20030128309

Best Available Copy

DTIC FILE COPY

The Installation Restoration Program Toxicology Guide

Volume 2

DTIC
ELECTE
MAR 2 8 1988
S C D

AD-A191 175

Arthur D. Little, Inc.
Acorn Park
Cambridge, MA 02140

May 1987

DISTRIBUTION STATEMENT A
Approved for public release;
Distribution Unlimited

Harry G. Armstrong Aerospace Medical Research Laboratory
Aerospace Medical Division
Air Force Systems Command
Wright-Patterson Air Force Base, Ohio
45433-6573

88 3 9 05

The Installation Restoration Program Toxicology Guide

Volume 2

DTIC COPY INSPECTED 3

Accesion For
NTIS CRA&I ☑
DTIC TAB ☐
Unannounced ☐
Justification
By per ltr
Distribution /
Availability Codes
Dist | Avail and / or Special
A-1

Arthur D. Little, Inc.
Acorn Park
Cambridge, MA 02140

May 1987

Harry G. Armstrong Aerospace Medical Research Laborat
Aerospace Medical Division
Air Force Systems Command
Wright-Patterson Air Force Base, Ohio
45433-6573

88 3 09 052

PREFACE

One of the objectives of the U S Air Force Installation Restoration Program is to provide individuals responsible for the management and implementation of the Installation Restoration Program (IRP) with information to evaluate the health hazards associated with actual or potential contamination of drinking water supplies. The Harry G. Armstrong Aerospace Medical Research Laboratory was requested by HQ USAF/SGPA to develop health and environmental information for each potential contaminant of drinking water supplies associated with USAF installations, i.e., a ground water contamination information data base. This IRP Toxicology Guide, Volume 2 of a three volume set, is a product of that effort. Volume 1 of the Guide (AD A171 095) was issued in October 1985. Both documents were produced under Contract F33615-81-D-0508 by Arthur D. Little, Inc., for the Biochemical Toxicology Branch, Toxic Hazards Division, Harry G. Armstrong Aerospace Medical Research Laboratory (AAMRL), Wright-Patterson AFB, OH.

Each volume of the IRP Toxicology Guide outlines the environmental fate and effects, exposure pathways, toxicity and sampling and analysis techniques for a selected list of chemical contaminants. The material provided is intended as an overview of key topic areas; no attempt was made to provide a comprehensive review. The Guide is not a technical report. Users are encouraged to read the Introduction to Volume 1 of the IRP Toxicology Guide before applying chemical-specific information.

The 35 chemicals included in Volume 1 of the IRP Toxicology Guide resulted from an Occupational and Environmental Health Laboratory (OEHL) review of all IRP Phase II reports available in March 1984. The selected chemicals were detected in ground water as part of the Phase II effort. An additional 24 chemicals are included in Volume 2 of the IRP Toxicology Guide. Volume 3 of the Guide is in preparation. Volume 3 will include pesticides and POL (petroleum, oil and lubricant) products of interest to the USAF Medical Service. Candidate chemicals for inclusion in future Guide expansion should be forwarded through MAJCOM bioenvironmental engineers to HQ USAF/SGPA. Consultant service concerning the current status of the toxicological information contained in this Guide should be obtained from the USAF OEHL/ECO, Brooks AFB, TX 78235-5000.

Every effort was made to assure that information was current and reliable at the time of publication. Users are encouraged to report apparent discrepancies or errors to AAMRL/TH, Wright-Patterson AFB, OH 45433-6573. Copies of this document were distributed to all Air Force bioenvironmental engineers and other Air Force personnel selected by HQ USAF/SGPA.

A brief sampling and analysis section was included for each of the chemicals in the Guide. Since sampling and analysis instructions are available to bioenvironmental engineering personnel (i.e., OEHL Recommended Sampling Procedures), the recommended methods were identified but were not described in detail.

ACKNOWLEDGEMENTS

Funding for this project originated from the Defense Environmental Restoration Account, Program Element 780008F. Program Manager for Arthur D. Little, Inc., was Andrew Sivak. Task Manager for this project was Muriel M. Goyer. Other major contributors were Marie L. Bonfiglio, Patricia M. Capomaccio, Deborah L. Cerundolo, Susan F. Coons, John H. Hagopian, Christoper P. Loreti, Warren L. Lyman, and Joanne H. Perwak. Charlene J. Doucette was responsible for report production. Computerized and manual literature searches were conducted by Margaret Miller and Marie C. Dellovo.

Marilyn E. George, Biochemical Toxicology Branch, Toxic Hazards Division, Harry G. Armstrong Aerospace Medical Research Laboratory, was Project Manager for the Air Force. Major Michael Shelley, Toxic Hazards Division, Harry G. Armstrong Aerospace Medical Research Laboratory served as technical monitor. This Guide is a product of the Air Force Systems Command, Human Systems Division's Health Effects Research effort in support of the Air Force Installation Restoration Program.

THE INSTALLATION RESTORATION PROGRAM TOXICOLOGY GUIDE

VOLUME 2

TABLE OF CONTENTS

		Page
List of Tables		vi
List of Figures		viii
List of Abbreviations, Acronyms, Terms and Symbols		ix
Chapter:		
36	Phenol	36-1
37	[illegible]chlorophenol	37-1
38	2,6 Dichlorophenol	38-1
39	Pentachlorophenol	39-1
40	Acetone	40-1
41	Methyl Ethyl Ketone	41-1
42	Methyl Cellosolve®	42-1
43	Ethylene Glycol	43-1
44	Bromochloromethane	44-1
45	Ethylene Dibromide	45-1
46	Butyl Benzyl Phthalate	46-1
47	Lindane	47-1
48	Chlordane	48-1
49	TOCP	49-1
50	Malathion	50-1
51	Dieldrin®	51-1
52	Aroclor® 1016, 1242, 1254, 1260	52-1
53	Sodium Chromate	53-1
54	Tetraethyl Lead	54-1
55	Hydrazine	55-1
56	Cyanide	56-1
Reference List		R-61
Index 1	Cross Index of Chemical, Common and Trivial Names	I-1
Index 2	Molecular Formula Index	I-6
Index 3	CAS Number Index	I-8
Index 4	RTECS Number Index	I-9

LIST OF TABLES

VOLUME 2

Table		Page
36-1	Equilibrium Partitioning Calculations for Phenol Model Environments	36-11
36-2	Soil Adsorption Constants Reported for Phenol	36-13
37-1	Equilibrium Partitioning Calculations for O-Chlorophenol in Model Environments	37-9
38-1	Equilibrium Partitioning Calculations for 2,6-Dichlorophenol in Model Environments	38-9
39-1	Equilibrium Partitioning Calculations for Pentachlorophenol in Model Environments	39-14
40-1	Equilibrium Partitioning Calculations for Acetone in Model Environments	40-7
40-2	Permeability of Acetone in Three Clay-sites	40-9
41-1	Equilibrium Partitioning Calculations for Methyl Ethyl Ketone in Model Environments	41-8
42-1	Equilibrium Partitioning Calculations for Methyl Cellosolve® in Model Environments	42-8
43-1	Equilibrium Partitioning Calculations for Ethylene Glycol in Model Environments	43-6
44-1	Equilibrium Partitioning Calculations for Bromochloromethane in Model Environments	44-7
45-1	Equilibrium Partitioning Calculations for Ethylene Dibromide in Model Environments	45-10
46-1	Equilibrium Partitioning Calculations for Butyl Benzyl Phthalate in Model Environments	46-7
46-2	Biodegradation of Butyl Benzyl Phthalate	46-9
47-1	Equilibrium Partitioning Calculations for Lindane in Model Environments	47-12
47-2	Freundlich Sorption Constants for Lindane	47-14
48-1	Equilibrium Partitioning Calculations for Chlordane in Model Environments	48-9
49-1	Equilibrium Partitioning Calculations for TOCP in Model Environments	49-7
50-1	Equilibrium Partitioning Calculations for Malathion in Model Environments	50-9
50-2	Hydrolysis Half-lives for Malathion in Aqueous Solutions at Temperatures near 20°C	50-12
51-1	Equilibrium Partitioning Calculations for Diazinon® in Model Environments	51-9
51-2	Hydrolysis Half-lives for Diazinon® in Aqueous Solutions at Temperatures Near 20°C	51-12

LIST OF TABLES - Continued

VOLUME 2

Table		Page
32-1	Approximate Composition (%) of Aroclor® Formulations	32-4
32-2	Equilibrium Partitioning Calculations for Aroclor® 1016, 1242, 1254 and 1260 in Model Environments	32-10
32-3	Equilibrium Partition Coefficients for PCBs	32-11
32-4	Mobility of Aroclor® 1242 and Aroclor® 1254 in Several Soil Materials with Various Leaching Solvents	32-14
32-5	Mobility of Aroclor® 1242 and Aroclor® 1254 on Silica gel Thin Plates Using Various Leaching Solvents	32-17
33-1	Chromate Sorption	33-13
33-2	Perforation of Nasal Septum in Chromate Workers	33-24
34-1	Equilibrium Partitioning Calculations for Tetraethyl Lead in Model Environments	34-13
41-1	Soil Properties and Percent Hydration Recovery	41-8
41-2	Hydration Behavior in Soil Sorption Studies	41-10

LIST OF FIGURES

VOLUME 2

Figure		Page
39-1	Relation of the Apparent Adsorption to the pH of the Supernatant Liquid	39-13
49-1	Biodegradation of Tricresyl Phosphate in Mississippi River Water	49-8
49-2	Loss of Tricresyl Phosphate Isomers in Lake Ontario Water	49-8
50-1	Temperature and pH Effects on Malathion Degradation	50-11
51-1	Decomposition of Diazinon® as a Function of Temperature	51-11
51-2	Decomposition of Diazinon® as a Function of pH	51-11
52-1	Structural Formula of PCBs	52-12
53-1	Eh-pH Diagram of Cr Species in Water at 25°C	53-14

This list of abbreviations, acronyms, terms and symbols is selected from the pages of the Guide. Words and phrases defined here include those occurring in more than one chapter, those indispensable to understanding the material in the chapter and those that may help clarify some of the definitions themselves. Not listed are those not commonly encountered which can be found in the chemical index and words adequately defined at the point of use.

AA	Atomic absorption spectroscopy
ACGIH	American Conference of Governmental Industrial Hygienists
Active metals	This refers to metals such as aluminum, calcium, magnesium, potassium, sodium, tin, zinc, and their alloys
ADI	Acceptable daily intake
ADL	Arthur D. Little, Inc.
Adeno carcinoma	A malignant tumor originating in glandular or dermal epithelium
Adenoma	A benign growth of glandular tissue
Aerosol	A suspension or dispersion of small solid or liquid particles in air or gas
AFOSH	Air Force Occupational Safety and Health Standard
Alkali metals	Metals (in Group IA of the Periodic Table), such as lithium, sodium, potassium, rubidium, cesium, and francium. The alkali metals react vigorously or at times violently with water. These metals present a dangerous fire risk when in contact with moisture or oxidizing materials
Alkaline earth metals	Calcium, barium, strontium, and radium (Group IIA of Periodic Table). Alkaline earth metals are less reactive than sodium and potassium and have higher melting and boiling points
Ambient water	Surface water

Ambient water criterion	That concentration of a pollutant in a navigable water that, based upon available data, will not result in adverse impact on important aquatic life, or on consumers of such aquatic life, after exposure of that aquatic life for periods of time exceeding 96 hours and continuing at least through one reproductive cycle; and will not result in a significant risk of adverse health effects in a large human population based on available information such as mammalian laboratory toxicity data, epidemiological studies of human occupational exposures, or human exposure data, or any other relevant data.
Amines	A class of organic compounds of nitrogen that may be considered as derived from ammonia (NH_3) by replacing one or more of the hydrogen atoms (H) with straight or branched hydrocarbon (alkyl) groups. All amines are basic in nature and usually combine readily with hydrochloric or other strong acids to form salts.
Aquifer	An underground, permeable saturated strata of rock, sand or gravel containing ground water.
Aromatic	A major group of hydrocarbons containing one or more rings like benzene, which has a six-carbon ring containing three double bonds. Most compounds in this group are derived from petroleum and coal tar and are reactive and chemically versatile. The name characterizes the strong and pleasant odor of most substances of this group. NOTE: The term "aromatic" is often used in perfume and fragrance industries to describe essential oils, which are not aromatic in the chemical sense.
atm	Atmosphere (760 Torr)
ATP	Adenosine triphosphate, a nucleotide cofactor important in many biological reactions where energy is transferred.
Autoignition temperature	The minimum temperature at which the material will ignite without a spark or flame being present. Along with the flash point, autoignition temperature gives an indication of rolative flammability.
BCF	Bioconcentration factor, a measure of the cumulative build-up of a specific compound sequentially through a food chain.
Benign	A term meaning noncancerous.
BOD	Biochemical oxygen demand

[illegible]	[illegible]
[illegible]	[illegible]
[illegible]	[illegible]

CWA	Clean Water Act
d	Density
da	Day(s)
DNA	Deoxyribonucleic acid
DOT	U.S. Department of Transportation
Drinking water	Water which meets the specifications of the water quality standards and is therefore suitable for human consumption and for all usual domestic purposes.
ECD	Electron capture detector
EEC	European Economic Community
EEG	Electroencephalogram, it detects abnormalities in the electrical waves emanating from different areas of the brain.
EKG	Electrocardiogram, a recording of the changes in electrical potential that occur during a cycle of heart muscle activity, producing a characteristic series of waves.
EPA	Environmental Protection Agency
Epithelium	The covering of internal and external surfaces of the body, including the lining of vessels and small cavities.
Epoxide	An organic compound containing a reactive group resulting from the union of an oxygen atom with other atoms (usually carbon) that are joined as shown below:  This group, commonly called "epoxy", characterizes the epoxy resins. Epichlorohydrin and ethylene oxide are well-known epoxides.
estim	Estimated value
F	Fahrenheit
f_{oc}	Fraction organic carbon in soil ($0 \leq f_{oc} \leq 1$)
FDA	Food and Drug Administration (U.S.A.)

FDCA	Food, Drug and Cosmetic Act
FID	Flame ionization detector
FIFRA	Federal Insecticide, Fungicide and Rodenticide Act
Finished	"End-of-tap" drinking water, i.e., water that has undergone drinking water treatment
Flammable limits in air	The range of gas or vapor concentrations in air, generally expressed in units percent by volume, capable of supporting combustion when ignited. The lower end of the range is commonly referred to as the lower flammable limit (LFL) and sometimes as the lower explosive limit (LEL). The upper end of the range is called the upper flammable limit (UFL) or the the upper explosive limit (UEL).
FR	Federal Register
ft	Foot
g	Grams(s)
Gavage	Forced feeding through a tube passed into the stomach.
GC	Gas chromatography
GI	Gastro-intestinal
Ground water	Subsurface water that occurs beneath the water table in soils and geologic forms that are fully saturated.
H	Henry's law constant ($atm \cdot m^3/mol$)
^3H	Chemical symbol for the radioactive isotope of hydrogen of atomic mass 3.
ha	Hectare, a unit of area equal to 10,000 square meters
HA	EPA's Health Advisory (formerly termed SNARL), an estimate of the no adverse response level for short and long-term exposures to a chemical via drinking water.
Half-life	Time required for removal or degradation of one-half of the original quantity.
Halogen	One of the electronegative elements of Group VIIA of the Periodic Table: fluorine, chlorine, bromine, iodine, and astatine. Fluorine is the most active of all chemical elements.

Halogenated	Containing one or more atoms of halogens.
Hemangioma	A tumor composed of blood vessels.
Hemangio-sarcoma	A malignant tumor composed of endothelial cells which line the heart and vessels of the circulatory system.
Hg	Mercury
HMTA	Hazardous Materials Transportation Act
HPLC	High-pressure liquid chromatography
hr	Hour(s)
Hydrocarbon	An organic compound (as acetylene or benzene) consisting exclusively of the elements carbon and hydrogen and often occurring in petroleum, natural gas, coal and bitumens.
Hydrolysis	The addition of the hydrogen and hydroxyl ions of water to a molecule, with its consequent splitting into 2 or more simpler molecules.
IARC	International Agency for Research on Cancer
IDLH	Immediately dangerous to life or health concentration; represents the maximum level from which one could escape within 30 minutes without any escape-impairing symptoms or any irreversible health effects.
im	Intramuscular
in	Inch
intradermal	Situated or applied within the skin
in vitro	Describes biological experiments in laboratory apparatus rather than in a living organism.
in vivo	Describes process that occur within a living organism.
ip	Intraperitoneal
IR	Infrared spectroscopy
IRP	Installation Restoration Program
IU	International units
iv	Intravenous

K_d(or K_p)	Soil sorption coefficient
kg	Kilogram(s) (10^3 grams)
K_{oc}	Soil absorption coefficient normalized to represent amount sorbed per unit weight of organic carbon in soil.
L	Liter(s)
lb	Pound(s)
LC_{50}	The concentration required to kill 50% of test individuals.
LCLo	Lowest reported lethal concentration.
$LC \cdot t_{50}$	Product of the concentration times time which causes lethality in 50% of the exposed population.
LD_{50}	The dose required to kill 50% of test individuals.
LDLo	Lowest reported lethal dose.
Lesion	An abnormal change in an organ because of injury or disease.
log K_{ow}	Log of the octanol-water partition coefficient.
Lower flammable limit	The lowest concentration of the material in air which will support combustion.
m	Meter
m^3	Cubic meter(s)
MAC	Maximum allowable concentration
Malignant	Pertaining to the growth and proliferation of certain tumors which terminate in death if not checked by treatment.
MCL	Maximum contaminant level
MDL	Minimum detection limit(s)
mEq	Milliequivalent (1/1000 of an equivalent)
mg	Milligram(s) (10^{-3} gram)
mg%	The concentration of a solution expressed in milligrams per 100 ml.

min	Minute(s)
Mineral acids (non-oxidizing)	Examples include boric, disulfuric, fluosilicic, hydriodic, hydrobromic, hydrochloric, hydrocyanic, hydrofluoric, permonosulfuric, phosphoric, and selenous acids as well as chlorosulfonic acid and various fluorophosphoric acids.
Mineral acids (oxidizing)	Examples include bromic, chloric, chromic acids hypochlorous, nitric, nitrohydrochloric, perbromic, perchloric, perchlorous, periodic and sulfuric acids.
mL	Milliliter (10^{-3} liter)
MLD	Minimum lethal dose
mm	Millimeter(s) (10^{-3} meter)
mM	Millimoles
mol	Gram mole
MPRSA	Marine Protection Research and Sanctuaries Act
MS	Mass spectrometry
Mutagen	A material that induces genetic damage.
MW	Molecular weight
n	Normal (isomer), as in n-butyl.
N	Normal (equivalents per liter, as applied to concentration); nitrogen (as in N-methylpyridine)
Narcosis	A state of stupor, unconsciousness or arrested activity.
NCI	National Cancer Institute
NEPA	National Environmental Policy Act
NFPA	National Fire Protection Association
NIOSH	The National Institute for Occupational Safety and Health
NIOSH No.	A unique, nine-position accession number assigned to each substance listed in the Registry of Toxic Effects of Chemical Substances published by NIOSH.

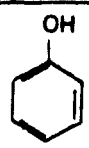
Nitride	Compounds of nitrogen with N^{-3} as the anion. These compounds may react with moisture to evolve flammable ammonia gas.
NOEL/NOAEL	No observed (adverse) effect level
NPL	National Priority List
NTP	National Toxicology Program
ng	Nanogram(s) (10^{-9} gram)
OHM/TADS	Oil and Hazardous Materials Technical Assistance Data System
OSHA	Occupational Safety and Health Act (or Administration)
Oxidation	Any process involving the addition of oxygen, loss of hydrogen, or loss of electrons from a compound.
Oxidizing materials	Any compound that spontaneously evolves oxygen either at room temperature or under slight heating. The term includes such chemicals as peroxides, chlorates, perchlorates, nitrates, and permanganates. These can react vigorously at ambient temperatures when stored near or in contact with reducing materials such as cellulosic (i.e., cotton, paper, rayon) and other organic compounds. In general, storage areas for oxidizing materials should be well ventilated and kept as cool as possible.
PEL	Permissible exposure limit, as found in 29CFR 1910.1000.
Percutaneous	Penetration of the skin
pH	A measure of acidity or alkalinity of a solution on a scale of 0-14; log of the reciprocal of the hydrogen ion concentration
PID	Photo ionization detector
Pk	Peak concentration.
Plasma	The straw-colored, fluid portion of blood that remains when all cells are removed.
po	By mouth
Polymerizable material	A substance capable of self-polymerization under appropriate conditions. Polymerization reactions are often violent, exothermic, and capable of causing violent rupture of sealed containers.

Polymerization	A chemical reaction, usually carried out with a catalyst, heat, or light, and often under high pressure. In this reaction, a large number of relatively simple molecules combine to form a chain-like macromolecule. This reaction can occur with the release of heat. In a container, the heat associated with polymerization may cause the substance to expand and/or release gas and cause the container to rupture, sometimes violently. The polymerization reaction occurs spontaneously in nature; industrially it is performed by subjecting unsaturated or otherwise reactive substances to conditions that will bring about the combination.
POTWs	Publicly owned treatment works
ppb	Part(s) per billion
ppm	Part(s) per million
ppt	Part(s) per thousand
PVA	Polyvinyl acetate
PVC	Polyvinyl chloride
R&W	Applies to water or waste water that has undergone no treatment
RCRA	Resource Conservation and Recovery Act
Reactivity (chemical)	Relating to the potential for a substance to undergo chemical transformation or change in the presence of other materials. Such chemical reactions often (but not always) are hazardous and involve evolution of heat, toxic or flammable gases, fires or explosions. The products formed by the reaction may have properties or hazards different from those of the chemical reactants.
RBC	Red blood cells
Reducing agents	These agents act to extract and liberate hydrogen from organic substances and may generate toxic and/or flammable gases and heat in contact with water. Many reducing agents may be pyrophoric and may ignite combustible materials in the presence of air. Contact with oxidizing materials may result in violent or explosive reactions. Examples of reducing agents include calcium, phosphorus, sodium, hydrazine, arsine, and metallic acetylides, aluminates, boranes, bromides, carbides, chlorides, hybrides, hydroborates, hyposulfites, iodides, phosphides, salenides, and silanes, as well as metal alkyls such as triethyl aluminum and diethyl zinc.

Reduction	Decreasing the oxygen content or increasing the proportion of hydrogen in a chemical compound or adding an electron to an atom or ion.
Rf	Retardation factor, i.e., the ratio of the velocity of the interstitial water to the velocity of a pollutant in soil.
RMCL	Recommended maximum contaminant level
RNA	Ribonucleic acid
RQ	Reportable quantities
sc	Subcutaneous, beneath the skin
SD	Standard deviation, a measure of the spread of individual measurements of a normally distributed variable.
SDWA	Safe Drinking Water Act
sec	Second(s)
Serum	The clear amber fluid that remains after blood has clotted; plasma without any of the substances involved in clotting.
SGOT	Serum glutamic oxalacetic transaminase, an enzyme released into the serum as the result of tissue injury, especially injury to the heart and/or liver.
SGPT	Serum glutamic pyruvic transaminase, an enzyme released into the serum as a result of tissue injury, especially damage to liver cells.
SH	Sulfhydryl group
SNARL	Suggested no adverse response level
STEL	Short-term exposure limit; an ACGIH-recommended concentration to which workers can be exposed continuously for a short period of time without suffering irritation, chronic or irreversible tissue damage or narcosis of sufficient degree to increase the likelihood of accidental injury, impair self-rescue or materially reduce work efficiency, provided that the daily threshold limit value is not exceeded.
Subcutaneous	Beneath the skin

Surface water	The water contained on the exterior or upper portion of the earth's surface; it does not include ground water.
Sym	Symmetrical
$t_{\frac{1}{2}}$	Half-life
TDLo	Lowest reported toxic dose
Teratogen	A material that induces nontransmissible changes (birth defects) in the offspring.
TLV®	Threshold limit value; an ACGIH-recommended time-weighted average concentration for a normal 8-hour work-day and a 40-hour work-week to which most workers can be exposed without adverse effect.
TNT	Trinitrotoluene, an explosive used in the munitions industry.
Toxic metals and their compounds	These include antimony, arsenic, barium, beryllium, bismuth, cadmium, chromium, cobalt, copper, indium, lead, manganese, mercury, molybdenum, nickel, osmium, selenium, thallium, thorium, titanium, zinc and zirconium; compounds containing these metals; and metallic compounds containing arsines, boron, calcium, cesium, magnesium, silver, strontium, tellurium, tin, tungsten or vanadium, among others.
TSCA	Toxic Substances Control Act
TWA	Time-weighted average
µg	Microgram(s) (10^{-6} gram)
µl	Microliter(s) (10^{-6} liter)
uns	Unsymmetrical
Upper flammable limit	The highest concentration of the material in air which will support combustion.
USAF	United States Air Force
USEPA	United States Environmental Protection Agency
Water quality standards	Legally enforceable provisions of state or Federal law which consist of a designated use or uses for the waters of the United States and water quality criteria for such waters based upon such uses.

WHO	World Health Organization
wk	Week(s)
w/v	Weight per unit volume
°	Degrees, as in 37°C
%	Percent
>	Greater than
<	Less than
~	Approximately
→	Yields or causes
+	Plus
®	Registered trademark

COMMON SYNONYMS:	CAS REG. NO.:	FORMULA:	AIR W/V CONVERSION FACTORS at 25°C (12)
Benzenol Carbolic acid Hydroxybenzene Phenic acid Phenyl hydroxide Phenylic acid	108-95-2 NIOSH NO.: SJ3325000	C_6H_6O	3.84 mg/m³ ≈ 1 ppm 0.260 ppm ≈ 1 mg/m³
	STRUCTURE: 		MOLECULAR WEIGHT: 94.11

REACTIVITY	Reactions of phenols or cresols with organic peroxides, organic hydroperoxides or non-oxidizing mineral acids typically generate heat, while those with oxidizing mineral acids or strong oxidizing agents generate heat and possibly fire. Reactions with elemental alkali or alkaline earth metals, nitrides or strong reducing agents evolve heat and flammable gases, while those with isocyanates, epoxides or polymerizable compounds may evolve heat and initiate violent polymerization reactions. Reactions with explosive compounds may cause explosions, while those with hydrazines or azo or diazo compounds may produce heat and generally innocuous gases. Reaction of phenol with calcium hypochlorite is exothermic and produces toxic fumes which may ignite. Addition of aluminum chloride to nitrobenzene containing 5% phenol may cause a violent explosion. Reaction of phenol with butadiene in a petroleum ether solution, catalyzed by boron trifluoride diethyletherate, may cause a closed container to pressurize and explode. Aluminum, magnesium, lead and zinc are attacked by hot phenol (505,507,511).

PHYSICO-CHEMICAL DATA	• Physical State (at 20°C): crystalline	(23)
	• Color: white; pink to red with light exposure	(23)
	• Odor: medicinal	(263)
	• Odor Threshold: 0.047 ppm	(263)
	• Liquid Density (g/ml): 1.0576 at 41°C	(14)
	• Freezing/Melting Point (°C): 40.9	(14)
	• Boiling Point (°C): 181.8	(14)
	• Flash Point (°C): 79 (closed cup)	(69)
	• Flammable Limits in Air, % by Volume: 1.4 to 8.6	(60,506, 507)
	• Autoignition Temperature (°C): 715	(51,60,504)
	• Vapor Pressure (mm Hg at 20°C): 0.5293	(10)
	• Saturated Concentration in Air (mg/m³ at 20°C): 2730	(ADL estim)
	• Solubility in Water (mg/L at 20°C): 84,000	(38)
	• Viscosity (cp): 3.02 at 50°C	(48)
	• Surface Tension (dyne/cm at 20°C): solid	(23)
	• Log (Octanol-Water Partition Coefficient), log K_{ow}: 1.46	(29)
	• Soil Adsorption Coefficient, K_{oc}: 14, 135	(652,654)
	• Henry's Law Constant (atm•m³/mol at 20°C): 7.0×10^{-7} (estim)	(964)
	• Bioconcentration Factor: 2 (goldfish) 1.4 (estim)	(940,659)

PERSISTENCE IN THE SOIL-WATER SYSTEM	Relatively mobile in soil-water systems. Volatilization also important for near-surface soils. Chemical is resistant to hydrolysis but is fairly susceptible to photo-oxidation, catalytic or free-radical oxidation (somewhat speculative), and to biodegradation.

PATHWAYS OF EXPOSURE	The primary pathway of concern from soil-water systems is the migration of phenol to ground-water supplies of drinking water. Data suggest that such migration has occurred in the past. The consumption of fish or other organisms is not expected to be a significant route of exposure.

HEALTH HAZARD DATA	Signs and Symptoms of Short-term Human Exposure (38,54): Phenol has a marked corrosive action on tissue. On contact with the eyes, it may cause severe damage and blindness. On skin, it induces anesthesia and blanching of the exposed area. If not removed promptly, it may cause a severe burn and systemic intoxication. Systemic effects, which can result from any route of exposure, include paleness, weakness, sweating, headache, ringing of the ears, cyanosis, shock, excitement, frothing of the nose and mouth and death.
	Toxicity Based on Animal Studies: LD_{50} (mg/kg) oral 414 [rat] (59) skin 669 [rat] (59) LC_{50} (mg/m^3) inhalation 316 [rat] (47) no time given
	Long-Term Effects: Liver and kidney damage, skin discoloration
	Pregnancy/Neonate Data: Negative
	Mutation Data: Conflicting evidence
	Carcinogenicity Classification: NTP - none assigned; IARC - none assigned

HANDLING PRECAUTIONS (38,52,54)	Handle chemical only with adequate ventilation • Vapor concentrations of 5-50 ppm: any self-contained breathing apparatus or supplied-air respirator; any chemical cartridge respirator with an organic vapor cartridge and dust and mist filters • 50-100 ppm: any supplied-air respirator or self-contained breathing apparatus with full facepiece; chemical cartridge respirator with full facepiece, organic vapor cartridge and dust and mist filter • Protective clothing, gloves, rubber boots and apron to prevent skin contact with solid or liquid phenol • Dust and splash-proof chemical goggles if there is probability of eye contact.

EMERGENCY FIRST AID TREATMENT (59,38,1311)	Ingestion: Dilute with water or milk as soon as possible. Do not induce vomiting if solution ingested is 5% or greater. Get medical attention immediately • Inhalation: Move victim to fresh air at once. If necessary give artificial respiration. Get medical attention • Skin: Remove contaminated clothing immediately; wash skin preferably with polyethylene glycol 30 or 400, or soap and water. Get medical attention immediately • Eye: Irrigate immediately with large amounts of water. Get medical attention immediately.

ENVIRONMENTAL AND OCCUPATIONAL STANDARDS AND CRITERIA

AIR EXPOSURE LIMITS:

Standards
- OSHA PEL (8-hr TWA): 5 ppm (skin)
- AFOSH PEL (8-hr TWA): 5 ppm (skin)

Criteria
- NIOSH IDLH (30-min): 100 ppm (skin)
- ACGIH TLV® (8-hr TWA): 5 ppm (skin)
- ACGIH STEL (15-min): 10 ppm (skin)

WATER EXPOSURE LIMITS:

Drinking Water Standards - None established

EPA Health Advisories - None established

EPA Ambient Water Quality Criteria (355)
- Human Health
  - Based on available toxicity data, for the protection of public health, the derived level is 3.5 mg/L.
  - Using available organoleptic data, for controlling undesirable taste and odor quality, the estimated level is 0.3 mg/L.
- Aquatic Life
  - Freshwater species
    acute toxicity: no criterion, but lowest effect level occurs at 10,200 µg/L.

    chronic toxicity: no criterion, but lowest effect level occurs at 2560 µg/L.
  - Saltwater species
    acute toxicity: no criterion, but lowest effect level occurs at 5800 µg/L.

    chronic toxicity: no criterion established due to insufficient data.

REGULATORY STATUS (as of January 1, 1987)

Promulgated Regulations

- Federal Programs

Clean Water Act (CWA)

Phenol is designated a hazardous substance. It has a reportable quantity (RQ) limit of 454 kg (347,985). It is also listed as a toxic pollutant (351). Water quality criteria have been set. Guidelines exist for phenol effluent in the glass manufacturing, textile mills and pesticide chemicals categories (897,893,891). Guidelines also exist for effluents containing phenols in the timber products processing, petroleum refining, and metal molding and casting point source categories (899,896,892) and in the point source categories for the manufacture of iron and steel, non-ferrous metals and ferroalloys (354,894,895).

Safe Drinking Water Act (SDWA)

In states with an approved Underground Injection Control program, a permit is required for the injection of phenol-containing wastes designated as hazardous under RCRA (295).

Resource Conservation and Recovery Act (RCRA)

Phenol is identified as a hazardous waste (U188) and listed as a hazardous waste constituent (328,329). Waste streams from the following industries contain phenol and are listed as specific sources of hazardous wastes: wood preservation (creosote and/or pentachlorophenol preserving processes), organic chemicals (phenol/acetone production) and coking (operational residues) (326,327).

Comprehensive Environmental Response Compensation and Liability Act (CERCLA)

Phenol is designated a hazardous substance under CERCLA. It has a reportable quantity (RQ) limit of 454 kg. Reportable quantities have also been issued for RCRA hazardous waste streams containing phenol but these depend upon the concentrations of the chemicals in the waste stream (985,1733).

Any facility at which phenol is present in excess of its threshold planning quantity of 500 pounds must notify state and local emergency planning officials. If phenol is released from the facility in excess of its reportable quantity (RQ), local emergency planning officials must be notified (1751).

Federal Insecticide, Fungicide and Rodenticide Act (FIFRA)

Phenol is exempt from a tolerance requirement when used as a solvent in pesticide formulations applied to animals (315).

Marine Protection Research and Sanctuaries Act (MPRSA)
Ocean dumping of organohalogen compounds as well as the dumping of known or suspected carcinogens, mutagens or teratogens is prohibited except when they are present as trace contaminants. Permit applicants are exempt from these regulations if they can demonstrate that such chemical constituents are non-toxic and non-bioaccumulative in the marine environment or are rapidly rendered harmless by physical, chemical or biological processes in the sea (309).

Occupational Safety and Health Act (OSHA)
Employee exposure to phenol shall not exceed an 8-hour time-weighted-average (TWA) of 5 ppm (298).

Hazardous Materials Transportation Act (HMTA)
The Department of Transportation has designated phenol as a hazardous material which is subject to requirements for packaging, labeling and transportation (306).

Food, Drug and Cosmetic Act (FDCA)
Phenol is approved for use as an indirect food additive (362).

The level for phenols in bottled drinking water is 0.001 mg/L (365).

- State Water Programs

  Missouri has a criterion of 1 μg/L for phenol in drinking water (731).

  The following states have a criterion of 1 μg/L for phenolics (731):
  - Florida - in surface water
  - Illinois, Mississippi, Oregon - in the public water supply
  - North Carolina - in fresh water
  - Minnesota - in water for domestic consumption
  - New York - in Class AA drinking water
  - New Hampshire - in Class A and B waters

  The following states have a criterion of 5 μg/L for phenolics (731):
  - Georgia - in all waters
  - Louisiana - in the public water supply
  - New York - in Class A drinking water
  - West Virginia - in drinking water

  The following states have a criterion of 50 μg/L for phenolics (731):
  - Iowa - in drinking water
  - Louisiana - in fresh water

The following states have ground water quality standards for phenolics (981):

Missouri - 0.3 mg/L for fast recharge
0.1 mg/L for slow recharge
New Jersey - 0.3 mg/L in Class GW 1
New York - 1 µg/L in Class GA
New Mexico - 5 µg/L
Virginia - 1 µg/L
Wyoming - 1 µg/L in Class 1

Other states follow EPA Ambient Water Quality Criteria.

Proposed Regulations

- Federal Programs

Clean Water Act (CWA)
Effluent guidelines for phenol have been proposed in the organic chemicals, plastics and synthetic fibers category (357).

Resource Conservation and Recovery Act (RCRA)
EPA has proposed that hazardous waste treatment, storage and disposal facilities monitor ground water for phenol when EPA suspects the facilities of leaking contaminants (1754).

EPA has proposed that solid wastes which contain a concentration equal to or greater than 14.4 mg/L phenol be listed as hazardous in that they exhibit the characteristic defined as EP toxicity (1565).

Toxic Substances Control Act (TSCA)
EPA has proposed that manufacturers, importers and processors of phenol submit health and safety studies (1753).

- State Water Programs - No proposed regulations are pending.

EEC Directives

Directive on Drinking Water (533)
The mandatory values for phenols (phenol indices) in surface water treatment categories A1, A2 and A3 used or intended for abstraction of drinking water are 0.001, 0.005 and 0.1 mg/L, respectively. Guideline values for phenols (phenol indices) under treatment categories A2 and A3 are 0.001 and 0.01 mg/L respectively. No guideline value is given for treatment category A1.

Directive Relating to the Quality of Water for Human Consumption (540)
The maximum admissible concentration for phenols (phenol indices) is 0.5 µg/L. Excluded from this category are natural phenols which do not react to chlorine. No guideline levels for phenols (phenol indices) are given.

Directive on Ground Water (538)
Direct and indirect discharge into ground water of substances which have a deleterious effect on the taste and/or odor of ground water, and compounds liable to cause the formation of such substances in ground water and to render it unfit for human consumption shall be subject to prior review so as to limit such discharges.

Directive on Bathing Water Quality (534)
Mandatory values for phenols (phenol indices) in bathing water are: (1) no specific odor and (2) concentrations ≤ 0.05 mg/L. Guideline values for phenols (phenol indices) suggest concentrations ≤ 0.005 mg/L.

Directive on Fishing Water Quality (536)
Phenolic compounds in both salmonid and cyprinid waters must not be present in such concentrations that they adversely affect fish flavor.

Directive on the Quality Required of Shellfish Waters (537)
The mandatory specifications for substances affecting the taste of shellfish require that their concentrations be lower than that liable to impair the taste of the shellfish.

Directive Relating to the Classification, Packaging and Labeling of Dangerous Preparations (Solvents) (544)
Phenol is listed as a Class I/b toxic substance and is subject to packaging and labeling regulations.

Directive on the Discharge of Dangerous Substances (535)
Organohalogens, organophosphates, petroleum hydrocarbons, carcinogens or substances which have a deleterious effect on the taste and/or odor of human food derived from aquatic environments cannot be discharged into inland surface waters, territorial waters or internal coastal waters without prior authorization from member countries which issue emission standards. A system of zero-emmission applies to discharge of these substances into ground water.

Directive on Marketing and Use of Dangerous Substances (541)
Phenol may not be used in ornamental objects intended to produce light or color effects by means of different phases.

Directive on Toxic and Dangerous Wastes (542)
Any installation establishment, or undertaking which produces, holds and/or disposes of certain toxic and dangerous wastes including phenols and phenol compounds; organic-halogen compounds; chrome compounds, lead compounds, cyanides, ethers and aromatic polycylic compounds (with carcinogenic effects) shall keep a record of the quantity, nature, physical and chemical characteristics and origin of such waste, and of the methods and sites used for disposing of such waste.

Directive on the Classification, Packaging and Labeling of Dangerous Substances (787)
Phenol is classified as a toxic substance and is subject to packaging and labeling regulations.

Directive on Transfrontier Shipment of Hazardous Waste (1433)
When the holder of a hazardous waste such as phenol intends to ship it to another member state, authorities of the member states concerned must be provided with information on the source and composition of the waste, measures to be taken to ensure safe transport, insurance against damage and the existence of a contractual agreement with the consignee of the waste. All transfrontier shipments must be properly packed and labeled and must be accompanied by instructions to be followed in the event of danger of accident.

36.1 MAJOR USES

The major use of phenol is as a chemical intermediate in the synthesis of organic chemicals, primarily phenolic resins. Phenol is also utilized in the production of bis-phenol-A, caprolactam, plasticizers, adipic acid, salicylic acid, 2,4-D, alkyl phenols and chlorinated phenols. A small amount is used as a solvent in petroleum refining (939). It is also employed as a disinfectant (2).

36.2 ENVIRONMENTAL FATE AND EXPOSURE PATHWAYS

36.2.1 Transport in Soil/Ground-water Systems

36.2.1.1 Overview

Phenol is expected to be relatively mobile in the soil/ground-water system when present at low concentrations (dissolved in water). Pure phenol is a solid at ambient temperatures (melting point is 41°C) and thus bulk quantities (e.g., from a spill or large dumping) would not be immediately mobile.

Transport pathways can be generally assessed by using an equilibrium partitioning model as shown in Table 36-1. These calculations predict the partitioning of low soil concentrations of phenol among soil particles, soil water and soil air. The estimates for the unsaturated topsoil model show that while most of the phenol is associated with the stationary soil phase, a significant amount (12.6%) is in the mobile water phase and thus easily leached. Diffusion of phenol vapors through the soil-air pores up to the ground surface would not appear to be a significant loss pathway based upon the model results. (Other data and model results given below, however, show volatilization losses may be significant.) In saturated, deep soils (containing no air and negligible soil organic carbon), a much higher fraction of the phenol is likely to be present in the soil water phase (Table 36-1) and available to be transported with flowing ground water.

The actual distribution of phenol in a model laboratory ecosystem has been measured by Figge et al. (807). Thirty (30) days after the non-sterile ecosystem was innoculated with C-14 labeled phenol, the percentage of the initial dose found in each "compartment" of the ecosystem was as follows: air, 23%; percolating water, 0.03%; soil, 24%; and plants, 43%. Total recovery was 90%. Two-thirds of the phenol "recovered" from the air compartment was identified as $^{14}CO_2$ which must have come from the chemical or biological degradation of phenol in the water, soil or plants. Thus, the actual "air" concentrations (meaning the free air above the ecosystem, not confined soil-air) were probably nearer 9%. The relatively large "true" air concentrations are a result of the fact that, during the 30-day test, the air in the test chamber was continuously exchanged, with the exhaust air passing through an absorber unit.

TABLE 36-1

EQUILIBRIUM PARTITIONING CALCULATIONS FOR PHENOL IN MODEL ENVIRONMENTS[a]

Soil Environment	Estimated Percent of Total Mass of Chemical in Each Compartment		
	Soil	Soil-Water	Soil-Air
Unsaturated topsoil at 25°C[b,c]	87.4	12.6	2.0×10^{-3}
Saturated deep soil[d]	13.1	86.9	-

a) Calculations based on Mackay's equilibrium partitioning model (34,35,36); see Introduction in Volume 1 for description of model and environmental conditions chosen to represent an unsaturated topsoil and saturated deep soil. Calculated percentages should be considered as rough estimates and used only for general guidance.

b) Utilized estimated soil sorption coefficient: K_{oc} = 36 (calculated average of data for soils given in reference 806).

c) Henry's law constant taken as 1.3×10^{-6} atm·m³/mol at 25°C (81).

d) Used sorption coefficient $K_p = 0.001\ K_{oc}$.

Two other modeling studies serve to elucidate the important transport and fate mechanisms for phenol in the natural environment. Jury et al. (808) used a soil chemical screening model to classify chemicals with regard to the importance of volatilization as a loss pathway after soil application (e.g., of a phenol-containing waste). The model assumed uniform application of the chemical to a depth of 10 cm in the soil, a soil-water content of 30% (by volume), and a soil organic carbon content of 1.25% (by weight). Under these conditions, the model results led Jury et al. (808) to classify phenol in a "moderately short-lived" group of chemicals having an effective volatilization half-life between 15 and 30 days. The actual half-life calculated for phenol was 21 days.

The second study by Pollard and Hern (809) simulated the transport and fate of phenol in a surface water body (Monongahela River) using the EXAMS model. Some of what was learned will help in understanding

soil/ground-water fate and transport. The model predicted oxidation (by photochemically-generated free radicals in the water) and biodegradation to be the most important fate pathways. The model showed volatilization to be an unimportant loss mechanism. Associated field testing showed sediment sorption was also a relatively unimportant process; the field testing provided data that allowed the model to be validated when certain assumptions were made about the concentration of free-radical oxidants.

A number of field and laboratory studies point to the relative mobility and non-persistence of phenol in soil/ground-water systems. In a study of land treatment of phenol-containing wastes, Demirjian et al. (522) found no detectable phenol in the soil at the end of the treatment cycle. Goerlitz et al. (810) found that sorption did not appreciably retard the movement of phenol in the leachate plume from an unlined surface impoundment. Laboratory sorption experiments using soil collected at the 30-m depth at the site also showed no significant sorption of phenol. The researchers did note disproportionate decreases in the downgradient concentration of phenol which were tentatively attributed to biodegradation. Phenol has been found in the leachate plume from a sanitary landfill (811), in peat soils 500 meters from a catchment pit (939), and in ground water (where it persisted 19 months) following a spill of phenol onto a soil consisting primarily of sand, gravel and undifferentiated dolomite (939).

36.2.1.2 Sorption on Soils

Table 36-2 lists several soil sorption constants that have been reported for phenol. In general, except for the Lake Zoar sediments, the data indicate that phenol is only weakly sorbed by soils containing organic matter. There is essentially no sorption on clays and minerals that contain no organic matter. Nevertheless, in unsaturated topsoils containing significant amounts of organic carbon (2%) and relatively small amounts of water (10% by volume), the model results shown in Table 36-1 show that a significant amount of the phenol may be associated with the stationary soil phase.

There is no ready explanation for the relatively high sorption constant associated with the Lake Zoar sediments. Some degree of excess sorption over that expected for simple hydrophobic sorption to organic matter, due to hydrogen bonding, has been suggested by Boyd (816).

36.2.1.3 Volatilization from Soils

Transport of phenol vapors through the air-filled pores of unsaturated soils can be an important transport mechanism for near-surface soils. This was demonstrated by the model ecosystem and modeling results discussed above (Section 36.2.1.1). However, due to the low value of the Henry's law constant (H) for phenol:

$$H = 7 \times 10^{-7} atm \cdot m^3/mol \text{ at } 20°C$$

TABLE 36-2

SOIL ADSORPTION CONSTANTS REPORTED FOR PHENOL*

Type of Soil	K_{oc}	Comment	Ref.
(Not specified)	27		812
Batcombe Silt Loam	30.2	2.51% OC, pH 6.7	813
Molokai clay	440	0.5% OC, pH 6.2	814
Davidson clay	700	0.3% OC, pH 6.4	814
Ava silty clay	150	0.4% OC, pH 4.5	814
Mohave clay loam	250	0.4% OC, pH 7.8	814
Fanno clay	144	0.9% OC, pH 7.0	814
Captina silt loam	90	0.64% OC, pH 5.4	815
Palouse silt loam	57	2.1% OC, pH 5.4	815
Brookston clay loam	16.1	3.0% OC, pH 5.7	816
Captina silt loam	91	0.64% OC, pH 5.4	817
Palouse silt loam	38.8	2.1% OC, pH 5.4	817
Lake Zoar sediment	2900	Fine fraction, 10.2% OC	818
Lake Zoar sediment	3100	Coarse fraction, 4.2% OC	818
(Generic)	135	Estimated	654
(Generic)	14	Estimated	652
(Generic)	9	Estimated	812
Montmorillonite	--	K_d=1.08 x 10^{-4}, 1/n=0.132	819
Cottage Grove sandstone (38°C)	--	k_d=7x10^{-3}, 1/n=1.01	
Silty Clay	--	No adsorption	821
Kaolinite, montmorillonite	--	No adsorption	822
Geothite (ε-FeOOH)	--	No adsorption	823

* K_{oc} = soil adsorption constant per unit weight organic carbon.

K_d = Freundlich adsorption coefficient.

1/n = Exponential factor on concentration in Freundlich adsorption equation.

OC = organic carbon content (by weight) of soil.

the vapor phase concentration in soil air will be very low whenever water is present.

36.2.2 Transformation Processes in Soil/Ground-water Systems

Phenol is a weak acid (pK_a = 9.90) and thus has a slight tendency to dissociate in water with the loss of a hydrogen ion: C_6H_5OH----> $C_6H_5O^- + H^+$. In pure water, only 0.13% would be expected to dissociate at pH 7, and 1.3% at pH 8.

Phenol is apparently susceptible to one or more chemical (non-biological) degradation mechanisms that can operate in the soil/ground-water system. Simple hydrolysis (reaction with water), however, does not take place rapidly under environmental conditions. An aqueous hydrolysis rate constant of 8.2-85. x 10^{-9} cm^3/mole sec has been reported (824). Conrad and Seiler (825) demonstrated abiological degradation of phenol and resulting CO formation, in sterile soils. They speculated that a radical mechanism, most probably initiated by reactions with molecular oxygen, were involved. Such a mechanism is consistent with the speculation of others (10) that phenol could be non-photolytically (and non-biologically) oxidized in oxygen-rich water, especially if certain iron or copper species were present which might catalyze the reaction.

Baker and Mayfield (826) also found that phenol underwent rapid non-biological degradation in sterile silica sand. The rate of this degradation reaction increased with temperature and decreased with concentration. In one test at 26°C, the phenol concentration in the silica sand/water mixture fell from 105 µg/g of silica to 29 µg/g silica after 32 days. Volatilization losses and photodegradation were clearly ruled out. These authors also speculated on an auto-oxidation mechanism that might be catalyzed.

There is good evidence to suggest that photo-oxidation should be an important degradation mechanism for phenol in aerated, near-surface surface waters (10,939,827).

Numerous studies have clearly shown that phenol is fairly easily biodegraded by microorganisms which are prevelant in the natural environment (10,939,806,828,829,830,831). Several types of microorganisms can use phenol as their sole source of carbon; however, at high phenol concentrations (e.g., above 100 mg/L) the microorganisms may be inhibited or killed. Evidence of the extent or rate of biodegradation at very low concentration (<1 mg/L) is contradictory. Degradation, both aerobic and anaerobic, has been demonstrated in a variety of natural water and natural soil conditions. Thus, it may be concluded that phenol should not persist (more than weeks to a few months at most) in environments with sufficient populations of active microorganisms. Although many rate studies have been carried out (see references 939 and 806 for a listing of data), prediction of biodegradation rate constants for specific environments is still difficult.

36.2.3 Primary Routes of Exposure from Soil/Ground-water Systems

The above discussion of fate pathways suggests that phenol has a low volatility, is weakly adsorbed to soil and has no significant potential for bioaccumulation. Although some data indicate volatilization of this compound from near surface soils does occur, in general, inhalation exposure to phenol from soil is not expected to be a dominant pathway. Phenol is likely to be mobile in ground water and may result in drinking water exposure via this route. Exposure pathways involving the accumulation of phenol by biota are not likely to be important due to its low bioconcentration factor.

The potential for ground water contamination is demonstrated by the common occurrence of phenol at hazardous waste sites. Mitre (83) reported that phenol has been found at 55 of the 546 National Priority List (NPL) sites. It was detected at 37 sites in ground water, 27 sites in surface water and 3 sites in air. These data indicate that both ground and surface-water pathways of exposure may be important. In the National Organics Monitoring Survey (NOMS) conducted by the USEPA (90), phenol was detected in 2 of 110 raw water supplies, including both surface and ground-water supplies.

The properties of phenol, and its common occurrence in ground water at NPL sites, suggest that exposure through drinking water may result from soil/ground-water systems. In addition, the movement of phenol in ground water may result in other exposure pathways. These pathways would include ingestion exposure through the consumption of surface water as a drinking water supply or dermal exposure through recreational use of surface waters. Bioaccumulation of phenol from surface waters, either by aquatic organisms or domestic animals, is not expected to be a dominant exposure pathway due to the low bioconcentration factor for phenol.

36.2.4 Other Sources of Human Exposure

As phenol is a large-volume industrial chemical, there are a number of other potential sources of human exposure. Exposure through drinking water (other than ground water associated with hazardous waste sites) does not generally appear to be a major source of exposure; phenol was detected in only 2 of 110 raw water supplies (90).

The production and use of phenol, however, has led to its presence in the atmosphere. Brodzinsky and Singh (84) summarized air monitoring data for phenol. They reported 90 data points. No data were available for rural and remote areas. In urban and suburban areas, the median concentration was 0.12 $\mu g/m^3$ (7 data points), and in source-dominated areas, the median concentration was 19 $\mu g/m^3$ (83 data points).

In addition to these environmental exposures, phenol is used in several medicinal preparations (antiseptic mouthwash and lozenges) that may result in ingestion exposure. It 's also a component of a number

of medicinal preparations that are dermally applied, such as cream for burns or poison ivy (940). The use of these products may result in significant exposure to phenol for short periods of product use.

Phenol has been found in some food products. Lustre and Issenberg (832) reported 7 mg/kg phenol in smoked summer sausage and 28.6 mg/kg in smoked pork belly. The authors speculated that the phenol originated from the wood used in processing the meat.

36.3 HUMAN HEALTH CONSIDERATIONS

36.3.1 Animal Studies

36.3.1.1 Carcinogenicity

In a study conducted by the National Cancer Institute, phenol was not carcinogenic for either male or female F344 rats or B6C3F1 mice. Both species were given drinking water containing 2500 or 5000 ppm phenol for 103 weeks. In low-dose male rats, there was an increased incidence of leukemias and lymphomas; the incidence in the high-dose group, however, was not significantly different from that of the control group. There was also no dose-response in female dosed groups. Therefore, evidence that phenol was the cause of these tumors was not clearly established. In mice, no tumor at any site was clearly associated with phenol administration (941).

A number of studies have shown that phenol promotes skin tumors in strains of mice specially inbred for sensitivity to tumor development. Benign tumors developed in these mice after a single application of 75 μg of the carcinogen 9,10-dimethylbenz(a)anthracene (DMBA) followed one week later by twice weekly applications of 2.5 mg phenol (as a 10% solution in benzene) to the same area for a period of 42 weeks. At 13 weeks, 22 of 23 mice (96%) had papillomas and 73% had carcinomas. The effect of benzene as the solvent must also be considered. Few tumors developed in the mice treated with DMBA alone (3/21 mice with papillomas at 42 weeks) or with phenol alone (5/14 mice with papillomas at one year). Standard inbred strains of mice similarly treated exhibited only a few papillomas (902).

In summary, there are no indications that phenol is carcinogenic by the oral route. Skin application of phenol, however, is tumorigenic in sensitive strains of mice but not in standard inbred mouse strains. This activity appears to be associated with phenol's irritancy and subsequent skin hyperplasia.

36.3.1.2 Mutagenicity

The mutagenic activity of phenol has been evaluated in several systems. Data from bacterial and yeast studies conflict. Gocke et al. (942) reported that phenol induced mutations in Salmonella strain

TA1538 in the presence of activation while another team of investigators (943) using strains TA 1535, 1537, 98 and 100 achieved negative results both with and without metabolic activation. Negative results were also obtained in the yeast, Saccharomyces cerevisiae D3 (944).

Phenol was found to induce statistically significant, concentration-dependent increases in sister chromatid exchanges in human T-lymphocytes in vitro. Phenol concentrations ranged from 5 to 3000 μM (945).

Hadorn and Niggli (946) found an increased frequency of dominant lethal mutations after in vivo treatment of Drosophila ovaries with 0.01% phenol followed by implantion into host larvae.

A five-generation study conducted with Porton-strain mice examined the influence of aqueous solutions of phenol on chromosomes in the process of spermatogenesis. Mice in each generation were given daily gavage doses of approximately 0, 6.5, 64 or 640 μg/kg/day for 30 days. Six males and females from each group per generation were then mated. The females continued to receive phenol during pregnancy and lactation. Testes from six males per group for each generation were examined for chromosomal defects in spermatogonia and primary spermatocytes. Dose-related increases in the incidence of aberrations were found in both cell types. Aberrations included chromatid and chromosome breaks, ring chromosomes, centric fusions, acentric fragments, aneuploidy (any deviation from the exact multiple of the haploid number of chromosomes) and polyploidy (more than two full sets of homologous chromosomes). There was also an apparent trend toward increased aberrations in each successive generation. However, the experimental protocol as well as the inadequacy of information presented by the investigation make interpretation of this latter point difficult. The complications associated with interpretation of the results in successive generations do not, however, mitigate the marked increase in chromosomal aberrations seen in the parental and F1 generations, i.e., two to four-fold above controls (963). These results are cause for concern in that equivalent human exposures (0.45-4.5 mg/70-kg man/day) could conceivably be ingested by the population at large. Unknown factors, however, such as tissue distribution and DNA repair capabilities of different tissues and species make any discussion of the genetic implications for man more speculative than factual. Further studies such as the effect of gavage administration compared to the more intermittent nature of human exposure via drinking water are needed to clarify the significance of this single report to humans (963).

36.3.1.3 Teratogenicity, Embryotoxicity and Reproductive Effects

Phenol has not been reported to cause any teratogenic or embryotoxic effects. Minor and Becher (947) found no increase in terata or resorptions in Sprague-Dawley rats given intraperitoneal injections of 20, 63 or 200 mg/kg either on days 9 to 11 or 12-14 of gestation. Similarly, no teratogenic effects were seen in CD-1 mice given oral doses of 70, 140 or 280 mg/kg/day on gestational days 6 through 15. Maternal toxicity was noted in the high-dose group (948).

36.3.1.4 Other Toxicologic Effects

36.3.1.4.1 Short-term Toxicity

Disturbance of the central nervous system is the predominant toxic response to phenol regardless of the route of administration. In rats, the oral LD_{50} ranges from 530 to 550 mg/kg (59). An acute lethal dose produces initial increases in pulse and respiration which later become slow, weak, and irregular. After an initial rise, blood pressure falls significantly The pupils constrict in the early stages but later dilate. Salivation may be evident and dyspnea is marked. Rats usually exhibit muscle twitching and uncoordinated leg movements until death occurs, usually due to respiratory arrest (12).

Cats appear to be the species most susceptible to the effects of phenol due to significant metabolic differences in the manner phenol is detoxified by this species. Oral doses of 50 to 100 mg/kg and intravenous doses of 50 mg/kg (dissolved in water) caused death in all animals tested (950).

In guinea pigs, inhalation exposures of 26-52 ppm, 7 hours daily, 5 days per week for 4 weeks caused weight loss, respiratory difficulty and signs of paralysis. At autopsy, pathologic examination revealed extensive myocardial necrosis and acute lobar pneumonia (951).

Cosgrove and Hubbard (952) reported that the eyes of rabbits were completely destroyed by one drop of 87% phenol in glycerin. However, if the eyes were immediately irrigated with water, corneas remained clear. If irrigation was delayed 10 seconds or longer, 40% of the animals sustained corneal damage. Solutions of 50% phenol in glycerin left in the eyes 10 seconds or longer before irrigation with water resulted in transparent corneas within 3 or 5 days in 30% of the animals. Solutions of 10 or 20% phenol in glycerin gave similar results. In another study, Murphy et al. (953) found that 0.1 ml of 5% phenol solution caused corneal opacities in 4 of 9 rabbits whose eyes were either not irrigated or irrigated with water for 2 minutes following 30 seconds of eye contact with the phenol solution.

The dermal LD_{50} for liquified phenol in rats is 670 mg/kg (0.625 ml/kg) by both occulsive and non-occlusive methods. Severe muscle tremors with twitching developed into generalized convulsions with loss of consciousness 5-10 minutes after administration of the dose in all animals. Severe hemoglobinuria developed 45-90 minutes after phenol application, with the severity increasing as a function of the dose. Skin lesions and edema with subsequent tissue necrosis and discoloration were also noted as well as pathologic evidence of kidney damage in all animals. The lowest dose applied was 0.1 mg/kg (954).

36.3.1.4.2 Chronic Toxicity

Damage to the lungs, liver, kidneys and heart has been reported following prolonged administration of phenol. Rabbits exposed to vapor

levels of 26 to 52 ppm, 7 hours daily, 5 days per week for 63 exposures in 88 days showed no signs of illness or discomfort. However, post-mortem examination revealed lobular pneumonia, chronic bronchitis, degeneration of the pulmonary blood vessels, myocardial degeneration, and indications of liver and kidney damage. Rats exposed to the same levels for 52 exposures in 74 days exhibited no signs of illness or pathologic changes (951).

Deichmann and Oesper (955) reported no significant effects in rats receiving 21-55 mg/rat/day (about 280 mg/kg for 200 g rat) in their drinking water for 12 months. However, pathological studies were not done. In another study, rats receiving 135 doses of 50 mg/kg phenol by gavage over a 6-month-period experienced "slight" kidney damage while those receiving 100 mg/kg had "slight to moderate" kidney damage and "very slight" liver changes (939). The apparent ability of rats to tolerate much larger doses of phenol in drinking water may be due to its rapid metabolism as well as the intermittent nature of dosing in contrast to exposure by gavage.

36.3.2 Human and Epidemiologic Studies

36.3.2.1 Short-term Toxicologic Effects

Phenol is readily absorbed from all routes of entry, distributed throughout the body, metabolized and rapidly excreted. The biological half-life of phenol in man is approximately 3.5 hours (939). Phenol is also produced endogenously by the degradative action of bacteria on tyrosine in the gut; between 1.5 and 5 mg of phenol are normally excreted per liter of human urine per day (939).

The most frequent adverse effects of phenol reported in humans result from skin contact (949). The skin is a primary route of entry for the solid, liquid and vapor. The vapor readily penetrates the skin with an absorption efficiency equal to that for inhalation (46). Signs and symptoms can develop rapidly with serious consequences including shock, convulsions, cyanosis, coma and death (949). Sax (51) reports that death can occur if 64 square inches of body surface are covered with phenol. Damage to internal organs has also been described. In addition, direct contact with the skin results in chemical burns.

Johnstone and Miller (956) described the case of an ink-manufacturing employee who spilled phenol on his leg, abdomen and chest. Although he immediately flushed the areas with water, he died within 15 minutes. Post-mortem examination revealed extensive first and second degree burns, edema and hyperemia of the lungs, kidneys, pancreas and spleen. In another case, a man died after application of benzyl benzoate (a scabicide) to his body with a brush that had been soaked overnight in an 80% phenol solution. Ten minutes after the application, he collapsed and began convulsing. He died shortly thereafter. Blood samples were found to contain 4.7 μg/ml phenol (957).

Cardiac arrhythmias have been reported in people undergoing chemical peeling of skin lesions with 40-80% phenol solutions. Arrhythmias are the primary type of morbidity associated with these procedures (958).

The lowest oral lethal dose reported in humans is 140 mg/kg (59); however, ingestion of 65 g of pure phenol or 120 g crude phenol have been survived (12). Ingestion causes severe burns of the mouth and throat, abdominal pain, cyanosis, muscular weakness, coma and death. Tremor, convulsions and muscle twitching may also occur (46). In one case, a woman committed suicide by ingesting 10-20 g of phenol. She became comatose with partial absence of reflexes, skin pallor, accelerated respiration, rapid pulse and dilated pupils. One hour after ingestion, she experienced cardiorespiratory arrest. Attempts at resuscitation were made for 2 hours, but to no avail. Autopsy revealed hyperemia of the tracheal and bronchial membranes. Histologic examination revealed edema of the liver and lungs and hyperemia of the intestines (959).

One incident of environmental poisoning occurred in 1974 when a derailed train spilled 37,900 liters of 100% phenol in rural Wisconsin. Over the next 6 months, phenol concentrations as high as 1130 mg/L were noted in well water. Individuals living near the site who ingested the phenol-contaminated water experienced burning sensations in the mouth, mouth sores, skin rashes, diarrhea and darkened urine (probably from oxidation products of phenol). Exposed individuals had estimated phenol intakes of 10-240 mg/person/day. Physical and laboratory examinations 6 months after the spill revealed no abnormalities in individuals who had consumed the contaminated water (961).

Owing in part to its low volatility, phenol is not considered a serious respiratory hazard (46). Inhalation of 15-52 ppm phenol for 8 hours (with two 30-minute breaks) using a face mask produced no ill effects in 8 human volunteers (960).

Phenol is irritating to the eyes, nose and throat. Concentrated phenol solutions are severely irritating to the human eye, causing conjunctival and corneal damage. In some cases, the eye lids have been severely damaged. In one case, severe iritis accompanied corneal injury (19).

36.3.2.2 Chronic Toxicologic Effects

Chronic phenol poisoning is infrequently reported. Severe chronic poisoning in man is characterized by systemic disorders which may include anorexia, vomiting, excessive salivation, headache, dizziness and skin eruption. Fatalities occur when there is extensive damage to the liver and kidneys (949,12).

Prolonged cutaneous exposure may result in ochronosis, a discoloration of collagenous tissue. NIOSH (949) cites numerous reports of ochronosis occurring in the early part of this century attributed to

the use of dressings impregnated with 5-10% phenol solutions for periods ranging from 3 to 24 years. Merliss (962) reported a case of a laboratory worker exposed to phenol, cresol and xylenol both dermally and by inhalation. Signs and symptoms appeared slowly and included loss of appetite and body weight, muscle pain, weakness and dark urine. After 13.5 years of exposure, examination revealed an emaciated individual with an enlarged liver and elevated liver enzyme levels. After exposure was discontinued, recovery was slow. Seven months later he had gained 7.6 kg and his liver was no longer palpable.

36.3.3 Levels of Concern

The USEPA (355) has established an ambient water quality criterion for the protection of human health for phenol of 3.5 mg/L. This criterion was developed based on the lowest-observed-adverse-effect level (i.e., slight kidney damage) in chronic oral studies with rats, an uncertainty factor of 500 and the assumption that two liters of drinking water are consumed by a 70-kg adult daily. An acceptable daily intake of 7 mg/kg was calculated for phenol (670).

OSHA (298) currently permits exposure to 5 ppm (19 mg/m^3) averaged over an 8-hour work-shift. The ACGIH (1003) recommends a threshold limit value of 5 ppm (19 mg/m^3), with a short-term exposure limit of 10 ppm (38 mg/m^3). These values were set to prevent systemic intoxication, provided skin absorption is avoided.

36.3.4 Hazard Assessment

Phenol is readily absorbed from all routes of entry. The majority of human lethal values are in the 5-40 g range. Central nervous system disturbances together with peripheral vasodilation result from an acute lethal dose of phenol, leading to sudden collapse, unconsciousness and death due to respiratory arrest. Ingestion of nonlethal amounts of phenol can result in burning in the mouth, mouth sores, headache, vomiting, diarrhea, back pain and production of dark urine.

The addition of up to 5000 ppm phenol to the drinking water of both mice and rats was found not to be carcinogenic for either species (941). Repeated skin application of large amounts of phenol does appear to promote tumor development in sensitive mouse strains but not in standard inbred strains of mice. The tumorigenic activity of phenol on mouse skin appears to be related to its irritancy and the resulting skin hyperplasia. Neither IARC (803) nor the NTP (883) have classified phenol with regard to carcinogenic activity.

Bacterial mutagenicity tests provide primarily negative findings for phenol. Phenol has been shown to increase sister chromatid exchanges in human lymphocytes *in vitro*. Phenol also induced lethal mutations in the fruit fly. The greatest concern, however, is an unconfirmed report of dose-related changes in the chromosomes of mouse spermatogonia and primary spermatocytes following gavage administration of aqueous phenol solutions at dosages as low as 6.5 µg/kg/day (963).

Unknown factors such as tissue distribution and DNA repair capabilities of different tissues and species make any discussion of the genetic implications for humans more speculative than factual. The negative carcinogenic response in lifetime studies with both rats and mice given 5000 ppm phenol in their drinking water plus the fact that phenol is a normal constituent of human tissues and fluids indicate that both humans and laboratory animals can handle long-term, low-level exposures to phenol with no apparent untoward effects. Nevertheless, this particular finding warrants validation in order to clarify the variance of its effect level from other reported effect levels as well as the potential implications of this study to humans if the results are substantiated.

Animal studies suggest no indications of embryotoxic nor teratogenic effects associated with phenol exposure. Slight to moderate kidney damage and slight liver changes have been reported in rats given 135 daily dosees of 100 mg/kg phenol by gavage. Rats, however, have been able to tolerate much larger doses in drinking water (55 mg/rat/-day or about 280 mg/kg for 200 g rat) probably due to its rapid metabolism as well as the intermittent nature of dosing in contrast to exposure by gavage.

36.4 SAMPLING AND ANALYSIS CONSIDERATIONS

Determination of phenol concentrations in soil and water requires collection of a representative field sample and laboratory analysis. Soil and water samples are collected in glass containers; extraction of samples should be completed within 7 days of sampling and analysis completed within 30-40 days. In addition to the targeted samples, quality control samples such as field blanks, duplicates, and spiked samples matrices may be specified in the recommended methods.

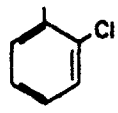
EPA-approved procedures for the analysis of phenol, one of the EPA priority pollutants, in aqueous samples include EPA Methods 604, 625, and 1625 (65), 8040 and 8250 (63). Prior to analysis, samples are extracted with methylene chloride as a solvent using a separatory funnel or a continuous liquid-liquid extractor. Methods 604 and 8040 also provide for a perfluorobenzyl bromide (PFB) derivatization of the sample extract with additional clean-up procedures if interferences are present in the sample matrix. An aliquot of the concentrated sample extract with or without derivatization is injected onto a gas chromatographic (GC) column using a solvent flush technique. The GC column is programmed to separate the semi-volatile organics; phenol is then detected with a flame ionization detector (Methods 604 and 8040 without derivatization), as its PFB derivative with an electron capture detector (Methods 604 and 8040 with derivatization) or with a mass spectrometer (Methods 625 and 1625).

The EPA procedures recommended for phenol analysis in soil and waste samples, Methods 8040 and 8250 (63), differ from the aqueous procedures primarily in the preparation of the sample extract. Solid

samples are extracted using either soxhlet extraction or sonication methods. Neat and diluted organic liquids may be analyzed by direct injection.

Typical phenol detection limits that can be obtained in waste waters and non-aqueous samples (wastes, soils, etc.) are shown below. The actual detection limit achieved in a given analysis will vary with instrument sensitivity and matrix effects.

Aqueous Detection Limit	Non-Aqueous Detection Limit
0.14 µg/L (Methods 604 and 8040 without derivatization)	1 µg/g (Method 8040)
2.2 µg/L (Methods 604 and 8040 with derivatization)	
1.5 µg/L (Methods 625 and 8250)	1 µg/g (Method 8250)
10 µg/L (Method 1625)	

COMMON SYNONYMS:	CAS REG. NO.:	FORMULA:	AIR W/V CONVERSION FACTORS at 25°C
2-Chlorophenol 2-Hydroxychloro-benzene 2-Chloro-1-hydroxy-benzene	95-57-8 NIOSH NO.: SK2625000	C_6H_5ClO	5.26 mg/m³ ≈ 1 ppm 0.1903 ppm ≈ 1 mg/m³
	STRUCTURE: 		MOLECULAR WEIGHT: 128.56

REACTIVITY	Phenols such as o-chlorophenol typically evolve heat in reactions with non-oxidizing mineral acids, organic peroxides or organic hydroperoxides; heat and possibly fire with oxidizing mineral acids or other strong oxidizing agents; and heat and flammable gases with alkali or alkaline earth metals, nitrides or strong reducing agents. Reactions with azo or diazo compounds or hydrazines typically evolve heat and usually innocuous gases. Those with isocyanates, epoxides, or polymerizable compounds may evolve heat and initiate violent polymerization reactions, while those with explosive compounds may initiate an explosion (511).

PHYSICO-CHEMICAL DATA	• Physical State (at 20°C): liquid	(23)
	• Color: colorless to yellow brown	(23)
	• Odor: medicinal	(67)
	• Odor Threshold: 3.6 ppb	(67)
	• Liquid Density (g/ml at 20°C): 1.2634	(68)
	• Freezing/Melting Point (°C): 9.3	(69)
	• Boiling Point (°C): 175	(69)
	• Flash Point (°C): 63.9 (closed cup)	(51,506)
	• Flammable Limits in Air, % by Volume: no data	( )
	• Autoignition Temperature (°C): no data	( )
	• Vapor Pressure (mm Hg at 20°C): 2.2	(901)
	• Saturated Concentration in Air (mg/m³ at 20°C): 16,600	(901)
	• Solubility in Water (mg/L at 20°C): 28,500	(67)
	• Viscosity (cp at 25°C): 4.11	(68)
	• Surface Tension (dyne/cm): 42.25 @ 12.7°C	(68)
	• Log (Octanol-Water Partition Coefficient), log K_{ow}: 2.15	(29)
	• Soil Adsorption Coefficient, K_{oc}: 68	(652)
	• Henry's Law Constant (atm·m³/mol at 25°C): 1.8×10^{-5} (estim)	(964)
	• Bioconcentration Factor: 214 (bluegill) 6.8 (estim)	(907,659)

PERSISTENCE IN THE SOIL-WATER SYSTEM	Relatively mobile in soil-water systems. Volatilization probably important for near-surface soils. Resistant to hydrolysis but fairly easily degraded by photo-oxidation, free-radical oxidation (speculative), and biodegradation.

PATHWAYS OF EXPOSURE	The primary pathway of concern from soil-water system is the migration of o-chlorophenol in ground-water drinking water supplies. Inhalation may also be important in some situations. Ingestion of fish or domestic animals is not likely to be important due to the low potential for bioaccumulation.

HEALTH HAZARD DATA	Signs and Symptoms of Short-term Human Exposure (972): o-Chlorophenol is harmful if swallowed, inhaled or absorbed through skin. Symptoms of exposure may include coughing, wheezing, shortness of breath, laryngitis, headache, nausea and vomiting.
	Toxicity Based on Animal Studies: LD_{50} (mg/kg) oral 670 [rat, mouse] (59) skin -- no data LC_{50} (mg/m^3) inhalation -- no data
	Long-Term Effects: No data
	Pregnancy/Neonate Data: Embryotoxic in rats at high doses
	Mutation Data: Limited evidence of mutagenic potential
	Carcinogenicity Classification: IARC - none assigned; NTP - none assigned

HANDLING PRECAUTIONS (52,54)	Handle chemical only with adequate ventilation • There are no formal guidelines available for this chemical with respect to respirator use. A self-contained breathing apparatus is recommended • Chemical goggles if there is probability of eye contact • Neoprene, nitrile, PVA or PVC protective clothing to prevent repeated or prolonged skin contact.

EMERGENCY FIRST AID TREATMENT (59,972, 1311)	Ingestion: Dilute ingested material with water or milk as soon as possible to prevent corrosion of upper GI tract; emesis may be induced if ingested solution is 5% or less. Get medical attention • Inhalation: Move victim to fresh air. If necessary, give artificial respiration. Get medical attention • Skin: Remove contaminated clothing; wash skin with soap and water or polyethylene glycol 300 or 400. If irritation persists, get medical attention • Eye: Irrigate with large amounts of water for 15 minutes. If irritation or pain persists, get medical attention.

ENVIRONMENTAL AND OCCUPATIONAL STANDARDS AND CRITERIA

AIR EXPOSURE LIMITS:

Standards
- OSHA PEL (8-hr TWA): none established
- AFOSH PEL (8-hr TWA): none established

Criteria
- NIOSH IDLH (30-min): none established
- ACGIH TLV® (8-hr TWA): none established
- ACGIH STEL (15-min): none established

WATER EXPOSURE LIMITS:

Drinking Water Standards - None established

EPA Health Advisories - None established

EPA Ambient Water Quality Criteria (355)
- Human Health
  - Based on ingestion of contaminated water and aquatic organisms, no criterion established due to insufficient data.

  - Based on organoleptic data for controlling undesirable taste and odor quality, the estimated level is 0.1 μg/L.

- Aquatic Life
  - Freshwater species
    acute toxicity: no criterion, but lowest effect level occurs at 4380 μg/L.

    chronic toxicity: no criterion, but impairment of fish flavor occurs at concentrations as low as 2000 μg/L.

  - Saltwater species
    acute toxicity: no criterion established due to insufficient data.

    chronic toxicity: no criterion established due to insufficient data.

REGULATORY STATUS (as of January 1, 1987)

Promulgated Regulations

- Federal Programs

Clean Water Act (CWA)

o-Chlorophenol is listed as a toxic pollutant (351). Water quality criteria have been set. Guidelines exist for effluent containing phenols in the timber products processing, petroleum refining, metal molding and casting, and textile mills point source categories (899, 896,892,893). Guidelines also exist in point source categories for the manufacture of iron and steel, non-ferrous metals and ferroalloys (354,894,895).

Safe Drinking Water Act (SDWA)

In states with an approved Underground Injection Control program, a permit is required for the injection of o-chlorophenol-containing wastes designated as hazardous under RCRA (295).

Resource Conservation and Recovery Act (RCRA)

o-Chlorophenol is identified as a hazardous waste (U048) and listed as a hazardous waste constituent (328,329). Waste streams from the following industries contain o-chlorophenol and are listed as specific sources of hazardous wastes: wood preservation (creosote and/or pentachlorophenol preserving processes) and coking (operational residues) (326,327).

Effective July 8, 1987, the land disposal of hazardous wastes containing halogenated organic compounds in total concentrations greater than or equal to 1000 mg/kg will be prohibited. The only exception will be underground injection (1755).

Comprehensive Environmental Response Compensation and Liability Act (CERCLA)

o-Chlorophenol is designated a hazardous substance under CERCLA. It has a reportable quantity (RQ) limit of 45.4 kg. Reportable quantities have also been issued for RCRA hazardous waste streams containing o-chlorophenol but these depend upon the concentrations of the chemicals in the waste stream (985).

Marine Protection Research and Sanctuaries Act (MPRSA)

Ocean dumping of organohalogen compounds as well as the dumping of known or suspected carcinogens, mutagens or teratogens is prohibited except when they are present as trace contaminants. Permit applicants are exempt from these regulations if they can demonstrate that such chemical constituents are non-toxic and non-bioaccumulative in the marine environment or are rapidly rendered harmless by physical, chemical or biological processes in the sea (309).

Hazardous Materials Transportation Act (HMTA)
The Department of Transportation has designated o-chlorophenol as a hazardous material which is subject to requirements for packaging, labeling and transportation (306).

Food, Drug and Cosmetic Act (FDCA)
The level for phenols in bottled drinking water is 0.001 mg/L (365).

- State Water Programs

Louisiana and Missouri have criteria of 0.1 µg/L for o-chlorophenol in public water and drinking water, respectively (731).

The following states have a criterion of 1 µg/L for phenolics (731):

Florida - in surface water
Illinois, Mississippi, Oregon - in the public water supply
North Carolina - in fresh water
Minnesota - in water for domestic consumption
New York - in Class AA drinking water
New Hampshire - in Class A and B waters

The following states have a criterion of 5 µg/L for phenolics (731):

Georgia - in all waters
Louisiana - in the public water supply
New York - in Class A drinking water
West Virginia - in drinking water

The following states have a criterion of 50 µg/L for phenolics (731):

Iowa - in drinking water
Louisiana - in fresh water

The following states have ground water quality standards for phenolics (981):

Missouri - 0.3 mg/L for fast recharge;
0.1 mg/L for slow recharge
New Jersey - 0.3 mg/L in Class GW 1
New York - 1 µg/L in Class GA
New Mexico - 5 µg/L
Virginia - 1 µg/L
Wyoming - 1 µg/L in Class 1

Other states follow EPA Ambient Water Quality Criteria.

Proposed Regulations

- Federal Programs

Clean Water Act (CWA)
Effluent guidelines for o-chlorophenol have been proposed in the organic chemicals, plastics and synthetic fibers category (357).

Resource Conservation and Recovery Act (RCRA)
EPA has proposed that non-liquid hazardous wastes containing halogenated organic compounds (HOCs) in total concentrations greater than or equal to 1000 mg/kg or liquid hazardous wastes containing HOCs in total concentrations greater than or equal to 1% HOCs must be incinerated in accordance with the requirements of 40CFR264.343 or 265.343 (1767).

EPA has also proposed that hazardous waste treatment, storage and disposal facilities monitor ground water for o-chlorophenol when EPA suspects the facilities of leaking contaminants (1754).

Toxic Substances Control Act (TSCA)
EPA has proposed that manufacturers of o-chlorophenol submit production, use, exposure and disposal data in order to determine whether there is further need for dioxin and furan testing of the chemical products for which it is a precursor (1435).

- State Water Programs
  No proposed regulations are pending.

EEC Directives

Directive on Drinking Water (533)
The mandatory values for phenols (phenol indices) in surface water treatment categories A1, A2 and A3 used or intended for abstraction of drinking water are 0.001, 0.005 and 0.1 mg/L, respectively. Guideline values for phenols (phenol indices) under treatment categories A2 and A3 are 0.001 and 0.01 mg/L, respectively. No guideline value is given for treatment category A1.

Directive Relating to the Quality of Water for Human Consumption (540)
The maximum admissible concentration for phenols (phenol indices) is 0.5 µg/L. Excluded from this category are natural phenols which do not react to chlorine. No guideline levels for phenols (phenol indices) are given.

Directive on Ground Water (538)
Direct and indirect discharge into ground water of substances which have a deleterious effect on the taste and/or odor of ground water, and compounds liable to cause the formation of such substances in ground water and to render it unfit for human consumption shall be subject to prior review so as to limit such discharges.

Directive on Bathing Water Quality (534)
Mandatory values for phenols (phenol indices) in bathing water are: (1) no specific odor and (2) concentrations ≤ 0.05 mg/L. Guideline values for phenols (phenol indices) suggest concentrations ≤ 0.005 mg/L.

Directive on Fishing Water Quality (536)
Phenolic compounds in both salmonid and cyprinid waters must not be present in such concentrations that they adversely affect fish flavor.

Directive on the Quality Required of Shellfish Waters (537)
The mandatory specifications for substances affecting the taste of shellfish require that their concentrations be lower than that liable to impair the taste of the shellfish.

Directive on the Discharge of Dangerous Substances (535)
Organohalogens, organophosphates, petroleum hydrocarbons, carcinogens or substances which have a deleterious effect on the taste and/or odor of human food derived from aquatic environments cannot be discharged into inland surface waters, territorial waters or internal coastal waters without prior authorization from member countries which issue emission standards. A system of zero-emission applies to discharge of these substances into ground water.

Directive on Marketing and Use of Dangerous Substances (541)
o-Chlorophenol may not be used in ornamental objects intended to produce light or color effects by means of different phases.

Directive on Toxic and Dangerous Wastes (542)
Any installation, establishment, or undertaking which produces, holds and/or disposes of certain toxic and dangerous wastes including phenols and phenol compounds; organic-halogen compounds; chrome compounds; lead compounds; cyanides; ethers and aromatic polycylic compounds (with carcinogenic effects) shall keep a record of the quantity, nature, physical and chemical characteristics and origin of such waste, and of the methods and sites used for disposing of such waste.

Directive on the Classification, Packaging and Labeling of Dangerous Substances (787)
o-Chlorophenol is classified as a harmful substance and is subject to packaging and labeling regulations.

Directive on Transfrontier Shipment of Hazardous Waste (1433)
When the holder of a hazardous waste such as o-chlorophenol intends to ship it to another member state, authorities of the member states concerned must be provided with information on the source and composition of the waste, measures to be taken to ensure safe transport, insurance against damage and the existence of a contractual agreement with the consignee of the waste. All transfrontier shipments must be properly packed and labeled and must be accompanied by instructions to be followed in the event of danger or accident.

EEC Directives - Proposed

Proposal for a Council Directive on the Dumping of Waste at Sea (1793)
EEC has proposed that the dumping of organohalogen compounds at sea be prohibited.

37.1 MAJOR USES

About 99% of the o-chlorophenol produced in the United States is used as a chemical intermediate in the production of higher chlorinated phenols. Other minor uses include their use in the production of specialized phenolic resins, as specialty solvents in the rubber industry, as a polymer intermediate in the manufacture of fire-retardant varnishes and as an aminizing agent for cotton fabric (901).

37.2 ENVIRONMENTAL FATE AND EXPOSURE PATHWAYS

37.2.1 Transport in Soil/Ground-water Systems

37.2.1.1 Overview

o-Chlorophenol is expected to be relatively mobile in the soil/ground-water environment when present at low concentrations (dissolved in water) or as a separate organic phase (e.g., resulting from a spill).

Transport pathways can be generally assessed by using an equilibrium partitioning model as shown in Table 37-1. These calculations predict the partitioning of low soil concentrations of o-chlorophenol among soil particles, soil water and soil air. The estimates for the unsaturated topsoil model show that while most of the o-chlorophenol is associated with the stationary soil phase, a significant amount (9.8%) is in the mobile water phase and thus easily leached. Diffusion of o-chlorophenol vapors through the soil-air pores up to the ground surface would appear to be a minor loss pathway based upon the model results. In saturated, deep soils (containing no air and negligible soil organic carbon), a much higher fraction of the o-chlorophenol is likely to be present in the soil water phase (Table 37-1) and available to be transported with flowing ground water.

o-Chlorophenol is a weak acid (pK_a = 8.52) and thus has a slight tendency to dissociate in water with the loss of a hydrogen ion. In pure water, only 2.9% would be dissociated at pH 7, but 23.2% would be dissociated at pH 8. Thus, in more alkaline waters (pH ≥ 8) the apparent mobility of o-chlorophenol should be increased since the ionic (dissociated) form would be only weakly sorbed by the stationary soil phase.

37.2.1.2 Soil Sorption on Soils

Based upon its octanol-water partition coefficient of 141, the soil sorption coefficient (K_{oc}) of o-chlorophenol is estimated to be 68. This estimate agrees well with a measured K_{oc} of 51 for a Brookston clay loam at a pH of 5.7 (816), and a second measured value of 75 from a surface soil in Calumet, MI with a pH of 5.4 (833). However, much higher values of K_{oc} (4900 to 23,000) have been reported based on studies with lake sediments (818).

TABLE 37-1

EQUILIBRIUM PARTITIONING CALCULATIONS FOR O-CHLOROPHENOL IN MODEL ENVIRONMENTS[a]

Soil Environment	Estimated Percent of Total Mass of Chemical in Each Compartment		
	Soil	Soil-Water	Soil-Air
Unsaturated topsoil at 25°C[b,c]	92.9 (90.2)	7.1 (9.8)	1.6×10^{-2} (1.6×10^{-2})
Saturated deep soil[d]	22.2 (21.6)	77.8 (78.4)	- -

a) Calculations based on Mackay's equilibrium partitioning model (34,35,36); see Introduction in Volume 1 for description of model and environmental conditions chosen to represent an unsaturated topsoil and saturated deep soil. Calculated percentages should be considered as rough estimates and used only for general guidance.

b) Utilized estimated soil sorption coefficient: $K_{oc} = 68$.

c) Henry's law constant taken as 1.8×10^{-5} atm•m³/mol at 25°C (964).

d) Used sorption coefficient $K_p = 0.001\ K_{oc}$.

e) Top number in each entry is for undissociated fraction of chemical. Bottom number, in parenthesis, is for total chemical concentration and is based upon the assumptions that the pH = 7, and that all of the dissociated fraction is in the soil-water compartment.

As noted above, sorption would be expected to decrease dramatically for pH > 8 because of the chemical's dissociation in this pH range. Sorption will also decrease with decreasing soil organic carbon content.

37.2.1.3 Volatilization from Soils

There are no data providing direct evidence on the importance of volatilization, through the air-filled pores of a soil, as a transport mechanism for o-chlorophenol. However, comparisons may be made with phenol for which some data are provided in Chapter 36 of this Guide. Those data showed that, given a sufficient time span (weeks to months),

volatilization was important for phenol in near-surface soils. Since o-chlorophenol has a vapor pressure about four times that of phenol, and a Henry's law constant about a factor of ten times that of phenol, it may be surmised that volatilization from surface soils will also be an important loss mechanism for o-chlorophenol.

37.2.2 Transformation Processes in Soil/Ground-water Systems

o-Chlorophenol is not likely to be susceptible to hydrolysis, in part because it contains no hydrolyzable functional groups (10,33,529). It is probably, like phenol, subject to slow degradation by free radical oxidation. Mabey et al. (33) give estimated oxidation rate constants of $< 7 \times 10^5$ M^{-1} hr^{-1} for reaction with singlet oxygen and 1×10^7 M^{-1} hr^{-1} for reaction with a peroxy radical. (The same estimates were given for phenol by Mabey et al. (33).) Baker and Mayfield (826) found that o-chlorophenol underwent rapid non-biological degradation in sterile soil. The rate of this degradation increased with temperature and decreased with concentration. In one test in a silica sand/water mixture at 26°C, the o-chlorophenol concentration fell from 100 μg/g of silica to about 15 μg/g after 7 days. These authors speculated that an auto-oxidation mechanism was involved, possibly catalyzed.

A number of studies have shown that o-chlorophenol can be photolytically degraded (10,806) but only with low wavelength light (below 300 nm) which is of very low intensity in the solar spectrum (10). Because of this, photolysis is not expected to be a significant degradation pathway. When photolysis does occur, reaction products initially formed include pyrocatechol and cyclopentadienic acids (857).

A variety of studies have shown that o-chlorophenol can be biodegraded with reasonable facility (10,901,806,55,826,830,833,834,835). Concentrations above 10 mg/L may be toxic and/or inhibitory to degrading microorganisms (806).

The data on biodegradation in soils are somewhat contradictory or confusing. Baker and Mayfield (826), for example, showed o-chlorophenol to be rapidly degraded by microorganisms in aerobically-incubated soil, but not biodegraded in anaerobically incubated soil (both at 23°C). (Non-biological degradation was, however, noted under "anerobic" conditions, not only at 23°C but also at 4°C (826).) Usipoff et al. (833) found that the chemical was not biodegraded by unacclimated soil cultures (at 20°C) based on data from an electrolytic respirometer (to measure oxygen uptake). However, the CHEMFATE data base (806) provides data from seven other studies on biodegradation in soils or sediments (or using microbes isolated from soils); in all cases, some degradation of o-chlorophenol was noted although the time scales for significant degradation were usually on the order of weeks to a few months.

o-Chlorophenol is easily biodegraded in tests using acclimated seed from sewage treatment plants. Tabak et al. (55), for example, classified the chemical as undergoing significant degradation with rapid adaptation in shake-flask tests.

Based upon the above information, it is concluded that o-chlorophenol can be biodegraded in the natural soil/ground-water environment as long as there are sufficient populations of active microorganisms present. If only low concentrations of microbes are present, biodegradation half-lives might be quite long (months to years).

37.2.3 Primary Routes of Exposure from Soil/Ground-water Systems

The above discussion of fate pathways suggests that o-chlorophenol has a moderate volatility, is weakly adsorbed to soil and has a low potential for bioaccumulation. This compound may volatilize from the soil surface, but that portion not removed by volatilization is likely to be mobile in ground water. These fate characteristics suggest several potential exposure pathways.

Volatilization of o-chlorophenol from a disposal site could result in inhalation exposures to workers or residents in the area. In addition, the potential for ground water contamination is high, particularly in sandy soils. It has been detected in ground water associated with hazardous waste sites, although infrequently. Mitre (83) reported that o-chlorophenol has been found at 3 of the 546 National Priority List (NPL) sites. It was detected at two sites in ground water and in the air at one site. While these data suggest that drinking water exposure from ground-water contamination is possible, it does not appear to be common. The reason for this may be the limited direct uses of this compound which is primarily used as a chemical intermediate (901).

The movement of o-chlorophenol in ground water may result in discharge to surface waters. Several additional exposure routes may result, including:

- Ingestion exposure resulting from the use of surface waters as drinking water supplies;
- Dermal exposure resulting from the recreational use of surface waters;
- Ingestion exposure resulting from consumption of aquatic organisms that have accumulated o-chlorophenol;
- Ingestion exposure resulting from consumption of meat or poultry that has accumulated o-chlorophenol through dermal contact with or ingestion of surface waters.

In general, exposures to o-chlorophenol associated with surface water contamination from a hazardous waste site can be expected to be lower than exposures from drinking contaminated ground water. The compound may be adsorbed or biodegraded before reaching surface water. Some volatilization of o-chlorophenol may occur from surface waters. In addition, the bioaccumulation factor for o-chlorophenol is low, and bioaccumulation in fish or domestic animals would likely be limited.

There is little evidence of exposure of the general population to o-chlorophenol (900,901). No monitoring data for this compound in drinking water, food or air have been reported (84,901).

37.3 HUMAN HEALTH CONSIDERATIONS

37.3.1 Animal Studies

37.3.1.1 Carcinogenicity

The carcinogenic potential of o-chlorophenol has not been tested by the oral route but it does appear to possess tumor-promoting activities in mice, probably a result of an irritant response. Boutwell and Bosch (902), in a 15-week experiment, initiated female Sutter mice with a single dermal application of 0.3% dimethylbenzanthracene in benzene. They followed this with twice weekly applications of ~ 25 μL of a 20% o-chlorophenol solution. Ten percent of the treated mice developed epithelial carcinomas and 61% developed papillomas. The promoting activity of o-chlorophenol is probably associated with its irritant effects and subsequent skin hyperplasia and is thus not appropriate for assessment of human hazard by ingestion.

In a separate study, Boutwell and Bosch (902) treated female Sutter mice with 20% o-chlorophenol in dioxane twice weekly for 12 weeks without prior initiation. At the conclusion of the study, 46% of the survivors had developed papillomas but no epithelial carcinomas were found.

37.3.1.2 Mutagenicity

Chung (903) noted a fivefold increase in chromatid deletions in the bone-marrow cells of Sprague-Dawley rats given oral doses of 130 mg/kg o-chlorophenol every other day for 1 week. After two to three weeks of exposure, complete inhibition of mitosis in bone marrow cells was noted.

37.3.1.3 Teratogenicity, Embryotoxicity and Reproductive Effects

A study conducted by Exon and Koller (904) gave some indication that o-chlorophenol may be feto- or embryotoxic at high doses. They exposed female Sprague-Dawley rats to 0, 5, 50 or 500 ppm o-chlorophenol in drinking water from the 21st day of age through parturition (the rats were bred at 90 days of age). Litter size was significantly decreased in a dose-related manner. Also, the number of stillborn pups born to dams receiving 500 ppm was greater than that seen in controls.

37.3.1.4 Other Toxicologic Effects

37.3.1.4.1 Short-term Toxicity

Toxicity data on o-chlorophenol are limited. It is considered to be an uncoupler of oxidative phosphorylation (i.e., inhibits production of ATP) and a convulsant poison (908). In general, the monochlorophenols produce kidney injury with red cell casts in the tubules, fatty infiltration of the liver and hemorrhages in the intestines of rats (12).

Ortho-chlorophenol is more toxic by the oral than the subcutaneous route. Oral LD_{50} values for both the mouse and rat are 670 mg/kg; a subcutaneous LD_{50} value of 950 mg/kg has been recorded for the rat (47).

Signs of intoxication in rats are similar whether the compound is administered orally, subcutaneously or intraperitoneally. They include restlessness and increased respiratory rate a few minutes after exposure. A few minutes later, motor weakness develops along with tremors and clonic convulsions which can be induced by noise or touch. Eventually, dyspnea and coma result and continue until death (12).

In rats treated orally every other day for 3 weeks with 65 or 130 mg/kg of o-chlorophenol dissolved in olive oil, weight gain was significantly reduced and liver weight was increased. Liver function was altered as indicated by elevated enzyme levels. Histologically, liver tissue was found to be degenerated (903).

In mice, exposure to 175 mg/kg o-chlorophenol daily by gavage for 14 days resulted in significant body weight reduction and 80% lethality. Mice given 35 or 69 mg/kg/day for the same duration were hyperactive from day 4 onward (858).

No data on dermal exposure are available but since it is lipid soluble and likely to be poorly ionized at physiological pH, absorption by this route is likely (905).

37.3.1.4.2 Chronic Toxicity

No chronic toxicity data are available.

37.3.2 Human and Epidemiologic Studies

There are no data on the effects of o-chlorophenol in humans.

37.3.3 Levels of Concern

No criteria or standards based on toxicity considerations have been established to date regarding this chemical. A criterion of 0.1 μg/L of o-chlorophenol is recommended by the USEPA based on organoleptic considerations (355). In view of the limited data available on the adverse health effects and effect levels associated with exposure to o-chlorophenol, estimates of exposure levels of concern cannot be made with any confidence.

37.3.4 Hazard Assessment

The available data on the toxicity of o-chlorophenol are limited. Acute median lethal doses in rodents are in the 670 to 950 mg/kg range. Subchronic studies are few but alteration of liver function appears to be the principal finding. A single report indicated the induction of chromosomal damage in mammalian somatic tissues by o-chlorophenol (903). The compound may also be embryotoxic at high doses. There is no information to suggest o-chlorophenol is a direct carcinogen. Some tumor-promoting capability has been demonstrated in mice for o-chlorophenol but it is probably associated with its irritant effects and subsequent skin hyperplasia, and thus, not appropriate for assessment of the systemic hazards associated with o-chlorophenol exposure. Neither IARC (803) nor the NTP (883) have classified this compound.

37.4 SAMPLING AND ANALYSIS CONSIDERATIONS

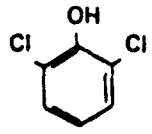
Determination of o-chlorophenol concentrations in soil and water requires collection of a representative field sample and laboratory analysis. Soil and water samples are collected in glass containers; extraction of samples should be completed within 7 days of sampling and analysis completed within 30-40 days. In addition to the targeted samples, quality control samples such as field blanks, duplicates, and samples matrices may be specified in the recommended methods.

EPA-approved procedures for the analysis of o-chlorophenol, one of the EPA priority pollutants, in aqueous samples include EPA Methods 604, 625, and 1625 (65), 8040 and 8250 (63). Prior to analysis, samples are extracted with methylene chloride as a solvent using a separatory funnel or a continuous liquid-liquid extractor. Methods 604 and 8040 also provide for a perfluorobenzyl bromide (PFB) derivatization of the sample extract with additional clean-up procedures if interferences are present in the sample matrix. An aliquot of the concentrated sample extract with or without derivatization is injected onto a gas chromatographic (GC) column using a solvent flush technique. The GC column is programmed to separate the semi-volatile organics; o-chlorophenol is then detected with a flame ionization detector (Methods 604 and 8040 without derivatization), as its PFB derivative with an electron capture detector (Methods 604 and 8040 with derivatization) or with a mass spectrometer (Methods 625 and 1625).

The EPA procedures recommended for o-chlorophenol analysis in soil and waste samples, Methods 8040 and 8250 (63), differ from the aqueous procedures primarily in the preparation of the sample extract. Solid samples are extracted using either soxhlet extraction or sonication methods. Neat and diluted organic liquids may be analyzed by direct injection.

Typical o-chlorophenol detection limits that can be obtained in waste waters and non-aqueous samples (wastes, soils, etc.) are shown below. The actual detection limit achieved in a given analysis will vary with instrument sensitivity and matrix effects.

Aqueous Detection Limit	Non-Aqueous Detection Limit
0.31 µg/L (Methods 604 and 8040 without derivatization)	1 µg/g (Method 8040)
0.58 µg/L (Methods 604 and 8040 with derivatization)	
3.3 µg/L (Methods 625 and 8250)	1 µg/g (Method 8250)
10 µg/L (Method 1625)	

COMMON SYNONYMS:	CAS REG. NO.:	FORMULA:	AIR W/V CONVERSION FACTORS at 25°C
RCRA Waste Number U082	87-65-0 NIOSH NO.: SK8750000	$C_6H_4Cl_2O$	6.66 mg/m³ ≈ 1 ppm 0.15 ppm ≈ 1 mg/m³
	STRUCTURE: 		MOLECULAR WEIGHT: 163.0

REACTIVITY	Dichlorophenols are considered to be both phenols and halogenated organics for compatibility classification purposes. Phenols typically evolve heat in reactions with non-oxidizing mineral acids and organic peroxides or hydroperoxides; heat and possibly fire with oxidizing mineral acids or other strong oxidizing agents; and heat and flammable gases with alkali or alkaline earth metals, nitrides or strong reducing agents. Reactions with azo or diazo compounds or hydrazines typically generate heat and usually innocuous gases. Those with isocyanates, epoxides or polymerizable compounds may evolve heat and initiate violent polymerization reactions, while those with explosive compounds may initiate an explosion. Halogenated organic compounds typically generate heat in reactions with cyanides, mercaptans and other organic sulfides. Those with non-oxidizing mineral acids, amines and strong oxidizing agents typically evolve heat and toxic gases, while those with caustics or nitrides evolve heat and flammable gases. Reactions with oxidizing mineral acids may generate heat, toxic gases and fire, while those with azo or diazo compounds or hydrazines may evolve heat and usually innocuous gases. Certain elemental metals and alloys as sheets, rods, drops, etc. may evolve heat and fire in reactions with these compounds, while alkali and alkaline earth metals and certain metals as powders, vapors or sponges may evolve heat and initiate an explosion. Heat evolution and explosion are also possible results of reactions with organic peroxides or hydroperoxides and strong reducing agents (511).

PHYSICO-CHEMICAL DATA	• Physical State (at 20°C): crystalline	(54)
	• Color: white	(54)
	• Odor: strong, penetrating, medicinal	(971)
	• Odor Threshold: .003 mg/L	(971)
	• Freezing/Melting Point (°C): 65-68	(14)
	• Boiling Point (°C): 218-220	(14)
	• Flash Point (°C): >100 (by analogy to 2,4 isomer)	(1)
	• Flammable Limits in Air, % by Volume: no data	( )
	• Autoignition Temperature (°C): no data	( )
	• Vapor Pressure (mm Hg at 20°C): 0.032	(969)
	• Saturated Concentration in Air (mg/m³ at 20°C): 286	(ADL estim)

PHYSICO-CHEMICAL DATA (Continued)	• Solubility in Water (mg/L at 25°C): 2300 (967) • Log (Octanol-Water Partition Coefficient), log K_{ow}: 2.64 (29) • Soil Adsorption Coefficient, K_{oc}: 210 (652) • Henry's Law Constant ($atm \cdot m^3/mol$ at 20°C): 3.0×10^{-6} (estim) (964) • Bioconcentration Factor: 21 (estim) (659)

PERSISTENCE IN THE SOIL-WATER SYSTEM	Mobile in soil-water systems due, in part, to acid dissociation. Resistant to hydrolysis, but susceptible to free-radical oxidation (speculative). May be susceptible to slow biodegradation; data are contradictory.

PATHWAYS OF EXPOSURE	The primary pathway of concern from soil-water systems is the migration of 2,6-dichlorophenol in ground-water drinking water supplies, although little evidence of such exposure presently exists. Inhalation and the consumption of this compound in fish are not expected to be important exposure pathways.

HEALTH HAZARD DATA	Signs and Symptoms of Short-term Human Exposure (972): 2,6-Dichlorophenol may be harmful by inhalation, ingestion or skin absorption. It is irritating to the mucous membranes and upper respiratory tract. Prolonged contact can induce severe irritation or burns.
	Toxicity Based on Animal Studies: LD_{50} (mg/kg): oral 2940 [rat] (47); skin -- no data LC_{50} (mg/m^3): inhalation -- no data
	Long-Term Effects: No data
	Pregnancy/Neonate Data: No data
	Mutation Data: Limited evidence of mutagenic potential
	Carcinogenicity: No data

HANDLING PRECAUTIONS (52,54)	Handle chemical only with adequate ventilation • There are no formal guidelines available for this chemical with respect to respirator use. A self-contained breathing apparatus is recommended • Chemical goggles if there is probability of eye contact • Natural rubber, neoprene, nitrile, PVC, or PVA protective clothing to prevent repeated or prolonged skin contact.

EMERGENCY FIRST AID TREATMENT (972)	Ingestion: If victim is conscious, induce vomiting. Get medical attention • Inhalation: Move victim to fresh air; give artificial respiration if necessary. Get medical attention • Skin: Remove contaminated clothing. Wash skin with soap and water. If irritation persists after washing, get medical attention • Eye: Irrigate for at least 15 minutes. If burning is present after washing, get medical attention.

ENVIRONMENTAL AND OCCUPATIONAL STANDARDS AND CRITERIA

AIR EXPOSURE LIMITS:

Standards
- OSHA PEL (8-hr TWA): none established
- AFOSH PEL (8-hr TWA): none established

Criteria
- NIOSH IDLH (30-min): none established
- ACGIH TLV® (8-hr TWA): none established
- ACGIH STEL (15-min): none established

WATER EXPOSURE LIMITS:

Drinking Water Standards - None established

EPA Health Advisories - None established

EPA Ambient Water Quality Criteria (355)
- Human Health
  - No criterion established due to insufficient data.
  - Based on available organoleptic data for controlling undersirable taste and odor, a level of 0.2 µg/L is recommended.
- Aquatic Life
  - Freshwater species
    acute toxicity: no criterion established due to insufficient data.

    chronic toxicity: no criterion established due to insufficient data.
  - Saltwater species
    acute toxicity: no criterion established due to insufficient data.

    chronic toxicity: no criterion established due to insufficient data.

REGULATORY STATUS (as of January 1, 1987)

Promulgated Regulations

- Federal Programs

Clean Water Act (CWA)

2,6-Dichlorophenol is listed as a toxic pollutant (351). Water quality criteria have been set. Guidelines exist for effluent containing phenols in the timber products processing, petroleum refining, metal molding and casting, and textile mills point source categories (899,896,892,893). Guidelines also exist in point source categories for the manufacture of iron and steel, non-ferrous metals and ferroalloys (354,894,895).

Safe Drinking Water Act (SDWA)

In states with an approved Underground Injection Control program, a permit is required for the injection of 2,6-dichlorophenol-containing wastes designated as hazardous under RCRA (295).

Resource Conservation and Recovery Act (RCRA)

2,6-Dichlorophenol is identified as a hazardous waste (U082) and listed as a hazardous waste constituent (328,329). Waste streams from the following industries contain 2,6-dichlorophenol and are listed as specific sources of hazardous wastes: pesticides (2,4-D production) and coking (operational residues) (326,327).

Effective July 8, 1987, the land disposal of hazardous wastes containing halogenated organic compounds in total concentrations greater than or equal to 1000 mg/kg will be prohibited. The only exception will be underground injection (1755).

Comprehensive Environmental Response Compensation and Liability Act (CERCLA)

2,6-Dichlorophenol is designated a hazardous substance under CERCLA. It has a reportable quantity (RQ) limit of 45.4 kg. Reportable quantities have also been issued for RCRA hazardous waste streams containing 2,6-dichlorophenol but these depend upon the concentrations of the chemicals in the waste stream (985).

Marine Protection Research and Sanctuaries Act (MPRSA)

Ocean dumping of organohalogen compounds as well as the dumping of known or suspected carcinogens, mutagens or teratogens is prohibited except when they are present as trace contaminants. Permit applicants are exempt from these regulations if they can demonstrate that such chemical constituents are non-toxic and non-bioaccumulative in the marine environment or are rapidly rendered harmless by physical, chemical or biological processes in the sea (309).

Hazardous Materials Transportation Act (HMTA)
The Department of Transportation has designated 2,6-dichlorophenol as a hazardous material which is subject to requirements for packaging, labeling and transportation (306).

Food, Drug and Cosmetic Act (FDCA)
The level for phenols in bottled drinking water is 0.001 mg/L (365).

- State Water Programs

  Louisiana has a criterion of 0.2 µg/L for 2,6-dichlorophenol in the public water supply (731).

  The following states have a criterion of 1 µg/L for phenolics (731):

  Florida - in surface water
  Illinois, Mississippi, Oregon - in the public water supply
  North Carolina - in fresh water
  Minnesota - in water for domestic consumption
  New York - in Class AA drinking water
  New Hampshire - in Class A and B waters

  The following states have a criterion of 5 µg/L for phenolics (731):

  Georgia - in all waters
  Louisiana - in the public water supply
  New York - in Class A drinking water
  West Virginia - in drinking water

  The following states have a criterion of 50 µg/L for phenolics (731):

  Iowa - in drinking water
  Louisiana - in fresh water

  The following states have ground water quality standards for phenolics (981):

  Missouri - 0.3 mg/L for fast recharge;
  0.1 mg/L for slow recharge
  New Jersey - 0.3 mg/L in Class GW 1
  New York - 1 µg/L in Class GA
  New Mexico - 5 µg/L
  Virginia - 1 µg/L
  Wyoming - 1 µg/L in Class 1

  Other states follow EPA Ambient Water Quality Criteria.

Proposed Regulations

- Federal Programs

  Resource Conservation and Recovery Act (RCRA)

  EPA has proposed that non-liquid hazardous wastes containing halogenated organic compounds (HOCs) in total concentrations greater than or equal to 1000 mg/kg or liquid hazardous wastes containing HOCs in total concentrations greater than or equal to 1% HOCs must be incinerated in accordance with the requirements of 40CFR264.343 or 265.343 (1767).

  EPA has also proposed that hazardous waste treatment, storage and disposal facilities monitor ground water for 2,6-dichlorophenol when EPA suspects the facilities of leaking contaminants (1754).

  Toxic Substances Control Act (TSCA)

  EPA has proposed that if manufacture or import of 2,6-dichlorophenol should resume it must be tested for the presence of dioxins and furans and existing test data must be submitted (1435).

- State Water Programs - No proposed regulations are pending.

EEC Directives

Directive on Drinking Water (533)

The mandatory values for phenols (phenol indices) in surface water treatment categories A1, A2 and A3 used or intended for abstraction of drinking water are 0.001, 0.005 and 0.1 mg/L, respectively. Guideline values for phenols (phenol indices) under treatment categories A2 and A3 are 0.001 and 0.01 mg/L, respectively. No guideline value is given for treatment category A1.

Directive Relating to the Quality of Water for Human Consumption (540)

The maximum admissible concentration for phenols (phenol indices) is 0.5 µg/L. Excluded from this category are natural phenols which do not react to chlorine. No guideline levels for phenols (phenol indices) are given.

Directive on Ground Water (538)

Direct and indirect discharge into ground water of substances which have a deleterious effect on the taste and/or odor of ground water, and compounds liable to cause the formation of such substances in ground water and to render it unfit for human consumption shall be subject to prior review so as to limit such discharges.

Directive on Bathing Water Quality (534)

Mandatory values for phenols (phenol indices) in bathing water are: (1) no specific odor and (2) concentrations ≤ 0.05 mg/L. Guideline values for phenols (phenol indices) suggest concentrations ≤ 0.005 mg/L.

Directive on Fishing Water Quality (536)
Phenolic compounds in both salmonid and cyprinid waters must not be present in such concentrations that they adversely affect fish flavor.

Directive on the Quality Required of Shellfish Waters (537)
The mandatory specifications for substances affecting the taste of shellfish require that their concentrations be lower than that liable to impair the taste of the shellfish.

Directive on the Discharge of Dangerous Substances (535)
Organohalogens, organophosphates, petroleum hydrocarbons, carcinogens or substances which have a deleterious effect on the taste and/or odor of human food derived from aquatic environments cannot be discharged into inland surface waters, territorial waters or internal coastal waters without prior authorization from member countries which issue emission standards. A system of zero-emission applies to discharge of these substances into ground water.

Directive on Toxic and Dangerous Wastes (542)
Any installation, establishment, or undertaking which produces, holds and/or disposes of certain toxic and dangerous wastes including phenols and phenol compounds; organic-halogen compounds; chrome compounds; lead compounds; cyanides; ethers and aromatic polycylic compounds (with carcinogenic effects) shall keep a record of the quantity, nature, physical and chemical characteristics and origin of such waste, and of the methods and sites used for disposing of such waste.

Directive on Transfrontier Shipment of Hazardous Waste (1433)
When the holder of a hazardous waste such as 2,6-dichlorophenol intends to ship it to another member state, authorities of the member states concerned must be provided with information on the source and composition of the waste, measures to be taken to ensure safe transport, insurance against damage and the existence of a contractual agreement with the consignee of the waste. All transfrontier shipments must be properly packed and labeled and must be accompanied by instructions to be followed in the event of danger or accident.

EEC Directives - Proposed

Proposal for a Council Directive on the Dumping of Waste at Sea (1793)
EEC has proposed that the dumping of organohalogen compounds at sea be prohibited.

38.1 MAJOR USES

The 2,6-isomer of dichlorophenol is used primarily as a feedstock in the manufacture of trichlorophenols, tetrachlorophenols and pentachlorophenol (54).

38.2 ENVIRONMENTAL FATE AND EXPOSURE PATHWAYS

38.2.1 Transport in Soil/Ground-water Systems

38.2.1.1 Overview

2,6-Dichlorophenol is expected to be quite mobile in the soil/ground-water environment when present at low concentrations (dissolved in water). The pure chemical is solid at ambient temperatures (melting point is 65-66°C) and thus bulk quantities (e.g., from a spill) would not be immediately mobile.

2,6-Dichlorophenol is a moderately strong organic acid (reported pK_a values are 6.63 (29) and 6.79 (856)), and thus it has a significant tendency to dissociate in natural waters with the loss of a hydrogen ion. In pure water, the percent dissociation at pH values of 6, 7 and 8 are, respectively, 19%, 70% and 96%. In general, the dissociated form of the chemical (the 2,6-dichlorophenate anion) is more water soluble and less strongly sorbed to soils than the neutral undissociated form.

Transport pathways can be generally assessed by using an equilibrium partitioning model as shown in Table 38-1. These calculations predict the partitioning of low soil concentrations of the 2,6-dichlorophenol among soil particles, soil water, and soil air. The estimates in this case are given for both the total chemical concentration and for the undissociated fraction. The estimates for the unsaturated topsoil model show that, based on total chemical concentration, most of the chemical (70.7%) is in the mobile water phase and thus easily transported with percolating ground water. Diffusion of chemical vapors through the soil-air pores up to the ground surface would not appear to be a significant loss pathway based upon the model results. In saturated deep soils (containing no air and negligible soil organic carbon), an even higher fraction of 2,6-dichlorophenol (85.9%) is predicted to be in the soil-water phase and available to be transported with flowing ground water.

38.2.1.2 Sorption on Soils

Based upon its octanol-water partition coefficient of 436, the soil sorption coefficient (K_{oc}) is estimated to be 210. This is a relatively low number indicative of fairly weak sorption. As noted above, the chemical would be expected to be more strongly sorbed at lower pH values due to less dissociation of the chemical. No measured sorption data were found in the literature.

TABLE 38-1

EQUILIBRIUM PARTITIONING CALCULATIONS FOR 2,6-DICHLOROPHENOL IN MODEL ENVIRONMENTS[a]

Soil Environment	Estimated Percent of Total Mass of Chemical in Each Compartment		
	Soil	Soil-Water	Soil-Air
Unsaturated topsoil at 25°C[b,c]	97.6 (29.3)	2.4 (70.7)	9×10^{-4} (9×10^{-4})
Saturated deep soil[d]	46.9 (14.1)	53.1 (85.9)	- -

a) Calculations based on Mackay's equilibrium partitioning model (34,35,36); see Introduction in Volume 1 for description of model and environmental conditions chosen to represent an unsaturated topsoil and saturated deep soil. Calculated percentages should be considered as rough estimates and used only for general guidance.

b) Utilized estimated soil sorption coefficient: $K_{oc} = 210$.

c) Henry's law constant taken as 3.0×10^{-6} atm•m³/mol at 25°C (964).

d) Used sorption coefficient $K_p = 0.001\ K_{oc}$.

e) Top number in each entry is for undissociated fraction of chemical. Bottom number, in parenthesis, is for total chemical concentration and is based upon the assumptions that the pH = 7 and that all of the dissociated fraction is in the soil-water compartment.

38.2.1.3 Volatilization from Soils

The Henry's law constant for 2,6-dichlorophenol (3.0×1.0^{-6} atm•m³/mol at 20°C (964)) is approximately the same as that for phenol (7.0×10^{-6} atm•m³/mol at 20°C (964)). Given that phenol is relatively easily lost from topsoils (see Chapter 36, Section 36.2), it is surmised that 2,6-dichlorophenol would also be relatively easily lost from toposoils. No data are available in the literature to support this conjecture.

38.2.2 Transformation Processes in Soil/Ground-water Systems

2,6-Dichlorophenol is probably not susceptible to degradation by hydrolysis since it has no hydrolyzable functional groups (529).

Baker and Mayfield (826) found that 2,6-dichlorophenol underwent non-biological degradation in sterile soil. In tests at 23°C, 55% of the 2,6-dichlorophenol was decomposed after 40 days in sterile, aerobic (clay loam) soil, while 81% was decomposed after 80 days in sterile, anaerobic soil. The researchers speculated that a radical mechanism, most probably initiated by reactions with molecular oxygen, was involved. A similar phenomenon was noted for other chlorophenols with the degradation rate increasing with temperature and decreasing with chemical concentration.

Baker and Mayfield (826) also reported studies showing 2,6-dichlorophenol to be "rapidly degraded" by microorganisms in aerobically-incubated soil at 23°C. No biodegradation was seen in anaerobically-incubated soil at this temperature. Haider et al. (836) reported the biodegradation of 2,6-dichlorophenol in a para-brown soil (1.26% organic carbon, pH 7.1). Other data reported in the literature provided contradictory information on the biodegradability of this chemical. Boyd and Shelton (834), for example, found no degradation in fresh anaerobic sludge at 37°C.

38.2.3 Primary Routes of Exposure from Soil/Ground-water Systems

The above discussion of fate pathways suggests that 2,6-dichlorophenol has a low volatility, is moderately sorbed to soil, and has a low potential for bioaccumulation. The volatilization of this compound from surface soil is not likely to represent a primary route of exposure. 2,6-Dichlorophenol may be mobile in ground water, particularly in sandy soils, and may result in drinking water exposure via this route. Exposure pathways involving the accumulation of 2,6-dichlorophenol are likely to be less important than drinking water exposure due to its low bioconcentration factor.

Human exposure as a result of ground water contamination has not been documented. Mitre (83) did not specifically report the presence of 2,6-dichlorophenol in ground water associated with any of the 546 National Priority List (NPL) sites. In addition, this compound has not been included in the National surveys of drinking water conducted by EPA (90,531). However, based on its chemical properties, 2,6-dichlorophenol has some potential to result in drinking water exposure through ground water contamination. In addition, the movement of this compound in ground water may result in indirect exposure pathways upon discharge to surface waters. These pathways would include ingestion exposure through the consumption of surface water as a drinking water supply, or dermal exposure through recreational use of surface waters. Bioaccumulation of 2,6-dichlorophenol from surface waters, either by aquatic organisms or domestic animal, are not expected to be dominant exposure pathways due to the low bioconcentration factor for 2,6-dichlorophenol.

38.2.4 Other Sources of Human Exposure

No other sources of exposure to 2,6-dichlorophenol have been identified.

38.3 HUMAN HEALTH CONSIDERATIONS

38.3.1 Animal Studies

38.3.1.1 Carcinogenicity

No carcinogenicity data are available for 2,6-dichlorophenol.

38.3.1.2 Mutagenicity

The 2,6-isomer of dichlorophenol gave negative results in the Ames test both with and without metabolic activation (970). A single report indicated that 2,6-dichlorophenol produced chromosome aberrations in rat bone marrow cells, but details of this Korean study were unavailable for evaluation (54,59).

38.3.1.3 Teratogenicity, Embryotoxicity and Reproductive Effects

No data are available.

38.3.1.4 Other Toxicologic Effects

38.3.1.4.1 Short-term Toxicity

The toxicity of 2,6-dichlorophenol has not been well studied. It is a severe eye (250 μg/24 hr) and skin (500 mg/24 hr) irritant in rabbits (59). By comparison with other chlorophenols, it is expected that 2,6-dichlorophenol is absorbed through the skin and from the gastrointestinal tract and rapidly eliminated (971).

In rats, the LD_{50} by the oral route is 2940 mg/kg compared to 390 mg/kg by the intraperitoneal route (59). Chlorinated phenols, in general, cause restlessness and an increased respiratory rate which are followed a few minutes later by motor weakness. Tremors, clonic convulsions, dyspnea and coma set in promptly and continue until death (12). The 2,6-isomer of dichlorophenol produces these signs but the decreased activity and motor weakness do not appear as promptly as they do with other chlorinated phenols (12).

In vitro tests have indicated that 2,6-dichlorophenol (at unspecified levels), inhibits rat liver mitochondrial respiration (971).

38.3.1.4.2 Chronic Toxicity

Administration of 2,6-dichlorophenol to rats at unspecified dosages and routes has been reported to inhibit rat growth, increase the liver to body weight ratio, decrease both the hemoglobin content and hematocrit ratio and to produce hepatic degeneration (59,971).

38.3.2 Human and Epidemiologic Studies

No human data were found in the literature.

33.3.3 Levels of Concern

The USEPA (355) has not established an ambient water quality criterion for the protection of human health for 2,6-dichlorophenol due to insufficient data; a criterion of 0.2 μg/L is suggested by the USEPA on an organoleptic basis (355).

An acceptable daily intake (ADI) for the 2,4-isomer of dichlorophenol was set by the USEPA at 7 mg/day based on a mouse subchronic oral no-effect level and an uncertainty factor of 1000 (670).

38.3.4 Hazard Assessment

The absence of human effects data as well as the lack of carcinogenic, reproductive and long-term animal exposure data for 2,6-dichlorophenol precludes an assessment of the human health hazards associated with exposure to this compound at this time. The compound has been documented to be a severe eye and skin irritant in rabbits (59). A single report indicated induction of chromosomal aberrations in rat marrow cells subsequent to exposure to 2,6-dichlorophenol (54,59); details of dosing and exposure regimen, however, were not available for evaluation. The compound has also been linked to liver degeneration in rats but again, the dose, route and duration of exposure were unspecified (971).

38.4 SAMPLING AND ANALYSIS CONSIDERATIONS

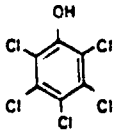
Determination of 2,6-dichlorophenol concentrations in soil and water requires collection of a representative field sample and laboratory analysis. Soil and water samples are collected in glass containers; extraction of samples should be completed within 7 days of sampling and analysis completed within 30-40 days. In addition to the targeted samples, quality control samples such as field blanks, duplicates, and fortified samples matrices may be specified in the recommended methods.

2,6-Dichlorophenol is not included among the EPA-designated priority pollutants. However, EPA Methods 604, 625, 1625 (65), 8040 and 8250 (63) would be appropriate methods of choice for the analysis of 2,6-dichlorophenol in aqueous samples. Prior to analysis, samples are extracted with methylene chloride as a solvent using a separatory funnel or a continuous liquid-liquid extractor. Methods 604 and 8040 also provide for a perfluorobenzyl bromide (PFB) derivatization of the sample extract with additional clean-up procedures if interferences are present in the sample matrix. An aliquot of the concentrated sample extract with or without derivatization is injected onto a gas chromatographic (GC) column using a solvent flush technique. The GC column is

programmed to separate the semi-volatile organics; 2,6-dichlorophenol is then detected with a flame ionization detector (Methods 604 and 8040 without derivatization), as its PFB derivative with an electron capture detector (Methods 604 and 8040 with derivatization) or with a mass spectrometer (Methods 625 and 1625).

The EPA procedures recommended for 2,6-dichlorophenol analysis in soil and waste samples, Methods 8040 and 8250 (63), differ from the aqueous procedures primarily in the preparation of the sample extract. Solid samples are extracted using either soxhlet extraction or sonication methods. Neat and diluted organic liquids may be analyzed by direct injection.

2,6-Dichlorophenol detection limits for the various methods were not determined but would be in the range of 0.4-10 μg/L for aqueous samples and 1 μg/g for non-aqueous samples.

COMMON SYNONYMS:	CAS REG. NO.:	FORMULA:	AIR W/V CONVERSION FACTORS at 25°C (12)
PCP Penta Chlorophen Pentachlorophenate Penchlorol	87-86-5 NIOSH NO.: SM6300000	C_6HCl_5O	10.88 mg/m³ ≈ 1 ppm 0.0919 ppm ≈ 1 mg/m³
	STRUCTURE: 		MOLECULAR WEIGHT: 266.35

REACTIVITY	Pentachlorophenol may be considered to be both a phenol and halogenated organic for compatibility classification purposes. Phenols typically evolve heat in reactions with non-oxidizing mineral acids, organic peroxides or hydroperoxides; heat and possibly fire with oxidizing mineral acids or other strong oxidizing agents; and heat and flammable gases with alkali or alkaline earth metals, nitrides or strong reducing agents. Reactions with azo or diazo compounds or hydrazines typically generate heat and usually innocuous gases. Those with isocyanates, epoxides, or polymerizable compounds may evolve heat and initiate violent polymerization reactions, while those with explosive compounds may initiate an explosion. Halogenated organic compounds typically generate heat in reactions with cyanides, mercaptans, and other organic sulfides. Those with non-oxidizing mineral acids, amines, and strong oxidizing agents typically evolve heat and toxic gases, while those with caustics or nitrides evolve heat and flammable gases. Reactions with oxidizing mineral acids may generate heat, toxic gases, and fire, while those with azo or diazo compounds or hydrazines may evolve heat and usually innocuous gases. Certain elemental metals and alloys as sheets, rods, drops, etc. may evolve heat and fire in reactions with these compounds, while alkali and alkaline earth metals and certain metals as powders, vapors, or sponges may evolve heat and initiate an explosion. Heat evolution and explosion are also possible results of reactions with organic peroxides and hydroperoxides or strong reducing agents (511).

PHYSICO-CHEMICAL DATA	• Physical State (at 20°C): powder or crystals	(23)
	• Color: white-brown	(23,67)
	• Odor: phenolic	(3)
	• Odor Threshold: 0.857-12 mg/L of water	(67)
	• Liquid Density (g/ml at 20°C): 1.978	(3)
	• Freezing/Melting Point (°C): 190	(23)
	• Boiling Point (°C): 310 with decomposition	(23)
	• Flash Point (°C): non-flammable	(60)
	• Flammable Limits in Air, % by Volume: none	(60)
	• Autoignition Temperature (°C): non-flammable	(60)
	• Vapor Pressure (mm Hg at 20°C): .00011	(67)

PHYSICO-CHEMICAL DATA (Continued)	• Saturated Concentration in Air (mg/m^3 at 20°C): 1.6 (ADL estim) • Solubility in Water (mg/L at 20°C): 14 (67) • Log (Octanol-Water Partition Coefficient), log K_{ow}: 5.12 (29) • Soil Adsorption Coefficient, K_{oc}: 63,500 (for neutral, undissociated molecule) (652) • Henry's Law Constant ($atm \cdot m^3/mol$ at 20°C): 2.8×10^{-6} (estim) (964) • Bioconcentration Factor: 13 (sheepshead minnow) (910,659) 6300 (estim)

PERSISTENCE IN THE SOIL-WATER SYSTEM	Mobile in soil-water system due largely to acid behavior (formation of phenate anion). Easily photolyzed, resistant to hydrolysis, possibly susceptible to free-radical oxidation, and fairly easily biodegraded, after acclimation, in natural environments.

PATHWAYS OF EXPOSURE	The primary pathway of concern from soil-water systems is the migration of pentachlorophenol in ground-water drinking water supplies, based on its presence at NPL sites and its detection in drinking water surveys. Inhalation exposures are not likely to be important, but consumption of fish or domestic animals may be as a result of bioaccumulation.

HEALTH HAZARD DATA	Signs and Symptoms of Short-term Human Exposure (38): Pentachlorophenol dust or mist may cause irritation of the eyes and respiratory tract. It readily penetrates skin. Prolonged dermal exposure may cause an acne-like dermatitis. Systemic effects include weakness, loss of appetite, nausea, vomiting, shortness of breath, chest pain, headache, excessive sweating and dizziness. In fatal cases, body temperature is often extremely high; death generally is due to cardiac arrest.
	Toxicity Based on Animal Studies: LD_{50} (mg/kg): oral 50 [rat] (59); skin 105 [rat] (59) LC_{50} (mg/m^3): inhalation 355 [rat] (47), no time given
	Long-Term Effects: Liver and kidney damage
	Pregnancy/Neonate Data: Embryo- and fetotoxic
	Mutation Data: Limited evidence of mutagenic potential
	Carcinogenicity Classification: IARC - Category 3; NTP - none assigned (studies in progress)

HANDLING PRECAUTIONS (38,52,54, 59)	Handle chemical only with adequate ventilation • Vapor concentrations of 0.5-2.5 mg/m^3: any supplied-air respirator or self-contained breathing apparatus (if eye irritation occurs, full-facepiece respiratory equipment should be used) • 2.5-25 mg/m^3: any supplied-air respirator or self-contained breathing apparatus with full-facepiece • Chemical goggles to avoid eye contact • Natural rubber, neoprene, nitrile, PVC or other protective clothing to prevent prolonged or repeated skin contact with the liquid; no skin surface should be exposed.

EMERGENCY FIRST AID TREATMENT (38,54,59)	Ingestion: Because many pesticide formulations are combined with other pesticides, fungicides or insecticides and are frequently dissolved in petroleum distillates, vomiting involves a serious risk that solvent will be aspirated, leading to chemical pneumonitis. For these reasons, if the ingested pentachlorophenol is dissolved in a petroleum-based carrier or a mixed formulation, do not induce vomiting. Contact physician or emergency medical facility immediately. If the ingested pentachlorophenol is in an aqueous carrier, induce vomiting. Get medical attention immediately. If body temperature is elevated, reduce by physical means • Inhalation: Move victim to fresh air, give artificial respiration if necessary. Get medical attention • Skin: Remove contaminated clothing. Wash skin with soap and water. If irritation persists, get medical attention • Eye: Flush with large amounts of water. Get medical attention.

ENVIRONMENTAL AND OCCUPATIONAL STANDARDS AND CRITERIA

AIR EXPOSURE LIMITS:

Standards
- OSHA PEL (8-hr TWA): 0.5 mg/m³ (skin)
- AFOSH PEL (8-hr TWA): 0.5 mg/m³ (skin)

Criteria
- NIOSH IDLH (30-min): 150 mg/m³
- ACGIH TLV® (8-hr TWA): 0.5 mg/m³ (skin)
- ACGIH STEL (15-min): deleted

WATER EXPOSURE LIMITS:

Drinking Water Standards - None established

EPA Health Advisories (890)

In the absence of formal drinking water standards, the EPA (992) has developed the following Health Advisories (formerly termed SNARLs) for noncarcinogenic risk for short and long-term exposure to pentachlorophenol in drinking water:

- 1 day: 3.5 mg/L
- 10 days: 1.1 mg/L
- long-term: none established

EPA Ambient Water Quality Criteria (355,1626)

- Human Health
  - Based on available toxicity data for the protection of public health, the derived level is 1.01 mg/L.
  - Using available organoleptic data for controlling undersirable taste and odor quality, the estimated level is 30 μg/L.
- Aquatic Life
  - Freshwater species

    Freshwater aquatic organisms and their uses should not be affected unacceptably if the 4-day average concentration (in μg/L) of pentachlorophenol does not exceed the numerical value given by e[1.005(pH)-5.290] more than once every 3 years on the average, and if the 1-hour average concentration (in μg/L) does not exceed the numerical value given by e[1.005(pH)-4.830] more than once every 3 years on the average.

- Saltwater species

  Saltwater aquatic organisms and their uses should not be affected unacceptably if the 4-day average concentration of pentachlorophenol does not exceed 7.9 µg/L more than once every 3 years on the average and if the 1-hour average concentration does not exceed 13 µg/L more than once every 3 years on the average.

WHO Drinking Water Guideline (666)

A health-based guideline for drinking water of 10 µg/L is recommended for pentachlorophenol. A daily per capita consumption of two liters of water was assumed.

REGULATORY STATUS (as of January 1, 1987)

Promulgated Regulations

- Federal Programs

Clean Water Act (CWA)

Pentachlorophenol is designated a hazardous substance. It has a reportable quantity (RQ) limit of 4.54 kg (347,985). It is also listed as a toxic pollutant (351). Water quality criteria have been set. Guidelines exist for pentachlorophenol effluent in the pesticide chemicals category and the pulp paper and paperboard point source category (891,893). Guidelines also exist for effluent containing phenols in the timber products processing, petroleum refining, metal molding and casting and textile mills point source categories (899,896,892,893) and in the iron and steel, non-ferrous metals and ferroalloy manufacturing point source categories (354,894, 895).

Safe Drinking Water Act (SDWA)

In states with an approved Underground Injection Control program, a permit is required for the injection of pentachlorophenol-containing wastes designated as hazardous under RCRA (295).

Resource Conservation and Recovery Act (RCRA)

Pentachlorophenol is identified as a hazardous waste (U242) and listed as a hazardous waste constituent (328,329). Non-specific sources of pentachlorophenol-containing waste are discarded, unused formulations containing PCP or compounds derived from it, residues resulting from incineration or thermal treatment of soil contaminated with these formulations and wastes from the production or manufacturing use of PCP or of intermediates used to produce its derivatives (325). Waste streams from the following industry contain pentachlorophenol and are listed as specific sources of hazardous wastes: wood preservation (creosote and/or pentachlorophenol preserving processes) (326,327).

Effective July 8, 1987, the land disposal of hazardous wastes containing halogenated organic compounds in total concentrations greater than or equal to 1000 mg/kg will be prohibited. The only exception will be underground injection (1755).

Comprehensive Environmental Response Compensation and Liability Act (CERCLA)

Pentachlorophenol is designated a hazardous substance under CERCLA. It has a reportable quantity (RQ) limit of 4.54 kg. Reportable quantities have also been issued for RCRA hazardous waste streams containing pentachlorophenol but these depend upon the concentrations of the chemicals in the waste stream (985).

Any facility at which pentachlorophenol is present in excess of its threshold planning quantity of 10,000 pounds must notify state and local emergency planning officials. If pentachlorophenol is released from the facility in excess of its reportable quantity (RQ), local emergency planning officials must be notified (1751).

Marine Protection Research and Sanctuaries Act (MPRSA)
Ocean dumping of organohalogen compounds as well as the dumping of known or suspected carcinogens, mutagens or teratogens is prohibited except when they are present as trace contaminants. Permit applicants are exempt from these regulations if they can demonstrate that such chemical constituents are non-toxic and non-bioaccumulative in the marine environment or are rapidly rendered harmless by physical, chemical or biological processes in the sea (309).

Occupational Safety and Health Act (OSHA)
Employee exposure to pentachlorophenol shall not exceed an 8-hour time-weighted-average (TWA) of 0.5 mg/m^3 (298).

Hazardous Materials Transportation Act (HMTA)
The Department of Transportation has designated pentachlorophenol as a hazardous material which is subject to requirements for packaging, labeling and transportation (306).

Food, Drug and Cosmetic Act (FDCA)
Pentachlorophenol is approved for use as an indirect food additive (362).

The level for phenols in bottled drinking water is 0.001 mg/L (365).

- State Water Programs

  The following states have a criterion of 1 µg/L for phenolics (731):

  Florida - in surface water
  Illinois, Mississippi, Oregon - in the public water supply
  North Carolina - in fresh water
  Minnesota - in water for domestic consumption
  New York - in Class AA drinking water
  New Hampshire - in Class A and B waters

  The following states have a criterion of 5 µg/L for phenolics (731):

  Georgia - in all waters
  Louisiana - in the public water supply
  New York - in Class A drinking water
  West Virginia - in drinking water

The following states have a criterion of 50 μg/L for phenolics (731):

Iowa - in drinking water
Louisiana - in fresh water

The following states have ground water quality standards for phenolics (981):

Missouri - 0.3 mg/L for fast recharge;
0.1 mg/L for slow recharge
New Jersey - 0.3 mg/L in Class GW 1
New York - 1 μg/L in Class GA
New Mexico - 5 μg/L
Virginia - 1 μg/L
Wyoming 1 μg/L

Other states follow EPA Ambient Water Quality Criteria.

Proposed Regulations

- Federal Programs

Clean Water Act (CWA)
Effluent guidelines for pentachlorophenol have been proposed in the organic chemicals, plastics and synthetic fibers category (357).

Safe Drinking Water Act (SDWA)
EPA has proposed a Recommended Maximum Contaminant Level (RMCL) of 0.22 mg/L for pentachlorophenol as part of the National Primary Drinking Water Regulations (992).

Resource Conservation and Recovery Act (RCRA)
EPA has proposed that non-liquid hazardous wastes containing halogenated organic compounds (HOCs) in total concentrations greater than or equal to 1000 mg/kg or liquid hazardous wastes containing HOCs in total concentrations greater than or equal to 1% HOCs must be incinerated in accordance with the requirements of 40CFR264.343 or 265.343 (1767).

EPA has also proposed that hazardous waste treatment, storage and disposal facilities monitor ground water for pentachlorophenol when EPA suspects the facilities of leaking contaminants (1754).

EPA has proposed that solid wastes which contain a concentration equal to or greater than 3.6 mg/L pentachlorophenol be listed as hazardous in that they exhibit the characteristic defined as EP toxicity (1565).

EPA has proposed listing waste residues containing 10 ppm or less of TCDD equivalents as non-specific sources of pentachlorophenol-containing waste (1398).

Comprehensive Environmental Response Compensation and Liability Act (CERCLA)
EPA has proposed that the emergency reporting requirements and the threshold planning quantity for pentachlorophenol be eliminated (1752).

Federal Insecticide, Fungicide and Rodenticide Act (FIFRA)
EPA has proposed canceling the registrations of pesticide products containing pentachlorophenol for non-wood preservative uses (974). For those products with wood preservative uses, EPA has proposed restricting their use to certified applicators. Manufacturers of wood preservative products will be required to make labeling changes and provide consumer information sheets (975).

- State Water Programs
  No proposed regulations are pending.

EEC Directives

Directive on Drinking Water (533)
The mandatory values for phenols (phenol indices) in surface water treatment categories A1, A2 and A3 used or intended for abstraction of drinking water are 0.001, 0.005 and 0.1 mg/L, respectively. Guideline values for phenols (phenol indices) under treatment categories A2 and A3 are 0.001 and 0.01 mg/L, respectively. No guideline value is given for treatment category A1.

Directive Relating to the Quality of Water for Human Consumption (540)
The maximum admissible concentration for phenols (phenol indices) is 0.5 µg/L. Excluded from this category are natural phenols which do not react to chlorine. No guideline levels for phenols (phenol indices) are given.

Directive on Ground Water (538)
Direct and indirect discharge into ground water of substances which have a deleterious effect on the taste and/or odor of ground water, and compounds liable to cause the formation of such substances in ground water and to render it unfit for human consumption shall be subject to prior review so as to limit such discharges.

Directive on Bathing Water Quality (534)
Mandatory values for phenols (phenol indices) in bathing water are: (1) no specific odor and (2) concentrations ≤ 0.05 mg/L. Guideline values for phenols (phenol indices) suggest concentrations ≤ 0.005 mg/L.

Directive on Fishing Water Quality (536)
Phenolic compounds in both salmonid and cyprinid waters must not be present in such concentrations that they adversely affect fish flavor.

Directive on the Quality Required of Shellfish Waters (537)
The mandatory specifications for substances affecting the taste of shellfish require that their concentrations be lower than that liable to impair the taste of the shellfish.

Directive on the Discharge of Dangerous Substances (535)
Organohalogens, organophosphates, petroleum hydrocarbons, carcinogens or substances which have a deleterious effect on the taste and/or odor of human food derived from aquatic environments cannot be discharged into inland surface waters, territorial waters or internal coastal waters without prior authorization from member countries which issue emission standards. A system of zero-emission applies to discharge of these substances into ground water.

Directive on Marketing and Use of Dangerous Substances (541)
Pentachlorophenol may not be used in ornamental objects intended to produce light or color effects by means of different phases.

Directive on Toxic and Dangerous Wastes (542)
Any installation, establishment, or undertaking which produces, holds and/or disposes of certain toxic and dangerous wastes including phenols and phenol compounds; organic-halogen compounds; chrome compounds; lead compounds; cyanides; ethers and aromatic polycylic compounds (with carcinogenic effects) shall keep a record of the quantity, nature, physical and chemical characteristics and origin of such waste, and of the methods and sites used for disposing of such waste.

Directive on Classification, Packaging and Labeling of Pesticides (786)
Pentachlorophenol is listed as a Class I/a substance and is subject to packaging and labeling regulations.

Directive on the Classification, Packaging and Labeling of Dangerous Substances (787)
Pentachlorophenol is classified as a toxic substance and is subject to packaging and labeling regulations.

Directive on Paints, Varnishes, Printing Inks, Adhesives and Similar Products (1334)
Pentachlorophenol is classified as a toxic substance when present in concentrations greater than 5% and as a harmful substance when present in concentrations ranging from 0.5 to 5%.

Directive on Transfrontier Shipment of Hazardous Waste (1433)
When the holder of a hazardous waste such as pentachlorophenol intends to ship it to another member state, authorities of the member states concerned must be provided with information on the source and composition of the waste, measures to be taken to ensure safe transport, insurance against damage and the existence of a contractual agreement with the consignee of the waste. All transfrontier shipments must be properly packed and labeled and must be accompanied by instructions to be followed in the event of danger or accident.

Directive on Limit Values and Quality Objectives for Discharges of Certain Dangerous Substances (1792)
Pursuant to the Directive on the Discharge of Dangerous Substances, the quality objective for pentachlorophenol is 2 µg/L. The emission standard of pentachlorophenol for the production of sodium pentachlorophenate by hydrolysis of hexachlorobenzene is 1 mg/L water discharged as a monthly average and 2 mg/L water discharged as a daily average. These regulations must be complied with as of January 1, 1988.

EEC Directives - Proposed

Proposal for a Council Directive on the Dumping of Waste at Sea (1793)
EEC has proposed that the dumping of organohalogen compounds at sea be prohibited.

39.1 MAJOR USES

Until recently, most of the pentachlorophenol (PCP) produced in the United States was consumed in the wood preserving industry (≈ 90%) where it was used to prevent discoloration, enhance toughness and prevent attack by insects and fungi. About 9% was used in the manufacture of sodium pentachlorophenate. Additional minor applications included its use in the textile, tanning and paint industries (909). EPA has proposed canceling the registrations of pesticide products containing PCP for non-wood preservative uses (974) and restricting the use of wood preservative applications to certified applicators (975).

Commercial PCP formulations contain from 85% to 99% PCP as well as different chlorophenol impurities (5-10% tetrachlorophenol, 1% trichlorophenol, about 5% chlorinated phenoxyphenols) and minor amounts of highly toxic polychlorinated dibenzo-p-dioxins and dibenzofurans (10-1000s mg/kg) (909).

39.2 ENVIRONMENTAL FATE AND EXPOSURE PATHWAYS

39.2.1 Transport in the Soil/Ground-water Systems

39.2.1.1 Overview

Pentachlorophenol is expected to be relatively mobile in the soil/ground-water environment when present at low concentrations (dissolved in water). The pure chemical is a solid at ambient temperatures (melting point is 190°C) and thus bulk quantities (e.g., from a spill) would not be immediately mobile.

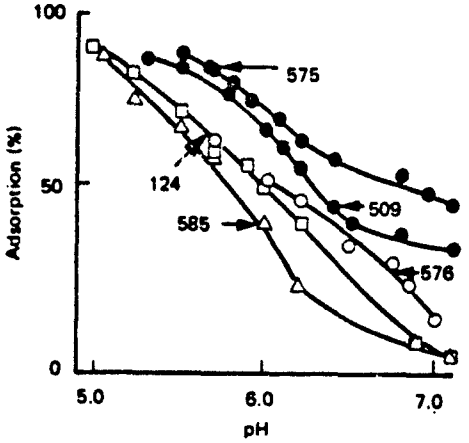
PCP is a moderately strong organic acid (reported pK_a values are 4.5 (856), 4.59 (29) and 4.74 (10)), and thus it is essentially completely dissociated into the phenate anion and hydrogen cation under typical pH conditions. In pure water, the percent dissociation at pH values of 6, 7 and 8 are, respectively, 96.2%, 99.6% and 99.96% based on pK_a = 4.59. PCP would be 50% dissociated when the pH was equal to the pK_a (i.e., at pH 4.6). In general, the dissociated form of the chemical (the phenate anion) is more soluble in water, less strongly sorbed to soils, and less bioaccumulated in biota than the neutral, undisssociated form. The solubility as a function of pH has been given by Branson and Blau (847) as follows:

pH	% Dissociated	Solubility (mg/L)
3	1.8	14
5	64.0	34
6	95.0	75
7	99.5	1,950
8	99.95	19,300

The change in soil sorption with pH has been measured by Choi et al. (848) and does indeed show a dramatic decrease in sorption as the pH goes from 5 to 7 (Figure 39-1). Thus, the importance of pH in the soil/ground-water mobility of PCP is difficult to overstate.

Transport pathways can be generally assessed by using an equilibrium partitioning model as shown in Table 39-1. These calculations predict the partitioning of low soil concentrations of PCP among soil particles, soil water, and soil air. The estimates in this case are given both for the total chemical concentrations and for the undissociated fraction, the latter being only technically valid for very low pH values (e.g., < 4). The estimates for the unsaturated topsoil model show that, based on total chemical concentration, essentially all of the chemical (99.6%) is predicted to be in the mobile water phase and thus easily transported with percolating ground water.

Diffusion of the chemical vapors through the soil-air pores and up to the ground surface would not appear to be a significant loss pathway based upon the model results. (Data presented below, however, indicate that both volatilization and sorption are, perhaps, more important than are predicted by this model). In saturated deep soils (containing no



Note: Numbers represent different soil samples.

No.	Soil Type
124	Montmorillonitic
509	Humus-rich allophanic
575	Humus-rich allophanic
576	Allophanic
585	Halloystic

Source: Choi et al. (848)

FIGURE 39-1

RELATION OF THE APPARENT ADSORPTION TO THE pH OF THE SUPERNATANT LIQUID
(Initial concentration: 100 ppm)

TABLE 39-1

EQUILIBRIUM PARTITIONING CALCULATIONS FOR PENTACHLOROPHENOL IN MODEL ENVIRONMENTS[a]

Soil Environment	Estimated Percent of Total Mass of Chemical in Each Compartment		
	Soil	Soil-Water	Soil-Air
Unsaturated topsoil at 25°C[b,c]	99.99 (0.4)	8.2×10^{-3} (99.6)	3×10^{-6} (3×10^{-6})
Saturated deep soil[d]	99.6 (0.4)	0.4 (99.6)	- -

a) Calculations based on Mackay's equilibrium partitioning model (34,35,36); see Introduction in Volume 1 for description of model and environmental conditions chosen to represent an unsaturated topsoil and saturated deep soil. Calculated percentages should be considered as rough estimates and used only for general guidance.

b) Utilized estimated soil sorption coefficient: K_{oc} = 63,500. (Valid only for neutral molecule.)

c) Henry's law constant taken as 2.8×10^{-6} atm•m³/mol at 20°C (964).

d) Used sorption coefficient $K_p = 0.001\ K_{oc}$.

e) Top number in each entry is for undissociated fraction of chemical. Bottom number, in parenthesis, is for total chemical concentration and is based upon the assumptions that the pH = 7 and that all of the dissociated fraction is in the soil-water compartment.

air and negligible soil organic carbon), the model predicts the same high proportion of PCP (99.6%) in the mobile aqueous phase if total concentrations of PCP (dissociated + undissociated) are used as the basis.

39.2.1.1.2 Experimental Fate and Transport Studies

Numerous laboratory and field studies have been carried out to study the mobility and persistance of PCP under various environmental conditions (307,810,826,835,837,838,839,840,841,842,843,844,845,846). Although few of these studies focused on fate and transport in just the

soil/ground-water environment, all the studies (including those simulating surface waters) provide valuable information on the relative importance of various fate and transport processes under fairly realistic conditions.

The basic findings of the laboratory and field studies cited above provide a reasonably consistent picture of PCP environmental fate and transport. This includes: (1) fairly rapid photodegradation in sunlit surface waters; (2) moderate to weak sorption on soils and sediments (sorption weakest on alkaline and reduced soils); and (3) reasonable susceptibility to biodegradation, at least under aerobic conditions. Some evidence of a non-biological, non-photolytic degradation mechanism is also provided. Some evidence of volatilization is also provided; however, most of the experiments used ^{14}C-labeled PCP and apparent concentrations in air are probably due mostly to $^{14}CO_2$ which would be derived from the biodegradation of ^{14}C-PCP.

Other laboratory ecosystem and field studies of the fate and transport of PCP have been summarized by Callahan (10), Scow and coworkers (909) and the Syracuse Research Corporation (806).

39.2.1.2 Sorption on Soils

No accurate prediction can be made of the soil sorption coefficient (K_{oc}) from the octanol-water partition coefficent (K_{ow}) of PCP because of the strong dissociation of PCP, and the uncertain effect of pH on the value of K_{ow} and the K_{ow}-K_{oc} correlation. As noted above, soil sorption of PCP is generally weak, but does become significant at lower pH values as shown by the data in Figure 39-1.

The data of Choi and Aomine (848) do show some increased sorption with increasing soil organic matter as would be expected. Other data show that PCP is somewhat more strongly sorbed to oxidized sediments than to reduced sediments (845,846). The soil sorption constant calculated from the data of DeLaune et al. (845) is K_{oc} = 2900 (reduced sediment, pH 6.8) and K_{oc} = 4200 (oxidized sediment, pH 6.8).

39.2.1.3 Volatilization from Soils

Based upon the relatively low vapor pressure of PCP (10^{-4} mm Hg @ 20°C) and low value of Henry's law constant (2.8×10^{-6}) atm•m^3/mol @ 20°C, volatilization from soils would not be expected to be an important loss pathway. However, some of the laboratory and field studies cited in Section 39.2.1.1.2 had PCP losses which were attributed to volatilization (838,839,842,843). Other ecosystem studies also show significant air concentrations (806). (See especially the studies by Kilzer et al. (849), Gile and Gillett (850), and Metcalf et al. (851)). Any such volatilization would only be important for surface soils.

39.2.2 Transformation Processes in Soil/Ground-water Systems

The ease of photolytic degradation in sunlit surface waters was mentioned above and is documented by several laboratory and field studies (838,840,841,844,852) and by other studies (10,909,806). Initial photochemical reactions commonly involve the loss of a chlorine or the substitution of a hydroxy group for a chlorine.

Pentachlorophenol is probably not susceptible to hydrolysis since it has no hydrolyzable functional groups (529).

The possibility of degradation by some other non-biological process is raised by the studies of Baker and Mayfield (826) and Baker et al. (835) where some degradation was seen, over time scales of 1 to 6 months, in test systems using sterile soils. A free-radical oxidation mechanism may be involved.

A fairly large body of data from studies on the biodegradability of PCP is available (10,909,806,853,854,855,826,839,842). The conclusions from these studies span a wide range, all the way from "no degradation" after 40 days in a stream water die-away test to "significant degradation with gradual adaptation" in a shake-flask static incubation test with municipal sewage seed. The weight of evidence does show, however, that PCP is moderately, easily biodegraded in the natural environment, including aerobic soils (but probably not anerobic soils).

Numerous factors will affect the rate at which PCP biodegrades including temperature, soil composition (especially concentration of organic carbon and nutrients, and pH), redox potential, microorganism population and PCP concentration. Valo et al. (854), for example, found no PCP degradation below 8°C or above 50°C in small-scale trickling filter tests; they also found the optimum pH for biodegradation in their system to be from 6.4 to 7.2, and that while PCP degradation continued when the partial pressure of oxygen (pO_2) was lowered to 0.0002 atm, the degradation ceased when pO_2 was further decreased to 0.00002 atm. Concentrations of PCP above 0.2 mg/L may inhibit biodegradation. Under optimum conditions, biodegradation half-lives may be on the order of just a few days; under less than optimum conditions, the half-lives may extend to weeks or months; under poor conditions it could be months to many years. Finally, it is worth noting that PCP undergoes ultimate (complete) biodegradation in which all carbon is converted to CO_2.

39.2.3 Primary Routes of Exposure from Soil/Ground-water Systems

The above discussion of fate pathways suggests that pentachlorophenol has a low volatility, is strongly sorbed* to soil, and has a moderate potential for bioaccumulation. The volatilization of this

---

*Categorization ignores dissociation, estimated K_{oc} value too high.

compound from surface soil is not likely to represent a primary route of exposure. Although PCP is strongly sorbed to soil, it may be mobile in alkaline and sandy soils with a potential for drinking water exposure through ground-water contamination. Exposure pathways involving the accumulation of PCP by biota may be important due to its moderate bioconcentration factor.

Pentachlorophenol is a relatively common contaminant at hazardous waste disposal sites. Mitre (83) reported that pentachlorophenol was found at 16 of the 546 National Priority List (NPL) sites. It was detected at 12 sites in ground water, 8 sites in surface water, and at 1 site in the air. These data suggest that both ground-water and surface-water pathways may be important.

Although its properties suggest it can be strongly sorbed to soil, the occurrence of pentachlorophenol in ground water at NPL sites indicates that drinking water exposure may result from soil/ground-water systems. In addition, surface water contamination may result either from run-off of pentachlorophenol adsorbed to soil particles, or from the discharge of ground water to surface water. A number of exposure pathways may result from surface water contamination. They are:

- Direct ingestion exposure as a result of the use of surface waters as drinking water supplies;

- Dermal exposure resulting from recreational use of surface waters;

- Ingestion exposure resulting from the consumption of aquatic organisms or domestic animals that have accumulated pentachlorophenol.

In general, these exposure pathways are not likely to be the primary routes of exposure from a soil/ground-water system because PCP is likely to be photolyzed and/or biodegraded upon reaching surface waters (909). The bioaccumulation of pentachlorophenol from surface waters, either by aquatic organisms or domestic animals, may be important in some situations due to the moderate bioconcentration factor for PCP.

39.2.4 Other Sources of Human Exposure

Pentachlorophenol is widely distributed in the environment, and there are a number of potential sources of exposure. Exposure through drinking water is prevalent, but exposure levels are low. In the National Organics Monitoring Survey, EPA detected PCP in 86 of 108 water supplies, with a mean of 0.07 μg/L and a maximum of 0.70 μg/L (90).

PCP has also been found in a variety of food products including dairy products, grains and cereals, root vegetables, and sugars and

adjuncts. On the basis of available data, FDA estimated an average intake of 0.76 mg/day for a 15-year-old male (884). EPA calculated an average intake of 1.5 mg/day for adults (885).

The nature of present and past uses of pentachlorophenol have led to releases to air and inhalation exposures, particularly to workers and persons using these products. As all non-wood uses of PCP are or will be cancelled, inhalation exposure resulting from these uses will be eliminated (974). In addition, most uses of PCP as a wood preservative will be restricted to use by certified applicators (975). PCP will also be restricted from use on logs intended for homes (975), although individuals residing in currently existing log homes will still be exposed to PCP in the home.

Dermal exposure to PCP will also be limited, as consumer uses of this wood-preserving product will be eliminated (974,975).

39.3 HUMAN HEALTH CONSIDERATIONS

39.3.1 Animal Studies

39.3.1.1 Carcinogenicity

No carcinogenic effects were reported in either rats or mice treated with oral doses of pentachlorophenol. Innes et al. (911) administered technical PCP by gavage to (C57BL/6xC3H/Anf)F1 and (C57BL/6xAKR)F1 mice at doses of 46.4 mg/kg on days 7-28 of age followed by 130 mg/kg in the diet up to 18 months of age. The tumor incidence above control values was not statistically significant. In Sprague-Dawley rats fed up to 30 mg/kg/day purified PCP for 22-24 months, no alteration in tumor incidence or duration of lifespan was noted (919).

Feeding studies in B6C3F1 mice conducted by the National Toxicology Program with technical-grade PCP (0, 100 or 200 ppm in the diet) and a commercial PCP formulation, Dowicide® EC7, (0, 200, 600 or 1200 ppm in the diet) are nearing completion (883). Preliminary data on the commercial formulation indicate liver damage in all treatment groups and goblet-cell hyperplasia in both sexes at the top two treatment levels.

39.3.1.2 Mutagenicity

The data concerning the mutagenicity of pentachlorophenol are conflicting, but the majority of test results are negative. Fahrig et al. (913) reported a significant increase in forward mutations and mitotic gene conversions in Saccharomyces cerevisiae following a 3.5-hour in vitro exposure to 400 mg/L PCP. No positive controls were run.

The same investigators reported weak mutagenic results in a spot test with mice; however, the results were inconclusive due to the lack of data on the controls and on the incidence of treatment-related maternal toxicity. Upon subsequent review, the data were determined not to be statistically significant (913).

Andersen et al. (915) reported that PCP did not induce point mutations in eight histidine-requiring mutants of Salmonella typhimurium; the tests did not emplo liver microsomal activation. PCP also produced negative mutagenic responses in a host-mediated assay (916) and in a sex-linked recessive lethal test with Drosophila (917).

In a human study, Bauchinger et al. (918) found a small but significant increase in the frequency of structural chromosome changes in the lymphocytes of 22 male workers employed in a PCP plant for up to 30 years. Chromosomal aberrations consisted of acentrics and dicentrics (i.e., lacking or having two centromeres, the portion of the chromosome to which the chromatids are joined). There was no significant increase in sister chromatid exchanges as compared with matched controls. An earlier study by Wyllie and coworkers (1200) found no significant difference in the incidence of chromosome breaks or gaps in 6 occupationally exposed workers when compared to 4 controls.

39.3.1.3 Teratogenicity, Embryotoxicity and Reproductive Effects

The embryonal and fetal effects of pentachlorophenol in rats were assessed in a series of studies by Schwetz et al. (912). In one study, 5, 15, 30 or 50 mg/kg/day of purified PCP (>98%) or 5.8, 15, 34.7 or 50 mg/kg/day of commercial PCP (88.4%) were administered by gavage to Sprague-Dawley rats on days 6 through 15 of gestation. Statistically significant, dose-related decreases in maternal weight gain were noted with both PCP samples at the top two treatment levels. In the offspring, purified PCP exerted a more pronounced effect than commercial-grade PCP. Fetal resorptions were statistically significant in dams given 15, 34.7 or 50 mg/kg/day of commercial PCP or 30 or 50 mg/kg/day purified PCP. Resorption rates were 9, 27 and 58%, respectively, for commercial PCP and 98 and 100%, respectively, for the purified grade compared to 4.2% in controls. The no-effect levels for resorptions were 5.8 mg/kg/day commercial PCP and 15 mg/kg/day purified PCP. The occurrence of subcutaneous edema, dilated ureters, and anomalies of the skull and vertebrae increased with increasing PCP dose (both grades) but were not significantly different from controls. Decreases in fetal body weight and crown rump length were seen at the upper dosage levels of either grade. Dosages of 15 mg/kg or less of either grade had no effects on fetal body measurements. In a second study, these investigators (912) showed that the developing rat embryo was more susceptible to a given dose of PCP during the period of early organogenesis (days 8-11) than during the later period (days 12-15).

Daily oral administration of 1.25 to 20 mg/kg PCP to Syrian golden hamsters on days 5 to 10 of pregnancy resulted in fetal deaths and/or resorptions in three of six test groups (1201). No other data were provided.

In a single generation reproduction study, Sprague-Dawley rats were fed 0, 3 or 30 mg/kg/day of purified PCP for 62 days prior to mating, throughout gestation and up to 21 days postpartum. The 30 mg/kg dose resulted in a significant decrease in the number of pups born alive and significantly decreased survival to days 7, 14 and 21 of lactation, but had no effect on fertility. A significantly increased number of litters showed skeletal anomalies at this dose, the average litter size was decreased and mean neonatal body weight was significantly less than controls. No adverse effects were noted at doses of 3 mg/kg/day (919).

39.3.1.4 Other Toxicologic Effects

39.3.1.4.1 Short-term Toxicity

Assessment of the toxicity data on pentachlorophenol is complicated by the presence of varying quantities of tetrachlorophenols, dioxins and furans in the technical-grade material. Although several studies compare the toxic effects of technical and pure PCP, in some studies, it is difficult to determine which effects are truly caused by PCP and which are due to the toxic contaminants (914).

The oral LD_{50} values in rodents range from 50-168 mg/kg (grade unspecified) (59). Fuel oil-type solvents reduce the lethal dose (i.e., increase toxicity), while aqueous solutions of the sodium salt are less toxic (910). The oral LD_{50} of purified pentachlorophenol in the rat has been reported to be 150-200 mg/kg (924). Signs of acute intoxication result from the ability of PCP to uncouple oxidative phosphorylation; they include an increase in the basal metabolic rate and a subsequent rise in body temperature, respiratory rate and heart rate. Progressive neuromuscular weakness, with convulsions and cardiac failure are observed in fatal cases. Death is characterized by the rapid onset of rigor mortis (12,924).

Pentachlorophenol readily penetrates the skin. A dermal LD_{50} of 105 mg/kg has been reported for the rat (59). Local effects of skin contact depend upon the amount of impurities in the sample. In a rabbit ear bioassay test using both pure and technical-grade PCP, a positive acnegenic response was noted with technical-grade PCP which contained 1980 ppm octachlorodibenzo-p-dioxin and 19 ppm hexachlorodibenzo-p-dioxin (HCDD). Pure PCP gave a negative response. Purified technical-grade PCP containing 1 ppm HCDD also gave a negative response (922).

In another dermal study, McGavack et al. applied varying amounts of aqueous PCP solutions of unspecified purity to the intact shaved skin of rabbits. Within 14 days, 1% PCP solutions produced redness, while 1.5% solutions caused microscopic evidence of skin irritation. A single application of a 10% PCP solution in doses ranging from 60 to 600 mg/kg produced swelling, inflammation, excoriation, desquamation and brown pigmentation of the skin (921).

PCP has been shown to be a severe eye irritant (924). Rabbit eyes exposed to solid PCP showed conjunctival and iritic congestion (923).

39.3.1.4.2 Chronic Toxicity

Chronic exposure to technical-grade PCP produces a number of hepatic changes. In an 8-month study, Goldstein et al. (925) fed rats 20, 100 or 500 ppm technical or pure PCP (equivalent to 1.2, 6 and 30 mg/kg, respectively). Feeding of 20 or 100 ppm pure PCP had no effect, but feeding of the technical-grade resulted in increased levels of liver enzymes and uroporphyrin. Body weight gain was reduced for both samples at the 500 ppm treatment level of PCP. Kociba et al. (926) also compared the toxicity of purified versus technical-grade PCP in a 90-day study with rats fed 3, 10 or 30 mg/kg/day. The investigators noted increased relative liver and kidney weights at all technical PCP treatment levels. With the purified PCP, increased relative liver weights were noted at the top two treatment levels only and increased relative kidney weights seen at the 30 mg/kg level. Focal hepatocellular degeneration and necrosis as well as elevated serum liver enzymes were observed in animals that received 30 mg/kg doses of technical-grade PCP.

With a PCP sample that contained "low amounts" of non-phenolic impurities, Schwetz et al. (919) observed mild toxicity in weanling Sprague-Dawley rats fed 30 mg/kg/day in their diet for 2 years. This resulted in decreased body weight gain, increased SGPT and increased urine specific gravity. The NOAEL was 3 mg/kg in females and 10 mg/kg in males.

The immune response in mice was compromised by exposure to technical-PCP. Kerkvliet et al. (927) found that PCP altered humoral immune functions in adult mice fed diets containing 50 or 500 ppm technical-grade (86%) for 10-12 weeks. The animals also exhibited greatly enhanced tumor susceptibility to low-dose, sarcoma-tumor-cell challenge (67% and 82% tumor incidence in mice exposed to 50 and 500 ppm, respectively, compared to 35% for controls). No significant changes were noted in mice fed pure PCP (>99%) for the same time period.

39.3.2 Human and Epidemiologic Studies

39.3.2.1 Short-term Toxicologic Effects

Pentachlorophenol intoxication is characterized by weakness, fatigue, dizziness, headache, abdominal pain, congestion of ocular and nasal mucosae, profuse sweating and high fever (≈ 106-108°F). PCP readily penetrates the skin and most cases of human exposure are through this route (909). Bevenue et al. (928) reported reddening and painful sensations in the hands of a male 10 minutes after immersion of his hands in a 0.4% PCP solution. The pain persisted for 2 hours. Urinary PCP levels returned to background levels within one month. Local skin irritation and chloracne have also been associated with dermal contact to technical PCP but dioxin contaminants are believed to be the causative agents in these cases (909).

Dust and mist concentrations greater that 1 mg/m^3 cause sneezing coughing and painful irritation of the eyes, nose and throat and 0.3 mg/m^3 may cause some nose irritation. Up to 2.4 mg/m^3 can be tolerated by persons acclimated to PCP (38).

Sangster et al. (929) reported symptoms of a generalized itching dermatosis, drowsiness, nausea, loss of appetite, swelling of the eyelids and dryness and scaling of the face and hands in 15 members of 3 families living in houses where large volumes of PCP solutions (5 to 5.5%) had been applied to the timbers and/or furniture. Plasma PCP concentrations ranged from 25 to 660 µg/L; the mean plasma PCP concentration in 99 military draftees used as a control population was 128 µg/L.

Throat irritation, facial flushing and hand and leg weakness were noted in 4 families after drinking and bathing in water from a well containing 12.5 mg/L PCP. Recovery occurred within 2-3 days (928). In a similar case, a 4-year-old child was hospitalized with fever, intermittent delerium, acidosis, aminoaciduria and ketonuria after bathing daily for 13 days with water from a PCP-contaminated holding tank (930).

Numerous industry-related PCP fatalities have been reported. Among the changes reported at autopsy were edematous brain and lungs, tubular degeneration of the kidneys, congestion of the liver with centrilobular degeneration and heart dilation (931). In fatal cases, the body temperature may be extremely high and death may occur as early as 3 hours after the onset of symptoms (46). A recent report of a fatal case involved a 33-year-old chemical plant worker who had been breaking up blocks of PCP. For 2 weeks prior to hospital admission, he experienced lethargy, breathing difficulties, profound thirst and sweating. On admittance to the hospital, the worker was comatose, his respiratory rate was 56/minute and his rectal temperature was 105°F. The patient succumbed 1 hour after admission despite treatment aimed at control of body temperature. Postmortem examination revealed an extreme degree of rigor in the thigh and leg muscles, edema of the brain and lungs and congestion of the liver (932).

PCP has also been reported to cause conjunctival irritation, corneal opacity, corneal numbness and slight mydriasis (2).

39.3.2.2 Chronic Toxicologic Effects

Symptoms of chronic toxicity are similar to those seen in acute intoxications. These include muscle weakness, headache, anorexia, abdominal pain and weight loss in addition to skin, eye and respiratory tract irritation (910). Another chronic health effect associated with commercial PCP exposure is chloracne, a type of acneform dermatitis commonly associated with exposure to dioxins. Baader and Bauer (933) reported chloracne in 10 workers engaged in PCP production for 5-10 months. Seven of these workers also developed severe bronchitis. More

than one year after cessation of exposure, all but one worker still showed signs of extensive dermatitis and 4 still complained of bronchitis. One fatal case of aplastic anemia has been linked to dermal exposure to PCP for one year (934).

Long-term exposure to pentachlorophenol may also affect the liver, kidneys and nervous system but interpretation of the data are complicated by the presence of PCP impurities as well as solvents. Among the effects reported with occupational exposure were slight decreases in nerve conduction velocity (937), liver enzymes which were elevated but still within normal limits (936) and reversible decreases in glomerular filtration rate and renal tubular function (935). One study suggests that PCP may alter human immune response as evidenced by a higher incidence of low-grade infection and inflammations in PCP-exposed workers (938).

Recently there have been several reports suggesting a possible association between pentachlorophenol use and production and development of leukemia, Hodgkin's disease and soft tissue sarcomas. Pentachlorophenol exposure could not be distinguished from dioxin exposure in any of these studies and in some cases, exposure to other chemicals also occurred. IARC (25) considers this evidence to be inadequate for assessment of human carcinogenicity of PCP.

39.3.3 Levels of Concern

The USEPA (388) has established a water quality criterion for pentachlorophenol of 1.01 mg/L for the protection of public health. The criterion is based on the oral no-observed adverse effect level of 3 mg/kg for the rat (919) and an uncertainty factor of 100. An acceptable daily intake of 2.1 mg/day of PCP was calculated for a 70 kg adult by EPA (670).

In the absence of formal drinking water standards, the USEPA (992) has developed the following Health Advisories for noncarcinogenic risks for pentachlorophenol concentrations in drinking water. They are - 1 day: 3.5 mg/L; 10 days - 1.1 mg/L; and long-term: none established.

The World Health Organization (666) has proposed a health-based guideline of 10 μg/L pentachlorophenol for drinking water; daily per capita consumption of two liters of drinking water was assumed.

IARC (803) lists pentachlorophenol in category 3 (insufficient evidence) in its weight-of-evidence ranking for potential carcinogens. The NTP has not assigned a classification as yet to pentachlorophenol; studies are in progress.

OSHA (298) currently permits and the ACGIH (1003) recommends exposure to pentachlorophenol be limited to 0.5 mg/m^3 averaged over an 8-hour work shift. These exposure limits were selected to prevent systemic toxicity.

39.3.4 Hazard Assessment

Pentachlorophenol may be absorbed through the skin, by inhalation or by ingestion. Assessment of the toxicity of pentachlorophenol is complicated by the presence of varying amounts of toxic contaminants; grades of purity ranges from 86% to > 99%.

Acute exposure hazards for pentachlorophenol result from its ability to uncouple oxidative phosphorylation and inhibit mitochondrial ATPase, causing a markedly increased metabolic rate and elevated body temperature. Risk of serious intoxication with pentachlorophenol is increased in hot weather. Human fatalities have been documented (931,932). Long-term exposure to pentachlorophenol produces hepatic and renal changes in laboratory animals (925,926) and humans (931,932,-935,936) and may compromise immune response (927,938). Absorption of pentachlorophenol by any route may result in chloracne in humans (933).

Technical-grade pentachlorophenol has been evaluated for cancer-causing effects in rats and two strains of mice. Rats ingested up to 30 mg/kg/day for 2 years while mice ingested up to 46.4 mg/kg/day. No increased incidences of tumors were seen (911,919). There are limited data to suggest possible mutagenic activity for pentachlorophenol but the majority of mutagenic test results are negative.

Embryotoxic and fetotoxic effects such as resorptions, subcutaneous edema, dilated ureters and anomalies of the skull and ribs were observed in rats exposed to pentachlorophenol during gestation (912,919). Purified PCP appears to be somewhat more toxic than technical-grade PCP with respect to embryonal and fetal effects. A no-observed adverse effect level of 3 mg/kg/day of purified PCP was recorded for rats (919).

39.4 SAMPLING AND ANALYSIS CONSIDERATIONS

Determination of pentachlorophenol concentrations in soil and water requires collection of a representative field sample and laboratory analysis. Soil and water samples are collected in glass containers; extraction of samples should be completed within 7 days of sampling and analysis completed within 30-40 days. In addition to the targeted samples, quality control samples such as field blanks, duplicates, and fortified samples matrices may be specified in the recommended methods.

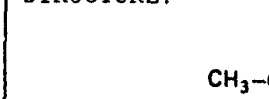
EPA-approved procedures for the analysis of pentachlorophenol, one of the EPA priority pollutants, in aqueous samples include EPA Methods 604, 625 and 1625 (65), 8040 and 8250 (63). Prior to analysis, samples are extracted with methylene chloride as a solvent using a separatory funnel or a continuous liquid-liquid extractor. Methods 604 and 8040 also provide for a perfluorobenzyl bromide (PFB) derivatization of the sample extract with additional clean-up procedures if interferences are present in the sample matrix. An aliquot of the concentrated sample

extract with or without derivatization is injected onto a gas chromatographic (GC) column using a solvent flush technique. The GC column is programmed to separate the semi-volatile organics; pentachlorophenol is then detected with a flame ionization detector (Methods 604 and 8040 without derivatization), as its PFB derivative with an electron capture detector (Methods 604 and 8040 with derivatization) or with a mass spectrometer (Methods 625 and 1625).

The EPA procedures recommended for pentachlorophenol analysis in soil and waste samples, Methods 8040 and 8250 (63), differ from the aqueous procedures primarily in the preparation of the sample extract. Solid samples are extracted using either soxhlet extraction or sonication methods. Neat and diluted organic liquids may be analyzed by direct injection.

Typical pentachlorophenol detection limits that can be obtained in waste waters and non-aqueous samples (wastes, soils, etc.) are shown below. The actual detection limit achieved in a given analysis will vary with instrument sensitivity and matrix effects.

Aqueous Detection Limit	Non-Aqueous Detection Limit
7.4 µg/L (Methods 604 and 8040 without derivatization)	1 µg/g (Method 8040)
0.59 µg/L (Methods 604 and 8040 with derivatization)	
3.6 µg/L (Methods 625 and 8250)	1 µg/g (Method 8250)
50 µg/L (Method 1625)	

COMMON SYNONYMS:	CAS REG. NO.:	FORMULA:	AIR W/V CONVERSION FACTORS at 25°C (13)
2-Propanone Dimethyl ketone Pyroacetic ether Pyroacetic acid Methyl acetal Methyl ketone	67-64-1 NIOSH NO.: AL3150000	C_3H_6O	2.37 mg/m³ ≈ 1 ppm 0 . ppm ≈ 1 mg/m³
	STRUCTURE: 		MOLECULAR WEIGHT: 58.09

REACTIVITY	Reactions of ketones such as acetone with non-oxidizing mineral acids, caustics, cyanides, mercaptans, or other organic sulfides typically produce heat, while those with alkali or alkaline earth elemental metals, nitrides or strong reducing agents evolve heat and flammable gases. Reactions with oxidizing mineral acids or other strong oxidizing agents may generate heat, fires, and/or explosions. Those with azo or diazo compounds or hydrazines may generate heat and usually innocuous gases. Reactions with organic peroxides or hydroperoxides typically result in explosions, while those with chlorinated melamines may result in rapid reaction, fumes, fire, and explosion. Explosive reactions have also been reported with chloroform and a base and with nitrosyl chloride and a platinum catalyst in closed containers (505,511).

PHYSICO-CHEMICAL DATA	• Physical State (at 20°C): volatile liquid	(45)
	• Color: colorless	(45)
	• Odor: sweet, pungent	(45)
	• Odor Threshold: 20 ppm	(13)
	• Liquid Density (g/ml at 20°C): 0.791	(21)
	• Freezing/Melting Point (°C): -95.3	(23)
	• Boiling Point (°C): 56.2	(13)
	• Flash Point (°C): -20 to -17 (cc); -15.6 to -9.4 (oc)	(23,51,60, 507)
	• Flammable Limits in Air, % by Volume: 2.15 or 2.6 - 12.8	(51,60, 506,507)
	• Autoignition Temperature (°C): 465, 538 or 560	(23,51, 506,514)
	• Vapor Pressure (mm Hg at 20°C): 186	(21)
	• Saturated Concentration in Air (mg/m³ at 20°C): 5.9×10^5	(ADL estim)
	• Solubility in Water (mg/L at 20°C): infinite	(21)
	• Viscosity (cp at 20°C): 0.33	(21)
	• Surface Tension (dyne/cm at 20°C): 23.7	(21)
	• Log (Octanol-Water Partition Coefficient), log K_{ow}: -0.24	(29)
	• Soil Adsorption Coefficient, K_{oc}: 0.28	(65)
	• Henry's Law Constant (atm·m³/mol at 25°C): 3.97×10^{-5}	(966)
	• Bioconcentration Factor: 0.03	(659)

PERSISTENCE IN THE SOIL-WATER SYSTEM	Acetone is expected to migrate freely through the soil/ground water system. Volatilization may occur in near surface soils; however, vapor phase concentrations in soil are expected to be very low whenever water is present. Biodegradation of acetone has been demonstrated and persistence in environments with active microbial populations is not expected.
PATHWAYS OF EXPOSURE	The primary pathway of concern from a soil/ground-water system is the migration of acetone to ground-water drinking water supplies. Inhalation may be important in some situations. Bioaccumulation of acetone is not likely to be an important exposure pathway.
HEALTH HAZARD DATA	Signs and Symptoms of Short-Term Human Exposure (2,61): Dryness and irritation of eyes, nose and throat are usual signs of acute exposure to acetone vapor. Exposure to high concentrations of acetone can produce dizziness, nausea, narcosis and in extreme cases, coma.
	Toxicity Based on Animal Studies: LD_{50} (mg/kg) oral 9750 [rat] (51) skin 20,000 [rabbit] (51) LC_{50} (mg/m³) inhalation [mouse] (51) 110,000·62 min
	Long-Term Effects: Respiratory tract irritation, dermatitis Pregnancy/Neonate Data: Negative Mutation Data: Limited evidence Carcinogenicity Classification: IARC - none assigned; NTP - none assigned
HANDLING PRECAUTIONS (54)	Handle chemical only with adequate ventilation • Vapor concentrations of 750-5000 ppm: gas mask with organic vapor canister • Vapor concentrations of 5000-20,000 ppm: gas mask with organic vapor canister, any supplied air respirator or self-contained breathing apparatus with full facepiece • Butyl, natural rubber, neoprene, nitrile, PE, PVA or PVC gloves, apron and boots to prevent repeated or prolonged skin contact with the liquid • Chemical goggles if there is probability of eye contact.
EMERGENCY FIRST AID TREATMENT (59)	Ingestion: Give large quantities of water and induce vomiting if victim is conscious. Get medical attention • Inhalation: move victim to fresh air immediately and perform artificial respiration if necessary • Skin: Remove contaminated clothing immediately to avoid flammability hazard. Wash skin with soap and water • Eye: Irrigate with water copiously for at least 15 minutes. If irritation or pain persists, get medical attention.

ENVIRONMENTAL AND OCCUPATIONAL STANDARDS AND CRITERIA

AIR EXPOSURE LIMITS:

Standards
- OSHA PEL (8-hr TWA): 1000 ppm
- AFOSH PEL (8-hr TWA): 1000 ppm

Criteria
- NIOSH IDLH (30-min): 20,000 ppm
- ACGIH TLV® (8-hr TWA): 750 ppm
- ACGIH STEL (15-min): 1000 ppm

WATER EXPOSURE LIMITS:

Drinking Water Standards - None established

EPA Health Advisories - None established

EPA Ambient Water Quality Criteria (355)
- Human Health
  No criterion established; acetone is not a priority pollutant.
- Aquatic Life
  No criterion established; acetone is not a priority pollutant.

REGULATORY STATUS (as of January 1, 1987)

Regulated Pollutants

- Federal Programs

Safe Drinking Water Act (SDWA)
In states with an approved underground injection control program a permit is required for the injection of acetone-containing wastes designated as hazardous under RCRA (295).

Resource Conservation and Recovery Act (RCRA)
Acetone is identified as an ignitable hazardous waste (D001) (329). Non-specific sources of acetone-containing waste that contain at least 10% acetone are solvent use (or recovery) activities (987).

Spent solvent wastes containing acetone are prohibited from land disposal unless one or more of the following conditions apply:

- the generator is a small quantity generator;
- the waste is generated from a response action under CERCLA or a corrective action under RCRA;
- the waste is a solvent-water mixture, solvent-containing sludge, or solvent-contaminated soil containing less than 1% total solvent constituents listed in 40CFR268.41.

Between November 8, 1986 and November 8, 1988, these wastes may be disposed of in a landfill or surface impoundment only if the facility is in compliance with the requirements specified in 40CFR268.5(h)(2). After November 8, 1988, all land disposal of these wastes is prohibited. These requirements do not apply if the wastes are disposed at a facility that has been granted a petition under 40CFR268.6 or an extension under 40CFR268.5 or if the waste is treated to meet specific treatment standards (1755).

Comprehensive Environmental Response Compensation and Liability Act (CERCLA)
Acetone is designated a hazardous substance under CERCLA. It has a reportable quantity (RQ) limit of 2270 kg. Reportable quantities have also been issued for RCRA hazardous waste streams containing acetone but these depend upon the concentrations of the chemicals in the waste stream (985).

Federal Insecticide, Fungicide and Rodenticide Act (FIFRA)
Acetone is exempt from a tolerance requirement when used as a solvent in pesticide formulations applied to growing crops or to raw agricultural commodities after harvest (315).

Marine Protection Research and Sanctuaries Act (MPRSA)
Ocean dumping of organohalogen compounds as well as the dumping of known or suspected carcinogens, mutagens or teratogens is prohibited except when they are present as trace contaminants. Permit applicants are exempt from these regulations if they can demonstrate that such chemical constituents are non-toxic and non-bioaccumulative in the marine environment or are rapidly rendered harmless by physical, chemical or biological processes in the sea (309).

Occupational Safety and Health Act (OSHA)
Employee exposure to acetone shall not exceed an 8-hour time-weighted-average (TWA) of 1000 ppm (298).

Hazardous Materials Transportation Act (HMTA)
The Department of Transportation has designated acetone as a hazardous material which is subject to requirements for packaging, labeling and transportation (306).

Food, Drug and Cosmetic Act (FDCA)
Acetone is approved for use as an indirect food additive (362).

A tolerance of 30 ppm is established for acetone in spice oleoresins when present as a residue from extraction of spice (361).

- State Water Programs
  There are no specific state regulations for acetone.

Proposed Regulations

- Federal Programs
  Resource Conservation and Recovery Act (RCRA)
  EPA has proposed that hazardous waste treatment, storage and disposal facilities monitor ground water for acetone when EPA suspects the facilities of leaking contaminants (1754).

- State Water Programs
  No proposed regulations are pending.

EEC Directives

Directive on Marketing and Use of Dangerous Substances (541)
Acetone may not be used in ornamental objects intended to produce light or color effects by means of different phases.

Directive on the Classification, Packaging and Labeling of Dangerous Substances (787)
Acetone is classified as a flammable substance and is subject to packaging and labeling regulations.

60.1 MAJOR USES

Acetone is used primarily as a solvent and chemical intermediate. Uses include the production of lubricating oils and as an intermediate in the manufacturing of chloroform and of various pharmaceuticals and pesticides. Acetone can also be found in paints, varnishes and lacquers and is used as a solvent for cements in the leather and rubber industry (No. 1, 3).

60.2 ENVIRONMENTAL FATE AND EXPOSURE PATHWAYS

60.2.1 Transport in Soil/Ground-water Systems

60.2.1.1 Overview

Acetone is expected to be mobile in the soil/ground water system when present at relatively low concentrations or as a separate organic phase (resulting from a spill of significant quantities of the chemical). In general, transport pathways can be assessed by using an equilibrium partitioning model, as shown in Table 60.1. These calculations predict the partitioning of low ppm concentrations of acetone among soil particles, soil water and soil air. Portions of acetone associated with the water and air phases of the soil have higher mobility than the adsorbed portion.

Estimates for the unsaturated topsoil model indicate that only 9.1% of the acetone is expected to be sorbed onto soil particles. Approximately 91% is expected to partition to the soil-water phase, and is thus available to migrate by bulk transport (e.g., the downward movement of infiltrating water), dispersion and diffusion. For the small portion of acetone in the gaseous phase of the soil (0.3%), diffusion through the soil-air pores up to the ground surface, and subsequent removal by wind, may be a significant loss pathway.

In saturated, deep soils (containing no soil air and negligible soil organic carbon), almost all of the acetone (99.9%) is predicted to be present in the soil-water phase (Table 60.1) and available for transport with flowing ground water. Sorption onto deep soils (0.1%) is not expected to be significant. Overall, ground water underlying acetone-contaminated soils with low organic content is expected to be vulnerable to contamination.

60.2.1.2 Sorption on Soils

The mobility of acetone in the soil/ground-water system (and its eventual migration into aquifers) is governed by the extent of its sorption on soil particles. In general, sorption on soils is expected to

TABLE 40-1

EQUILIBRIUM PARTITIONING CALCULATIONS FOR ACETONE IN MODEL ENVIRONMENTS[a]

Soil Environment	Estimated Percent of Total Mass of Chemical in Each Compartment		
	Soil	Soil-Water	Soil-Air
Unsaturated topsoil at 25°C[b,c]	5.1	94.4	0.5
Saturated deep soil[d]	0.1	99.9	-

a) Calculations based on Mackay's equilibrium partitioning model (34,35,36); see Introduction in Volume 1 for description of model and environmental conditions chosen to represent an unsaturated topsoil and saturated deep soil. Calculated percentages should be considered as rough estimates and used only for general guidance.

b) Utilized estimated soil sorption coefficient: K_{oc} = 0.28 (611).

c) Henry's law constant taken as 3.97 x 10^{-5} atm·m³/mol at 25°C (966).

d) Used sorption coefficient $K_p = 0.001\ K_{oc}$.

- increase with increasing soil organic matter content;
- increase slightly with decreasing temperature;
- increase moderately with increasing salinity of the soil water; and
- decrease moderately with increasing dissolved organic matter in the soil water.

Acetone is infinitely soluble in water and, as evidenced by its negative log K_{ow} and low K_{oc}, adsorption to soil/sediments is not expected to contribute significantly to its environmental fate. Acetone has been detected in various types of water including drinking water; it has also been identified in leachates from landfills (1119).

Some sorption, however, has been reported. Rathbun et al. (1119) report studies indicating that acetone vapor was slightly sorbed to montmorillonite, but only if the clay was previously hydrated with water. Adsorption of acetone on activated carbon was also reported.

Green et al. (1127) provided data on the permeability of acetone in Ranger Shale, Keese Kaolin, and Fire Clay. All three clay soils are classified as virtually impervious to solvents and were observed to be more permeable to water than to solvents. The characteristics of the clay soils and the reported permeability are presented in Table 60-2. Of the compounds tested, acetone was the most mobile organic solvent in all matrices except Ranger Shale. (It was postulated that microbial decomposition of acetone in the biologically active Ranger Shale resulted in CO_2 production and clogging of pores.) Data from this study also indicate that the solvent that caused the greatest swelling (H_2O) had the highest coefficient of permeability. Swelling reported for acetone was also relatively high.

In summary, acetone is expected to migrate freely through the soil/ground-water system with little or no retardation. Permeability to acetone has also been shown for materials known to be relatively impervious to organic solvents (e.g., clays).

60.2.1.3 Volatilization from Soils

In spite of the fact that acetone is a volatile compound, the potential for volatilization is reduced due to its high aqueous solubility. Transport of vapors through the air-filled pores of unsaturated soils may occur in near-surface soils. However, modeling results suggest that a very small fraction of the acetone loading will be present in the soil-air phase.

In general, important soil and environmental properties influencing the rate of volatilization include soil porosity, temperature, convection currents and barometric pressure changes; important physicochemical properties include the Henry's Law constant, the vapor-soil sorption coefficient and, to the lesser extent, the vapor phase diffusion coefficient (31).

The Henry's law constant (H), which provides an indication of a chemical's tendency to volatilize from solution, is expected to increase significantly with increasing temperature. Moderate increases in H have also been observed with increasing salinity and the presence of other organic compounds (18). These results suggest that the presence of other materials may significantly affect the volatilization of acetone, particularly from surface soils. No information was available for the two other physicochemical properties influencing volatilization, i.e., the vapor-soil sorption coefficient and the vapor phase diffusion coefficient.

Volatilization coefficients (K_v) for acetone in water have been reported (1119,1121) to range from 0.6 $days^{-1}$ to 2.3 $days^{-1}$, corresponding to half-lives of 1.3 days to 0.34 days, for very low mixing conditions to very high mixing conditions, respectively. Experimental conditions used correspond to low air mixing, variable stirring rate of 0 - 2020 rpm and water depths of 200-267 mm. It is expected that these coefficients would increase for higher mixing conditions or increased air velocity in environmental aquatic systems.

TABLE 40-2

PERMEABILITY OF ACETONE IN THREE CLAY-SITES

	Ranger Shale	Kosse Kaoline	Fire Clay
Packed density (g/cc)	1.73	1.36	1.81
% Organic carbon	0.28	0.12	0.03
% Swell (H_2O)	11.7	11.7	8.2
% Swell (acetone)	4	8.7	3.6
Permeability (x 10^{-9} cm/sec) for H_2O	38	220	13.5
Permeability (x 10^{-9} cm/sec) for acetone	2.5	65	7

Source: Green et al. (1122)

The significance of acetone volatilization in the environment is not well known; data on volatilization from soils, in particular, are not available. Since acetone is not strongly adsorbed to soil, some volatilization at the surface may occur; however, the ability of acetone to be transported with soil water is significant. Furthermore, any acetone lost due to volatilization will be rapidly washed out of the atmosphere, due to its high water solubility, and returned to the soil/water system.

40.2.2 Transformation Processes in Soil/Ground-water Systems

The portion of acetone that has been released from the soil into the air will either return to the soil via atmospheric washout or eventually undergo photochemical oxidation; a photodissociation lifetime of 14.8 days has been reported for acetone in air under troposperic conditions (1120).

No information on the hydrolysis of acetone was available; under normal environmental conditions, hydrolysis is not expected to occur at a rate competitive with volatilization or bicdegradation. Rathbun et al. (1119) reported no significant photodegradation of acetone in water.

Acetone is expected to be highly susceptible to microbial biodegradation. It is rapidly oxidized by most sewage microorganisms (1130) and has been classified as having low persistence (1123-1125). Several authors (1132,1133) have reported the biodegradation of acetone by microbes grown on acetone or propane, or by soil bacteria grown on C1-C8 aliphatic hydrocarbons. No acetone degradation with four yeast cultures was reported (1131).

Degradation of acetone, determined by BOD_5 tests with acclimated sewage seed or microbes from polluted waters, ranged from 31% to 84% degradation after 20 days was observed to be 76% to 84% (891,880,1127,1134). Experimental biodegradation results (1119) with initial concentrations of 15 - 150 mg/L acetone showed the importance of acclimation of a bacterial culture to acetone. Without acclimation, the lag time before degradation averaged about 13 hours; with pretreatment, the lag time was reduced to 1.8 hours. The degradation coefficient (K_1) showed considerable scatter and ranged from 0.41 to 7.9 $days^{-1}$; there was no clear correlation of degradation rate with acclimation. Chou et al. (1126) reported 55% utilization of acetone in an anaerobic reactor.

Two studies (1128,1129) reported some toxicity to activated sludge and domestic sewage seed at acetone concentrations of 500 mg/L.

In actual soil/ground-water systems, the concentration of microorganisms capable of biodegrading acetone may be low, and is expected to drop off sharply with increasing depth; prediction of biodegradation rates in the environment is not possible. However, persistence of acetone in environments with sufficient active microbial populations is not expected.

60.2.3 Primary Routes of Exposure from Soil/Ground-water Systems

The above discussion of fate pathways suggests that acetone has a moderate volatility, is very weakly adsorbed to soil, and has no significant potential for bioaccumulation. This compound may volatilize from the soil surface, but that portion not removed by volatilization is likely to be mobile in ground water. These fate characteristics suggest several potential exposure pathways.

Volatilization of acetone from a disposal site could result in inhalation exposure to workers or residents in the area. In addition, the potential for ground water contamination is high, particularly in sandy soils. Acetone has been detected in ground water associated with hazardous waste sites. Nitro (83) reported that acetone has been found at 8 of the 546 National Priority List (NPL) sites. It was detected at 3 sites in ground water, 3 in surface water and 3 in air. However, analysis for acetone may not be commonly done at NPL sites as it is not a priority pollutant and is not generally considered a public health concern. These data, as well as the properties of acetone, suggest that drinking water exposure from ground water contamination is likely to be its primary route of exposure from soil/ground-water systems.

The movement of acetone in ground water may result in discharge to surface water. As a result, ingestion exposures may occur resulting from the use of surface waters as drinking water supplies; dermal exposures may result from the recreational use of contaminated surface waters. Such exposures are likely to be lower than those obtained from drinking contaminated ground water due to biodegradation and/or volatilization of acetone in surface water. Any pathways related to

the uptake of acetone by aquatic organisms or domestic animals from surface waters are likely to be less significant than other sources of exposure due to the low BCF for acetone.

40.2.4 Other Sources of Human Exposure

Acetone is a widely used industrial solvent As such, there are a number of potential sources of human exposure. However, data to support these exposures are lacking. For example, acetone is not commonly measured in drinking water.

The production and use of acetone has led to its presence in the atmosphere. Brodzinsky and Singh (84) summarized air monitoring data for a number of pollutants. For acetone, they reported 22 data points for source-dominated areas. The median concentration reported was 0.83 $\mu g/m^3$. Acetone was also detected in the indoor air of an energy-efficient office building at approximate levels of 1-75 ppb (906).

Dermal exposure is expected to be common due to the prevalence of acetone as a solvent in various products. For example, two surveys were conducted in Japan on the solvent content of a variety of products. They found acetone in 4% of the paints, 4% of the inks, 12% of the adhesives, 9% of the thinners, and 8% of the degreasers that were sampled. While most of these products were used in occupational settings, some may be used by consumers (1140,1141).

40.3 HUMAN HEALTH CONSIDERATIONS

40.3.1 Animal Studies

40.3.1.1 Carcinogenicity

The data available regarding the carcinogenicity of acetone are limited to a skin-painting study in mice of inadequate time duration. Van Duuren et al. (1043) applied 0.1 ml of acetone to the skin of female ICR/Ha Swiss mice three times a week for one year. No evidence of tumors were reported up to 208 days later.

40.3.1.2 Mutagenicity

Acetone was negative in a reverse mutation assay with strains TA98, TA100, TA1535, TA1537 and TA1538 of Salmonella typhimurium, both with and without metabolic activation (1017,1054).

It did, however, significantly inhibit metabolic cooperation in Chinese hamster V-79 cells. This inhibition of metabolic cooperation is indicative of an inhibition of intercellular communication (1013). A recent report by Zimmerman et al. (1011) showed acetone to induce aneuploidy in the D61.M strain of Saccharomyces cervisiae, but not to induce point mutations or recombinations.

40.3.1.3 Teratogenicity, Embryotoxicity and Reproductive Effects

McLaughlin et al. (1042) injected 39 or 78 mg of acetone/kg of egg into the yolk sac of fresh fertile chick eggs before incubation. The eggs were then incubated and hatched. Reduced hatchability was shown at both the 39 mg level (80% hatchability) and the 78 mg level (50% hatchability). The percent hatchability for control eggs (i.e., injected with needle only) was not reported. No evidence of teratogenicity was found at either treatment level.

40.3.1.4 Other Toxicologic Effects

40.3.1.4.1 Short-term Toxicity

The oral LD_{50} of acetone for mice is reported to be 3000 mg/kg (51), while the oral LD_{50} for rats is listed as 9750 mg/kg (51). Acetone primarily acts as an irritant and as a depressant of the CNS. Common signs of acetone toxicity include eczema, conjunctivitis and corneal erosion, pharyngitis and bronchitis, CNS depression, weakness and narcosis (59).

Early studies revealed that acetone produces depression of the respiratory and vasomotor centers in a variety of experimental animals (1029). Specht et al. (1041) exposed guinea pigs to 20,000 ppm of acetone. Irritation of the mucous membranes, narcosis, CNS depression and respiratory dysfunction were observed. A decrease of 30 breaths/minute and 50 heartbeats/minute were recorded at 4800 ppm, while a decrease in body temperature 4°C below normal occurred at 10,800 ppm. Histological examination revealed congestion of the lungs and kidney as well as hemorrhaging in the pulp of the spleen.

Goldberg et al. (1051) studied the behavioral effects of acetone on rats. Rats were trained to climb a pole within two seconds of a stimulus. A delay of more than 6 seconds was considered to be a significant change in behavior. Rats were then exposed to 3000, 6000, 12,000 or 16,000 ppm of acetone vapor for 4 hours/day, 5 days/week for two weeks. Performance of each rat was tested before and after each exposure. Acetone at concentrations of 6000 ppm or above resulted in a significant modification of the avoidance and escape behavior pattern. Several rats exposed to the 12,000 or the 16,000 ppm level initially developed muscular incoordination after exposure, however, no signs of incoordination were reported on subsequent exposures.

Due to the narcotic effect of acetone at high concentrations, Geller et al. (1012) attempted to determine if exposure to half the TLV concentration would produce similar low level effects on CNS function. A match-to-sample discrimination task was used to measure the behavioral response of baboons exposed to acetone compared with performance under normal conditions. Baboons subjected to 500 ppm acetone, 6 hours/day for 7 days exhibited a marked change in the number of extra responses made during exposure. An increase in response time

was also demonstrated. Geller concluded that these effects were the result of a slight narcosis associated with acetone exposure at very low levels.

40.3.1.4.2 Chronic Toxicity

Male ICR mice and albino rats were exposed to 19,000 ppm of acetone vapor 3 hours/day, 5 days/week for 8 weeks. Animals were sacrificed after 2, 4, 8 and 10 weeks. Histopathological examination of tissues did not reveal any organ damage. Depression of body weight gain was the only adverse effect of chronic acetone exposure indicated (1078).

Rengstorff (1045) investigated the effects of dermal or subcutaneous injections of acetone in albino guinea pigs. Animals were exposed cutaneously to 0.5 ml of acetone or were injected subcutaneous on the back with either a 5% or 50% acetone in saline solution. Animals were dosed 3 times a week for 3 weeks. Examinations were conducted 60 to 90 days after the first application or injection, and every thirty days thereafter for 6 months. Two of the twelve animals cutaneously exposed to undiluted acetone developed bilateral cataracts involving the entire periphery of the lens. Two out of four animals treated subcutaneously with the 50% solution and five out of twelve animals injected with the 5% acetone solution developed cataracts. Three of the animals in this 5% acetone solution treatment group showed a disappearance of lens damage as time elapsed, and by 6 months, lenses had returned to normal.

Due to the unexpected effect acetone had on the eyes of guinea pigs, Rengstorff dropped 1.0 ml of acetone on the dorsal thorax area of 8 albino guinea pigs and 8 New Zealand white rabbits two times a day, 5 days a week for 4 or 8 weeks. Saline was substituted for acetone in the control group in addition to 4 guinea pigs receiving no treatment. Examinations were made each week for 8 weeks and then every other week for the remainder of the 6 month period. Two of the 8 guinea pigs developed bilateral cataracts in the 8-week-treatment group. No lens abnormalities were observed in any of the experimental or control rabbits or in the control guinea pigs. Histological appearance of the acetone-treated eyes showed advanced lens lesions suggesting a progressive sclerotic change (1045). Rengstorff theorized that the mechanism which induces the crystalline lens opacities in acetone-treated guinea pigs is the same metabolic mechanism involved in the pathology of diabetic cataracts, and is related to the accumulation of ketone bodies such as acetone in the aqueous humor.

40.3.2 Human and Epidemiologic Studies

40.3.2.1 Short-term Toxicologic Effects

Exposure to acetone vapor usually results in irritation to the eyes, nose and throat. Dizziness and narcosis occur with continued exposure.

Ross (1044) reported an incident of acute acetone intoxication in workmen cleaning out a 12-foot-deep pit. Tanks of acetone and 1,1,1-trichloroethane were stored next to the pit. Two men descended into the pit and filled water into 2 buckets which were hoisted up and out of the pit by two men at the top of the ladder. All four men noticed a sickly sweet odor while working. One man working in the pit felt throat irritation, weakness in the legs and had a severe headache. The other man in the pit experienced eye irritation and felt "drunk" just before noontime. After an one hour lunch break, this man descended into the pit, filled one bucket of water and fainted. Four men came to assist the unconscious man out of the pit. All immediately experienced eye irritation and dizziness. Urine samples of the 8 men ranged from 4.6-7.2 mg acetone/100 ml urine. Samples taken 7 days later showed acetone levels had returned to normal, ranging between 0.39-1.29 mg acetone/100 ml urine. Air samples taken 3 hours after the men were taken to the hospital revealed acetone levels in excess of 12,000 ppm and 1,1,1-trichloroethane levels of up to 50 ppm.

Matsushita et al. (1052) conducted an inhalation study using five groups of five male volunteers. Each group was subjected to 0, 100, 200, 500 or 1000 ppm of acetone for 6 hours. Most of the subjects in the 500 and 1000 ppm groups experienced irritation of the nose, eyes, throat and trachea. Men in these groups also complained of tension, general weakness, heavy eyes or lack of energy the following morning. The 250 ppm group experienced similar complaints, but to a lesser extent. No complaints were reported in the 100 ppm group.

Lupulescu et al. (1053) studied the effect of 1 ml of acetone when applied to the skin of 7 volunteers for 90 minutes. Mild edema and hyperemia were the only clinical signs observed. Electron microscopic examination of the affected skin revealed cell damage and cytoarchitectural disorganization in the stratum corneum. These findings indicate that acetone affects the organization and cell homeostasis of the upper layers of human skin.

Ingestion of 200 ml of acetone resulted in a stuporous condition with flushed cheeks, shallow breathing, and a pulse rate of 108. The throat was red and swollen and erosion was observed on the soft palate and around the entrance to the esophagus. The individual lapsed into a coma shortly after admission to the hospital. Supportive therapy was given and the individual regained consciousness 12 hours later. Pain and an increased sensitivity in the legs and hips developed 6 days later and persisted for two months. Four weeks after the initial ingestion of acetone, the subject had an increased fluid intake along with an increased urine output. An oral glucose tolerance test gave values in the diabetic range, but levels gradually returned to normal over a 2.5 months period (1048). Recent work by Casazza et al. (1049) indicates that hepatocytes isolated from chronic acetone-fed rats are capable of converting acetone to glucose in vitro.

40.3.2.2 Chronic Toxicologic Effects

Chronic exposure to acetone may cause harmful effects resulting in hyperemia of the conjunctiva and pharynx, lung irritation and rough breathing, dizziness, headaches, insomnia, and epigastric pain (1055).

Vigliani and Zurlo (1050) studied the health of factory workers exposed to 1000 ppm of acetone, 3 hours/day for 7-15 years. All the workers examined had inflamed respiratory tracts, stomachs and duodenums. They also reportedly experienced dizzy spells and loss of strength.

40.3.3 Levels of Concern

No water quality criteria or standards have been established for acetone. The OSHA (298) standard is 1000 ppm averaged over an 8-hour work-shift. The ACGIH (3) recommend a threshold limit value of 750 ppm, with a short-term exposure limit of 1000 ppm.

40.3.4 Hazard Assessment

Acetone is generally considered to be among the least toxic solvents used in industry (12). Human exposure to vapor concentrations of 250-1000 ppm results in irritation of eyes, nose and throat (1052); higher vapor concentrations can produce depression of the central nervous system and narcosis (59,1044). Oral LD_{50} values for acetone range from 3 to 10 g/kg in rodents (51). Human ingestion of 200 mL of acetone induced gastroenteritis, narcosis and possible renal injury (1048).

Animal studies indicate signs of slight narcosis in baboons exposed to 500 ppm acetone (1012). Chronic dermal application of acetone resulted in the development of reversible cataracts in guinea pigs but not rabbits (1045); these cataracts may be related to the same metabolic mechanism associated with cataract formation in diabetics, i.e., the rise in ketone bodies in the eye.

Carcinogenicity tests are limited to a single skin-painting experiment of inadequate duration in mice (1043). No indications of tumor production were observed and there are no reports in the literature to implicate acetone as a carcinogen. Negative results were obtained in two Ames mutagenicity tests (1017,1054). Acetone, however, was shown to induce aneuploidy in yeast (1011). Injection of acetone directly into the yolk sacs of chick eggs produced no evidence of terata (1042).

The widespread use of acetone in industrial applications without indications of serious health effects suggest low level acetone exposure does not pose a significant health hazard.

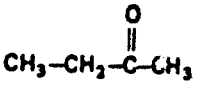
40.4 SAMPLING AND ANALYSIS CONSIDERATIONS

Determination of the concentrations of acetone in soil and water requires collection of a representative field sample and laboratory analysis. Due to the volatility of acetone, care is required to prevent losses during sample collection and storage. Soil and water samples are collected in airtight containers with no headspace; analysis should be completed within 14 days of sampling. In addition to the targeted samples, quality assurance samples such as field blanks, duplicates, and spiked matrices should be included in the analytical program.

Acetone is not included among the EPA-designated priority pollutants. However, EPA Methods 624, 1624 (65) 8015 and 8240 (63) should be appropriate methods of choice for the analysis of acetone in aqueous samples. An inert gas is bubbled through the aqueous sample in a purging chamber at ambient temperature, transferring the acetone from the aqueous phase to the vapor phase and onto a sorbent trap. The trap is then heated and backflushed to desorb the acetone and transfer it onto a gas chromatographic (GC) column. The GC column is programmed to separate the volatile organics; acetone is then detected with a flame ionization detector (Method 8015) or a mass spectrometer (Methods 624, 1624 and 8240).

The EPA procedures recommended for analysis of chemicals such as acetone in soil and waste samples, Methods 8015 and 8240 (63), differ from the aqueous procedures primarily in the method by which the analyte is introduced into the GC. The recommended method involves dispersing the soil or waste sample in methanol or polyethylene glycol to dissolve the acetone. A portion of the solution is then combined with water and purged as described above. Other sample introduction techniques include direct injection and a headspace method.

Acetone detection limits for the various methods were not determined but would be in the range of 1-50 $\mu g/L$ for aqueous samples and 1 $\mu g/g$ for non-aqueous samples.

COMMON SYNONYMS:	CAS REG. NO.:	FORMULA:	AIR W/V CONVERSION FACTORS at 25°C (59)
2-Butanone MEK Ethyl methyl ketone Methyl acetone	78-93-3 NIOSH NO.: EL6475000	C_4H_8O	2.94 mg/m³ = 1 ppm 0.340 ppm = 1 mg/m³
	STRUCTURE: 		MOLECULAR WEIGHT: 72.10

REACTIVITY	Reactions of ketones such as methyl ethyl ketone with non-oxidizing mineral acids, caustics, cyanides, mercaptans, or other organic sulfides typically produce heat, while those with alkali or alkaline earth elemental metals, nitrides or strong reducing agents evolve heat and flammable gases. Reactions with oxidizing mineral acids or other strong oxidizing agents may generate heat and fire. Those with azo or diazo compounds or hydrazines may generate heat and usually innocuous gases. Reactions with organic peroxides or hydroperoxides typically result in explosions. Various manufacturers list oxidizing agents, chlorinated hydrocarbons in the presence of alkalies, alkanolamines, amines, pyridines, ammonia, caustics, inorganic acids, isocyanates, and halogens as incompatible materials (505,507,511).

PHYSICO-CHEMICAL DATA	• Physical State (at 20°C): liquid	(23)
	• Color: colorless	(23)
	• Odor: acetone-like	(23)
	• Odor Threshold: 5.4 ppm, 10 ppm	(384,2)
	• Liquid Density (g/ml at 20°C): 0.805	(14)
	• Freezing/Melting Point (°C): -86.4	(23)
	• Boiling Point (°C): 79.6	(14)
	• Flash Point (°C): -5.6 to -1.1 (oc); -6.7 to -3.9 (cc)	(60,507, 514)
	• Flammable Limits in Air, % by Volume: 1.7 - 2.0 to 10 - 12	(51,60, 506,507)
	• Autoignition Temperature (°C): 404 or 516	(51,60, 506,510)
	• Vapor Pressure (mm Hg at 20°C): 70.6	(59)
	• Saturated Concentration in Air (mg/m³ at 20°C): 279,071	(ADL estim)
	• Solubility in Water (mg/L at 10°C): 353,000	(67)
	• Viscosity (cp at 25°C): 0.4	(23)
	• Surface Tension (dyne/cm at 20°C): no data	( )
	• Log (Octanol-Water Partition Coefficient), log K_{ow}: 0.29	(29)
	• Soil Adsorption Coefficient, K_{oc}: 0.94	(611)
	• Henry's Law Constant (atm·m³/mol at 20°C): 4.35×10^{-6}	(1138)
	• Bioconcentration Factor: 1.86, 0.09	(1137,659)

PERSISTENCE IN THE SOIL-WATER SYSTEM	Methyl ethyl ketone is expected to migrate in the soil/ground-water system with very little retardation. Volatilization from near-surface soils may occur; however, vapor concentrations in soil are expected to be very low whenever water is present. Biodegradation of methyl ethyl ketone has been demonstrated and persistence in environments with active microbial populations is not expected.

PATHWAYS OF EXPOSURE	The primary pathway of concern from a soil/ground-water system is the migration of methyl ethyl ketone to ground-water drinking water supplies. Inhalation may be important in some situations. Bioaccumulation of methyl ethyl ketone is not likely to be an important exposure pathway.

HEALTH HAZARD DATA	Signs and Symptoms of Short-term Human Exposure (13): Eye, nose and throat irritation are usually the first symptoms to appear in methyl ethyl ketone exposure. At high concentrations, CNS depression and narcosis along with congestion of the lungs, liver and kidneys are observed.
	Toxicity Based on Animal Studies: LD_{50} (mg/kg): oral 2737 [rat] (47); skin 13,000 [rabbit] (47). LC_{50} (mg/m^3): inhalation [mouse] 40,000•2 hr (47)
	Long-Term Effects: Dermatitis
	Pregnancy/Neonate Data: Fetotoxic at 3000 ppm
	Mutation Data: Conflicting data
	Carcinogenicity: No data

HANDLING PRECAUTIONS (54)	Handle chemical only with adequate ventilation • Vapor concentration of 200 - 1000 ppm: chemical cartridge respirator with organic vapor cartridge and full facepiece • 1000 - 30,000 ppm: gas mask with organic vapor canister, any supplied air respirator or self-contained breathing apparatus with full facepiece • Butyl, natural rubber, neoprene, nitrile, PE, PVA or PVC gloves, apron and boots to prevent repeated or prolonged skin contact with the liquid • Chemical goggles if there is probability of eye contact.

EMERGENCY FIRST AID TREATMENT (54)	Ingestion: Give large quantities of salt water and induce vomiting if victim is conscious. Get medical attention • Inhalation: Move victim to fresh air immediately and perform artifical respiration if necessary • Skin: Remove contaminated clothing. Wash skin with soap and water • Eye: Irrigate with large amounts of water immediately.

ENVIRONMENTAL AND OCCUPATIONAL STANDARDS AND CRITERIA

AIR EXPOSURE LIMITS:

Standards
- OSHA PEL (8-hr TWA): 200 ppm
- AFOSH PEL (8-hr TWA): 200 ppm

Criteria
- NIOSH IDLH (30-min): 3000 ppm
- ACGIH TLV® (8-hr TWA): 200 ppm
- ACGIH STEL (15-min): 300 ppm

WATER EXPOSURE LIMITS:

Drinking Water Standards - None established

EPA Health Advisories

In the absence of formal drinking water standards, the EPA (1770) has developed the following Health Advisories (formerly termed SNARLs) for noncarcinogenic risk for short and long-term exposure to methyl ethyl ketone in drinking water:

- 1 day: none established
- 10 days: none established
- long-term: 8.6 mg/L

EPA Ambient Water Quality Criteria (355)

- Human Health

  No criterion established; methyl ethyl ketone is not a priority pollutant.

- Aquatic Life

  No criterion established; methyl ethyl ketone is not a priority pollutant.

REGULATORY STATUS (as of January 1, 1987)

Promulgated Regulations

- Federal Programs

Safe Drinking Water Act (SDWA)
In states with an approved Underground Injection Control program, a permit is required for the injection of methyl ethyl ketone-containing wastes designated as hazardous under RCRA (295).

Resource Conservation and Recovery Act (RCRA)
Methyl ethyl ketone is identified as a toxic, ignitable hazardous waste (U159) and listed as a hazardous waste constituent (328,329). Non-specific sources of methyl ethyl ketone-containing waste that contain at least 10% methyl ethyl ketone are solvent use (or recovery) activities (987).

Spent solvent wastes containing methyl ethyl ketone are prohibited from land disposal unless 1 or more of the following conditions apply:

- the generator is a small quantity generator;
- the waste is generated from a response action under CERCLA or a corrective action under RCRA;
- the waste is a solvent-water mixture, solvent-containing sludge or solvent-contaminated soil containing less than 1% total solvent constituents listed in 40CFR268.41.

Between November 8, 1986 and November 8, 1988, these wastes may be disposed of in a landfill or surface impoundment only if the facility is in compliance with the requirements specified in 40CFR268.5(h)(2). After November 8, 1988, all land disposal of these wastes is prohibited. These requirements do not apply if the wastes are disposed at a facility that has been granted a petition under 40CFR268.6 or an extension under 40CFR268.5 or if the waste is treated to meet specific treatment standards (1755).

Toxic Substances Control Act (TSCA)
Manufacturers, processors or distributors of methyl ethyl ketone must report production, usage and disposal information to EPA. They, as well as others who possess health and safety studies on methyl ethyl ketone, must submit them to EPA (334,335).

Comprehensive Environmental Response Compensation and Liability Act (CERCLA)
Methyl ethyl ketone is designated a hazardous substance under CERCLA. It has a reportable quantity (RQ) limit of 2270 kg. Reportable quantities have also been issued for RCRA hazardous waste streams containing methyl ethyl ketone but these depend upon the concentrations of the chemicals in the waste stream (985).

Federal Insecticide, Fungicide and Rodenticide Act (FIFRA)
Methyl ethyl ketone is exempt from a tolerance requirement when used as a surfactant in pesticide formulations applied to growing crops (315).

Marine Protection Research and Sanctuaries Act (MPRSA)
Ocean dumping of organohalogen compounds as well as the dumping of known or suspected carcinogens, mutagens or teratogens is prohibited except when they are present as trace contaminants. Permit applicants are exempt from these regulations if they can demonstrate that such chemical constituents are non-toxic and non-bioaccumulative in the marine environment or are rapidly rendered harmless by physical, chemical or biological processes in the sea (309).

Occupational Safety and Health Act (OSHA)
Employee exposure to methyl ethyl ketone shall not exceed an 8-hour time-weighted-average (TWA) of 200 ppm (298).

Hazardous Materials Transportation Act (HMTA)
The Department of Transportation has designated methyl ethyl ketone as a hazardous material which is subject to requirements for packaging, labeling and transportation (306).

Food, Drug and Cosmetic Act (FDCA)
Methyl ethyl ketone is approved for use as an indirect food additive (362).

- State Water Programs
  There are no specific state regulations for methyl ethyl ketone.

Proposed Regulations

- Federal Programs

  Resource Conservation and Recovery Act (RCRA)
  EPA has proposed that solid wastes which contain a concentration equal to or greater than 7.2 mg/L methyl ethyl ketone be listed as hazardous in that they exhibit the characteristic defined as EP toxicity (1565).

  EPA has proposed that hazardous waste treatment, storage and disposal facilities monitor ground water for methyl ethyl ketone when EPA suspects the facilities of leaking contaminants (1754).

- State Water Programs
  No proposed regulations are pending.

EEC Directives

Directive on Marketing and Use of Dangerous Substances (541)
Methyl ethyl ketone may not be used in ornamental objects intended to produce light or color effects by means of different phases.

Directive on the Classification, Packaging and Labeling of Dangerous Substances (787)
Methyl ethyl ketone is classified as a flammable substance and is subject to packaging and labeling regulations.

41.1 MAJOR USES

Methyl ethyl ketone is used primarily as a solvent. The coating industry uses methyl ethyl ketone extensively, accounting for 61% of its production, to manufacture gums, resins and nitrocellulose. Approximately 18% of the methyl ethyl ketone produced is used to make cements and adhesives. Other manufacturers utilize methyl ethyl ketone to produce printing ink, cleaning fluids, smokeless powders and wax (200,59,67).

41.2 ENVIRONMENTAL FATE AND EXPOSURE PATHWAYS

41.2.1 Transport in Soil/Ground-water Systems

41.2.1.1 Overview

Methyl ethyl ketone is expected to be fairly mobile in the soil/ground-water system when present at low concentrations or as a separate organic phase (resulting from a spill of significant quantities of the chemical). In general, transport pathways can be assessed by using an equilibrium partitioning model, as shown in Table 41-1. These calculations predict the partitioning of low soil concentrations of methyl ethyl ketone among soil particles, soil water and soil air. Portions of methyl ethyl ketone associated with the water and air phases of the soil have higher mobility than the adsorbed portion.

Estimates for the unsaturated topsoil model indicate that only 15.2% of the methyl ethyl ketone is expected to be sorbed onto soil particles. Approximately 84% is expected to partition to the soil-water phase, and is thus available to migrate by bulk transport (e.g., the downward movement of infiltrating water), dispersion and diffusion. For the small portion of methyl ethyl ketone in the gaseous phase of the soil (0.5%), diffusion through the soil-air pores up to the ground surface, and subsequent removal by wind, may be a significant loss pathway.

In saturated, deep soils (containing no soil air and negligible soil organic carbon), almost all of the methyl ethyl ketone (99.6%) is predicted to be present in the soil-water phase (Table 41-1) and available for transport with flowing ground water. Sorption onto deep soils (0.4%) is not expected to be significant. Overall, ground water underlying methyl ethyl ketone-contaminated soils with low organic content is expected to be vulnerable to contamination.

41.2.1.2 Sorption on Soils

The mobility of methyl ethyl ketone in the soil/ground-water system (and its eventual migration into aquifers) is governed by the extent of its sorption on soil particles. In general, sorption on soils is expected to:

TABLE 41-1

EQUILIBRIUM PARTITIONING CALCULATIONS FOR METHYL ETHYL KETONE IN MODEL ENVIRONMENTS[a]

Soil Environment	Estimated Percent of Total Mass of Chemical in Each Compartment		
	Soil	Soil-Water	Soil-Air
Unsaturated topsoil at 25°C[b,c]	15.2	84.3	0.5
Saturated deep soil[d]	0.4	99.6	-

a) Calculations based on Mackay's equilibrium partitioning model (34,35,36); see Introduction in Volume 1 for description of model and environmental conditions chosen to represent an unsaturated topsoil and saturated deep soil. Calculated percentages should be considered as rough estimates and used only for general guidance.

b) Utilized estimated soil sorption coefficient: K_{oc} = 0.94 (611).

c) Henry's law constant taken as 4.35 x 10^{-5} atm·m³/mol at 25°C (1138).

d) Used sorption coefficient K_p = 0.001 K_{oc}.

- increase with increasing soil organic matter content;
- increase slightly with decreasing temperature;
- increase moderately with increasing salinity of the soil water; and
- decrease moderately with increasing dissolved organic matter in the soil water.

No information specific to the adsorption of methyl ethyl ketone in the environment was available. Methyl ethyl ketone is highly soluble in water and its low values for log K_{ow} and K_{oc} suggest that sorption to soils/sediments does not contribute significantly to its environmental fate. Methyl ethyl ketone in the soil/ground-water system is expected to be only slightly less mobile than acetone, which was reported to migrate freely with little or no retardation.

41.2.1.3 Volatilization from Soils

Transport of methyl ethyl ketone vapors through the air-filled pores of unsaturated soils may occur in near-surface soils. However, modeling results suggest that a very small fraction of the methyl ethyl ketone loadings will be present in the soil-air phase.

In general, important soil and environmental properties influencing the rate of volatilization include soil porosity, temperature, convection currents and barometric pressure changes; important physicochemical properties include the Henry's law constant, the vapor-soil sorption coefficient, and, to a lesser extent, the vapor phase diffusion coefficient (31).

The Henry's law constant (H), which provides an indication of a chemical's tendency to volatilize from solution, is expected to increase significantly with increasing temperature. Moderate increases in H have also been observed with increasing salinity and the presence of other organic compounds (18). These results suggest that the presence of other materials may significantly affect the volatilization of acetone, particularly from surface soils. No information was available for the two other physicochemical properties influencing volatilization, i.e., the vapor-soil sorption coefficient and the vapor phase diffusion coefficient.

Experimental mass transfer coefficient (25°C) were determined for methyl ethyl ketone at several depths and mixing rates (1121). Volatilization half-lives calculated from the mass transfer coefficients ranged from 1.05 days for high mixing (2020 rpm) of a 15 cm aqueous solution to 2.25 days for low mixing (557 rpm) of a 20 cm aqueous solution. Lande et al. (1137) calculated an approximate half-life of 138 hours (5.75 days) for the evaporation (20°C) of methyl ethyl ketone from aqueous solution. It can be expected that the rate of volatilization may vary for aqueous environmental systems.

The significance of methyl ethyl ketone volatilization in the environment is not documented; data on volatilization from soils, in particular, are not available. Since methyl ethyl ketone is not strongly adsorbed to soil, some volatilization at the surface may occur; however, the ability of methyl ethyl ketone to be transported with soil water is significant. Furthermore, methyl ethyl ketone has been reported in rainwater samples (1136) suggesting that, due to its high water solubility, any methyl ethyl ketone lost due to volatilization may be washed out of the atmosphere and returned to the soil/water system.

41.2.2 Transformation Processes in Soil/Ground-water Systems

No information on the hydrolysis of methyl ethyl ketone in the soil/ground-water system was available; under normal environmental conditions, hydrolysis is not expected to occur at a rate competitive with volatilization or biodegradation. The portion of methyl ethyl

ketone that has been released from the soil into the air will either return to the soil via atmospheric washout or eventually undergo photochemical oxidation.

Methyl ethyl ketone is expected to be susceptible to extensive microbial biodegradation in pure cultures, mixed cultures, and activated sludge systems (1137). Several authors (1132,1133) have reported the biodegradation of methyl ethyl ketone by microbes grown on propane, or by soil bacteria grown on C1-C8 aliphatic hydrocarbons; oxidation was observed even where methyl ethyl ketone was unable to support growth of the organism. Methyl ethyl ketone degradation by one of four tested yeast cultures was also reported (1131).

After five days of incubation, degradation of methyl ethyl ketone, as determined by BOD_5 tests with acclimated sewage seed or microbes from polluted waters, ranged from 48% to 88%; degradation after 20 days was observed to be 69% to 89% (880,881,882,1127). Dojlido (1135) reported 100% degradation in 8 days for 200 mg/L methyl ethyl ketone and in 9 days for 400 mg/L. Chou et al. (1126) report 77% utilization of methyl ethyl ketone in an anaerobic reactor; the same authors report 100% anaerobic degradation by enriched methane cultures after an 8-day lag.

In actual soil/ground-water systems, the concentration of microorganisms capable of biodegrading methyl ethyl ketone may be low, and is expected to drop off sharply with increasing depth; prediction of biodegradation rates in the environment is not possible. However, in environments with sufficient microbial populations, methyl ethyl ketone is not expected to persist.

41.2.3 Primary Routes of Exposure from Soil/Ground-water Systems

The above discussion of fate pathways suggests that methyl ethyl ketone has a moderate volatility, is very weakly adsorbed to soil, and has no significant potential for bioaccumulation. This compound may volatilize from the soil surface, but that portion not removed by volatilization is likely to be mobile in ground water. These fate characteristics suggest several potential exposure pathways.

Volatilization of methyl ethyl ketone from a disposal site could result in inhalation exposure to workers or residents in the area. In addition, the potential for ground water contamination is high, particularly in sandy soils. It has been detected in ground water associated with hazardous waste sites. Mitre (83) reported that methyl ethyl ketone has been found at 10 of the 546 National Priority List (NPL) sites. It was detected at 4 sites in ground water, 4 in surface water, and 4 in air. However, it may not be commonly analyzed for at NPL sites as it is not a priority pollutant. These data, as well as the properties of methyl ethyl ketone, suggest that drinking water exposure from ground water contamination is likely to be its primary route of exposure from soil/ground-water systems.

The movement of methyl ethyl ketone in ground water may result in discharge to surface water. As a result, ingestion exposures may occur resulting from the use of surface waters as drinking water supplies, and dermal exposures may result from the recreational use of surface waters. Such exposures are likely to be lower than those from drinking contaminated ground water due to biodegradation and/or volatilization of methyl ethyl ketone in surface water. Any pathways related to the uptake by aquatic organisms or domestic animals from surface waters are likely to be less significant than other sources of exposure due to the low BCF for methyl ethyl ketone.

41.2.4 Other Sources of Human Exposure

Methyl ethyl ketone is widely used as a industrial solvent, coating, and adhesive. As such, there are a number of sources of human exposure. Data, however, are somewhat lacking. For example, it is not commonly measured in drinking water.

The production and use of methyl ethyl ketone has led to its presence in the atmosphere. Brodzinksy and Singh (84) summarized air monitoring data for a number of pollutants. For methyl ethyl ketone, they reported 181 data points for urban/suburban areas. All results for these samples were less than the detection limit. In source-dominated areas, the median concentration reported was 0.19 $\mu g/m^3$ for 33 data points.

Dermal exposure is expected to be common due to the prevalence of methyl ethyl ketone as a solvent in various products. For example, two surveys were conducted in Japan on the solvent content of a variety of products. They found methyl ethyl ketone in 26% of the paints, 21% of the inks, 23% of the adhesives, 11% of the thinners, and 8% of the degreasers that were sampled. While most of these products were used in occupational settings, some may be used by consumers (1140,1141).

The ketones are naturally occurring components of food. Lande et al. (1137) reviewed the literature and found methyl ethyl ketone in a wide variety of foods including cheese (0.3 ppm), milk (0.08 ppm), cream (0.2 ppm), bread, oranges and rum. This compound appears to be a common component of the diet although a total exposure from this source can not be evaluated without additional data (1137).

41.3 HUMAN HEALTH CONSIDERATIONS

41.3.1 Animal Studies

41.3.1.1 Carcinogenicity

No data were available with regard to the carcinogenic potential of methyl ethyl ketone.

41.3.1.2 Mutagenicity

Methyl ethyl ketone showed no evidence of mutagenicity when tested in TA1C2 and TA104 strains of Salmonella typhimurium (1001). It was shown to be marginally positive, at best, in a Chinese V-79 hamster cell assay which indicates the ability of compounds to inhibit gap junction-mediated intercellular communication (1013). Zimmerman (1011), using the diploid yeast strain D61.M of Saccharomyces cerevisiae, found methyl ethyl ketone strongly induced mitotic aneuploidy (having more or less than the normal number of chromosomes), but no other types of detectable genetic effects.

41.3.1.3 Teratogenicity, Embryotoxicity and Reproductive Effects

Schwetz et al. (1003) exposed pregnant Sprague-Dawley rats to 1000 or 3000 ppm of methyl ethyl ketone vapor in a chamber for 7 hours a day on days 6 through 15 of gestation. No evidence of maternal toxicity was observed. A retardation of fetal development and a significant increase in the number of anomalous skeletons (19% vs. 0 in the control group) were observed at both the 1000 and 3000 ppm treatment levels. Examination of the litters of the dams exposed to 3000 ppm methyl ethyl ketone revealed 2 fetuses with acaudia (no tails) and imperforated anus, and 2 fetuses with brachygnathia (shortened lower jaw). Though these unusual anomalies were not statistically significant, Schwetz did note that they had never before been observed in control animals in the Sprague-Dawley strain in his laboratory.

Due to a lack of dose-related response in the previous experiment, Deacon et al. (1005) duplicated the study in order to determine the repeatability of the unusual anomalies observed by Schwetz. Experimental design was identical. Exposure to 3000 ppm methyl ethyl ketone produced a slight maternal toxicity as shown by a decreased maternal weight gain. Minor anomalies in fetal development included an extra lumbar rib and delayed ossification of the cervical centra which were noted by Deacon to occur at low incidence historically among control rats in his laboratory. The findings presented in this follow-up study indicate that methyl ethyl ketone produced a slight fetotoxic effect at the 3000 ppm exposure level, but no embryotoxic or teratogenic response in rats.

41.3.1.4 Other Toxicologic Effects

41.3.1.4.1 Short-term Toxicity

Acute exposure to methyl ethyl ketone generally results in irritation to the eyes, nose and throat, CNS depression, emphysema and congestion of the liver and kidneys. The oral LD_{50} range for rats is reported to be 2.7-3.6 g/kg (47,13) while the reported LC_{50} value in the mouse is a two-hour exposure to 40,000 mg/m^3 methyl ethyl ketone (47).

Patty et al. (1028) describe the effects of airborn methyl ethyl ketone on guinea pigs at concentrations of 0.33, 1.0, 3.3 or 10.0% for up to 810 minutes. Signs of toxicity included irritation of the nose and eyes, incoordination, narcosis, gasping and death. Necropsy revealed emphysema, slight congestion of the brain and marked congestion of the systemic organs, particularly the lungs.

Exposure of guinea pigs to 10% methyl ethyl ketone vapor for 30 minutes resulted in opaque corneas. Examination eight days later showed that the eyes had returned to normal, indicating a reversibility of the damage (1028).

It has been well established that ketones as a class can cause narcosis at high concentrations (13,1029). However, it is believed (1012) that ketones may also be capable of producing a modification of behavior or impairment of judgement at lower concentrations. Geller et al. (1012) evaluated the effect of low-level methyl ethyl ketone exposure on delayed match-to-sample tasks in the baboon. Four juvenile baboons were exposed to 100 ppm methyl ethyl ketone, 24 hours a day for 7 days. Accuracy of performance was minimally affected. However, extra responses during the delay period were recorded and the response time was significantly increased. These effects were considered to be an early manifestation of the incoordination and narcosis which are observed at much higher concentrations.

Tham et al. (1006) demonstrated that a component of the equilibrium system, the vestibulo-ocular reflex (VOR), was depressed in rats when methyl ethyl ketone was infused into the circulatory system at a rate of 70 μM/kg/minute for 60 minutes, resulting in blood levels of 100 ppm. Nystagmus (a rapid, involuntary movement of the eye ball) was induced by accelerated rotation to study vestibular function. Depression of the VOR is considered an early sign of intoxication prior to the onset of a general depression of the central nervous system.

41.3.1.4.2 Chronic Toxicity

A subchronic inhalation study performed by Cavender et al. (1008) exposed male and female Fischer 344 rats to 1250, 2500 or 5000 ppm methyl ethyl ketone in a chamber for 6 hours/day, 5 days/week for 13 weeks. The only clinical observation was a decrease in mean body weight in the group receiving 5000 ppm methyl ethyl ketone. Increases in liver weight and liver to body weight ratios were noted in both males and females in the 5000 ppm group and a depression of brain weight in females in the 5000 ppm group at necropsy. No lesions were found that could be attributed to methyl ethyl ketone.

Methyl ethyl ketone has been shown to shorten the latency period for the onset of neurotoxic effects of methyl butyl ketone and n-hexane in a number of species. Altenkirch (1002) studied the response of the nervous system to chronic repeated exposures of 10,000 ppm pure hexane, 10,000 ppm methyl ethyl ketone/n-hexane (ratio of 1:9) or 6000 ppm pure methyl ethyl ketone in rats. Motor neuropathy with giant swelling of

axons in the peripheral and central nervous system, as well as severe potentiation of hexane neurotoxicity and shortened onset of morphological and clinical signs developed in animals exposed to the methyl ethyl ketone/hexane mixture. Motor impairment of the methyl ethyl ketone/hexane treated rats varied from a waddling gait and eversion of hind limbs to quadriplegia. Methyl ethyl ketone alone did not produce neuropathy. Rats exposed to extremely high concentrations of pure methyl ethyl ketone (6000-10,000 ppm), however, developed severe bronchopneumonia and died.

The potentiation effect of methyl ethyl ketone on hexane-induced neuropathy has also been observed with methyl butyl ketone (1029,1030). Rats intoxicated by continuous exposure to air containing methyl ethyl ketone and methyl butyl ketone vapor in a ratio of 1125:225 ppm developed clinical evidence of neuropathy after 25 days; rats inhaling 225 ppm methyl butyl ketone alone exhibited neuropathy after 66 days.

Methyl ethyl ketone potentiates the neurotoxic effects of methyl butyl ketone and hexane presumably by stimulating their metabolism to neurotoxic metabolites (1015). Both hexane and methyl butyl ketone share common products in their metabolic pathways, i.e., 2,5-hexanediol and 2,5-hexanedione. Hexanedione is believed to be the neurotoxic agent (1030,1014). Administration of hexane and methyl ethyl ketone together results in a significant increase in the activity of mixed-function oxygenase enzymes in rats (1004) and the urinary excretion of 2,5-hexanedione is increased after administration of the methyl ethyl ketone/methyl butyl ketone mixture to rats (1002). Furthermore, administration of 2,5-hexanedione produced effects indistinguishable from hexane or methyl butyl ketone neurotoxicity (1014).

41.3.2 Human and Epidemiologic Studies

41.3.2.1 Short-term Toxicologic Effects

Berg et al. (1016) reported a case of retrobular neuritis in an 18-year-old male exposed to methyl ethyl ketone while removing paint in an enclosed area. Symptoms included a dull headache, mild vertigo and diminished vision in both eyes. Ophthalmic examination and testing 2 hours later revealed marked enlargment of the blind spot and superior arcuate-type defects in both eyes. Blood analysis showed the presence of methanol and formaldehyde. Thirty-six hours after exposure, vision returned to normal. Berg postulated that the patient had suffered optic nerve toxicity induced by methanol formed from the metabolism of methyl ethyl ketone.

Munies and Wurster (1031) demonstrated that methyl ethyl ketone in contact with the skin resulted in a partial dehydration of the stratum corneum. Wahlberg (1009) showed that the spontaneous transient whitening of the skin caused by excessive exposure to methyl ethyl ketone is due to a change in structure and the removal of the skin lipids rather than by vasoconstriction.

41.3.2.2 Chronic Toxicologic Effects

Smith and Mayer (1032) investigated the effects of methyl ethyl ketone on a group of factory workers using methyl ethyl ketone as a solvent. Routes of exposure included both immersion of bare hands in the solvent and inhalation of 300-600 ppm. No duration of exposure was given. A number of workers developed severe dermatitis. Several workers also experienced numbness in the fingers, arms and legs. Symptoms disappeared when exposure to methyl ethyl ketone was discontinued.

The potentiation of various hexacarbon neuropathies by methyl ethyl ketone is of particular interest in cases of solvent abuse. Altenkirch (1033) reported 25 cases of clinically severe toxic polyneuropathy in people addicted to inhaling methyl ethyl ketone-containing solvents. The peripheral motor defects took 2.5-3 years to become apparent. The effects were considered to be due to an axonal transmission disorder which destroyed peripheral and central axons (0049).

Altenkirch (1004) also described what was known as the Berlin Poisoning Affair. In 1974, a solvent manufacturer changed its formulation to help stop inhalation abuse. The hexane content was reduced from 31 to 16% and 11% methyl ethyl ketone was added as a denaturant. An epidemic-like outbreak of 19 severe neuropathy syndromes occurred soon after the new formulation was available to the public. Neurological effects included considerable weight loss, muscular weakness affecting all four extremities or paralysis of all four extremities, extreme muscular atrophy, and respiratory disorders. In some cases, visual disturbances occurred and facial nerves were affected. Individuals examined up to 4 years after the incident still exhibited muscular atrophy, muscular weakness and sensory defects. This incident further supports findings that the neurotoxic properties of hexane can be potentiated by methyl ethyl ketone.

A female shoe-factory worker developed sensorimotor neuropathy after years of working with a glue containing 20% methyl ethyl ketone and 8% hexane (1007). The woman developed sensory and motor neuropathy in the lower limbs, and the absence of deep reflexes. This condition slowly regressed once exposure to the solvent mixture ceased.

41.3.3 Levels of Concern

The EPA (1770) has established a Health Advisory for noncarcinogenic risk for long-term exposure to methyl ethyl ketone of 8.6 mg/L in drinking water.

The OSHA (298) standard is 200 ppm (590 mg/m^3) averaged over an 8-hour work-shift. The ACGIH (3) recommends a threshold limit value of 200 ppm, with a short-term exposure limit of 300 ppm (885 mg/m^3). The threshold limit value was set to prevent injurious effects and minimize complaints about odor and irritation (46).

41.3.4 Hazard Assessment

Methyl ethyl ketone exhibits a low toxicity subsequent to acute and chronic exposures. The oral LD_{50} value for rats is in the 2.7 to 3.6 g/kg range (47,13); the inhalation LC_{50} for mice for a two hour exposure is 40,000 mg/m^3 (47). At high concentrations (e.g., 10% in air), methyl ethyl ketone can induce narcosis (1028) but low level chronic exposure (2500 ppm for 90 days) produced no adverse effects in rats (1008).

Exposure to methyl ethyl ketone can produce local irritation of the eyes, upper respiratory tract and skin (1016,1031,1032). If splashed into the eyes, painful irritation and corneal injury may result (1028). Direct skin contact may produce dermatitis and defat the skin (1032,1009). Short-term human exposure to methyl ethyl ketone can produce headache, eye and throat irritation.

Studies in both humans and animals indicate that methyl ethyl ketone potentiates (i.e., shortens the time of onset) of peripheral neuropathy caused by either n-hexane or methyl n-butyl ketone. Methyl ethyl ketone itself does not induce peripheral neuropathy (1002,1029,1030).

The reproductive, mutagenic and carcinogenic activity of methyl ethyl ketone have not been thoroughly investigated and require further research. Female rats exposed via inhalation to over 1000 ppm methyl ethyl ketone resulted in fetotoxic effects. A low incidence of malformations was observed in one study (1003) but could not be duplicated using an identical experimental design (1005), suggesting that methyl ethyl ketone produces minor fetotoxic effects but is not a teratogen in rats.

Conflicting data are available regarding the mutagenicity of methyl ethyl ketone. Negative results were obtained in an Ames assay (1001), a marginally positive response at best in a Chinese V-79 hamster cell test (1013) and a strongly positive induction of aneuploidy in a yeast test (1011). There are no data available on the carcinogenic activity of methyl ethyl ketone.

41.4 SAMPLING AND ANALYSIS CONSIDERATIONS

Determination of the concentration of methyl ethyl ketone in soil and water requires collection of a representative field sample and laboratory analysis. Due to the volatility of methyl ethyl ketone, care is required to prevent losses during sample collection and storage. Soil and water samples are collected in airtight containers with no headspace; analysis should be completed within 14 days of sampling. In addition to the targeted samples, quality assurance samples such as field blanks, duplicates, and spiked matrices should be included in the analytical program.

Methyl ethyl ketone is not included among the EPA-designated priority pollutants. However, EPA Methods 624, 1624 (65) 8015 and 8240 (63) would be appropriate methods of choice for the analysis of methyl ethyl ketone in aqueous samples. An inert gas is bubbled through the aqueous sample in a purging chamber at ambient temperature, transferring the methyl ethyl ketone from the aqueous phase to the vapor phase and onto a sorbent trap. The trap is then heated and backflushed to desorb the methyl ethyl ketone and transfer it onto a gas chromatographic (GC) column. The GC column is programmed to separate the volatile organics; methyl ethyl ketone is then detected with a flame ionization detector (Method 8015) or a mass spectrometer (Methods 624, 1624, and 8240).

The EPA procedures recommended for methyl ethyl ketone analysis in soil and waste samples, Methods 8015 and 8240 (63), differ from the aqueous procedures primarily in the method by which the analyte is introduced into the GC. The recommended method involves dispersing the soil or waste sample in methanol or polyethylene glycol to dissolve the methyl ethyl ketone. A portion of the solution is then combined with water and purged as described above. Other sample introduction techniques include direct injection and a headspace method.

Methyl ethyl ketone detection limits for the various methods were not determined but would be in the range of 1-50 $\mu g/L$ for aqueous samples and 1 $\mu g/g$ for non-aqueous samples.

COMMON SYNONYMS:	CAS REG. NO.:	FORMULA:	AIR W/V CONVERSION FACTORS at 25°C (12)
2-Methoxyethanol Ethylene glycol monomethyl ether Ethylene glycol methyl ether Methyl glycol EGME	109-86-4 NIOSH NO.: KL5775000	$C_3H_8O_2$	3.11 mg/m³ ≈ 1 ppm 0.322 ppm ≈ 1 mg/m³
	STRUCTURE: $HO-CH_2-CH_2-O-CH_3$		MOLECULAR WEIGHT: 76.1

REACTIVITY	The NFPA reports that contact of air with Methyl Cellosolve® forms peroxides that are highly explosive. NIOSH reports that contact with strong oxidizing agents may cause fires and/or explosions and that contact with strong caustics may cause decomposition. For compatibility classification purposes, Methyl Cellosolve® is considered to have attributes of both glycols and ethers. Reactions of glycols with non-oxidizing mineral acids typically generate heat, while those with oxidizing mineral acids, organic peroxides or hydroperoxides, or other strong oxidizing agents may evolve heat and fire. Those with organic acids, isocyanates, or epoxides may initiate violent polymerization, while reactions with alkali or alkaline earth elemental metals or strong reducing agents may evolve heat, flammable gases and fire. Reactions with nitrides may produce heat, flammable gases, and an explosion, while those with azo or diazo compounds or hydrazines may generate heat and generally innocuous gases. Reactions of ethers with mineral acids or strong oxidizing agents are listed as producing effects similar to those of glycols with these sunstances (38,505,511).

PHYSICO-CHEMICAL DATA	• Physical State (at 20°C): liquid	(45)
	• Color: colorless	(45)
	• Odor: mild, pleasant	(45)
	• Odor Threshold: 60 ppm	(2)
	• Liquid Density (g/ml at 20°C): 0.97459	(21)
	• Freezing/Melting Point (°C): -85	(21)
	• Boiling Point (°C): 124	(21)
	• Flash Point (°C): 38.9-41.7 (cc); 48.9 (oc)	(60,506,507)
	• Flammable Limits in Air, % by Volume: 2.5% (1.8% at STP) - 19.8% (14% at STP)	(38,60, 506)
	• Autoignition Temperature (°C): 285-288.3	(38,60,506)
	• Vapor Pressure (mm Hg at 20°C): 6	(2)
	• Saturated Concentration in Air (mg/m³ at 20°C): 25,000	(ADL estim)
	• Solubility in Water (mg/L at 20°C): miscible in all proportions	(38)
	• Viscosity (cp at 20°C): no data	( )
	• Surface Tension (dyne/cm at 20°C): 3.3 x 10^5	(60)

PHYSICO-CHEMICAL DATA (Continued)	• Log (Octanol-Water Partition Coefficient), log K_{ow}: -0.77 (29) • Soil Adsorption Coefficient, K_{oc}: 0.08 (611) • Henry's Law Constant ($atm \cdot m^3/mol$ at 20°C): 8×10^{-9} estim. (966) • Bioconcentration Factor: 0.008 (659)
PERSISTENCE IN THE SOIL-WATER SYSTEM	Methyl Cellosolve® is expected to be mobile in the soil/ground-water system due to its weak sorption on soils and high water solubility. Volatilization may occur at the surface but is expected to be of minimal importance whenever water is present. Data on biodegradation are inconclusive.
PATHWAYS OF EXPOSURE	The primary pathway of concern from a soil/ground-water drinking system is the migration of Methyl Cellosolve® to ground-water drinking water supplies, although no data confirm this. Inhalation or bioaccumulation of Methyl Cellosolve® from surface waters or soils are not likely to be important exposure pathways.
HEALTH HAZARD DATA	Signs and Symptoms of Short-term Human Exposure (12,38,54): Acute exposure by inhalation to Methyl Cellosolve® generally results in narcosis, pulmonary edema and severe liver and kidney damage. Poisoning by ingestion resembles ethylene glycol toxicity, possibly resulting in renal failure and death.
	Toxicity Based on Animal Studies: LD_{50} (mg/kg): oral 2460 [rat] (51); skin 1280 [rabbit] (51) LC_{50} (ppm): inhalation [mouse] (59) 1480•7 hr
	Long-Term Effects: Hematological and neurological effects
	Pregnancy/Neonate Data: Testicular atrophy, teratogenicity, fetotoxicity
	Mutation Data: Negative
	Carcinogenicity: No data
HANDLING PRECAUTIONS (54)	Handle chemical only with adequate ventilation • Vapor concentration of 250 ppm or less: any supplied-air respirator or self-contained breathing apparatus • Vapor concentrations of 250-1250 ppm: any supplied-air respirator or self contained breathing apparatus with full facepiece • Vapor concentrations of 1250-2000 ppm: type C supplied-air respirator with full facepiece operated in pressure-demand mode.

EMERGENCY FIRST AID TREATMENT (54)	Ingestion: Do not induce vomiting if victim is conscious. Get medical attention immediately • Inhalation: Move victim to fresh air immediately and perform artificial respiration if necessary • Skin: Remove contaminated clothing immediately and wash with water • Eye: Irrigate with large amounts of water immediately.

ENVIRONMENTAL AND OCCUPATIONAL STANDARDS AND CRITERIA

AIR EXPOSURE LIMITS:

Standards
- OSHA PEL (8-hr TWA): 25 ppm
- AFOSH PEL (8-hr TWA): 25 ppm

Criteria
- NIOSH IDLH (30-min): 2000 ppm
- ACGIH TLV® (8-hr TWA): 5 ppm (skin)
- ACGIH STEL (15 min): none established

WATER EXPOSURE LIMITS:

Drinking Water Standards - None established

EPA Health Advisories - None established

EPA Ambient Water Quality Criteria (355)
- Human Health
  No criterion established, Methyl Cellosolve® is not a priority pollutant.
- Aquatic Life
  No criterion established, Methyl Cellosolve® is not a priority pollutant.

REGULATORY STATUS (as of January 1, 1987)

Promulgated Regulations

- Federal Programs

  Federal Insecticide, Fungicide and Rodenticide Act (FIFRA)
  Methyl Cellosolve® is exempt from a tolerance requirement when used as a solvent for formulations used before crops emerge from the soil (315).

  Marine Protection Research and Sanctuaries Act (MPRSA)
  Ocean dumping of organohalogen compounds as well as the dumping of known or suspected carcinogens, mutagens or teratogens is prohibited except when they are present as trace contaminants. Permit applicants are exempt from these regulations if they can demonstrate that such chemical constituents are non-toxic and non-bioaccumulative in the marine environment or are rapidly rendered harmless by physical, chemical or biological processes in the sea (309).

  Occupational Safety and Health Act (OSHA)
  Employee exposure to Methyl Cellosolve® shall not exceed an 8-hour time-weighted-average (TWA) of 25 ppm (298).

  Hazardous Materials Transportation Act (HMTA)
  The Department of Transportation has designated Methyl Cellosolve® as a hazardous material which is subject to requirements for packaging, labeling and transportation (306).

  Food, Drug and Cosmetic Act (FDCA)
  Methyl Cellosolve® is approved for use as an indirect food additive (362).

- State Water Programs
  There are no specific state regulations for Methyl Cellosolve®.

Proposed Regulations

- Federal Programs

  Occupational Safety and Health Act (OSHA)
  OSHA has determined that the existing PEL for Methyl Cellosolve® is inadequate to protect workers from significant health risks and will propose a revised standard at a later date (1235).

- State Water Programs
  No proposed regulations are pending.

EEC Directives

Directive on Ground Water (538)

Direct discharge into ground water (i.e., without percolation through the ground or subsoil) of organophosphorous compounds, organohalogen compounds and substances which may form such compounds in the aquatic environment, substances which possess carcinogenic, mutagenic or teratogenic properties in or via the aquatic environment and mineral oils and hydrocarbons is prohibited. Appropriate measures deemed necessary to prevent indirect discharge into ground water (i.e., via percolation through ground or subsoil) of these substances shall be taken by member countries.

Directive Relating to the Classification, Packaging and Labeling of Dangerous Preparations (Solvents) (544)

Methyl Cellosolve® is listed as a Class II/c harmful substance and is subject to packaging and labeling regulations.

Directive on Marketing and Use of Dangerous Substances (541)

Methyl Cellosolve® may not be used in ornamental objects intended to produce light or color effects by means of different phases.

Directive on Toxic and Dangerous Wastes (542)

Any installation, establishment, or undertaking which produces, holds and/or disposes of certain toxic and dangerous wastes including phenols and phenol compounds; organic-halogen compounds; chrome compounds; lead compounds; cyanides; ethers and aromatic polycyclic compounds (with carcinogenic effects) shall keep a record of the quantity, nature, physical and chemical characteristics and origin of such waste, and of the methods and sites used for disposing of such waste.

Directive on the Classification, Packaging and Labeling of Dangerous Substances (787)

Methyl Cellosolve® is classified as a harmful substance and is subject to packaging and labeling regulations.

42.1 MAJOR USES

Methyl Cellosolve® is an industrial solvent used primarily in the aviation industry. Approximately 47% of the Methyl Cellosolve® produced is used as a jet fuel anti-icing additive. The remainder is used for resins, lacquers, paints, varnishes, gum, perfume, dyes and inks and as a constituent of cleaning compounds, liquid soaps, cosmetics and hydraulic fluids (2,54,59).

42.2 ENVIRONMENTAL FATE AND EXPOSURE PATHWAYS

42.2.1 Transport in Soil/Ground-water Systems

42.2.1.1 Overview

Methyl Cellosolve® is expected to be highly mobile in the soil/ground-water system when present at relatively low concentrations or as a separate organic phase (resulting from a spill of significant quantities of the chemical). In general, transport pathways can be assessed by using an equilibrium partitioning model, as shown in Table 42-1. These calculations predict the partitioning of low soil concentrations of Methyl Cellosolve® among soil particles, soil water and soil air. Portions of Methyl Cellosolve® associated with the water and air phases of the soil have higher mobility than the adsorbed portion.

Estimates for the unsaturated topsoil model indicate that 1.5% of the Methyl Cellosolve® is expected to be sorbed onto soil particles. Approximately 98.5% is expected to partition to the mobile soil-water phase, and is thus available to migrate by bulk transport (e.g., the downward movement of infiltrating water), dispersion and diffusion. Since an insignificant portion of the Methyl Cellosolve® is expected to be in the gaseous phase of the soil (0.0001%), diffusion through the soil-air pores up to the ground surface and subsequent removal by wind would appear to be a minor loss pathway. In saturated, deep soils (containing no soil air and negligible soil organic carbon), almost all of the Methyl Cellosolve® (99.97%) is predicted to be present in the soil-water phase (Table 42-1) and available for transport with flowing ground water. Sorption onto deep soils (0.03%) is not expected to be significant. Overall, ground water underlying Methyl Cellosolve® contaminated soils with low organic content is expected to be vulnerable to contamination.

42.2.1.2 Sorption on Soils

The mobility of Methyl Cellosolve® in the soil/ground-water system (and its eventual migration into aquifers) is controlled by the extent of its sorption onto soil particles. Methyl Cellosolve® is miscible in water and, as evidenced by its negative log K_{ow} and low K_{oc}, adsorption to soil/sediments is not expected to significantly influence its environmental fate.

TABLE 42-1

EQUILIBRIUM PARTITIONING CALCULATIONS FOR METHYL CELLOSOLVE® IN MODEL ENVIRONMENTS[a]

Soil Environment	Estimated Percent of Total Mass of Chemical in Each Compartment		
	Soil	Soil-Water	Soil-Air
Unsaturated topsoil at 25° C[b,c]	1.5	98.5	1×10^{-4}
Saturated deep soil[d]	0.03	99.97	-

a) Calculations based on Mackay's equilibrium partitioning model (34,35,36); see Introduction in Volume 1 for description of model and environmental conditions chosen to represent an unsaturated topsoil and saturated deep soil. Calculated percentages should be considered as rough estimates and used only for general guidance.

b) Utilized soil sorption estimated with equations of Means et al. (611): $K_{oc} = 0.08$.

c) Henry's law constant taken as 8×10^{-9} atm·m³/mol at 25°C estimated according to method of Hine and Mookerjee (966).

d) Sorption coefficient calculated as a function of K_{oc} assuming 0.1% organic carbon: $K_p = 0.001 \times K_{oc}$.

No data specific to sorption of Methyl Cellosolve® on soils were available. However, behavior of Methyl Cellosolve® is expected to be similar to that of ethylene glycol or acetone which both migrate freely through the soil/ground-water system with little or no retardation (862,1122).

42.2.1.3 Volatilization from Soils

Transport of Methyl Cellosolve® vapors through the air-filled pores of unsaturated soils may occur in near-surface soils. However, modeling results suggest that only a small fraction of the Methyl Cellosolve® loading will be present in the soil-air phase.

In general, important soil and environmental properties influencing the rate of volatilization include soil porosity, temperature,

convection currents and barometric pressure changes; important physicochemical properties include the Henry's law constant, the vapor-soil sorption coefficient, and, to the lesser extent, the vapor phase diffusion coefficient (31).

Data on Methyl Cellosolve® volatilization from soils, in particular, are not available. Methyl Cellosolve® is not strongly adsorbed to soil and is highly soluble in water. Although some volatilization may occur at the surface, the low value estimated for the Henry's law constant (8×10^{-9} atm•m^3/mole) suggests that vapor concentrations will be low whenever water is present and volatilization will be minimal.

42.2.2 Transformation Processes in Soil/Ground-water Systems

No information was available on the non-biological degradation of Methyl Cellosolve® under environmental conditions.

The data on microbial degradation of Methyl Cellosolve® in pure cultures are limited and inconclusive (859,861). Degradation using activated sludge and acclimated sewage seed has been reported to be fairly significant with BOD_5 values ranging from 7% to 65% (880,860, 881,882).

Based on the limited data available, prediction of biodegradation rates in the environment is not possible. Furthermore, in most soil/ground-water systems, the concentrations of microorganisms capable of biodegrading Methyl Cellosolve® may be low, and drop off sharply with depth. Thus, biodegradation may be of minimal importance except, perhaps, near landfills with active microbiological populations.

42.2.3 Primary Routes of Exposure from Soil/Ground-water Systems

The above discussion of fate pathways suggests that Methyl Cellosolve® is effectively nonvolatile, is very weakly adsorbed to soil, and has no significant potential for bioaccumulation. These fate characteristics suggest several potential exposure pathways.

The potential for ground water contamination with Methyl Cellosolve® is high, particularly in sandy soils. It has not been reported in ground water associated with hazardous waste sites, but the properties of Methyl Cellosolve® suggest the drinking water exposure from ground water contamination is likely to be its primary route of exposure from soil/ground-water systems.

The movement of Methyl Cellosolve® in ground water may result in discharge to surface water. As a result, ingestion exposures may occur resulting from the use of surface waters as drinking water supplies, and dermal exposures may result from the recreational use of surface waters. Such exposures are likely to be lower than those from drinking contaminated ground water due to degradation of Methyl Cellosolve® in surface water. Any pathways related to the uptake by aquatic organisms

or domestic animals from surface waters are likely to less significant than other sources of exposure due to the low BCF for Methyl Cellosolve®.

42.2.4 Other Sources of Human Exposure

Methyl Cellosolve® is used as a solvent in a variety of products and as a constituent of printing pastes, cleaning compounds, liquid soaps and cosmetics. As such, there are likely to be a number of sources of human exposure.

Dermal exposure, in particular, is possible in some situations due to the use of Methyl Cellosolve® in these products. For example, two surveys were conducted in Japan on the solvent content of a variety of products. They found Methyl Cellosolve® in 4% of the inks, 1% of the adhesives and 3% of the thinners that were sampled. While most of these products were used in occupational settings, some may be used by consumers (1140,1141).

42.3 HUMAN HEALTH CONSIDERATIONS

42.3.1 Animal Studies

42.3.1.1 Carcinogenicity

No data were found.

42.3.1.2 Mutagenicity

Methyl Cellosolve® did not produce mutagenic effects when tested in strains TA1535, TA1537, TA98 and TA100 of Salmonella typhimurium, both with and without metabolic activation (1060). It did, however, block junction-mediated intercellular communication in Chinese hamster V-79 cells (1061).

Exposure of male and female rats to 500 ppm Methyl Cellosolve® vapor for 7 hours a day for 5 days failed to reveal any significant increase in chromosome aberrations in bone marrow cells (1284). Also no increase in unscheduled DNA synthesis was observed in human cell lines when up to 10 mg/mL Methyl Cellosolve® was added to the culture (1284).

A dominant lethal study in rats was conducted by McGregor (1285). Results from exposure to 500 ppm Methyl Cellosolve® vapor for 7 hours per day on 5 consecutive days were inconclusive. Pregnancy frequencies and total implantations per female were not significantly different from those of controls at weeks 1 and 2, but were greatly reduced at weeks 3 and 4 and totally absent at week 5. Due to a profound decrease in male fertility, it was not possible to detect an increase in early fetal deaths indicative of a true dominant lethal effect. Exposure at a level of 25 ppm produced no reduction in the above parameters.

42.3.1.3 Teratogenicity, Embryotoxicity and Reproductive Effects

Methyl Cellosolve® causes both teratogenic and adverse male reproductive effects in several species. The effect of Methyl Cellosolve® vapor on pregnant rats was evaluated by Nelson et al. (1059). Sprague-Dawley rats were exposed to 0, 50, 100 or 200 ppm of Methyl Cellosolve® vapor for 7 hours/day on days 7-15 of gestation. No signs of maternal toxicity were observed. Fetuses were examined on day 20. Methyl Cellosolve® was highly embryotoxic at all treatment levels with an increase in resorption and reduced fetal weight occurring at both the 50 and 100 ppm level. Complete fetal resorption occurred at the 200 ppm level. Heart abnormalities were the predominant malformation observed in both the 50 and 100 ppm groups. Other terata occurring at a lower frequency affected the retina, the eyes, the umbilicus and the lungs. Skeletal aberrations at both the 50 and 100 ppm levels included wavy, fused and absent ribs, and extra vertebrae. Tail malformations were also observed in the 100 ppm group (1059).

Groups of 24-32 pregnant Fischer 344 rats, CF-1 mice and New Zealand white rabbits were exposed to 0, 50, 200 or 400 ppm Methyl Cellosolve® vapor for 6 hours/day on days 6-15 (rats and mice) or on days 6-18 (rabbits) of gestation. Complete embryolethality resulted at the 200 and 400 ppm levels. Mice were then exposed to 0, 10 or 50 ppm Methyl Cellosolve® vapor, while rats and rabbits were exposed to 0, 3 10 or 50 ppm Methyl Cellosolve® vapor during the period of major organogenesis. Methyl Cellosolve® was not teratogenic in Fischer 344 rats exposed to concentrations of up to 50 ppm for 6 hours/day, although a slight fetotoxic effect was observed at the 50 ppm level as shown by a statistically significant increase in the incidence of lumbar spurs (57 vs. 18 in the control group) and a delayed vertebrae centra ossification (19 vs. 4 in the control group). No teratogenic response was observed in the CF-1 mice at any treatment level, however, there was an indication of fetotoxicity at the 50 ppm level. Minor fetal effects at this level included an increased incidence of extra lumbar ribs (82 vs. 48 in the control groups) and an increased incidence of unilateral testicular hypoplasia (8 vs. 2 in the control group). Rabbits exposed to 50 ppm experienced a significant increase in the resorption rate (24 vs. 4 in the control groups). Also, mean fetal body weight in this group was significantly reduced (35.88 vs. 39.57 in the control groups). At this level, all organ systems in the rabbit were involved in a significant incidence of malformations. The most frequent major malformations included arthrogryposis (persistent joint contracture), anonychia (absence of nails), brachydatyly (shortness of digits) and ectrodactyly (absence of digits). Forty-three percent of the fetuses had ventricular septal defects, 16% of which exhibited a constriction of the aortic arch. Severe splenic hypoplasia was evident and in several cases, the spleen was nearly invisible. Low incidences of other malformations, such as, missing bones of the paws, and extra, shortened, fused, forked or calloused ribs were also considered terata induced by 50 ppm Methyl Cellosolve® in the rabbit. No effects were reported in fetuses of rabbits exposed to the 3 or 10 ppm levels (1062).

Nagano et al. (1063) investigated the effects of Methyl Cellosolve® ingestion upon fetal development in mice. Pregnant JCL-ICR mice were given 31.25, 62.5, 125, 250, 500 or 1000 mg of Methyl Cellosolve®/kg of body weight/day by gastric intubation on days 7-14 of gestation. A decrease in maternal body weight gain was observed in the 250, 500 and 1000 mg/kg groups. The 1000 mg/kg group also exhibited a significant decrease in the white blood cell count. All fetuses in the 1000 mg/kg group were dead and only one fetus survived in the 500 mg/kg group. This fetus had exencephaly and abnormal digits. There was a significant reduction in fetal weight at both the 125 and 250 mg/kg doses. Exencephaly, abnormal digits and umbilical hernias were the major gross abnormalities observed in the 250 mg/kg group. The incidence of oligodactyly (less than usual number of digits) was statistically significant in the 250 mg/kg group (17 cases). Syndactyly (webbing between adjacent digits) was observed in 9 fetuses in the 250 mg/kg group, but was not considered to be statistically significant. All examined fetuses of the 250 mg/kg group had skeletal malformations including fused and/or poorly developed ribs and vertebrae, and spine bifida occulta. In the 125 mg/kg group, 51.12% of the fetuses exhibited these same types of malformations. Similar but not statistically significant malformations were also observed in the 31.25 and 62.5 mg/kg groups. All skeletal effects followed a dose-dependent trend. Nagano et al. concluded that Methyl Cellosolve® was capable of producing teratogenic effects in mice although only mild maternal toxicity was observed.

The male reproductive system is also adversely affected by Methyl Cellosolve®. Rao et al. (1056) exposed groups of male and female Sprague-Dawley rats to 0, 30, 100 or 300 ppm Methyl Cellosolve® vapor for 6 hours/day, 5 days/week for 13 consecutive weeks. At the end of the exposure period, rats were allowed to breed with unexposed rats. The mean body weights of male rats treated with 300 ppm of Methyl Cellosolve® were significantly decreased throughout the study. Female rats exposed to 300 ppm of Methyl Cellosolve® also showed a statistically significant decrease in body weight beginning on the seventh week of exposure. No decrease in fertility was observed among any of the treated females. Male fertility was based on the ability to impregnate unexposed females. There was no apparent effect on mating behavior, however, the fertility indices of the male rat exposed to 300 ppm were significantly decreased (20% vs. 97%). Only 4 of 20 females were impregnated and all 4 impregnations resulted in complete resorption. These males were bred again at 13 and 19 weeks post-exposure. Fertility was still decreased during these breeding periods, however, 50% of the males previously exposed to 300 ppm Methyl Cellosolve® sired litters in which the majority of implantations appeared viable (1056).

In order to determine the nature of the infertility observed in males, male F344 rats were given 150 mg/kg/day Methyl Cellosolve® in distilled water perorally 5 days/week. Animals were sacrificed 1, 2, 4, 7 and 10 days after the first dose and testicular tissue was examined. By the fourth day, the spermatid population decreased in affected tubules as the precursor spermatocytes died. Effects appeared

to be specific for the spermatocyte stage of development and resulted in a depletion of the spermatid population which was not being replenished. Analysis of several indices of sertoli cell function were examined and found to be unaffected by Methyl Cellosolve®. Chapin et al. (1057) concluded that the spermatocytes were the first cells to undergo necrotic changes after treatment of F344 rats with Methyl Cellosolve®.

Foster et al. (1058) administered 50, 100, 250 or 500 mg/kg/day of Methyl Cellosolve® by gavage to rats (strain not specified). Six animals from each treatment group were killed 6 and 24 hours after the first dose. Other animals from each treatment group were killed on days 2, 4, 7 and 11. Another group of animals were given 500 mg/kg/day of Methyl Cellosolve® for 4 days. Rats were then killed at 0, 2, 4 and 8 weeks post-ingestion. A decrease in testicular weight was observed in the 500 mg/kg/day treatment group on day 2 of testing, which became more pronounced as time progressed. By day 7, testes weights for both the 250 mg and the 500 mg groups were significantly less than the control weights. Histological examination again revealed degeneration of the spermatocytes, but in this case, damage was evident 24 hours after a single treatment of 100, 250 or 500 mg/kg/day and necrosis progressed in a dose-related fashion. By day 11, treatment with 250 or 500 mg/kg/day had resulted in a cessation of the sperm maturation process. Testis weight did not begin to recover until 2 weeks after the last treatment and testes weights did not reach control levels until 8 weeks after the last treatment was given (1058).

The major metabolite of Methyl Cellosolve® is methoxyacetic acid (MAA) which accounts for 73.1% of the Methyl Cellosolve® metabolites in the urine. In vivo experiments with MAA induced identical testicular lesions as was seen with Methyl Cellosolve®. There was a decrease in testes weight associated with testicular cell damage. The degree of degeneration was dose-related. The testicular lesions were reversible in a large number of tubules once treatment had ceased. In addition, alcohol dehydrogenase inhibited Methyl Cellosolve® metabolism and provided complete protection against any degenerative effects on the testes. This information suggests that Methyl Cellosolve® is not responsible for testicular damage, but rather its metabolite MAA that causes the damage (1058).

A recent study by Rawlings et al. (1287) reported that MAA is also teratogenic to rat embryos in culture. Structural defects occurred in 67% of the conceptuses exposed to 2 mM MAA and 100% of the conceptuses exposed to 5 mM MAA. All of the 5 mM-treated embryos had infused brain folds. Based on this and other research (1076), MAA may be a key factor in the teratogenic effects associated with Methyl Cellosolve® exposure.

42.3.1.4 Other Toxicologic Effects

42.3.1.4.1 Short-term Toxicity

In addition to the adverse reproductive effects of Methyl Cellosolve®, the blood and nervous system are prime targets of toxicity. Anemia, abnormal leucocytes, kidney damage and metabolic acidosis are signs associated with Methyl Cellosolve® poisoning. The oral LD_{50} is listed as 2460 mg/kg for rats and 2.8 g/kg for mice (1251). The LC_{50} for mice inhaling Methyl Cellosolve® for 7 hours is 1480 ppm (59).

Heinonen and Vainio (1065) studied the dose-dependent toxicity of Methyl Cellosolve® vapor on the liver and kidney of the rat. Male Wistar rats were exposed to 50, 100 or 400 ppm of Methyl Cellosolve® for 6 hours/day, 5 day/week for 1 or 2 weeks. NADPH cytochrome c reductase activity showed a significant dose-related decrease in the liver, while UDP-glucuronosyl transferase activity showed a significant dose-related increase. Glutathione levels showed a dose-related increase in the liver and kidneys. Oxalate crystals were present in the renal tubules. Heinonen and Vainio speculated that the calcium oxalate and the resultant metabolic acidosis was possibly the result of the decomposition of Methyl Cellosolve® to methanol and ethylene glycol.

Male and female Fischer 344 rats and B6C3F1 mice were exposed to 0, 100, 300 or 1000 ppm Methyl Cellosolve® vapor for 6 hours/day on 5 consecutive days followed by 4 additional consecutive exposures after a 2 day interruption (9 exposures in an 11 day interval) (1066). Growth of both the male and female rats in the 1000 ppm Methyl Cellosolve® group was significantly retarded. The mean body weight gains of female rats in the 100 and 300 ppm groups were significantly lower than the controls. The packed cell volume, red and white blood cell counts and hemoglobin of both male and female rats in the 1000 ppm Methyl Cellosolve® group were significantly decreased over the controls. Significant, but less severe alterations of the hematological parameters were observed in the groups of rats and mice exposed to 300 ppm Methyl Cellosolve®. Rats exposed to 1000 ppm Methyl Cellosolve® exhibited severe degeneration of the germinal epithelium in the testes, severe lymphoid depletion in the cortex of the thymus and a reduced number of lymphoid cells in the spleen and mesenteric lymph nodes. Effects were similar but less severe in the 300 ppm groups, while no treatment-related changes were observed in the 100 ppm groups. A markedly reduced bone marrow cellularity, shown by a drastically reduced number of myeloid and erythroid cells and a slight increase in immature cells was also observed. The tissues primarily affected by Methyl Cellosolve® all have a relatively high rate of cell division which suggests that Methyl Cellosolve® many produce its toxic effects

by inhibiting mitotic processes. However, since all tissue with a high rate of cellular division are not affected, Methyl Cellosolve®-target organ specificity must involve other factors.

Romer et al. (1070) found that administration of Methyl Cellosolve® in combination with ethanol to rats produced an accumulation of Methyl Cellosolve® in the blood stream. Both Methyl Cellosolve® and ethanol are believed to compete for the metabolizing enzyme, alcohol dehydrogenase (ADH). The affinity of ADH for ethanol is greater than its affinity for Methyl Cellosolve®. This results in a metabolism of the ethanol but an inhibition of the degradation of Methyl Cellosolve®.

42.3.1.4.2 Chronic Toxicity

Miller et al. (1067) exposed Sprague-Dawley rats and New Zealand white rabbits to 0, 30, 100 or 300 ppm Methyl Cellosolve® vapor 6 hours/day, 5 days/week for 13 weeks. Mean body weight of both rats and rabbits exposed to 300 ppm were significantly lower than the control animals. In rats, gross lesions attributed to Methyl Cellosolve® exposure occurred at the 300 ppm level only. There was a decrease in thymus size and weight, small flaccid testes in the males and a decrease in abdominal adipose tissue in some of the females. In rabbits, the males appeared to be affected at all 3 exposure levels while female rabbits were affected at only the 100 and 300 ppm levels. Effects were similar to those observed in the rat, however, they were more severe and followed a dose-dependent pattern. Signs included a reduction of body weight, hematologic changes, lymphoid tissue atrophy and degeneration of testicular germinal epithelium. Miller believed that despite the lack of bone marrow response in this study, the primary effect of Methyl Cellosolve® is on hematopoiesis (1067).

Male Hartley guinea pigs dermally exposed to 1 g/kg/day Methyl Cellosolve® 6 hours/day, 5 days/week for 13 weeks developed body weight loss and reduced testicle and spleen weights. Hematologic alterations include mild anemia and a lymphopenia with increased neutrophils. These data indicate Methyl Cellosolve® readily penetrates the skin and produces toxic effects similar to other routes of exposure (1789).

42.3.2 Human and Epidemiologic Studies

42.3.2.1 Short-term Toxicologic Effects

Human exposure to Methyl Cellosolve® generally results in hematologic and CNS disorders. Symptoms tend to mimic those of ethylene glycol intoxication.

Nitter-Hauge (1068) reported two cases of Methyl Cellosolve® poisoning. Two men inadvertently drank approximately 100 mL of Methyl Cellosolve®. Several hours later, after a symptom-free interval of 8-18 hours, they appeared ill and were taken to a hospital. Symptoms included cerebral confusion, deep and frequent respiration and a

profound metabolic acidosis. One man exhibited renal failure with persistent oxaluria. Both men recovered and were discharged 3-4 weeks after admission.

Young and Woolner (1069) reported another case of Methyl Cellosolve® ingestion. The man was believed to have consumed 200 mL of Methyl Cellosolve® mix with liquor. He was admitted to the hospital in a comatose condition and died 5 hours later. Autopsy revealed hemorrhagic gastritis, marked degeneration of the kidney tubules and fatty degeneration of the liver. The fatal outcome of this case may be linked to the patient's simultaneous ingestion of ethanol with Methyl Cellosolve®.

42.3.2.2 Chronic Toxicologic Effects

Chronic Methyl Cellosolve® toxicity is a condition which is very difficult to diagnose unless definite knowledge of exposure is known to have occurred. Symptoms of chronic exposure to Methyl Cellosolve® usually include headache, dizziness, lethargy, weakness, unequal pupil size, disorientation, the appearance of mental retardation and personality changes. Ataxia, anemia and disturbances in vision and hearing have been reported. The overall chronic condition has on occasion been mistakenly diagnosed as schizophrenia (17).

Zavon (1072) described a case involving the admission of a young man to a hospital in a nervous and tense state. Prior to hospitalization he complained of weakness, a need for more sleep than usual, loss of appetite, dazed preoccupied look and the reoccurrence of a stutter. Physical examination was normal. The individual was diagnosed as suffering from a confused state and was treated for schizophrenia with a series of electroshock treatments. He was released from the hospital 2 weeks later. He still complained of nervousness but the stuttering had disappeared. It was later discovered that this man worked in the printing department of a plastics plant where Methyl Cellosolve® was frequently used to clean the presses. A diagnosis of Methyl Cellosolve® intoxication was made retrospectively. Estimated atmospheric concentrations of Methyl Cellosolve® to which this worker was exposed ranged from 61-3960 ppm.

Ohi and Wegman (1073) investigated 2 reports of encephalopathy resulting from dermal exposure to Methyl Cellosolve®. Both individuals were employed in an electroplating facility where jets of acetone spray were used on the equipment and cleaned by rubbing the metal with bare hands. For about 6 months, from spring to fall, Methyl Cellosolve® was substituted for acetone. Air samples showed an average Methyl Cellosolve® concentration of 8 ppm, well below the 25 ppm TLV®. The first affected employee was hospitalized in August in a confused state. During examination he was disoriented and lapsed in and out of sleep. During the preceding 2-3 months he suffered from lethargy, unusual sleepiness, decreased hearing, anorexia and weight loss. The white cell count was 2600 (4300-10,800 is the normal range) and bone marrow aspiration revealed marrow depression with some signs of recovery. The

worker was treated for encephalopathy and his condition improved over several weeks. The second case was admitted in September with a cough, shortness of breath, fever, lethargy, staggering gait, blurred vision, slurred speech, poor memory, headache, confusion, anorexia, nausea, vomiting and bed wetting. The blood test appeared normal, however, a bone marrow aspiration revealed severe marrow damage. The worker was not treated, but remained in the hospital for observation. All symptoms disappeared within one week. These 2 cases of Methyl Cellosolve® poisoning occurred via a strictly cutaneous route, and in an environment in which air concentrations were considerably below the threshold limit of 25 ppm (1073).

Nakaaki et al. (1075) investigated the ability of Methyl Cellosolve® to penetrate human skin. High blood levels of Methyl Cellosolve® were found following dermal exposure to 15 mL of undiluted Methyl Cellosolve® for 2 hours. The information provided by Ohi (1073) and Nakaaki (1075) also indicates that dermal absorption is a significant route of exposure for Methyl Cellosolve®.

Another report of Methyl Cellosolve® intoxication is of a coating and mixing operator in a microfilm lab. After approximately 6 months of exposure, this operator complained of an increase in sleeptime, a 20 pound increase in body weight despite a decreased appetite, and an increased feeling of reserve. White and red cell counts, hemoglobin, hematocrit and platelets had all dropped to abnormally low levels. The worker continued at his job, which involved regular inhalation and dermal exposure to 18.2-57.8 ppm of Methyl Cellosolve®, for another year. During this year, physical examinations were normal, but macrocytic anemia persisted. At one year, he was removed from all Methyl Cellosolve® exposure. Within one month, hematologic parameters had returned to normal (1074). Again, this hematologic picture typifies chronic Methyl Cellosolve® toxicity. The absence of CNS toxicity suggests that exposure levels were very low.

Recent toxicological studies have reported testicular atrophy and sterility in animals exposed to Methyl Cellosolve® (1056,1057,1058). A cross-sectional study was conducted by Cook et al. (1071) to determine if employees exposed to Methyl Cellosolve® had an increased prevalence of anemia, leukopenia or sterility than those not exposed. Only 6 potentially exposed and 9 control employees were used in the fertility portion of the study. The results indicated that no gross abnormalities or clinically meaningful differences in fertility existed among the potentially exposed and control employees other than a potentially decreased testicular size among the potentially exposed employees.

42.3.3 Levels of Concern

The current OSHA (298) standard is 25 ppm averaged over an 8-hour work-shift; revision of this standard, however, is under consideration (1235) based on recent animal studies which suggest that the presently recommended exposure limit may not afford an adequate safety margin.

The ACGIH (3) recommends a 5 ppm TWA, with a notation of possible skin absorption.

42.3.4 Hazard Assessment

Methyl Cellosolve® is moderately toxic by ingestion and inhalation and is readily absorbed through the skin. In humans, symptoms of intoxication with this compound include nausea, headache, vomiting, hematological disorders and kidney damage.

Animal data are remarkable in their consistency of effects across species lines within defined exposure ranges. Methyl Cellosolve® has been shown to induce hematological effects characterized by reduction in red and white blood cell counts, bone marrow depression, testicular atrophy, fetotoxicity and teratogenicity. These effects are observed following all routes of exposure.

Hematological effects have been documented in mice, rats, rabbits, guinea pigs and humans (1066,1067,1789,17,1074) within an exposure range of 100 to 1000 ppm. Degenerative changes in the testis have also been identified in a range of animal species (1058,1056) and fetotoxic and teratogenic effects have been noted in rats, mice and rabbits (1059,1062,1063) at exposure levels in the range of 50 ppm.

Effects on the testes and developing embryo do not appear to be associated with interactions with DNA. Methyl Cellosolve® does not appear to pose a genotoxic hazard. It did not induce mutations in either bacteria or mammalian cell culture systems (1016,1284) and provided negative indications of a dominant lethal effect in rats at the 25 ppm level (1285). There are no data available regarding the carcinogenicity of Methyl Cellosolve®.

The similarity of toxic effects resulting from exposure to Methyl Cellosolve® in several species and evidence of hematological effects in humans at exposure levels which induce hematological effects in animals suggest it is prudent to assume that effects on testes and the developing embryo seen in animals at lower exposure levels may also occur in similarly exposed humans.

42.4 SAMPLING AND ANALYSIS CONSIDERATIONS

Determination of the concentration of Methyl Cellosolve® in soil and water requires collection of a representative field sample and laboratory analysis. Due to the volatility of Methyl Cellosolve®, care is required to prevent losses during sample collection and storage. Soil and water samples should be collected in airtight containers with no headspace; analysis should be completed within 14 days of sampling. In addition to the targeted samples, quality assurance samples such as field blanks, duplicates, and spiked matrices should be included in the analytical program.

Methyl Cellosolve® is not included among the EPA-designated priority pollutants, and an EPA-approved procedure for the analysis of Methyl Cellosolve® is not available. However, the recommended analytical m ods for alcohols and ethers (1142) is gas chromatography with fla ionization detection (GC/FID). Samples may either be directly injected onto the gas chromatographic (GC) column (aqueous and organic liquid samples) or may first be extracted with methylene chloride or toluene and the concentrated extract injected onto the GC column (aqueous and solid samples). Detection of Methyl Cellosolve® is then accomplished by a flame ionization detector. A mass spectrometer using either electron impact (EI) or chemical ionization (CI) techniques may also be used to detect Methyl Cellosolve®.

A detection limit for Methyl Cellosolve® using these methods was not determined but would be in the range of μg/L for aqueous samples and μg/g for non-aqueous samples which have been extracted and part-per-million (ppm) range for samples which have been directly injected.

COMMON SYNONYMS:	CAS REG. NO.:	FORMULA:	AIR W/V CONVERSION FACTORS at 25°C (12)
1,2-Ethanediol Glycol alcohol Permanent anti-freeze EG	107-21-1 NIOSH NO.: KW2975000	$C_2H_6O_2$	2.54 mg/m³ ≃ 1 ppm 0.365 ppm ≃ 1 mg/m³
	STRUCTURE: $HO-CH_2-CH_2-OH$		MOLECULAR WEIGHT: 62.07

REACTIVITY	The National Fire Protection Association reports that mixture of ethylene glycol with chlorosulfonic acid, oleum, or sulfuric acid causes the pressure and temperature to increase in a closed container. Reactions of glycols with non-oxidizing mineral acids typically generate heat, while those with oxidizing mineral acids, organic peroxides or hydroperoxides, or other strong oxidizing agents may evolve heat and fire. Compatibility charts further indicate that reactions of glycols with organic acids, isocyanates, or epoxides may initiate violent polymerization, while those with alkali or alkaline earth elemental metals or strong reducing agents may evolve heat, flammable gases and fire. Reactions with nitrides may produce heat, flammable gases, and an explosion, while those with azo or diazo compounds or hydrazines may evolve heat and generally innocuous gases (505,511).

PHYSICO-CHEMICAL DATA	• Physical State (at 20°C): liquid	(54)
	• Color: colorless	(54)
	• Odor: none	(12)
	• Odor Threshold: no data	( )
	• Liquid Density (g/ml at 20°C): 1.1135	(69)
	• Freezing/Melting Point (°C): -13	(21)
	• Boiling Point (°C): 197.6	(21)
	• Flash Point (°C): 111 (cc), 116 (oc)	(60,506, 507)
	• Flammable Limits in Air, % by Volume: 3.2-?	(51,60, 506)
	• Autoignition Temperature (°C): 398-400 or 413	(51,60, 506)
	• Vapor Pressure (mm Hg at 20°C): 0.05	(67)
	• Saturated Concentration in Air (mg/m³ at 20°C): 340	(67)
	• Solubility in Water (mg/L at 20°C): complete	(507)
	• Viscosity (cp at 20°C): 19.83	(21)
	• Surface Tension (dyne/cm at 20°C): 48.4	(69)
	• Log (Octanol-Water Partition Coefficient), log K_{ow}: -1.36	(20)
	• Soil Adsorption Coefficient, K_{oc}: 0.02	(611)
	• Henry's Law Constant (atm•m³/mol at 25°C): 6.0×10^{-8}	(966)
	• Bioconcentration Factor: 0.002	(659)

PERSISTENCE IN THE SOIL-WATER SYSTEM	Ethylene glycol is expected to be highly mobile in the soil/ground-water system. Sorption onto soil is weak and volatilization is expected to be minimal. Although data on biodegradation in soil are limited, ethylene glycol is not expected to be highly persistent.

PATHWAYS OF EXPOSURE	The primary pathway of concern from a soil/ground-water system is the migration of ethylene glycol to ground-water drinking water supplies, although no data confirm this. Inhalation or bioaccumulation of ethylene glycol are not likely to be important exposure pathways.

HEALTH HAZARD DATA	Signs and Symptoms of Short-term Human Exposure (69): Clinical symptoms include CNS dysfunction with severe metabolic acidosis, cardiopulmonary failure and acute renal failure.
	Toxicity Based on Animal Studies: LD_{50} (mg/kg) oral 7500 [mouse] (47) skin 19530 [rabbit] (47) LC_{50} (mg/m^3) inhalation -- no data
	Long-Term Effects: CNS depression, severe renal damage
	Pregnancy/Neonate Data: Teratogenic
	Mutation Data: Negative
	Carcinogenicity Classification: IARC - none assigned; NTP - under study via dietary exposure

HANDLING PRECAUTIONS (507)	NIOSH approved breathing air equipment or NIOSH approved face mask with organic vapor cartridge and dust or mist prefilter (not for use in fire fighting or in atmospheres with reduced oxygen content).

EMERGENCY FIRST AID TREATMENT (507)	Ingestion: Give large quantities of salt water and induce vomiting immediately if individual is conscious. Get medical attention • Inhalation: Move victim to fresh air immediately and perform artificial respiration if necessary • Skin: Remove contaminated clothing. Wash skin with soap and water • Eye: Irrigate with large amounts of water immediately.

ENVIRONMENTAL AND OCCUPATIONAL STANDARDS AND CRITERIA

AIR EXPOSURE LIMITS:

Standards
- OSHA PEL (8-hr TWA): none established
- AFOSH PEL (8-hr TWA): none established

Criteria
- NIOSH IDLH (30-min): none established
- ACGIH TLV® (8-hr TWA): CL: 50 ppm
- ACGIH STEL (15-min): none established

WATER EXPOSURE LIMITS:

Drinking Water Standards
None established

EPA Health Advisories
In the absence of formal drinking water standards the EPA (383) has developed the following Health Advisories (formerly termed SNARLs) for noncarcinogenic risk for short- and long-term exposure to ethylene glycol in drinking water:

- 1 day: 19 mg/L
- 10 days: none established
- long-term: 5.5 mg/L

EPA Ambient Water Quality Criteria (355)
- Human Health
  No criterion established; ethylene glycol is not a priority pollutant.
- Aquatic Life
  No criterion established; ethylene glycol is not a priority pollutant.

REGULATORY STATUS (as of January 1, 1987)

Promulgated Regulations

- Federal Programs

  Federal Insecticide, Fungicide and Rodenticide Act (FIFRA)
  Ethylene glycol is exempt from a tolerance requirement when used as an antifreeze or deactivator for all pesticides used before a crop emerges from the soil and for herbicides used before or after a crop emerges (315).

  Marine Protection Research and Sanctuaries Act (MPRSA)
  Ocean dumping of organohalogen compounds as well as the dumping of known or suspected carcinogens, mutagens or teratogens is prohibited except when they are present as trace contaminants. Permit applicants are exempt from these regulations if they can demonstrate that such chemical constituents are non-toxic and non-bioaccumulative in the marine environment or are rapidly rendered harmless by physical, chemical or biological processes in the sea (309).

  Food, Drug and Cosmetic Act (FDCA)
  Ethylene glycol is approved for use as an indirect food additive (362).

  Consumer Product Safety Act (CPSA)
  Ethylene glycol-based radiator antifreeze distributed in containers intended or suitable for household use may be misbranded if they fail to bear a warning statement adequate for protection of the public health and safety (1236).

- State Water Programs
  There are no specific state regulations for ethylene glycol.

Proposed Regulations

- Federal Programs
  No proposed regulations are pending.

- State Water Programs
  No proposed regulations are pending.

EEC Directives

Directive on Marketing and Use of Dangerous Substances (541)
Ethylene glycol may not be used in ornamental objects intended to produce light or color effects by means of different phases.

Directive on the Classification, Packaging and Labeling of Dangerous Substances (787)
Ethylene glycol is classified as a harmful substance and is subject to packaging and labeling regulations.

43.1 MAJOR USES

Ethylene glycol is a colorless, odorless, hydroscopic liquid infinitely soluble in water and many organic liquids. Due to its ability to markedly reduce the freezing point of water, about 40% of all ethylene glycol production goes to the manufacturing of nonvolatile antifreeze and liquid coolant for motor vehicles. Approximately 35% is used to manufacture polyester fiber and film. Ethylene glycol is also used in hydraulic fluids, as a solvent and as a heat transfer agent, especially in solar powered hot-water heaters (59,507).

43.2 ENVIRONMENTAL FATE AND EXPOSURE PATHWAYS

43.2.1 Transport in Soil/Ground-water Systems

43.2.1.1 Overview

Ethylene glycol is expected to be highly mobile in the soil/ground-water system when present at relatively low concentrations or as a separate organic phase (resulting from a spill of significant quantities of the chemical). In general, transport pathways can be assessed by using an equilibrium partitioning model as shown in Table 43-1. These calculations predict the partitioning of low soil concentrations of ethylene glycol among soil particles, soil water and soil air. Portions of ethylene glycol associated with the water and air phases of the soil have higher mobility than the adsorbed portion.

Estimates for the unsaturated topsoil model indicate that only 0.4% of the ethylene glycol is expected to be sorbed onto soil particles. Approximately 99.6% is expected to partition to the mobile soil-water phase, and is thus available to migrate by bulk transport (e.g., the downward movement of infiltrating water), dispersion and diffusion. Since a very small portion of ethylene glycol is expected to be in the gaseous phase of the soil (less than 0.001%), diffusion through the soil-air pores up to the ground surface and subsequent removal by wind would appear to be a minor loss pathway. In saturated, deep soils (containing no soil air and negligible soil organic carbon), almost all of the ethylene glycol (99.99%) is predicted to be present in the soil-water phase (Table 43-1) and available for transport with flowing ground water. Sorption onto deep soils (less than 0.01%) is not expected to be significant. Overall, ground water underlying ethylene glycol-contaminated soils with low organic content is expected to be vulnerable to contamination.

43.2.1.2 Sorption on Soils

The mobility of ethylene glycol in the soil/ground-water system (and its eventual migration into aquifers) is governed by the extent of its sorption on soil particles. Ethylene glycol is miscible in water and, as evidenced by its negative log K_{ow} and low K_{oc}, adsorption to soil/sediments is not expected to significantly influence its environmental fate.

TABLE 43-1

EQUILIBRIUM PARTITIONING CALCULATIONS FOR ETHYLENE GLYCOL IN MODEL ENVIRONMENTS[a]

Soil Environment	Estimated Percent of Total Mass of Chemical in Each Compartment		
	Soil	Soil-Water	Soil-Air
Unsaturated topsoil at 25°C[b,c]	0.4	99.6	7×10^{-4}
Saturated deep soil[d]	8×10^{-3}	99.99	-

a) Calculations based on Mackay's equilibrium partitioning model (34,35,36); see Introduction in Volume 1 for description of model and environmental conditions chosen to represent an unsaturated topsoil and saturated deep soil. Calculated percentages should be considered as rough estimates and used only for general guidance.

b) Utilized estimated soil sorption coefficient: $K_{oc} = 0.02$.

c) Henry's law constant taken as 6×10^{-8} atm·m³/mol at 25°C (966).

d) Used sorption coefficient $K_p = 0.001\ K_{oc}$.

Lokke (862) studied the adsorption and leaching of ethylene glycol in subsoils. No adsorption was observed for ethylene glycol (0.1-90 mg/L) onto two sandy soils and one clay subsoil ranging from 0.1-0.2% organic carbon. Leaching studies performed with soil cores of sandy till showed that ethylene glycol (150-220 g/L) closely followed the movement of water with little or no retardation.

43.2.1.3 Volatilization from Soils

Transport of ethylene glycol vapors through the air-filled pores of unsaturated soils may occur in near-surface soils. However, modeling results suggest that an insignificant fraction of the ethylene glycol loading will be present in the soil-air phase.

In general, important soil and environmental properties influencing the rate of volatilization include soil porosity, temperature, convection currents and barometric pressure changes; important physicochemical properties include the Henry's law constant, the vapor-soil sorption coefficient, and, to the lesser extent, the vapor phase diffusion coefficient (31).

Data on ethylene glycol volatilization from soils, in particular, are not available. Ethylene glycol is not strongly adsorbed to soil and is highly soluble in water. Although some volatilization may occur at the surface, the low value of the Henry's law constant (6×10^{-8} atm•m^3/mole) suggests that vapor concentrations in soil will be low whenever water is present and volatilization will be minimal.

43.2.2 Transformation Processes in Soil/Ground-water Systems

No information was available on the non-biological degradation of ethylene glycol in the environment. Thermo-oxidative degradation to organic acids has been reported for ethylene glycol used as an anti-freeze mixture (866).

A variety of studies have reported that ethylene glycol can be readily biodegraded under both aerobic and anaerobic conditions (867, 865,868,864,869,879). Data on degradation by microorganisms isolated from soil are contradictory. Harada and Nagashima (871) reported growth and nongrowth with ethylene glycol as sole carbon source. Jensen (872) reported no degradation using microbes isolated from soil. Gaston and Stadtman (868) reported rapid degradation under anaerobic conditions using microbes isolated from mud.

Degradation using activated sludge microorganisms or sewage seed was rapid; complete degradation within a few days was reported in several studies (873,874,875,876,877,878). Concentrations up to 2000 ppm were shown to support microbial growth, with an optimum concentration of 200 ppm reported. However, some concentrations above 1000 ppm were inhibitory (879); concentrations above 10,000 ppm inhibited growth of activated sludge (863).

In actual soil/ground-water systems, the concentrations of microorganisms capable of degrading ethylene glycol may be low, and may drop off with increasing depth; prediction of biodegradation rates in the environment is not possible. However, since both aerobic and anaerobic degradation have been demonstrated, persistence of ethylene glycol in environments with sufficient active microbial populations is not expected.

43.2.3 Primary Routes of Exposure from Soil/Ground-water Systems

The above discussion of fate pathways suggests that ethylene glycol is essentially nonvolatile, is very weakly adsorbed to soil, and has no significant potential for bioaccumulation. These fate characteristics suggest several potential exposure pathways.

The potential for ground water contamination with ethylene glycol is high, particularly in sandy soils. It has been detected in ground water associated with hazardous waste sites. Mitre (83) reported that ethylene glycol has been found in 1 of the 546 National Priority List (NPL) sites. At this particular site it was detected in surface water. However, it may not be commonly analyzed for at NPL sites as it is not a priority pollutant and is not commonly thought to be of concern to

public health. The properties of ethylene glycol suggest that drinking water exposure from ground water contamination is likely to be its primary route of exposure from soil/ground-water systems.

The movement of ethylene glycol in ground water may result in discharge to surface water. As a result, ingestion exposures may occur resulting from the use of surface waters as drinking water supplies, and dermal exposures may result from the recreational use of surface waters. Such exposures are likely to be lower than those from drinking contaminated ground water due to the degradation of ethylene glycol in surface water. Any pathways related to the uptake by aquatic organisms or domestic animals from surface waters are likely to be less significant than other sources of exposure due to the low BCF for ethylene glycol.

41.2.4 Other Sources of Human Exposure

Ethylene glycol is used in antifreeze, hydraulic fluids, electrolytic condensors, heat exchangers and as an industrial solvent. As such, there are likely to be a number of sources of human exposure, however, data documenting these exposures are lacking.

43.3 HUMAN HEALTH CONSIDERATIONS

43.3.1 Animal Studies

43.3.1.1 Carcinogenicity

No tumors were reported when ethylene glycol was injected subcutaneously into rats and mice for 2-15 months; the levels used were not cited (1034,1035,1036). Blood (1037) found no increased incidence of tumors in rats after being fed a diet containing 1% ethylene glycol for 2 years. Ethylene glycol is currently under investigation by the NTP to determine possible carcinogenic effects via dietary exposure (0047).

43.3.1.2 Mutagenicity

Ethylene glycol was found to be inactive in the TA-98, TA-100, TA-1535 and TA-1537 strains of Salmonella typhimurium (1017,1038).

43.3.1.3 Teratogenicity, Embryotoxicity and Reproductive Effects

Maronpot et al. (1018) fed 80 pregnant Fischer 344 rats a diet containing 0, 0.04, 0.2 or 1 g/kg/day of ethylene glycol on days 6-15 of gestation. No maternal toxicity or increased incidence of teratogenic effects were observed at any of the dosage levels used. There was a statistically significant increase in delayed ossification (24% vs. 3% in control animals) and unossified (44% vs. 19% in control

animals) vertebrae centra observed in fetuses of the dams that received 1 g/kg/day of ethylene glycol. These effects were attributed to delayed maturation and were considered evidence of minimal embryotoxicity.

In a recent study, Lamb et al. (1019) continuously administered 0, 0.25, 0.5 or 1% ethylene glycol in the drinking water of male and female CD-1 mice. Mice from each treatment group were paired and allowed to mate. No treatment-related effects were observed on body weight or water consumption and no clinical signs of toxicity were evident in the parental generation. During a 14-week co-habitation period, exposure to 1% ethylene glycol in the drinking water was associated with a statistically significant decrease in the number of litters per fertile pair (4.5 vs. 4.9), the mean number of live pups per litter (10.2 vs. 10.8) and the mean live pup weight (1.53 vs. 1.63). The neonatal pups exhibited various malformations such as fused ribs, twisted spine, abnormally shaped or missing sternebrae, abnormally shaped vertebrae and cleft lip following continuous exposure of the parents to 1% (1.64 g/kg/day) ethylene glycol in the drinking water. No such defects were observed among control mice. The progeny of the F_1 generation, also continuously exposed to the 1% ethylene glycol drinking water, displayed modified craniofacial characteristics as adults which were not apparent in the neonatal period of growth. These facial abnormalities included a shortened snout and wide set eyes. Fertility in the F_1 generation was also decreased (61% vs. 80% in the control group).

Price et al. (1020) confirmed and expanded the results reported in the Lamb study (1019). Pregnant CD rats were dosed by gavage with 0, 1250, 2500 or 5000 mg/kg/day and CD-1 mice with 0, 750, 1500 or 3000 mg/kg/day of ethylene glycol on days 6-15 of gestation. No maternal deaths or distinctive clinical signs were noted, however, a significant dose-related decrease in maternal weight gain was observed at all levels in rats and at the 1500 and 3000 mg/kg/day levels in mice. Fetal body weight per litter was significantly reduced at the mid- and high-dosage levels in the rats and at all levels in the mice. The percentage of litters with malformed fetuses was significantly increased in all treatment groups and followed a dose-related trend. The most commonly observed malformations were cleft lip and palate, fused ribs, neural tube closure defects and abnormally shaped vertebrae and sternebrae. In mice, two fetuses in one litter in the 3000 mg/kg/day treatment group each exhibited a mid-facial cleft, which is an unusual defect for the CD-1 species. The shortened frontal, nasal and parietal bones observed in the F_1 mice following continuous pre- and postnatal exposure to ethylene glycol (1019) were not observed in fetal rats or mice in this study.

Union Carbide (1021) reported results of a recent inhalation study on the teratogenic effects of ethylene glycol in CD rats and CD-1 mice. The duration of the study was not provided. A reduced ossification in the humerous, zygomatic arch and hind limb metatarsals and phalanges indicated slight fetotoxicity in rats exposed to 1000 or 2500 mg/m^3

ethylene glycol. CD-1 mice also exposed to 1000 or 2500 mg/m³ ethylene glycol experienced reduced body weight and reduced ossification at numerous skeletal locations. Teratogenicity was demonstrated at both of these concentrations in mice as shown by a statistically significant increase of external, visceral and skeletal malformations. Predominant terata included exencephaly, cleft palate, abnormal faces and facial bones, fused vertebrae and abnormal ribs.

A possible mechanism of action for the teratogenic effects of ethylene glycol has been proposed by Lamb (1019). A metabolite of ethylene glycol, oxalic acid, is known to chelate calcium. Lamb suggests that this calcium chelation may lead to hypocalcemia and may act upon fetal development by altering the biological supply of the calcium cation.

43.3.1.4 Other Toxicologic Effects

43.3.1.4.1 Short-term Toxicity

Ingestion of ethylene glycol generally results in depression followed by respiratory and cardiac failure, renal damage and possibly brain damage (54). The oral LD_{50} for mice is listed as 7500 mg/kg (47). Inhalation of ethylene glycol primarily results in depression of the CNS and hematopoietic dysfunction but rarely results in death (54). No LC_{50} value was found in the literature for ethylene glycol. The dermal LD_{50} is listed as 19,530 mg/kg in rabbits (47).

Typical signs of ethylene glycol poisoning are best exemplified in the dog. Dogs were orally given 6 ml ethylene glycol per kilogram of body weight. Signs included incoordination, increased depth and rate of respiration and increased heart rate. As progression of the poisoning continued, collapse and labored breathing ensued. Coma and death occurred within 37 hours. Necropsy revealed pulmonary and gastric hyperemia, severe toxic tubular nephrosis and renal oxalosis (1022). One to three hours after feeding dogs 9.5 ml ethylene glycol per kilogram of body weight, Grauer et al. (1023) observed depression, incoordination and increased fluid intake and urine output. Severe metabolic acidosis developed as the osmolal and anion gap increased. Within 6 hours, calcium oxalate crystalluria was observed, but it was not until 48 hours post-ingestion that a diminished renal excretory function was seen.

McDonald et al. (1046) injected 0.5 ml of 0, 0.004, 0.04, 0.4, 4 or 40% ethylene glycol solution into the corneal shelf of albino New Zealand rabbits. One treatment per day was given for 5 days. The 0.4% solution was found to be the highest concentration that was nontoxic and non-irritating. Irritation resulting from the 4 and 40% solutions consisted of swelling, discharge and conjunctival redness. All eyes returned to normal within 7 days of the last treatment. No evidence of systemic toxicity was observed.

The effect of ethylene glycol on brain function was tested in the male albino rat by Rajagopal (1024). Rats were given 10 mg/kg of a 50% aqueous solution of ethylene glycol by an intragastric tube. Urinary pH, blood pH and plasma bicarbonate levels all fell indicating a condition of metabolic acidosis. In response to the acidotic state, the renal distal tubular cells synthesized 332% more ammonia. The calcium oxalate deposition in the kidney and the oliguria caused a back diffusion of ammonia into the blood stream, resulting in a 497% increase in blood ammonia. The levels of brain amino acids (glutamate, GABA and glutamine) were altered in an attempt to detoxify the large amounts of ammonia entering the brain via the blood stream. The glutamate levels dropped 15.2% in order to utilize the ammonia to synthesize glutamine (which increased by 29.7%). The GABA level was reduced by 20.5%. This change in amino acid balance affected neurotransmission, and may be a possible explanation for the brain damage and even death seen in several cases of ethylene glycol toxicity.

43.3.1.4.2 Chronic Toxicity

The primary effect of repeated oral doses of ethylene glycol is kidney damage. Injury may occur even though oxalate crystals are not deposited in the kidney.

The effect of ethylene glycol on the kidney was studied by Roberts and Seibold (1047). Ethylene glycol was administered in levels ranging from 0.25 - 10% in the drinking water of several macaque species of monkeys. The left kidney was removed from all animals between days 6 and 13 of the experiment. Animals were sacrificed when they were uremic (the build-up of protein by-products in the blood due to inadequate kidney function) or dying. Seven out of ten animals received 15 ml/kg or more ethylene glycol. Five of these animals had deposition of calcium oxalate crystals in the proximal tubules. Tubular epithelium adjacent to the crystals was necrotic. Six animals were continued on the experiment for longer than 12 days. Three of these animals (ethylene glycol dose ranging from 33 to 137 ml/kg) had renal changes proportional to the dose given. Well marked to extreme deposition of calcium oxalate crystals in the proximal tubules along with necrosis of epithelial cells were present. Monkeys given total doses of less than 15 ml/kg ethylene glycol developed mild glomerular damage, but no calcium oxalate crystals were present. This led Roberts and Seibold to speculate that ethylene glycol or its metabolic products other than oxalic acid are capable of causing renal damage. Deposition of calcium oxalate crystals were also found in tissues other than kidney. Three animals that were found in a dying state by day 31 of the experiment had oxalate crystals present in the walls of the cerebral vessels and adjacent tissues. This study concluded that high doses of ethylene glycol causes nephrotoxic necrosis in the proximal tubules while low doses of ethylene glycol cause abnormal glomerular permeability.

Rats maintained on a diet containing 1 or 2% ethylene glycol, developed calcium oxalate bladderstones and severe renal injury and degeneration (1039).

43.3.2 Human and Epidemiologic Studies

43.3.2.1 Short-term Toxicologic Effects

The primary route of exposure to ethylene glycol in humans is by accidental or deliberate ingestion. Ingestion of about 100 mL can be fatal (12). The effects of ethylene glycol poisoning usually appear in three distinct phases The onset of the first stage begins approximately 30 minutes to 12 hours following ingestion and predominately affects the CNS. With small doses, the victim appears drunk, but without the odor of alcohol on the breath; with large doses, stupor, coma, convulsions and possible death occur within the first 24 hours. If the individual survives beyond the initial 12-24 hours, cardiopulmonary signs become prominent. This phase is characterized by tachypnea, cyanosis, pulmonary edema and possible death within the next 24 hours. The final stage primarily affects the renal system and includes such signs and symptoms as flank pain, metabolic acidosis and anuria. Death may occur as late as 17 days post-ingestion (12).

Acute levels of ethylene glycol in the human body may lead to various metabolic problems. A 24-year-old man deliberately ingested an unknown quantity of ethylene glycol. The victim developed pulmonary edema and a decreased pulmonary compliance that fit the criteria for the Adult Respiratory Distress Syndrome (ARDS). Although many deaths from ethylene glycol have been attributed to cardiopulmonary dysfunction, this case is unusual because it represents a respiratory dysfunction in the presence of normal cardiac function (1025).

Cieciura (1026) examined renal biopsies of five patients with acute ethylene glycol poisoning on days 5, 10, 16 and 22 of hospitalization. Extensive calcium oxalate and carbonate crystals were present in the glomerular interloop spaces of the kidney which exerted mechanical as well as toxic effect on surrounding tissue. The crystals were shown to persist until 22 days post-ingestion.

Edelhauser *et al.* (1027) studied the effects of high concentrations of ethylene glycol on human corneas in culture. No damage to the corneal endothelium was reported when up to 5000 ppm ethylene glycol was exposed directly on the cornea for 2 hours.

43.3.2.2 Chronic Toxicologic Effects

Chronic exposure to ethylene glycol is rare in humans. Symptoms are generally listed as anorexia, oliguria, nystagmus, lymphocytosis and loss of consciousness (54).

An unusual case of chronic ethylene glycol toxicity due to inhalation was reported by Troisi (1040,1041). Thirty-eight women were exposed to a mixture containing 40% ethylene glycol, 55% boric acid and 5% ammonia at 105°C while working in an electrolytic condenser factory. Nine women suffered frequent attacks of unconsciousness 2-3 times a week. Fourteen women developed nystagmus (an involuntary rapid movement of the eye ball) and five showed an absolute lymphocytosis. The attacks ceased immediately once exposure to ethylene glycol vapor ceased.

43.3.3 Levels of Concern

The ACGIH (3) has established a ceiling limit of 50 ppm for ethylene glycol. OSHA (298) has no established standard.

The EPA (383) has developed health advisories of 19 mg/L for one-day exposure and 5.5 mg/L for long-term exposure to ethylene glycol in drinking water.

43.3.4 Hazard Assessment

Ethylene glycol is not considered to be either a carcinogenic or mutagenic hazard. A chronic feeding study using rats fed 1% ethylene glycol in the diet produced no evidence of carcinogenic activity (1037). There are no data to indicate any mutagenic activity either.

Ethylene glycol has been shown to produce dose-related teratogenic effects in rats and mice when administered by gavage or via the drinking water (1019,1020) as well as by inhalation (1037).

The principal hazard to humans appears to be associated with ingestion of large quantities of ethylene glycol. Depression of the central nervous system, serious renal injury and death may result from ingestion of about 100 mL (12). Early symptoms following ingestion are similar to alcoholic inebriation, but if untreated, can result in respiratory failure, convulsions, cardiovascular collapse and severe metabolic acidosis (12).

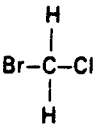
43.4 SAMPLING AND ANALYSIS CONSIDERATIONS

Determination of the concentration of ethylene glycol in soil and water requires collection of a representative field sample and laboratory analysis. Care is required to prevent losses during sample collection and storage. Soil and water samples should be collected in airtight containers with little or no headspace; analysis should be completed within 14 days of sampling. In addition to the targeted samples, quality assurance samples such as field blanks, duplicates, and spiked matrices should be included in the analytical program.

Ethylene glycol is not included among the EPA-designated priority pollutants, and an EPA-approved procedure for the analysis of ethylene glycol is not available. However, the recommended analytical method

for glycols (1142) is gas chromatography with flame ionization detection (GC/FID). Samples may either be directly injected onto the gas chromatographic (GC) column (aqueous and organic liquid samples) or they may first be extracted with an organic solvent (e.g., methylene chloride) and the concentrated extract injected onto the GC column (aqueous and solid samples). Detection of ethylene glycol is then accomplished by a flame ionization detector. A mass spectrometer using either electron impact (EI) or chemical ionization (CI) techniques may also be used to detect ethylene glycol.

A detection limit for ethylene glycol using these methods was not determined but would be in the range of µg/L for aqueous samples and µg/g for non-aqueous samples which have been extracted and parts-per-million (ppm) range for samples which have been directly injected.

COMMON SYNONYMS:	CAS REG. NO.:	FORMULA:	AIR W/V CONVERSION FACTORS at 25°C (12)
Chlorobromomethane Methylene chloro-bromide Fluorocarbon 1011 CBM Chloromethyl bromide	74-97-5 NIOSH NO.: PA5250000	CH_2BrCl	5.3 mg/m³ ≃ 1 ppm 0.189 ppm ≃ 1 mg/m³
	STRUCTURE: 		MOLECULAR WEIGHT: 129.40

REACTIVITY	Reactions of halogenated organic materials such as bromochloromethane with cyanides, mercaptans or other organic sulfides typically generate heat, while those with mineral acids, amines, azo compounds, hydrazines, caustics, or nitrides commonly evolve heat and toxic or flammable gases. Reactions with oxidizing mineral acids may generate heat, toxic gases, and fires. Those with alkali or alkaline earth elemental metals, certain other chemically active elemental metals like aluminum, calcium, zinc or magnesium, organic peroxides or hydroperoxides, strong oxidizing agents, or strong reducing agents typically result in heat generation and explosions and/or fires (38,54,56).

PHYSICO-CHEMICAL DATA	• Physical State (at 20°C): liquid	(23)
	• Color: colorless to pale yellow	(2)
	• Odor: chloroform-like	(23)
	• Odor Threshold: 400 ppm	(384)
	• Liquid Density (g/ml at 20°C): 1.9344	(68)
	• Freezing/Melting Point (°C): -86.5	(68)
	• Boiling Point (°C): 68.1	(68)
	• Flash Point (°C): not flammable	(23,38,51)
	• Flammable Limits in Air, % by Volume: not flammable	(23,38,51)
	• Autoignition Temperature (°C): not flammable	(23,38,51)
	• Vapor Pressure (mm Hg at 20°C): 117	(38)
	• Saturated Concentration in Air (mg/m³ at 20°C): 830,000	(ADL estim)
	• Solubility in Water (mg/L at 20°C): 9000	(38)
	• Viscosity (cp at 20°C): no data	( )
	• Surface Tension (dyne/cm at 20°C): no data	( )
	• Log (Octanol-Water Partition Coefficient), log K_{ow}: 1.41	(29)
	• Soil Adsorption Coefficient, K_{oc}: 12	(611)
	• Henry's Law Constant (atm·m³/mol at 20°C): 1.22×10^{-3}	(1219)
	• Bioconcentration Factor: 5.0	(1219)

PERSISTENCE IN THE SOIL-WATER SYSTEM	Bromochloromethane is expected to be relatively mobile in surface soils and highly mobile in deep soils or sandy soils. Removal by volatilization is the primary loss pathway, particularly for material at the surface or in the soil-air phase. Transformation in natural soils is not expected to be significant.

PATHWAYS OF EXPOSURE	The primary exposure pathway of concern from soil/ground-water systems is the migration of bromochloromethane to ground-water drinking water supplies. Exposures through inhalation may be important in some situations, but ingestion of foods containing this compound is not generally expected to be significant.

HEALTH HAZARD DATA	Signs and Symptoms of Short-term Human Exposure (54,38): Bromochloromethane may cause irritation of the eyes and throat. Inhalation may cause disorientation, dizziness, headaches, anorexia, nausea, vomiting, abdominal pain, weight loss, memory impairment, paralysis, weakness, tremors, convulsions and narcosis. Prolonged contact may cause skin irritation.
	Toxicity Based on Animal Studies: LD_{50} (mg/kg) oral 5000 [rat] (1297) skin -- no data LC_{50} (mg/m^3) inhalation [mouse] (1297) 12,047•7hr
	Long-Term Effects: Reversible liver injury
	Pregnancy/Neonate Data: No data
	Mutation Data: Conflicting in bacterium; negative in yeast
	Carcinogenicity: No data

HANDLING PRECAUTIONS (38)	Handle chemical only with adequate ventilation • Vapor concentrations of 200-1000 ppm: any chemical cartridge respirator with an organic vapor cartridge • 1000-2000 ppm: any supplied-air respirator or self-contained breathing apparatus • 2000-5000 ppm: gas mask with a chin-style or a front or back-mounted organic vapor canister • Chemical goggles if there is probability of eye contact • Appropriate clothing to prevent repeated or prolonged skin contact.

EMERGENCY FIRST AID TREATMENT (38,54)	Ingestion: Induce vomiting if victim is conscious. Get medical attention • Inhalation: Move victim to fresh air. Give artificial respiration if necessary. Get medical attention • Skin: Remove contaminated clothing. Wash skin with soap and water. If irritation persists after washing, get medical attention • Eye: Flush with large amount of water. If irritation persists after washing, get medical attention.

ENVIRONMENTAL AND OCCUPATIONAL STANDARDS AND CRITERIA

AIR EXPOSURE LIMITS:

Standards
- OSHA PEL (8-hr TWA): 200 ppm
- AFOSH PEL (8-hr TWA): 200 ppm

Criteria
- NIOSH IDLH (30-min): 5000 ppm
- ACGIH TLV® (8-hr TWA): 200 ppm
- ACGIH STEL (15-min): 250 ppm

WATER EXPOSURE LIMITS:

Drinking Water Standards - None established

EPA Health Advisories - None established

EPA Ambient Water Quality Criteria (355)
- Human Health
  No criterion established; bromochloromethane is not a priority pollutant.
- Aquatic Life
  No criterion established; bromochloromethane is not a priority pollutant.

REGULATORY STATUS (as of January 1, 1987)

Promulgated Regulations

- Federal Programs

  Resource Conservation and Recovery Act (RCRA)
  Effective July 8, 1987, the land disposal of hazardous wastes containing halogenated organic compounds in total concentrations greater than or equal to 1000 mg/kg will be prohibited. The only exception will be underground injection (1755).

  Marine Protection Research and Sanctuaries Act (MPRSA)
  Ocean dumping of organohalogen compounds as well as the dumping of known or suspected carcinogens, mutagens or teratogens is prohibited except when they are present as trace contaminants. Permit applicants are exempt from these regulations if they can demonstrate that such chemical constituents are non-toxic and non-bioaccumulative in the marine environment or are rapidly rendered harmless by physical, chemical or biological processes in the sea (309).

  Occupational Safety and Health Act (OSHA)
  Employee exposure to bromochloromethane shall not exceed an 8-hour time-weighted-average (TWA) of 200 ppm (298).

  Hazardous Materials Transportation Act (HMTA)
  The Department of Transportation has designated bromochloromethane as a hazardous material which is subject to requirements for packaging, labeling and transportation (306).

- State Water Programs
  There are no specific state regulations for bromochloromethane.

Proposed Regulations

- Federal Programs

  Resource Conservation and Recovery Act (RCRA)
  EPA has proposed that non-liquid hazardous wastes containing halogenated organic compounds (HOCs) in total concentrations greater than or equal to 1000 mg/kg or liquid hazardous wastes containing HOCs in total concentrations greater than or equal to 1% HOCs must be incinerated in accordance with the requirements of 40CFR264.343 or 265.343 (1767).

  Toxic Substances Control Act (TSCA)
  EPA has proposed that manufacturers, importers and processors of bromochloromethane submit health and safety studies (1753).

- State Water Programs
  No proposed regulations are pending.

EEC Directives

Directive on Ground Water (538)
Direct discharge into ground water (i.e., without percolation through the ground or subsoil) of organophosphorous compounds, organohalogen compounds and substances which may form such compounds in the aquatic environment, substances which possess carcinogenic, mutagenic or teratogenic properties in or via the aquatic environment and mineral oils and hydrocarbons is prohibited. Appropriate measures deemed necessary to prevent indirect discharge into ground water (i.e., via percolation through ground or subsoil) of these substances shall be taken by member countries.

Directive on the Quality Required of Shellfish Waters (537)
The mandatory specifications for organohalogenated substances specify that the concentration of each substance in the shellfish water or in shellfish flesh must not reach or exceed a level which has harmful effects on the shellfish and larvae. The guideline specifications for organohalogenated substances state that the concentration of each substance in shellfish flesh must be so limited that it contributes to the high quality of shellfish product.

Directive on the Discharge of Dangerous Substances (535)
Organohalogens, organophosphates, petroleum hydrocarbons, carcinogens or substances which have a deleterious effect on the taste and/or odor of human food derived from aquatic environments cannot be discharged into inland surface waters, territorial waters or internal coastal waters without prior authorization from member countries which issue emission standards. A system of zero-emission applies to discharge of these substances into ground water.

Directive on Toxic and Dangerous Wastes (542)
Any installation, establishment, or undertaking which produces, holds and/or disposes of certain toxic and dangerous wastes including phenols and phenol compounds; organic-halogen compounds; chrome compounds; lead compounds; cyanides; ethers and aromatic polycylic compounds (with carcinogenic effects) shall keep a record of the quantity, nature, physical and chemical characteristics and origin of such waste, and of the methods and sites used for disposing of such waste.

EEC Directives - Proposed

Proposal for a Council Directive on the Dumping of Waste at Sea (1793)
EEC has proposed that the dumping of organohalogen compounds at sea be prohibited.

44.1 MAJOR USES

The major use of bromochloromethane is as a fire extinguisher fluid. Its effectiveness per unit weight makes it suitable for use in aircraft and portable extinguishers. It also has limited use as a chemical intermediate (12,21).

44.2 ENVIRONMENTAL FATE AND EXPOSURE PATHWAYS

44.2.1 Transport in Soil/Ground-water Systems

44.2.1.1 Overview

Bromochloromethane may be relatively mobile in the soil/ground-water system when present at low concentrations (dissolved in water and sorbed in soil) or as a separate organic phase (resulting from a spill of significant quantities of the chemical).

Transport pathways for low soil concentrations can be generally assessed by estimating equilibrium partitioning as shown in Table 44-1. These calculations predict the partitioning of bromochloromethane among soil particles, soil water and soil air. The estimates for the unsaturated topsoil model indicate that significant amounts (29%) of the bromochloromethane are expected to be present in the soil-water phase, and can thus migrate by bulk transport (e.g., the downward movement of infiltrating water), and dispersion and diffusion. A smaller portion (4.4%) is expected to partition to the soil-air phase; therefore, diffusion through the soil-air pores up to the ground surface, and subsequent removal by wind is a less significant transport pathway. In saturated, deep soils (containing no soil air and negligible soil organic carbon), a much higher fraction of the bromochloromethane (95%) is likely to be present in the soil-water phase and available for transport with flowing ground water. Ground water underlying bromochloromethane-contaminated soils with low organic content is particularly vulnerable to contamination.

44.2.1.2 Sorption on Soils

The mobility of bromochloromethane in the soil/ground-water system (and its eventual migration into aquifers) is strongly affected by the extent of its sorption on soil particles. In general, sorption on soils is expected to:

- increase with increasing soil organic matter content;
- increase slightly with decreasing temperature;
- increase slightly with increasing salinity of the soil water; and
- decrease moderately with increasing dissolved organic matter content of the soil water.

TABLE 44-1

EQUILIBRIUM PARTITIONING CALCULATIONS FOR BROMOCHLOROMETHANE IN MODEL ENVIRONMENTS[a]

Soil Environment	Estimated Percent of Total Mass of Chemical in Each Compartment		
	Soil	Soil-Water	Soil-Air
Unsaturated topsoil at 25°C[b,c]	66.7	28.9	4.4
Saturated deep soil[d]	4.8	95.2	-

a) Calculations based on Mackay's equilibrium partitioning model (34,35,36); see Introduction in Volume 1 for description of model and environmental conditions chosen to represent an unsaturated topsoil and saturated deep soil. Calculated percentages should be considered as rough estimates and used only for general guidance.

b) Used estimated soil sorption coefficient: K_{oc} = 12 (611).

c) Henry's law constant taken as 1.22 x 10^{-3} atm·m^3/mol at 20°C (Arthur D. Little, Inc. estimate).

d) Used sorption coefficient (K_p) calculated as a function of K_{oc} assuming 0.1% organic carbon: $^pK_p = 0.001 \times K_{oc}$.

There are no available data on the extent of sorption of bromochloromethane on soils; data for other halomethanes indicate weak sorption. Schwarzenbach et al. (77) determined retardation rates, which represent interstitial water velocity/pollutant velocity ratios in the soil, for several chlorinated organics with higher K_{oc} values than bromochloromethane. The data indicate some retention in soils having 1-2% organic carbon content and little or no retention in soils with less than 0.1% organic carbon. Assuming analogous soil conditions, adsorption of bromochloromethane, particularly to deep soils, is not expected to be significant.

44.2.1.3 Volatilization from Soils

Transport of bromochloromethane vapors through the air-filled pores of unsaturated soils may occur, particularly in near-surface

soils. In general, important soil and environmental properties influencing the rate of volatilization include soil porosity, temperature, convection currents and barometric pressure changes; important physico-chemical properties include the Henry's law constant, the vapor-soil sorption coefficient, and, to a lesser extent, the vapor phase diffusion coefficient (31). No information is available on the latter two physico-chemical properties for bromochloromethane.

The Henry's law constant (H), which provides an indication of a chemical's tendency to volatilize from solution, is expected to increase significantly with increasing temperature; moderate increases in H were observed with increasing salinity and the presence of other organic compounds (18). The Henry's law constant for bromochloromethane is estimated to be 1.22×10^{-3} atm • m^3/mol (Arthur D. Little, Inc. estimate) suggesting moderate to high volatilization from aqueous solution. Even though volatilization from soil will be lower than volatilization from water, it is expected to be a primary loss process for near-surface soils due to the weak sorption on soils and slow rate of transformation.

No specific information regarding the rate of volatilization of bromochloromethane from soils was available. Evidence of volatilization of bromochloromethane from river water has been reported (1644), although no rates were determined. Volatilization half-lives on the order of 20-90 minutes have been reported for chloromethane and dichloromethane in stirred aqueous solutions (10); half-lives for dibromochloromethane from rivers and streams have been reported to range from 43 minutes to 16.6 days. Since the vapor pressure of bromochloromethane (~120 torr) is less than that of dichloromethane (350 torr) but greater than that of dibromochloromethane (15 torr), the half-life of volatilization for bromochloromethane is expected to be intermediate between the above values. Volatilization of some halogenated organics from near-surface soils has been shown to be slower than their volatilization from well-stirred aqueous solutions by approximately one order of magnitude (82).

44.2.2 Transformation Processes in Soil/Ground-water Systems

Data specific to the transformation of bromochloromethane in soil/ground-water systems were not available. Maximum hydrolytic half-lives ranging from 137 years to 3000 years have been reported for other di- and tri-halomethanes (10), suggesting that hydrolysis in the environment is not expected to be significant. Photolysis and oxidation are also not expected to occur in the environment at rates significant enough to compete with volatilization.

Most references indicate that low molecular weight chloroaliphatics are not metabolized by microorganisms (10). However, Thom and Agg (80) have included several halomethanes in a list of organic chemicals amenable to degradation by biological sewage treatment, provided that suitable acclimation can be achieved. Tabak et al. (79) report significant degradation and rapid acclimation for bromochloromethane using an

activated sludge population. In most soil/ground-water systems, however, the concentration of microorganisms capable of biodegrading chemicals such as bromochloromethane is very low and drops off sharply with increasing depth. Thus, biodegradation should be assumed to be of minimal importance except, perhaps, in landfills with active microbiological populations.

44.2.3 Primary Routes of Exposure from Soil/Ground-water Systems

The above discussion of fate pathways suggests that bromochloromethane has a high volatility, is weakly sorbed, and has no significant potential for bioaccumulation. Bromochloromethane on the soil surface is likely to volatilize, but that portion not subject to volatilization is likely to be mobile in ground water. These fate characteristics suggest several exposure pathways.

Volatilization of bromochloromethane from a disposal site could result in inhalation exposures. The potential for ground water contamination is high, particularly in sandy soils. Mitre (83) reported that bromochloromethane has been found at 2 of the 546 National Priority List (NPL) sites. It was detected in the ground water at both of these sites. Among the available drinking water surveys of ground water quality, bromochloromethane is not generally reported. It was detected, but not quantified, in the National Organics Monitoring Survey that was conducted in 1976-1977 (90). These data indicate that bromochloromethane is not a common contaminant in ground water, probably due to its limited use. However, its properties, and information available on its fate, suggest that it should be mobile in soil/ground-water systems, and the contamination of drinking water would be of primary concern at sites where it is present.

Discharges of bromochloromethane to surface water from soil/ground-water systems would probably not represent significant sources of exposure due to the volatility and low potential for bioaccumulation of bromochloromethane.

44.2.4 Other Sources of Human Exposure

No other sources of exposure to bromochloromethane were identified.

44.3 HUMAN HEALTH CONSIDERATIONS

44.3.1 Animal Studies

44.3.1.1 Carcinogenicity

No carcinogenicity studies have been conducted with bromochloromethane.

44.3.1.2 Mutagenicity

Simmon et al. (1294) found bromochloromethane to be mutagenic in Salmonella typhimurium TA100. Another source noted a negative response in both Salmonella typhimurium and Saccharomyces cerevisiae D3 (1295).

44.3.1.3 Teratogenicity, Embryotoxicity and Reproductive Effects

No reproductive studies have been conducted with bromochloromethane.

44.3.1.4 Other Toxicologic Effects

44.3.1.4.1 Short-term Toxicity

Bromochloromethane appears to be one of the least toxic of the halomethanes; the primary response to overexposure is CNS depression (12). Oral LD_{50} values for rats and mice are 5000 mg/kg and 4300 mg/kg, respectively (1297,47). Single oral doses of 1000 mg/kg or less have no apparent effect on rats, while single oral doses of 3000 and 4500 mg/kg caused fatty degeneration of the liver and kidneys in mice (12).

An LC_{50} of 2273 ppm for 7 hours has been reported for mice (1297). Concentrations of 3000 ppm produce light narcosis in rats within 15 minutes. Transient pulmonary edema was observed at concentrations below 27,000 ppm. Interstitial pneumonitis resulted in delayed deaths following exposure to 20,000 ppm. Deaths occurred during exposure only at concentrations above 27,000 ppm (1298).

When applied repeatedly to the open skin of rabbits, bromochloromethane produced moderate irritation and hyperemia; prolonged skin contact may cause dermatitis (46). A mean skin permeability constant of 0.79 cm/hr was calculated for rats exposed in a body-only chamber to vapor concentrations of 2500 to 40,000 ppm bromochloromethane for 4 hours. The total amount absorbed through the skin increased linearly with increasing vapor concentration at the skin surface (1299).

In rabbits, the liquid caused transient corneal epithelial injury and conjunctival edema (19).

44.3.1.4.2 Chronic Toxicity

Repeated inhalation of bromochloromethane causes little organic injury. Rats, rabbits and dogs exposed to a concentration of 1000 ppm, 7 hours daily, 5 days per week for 14 weeks showed no evidence of toxic response (1297). In another study, some liver pathology was observed in female rats and dogs exposed to 500 ppm in air for 6 months on the same dosing schedule. Rabbits, guinea pigs and male rats showed no

effect at this level except elevated blood bromide levels. Histopathological changes in the liver and testes as well as elevated blood bromide levels were noted at 1000 ppm (1407).

44.3.2 Human and Epidemiologic Studies

44.3.2.1 Short-term Toxicologic Effects

There are few reports of adverse effects in humans from bromochloromethane exposure. This is probably due to its limited usage and low toxicity (12). Rutstein (1408) reported acute poisoning in three fire fighters exposed to unknown but very high vapor concentrations of bromochloromethane. Symptoms included severe headache, nausea and eye and throat irritation. Two of the three victims became comatose. Of these, one had convulsions, the other had respiratory arrest but was resuscitated. Recovery was slow but complete. Liver biopsies revealed normal microanatomy. Liver function studies were normal a few days after exposure.

Bromochloromethane is an irritant to the eyes and mucous membranes. Accidental discharge of a fire extinguisher close to the face produced immediate severe burning sensation in the eyes, followed by partial loss of the corneal epithelium. Discomfort and photophobia gradually subsided over the course of three days (19). Prolonged skin contact may cause dermatitis (46).

44.3.2.2 Chronic Toxicologic Effects

There are no data on the effects of chronic exposure, however, it does occur in manufacturing and packaging operations (2).

44.3.3 Levels of Concern

No water quality criteria or standards have been established to date regarding this chemical.

The OSHA (298) and ACGIH (3) TWA value is 200 ppm (1050 mg/m^3).

44.3.4 Hazard Assessment

The impact on human health resulting from either acute or long-term exposure to bromochloromethane has not been adequately evaluated in humans. Bromochloromethane vapor is a narcotic and respiratory irritant (12). The primary response to bromochloromethane exposure is CNS depression (e.g., mental confusion, dizziness, weakness, tremors). Prolonged or repeated skin contact may cause dermatitis (46). Eye contact can result in transient loss of corneal epithelium and photophobia (19).

Animal data provide little evidence of organic injury from either acute or chronic exposure to bromochloromethane. No effects were reported for rats, rabbits and dogs after repeated inhalation exposures

to 1000 ppm for 14 weeks (1297), although another study indicated reversible liver pathology in rats (females only) and dogs but not rabbits, guinea pigs and male rats exposed to 500 ppm for six months under the same treatment regimen (1407).

No studies were found concerning the carcinogenic potential or reproductive effects associated with exposure to bromochloromethane. Two in vitro mutagenicity studies provide conflicting results in the Salmonella bacterium but negative results in the yeast, Saccaromyces cerevisiae. Additional studies are needed to clarify this issue. The potential impact on human health resulting from exposure to bromochloromethane cannot be clearly established at this time due to the extent and quality of health effects data available. However, based on limited data, bromochloromethane exposure does not appear to pose a major health hazard except at high vapor concentrations.

44.4 SAMPLING AND ANALYSIS CONSIDERATIONS

Determination of bromochloromethane concentrations in soil and water requires collection of a representative field sample and laboratory analysis. Due to the volatility of bromochloromethane, care is required to prevent losses during sample collection and storage. Soil and water samples are collected in airtight containers with no headspace; analysis should be completed within 14 days of sampling. In addition to the targeted samples, quality control samples such as field blanks, duplicates, and spiked matrices should be included in the analytical program.

Bromochloromethane is not included among the EPA-designated priority pollutants and an EPA-approved procedure for the analysis of bromochloromethane is not available. However, EPA Methods 601, 624, 1624 (65), 8010 and 8240 (63) would be appropriate methods of choice for the analysis of bromochloromethane in aqueous samples. An inert gas is bubbled through the aqueous sample in a purging chamber at ambient temperature, transferring the bromochloromethane from the aqueous phase to the vapor phase and onto a sorbent trap. The trap is then heated and backflushed to desorb the bromochloromethane and transfer it onto a gas chromatographic (GC) column. The GC column is programmed to separate the volatile organics; bromochloromethane is then detected with a halide specific detector (Methods 01 and 8010) or a mass spectrometer (Methods 624, 1624, and 8240).

The EPA procedures (Methods 8010 and 8240) recommended for analysis of halogenated volatile organic compounds such as bromochloromethane in soil and waste samples (63), differ from the aqueous procedures primarily in the method by which the analyte is introduced into the GC. The recommended method involves dispersing the soil or waste sample in methanol or polyethylene glycol to dissolve the bromochloromethane. A portion of the solution is then combined with water and purged as described above. Other sample introduction techniques include direct injection and thermal desorption.

Bromochloromethane detection limits for the various methods were not determined but would be in the range of 1-10 µg/L for aqueous samples and 1 µg/g for non-aqueous samples.

COMMON SYNONYMS:	CAS REG. NO.:	FORMULA:	AIR W/V CONVERSION FACTORS at 25°C (12)
1,2-Dibromoethane EDB Glycol dibromide	106-93-4 NIOSH NO.: KH9275000	$C_2H_4Br_2$	7.68 mg/m³ ≈ 1 ppm 0.13 ppm ≈ 1 mg/m³
	STRUCTURE: $Br-CH_2-CH_2-Br$		MOLECULAR WEIGHT: 187.88

REACTIVITY	Reactions of halogenated organic materials such as ethylene dibromide with cyanides, mercaptans or other organic sulfides typically generate heat, while those with mineral acids, amines, azo compounds, hydrazines, caustics, or nitrides commonly evolve heat and toxic or flammable gases. Reactions with oxidizing mineral acids may generate heat, toxic gases, and fires. Those with alkali or alkaline earth elemental metals, certain other chemically active elemental metals like aluminum, zinc or magnesium, organic peroxides or hydroperoxides, strong oxidizing agents, or strong reducing agents typically result in heat generation and explosions and/or fires. One source reports that ethylene dibromide slowly decomposes in the presence of light (light source unspecified) (38,54,56,504).

PHYSICO-CHEMICAL DATA	• Physical State (at 20°C): liquid	(23)
	• Color: colorless	(23)
	• Odor: mildly sweet, chloroform odor	(60)
	• Odor Threshold: 10 ppm	(38)
	• Liquid Density (g/ml at 20°C): 2.172	(21)
	• Freezing/Melting Point (°C): 9	(23)
	• Boiling Point (°C): 131	(23)
	• Flash Point (°C): not flammable	(23,504)
	• Flammable Limits in Air, % by Volume: not flammable	(23,504)
	• Autoignition Temperature (°C): not flammable	(23,504,507)
	• Vapor Pressure (mm Hg at 20°C): 11	(67)
	• Saturated Concentration in Air (mg/m³ at 20°C): 113,000	(67)
	• Solubility in Water (mg/L at 20°C): 3400	(21)
	• Viscosity (cp at 21°C): 1.676	(60)
	• Surface Tension (dyne/cm at 20°C): 38.75	(60)
	• Log (Octanol-Water Partition Coefficient), log K_{ow}: 1.76	(1645)
	• Soil Adsorption Coefficient, K_{oc}: 28	(611)
	• Henry's Law Constant (atm•m³/mol at 20°C): 3.18×10^{-4}	(74)
	• Bioconcentration Factor: 2.7 (estim)	(659)

PERSISTENCE IN THE SOIL-WATER SYSTEM	EDB is expected to be highly mobile in the soil/ground-water system. Adsorption onto soils, particularly soil of < 1% organic content, is low. Volatilization may be an important transport process. Degradation of EDB in soil systems is not expected to be significant.

PATHWAYS OF EXPOSURE	The primary exposure pathway of concern from soil/ground-water systems is the migration of EDB to ground-water drinking water supplies. Inhalation exposures may also be important in some situations. Exposures through ingestion of foods contaminated with EDB from soil/ground-water systems are not generally expected to be significant.

HEALTH HAZARD DATA	Signs and Symptoms of Short-term Human Exposure (38,54,45): Inhalation of EDB may cause irritation of the eyes, nose and throat. Systemic exposure via ingestion or inhalation can result in drowsiness, vomiting, nausea, abdominal pain, diarrhea and headache. Prolonged contact of the liquid with the skin may cause erythema, blisters and ulceration; these reactions may be delayed 24-48 hours.
	Toxicity Based on Animal Studies: LD_{50} (mg/kg): oral 146 [rat] (1759); skin 300 [rat] (47) LCLo (mg/m³): inhalation [rat] (47) 3124•2 hr
	Long-Term Effects: Lung, liver and kidney damage
	Pregnancy/Neonate Data: Testicular injury
	Mutation Data: Suggestive evidence of mutagenicity
	Carcinogenicity Classification: IARC-2B; NTP: Clear evidence

HANDLING PRECAUTIONS (38,507)	Handle chemical only with adequate ventilation • Vapor concentrations of 20-400 ppm: any supplied-air respirator or self-contained breathing apparatus with full facepiece; chemical cartridge respirator with full facepiece and an organic vapor cartridge • Greater than 400 ppm: self-contained breathing apparatus with a full facepiece operated in pressure demand or other positive pressure mode • Chemical goggles if there is probability of eye contact • Neoprene or PVC gloves.

EMERGENCY FIRST AID TREATMENT (38,54)	Ingestion: Because many pesticide formulations are combined with other pesticides, fungicides or insecticides and are frequently dissolved in petroleum distillates, vomiting involves a serious risk that solvent will be aspirated, leading to chemical pneumonitis. For these reasons, if the ingested EDB is dissolved in a petroleum-based carrier or a mixed formulation, do not induce vomiting. Contact physician or emergency medical facility immediately. If the ingested EDB is in an aqueous carrier, induce vomiting. Get medical attention immediately • Inhalation: Move victim to fresh air. Give artificial respiration if necessary. Get medical attention • Skin: Remove contaminated clothing immediately. Wash skin with soap and water. If irritation persists after washing, get medical attention • Eye: Flush with large amounts of water. If irritation persists after washing, get medical attention.

ENVIRONMENTAL AND OCCUPATIONAL STANDARDS AND CRITERIA

AIR EXPOSURE LIMITS:

Standards
- OSHA PEL (8-hr TWA): 20 ppm; CL: 30 ppm (8-hr TWA)
- AFOSH PEL (8-hr TWA): 20 ppm; PEAK: 50 ppm (5 min)

Criteria
- NIOSH IDLH (30-min): 400 ppm
- ACGIH TLV® (8-hr TWA): avoid exposure (A2, suspected human carcinogen [skin])
- ACGIH STEL (15-min): none established

WATER EXPOSURE LIMITS:

Drinking Water Standards: None established

EPA Health Advisories

In the absence of formal drinking water standards, the EPA (992) has developed the following Health Advisories (formerly termed SNARLS) for non-carcinogenic risk for short and long-term exposure to EDB in drinking water:

- 1 day: 0.027 mg/L
- 10 days: 0.027 mg/L
- long-term: none established

EPA Ambient Water Quality Criteria (355)
- Human Health

  No criterion established; ethylene dibromide is not a priority pollutant.

- Aquatic Life

  No criterion established; ethylene dibromide is not a priority pollutant.

REGULATORY STATUS (as of January 1, 1987)

Promulgated Regulations

- Federal Programs

Clean Water Act (CWA)
Ethylene dibromide is designated a hazardous substance. It has a reportable quantity (RQ) limit of 454 kg (347,985).

Safe Drinking Water Act (SDWA)
In states with an approved Underground Injection Control program, a permit is required for the injection of ethylene dibromide-containing wastes designated as hazardous under RCRA (295).

Resource Conservation and Recovery Act (RCRA)
Ethylene dibromide is identified as a hazardous waste (U067) and listed as a hazardous waste constituent (328,329). Waste streams from the organic chemicals industry (ethylene dibromide production) contain EDB and are listed as specific sources of hazardous waste (990).

Effective July 8, 1987, the land disposal of hazardous wastes containing halogenated organic compounds in total concentrations greater than or equal to 1000 mg/kg will be prohibited. The only exception will be underground injection (1755).

Comprehensive Environmental Response Compensation and Liability Act (CERCLA)
Ethylene dibromide is designated a hazardous substance under CERCLA. It has a reportable quantity (RQ) limit of 454 kg. Reportable quantities have also been issued for RCRA hazardous waste streams containing ethylene dibromide but these depend upon the concentrations of the chemicals in the waste stream (985).

Federal Insecticide, Fungicide and Rodenticide Act (FIFRA)
Tolerances have been established for inorganic bromide residues in or on raw agricultural commodities grown in soil treated with ethylene dibromide. Levels range from 5 to 125 ppm (977).

The following tolerances have been established for residues of ethylene dibromide (1399):

0.001 ppm in or on soybeans
0.25 ppm in citrus fruits or papayas
0.03 ppm in mangoes

Marine Protection Research and Sanctuaries Act (MPRSA)
Ocean dumping of organohalogen compounds as well as the dumping of known or suspected carcinogens, mutagens or teratogens is prohibited except when they are present as trace contaminants. Permit

applicants are exempt from these regulations if they can demonstrate that such chemical constituents are non-toxic and non-bioaccumulative in the marine environment or are rapidly rendered harmless by physical, chemical or biological processes in the sea (309).

Occupational Safety and Health Act (OSHA)
Employee exposure to ethylene dibromide shall not exceed an 8-hour time-weighted-average (TWA) of 20 ppm. A ceiling level of 30 ppm shall not be exceeded at any time during an 8-hour workshift except for a duration of 5 minutes when it may reach a ceiling level of 50 ppm (298).

Hazardous Materials Transportation Act (HMTA)
The Department of Transportation has designated ethylene dibromide as a hazardous material which is subject to requirements for packaging, labeling and transportation (306).

Food, Drug and Cosmetic Act (FDCA)
The following action levels have been established for residues of ethylene dibromide (1400):

150 ppb in milled products
30 ppb in finished (ready-to-eat) consumer products

- State Water Programs
  Wisconsin has an enforcement standard of 0.02 µg/L and a preventive action limit of 0.002 µg/L for ground water (981).

  Florida has a drinking water standard of 0.02 µg/L (981).

Proposed Regulations

- Federal Programs
  Safe Drinking Water Act (SDWA)
  EPA has proposed a Recommended Maximum Contaminant Level (RMCL) of zero for ethylene dibromide as part of the National Primary Drinking Water Regulations (992).

  Resource Conservation and Recovery Act (RCRA)
  EPA has proposed that non-liquid hazardous wastes containing halogenated organic compounds (HOCs) in total concentrations greater than or equal to 1000 mg/kg or liquid hazardous wastes containing HOCs in total concentrations greater than or equal to 1% HOCs must be incinerated in accordance with the requirements of 40CFR264.343 or 265.343 (1767).

  EPA has also proposed that hazardous waste treatment, storage and disposal facilities monitor ground water for ethylene dibromide when EPA suspects the facilities of leaking contaminants (1754).

EPA has proposed listing washwater from the formulation of mixed alkyl leads as specific source of ethylene dibromide-containing hazardous waste (1397).

Occupational Safety and Health Act (OSHA)
OSHA has proposed lowering the employee exposure limits to ethylene dibromide. They have proposed an 8-hour-time-weighted-average of 0.1 ppm and a ceiling limit of 0.5 ppm. Requirements for exposure monitoring, methods of control, personal protective equipment, hygiene practices, medical surveillance and employee training and education have also been proposed (1394).

- State Water Programs
  No proposed regulations are pending.

EEC Directives

Directive Relating to the Quality of Water for Human Consumption (540)
The maximum admissible concentration for ethylene dibromide is 0.1 μg/L. The total maximum allowable concentration for pesticides and related products is 0.5 μg/L.

Directive on Ground Water (538)
Direct discharge into ground water (i.e., without percolation through the ground or subsoil) of organophosphorous compounds, organohalogen compounds and substances which may form such compounds in the aquatic environment, substances which possess carcinogenic, mutagenic or teratogenic properties in or via the aquatic environment and mineral oils and hydrocarbons is prohibited. Appropriate measures deemed necessary to prevent indirect discharge into ground water (i.e., via percolation through ground or subsoil) of these substances shall be taken by member countries.

Directive on the Quality Required of Shellfish Waters (537)
The mandatory specifications for organohalogenated substances specify that the concentration of each substance in the shellfish water or in shellfish flesh must not reach or exceed a level which has harmful effects on the shellfish and larvae. The guideline specifications for organohalogenated substances state that the concentration of each substance in shellfish flesh must be so limited that it contributes to the high quality of shellfish product.

Directive Relating to the Classification, Packaging and Labeling of Dangerous Preparations (Solvents) (544)
Ethylene dibromide is listed as a Class I/a toxic substance and is subject to packaging and labeling regulations.

Directive on the Discharge of Dangerous Substances (535)
Organohalogens, organophosphates, petroleum hydrocarbons, carcinogens or substances which have a deleterious effect on the taste and/or odor

of human food derived from aquatic environments cannot be discharged into inland surface waters, territorial waters or internal coastal waters without prior authorization from member countries which issue emission standards. A system of zero-emission applies to discharge of these substances into ground water.

Directive on Marketing and Use of Dangerous Substances (541)
Ethylene dibromide may not be used in ornamental objects intended to produce light or color effects by means of different phases.

Directive on Toxic and Dangerous Wastes (542)
Any installation, establishment, or undertaking which produces, holds and/or disposes of certain toxic and dangerous wastes including phenols and phenol compounds; organic-halogen compounds; chrome compounds; lead compounds; cyanides; ethers and aromatic polycyclic compounds (with carcinogenic effects) shall keep a record of the quantity, nature, physical and chemical characteristics and origin of such waste, and of the methods and sites used for disposing of such waste.

Directive on the Classification, Packaging and Labeling of Dangerous Substances (787)
Ethylene dibromide is classified as a toxic substance and is subject to packaging and labeling regulations.

Directive on Major Accident Hazards of Certain Industrial Activities (1794)
Ethylene dibromide manufacturers are required to notify competent authorities if it is stored or processed in quantities in excess of 50 tons. If a major accident occurs, authorities must be provided with the circumstances of the accident, substances involved, emergency measures taken, and the data available for assessing the effects on man and the environment.

EEC Directives - Proposed

Proposal for a Council Directive on the Dumping of Waste at Sea (1793)
EEC has proposed that the dumping of organohalogen compounds at sea be prohibited.

EEC has proposed that the dumping of pesticides at sea be forbidden without prior issue of a special permit.

Proposal for a Council Directive Amending Directive 79/117/EEC Prohibiting the Placing on the Market and Use of Plant Protection Products Containing Certain Active Substances (1427)
EEC has proposed that plant protection products containing ethylene dibromide not be placed on the market or used unless necessary because of an unforeseeable danger threatening plant production which cannot be controlled by other means, such products may be permitted to be marketed and/or used for a maximum period of 120 days.

45.1 MAJOR USES

The major use of ethylene dibromide (EDB) is as a lead scavenger in antiknock mixtures added to gasolines. Due to EPA regulations limiting the lead content of gasolines, the use of EDB in this area is decreasing. The second major commercial use of EDB has been as an ingredient of soil and grain fumigants to protect stored grain from pest infestations and to control fruit flies; however, recent EPA regulations have eliminated about 97% of EDB's agricultural use.

The minor uses of EDB include use as a chemical intermediate and as a nonflammable solvent for resins, gums and waxes (1605).

45.2 ENVIRONMENTAL FATE AND EXPOSURE PATHWAYS

45.2.1 Transport in Soil/Ground-water Systems

45.2.1.1 Overview

EDB may move through the soil/ground-water system when present at low concentrations (dissolved in water and sorbed on soil) or as a separate organic phase (resulting from a spill of significant quantities of the chemical). In general, transport pathways can be assessed with the results of an equilibrium partitioning model as shown in Table 45-1. These calculations predict the partitioning of low soil concentrations of EDB among soil particles, soil water and soil air. The EDB associated with the water and air phases of the soil is more mobile than that which is adsorbed.

The estimates for the unsaturated topsoil model indicate that approximately 15% of the EDB is expected to be present in the soil-water phase and thus available to migrate by bulk transport (e.g., the downward movement of infiltrating water), dispersion and diffusion. For the small portion of EDB in the gaseous phase of the soil (1%), diffusion through the soil-air pores up to the ground surface, and subsequent removal by wind, may be a significant loss pathway. In saturated, deep soils (containing no soil air and negligible soil organic carbon), a much higher fraction of the EDB (89%) is expected to be in the soil-water phase (Table 45-1) and transported with flowing ground water. Ground water underlying EDB-contaminated soils with low organic content is highly vulnerable to contamination. Using an index designed to rank chemicals in terms of their relative potential to intrude into ground water, Rao et al. (1531) determined that EDB had the highest potential for ground water contamination of the 41 organic chemicals they examined.

Application of a screening model (808) to determine the behavior of trace organics in soil indicated that EDB is expected to be highly mobile by both diffusion and dispersion. Volatilization is expected to be significant with an effective half-life of 3.4 days under conditions of deep placement (10 cm) in soil containing 1.25% organic carbon.

TABLE 45-1

EQUILIBRIUM PARTITIONING CALCULATIONS FOR ETHYLENE DIBROMIDE IN MODEL ENVIRONMENTS[a]

Soil Environment	Estimated Percent of Total Mass of Chemical in Each Compartment		
	Soil	Soil-Water	Soil-Air
Unsaturated topsoil at 25°C[b,c]	83.8	15.6	0.6
Saturated deep soil[d]	10.5	89.5	-

a) Calculations based on Mackay's equilibrium partitioning model (34,35,36); see Introduction in Volume 1 for description of model and environmental conditions chosen to represent an unsaturated topsoil and saturated deep soil. Calculated percentages should be considered as rough estimates and used only for general guidance.

b) Use estimated soil sorption coefficient: K_{oc} = 28 (611).

c) Henry's law constant taken as 3.18×10^{-4} atm·m³/mol at 25°C (74).

d) Used sorption coefficient (K_p) calculated as a function of K_{oc} assuming 0.1% organic carbon: $K_p = 0.001 \times K_{oc}$.

45.2.1.2 Sorption on Soils

The mobility of EDB in the soil/ground-water system (and its eventual migration into aquifers) is strongly affected by the extent of its sorption on soil particles. In general, sorption on soils is expected to:

- increase with increasing soil organic matter content;
- increase slightly with decreasing temperature;
- increase moderately with increasing salinity of the soil water; and
- decrease moderately with increasing dissolved organic matter content of the soil water.

Values of the equilibrium soil sorption constant (K_{oc}) for EDB have been reported to range from 28 to 66 (1531,611,230,808,1645) suggesting weak sorption to soils; sorption is expected to increase as organic content of the soil increases. Chiou et al. (1646) examined

the transfer of nonionic chemicals, including EDB, from water to soil and indicated that the process is essentially one of partitioning (dissolution) rather than physical adsorption. The soil-water equilibrium isotherms showed no indication of curvature even at high concentrations, and the distribution coefficients were inversely proportional to the water solubilities.

Rogers and MacFarlane (1645) found only minimal sorption of EDB on soils (1.8-2.6% organic carbon content) and clay; only 0.3% to 4% of the available chemical was sorbed by the absorbent. Schwarzenbach et al. (77) determined retardation rates, which represent interstitial water velocity/ pollutant velocity in the soil, for several chlorinated organics with higher K_{ow} and K_{oc} values than EDB. The data indicate some retention in soils having 1-2% organic carbon content and little or no retention in soils with less than 0.1% organic carbon. Wilson et al. (82) reported a retardation factor of 1.2 in sandy soil for 1,2-dichloroethane with K_{ow} and K_{oc} values only slightly lower than those for EDB. Assuming analogous soil conditions, retention of EDB, particularly in deep soils of low organic content, is not expected to be significant.

45.2.1.3 Volatilization from Soils

Transport of EDB vapors through the air-filled pores of unsaturated soils may be an important transport mechanism for near-surface soils. In general, important soil and environmental properties influencing the rate of volatilization include soil porosity, temperature, convection currents and barometric pressure changes; important physicochemical properties include the Henry's law constant, the vapor-soil sorption coefficient, and, to a lesser extent, the vapor phase diffusion coefficient (31). No information was available on the latter two physico-chemical properties.

The Henry's law constant (H), which provides an indication of a chemical's tendency to volatilize from solution, is expected to increase significantly with increasing temperature. Moderate increases in H were also observed with increasing salinity and the presence of other organic compounds (18). The Henry's law constant for EDB is estimated to be 3.18×10^{-4} atm•m^3/mol (74), suggesting moderate volatility from aqueous solution. Although volatilization from soil will be slower than from water, it may be an important fate process due to the relatively weak sorption and slow transformation of EDB.

No specific information regarding the rate of EDB volatilization from soils was available. However, evidence of EDB emanating from selected hazardous and sanitary landfills in New Jersey has been provided (1647); ambient air concentrations in the vicinity of the hazardous waste sites were higher than levels measured at an urban/industrial site in Newark. No volatilization rates were determined.

Volatilization of EDB from water has been shown to be enhanced by subwater mixing (1597); the evaporation half-life from 1.6 cm of water with stirring was reported to be 6.8 minutes. Other studies have reported EDB volatilization half-lives ranging from 4-6 hours for 1 m water depth (1649). Volatilization half-lives for ethylene dichloride (1,2-dichloroethane), with a Henry's law constant of 1.1×10^{-3} atm•m^3/mol, in stirred aqueous solutions have been reported to range from 29-90 minutes depending on the degree of agitation (10); volatilization of EDB from similar aqueous solutions would be somewhat slower. Compared to their volatilization from well-stirred solutions, volatilization of some halogenated organics from near-surface soils has been reported to be slower by approximately one order of magnitude (82).

45.2.2 Transformation Processes in Soil/Ground-water Systems

The persistence of EDB in soil/ground-water systems is not well documented. Under normal environmental conditions, EDB is not expected to undergo rapid hydrolysis. The half-life of EDB due to hydrolysis has been reported to be 5-10 days, favored by acid conditions (1650); other authors report the rate of hydrolysis in neutral water to be quite slow, with half-lives on the order of 13-16 years (1651,1652). In soil-water culture, 10^{-4} M EDB required two months for degradation (1651).

EDB has been shown to undergo rapid photohydrolysis in aqueous solution (1652) in spite of the fact that the absorption spectrum for EDB trails only slightly into the visible. The photolytic reaction of EDB (10^{-2} M) was complete within two hours, representing a rate enhancement on the order of 10^5 over the nonphotolytic pathway for which the half-life was determined to be 16 years. No additional data on the photolysis or oxidation of EDB in soil were available.

Literature references to microbial degradation of EDB are few. One study reported no degradation of EDB in water under anaerobic conditions in the presence of primary sewage seed (1653), while another study reported degradation under methanogenic conditions but no degradation in aerobic cultures (1654). Castro and Belser (1655) reported 97% degradation of EDB in eight weeks with a soil inoculum added to autoclaved soil.

Most references indicate that low molecular weight chloroaliphatics are not rapidly metabolized in the environment (76) although biodegradation by acclimated populations may occur. Slow to moderate degradation of ethylene dichloride was observed by Tabak et al. (79) with an acclimated, activated-sludge population; and Thom and Agg (80) included ethylene dichloride in a list of organic chemicals amenable to degradation by biological sewage treatment, providing suitable acclimatization was achieved. In situ biodegradation by blended specialized bacterial seed cultures has been suggested as a decontamination procedure for soils contaminated with ethylene dichloride (650). There are insufficient data to determine whether EDB would behave similarly.

In most natural soil/ground-water systems, the concentration of microorganisms capable of biodegrading chemicals such as EDB is expected to be very low and to drop off sharply with increasing depth. Thus, biodegradation in the soil/ground-water system should be assumed to be of minimal importance except, perhaps, in landfills with active microbiological populations.

45.2.3 Primary Routes of Exposure from Soil/Ground-water Systems

The above discussion of fate pathways suggests that ethylene dibromide has a moderate volatility, is weakly sorbed to soil, and has no significant potential for bioaccumulation. Ethylene dibromide on the soil surface is likely to volatilize, but that portion not subject to volatilization is likely to be mobile in ground water. These fate characteristics suggest several exposure pathways.

Volatilization of EDB from a disposal site could result in inhalation exposures. Harkov et al. (1647) measured VOC levels at six abandoned hazardous waste sites, as well as a sanitary landfill, in New Jersey. They found mean levels of EDB ranging from 0.01 to 0.47 ppb (volume) for the seven sites, with a maximum concentration of 6.71 ppb (volume). EDB was not detected (at about 0.05 ppb (volume)) at an urban/industrial site in Newark, New Jersey. The authors concluded that some VOC, including EDB were found at higher concentrations at hazardous waste sites than in typical urban areas.

The potential for drinking water contamination resulting from the migration of EDB with ground water is high. In a monitoring study of pesticides in ground water, EDB was detected at levels of 0.05 to 20 ppb (1797). In addition, EDB has been detected in a number of states. In one state, levels of EDB from 0.02-560 μg/L were detected in 25 samples of ground water (992). While those levels are generally attributed to agricultural practices, the data indicate the mobility of EDB and its potential for contamination of ground-water drinking water supplies.

Discharges of EDB to surface water from soil/ground-water systems would probably not represent significant sources of exposure due to this compound's high volatility and its low potential for bioaccumulation.

45.2.4 Other Sources of Human Exposure

EDB has been widely used in the past as an additive in leaded gasoline as well as a pesticide. As a result, there are a number of other sources of human exposure. As discussed in the previous section, EDB has been found to some extent in ground-water drinking water supplies. According to EPA (1419), levels in drinking water range from 0-560 μg/L.

As a result of the use of EDB as a soil fumigant and as a post-harvest fumigant, residues of this compound in food were common, although most uses of EDB were cancelled in 1984. In the EPA Position Document 4 (1796), they estimate the EDB intake from citrus to be 0.00041 μg/kg/day for non-California citizens, and 0.0069 μg/kg/day for California residents. The mean dietary intake from EDB-contaminated grain was estimated to be 0.0063 μg/kg/day. It is likely that these intakes may have decreased since uses of EDB are now limited.

EDB has been detected in air resulting from its use in leaded gasoline. Brodzinsky and Singh (84) conducted an assessment of available data for volatile organic chemicals. They reported median levels of EDB below detection limits in rural/remote areas, 200 ng/m^3 in urban/suburban areas, and 1500 ng/m^3 in source-dominated areas. A total of 930 data points were evaluated.

34.3 HUMAN HEALTH CONSIDERATIONS

45.3.1 Animal Studies

45.3.1.1 Carcinogenicity

EDB has been demonstrated to be carcinogenic in rodents by oral, inhalation and dermal routes.

The NCI conducted a bioassay of technical grade EDB by the oral route using Osborne-Mendel rats and B6C3F1 mice (1606). EDB was administered in corn oil by gavage at time-weighted average doses of 41 or 38 mg/kg/day for male rats, 39 or 37 mg/kg/day for female rats, and 107 or 62 mg/kg/day for mice of both sexes. Due to excessive mortality, male and female rats were terminated in weeks 49 and 61, respectively, and all male and high dose female mice died or were sacrificed by week 78. In rats, squamous cell carcinomas of the forestomach were observed in a dose-related manner in both sexes at incidences ranging from 58 to 90%. Squamous cell carcinomas were also observed in both sexes of mice at incidences of 56 to 94%. None were found in controls of either species. These lesions were seen as early as week 12 in rats and week 24 in mice. There also were statistically significant incidences of hepatocellular carcinomas in female rats, hemangiosarcomas in male rats, and alveolar/bronchiolar adenomas in male and female mice.

A 78 to 103 week inhalation bioassay was conducted in F344 rats and B6C3F1 mice by the National Toxicology Program (1743). Animals of both sexes in each species were exposed to vapor levels of either 10 or 40 ppm, 6 hours per day, 5 days per week. In rats, there was a dose-related increase in the incidence of nasal cavity tumors in both sexes (58%-86%). In high-dose animals of both sexes, there was a statistically significant increase in circulatory system hemangiosarcomas - 30%

in males, 10% in females, none in controls. In high-dose males, there was a 50% incidence of mesotheliomas of the tunica vaginalis compared with none in the controls. In females, the incidence of fibroadenomas of the mammary gland was statistically significant in both low- and high-dose groups - 58% and 48%, respectively. There was 8% incidence in female controls. An 11% incidence of alveolar/bronchiolar adenomas and carcinomas was also observed in high-dose females.

In mice a statistically significant number of alveolar/bronchiolar carcinomas and adenomas were seen in high-dose males (50%) and females (82%). There was an overall incidence of 4% in controls. Fibroadenomas of the mammary gland were seen in the females but the trend was not dose-related (28% in the low-dose group vs. 16% in the high-dose group). Hemangiosarcomas occurred in low- (22%) and high-dose (46%) females. There was also a 22% incidence of subcutaneous fibrosarcomas and a 24% incidence of nasal cavity carcinomas in high-dose females (1743).

Another inhalation study was conducted by Wong et al. (1744) in Sprague-Dawley rats. Animals were exposed to vapor concentrations of 20 ppm with and without 0.05% disulfiram in the diet or to disulfiram alone. [Disulfiram decreases oxidative metabolism and increases the degree of glutathione conjugation of EDB, resulting in increased binding to DNA (1762).] Exposure was for 7 hours per day, 5 days per week over an 18 month period. Survival of the animals was poor. At the end of 18 months, males and females exposed to EDB alone had mortalities of 90% and 77%, respectively. All animals receiving EDB and disulfiram died within 15 months. Male rats receiving EDB alone had significantly higher tumor incidences in the spleen, adrenal and subcutaneous mesenchymal tissue than control males. Females exposed to EDB had significantly higher tumor incidences in the spleen, adrenals and mammary glands when compared with female controls. In animals receiving EDB with disulfiram there were significant increases in tumors of the liver, kidneys and thyroid when compared with animals receiving EDB or disulfiram alone. There were also high incidences of hemangiosarcoma in the liver, spleen and mesentery in animals receiving the EDB/disulfiram combination. Males receiving the combination had a higher incidence of lung tumors than males receiving EDB alone. No lung tumors were observed in either control or disulfiram treated rats. Generally, in rats receiving the combination treatment, neoplasms were found earlier and at a higher incidence than in rats receiving either chemical alone.

Van Duuren et al. (142) found that EDB induced a statistically significant incidence of skin papillomas, skin carcinomas and lung tumors in female Ha:ICR Swiss mice. EDB was applied to the dorsal skin 3 times weekly as a 50 mg dose in 0.2 mL of acetone. The first tumor was seen after 395 days.

Kowalski et al. (1763) demonstrated that the target tissues for EDB-induced carcinogenic effects can metabolize EDB to reactive products which become universally bound to tissue constituents. A good

correlation was found between reported organ sensitivities to EDB and the binding of EDB metabolites in the tissues. For example, a high degree of binding was found in the squamous epithelium of the forestomach, the bronchiolar epithelium, nasal epithelium and in the adrenal cortex, areas in which EDB has induced tumors in animals.

45.3.1.2 Mutagenicity

EDB is mutagenic to bacteria, fungi, insects and cultured mammalian cells in the absence of an activation system.

Reverse mutations have been reported in various strains of Salmonella typhimurium (1108,1725), E. coli (1108) and B. subtilis (1725). In fungi, EDB produced forward mutations in Streptomyces coelicolor and Aspergillus nidulans (1726). Recessive lethal mutations were induced in Drosophila melanogaster that were exposed to concentrations as low as 0.2 ppm for 11 hours (1727).

A significant and dose-dependent increase in the frequency of chromosomal aberrations and sister chromatid exchanges was seen in Chinese hamster cells exposed to EDB (1728). EDB has induced sister chromatid exchanges in human lymphocytes in vitro (1729) and in 2 human lymphoblastoid cell lines, it induced gene mutations at the hgprt locus (1730).

In vivo studies in animals and man have given negative or marginal results. No dominant lethal effects were seen in mice given single ip doses of 18 or 90 mg/kg or oral doses of 50 or 100 mg/kg daily for 5 days (998), but single ip doses of 84 or 168 mg/kg produced sister chromatid exchanges in bone marrow cells at a rate slightly higher than controls (1761). Steenland et al. (1731,1732) found that neither short- nor long-term exposures to EDB caused any chromosomal abnormalities in humans. Short-term exposures were for an average of 14 days with an 8-hour TWA of 60 ppb. Long-term exposures were for an average of 5 years with an 8 hour TWA of 88 ppb.

45.3.1.3 Teratogenicity, Embryotoxicity and Reproductive Effects

EDB induces testicular damage at low doses. There is also evidence that EDB may induce sperm abnormalities and sperm death. In the NTP bioassay conducted with F344 rats (1743), testicular atrophy was observed in 4% of the low-dose animals (10 ppm) and in 10.2% of the high-dose (40 ppm) animals. Many cases of atrophy in the high-dose group were associated with testicular tumors and may not reflect direct EDB toxicity. Testicular degeneration, however, was found in 20% of the low-dose and 36.7% of the high-dose animals.

Oral doses of 38 or 41 mg/kg/day caused testicular atrophy at rates of 29 and 36%, respectively, after 49 weeks of administration to Osborne-Mendel rats. B6C3F1 mice exhibited a 21% rate of atrophy after 78 weeks of oral doses of 107 mg/kg/day (1606). Intraperitoneal doses

of 10 mg/kg for 5 days produced transient sterility in Wistar rats which resulted from damage to spermatids. Normal fertility returned after 5 weeks (1740).

Rats and mice exposed to 0, 20, 38 or 80 ppm EDB, 23 hours per day on days 6 through 16 of gestation showed no evidence of teratogenic effects. There was some evidence of embryotoxicity as measured by increased resorptions but this was not statistically significant. There was also a minor incidence of external, soft-tissue and skeletal anomalies but these occurred only at concentrations that affected maternal welfare (1742).

45.3.1.4 Other Toxicologic Effects

45.3.1.4.1 Short-term Toxicity

Animal studies have confirmed that EDB is acutely toxic to the liver and kidneys, but near-lethal doses are required to produce observable organ damage (1745). Generally, the margin between the dose which is tolerated for long-term exposure and that causing severe injury and death is small (12).

Rowe et al. (1759) reported single oral dose LD_{50} values for several species of animals. These range from 55 mg/kg in female rabbits to 420 mg/kg in female mice. Values of 146 and 117 mg/kg were reported for male and female rats, respectively.

These investigators also studied the effects of EDB on various animal species by single and repeated inhalation exposures. The maximum survival times of rats exposed to EDB vapors were as follows: 3000 ppm for 6 minutes, 400 ppm for 30 minutes and 200 ppm for 2 hours. In female rats, the no adverse effect levels were 600 ppm for 6 minutes, 100 ppm for 2.5 hours and 50 ppm for 7 hours. The pathological changes noted were congestion, edema, hemorrhages and inflammation of the lungs, cloudy swelling, fatty degeneration and necrosis of the liver, and interstitial congestion, edema and cloudy swelling of the tubular epithelium of the kidney. No adverse effects were reported in rats and guinea pigs exposed to vapor levels of 25 ppm, 7 hours per day for 13 exposures in 17 days (1759).

In an early study by Kochman (1760), cats and rabbits were exposed to vapor levels of approximately 100 ppm for 30 minutes per day. The survival period for cats was approximately 10 days. Autopsy showed that the body cavities contained a clear, yellow liquid. The lungs were judged to be partially nonfunctional and contained dark red discolorations. The spleen was slightly enlarged and the kidneys were swollen and yellow colored. Fatty degeneration of the liver and tubular degeneration of the kidney were also noted. Rabbits survived from 4 to 22 days. Autopsy revealed hyperemia of the liver and kidneys, blood in the colon and an excessive amount of liquid in the small intestine.

Dermal contact lasting for 24 hours was survived by 14 of 15 rabbits at a dose of 210 mg/kg but resulted in 100% mortality after a dose of 1100 mg/kg. In all of the exposed animals, EDB produced moderate to severe erythema, edema, skin necrosis and marked CNS depression (1759). A dermal LD_{50} of 300 mg/kg in rabbits has been reported (47).

Undiluted EDB caused pain and conjunctival irritation when applied to the eyes of rabbits. Slight but superficial necrosis was also observed but healing was prompt and complete (1759).

45.3.1.4.2 Chronic Toxicity

Long-term exposure to EDB affects the lung, liver and kidneys. Rowe et al. (1759) investigated the chronic toxicity of EDB in rats, rabbits, guinea pigs and monkeys. Exposures to vapor levels of 25 ppm for 156 seven-hour exposures in 220 days caused no adverse effects, but exposures to 50 ppm, 7 hours per day, 5 days per week for 70-90 days was not well tolerated by any test species. Guinea pigs were the most sensitive exhibiting increased lung, liver and kidney weights, depressed body weight gain, slight central fatty degeneration of the liver and slight degeneration of the renal tubular epithelium. Rabbits showed only small increases in liver and kidney weights. Monkeys appeared ill, nervous and unkempt. Liver weights were increased and there was very slight central fatty degeneration of the liver. Rats exhibited increased liver and kidney weights, increased lung weights and decreased testis weights in males and decreased spleen weights in females. In a 13-week study, Reznik et al. (1764) found histopathological changes to be limited to the respiratory tract in rats and mice exposed to 75 ppm EDB vapor 6 hours daily, 5 days per week. Changes in the nasal cavity included loss of cilia, cytomegaly, focal hyperplasia and squamous metaplasia.

Other effects seen in the NCI carcinogenicity bioassay were degenerative changes in the liver and adrenal cortex in high and low dose rats and testicular atrophy in male rats and mice (1606).

45.3.2 Human and Epidemiologic Studies

45.3.2.1 Short-term Toxicologic Effects

Acute oral or inhalation exposure to EDB causes vomiting, diarrhea, abdominal pain and in some cases delayed lung damage and CNS depression (1745). In the past, EDB was occasionally confused with the anesthetic ethyl bromide. NIOSH (1741) reported an early case in which EDB was accidentally used in this manner. The female patient, after being administered the contents of a 70 g bottle, experienced symptoms of dizziness, vomiting, diarrhea, difficult breathing, thirst, abdominal pain and uterine hemorrhaging. She died within 44 hours of receiving the EDB. Autopsy results revealed skin vessels filled with blood and body cavities which contained clear, red liquid. There were signs of upper respiratory tract irritation with extensive surface

hemorrhage. The heart, liver and kidneys were in the advanced stages of parenchymatous degeneration. Microscopic examination showed fatty degeneration of the liver cells and cardiac musculature.

One case of ingestion of EDB has been reported (1746). In this instance, a 43-year-old woman ingested 4.5 mL (~140 mg/kg) EDB in capsule form. She began vomiting immediately and continued to do so periodically for the next 48 hours. Diarrhea began after 24 hours. There was both a darkening of the urine and a decrease in volume after 36 hours. The patient was hospitalized 48 hours after ingestion and was completely anuric at this time. She did not improve after supportive treatment and died 54 hours after ingestion. Autopsy revealed no excess fluid in body cavities and no gross cardiac abnormalities. Microscopic examination showed massive hepatic necrosis with red blood cells in the sinusoids and scattered areas of yellow pigment. The kidneys were intensely congested with local damage in the proximal tubular epithelium.

Acute occupational exposure of workers cleaning a storage tank led to 2 additional fatalities (1747). The first worker collapsed within 5 minutes of entering the tank and died 12 hours later. A supervisor attempting to rescue the first worker also collapsed inside the tank and died 64 hours later. Both workers experienced nausea, vomiting, diarrhea, acute renal and hepatic failure and metabolic acidosis. Two hours after the accident 7.5 cm of liquid was found at the bottom of the tank. Upon analysis, it was found to contain between 0.1 and 0.3% EDB and traces of dichloropropene and dichloropropane and high concentrations of nitrates and phosphates. EDB was the only airborne toxicant detected. Levels ranged from 15 to 41 ppm. Death was attributed to dermal exposure for a 20-60 minute period. The inhalation of EDB was not considered to be a significant factor in this case because the air levels that were measured in the tank would not produce toxic effects in animals. An alternative cause of these fatalities was thought to be clostridial infections since 2 species of pathogenic clostridia were isolated from lung tissue (1748). This hypothesis was disputed because of the long time period which elapsed before death and because the victims had no predisposing factors (1749).

Liquid EDB is highly irritating to human skin causing marked erythema and vesiculation (46). Pflesser (1750) conducted a series of experiments in which EDB was in contact with the skin for various periods of time. In the first experiment, 0.5 mL of EDB was rubbed into the forearm for 1 minute and washed with soap and water 30 minutes later. All subjects developed swelling, reddening and itching within 24 hours. These subsided within 2-3 days. In another experiment, the subjects applied 0.5 mL EDB with a swab and covered the area for 10 minutes. During this time, slight burning was noticed. The area was then cleansed with soap and water. During the next 24 hours, reddening and swelling developed but disappeared in 3-5 days. In a subsequent experiment, the same procedure was repeated and the site was covered for 30 minutes. During the exposure, subjects reported burning at the

application site. Within 15-20 minutes after exposure, there was painful inflammation of the skin, which included reddening, swelling and blistering. The damaged skin healed after 7-13 days of supportive treatment.

EDB vapor is irritating to the eyes and there have been no reports of corneal opacification (19).

45.3.2.2 Chronic Toxicologic Effects

There is no conclusive evidence that long-term exposure to EDB causes cancer or adverse reproductive effects to humans. To evaluate long-term effects in humans, epidemiologic studies of workers occupationally exposed to EDB have been reported but substantial deficiencies have limited the use of these data in risk analysis.

In 1980, Ott et al. (1756) reported a retrospective mortality study of 161 male workers who were exposed to EDB in 2 manufacturing facilities. All workers were reactor and still operators. Sixty-two were employed in plant A, which operated from the mid 1920's until 1976. Workers at this plant were exposed to vapor levels ranging from 1 to 70 ppm. Besides EDB, workers at this plant were reportedly exposed to 25 other substances including bromine, benzene, substituted phenols, vinyl bromide, carbon tetrachloride and other halogenated hydrocarbons. The remaining 99 workers were employed at plant B, which operated from 1942 to 1969. In addition to EDB, these workers were exposed to bromine, ethylene, chlorine and sulfur dioxide. Vapor levels at plant B were not reported. There were 9 deaths due to malignant neoplasms, but this included 2 deaths from lung cancer in workers also exposed to arsenic. Since arsenic is known to increase the risk of lung cancer, these workers were excluded from the analysis. At plant A, there were 5 deaths versus 2.2 expected while at plant B there were 2 deaths versus 3.6 expected. The results of this study are inconclusive due to the small sample size, lack of EDB exposure data at plant B and exposure to other halogenated solvents.

TerHaar (1757) reported that EDB exposure for periods ranging from 3 months to 10 years resulted in 1 death from kidney cancer in 53 employees. In evaluating the reproductive toxicity of EDB, exposures at less than 5 ppm had no adverse effect on sperm counts. A retrospective evaluation of workers reproductive histories found no significant difference between the observed and expected number of live births among 297 worker's wives.

NIOSH recently reported a reproductive study conducted in 46 men exposed to a mean vapor level of 88 ppb EDB for 5 years. Statistically significant adverse reproductive effects which were noted included decreased sperm count, decreased percentage of viable and motile sperm, and an increased proportion of sperm with morphologic abnormalities (1758).

45.3.3 Levels of Concern

In the absence of formal drinking water standards, the EPA (992) has established the following Health advisories for noncarcinogenic risk for short and long-term exposure to EDB in drinking water: 1-day - 0.027 mg/L; 10-days - 0.027 mg/L; long-term - none established.

The ACGIH (3) have given EDB an A2 (suspected human carcinogen) classification, with a recommendation that exposure be avoided. OSHA (298) currently permits exposure to an 8-hour time-weighted-average of 20 ppm EDB, with a not to be exceeded ceiling limit of 30 ppm during an 8-hour work-shift except for a peak level of 50 ppm for a duration of five minutes. OSHA (1398) has proposed but not yet enacted to lower employee exposure limits to 0.1 ppm (8-hr TWA) with a ceiling limit of 0.5 ppm.

45.3.4 Hazard Assessment

EDB is carcinogenic to mice and rats by oral administration, producing squamous-cell carcinomas of the forestomach in both species (1606). Inhalation of EDB vapors produced alveolar/bronchiolar carcinomas, hemangiosarcomas and numerous other tumors in rats and mice (1743,1744). EDB also produced skin, lung and forestomach tumors in mice after dermal application (142). Evidence for carcinogenicity to humans is inadequate. IARC has categorized EDB as a group 2B carcinogen. Results of NTP bioassay indicate clear evidence of carcinogenicity. The USEPA (667) has calculated an upper limit incremental unit cancer risk of 41 $(mg/kg/day)^{-1}$ for EDB.

There is also sufficient evidence to indicate mutagenic activity in a wide variety of non mammalian test systems and in cultures of mammalian cells (1108,1726,1728,1730).

EDB does not appear to be teratogenic in either rats or mice but it does induce testicular degeneration in these species at levels as low as 10 ppm (1742,1605,1743). A recent NIOSH report suggest possible human reproductive disorders in men exposed to a mean EDB vapor level of 88 ppb for 5 years (1758).

EDB vapor is irritant to eyes and mucous membranes, high vapor concentrations can result in CNS depression (1745). Acute exposures may cause lung, liver and kidney damage (1759,1745).

Prolonged contact of the liquid with the skin may cause erythema, blistering and skin ulcers; reactions may be delayed by 24-48 hours (46,1750). Deaths have occurred in humans after the inadvertent ingestion (4.5 m.) or inhalation of EDB (1746,1747).

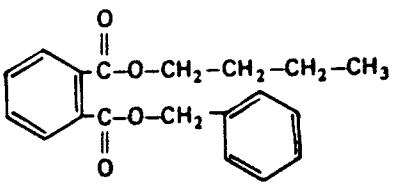
45.4 SAMPLING AND ANALYSIS CONSIDERATIONS

Determination of ethylene dibromide concentrations in soil and water requires collection of a representative field sample and laboratory analysis. Due to the volatility of ethylene dibromide, care is required to prevent losses during sample collection and storage. Soil and water samples e collected in airtight containers with no headspace; analysis should be completed within 14 days of sampling. In addition to the targeted samples, quality control samples such as field blanks, duplicates, and spiked matrices should be included in the analytical program.

Ethylene dibromide is not included among the EPA-designated priority pollutants and an EPA-approved procedure for the analysis of ethylene dibromide is not available. However, EPA Methods 601, 624, 1624 (65), 8010 and 8240 (63) would be appropriate methods of choice for the analysis of ethylene dibromide in aqueous samples. An inert gas is bubbled through the aqueous sample in a purging chamber at ambient temperature, transferring the ethylene dibromide from the aqueous phase to the vapor phase and onto a sorbent trap. The trap is then heated and backflushed to desorb the ethylene dibromide and transfer it onto a gas chromatographic (GC) column. The GC column is programmed to separate the volatile organics; ethylene dibromide is then detected with a halide specific detector (Methods 601 and 8010) or a mass spectrometer (Methods 624, 1624, and 8240).

The EPA procedures recommended for ethylene dibromide analysis in soil and waste samples, Methods 8010 and 8240 (63), differ from the aqueous procedures primarily in the method by which the analyte is introduced into the GC. The recommended method involves dispersing the soil or waste sample in methanol or polyethylene glycol to dissolve the ethylene dibromide. A portion of the solution is then combined with water and purged as described above. Other sample introduction techniques include direct injection and thermal desorption.

Ethylene dibromide detection limits for the various methods were not determined but would be in the range of 1-10 $\mu g/L$ for aqueous samples and 1 $\mu g/g$ for non-aqueous samples.

COMMON SYNONYMS:	CAS REG. NO.:	FORMULA:	AIR W/V CONVERSION FACTORS at 25°C (202)
1,2-Benzenedicarboxylic acid, butyl phenylmethyl ester Benzyl butyl phthalate BBP Phthalic acid, butyl benzyl ester	85-68-7 NIOSH NO.: TH9990000	$C_{19}H_{20}O_4$	12.8 mg/m³ = 1 ppm 0.078 ppm = 1 mg/m³
	STRUCTURE: 		MOLECULAR WEIGHT: 312.39

REACTIVITY	Butyl benzyl phthalate is considered to be an ester for compatibility classification purposes. Such compounds generally evolve heat in reactions with non-oxidizing mineral acids or caustics. Reactions with oxidizing mineral acids, other strong oxidizers, or strong reducing agents may result in heat evolution and fire. Those with alkali or alkaline earth metals or nitrides may evolve heat and flammable gases, while those with azo or diazo compounds or hydrazines may produce heat and typically innocuous gases. Reactions with explosive materials may result in an explosion (51, 507,511).

PHYSICO-CHEMICAL DATA	• Physical State (at 20°C): oily liquid	(23)
	• Color: clear	(23)
	• Odor: slight	(23)
	• Odor Threshold: no data	( )
	• Liquid Density (g/ml at 25°C): 1.113-1.121	(23)
	• Freezing/Melting Point (°C): -35	(59)
	• Boiling Point (°C): 370	(59,507)
	• Flash Point (°C): 199 (open cup)	(23,60, 506,507)
	• Flammable Limits in Air, % by Volume: 0.26 (calc.) - ?	(507)
	• Autoignition Temperature (°C): no data	( )
	• Vapor Pressure (mm Hg at 20°C): 8.6×10^{-6} (estim)	(507)
	• Saturated Concentration in Air (mg/m³ at 20°C): 0.147	(ADL estim)
	• Solubility in Water (mg/L at 25°C): 2.9	(507)
	• Viscosity (cp at 25°C): 47	(507)
	• Surface Tension (dyne/cm at 25°C): 39.9	(507)
	• Log (Octanol-Water Partition Coefficient), log K_{ow}: 4.77	(1657)
	• Soil Adsorption Coefficient, K_{oc}: 28,400	(ADL estim)
	• Henry's Law Constant (atm·m³/mol at 20°C): 1.2×10^{-6}	(1219)
	• Bioconcentration Factor: 663 (bluegill)	(399)

PERSISTENCE IN THE SOIL-WATER SYSTEM	BBP is expected to be relatively immobile due to strong soil sorption; however, complexation with organic substances may cause BBP to be mobilized and transported with ground water. Volatilization is not expected to be significant. BBP is resistant to chemical degradation but is fairly easily biodegraded.

PATHWAYS OF EXPOSURE	The primary exposure pathway of concern from soil/ground-water systems is the migration of BBP to ground water drinking water supplies, although the situations where this will occur may be limited. Exposures through ingestion of foods contaminated with BBP may be important in some situations.

HEALTH HAZARD DATA	Signs and Symptoms of Short-term Human Exposure : No reports of adverse effects associated with human exposure were found.
	Toxicity Based on Animal Studies: LD_{50} (mg/kg) oral 2330 [rat] (47) skin >10,000 [rabbit] (507) LC_{50} (mg/m^3) inhalation [mammal] (47) 13,100
	Long-Term Effects: Testicular degeneration in rats; no effect in mice or dogs
	Pregnancy/Neonate Data: Negative in rabbits
	Mutation Data: Negative
	Carcinogenicity Classification: IARC - not classified; NTP - some evidence

HANDLING PRECAUTIONS (59,507)	Handle chemical only with adequate ventilation • There are no formal guidelines available for this chemical with respect to respirator use. It is recommended that exposure be kept below 5 mg/m^3. When this concentration is exceeded, a self-contained breathing apparatus or supplied air respirator may be required • Chemical goggles if there is probability of eye contact • Wearing of protective gloves is recommended.

EMERGENCY FIRST AID TREATMENT (59)	Ingestion: If victim is conscious, induce vomiting. Get medical attention • Inhalation: Move victim to fresh air; give artificial respiration if needed • Skin: Remove any contaminated clothing; wash exposed skin with soap and water. If irritation persists, get medical attention • Eye: Irrigate with large amounts of water.

ENVIRONMENTAL AND OCCUPATIONAL STANDARDS AND CRITERIA

AIR EXPOSURE LIMITS:

Standards
- OSHA PEL (8-hr TWA): none established
- AFOSH PEL (8-hr TWA): none established

Criteria
- NIOSH IDLH (30-min): none established
- ACGIH TLV® (8-hr TWA): none established
- ACGIH STEL (15-min): none established

WATER EXPOSURE LIMITS:

Drinking Water Standards - None established

EPA Health Advisories - None established

EPA Ambient Water Quality Criteria (355)
- Human Health
  No criterion established due to insufficient data.

- Aquatic Life
  - Freshwater species
    acute toxicity: no criterion, but lowest effect level occurs at 940 µg/L phthalate esters.

    chronic toxicity: no criterion, but lowest effect level occurs at 3 µg/L phthalate esters.

  - Saltwater species
    acute toxicity: no criterion, but lowest effect level occurs at 2944 µg/L phthalate esters.

    chronic toxicity: no criterion established due to insufficient data.

REGULATORY STATUS (as of January 1, 1987)

Promulgated Regulations

- Federal Programs

Clean Water Act (CWA)
Butyl benzyl phthalate is listed as a toxic pollutant (351). Water quality criteria have not been set due to insufficient data. No effluent limitations specific to this chemical have been set.

Resource Conservation and Recovery Act (RCRA)
Butyl benzyl phthalate is listed as a hazardous waste constituent (328).

Toxic Substances Control Act (TSCA)
Manufacturers, processors or distributors of butyl benzyl phthalate must report production, usage and disposal information to EPA. They, as well as others who possess health and safety studies on butyl benzyl phthalate, must submit them to EPA (334,335).

Comprehensive Environmental Response Compensation and Liability Act (CERCLA)
Butyl benzyl phthalate is designated a hazardous substance under CERCLA. It has a reportable quantity (RQ) limit of 45.4 kg. Reportable quantities have also been issued for RCRA hazardous waste streams containing butyl benzyl phthalate but these depend upon the concentrations of the chemicals in the waste stream (985).

Federal Insecticide, Fungicide and Rodenticide Act (FIFRA)
Butyl benzyl phthalate is exempt from the requirement of a tolerance for residues in or on cotton seed when used as an inert plasticizer in the formulation of controlled release laminated dispensers of gossyplure. It is also exempt from a tolerance requirement for residues in or on artichokes when used as an inert plasticizer in multi-layered laminated controlled release dispensers of (≥)-11-hexadecenal (983).

Marine Protection Research and Sanctuaries Act (MPRSA)
Ocean dumping of organohalogen compounds as well as the dumping of known or suspected carcinogens, mutagens or teratogens is prohibited except when they are present as trace contaminants. Permit applicants are exempt from these regulations if they can demonstrate that such chemical constituents are non-toxic and non-bioaccumulative in the marine environment or are rapidly rendered harmless by physical, chemical or biological processes in the sea (309).

Food, Drug and Cosmetic Act (FDCA)
Butyl benzyl phthalate is approved for use as an indirect food additive (362).

- State Water Programs
  Kentucky, Virginia, Florida, Texas, Nevada and Oklahoma each have a criterion of 3 μg/L for phthalate esters (732).

Proposed Regulations

- Federal Programs
  Toxic Substances Control Act (TSCA)
  EPA has proposed that manufacturers and processers of butyl benzyl phthalate conduct toxicity, fate and bioconcentration testing (986).

  EPA has proposed that hazardous waste treatment, storage and disposal facilities monitor ground water for butyl benzyl phthalate when EPA suspects the facilities of leaking contaminants (1754).

- State Water Programs
  No proposed regulations are pending.

EEC Directives

Directive on Ground Water (538)
Direct discharge into ground water (i.e., without percolation through the ground or subsoil) of organophosphorous compounds, organohalogen compounds and substances which may form such compounds in the aquatic environment, substances which possess carcinogenic, mutagenic or teratogenic properties in or via the aquatic environment and mineral oils and hydrocarbons is prohibited. Appropriate measures deemed necessary to prevent indirect discharge into ground water (i.e., via percolation through ground or subsoil) of these substances shall be taken by member countries.

46.1 MAJOR USES

Butyl benzyl phthalate (BBP) is used exclusively as a plasticizer (202). Fifty percent goes into polyvinyl chloride-based flooring products; another important use is in polyvinyl acetate emulsions used as adhesives in the packaging industry (202). BBP is approved by the U.S. Food and Drug Administration for use in food contact articles (362). BBP is also used as a plasticizer with other polymers, including ethyl cellulose, acrylic resins, polyvinyl formal and polyvinyl butyral (202).

46.2 ENVIRONMENTAL FATE AND EXPOSURE PATHWAYS

46.2.1 Transport in Soil/Ground-water Systems

46.2.1.1 Overview

BBP may move through the soil/ground-water system when present at low concentrations (dissolved in water and sorbed on soil) or as a separate organic phase (resulting from a spill of significant quantities of the chemical). In general, transport pathways can be assessed with the use of an equilibrium partitioning model as shown in Table 46-1. These calculations predict the partitioning of low soil concentrations of BBP among soil particles, soil water, and soil air. The portions of BBP associated with the water and air phases of the soil are more mobile than the adsorbed portion.

The estimates (see Table 46-1) for the unsaturated topsoil model indicate that essentially all of the chemical (99.98%) would be sorbed on the soil; a relatively small amount (0.02%) of the chemical will be present in the soil-water phase and could thus migrate by bulk transport (e.g., the downward movement of infiltrating water), dispersion and diffusion. For the very small portion of BBP in the gaseous phase of the soil (10^{-6}%), diffusion through the soil-air pores up to the ground surface, and subsequent removal by wind, is possible.

In saturated, deep soils (containing no soil air and negligible soil organic carbon), a higher fraction of the BBP (0.8%) is likely to be present in the soil-water phase (Table 46-1) and transported with flowing ground water. However, most of the BBP is still expected to be adsorbed on soils, and ground waters underlying BBP-contaminated soils with low organic content may not be affected unless the BBP is mobilized by complexation with other species. It has been reported that phthalate esters readily interact with the fulvic acid in humic substances in water and soil. The interaction forms a fulvic acid-phthalate complex which is highly water soluble, allowing the otherwise insoluble phthalate esters to be mobilized and transported (766).

TABLE 46-1

EQUILIBRIUM PARTITIONING CALCULATIONS FOR BUTYL BENZYL PHTHALATE IN MODEL ENVIRONMENTS[a]

Soil Environment	Estimated Percent of Total Mass of Chemical in Each Compartment		
	Soil	Soil-Water	Soil-Air
Unsaturated topsoil at 25°C[b,c]	99.98	0.02	10^{-6}
Saturated deep soil[d]	99.2	0.8	-

a) Calculations based on Mackay's equilibrium partitioning model (34,35,36); see Introduction in Volume 1 for description of model and environmental conditions chosen to represent an unsaturated topsoil and saturated deep soil. Calculated percentages should be considered as rough estimates and used only for general guidance.

b) Used estimated soil sorption coefficient: K_{oc} = 28,400 (Estimated by Arthur D. Little, Inc.)

c) Henry's law constant taken as 1.2×10^{-6} atm • m^3/mol at 25°C (Estimated by Arthur D. Little, Inc.)

d) Used sorption coefficient calculated as a function of K_{oc} assuming 0.1% organic carbon: $K_p = 0.001 \times K_{oc}$.

46.2.1.2 Sorption on Soils

The mobility of BBP in the soil/ground-water environment (and its eventual migration into aquifers) is strongly affected by the extent of its sorption on soil particles. In general, sorption on soils is expected to:

- increase with increasing soil organic matter content (except that complexation with humic or fulvic acids may decrease the extent of sorption);
- increase slightly with decreasing temperatures;
- increase moderately with increasing salinity of the soil water (701); and
- decrease moderately with increasing dissolved organic matter content of the soil water.

Log K_{ow} values for BBP have been reported to range from 3.57 to 5.63 (657,1656,1657). Based upon log K_{ow} of 4.77 (1657), the soil sorption coefficient (K_{oc}) is estimated to be 28,400. This is a relatively high value, indicative of strong sorption to soils. Gledhill et al. (1657) determined partition coefficients ($\mu g/g + \mu g/mL$) for BBP sorption onto three soils with organic matter ranging from 1.2% to 3.4%; the measured partition coefficients ranged from 68 to 350. As mentioned above, phthalate esters have been shown to complex with natural organic substances (e.g., fulvic acid) to form water soluble complexes (765,766,767). Thus, sorption in soil/ground-water systems may be significantly weaker than might otherwise be expected.

46.2.1.3 Volatilization from Soils

Transport of BBP vapors through the air-filled pores of unsaturated soils is not expected to be an important transport mechanism except for near-surface dry soils. The very low value of Henry's law constant for BBP (1.2×10^{-6} atm·m^3/mol at 25°C) implies that, when water is present, nearly all the BBP will be in the water or soil compartment (see Table 46-1). No significant volatilization was observed in an experiment with phthalate esters in activated sludge (1658). In contrast, there is evidence that phthalate esters are slowly volatilized from plastics into the air (10). However, since BBP is expected to be readily sorped onto soils, volatilization is not expected to be a significant transport process in soil/ground-water systems.

46.2.2 Transformation Processes in Soil/Ground-water Systems

The persistence of BBP in soil/ground-water systems is not well documented. Photolysis and oxidation are not expected to be significant transformation processes in natural soils, and hydrolysis does not appear to be a major degradation pathway under normal environmental conditions. Wolfe et al. (658) examined the rate of hydrolysis for several phthalate esters, not including BBP, and found half-lives in water at pH 7 on the order of 3.2 to 2,000 years (10). Other investigators report half-lives ranging from 80 to 4,000 days at pH 8 and 30°C (1660). The hydrolysis of phthalate esters is catalyzed by both acids and bases (10). A 20°C drop in temperature (to a more typical ground-water temperature of 10°C) would increase the 30°C hydrolysis half-life by a factor of about 5.

Persistence studies indicate that biodegradation is the most important process for destruction of BBP in the environment (1657, 10,524,768). The data show that there are a number of microorganisms capable of using BBP as the sole source of carbon, and that ultimate degradation is possible. Biodegradation of BBP probably involves enzymic hydrolysis, and can depend on temperature, pH, oxygen content of environment, and other variables (10). Tabak et al. (55) have shown that BBP is easily degraded in active mixed cultures (and thus in sewage treatment plants), and have characterized BBP as undergoing "significant degradation [with] rapid adaptation."

Results of persistence studies for BBP are summarized in Table 46-2. There are no data available on BBP biodegradation in natural soil systems. Biodegradation of BBP proceeds rapidly in aerobic systems and more slowly under anaerobic conditions. Shelton et al. (1659) report that the initial steps in phthalate metabolism appear to be identical under aerobic and anaerobic conditions. In experiments with undiluted anaerobic digester sludge (1659), BBP was shown to be 75% degraded in two weeks; using sludge diluted to 10%, the degradation was slower (76 to 103% in 30 days). Lag times on the order of 1-2 weeks have been reported for BBP under both aerobic and anaerobic conditions; complete degradation may not occur within the retention times of some municipal sludge digesters (678,1659).

TABLE 46-2

BIODEGRADATION OF BUTYL BENZYL PHTHALATE

	Degradation			
	Primary	Ultimate	Time (days)	$t_{\frac{1}{2}}$ (days)
• Activated sludge, Aerobic	93-99%[a]		1	
Aerobic	99%[b]		2	
Anaerobic		75%[c]	14	
• Shake flask, acclimated	77%[b]	43%[b]	28	
• CO_2 evolution, aerobic	96%[a]	28		
• Gas production, anaerobic		<10%[a]	28	
• River water	100%[a]		9	2
• Lake water microcosm	>95%[a]		7	<4
		51-65%[a]	28	

[a]Reference 1657

[b]Reference 678

[c]Reference 1659

In most soil/ground-water systems, the concentration of naturally occurring microorganisms capable of biodegrading chemicals such as BBP may be low and would drop off sharply with increasing depth. Thus, biodegradation in the soil/ground-water environment may be of minimal importance except, perhaps, in near-surface soils and in landfills with active microbiological populations.

46.2.3 Primary Routes of Exposure from Soil/Ground-water Systems

The above discussion of fate pathways suggests that BBP has a low volatility, is strongly sorbed to soil, and has a high potential for bioaccumulation. These fate characteristics suggest several potential exposure pathways.

Volatilization of BBP from disposal sites in not likely to represent an important exposure pathway under most conditions. Drinking water contamination resulting from the migration of BBP with ground water may occur, particularly in deep or sandy soils. The potential for the formation of soluble complexes may make the possibility of drinking water contamination by BBP more likely than expected based on its properties. However, no data were found to indicate that BBP contamination of ground water is a common occurrence.

The movement of BBP in ground water, or its movement with soil particles, may result in discharges to surface waters. Consequently, ingestion exposures may occur through the use of surface waters as drinking water supplies, and dermal exposures may result from the recreational use of surface waters. In addition, BBP may be taken up by aquatic organisms and result in ingestion exposures for humans. The biodegradation of BBP may limit the extent to which these pathways are important.

46.2.4 Other Sources of Human Exposure

BBP is used as a plasticizer, particularly for polyvinyl chloride. Its primary use is in floor covering. As a result of its production and use, this compound is detected in surface waters and sediment in the U.S. An analysis of available data showed that 3% of the 1220 available data points had detectable concentrations of BBP. The median concentration in water was less than 10 μg/L, the most frequently stated detection limit. It was found in 6% of the 392 sediment stations with a median concentration of less than 500 μg/kg dry weight, and in 3% of 182 biota samples with a median concentration of less than 2.5 mg/kg (1417). These data suggest that ambient exposure to BBP is limited and at low levels.

The use of products containing BBP may result in exposure to the consumer. Releases of some phthalates from consumer products have been measured, however, no data were found for BBP.

46.3 HUMAN HEALTH CONSIDERATIONS

46.3.1 Animal Studies

46.3.1.1 Carcinogenicity

The National Toxicology Program conducted a carcinogenesis bioassay with BBP in B6C3F1 mice and F344/N rats. Both species were fed diets containing either 6000 or 12,000 ppm BBP for 28 to 103 weeks. There was no increased incidence of any type of tumor among male or female mice at 103 weeks. The male rat study was discontinued after 28 weeks due to unexplained but compound-related internal hemorrhaging which resulted in a large number of deaths. Mononuclear cell leukemias occurred at a statistically significant incidence in high dose female rats (36%) when compared with the low dose (14%) and control groups (14%). The historical incidence at the laboratory for female F344/N rats for this type of leukemia is 19%. Under the conditions of the study, BBP was not carcinogenic for mice of either sex, probably carcinogenic for female rats and inadequately tested in male F344 rats (1410).

Theiss et al. (1411) reported that groups of 20 Strain A male mice given intraperitoneal injections of up to 800 mg/kg BBP 3 times weekly for 8 weeks displayed no increased incidence of pulmonary adenomas compared with saline injected controls (0.10 to 0.25 lung tumors/mouse were found in treated animals vs. 0.19 in saline controls). In this case, the negative result cannot be taken as evidence of non-carcinogenicity because the length of the study was inadequate.

46.3.1.2 Mutagenicity

Mutagenicity tests conducted with BBP have given negative results. It has been tested with Salmonella typhimurium strains TA98, TA100, TA1535 and TA1537 with and without metabolic activation (1412), Saccharomyces cerevisiae D4, Escherichia coli, Bacillus subtilis and L5178Y mouse lymphoma cells (202) with negative results. Negative findings were also noted in mammalian cytogenetic studies using Chinese hamster ovary cells to detect chromosome aberrations and sister chromatid exchanges (1410).

46.3.1.3 Teratogenicity, Embryotoxicity and Reproductive Effects

BBP was shown to be lethal in the chick embryo system by Haberman et al. (1414). Nine-day chick embryos in ovo were injected with 0.1 mL of a 5% suspension of BBP in Hank's balanced salt solution into either the allantoic cavity or the chorioallantoic membrane (CAM). BBP injected into the CAM caused 68% mortality in the embryos compared with 27% in controls. Injection into the allantoic cavity caused 28% of the embryos to die in ovo compared with 18% in controls. Neonatal death rates at 21 days of age were not affected.

Bower et al. (1415) injected 0.05 ml of undiluted BBP into the yolk sac of fertilized chick eggs between the 65th and 72nd hour of development. Of the BBP-treated embryos, 48.8% died before hatching compared with 31.1, 53.4, and 44.8% in uninoculated, vegetable oil and sesame oil treated controls, respectively. There were no congenital malformations in any of the hatched chicks.

No evidence of fetotoxicity or teratogenicity was observed in the offspring in female rabbits treated with oral doses of 3 or 10 mg/kg BBP on days 6 through 18 of gestation (507).

In rats, BBP appears to exert a direct toxic effect on the testis with secondary effects on other reproductive organs. In adult male Fischer 344 rats fed levels of 0.625, 1.25, 2.5 or 5.0% BBP in their diet for 14 days, the absolute weights of testis, epididymis, prostate and seminal vesicles were reduced in a dose-dependent manner at the 2.5 and 5% levels. These weight reductions were associated with generalized histological atrophy of these tissues, with a clear relationship between dose and the severity of morphological changes in the testis, seminal vesicles, and prostate. Sperm granulomas were observed in one of the ten animals in both the 2.5 and 5.0% groups (1413).

Dermal application of 4 ml/kg (4.45 g/kg) to the testes of rats was found to cause deviations in sperm mobility but did not induce damage to the testis (59).

46.3.1.4 Other Toxicologic Effects

46.3.1.4.1 Short-term Toxicity

The acute toxicity of BBP is low; oral LD_{50} values of 2330 and 4170 mg/kg are reported for the rat and mouse, respectively (47). The dermal LD_{50} value for rabbits is greater than 10,000 mg/kg (507).

In a 1952 study, both oral doses of 1.8 g/kg and ip doses of 4 g/kg caused rats to die after 4 to 8 days. Histopathological studies revealed toxic splenitis and degeneration of CNS tissue with congestive encephalopathy (1416).

In four-week oral toxicity studies with rats fed diets containing concentrations equivalent to 500, 1000, 1500, 2000 or 3000 mg BBP/kg body weight, decreased food consumption and depressed body weight gain were noted in the "high dose" groups. Weakness and loss of coordination were observed in animals receiving a dosage of 2000 or 3000 mg/kg (507).

Rats exposed to vapor concentrations of 0.36, 1.0 or 2.1 mg/L (~332, 922 or 1936 mg/m^3), 6 hours per day, 5 days per week for 4 weeks had decreased body weight at the high dose levels. Atrophic spleens and reproductive organs were also noted in high dose males (507). In a

another four-week inhalation study, no significant adverse effects were observed in rats exposed to 40, 150 or 500 mg/m^3. No dosing schedule was reported (507).

A 14-day feeding study with male Fischer 344 rats resulted in testicular degeneration at dietary levels of 50,000 or 100,000 mg/kg but not at 25,000 mg/kg (1410).

Mice fed up to 25,000 mg/kg for 14-90 days exhibited no gross or histological effects (1410).

Calley et al. (292) administered daily intraperitoneal injections of 500 mg/kg BBP (as a 3% acacia emulsion) to albino mice for 6 weeks. BBP had no effect on the final body weight or organ weights. Pathological changes included acute peritonitis, periportal hepatitis and extra medullary hematopoiesis in both the liver and spleen.

BBP did not cause either immediate nor delayed hypersensitivity reactions when evaluated in mice and guinea pigs (507).

46.3.1.4.2 Chronic Toxicity

Long-term administration of BBP causes liver and kidney effects in rats. Ninety-day studies at dietary concentrations of 2000, 5000 and 12,000 ppm daily caused increased liver weights in the high dose groups and increased kidney weights in both the high and low dose groups. Depressed weight gain and focal liver necrosis were noted in high dose animals. Pancreatic lesions were seen in the mid-dose animals (507).

Dogs which ingested diets containing 1, 2 or 5% BBP for 90 days reportedly exhibited no alterations in urinary or hematological parameters and no gross or histopathological effects (202).

Inhalation studies in rats exposed to vapor concentrations of 0, 0.051, 0.218 or 0.799 mg/L (~ 3.7, 15.7, 57.4 ppm), 6 hours daily 5 days per week, for 13 weeks caused increased liver and kidney weights in the high exposure groups and increased kidney weights in mid-dose groups. The no-effect level was 0.051 mg/L (507).

46.3.2 Human and Epidemiologic Studies

46.3.2.1 Short-term Toxicologic Effects

Occupational exposure to BBP has not been reported to cause any significant adverse effects in humans. Dermal contact and inhalation are expected to be the primary routes of exposure.

A repeat insult patch test conducted on 200 human volunteers produced no positive reactions, leading to the conclusion that BBP is not a primary or cumulative skin irritant or sensitizing agent (507).

No specific exposure cases have been reported.

46.3.2.2 Chronic Toxicologic Effects

No data were found on the long-term effects of human exposure to BBP.

46.3.3 Levels of Concern

No criteria or standards have been established to date regarding BBP. The USEPA (355) has not established an ambient water quality criterion for the protection of human health due to insufficient data and neither OSHA (298) nor the ACGIH (3) have set a TWA exposure limit for BBP. Therefore, estimates of exposure levels of concern cannot be clearly defined at this time.

46.3.4 Hazard Assessment

BBP has a low order of acute toxicity in experimental animals by various routes of exposure. Long-term administration of BBP at dietary concentrations of 2000 ppm induced liver and kidney pathology in rats but not in dogs. Testicular degeneration has been reported in rats fed high levels (e.g., 50,000 mg/kg) of BBP in their diet (1410,1413), but it is not seen in mice (1410) or dogs (202). Additional data are required to establish the implications of these findings to humans in view of the marked species differences and the high dose levels administered.

Oral administration of BBP in the diet of rats and mice resulted in no increased incidence of tumors in mice but did result in an increased incidence of mononuclear cell leukemias in high-dose female rats. The incidence of this type of tumor in the low-dose female group was comparable to that in controls. The compound was inadequately studied in male rats due to internal hemorrhaging which appeared to be compound-related, and resulted in a large number of early deaths (1410).

Mutagenicity studies in bacteria, yeast and mammalian cells are negative (202,1410). Although lethal when injected directly into chick embryos, injection of BBP produced no congenital abnormalities and no adverse effects were observed in offspring of rabbits given 10 mg/kg BBP orally during gestation (507). Based on the lack of human data associated with exposure to BBP, no reliable assessment of hazard can be established for BBP without additional data. However, it should be noted, the adverse effects noted in animal studies all occur with very high exposure levels.

46.4 SAMPLING AND ANALYSIS CONSIDERATIONS

Determination of BBP concentrations in soil and water requires collection of a representative field sample and laboratory analysis. Care is required to prevent losses during sample collection and storage. Soil and water samples should be collected in glass containers;

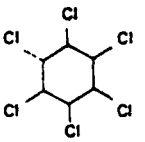
extraction of samples should be completed within 7 days of sampling and analysis completed within 40 days for aqueous samples and 30 days for non-aqueous samples. In addition to the targeted samples, quality control samples such as field blanks, duplicates, and spiked matrices may be specified in the recommended methods.

EPA-approved procedures for the analysis of BBP, one of the EPA priority pollutants, in aqueous samples include EPA Methods 606, 625, 1625 (65), 8060 and 8250 (63). Prior to analysis, samples are extracted with methylene chloride as a solvent using a separatory funnel or a continuous liquid-liquid extractor. An aliquot of the concentrated sample extract (after solvent exchanging the methylene chloride for hexane in Methods 606 and 8060) is injected onto a gas chromatographic (GC) column using a solvent flush technique. The GC column is programmed to separate the semi-volatile organics; BBP is then detected with an electron capture detector (Methods 606 and 8060), a flame ionization detector (Methods 8060) or a mass spectrometer (Method 625 and 1625).

The EPA procedures recommended for BBP analysis in soil and waste samples, Methods 8060 and 8250 (63), differ from the aqueous procedures primarily in the preparation of the sample extract. Solid samples are extracted using either soxhlet extraction or sonication methods. Neat and diluted organic liquids may be analyzed by direct injection.

Typical BBP detection limits that can be obtained in wastewaters and non-aqueous samples (wastes, soils, etc.) are shown below. The actual detection limit achieved in a given analysis will vary with instrument sensitivity and matrix effects.

Aqueous Detection Limit	Non-Aqueous Detection Limit
0.34 µg/L (Methods 606 and 8060/ECD)	1 µg/g (Method 8060)
15 µg/L (Method 8060/FID)	1 µg/g (Method 8250)
2.5 µg/L (Method 625)	
10 µg/L (Method 1625)	

COMMON SYNONYMS:	CAS REG. NO.:	FORMULA:	AIR W/V CONVERSION FACTORS at 25°C (1098)
Cyclohexane, 1,2,3,4,5,6-hexachloro-, gamma isomer Gamma-benzene hexachloride Gamma-BHC Gamma-HCH	58-89-9 NIOSH NO.: GV4900000	$C_6H_6Cl_6$	12.1 mg/m³ = 1 ppm 0.0826 ppm = 1 mg/m³
	STRUCTURE: 		MOLECULAR WEIGHT: 290.85

REACTIVITY	Lindane is considered to be a halogenated organic compound for compatibility classification purposes. Halogenated organic compounds typically generate heat in reactions with cyanides, mercaptans, and other organic sulfides. Those with non-oxidizing mineral acids, amines, and strong oxidizing agents typically evolve heat and toxic gases, while those with caustics or nitrides evolve heat and flammable gases. Reactions with oxidizing mineral acids may generate heat, toxic gases, and fire, while those with azo or diazo compounds or hydrazines may evolve heat and usually innocuous gases. Certain elemental metals and alloys as sheets, rods, drops, etc. may evolve heat and fire in reactions with these compounds, while alkali and alkaline earth elemental metals and metals as powders, vapors, or sponges may evolve heat and initiate an explosion. Heat and explosion are also possible results of reactions with organic peroxides organic hydroperoxides, or strong reducing agents (511).

PHYSICO-CHEMICAL DATA	• Physical State (at 20°C): solid, crystalline	(54)
	• Color: colorless - white	(54)
	• Odor: none	(38)
	• Odor Threshold: no data	( )
	• Density (g/ml at 20°C): 1.85	(59)
	• Freezing/Melting Point (°C): 112	(2)
	• Boiling Point (°C): decomposes (323.4)	(2)
	• Flash Point (°C): not flammable	(60,504)
	• Flammable Limits in Air, % by Volume: not flammable	(60,504)
	• Autoignition Temperature (°C): not flammable	(60,504)
	• Vapor Pressure (mm Hg at 20°C): 9.4×10^{-6}	(59)
	• Saturated Concentration in Air (mg/m³ at 20°C): 0.149	(ADL estim)
	• Solubility in Water (mg/L at 25°C): 7.8	(10,33)
	• Viscosity (cp at 20°C): no data	( )
	• Surface Tension (dyne/cm at 20°C): no data	( )
	• Log (Octanol-Water Partition Coefficient), log K_{ow}: 3.72	(10,29)
	• Soil Adsorption Coefficient, K_{oc}: 2500 (estim)	(611)
	• Henry's Law Constant (atm·m³/mol at 20°C): 4.8×10^{-7}	(31)
	• Bioconcentration Factor: 250	(659)

PERSISTENCE IN THE SOIL-WATER SYSTEM	Lindane is expected to be moderately mobile and non-persistent in soil due to moderate sorption, volatilization, and relatively rapid biodegradation, particularly under anaerobic conditions. Risk of ground-water contamination is low except under conditions of heavy application or frequent rainfall/irrigation. Changes in soil moisture content are expected to be important in dissipation of lindane from soil.

PATHWAYS of EXPOSURE	The primary pathway of concern from soil/ground-water systems is the migration of lindane to ground water drinking water supplies. Uptake by crops from soil or bioaccumulation by aquatic organisms or domestic animals may be important exposure pathways in some instances.

HEALTH HAZARD DATA	Signs and Symptoms of Short-term Human Exposure (2,15): Acute poisoning from ingestion or massive dermal exposure generally result in headache, nausea, vomiting and respiratory problems. Lindane also stimulates the CNS causing hyper-irritability, muscular incoordination, convulsions and coma.
	Toxicity Based on Animal Studies: LD_{50} (mg/kg) oral 76 [rat] (51) skin 500 [rat] (51) LC_{50} (mg/m^3) inhalation -- no data
	Long-Term Effects: Liver and kidney damage
	Pregnancy/Neonate Data: Possibly embryotoxic
	Mutation Data: Limited evidence
	Carcinogenicity Classification: IARC-2B; NTP-none assigned

HANDLING PRECAUTIONS (54)	Handle chemical only with adequate ventilation • Vapor concentrations of <5 mg/m^3: any chemical cartridge respirator with organic vapor cartridge and dust and mist filters or any supplied-air respirator or self-contained breathing apparatus • 5-25 mg/m^3: any chemical cartridge respirator with organic vapor cartridges, full facepiece and dust and mist filter or any gas mask with organic vapor canister with dust and mist filter or any supplied air respirator with full facepiece or any self-contained breathing apparatus with full facepiece • 25-500 mg/m^3: any powered air-purifying respirator with organic vapor cartridges and high-efficiency particulate filters or any Type C supplied-air respirator operated in pressure-demand or other positive pressure or continuous flow modes • Chemical goggles if there is a probability of eye contact • Protective clothing to prevent skin contact.

EMERGENCY FIRST AID TREATMENT (54)	Ingestion: Because many pesticide formulations are combined with other pesticides, fungicides or insecticides and are frequently dissolved in petroleum distillates, vomiting involves a serious risk that solvent will be aspirated, leading to chemical pneumonitis. For these reasons, if the ingested lindane is dissolved in a petroleum-based carrier or a mixed formulation, do not induce vomiting. Contact physician or emergency medical facility immediately. If the ingested lindane is in an aqueous carrier, induce vomiting. Get medical attention immediately • Inhalation: Move victim to fresh air and perform artificial respiration, if necessary • Skin: Remove contaminated clothing and wash skin with soap and water. If irritation persists, get medical attention • Eye: Irrigate for at least 15 minutes. If irritation persists, get medical attention.

ENVIRONMENTAL AND OCCUPATIONAL STANDARDS AND CRITERIA

AIR EXPOSURE LIMITS:

Standards
- OSHA PEL (8-hr TWA): 0.5 mg/m^3
- AFOSH PEL (8-hr TWA): 0.5 mg/m^3

Criteria
- NIOSH IDLH (30-min): 1000 mg/m^3
- ACGIH TLV® (8-hr TWA): 0.5 mg/m^3 (skin)
- ACGIH STEL (15-min): deleted

WATER EXPOSURE LIMITS:

Drinking Water Standards

Under the National Primary Drinking Water Regulations (296), the maximum contaminant level (MCL) for lindane is 0.004 mg/L. This MCL applies to community water systems which serve a population of 10,000 people or more and which add a disinfectant as part of their treatment process (991).

EPA Health Advisories

The EPA (992) has developed the following Health Advisories (formerly termed SNARLs) for non-carcinogenic risk for short and long-term exposure to lindane in drinking water:

- 1 day: none established
- 10 days: 4.3 mg/L
- long-term: none established

EPA Ambient Water Quality Criteria (355)
- Human Health
  - Based on ingestion of contaminated water and aquatic organisms, (10^{-5}, 10^{-6}, 10^{-7} cancer risk), 186 ng/L, 18.6 ng/L, 1.86 ng/L.
  - Based on ingestion of contaminated aquatic organism only, (10^{-5}, 10^{-6}, 10^{-7} cancer risk), 625 ng/L, 62.5 ng/L, 6.25 ng/L.
- Aquatic Life
  - Freshwater species
    The criterion to protect freshwater aquatic life as derived using the guidelines is 0.080 µg/L as a 24-hour average and the concentration should not exceed 2.0 µg/L at any time.
  - Saltwater species
    For saltwater aquatic life, the concentration of lindane should not exceed 0.16 µg/L at any time.

WHO Drinking Water Guideline (666)

A health based guideline for drinking water of 3 μg/L is recommended for lindane. A daily per capita consumption of two liters of water was assumed.

REGULATORY STATUS (as of January 1, 1987)

Promulgated Regulations

- Federal Programs

Clean Water Act (CWA)

Lindane is designated a hazardous substance. It has a reportable quantity (RQ) of 0.454 kg (347,985). It is also listed as a toxic pollutant (351). Water quality criteria have been set. No effluent limitations specific to this chemical have been set.

Safe Drinking Water Act (SDWA)

Under the National Primary Drinking Water Regulations (296), the maximum contaminant level (MCL) for lindane is 0.004 mg/L. This MCL applies to community water systems which serve a population of 10,000 people or more and which add a disinfectant as part of their treatment process (991).

In states with an approved Underground Injection Control program, a permit is required for the injection of lindane-containing wastes designated as hazardous under RCRA (295).

Resource Conservation and Recovery Act (RCRA)

Lindane is identified as a hazardous waste (U129) and listed as a hazardous waste constituent (328,329). A non-specific source of lindane-containing waste is chlorinated aliphatic hydrocarbon production (325). Solid wastes for which the extracts contain a concentration equal to or greater than 0.4 mg/L lindane are listed as hazardous in that they exhibit the characteristics defined as EP toxicity (988).

For ground water protection, the maximum concentration of lindane-containing hazardous waste allowed in ground water is 0.004 mg/L (989).

Effective July 8, 1987, the land disposal of hazardous wastes containing halogenated organic compounds in total concentrations greater than or equal to 1000 mg/kg will be prohibited. The only exception will be underground injection (1755).

Comprehensive Environmental Response Compensation and Liability Act (CERCLA)

Lindane is designated a hazardous substance under CERCLA. It has a reportable quantity (RQ) limit of 0.454 kg. Reportable quantities have also been issued for RCRA hazardous waste streams containing lindane but these depend upon the concentrations of the chemicals in the waste stream (985).

Any facility at which lindane is present in excess of its threshold planning quantity of 1000 pounds must notify state and local emergency planning officials. If lindane is released from the facility in excess of its reportable quantity (RQ), local emergency planning officials must be notified (1751).

Federal Insecticide, Fungicide and Rodenticide Act (FIFRA)
Tolerances have been established for lindane residues in or on raw agricultural commodities. Levels range from 0.01 to 7 ppm (978).

Marine Protection Research and Sanctuaries Act (MPRSA)
Ocean dumping of organohalogen compounds as well as the dumping of known or suspected carcinogens, mutagens or teratogens is prohibited except when they are present as trace contaminants. Permit applicants are exempt from these regulations if they can demonstrate that such chemical constituents are non-toxic and non-bioaccumulative in the marine environment or are rapidly rendered harmless by physical, chemical or biological processes in the sea (309).

Occupational Safety and Health Act (OSHA)
Employee exposure to lindane shall not exceed an 8-hour time-weighted-average (TWA) of 0.5 mg/m^3 (298).

Hazardous Materials Transportation Act (HMTA)
The Department of Transportation has designated lindane as a hazardous material which is subject to requirements for packaging, labeling and transportation (306).

Food, Drug and Cosmetic Act (FDCA)
The level for lindane in bottled drinking water is 0.004 mg/L. This level is identical to the maximum contaminant level (MCL) given under the Safe Drinking Water Act (365).

- State Water Programs

  All states follow the National Primary Drinking Water Regulations under the Safe Drinking Water Act.

  States with additional regulations for lindane (731,981):

  California - action level of 4 ppb;
  Florida - 0.01 µg/L in the public water supply;
  Georgia - 0.08 µg/L in all waters;
  Missouri - does not allow lindane to be present in state waters;
  New Jersey - 0.08 µg/L in surface waters;
  New York - None detected in class GA ground water;
  North Carolina - 0.01 µg/L in fresh water;
  Virginia - 0.01 µg/L in ground water;
  Wisconsin - 0.002 µg/L preventive action limit in ground water, 0.02 µg/L enforcement standard in ground water.

Proposed Regulations

- Federal Programs

  Safe Drinking Water Act (SDWA)
  EPA has proposed a Recommended Maximum Contaminant Level (RMCL) of 0.0002 mg/L for lindane as part of the National Primary Drinking Water Regulations (992).

Resource Conservation and Recovery Act (RCRA)
EPA has proposed listing spent filters, spent desiccants, light ends and filter aids from chlorinated aliphatic hydrocarbon production as a non-specific source of lindane-containing hazardous waste (330).

EPA has proposed that solid wastes for which the extracts contain a concentration equal to or greater than 0.06 mg/L lindane be listed as hazardous in that they exhibit the characteristic defined as EP toxicity (1565).

EPA has proposed that non-liquid hazardous wastes containing halogenated organic compounds (HOCs) in total concentrations greater than or equal to 1000 mg/kg or liquid hazardous wastes containing HOCs in total concentrations greater than or equal to 1% HOCs must be incinerated in accordance with the requirements of 40CFR264.343 or 265.343 (1767).

EPA has also proposed that hazardous waste treatment, storage and disposal facilities monitor ground water for lindane when EPA suspects the facilities of leaking contaminants (1754).

Federal Insecticide, Fungicide and Rodenticide Act (FIFRA)
EPA has proposed canceling the indoor use of lindane smoke fumigation devices and the use of lindane dog dips for control of all pests except mites. Lindane would be classified for restricted use in certain commercial applications. Specific label modifications would be required as would the submission of mutagenicity data (1335).

- State Water Programs
  No proposed regulations are pending.

EEC Directives

Directive on Drinking Water (533)
The mandatory values for total pesticides in surface water treatment categories A1, A2 and A3 used or intended for abstraction of drinking water are 0.001, 0.0025 and 0.005 mg/L, respectively. There are no guideline values.

Directive Relating to the Quality of Water for Human Consumption (540)
The maximum admissible concentration for lindane is 0.1 µg/L. The total maximum allowable concentration for pesticides and related products is 0.5 µg/L.

Directive on Ground Water (538)
Direct discharge into ground water (i.e., without percolation through the ground or subsoil) of organophosphorous compounds, organohalogen compounds and substances which may form such compounds in the aquatic environment, substances which possess carcinogenic, mutagenic or

teratogenic properties in or via the aquatic environment and mineral oils and hydrocarbons is prohibited. Appropriate measures deemed necessary to prevent indirect discharge into ground water (i.e., via percolation through ground or subsoil) of these substances shall be taken by member countries.

Directive on Bathing Water Quality (534)
When inspection of a bathing area shows that heavy metals, pesticides or cyanides may be present, concentrations should be checked by competent authorities.

Directive on the Quality Required of Shellfish Waters (537)
The mandatory specifications for organohalogenated substances state that the concentration of each substance in the shellfish water or in shellfish flesh must not reach or exceed a level which has harmful effects on the shellfish and larvae. The guideline specifications for organohalogenated substances state that the concentration of each substance in shellfish flesh must be so limited that it contributes to the high quality of shellfish product.

Directive on the Discharge of Dangerous Substances (535)
Organohalogens, organophosphates, petroleum hydrocarbons, carcinogens or substances which have a deleterious effect on the taste and/or odor of human food derived from aquatic environments cannot be discharged into inland surface waters, territorial waters or internal coastal waters without prior authorization from member countries which issue emission standards. A system of zero-emission applies to discharge of these substances into ground water.

Directive on Marketing and Use of Dangerous Substances (541)
Lindane may not be used in ornamental objects intended to produce light or color effects by means of different phases.

Directive on Classification, Packaging and Labeling of Pesticides (786)
Lindane is listed as a Class I/c substance and is subject to packaging and labeling regulations.

Directive on the Classification, Packaging and Labeling of Dangerous Substances (787)
Lindane is classified as a toxic substance and is subject to packaging and labeling regulations.

Directive on Plant Protection Products (1333)
Plant protection products containing hexachlorocyclohexane with less than 99% of the gamma isomer may be neither placed on the market nor used. If it appears necessary, because of an unforeseeable danger threatening plant production which cannot be controlled by other means, such products may be permitted to be marketed and/or used for a maximum period of 120 days.

Directive on Hexachlorocyclohexane (1332)
The monthly limit values applicable to the total quantity of hexachlorocyclohexane (HCH) present in all water discharges coming from industrial plant sites are as follows: (1) In plants used for HCH production - 3 mg/L; (2) In plants used for lindane extraction - 8 mg/L; (3) In plants used for HCH production and the extraction of lindane - 6 mg/L. The total HCH concentration in inland surface waters affected by discharges and in estuary and territorial sea waters must not exceed 100 and 20 ng/L, respectively. In the case of water used for the abstraction of drinking water, the HCH content must conform to the requirements of the Directive on Drinking Water.

EEC Directives - Proposed

Proposal for a Council Directive on the Dumping of Waste at Sea (1793)
EEC has proposed that the dumping of pesticides at sea be forbidden without prior issue of a special permit.

Proposal for a Council Regulation Concerning Export From and Import Into the Community of Certain Dangerous Chemicals (1795)
EEC has proposed that any export of hexachlorocyclohexane (containing less than 99% of the gamma isomer) on its own or in preparations must be reported by the exporter to a designated authority in the state of export and the state of import. The product must be packaged and labeled in accordance with the Directive on Classification, Packaging and Labeling of Dangerous Substances.

47.1 MAJOR USES

Lindane is the 99.5% pure gamma isomer of 1,2,3,4,5,6-hexachlorocyclohexane. It is used as an insecticide on cotton and other foliar plants, for soil and seed treatment of fruit and vegetable crops, and for the control of termites and other DDT-resistant insects (12). Lindane is also used as a therapeutic agent in veterinary and human medicine, i.e., for the ectoparasitic control of livestock, pets, and domestic animals; the 1% cream, lotion and shampoo are highly effective in combating human scabies and lice (12,25). Registration of some lindane products, including its use in continuous vaporizers, on some agricultural crops, on dairy cattle and in dairy barns and milk rooms have been cancelled (17).

Lindane replaced hexachlorocyclohexane (a mixture of alpha, beta, delta and gamma isomers) for various insecticidal applications when it was discovered that almost all of the insecticidal activity resided in the gamma isomer, i.e., lindane. Hexachlorocyclohexane (also called benzene hexachloride or BHC) is no longer produced in the U.S. (17).

47.2 ENVIRONMENTAL FATE AND EXPOSURE PATHWAYS

47.2.1 Transport in Soil/Ground-water Systems

47.2.1.1 Overview

Lindane is expected to be relatively immobile in the soil/ground-water system when present at low dissolved concentrations. Lindane is a solid at ambient temperature (melting point is 112°C) and is generally dissolved in a solvent prior to application. Bulk quantities of the solution (e.g., from a spill, heavy spray application, or improper disposal of excess formulations) could be transported through the unsaturated zone. Most studies, however, have shown that proper application of lindane to soil surfaces does not result in rapid transport through the soil. Furthermore, as discussed later in this section, lindane has been shown to be susceptible to degradation in the soil/ground-water system.

In general, transport pathways can be assessed by using an equilibrium partitioning model, as shown in Table 47-1. These calculations predict the partitioning of low soil concentrations of lindane among soil particles, soil water and soil air. Portions of lindane associated with the water and air phases of the soil have higher mobility than the adsorbed portion. Estimates for the unsaturated topsoil model indicate that almost all (99 8%) of the lindane is expected to be associated with the stationary phase. Less than 1% is expected to partition to the soil-water phase; therefore, only a small portion would be available to migrate by bulk transport (e.g., the downward movement of infiltrating water), dispersion and diffusion. An insignificant portion of lindane is expected in the gaseous phase of the soil; diffusion of vapors through the soil-air pores up to the ground

TABLE 47-1

EQUILIBRIUM PARTITIONING CALCULATIONS FOR LINDANE IN MODEL ENVIRONMENTS[a]

Soil Environment	Estimated Percent of Total Mass of Chemical in Each Compartment		
	Soil	Soil-Water	Soil-Air
Unsaturated topsoil at 25°C[b,c]	99.8	0.2	10^{-5}
Saturated deep soil[d]	91.4	8.6	-

a) Calculations based on Mackay's equilibrium partitioning model (34,35,36); see Introduction in Volume 1 for description of model and environmental conditions chosen to represent an unsaturated topsoil and saturated deep soil. Calculated percentages should be considered as rough estimates and used only for general guidance.

b) Utilized estimated soil sorption coefficient (611): K_{oc} = 2500.

c) Henry's law constant taken as 4.8×10^{-7} atm·m³/mol at 25°C (31).

d) Used sorption coefficient $K_p = 0.001\ K_{oc}$.

surface is not expected to be important (other data shown below indicate that entrainment with evaporating water may occur). In saturated, deep soils (containing no soil air and negligible soil organic carbon), a higher percentage of the lindane (8.6%) is predicted to be present in the soil-water phase (Table 47-1) and available for transport with flowing ground water. Sorption onto deep soils, however, is still expected to be significant.

Due to lindane's extensive use as an agricultural insecticide, several groups have studied its persistence in soil. Volatilization and biodegradation have been reported to be potentially important processes, while the leaching potential of lindane is expected to be relatively low compared to other commonly used chlorinated pesticides (1210). Bomberger et al. (1209) modeled the leachability of lindane in a soil system having 1% organic carbon, 50% porosity and 30% soil field capacity. After application of 305 cm water lindane migrated only 19 cm into the soil; the water front was estimated to be 1017 cm deep. In general, ground waters underlying lindane-contaminated soils are not

expected to be highly vulnerable. However, in climates where precipitation greatly exceeds evaporation, lindane could be leached deep into the soil and represent a threat to ground water.

Comparative studies of the retention times of various chlorinated hydrocarbon pesticides in soil indicate that lindane disappears from soil relatively rapidly. In an experimental study using two soils with organic content of 13% and 1%, the amounts of lindane found to persist after 128 days were 57% and 33%, respectively (1521). Another study (1530) reported lindane persistence in soil under very dry conditions with little or no runoff and under humid conditions with heavy rain. The observed half-lives for dry and humid soils were 50 days and 2 days, respectively; the corresponding periods for 99% disappearance were 500 days and 40 days. Maximum removal due to runoff was reported to be 0.03%.

A major review of lindane in soil presented the results of several investigators which indicated that lindane residues diminished 40-80% per year (1499). Other studies reported by the same author showed that 50% of surface-applied lindane disappeared within 4-6 weeks and 90% disappeared in 30-40 weeks. After being worked into the soil, however, it took 15-20 weeks for the disappearance of 50% of the lindane, and 2-3 years for disappearance of 90%. Additional data indicated only 0.2% of lindane applied at the rate of 10 kg/hectacre was found in the soil 15 years after application. Under tropical conditions, lindane residues were reported to virtually disappear within 30 days.

Several studies (1501,1502,1503,1504) have examined the persistence of lindane in soils used to grow crops. Under tropical conditions, reduction of lindane was generally reported to range from 70 to 90% over 2-3 months; one study reported reduction of 97.5% in 100 days. Reported uptake of lindane by the agricultural crops was minimal.

47.2.1.2 Sorption on Soils

There are several available studies addressing the adsorption and leachability of lindane on soils (1505,1506,1507). Values of the equilibrium soil sorption constant, K_{oc}, for lindane are in the range of 2500 (611) to 3800 (33). Sorption onto soils with organic content > 0.1% is expected to occur, but not to the extent that leaching is completely prevented.

As with all neutral organic chemicals, the extent of sorption is proportional to the soil organic content. Sharom et al. (1505) reported Freundlich sorption constants for lindane adsorbed on four different soils; these are shown in Table 47-2. Experimental leaching studies performed by the same authors indicated moderate mobility for adsorbed lindane; 92.6% of the lindane sorbed to sand and 34.2% of that sorbed to organic soil was leached after ten successive 200 mL water rinses.

TABLE 47-2

FREUNDLICH SORPTION CONSTANTS FOR LINDANE

	1/n	K	Organic Content	Reference
Organic soil	0.98	899	75%	1505
Big Creek Sediment	0.96	24	2.8%	1505
Beverly Sandy Loam	0.97	16	2.5%	1505
Plainfield Sand	0.99	8	0.7%	1505
Montmorillonite Clay/Water			-	
Sorption	0.662	1260		1515
Desorption	0.662	1260		1515
Sediment/Water			1.34%	
Sorption	0.926	350		1515
Desorption	1.96	4		1515
Sediment/Water			1.33%	
Sorption	1.265	60		1515
Desorption	0.529	11200		1515
Sediment/Water			0.55%	
Sorption	0.657	2200		1515
Desorption	1.72	4		1515

Chiou et al. (1508) examined the relative importance of soil organic matter and soil minerals in the sorption of lindane. They report that, in hydrated soils or aqueous systems, partitioning of lindane from water into the organic matter is the primary process of soil uptake and adsorption by soil minerals is relatively insignificant. However, in dehydrated soils, adsorption to soil minerals may be significant; the effectiveness of this adsorption is related to the ability of lindane to compete with the organic solvent for the polar mineral surfaces. Uptake of lindane applied to dry soils in nonpolar solvent, therefore, may be effected mainly through mineral adsorption. Due to the strong ability of water to compete for polar surfaces, the application of water to the soils may cause desorption of lindane from the mineral sites, making it available for transport or re-adsorption to the organic matter.

Several authors (1506,1507,1509) examined the effects of temperature, period of contact, and pesticide concentration on adsorption and leachability of lindane in soils. Leaching of lindane from sandy clay loam (2.6% organic content) was relatively slow at all concentrations (1.6 μg/g soil-43.2 μg/g soil); at the lowest concentration, leaching was not detected until 200 days after application (1506). In general, leachability increased with lindane concentration. The data also suggest the downward movement of lindane through the soil; surface adsorption after leaching was minimal at all concentrations while adsorption at 16 cm was much higher.

Adsorption of lindane has been reported to occur rapidly after application (1507,1509). In one experiment, lindane sorption onto a sand aquifer (1509) was reported to be rapid during the first four hours, with little additional sorption during the next 95 hours.

Retention of lindane on soil has also been shown to decrease progressively with increasing soil temperature (1507,1509). El Beit et al. (1507) exhibited a drop from 40% adsorption at 2°C to 15% at 45°C. The observed decrease may be due to an increase in the leaching, evaporation, or degradation of lindane.

In summary, the available data suggest that sorption of lindane onto soils of moderate to high organic content will occur. However, evidence of leaching exists, particularly under conditions of high concentration, elevated temperature or frequent rainfall/irrigation.

47.2.1.3 Volatilization from Soils

Transport of lindane vapors through the air-filled pores of unsaturated soils is not expected to be a major transport pathway. Modeling results indicate that a very small fraction of the lindane loading will be present in the soil-air phase. However, due to its relatively high vapor pressure (10^{-5}-10^{-4} mm Hg) and water solubility (~10 mg/L), volatilization of lindane transported to the surface by evaporating water may be important.

Several authors (1510,1511,1512,1513,1514) have studied the effect of soil moisture content on the volatilization of lindane. In general, volatilization from soil is controlled by diffusion of the pesticide and by the mass flow of water to the surface. Evaporating water has been shown to enhance volatilization of lindane from soil due to the "wick effect," whereby the pesticide is carried to the surface in evaporating water, but not due to co-distillation with water vapor (1512).

The results of field experiments indicate that, with adequate moisture, pesticides applied to the surface of soil initially volatilize at rates proportional to the vapor density of the pure chemical. If the soil remains moist, volatilization appears to be controlled by diffusion; the time required for the volatilization rate to decline to half the initial rate is similar for most pesticides and

ranges from 6-9 hours (1510). When moisture on soil surfaces decreases to an amount equal to one monomolecular layer, the effective vapor pressure of lindane and thus its volatilization is greatly reduced (above one to three molecular layers of absorbed water, soil moisture changes have less influence on volatilization). Laboratory and field studies have shown that relatively small amounts of moisture applied to the dry surface layer results in a marked increase in volatilization.

Glotfelty et al. (1511) presented volatilization data for lindane applied to the surface of a moist silt loam soil and a drier sandy loam. Initial rapid volatilization of lindane from the surface of the moist silt loam was observed: 50% lost in six hours, and 90% lost in six days. By contrast, losses from the surface of the sandy soil were much lower (12% lost after 50 hours), probably due to the lack of capillary wetting which created a dry soil surface; losses remained low until moisture was applied. Another study (1510) reported 78% volatilization from moist soil after 11 days.

Volatilization losses from environmental soils vary greatly with the extent of incorporation into the soil column and will generally be much lower than those reported for experimental surface soils. However, heavy application to vegetation or surface soils may yield extremely rapid volatilization and persistence within the affected area may be on the order of days rather than the longer times required for dissipation after incorporation into soil.

47.2.2 Transformation Processes in Soil/Ground-water Systems

Lindane has been reported to be susceptible to a number of degradation processes including hydrolysis, photolysis, and biodegradation. In persistence studies (1518), degradation (due to chemical and biological factors) was reported to increase with increases in pH, temperature, and ultraviolet irradiation.

The data addressing hydrolysis and photolysis in the soil/ground-water system are very limited. Lindane hydrolysis has been reported to be catalyzed by hydroxide and hydrogen ions; neutral hydrolysis was reported to be relatively unimportant. Experimental hydrolysis half-lives (first order) in natural water/sediment systems were determined to be 92 hours, 771 hours, and 648 hours for systems at pH 9.3, pH 7.3, and pH 7.8, respectively (1515). Other authors (1516,1517) have reported aqueous hydrolysis half-lives of one to four years at pH 7 to pH 8. Direct photolysis of lindane in the environment is expected to be minimal due to its limited solar absorption (10). However, an adjusted mid-winter photolysis half-life for lindane in distilled water was reported to be 65 days; photolysis rate retardation was noted for natural water/sediment systems at pH 7.3 and pH 7.8, while enhancement was noted in natural water/sediment at pH 9.3, possibly due to alkaline hydrolysis side reactions promoting photodegradable intermediates (1515). Photolysis studies for lindane in aqueous solution containing soil fulvic acid as a photosensitizer yielded a half-life of 48 days (1519).

Studies on the biodegradation of lindane have been presented in a number of reports (10,1499,1501,1520,1521,1522,1209). The general conclusion is that, compared to other chlorinated pesticides, lindane is relatively biodegradable with half-lives ranging from several days to months when introduced into biologically active environments. Microbial degradation is expected to be greater under anaerobic conditions than under aerobic conditions. Major degradation products have been reported to be pentachlorocyclohexane (PCCH) and α-BHC; other degradation products include other BHC isomers, tetrachlorocyclohexanes, pentachlorobenzene, and tetrachlorobenzenes. These degradation products are expected to be more volatile than lindane.

Seventy-one of 147 microorganisms isolated from a sandy loam soil exhibited the ability to utilize lindane in solution as the sole carbon source after six weeks incubation (1523). Thirteen microorganisms were studied further; of these, three showed adaptation times of less than a day while four required five to seven days adaptation. In another study (1524), 53 aerobes and 18 anaerobes, out of 354 bacterial and fungal isolates, were shown to metabolize lindane. An anaerobic bacterial species in pure culture was shown to degrade 3.7 ppm lindane to 0.02 ppm in 27 hours (1499). A 4000 ppm solution of lindane was shown to stimulate the growth of soil bacteria (1520).

Lindane added to a thick anaerobic sludge at 35°C was reported to be 95% transformed after several days; anaerobic processes were more effective than aerobic processes (1525). In an experiment using lake water/sediment, 15% and 90% degradation was observed after 87 days in aerobic and anaerobic environments, respectively (1526). In contrast, Mathur and Saha (1527) reported only 10% degradation after 42 days incubation of lindane in anaerobic flooded sandy soil.

Anaerobic degradation of lindane during composting has been shown to be rapid: 20-40% in 70 days during one experiment; 99% in 70 days during a second experiment (1522). In anaerobic soils, 50% of the applied lindane was transformed within 56 days (1528). When applied to an anaerobic mixed bacterial flora enriched from an arable soil, up to 90% of the lindane was degraded within four to five days (1529).

In most soil/ground-water systems, the natural concentration of microorganisms capable of biodegrading chemicals such as lindane is expected to be low and to drop off sharply with increasing depth. Thus, biodegradation in the soil environment may be slower than that reported in experimental data. The exception may be in areas with active microbiological populations, such as near landfills.

47.2.3 Primary Routes of Exposure from Soil/Ground-water Systems

The above discussion of fate pathways suggests that lindane has a low volatility; is moderately to strongly sorbed to soil, and has a moderate potential for bioaccumulation. These fate characteristics suggest several potential exposure pathways.

Volatilization of lindane from a disposal site is not likely to represent a major exposure pathway for workers or residents in the area. There is a potential for lindane to contaminate ground water, particularly in sandy soils. Mitre (83) reported that lindane has been found at 7 of the 546 National Priority List (NPL) sites. It was detected at 5 sites in ground water, 5 sites in surface water, and one site in air. However, contamination of ground-water drinking water supplies does not appear to be common or at high levels. Fractional compliance data show that no public ground water systems exceeded the MCL for lindane (0.004 mg/L) (992). In the Rural Water Survey, one out of 71 ground-water systems exceeded the minimum quantification limit (0.002 μg/L) for lindane. In the National Organics Reconaissance Survey (NORS), two ground-water systems contained lindane, but at levels less than the minimum quantifiable limit (992). In some cases, either related to high use areas or to specific site conditions, lindane can be found more commonly in ground water. EPA (992) reported that a survey of ground-water supplies in one state showed that 58.3% of the samples contained lindane at levels greater than 0.01 μg/L.

The movement of lindane in ground water may result in discharges to surface water. As a result, ingestion exposures may occur, resulting from the use of surface water as a drinking water supply, and dermal exposures may occur resulting from the recreational use of surface waters. In addition, lindane may be accumulated by aquatic organisms or domestic animals. The bioaccumulative potential of this compound suggests that these may be important exposure pathways.

47.2.4 Other Sources of Human Exposure

Lindane is registered for commercial and home use as an insecticide. Its use in shampoo to combat lice results in direct exposure to consumers, while its commercial insecticidal uses may result in exposure through environmental media.

As reported above, lindane is found to some extent in drinking water, although generally at low levels. Air exposures are also possible, but again concentrations are low. Lindane was detected in 68% of ambient air samples taken from 16 U.S. cities in 1970-1972. The mean of the positive values was 0.9 ng/m^3 and the maximum was 11.7 ng/m^3 (992). In a 1980 survey of 10 U.S. cities, lindane was detected in 0.8% of the 123 samples, with a mean level of 0.1 ng/m^3 and a maximum value of 1.5 ng/m^3. Pankow et al. (1795) detected lindane in some samples of rain from a semi-rural and an urban site in Oregon. The mean dissolved rain concentrations were 0.45 ng/L and 11 ng/L, respectively. From these concentrations, the authors estimated equilibrium atmospheric gas phase concentrations of 6.3×10^{-2} ng/m^3 and 1.5 ng/m^3. These data suggest that inhalation of lindane may occur in some locations at low levels.

Dietary intake, in general, also appears to be low. The average daily intake from market basket studies ranged from 0.002 to 0.004 μg/kg of body weight/day for adults over the years 1976-1979. The

largest source in the diet was meat, fish and poultry (1245). The average daily intake for infants during this same time period was 0.001-0.006 μg/kg/day, and for toddlers it was 0.005-0.010 μg/kg/day for the same years (1244). Other specialized surveys have been conducted that show the presence of lindane at low levels in human milk (1249), and bovine and porcine fat samples (1248). It was not detected in a 1977 survey of bovine milk in Canada (1247). These data suggest that the diet represents a source of exposure to lindane, but exposures are generally low.

47.3 HUMAN HEALTH CONSIDERATIONS

47.3.1 Animal Studies

47.3.1.1 Carcinogenicity

Data on the carcinogenicity of lindane are inconclusive due to the varied response obtained from the numerous mouse strains and species of animals investigated.

Thorpe and Walker (1083) fed CF1 mice 400 ppm lindane daily for 2 year . Liver enlargement was present by week 50 in both male and female mice. Examination of the liver at this stage revealed an irregular nodular surface with many lesions. The first liver tumor appeared in a treated female after 12 months. while the first tumor in a female control animal did not occur until 23 months. By the 110th week, 96% of the male mice fed 400 ppm lindane (compared with 24% in controls) and 95% of the female mice fed 400 ppm lindane (compared with 23% in controls) exhibited liver tumors. Hyperplastic nodules of the liver occurred in 38% of the treated males and 20% of the control males while hepatic neoplasms occurred in 55% of the treated males and only 4% in the control males Hyperplastic nodules of the liver occurred in 34% of the treated females and 23% of the control females, while hepatic neoplasms occurred in 34% of the treated females and none of the control females. Thorpe and Walker concluded that prolonged ingestion of 400 ppm lindane induced a statistically significant increase in the incidences of hyperplastic foci and parenchymal cell tumors in the liver of CF1 mice.

Weisse and Herbst (1082) studied the effect of lindane in the diet of Chbi:NMRI(SPF) mice in order to determine if the carcinogenic effect demonstrated in CF1 mice was representative of the effects for all strains of mice. Male and female mice were given 0, 12.5, 25 or 50 ppm lindane in the diet for 80 weeks. There was no increased incidence of tumors in any of the treatment groups tested. A 19% incidence of tumor development did occur, however the frequency of occurrence was the same in all treatment groups. Weisse and Herbst concluded that lindane in doses of up to 50 ppm per day for 80 weeks in Chbi:NMRI(SPF) mice was not carcinogenic and produced no observable adverse effects.

Morrissey and Wolff (1117) investigated the effect of lindane on female (YS x VY)F_1 hybrid mice grouped by color pattern into obese yellow, lean pseudoagouti and lean black groups. Half of each group was fed 160 ppm lindane for 24 months. Lindane treatment resulted in 68.4%, 74.5% and 82.3% incidence of alveolar bronchiolization in yellow, pseudoagouti and black mice, respectively, in comparison to 14.7%, 10.5% and 10.4% in the color-matched controls. The incidence of alveolar cell tumors was statistically significant in lindane-treated, genetically identical ($A^{vy/a}$) yellow (18.9%) and pseudogouti (13.8%) mice in comparison with 4.2% and 6.3% in the color-matched controls.

The NCI (1100) studied the effects of lindane on Osborne-Mendel rats and B6C3F1 mice. Male rats were fed 236 or 472 ppm lindane while female rats were fed 135 or 270 ppm lindane. Rats were treated for 80 weeks and observed for 29-30 weeks. Male and female mice were fed 80 or 160 ppm lindane for 80 weeks and observed for 10-11 weeks. Body weight was not affected by lindane in any of the treated animals. Clinical signs of toxicity increased as the study progressed and by the last 6 weeks of the experiment, rats had rough and discolored hair coats, pale mucous membranes, dermatitis and vaginal bleeding. There was no significant increase in the incidence of tumors in the rats treated with lindane in comparison to the control animals. It was concluded that lindane was not carcinogenic in Osborne-Mendel rats at the levels administered in this study. Signs of toxicity in mice included increased excitability, rough hair coats and abdominal distension. Hepatocellular carcinoma and neoplastic nodules of the liver were statistically significant in the low-dose male mice (39%) vs. the matched-control group (20%) or the pooled control group (10%). Due to a lack of dose-related response, NCI concluded that there was insufficient evidence of carcinogenicity in B6C3F1 mice induced by lindane in this study.

IARC (25) evaluated all available literature on lindane carcinogenicity and concluded that there is sufficient evidence that lindane is carcinogenic in CF1 mice. The carcinogenic nature of lindane in other strains and species is still in question. The low-dose treatment in the Weisse and Herbst (1082) and the NCI (1100) studies have led IARC to question the lack of response. IARC also noted the low number of control animals in the experimental groups in the NCI B6C3F1 mice study.

47.3.1.2 Mutagenicity

The results of reversion studies done by Buselmaier et al. (1101) showed lindane to be non-mutagenic in the G46 strain of Salmonella typhimurium and strain A21 of Serratia marcescens.

A 0.001% lindane solution produced no sex-linked recessive mutations when injected into Drosophila melanogaster (1102).

Also, no unscheduled DNA synthesis occurred in SV40-transformed human fibroblasts (VA-1) cultured with 1 or 1000 μM of lindane both with and without metabolic activation (1105).

Lindane did, however, cause a slight increase in the frequency of chromatid gaps and breaks in Chinese hamster fibroblasts in vitro (1103) and did inhibit cell division and produce chromatid breaks in human peripheral blood lymphocytes in vitro (1104). Rocchi et al. (1081) investigated the effect of lindane on scheduled and unscheduled DNA synthesis in the human lymphocyte. Lindane was shown to inhibit 72% of scheduled DNA synthesis and 55% of unscheduled DNA synthesis.

47.3.1.3 Teratogenicity, Embryotoxicity and Reproductive Effects

Mametkuliev (1139) investigated the effect of lindane on pregnancy and teratogenicity. Rats (strain not specified) were fed 0, 12 or 25 mg/kg lindane daily on days 1-20 of gestation. Other groups of rats were fed 25 mg/kg lindane daily on days 1-7 of gestation or on days 7-15 of gestation. Examination of fetuses on day 20 revealed no teratogenic effect. However, animals fed 25 mg/kg lindane throughout pregnancy did show an increase in postimplantation death of embryos (25.6% vs. 11.2% in rats fed 25 mg/kg lindane on days 7-15, 7.6% in rats fed 25 mg/kg lindane on days 1-7, 9.5% in rats fed 12 mg/kg lindane throughout gestation and 13.2% in control animals).

Palmer et al. (1079) studied the effect of lindane on the fetal development in rabbits and rats. Lindane was intragastrically administered to pregnant New Zealand white rabbits and CFY rats at dosages of 5, 10 or 20 mg/kg body weight daily on gestational days 6-18 for the rabbit and 6-15 for the rat. All dams were slightly lethargic during the dosing period, but no other changes were observed. Examination of the rabbit offspring revealed only one fetus in the 10 mg/kg treatment group with mild cebocephaly (monkey-like head, i.e., defective nose and close-set eyes) involving the partial fusion of the frontal and nasal bones. This was considered a spontaneous malformation. There was a dose-related increase in the incidence of extra 14th ribs in the rat, however, it was not statistically significant. Palmer et al. concluded that lindane was not teratogenic or even embryotoxic in CFY rats or New Zealand white rabbits.

In a 3-generation reproductive study, no malformations or compound related effects were reported in CD rats fed 25, 50 or 100 ppm lindane (1787). The significance of increased liver weight and enlarged hepatocytes in F^3 progeny was considered questionable.

47.3.1.4 Other Toxicologic Effects

47.3.1.4.1 Short-term Toxicity

Small amounts of lindane may cause dizziness, nausea, muscle weakness and tremors while a massive dose results in vomiting and diarrhea progressing to convulsions. Circulatory and respiratory failure may also appear (15). In the rat, the oral LD_{50} is listed as 76 mg/kg while the dermal LD_{50} is 500 mg/kg (51).

Frank and Braun (1085) reported 2 cases of accidental lindane ingestion in cattle. The first calf went into convulsions immediately after ingestion. It collapsed and died within one hour. The second calf developed convulsions 10 hours after ingestion. The convulsions persisted and increased in severity until the calf died 40 hours later. The esophagus was congested and the left lung was partially collapsed. It was later discovered that the calves had been given 3.6 g lindane. By examination of stomach content and tissue, it was determined that the first calf had consumed 2302 mg lindane while the second calf had consumed approximately 1100-1300 mg of lindane.

Cattabeni et al. (1087) examined the effect of lindane on the GABA (gamma-aminobutyric acid) system in rats. An alteration or decrease of GABA activity is correlated with convulsions and hyperexcitability. Male Sprague-Dawley rats were intraperitoneally injected with 100 mg/kg lindane and killed 10, 30 or 60 minutes later by microwave irradiation. Brains were examined and found to produce a statistically significant time-dependent increase in GABA in the cerebellum (a 76% increase in 60 minutes). Cattabeni concluded that the convulsions triggered by lindane were not due to an interference with GABA metabolism. The mechanism of the convulsive seizures associated with lindane is still unknown; however, once the seizures have begun, the GABAergic system is activated, most likely as a form of protection.

Male Wistar rats were treated with 800 ppm lindane for two weeks and then examined. Glucosuria accompanied by normal blood glucose was present in nearly all rats. The presence of glucose in the urine when levels of glucose in blood are normal, indicate a tubular defect in re-absorption. Urea is normally only partially re-absorbed through the tubules; however, in lindane-treated animals, there was an increase in the urinary urea and normal blood urea indicating a synthesis of urea in the renal tubules due to tissue destruction. Histopathological lesions were also observed in the kidney as shown by hypertrophy and degradation of renal epithelium (1084).

The hematological parameters of male Wistar rats were studied when fed 800 ppm lindane for 2 weeks. Blood clotting time was significantly increased (44.3 seconds vs. 27 seconds in control animals). Other parameters, such as red and white blood cell counts, packed cell volume, hemoglobin and serum calcium, were not significantly affected by lindane (1086).

Lindane tends to accumulate in fatty tissue during administration. However, once exposure has ceased, lindane is eliminated from the body relatively quickly. Rats administered lindane accumulated 102 ppm in the fatty tissue. This level dropped to zero one week after lindane treatment was suspended (1156). Evaluation of rats fed 100 mg/kg lindane daily for 10 days showed that the body accumulation had diminished to 0.1 ppm only 3 days after treatment had ceased (1157).

47.3.1.4.2 Chronic Toxicity

Heyroth (1155) reported results of long-term inhalation studies. Inhalation of 0.73 mg/m^3 lindane by rats for 7 hours/day, 5 days/week for 180 days resulted in no adverse clinical signs. Necropsy revealed slight liver enlargement. Two of 20 rats exposed to 3% lindane dust for 7 hours/day, 5 days/week for 218 days developed some doubtful liver and kidney alterations (1155).

Male and female beagle dogs were fed 0, 25, 50 or 100 ppm lindane daily for 104 weeks. Ophthalmoscopic examination as well as hematological analyses were performed on weeks 4, 13, 26, 52 and 102. Urinalyses were conducted on a monthly basis. No clinical lindane-related effects were observed in any of the treated animals. Electroencephalogram (EEG), ophthalmological, hematological examinations and urinalyses were all normal. The only abnormal finding was that the dogs in the 100 ppm treatment group had unusually dark livers, but histological examination revealed no abnormalities. Animals were then dosed with 200 ppm lindane for 32 weeks in order to determine adverse effects at a higher level. Two animals developed convulsions by day 54 and 92. These convulsions were considered to be due to hereditary canine epilepsy rather than lindane toxicity. EEG's from this group revealed high voltage slow wave activity which was most likely indicative of non-specific neuronal irritation. It was concluded that no toxic effects could be contributed to chronic feeding of 50 ppm of lindane to beagle dogs (1088).

Due to the variable carcinogenic nature of lindane in rodents, Oesch et al. (1097) studied the effects of lindane on enzyme induction as a possible role of liver tumor promotion. CF1 mice, B6C3F1 mice and Osborne-Mendel rats were fed a diet containing approximately 0, 50, 120, 270 ppm lindane for 3 days or 3 months. Enzyme activity and induction were not significantly different between the two mice strains, however, the B6C3F1 mice did not survive the 3-month treatment with the highest dose of lindane. The CF1 mice did differ enzymatically from Osborne-Mendel rats. At the 300 ppm treatment level, male and female CF1 mice showed a very high monooxygenase activity compared to rats of both sexes. After treatment with the highest dose of lindane, CF1 mice exhibited a lower epoxide hydrolase activity than the Osborne-Mendel rats, while a 5-6 fold increase in glutathione-S-transferase was seen. These variations in enzymes led Oesch et al. to speculate that the alterations of the enzymes involved in the metabolism of lindane in the liver may somehow relate to its carcinogenic nature in CF1 mice (1097).

47.3.2 Human and Epidemiologic Studies

47.3.2.1 Short-term Toxicologic Effects

Lindane poisoning in humans generally results from misuse or abuse of the 1% lindane preparation used to treat scabies and lice. Symptoms usually include vertigo, ataxia, agitation, tremors, headache, nausea,

vomiting, respiratory failure and slower or unreactive pupils to light. Convulsions and coma are present in severely affected people (1098). The severity of the symptoms is usually determined by the serum concentration of lindane. Symptoms generally appear when blood levels reach 20 ng/mL while convulsions occur at a serum value of 290 ng/mL (1095).

Over a one month period, 79 people were affected by a 40% lindane mixture applied to bed covers, clothing, floors as well as the subjects' body surfaces. Initial symptoms included lassitude, headache, vertigo and muscle pain followed by intestinal colic, diarrhea, and stomatitis. Next, CNS symptoms appeared and were characterized by mental confusion, dysarthria (imperfect articulation of speech due to poor muscle control resulting from nervous system damage), and convulsions. Blindness from optic atrophy was observed in one individual and complaints of diminished vision were reported in two other cases. One death following degeneration of the liver and kidneys was also reported (1566).

Severe poisoning was reported in a sixteen-year-old boy following ingestion of 392 g of 1% lindane shampoo. He was found unconscious and taken to the hospital where gastric lavage was performed. A deep coma and convulsions ensued. Breathing was erratic and the pupils were only sightly reactive to light. Phenobarbital was given to control the seizures. He slowly recovered and was released from the hospital on the 12th day. Examination one month later was normal and seizures were reported to have disappeared completely by the fifth month (1089).

A poisoning by cutaneous exposure was reported by Davies et al. (1089). A two-month-old infant was treated for scabies with spot applications of lindane to the abdomen and legs for two days. The infant was then treated with a whole-body application of 1% lindane lotion after a hot bath. The lotion was left on the infant's skin for 18 hours and then washed off. The infant was found dead in his crib 24 hours later. Autopsy revealed 110 ppb lindane in the brain tissue, 33 ppb in the blood and 2.5 ppb in the urine. This is the first reported case of the brain level of lindane being 3 times greater than the blood level.

Another case of acute toxicity involved a 23-year-old man diagnosed with scabies. He completely covered his trunk and limbs with 1% lindane. Within 12 hours, symptoms included fatigue, dizziness, nausea and vomiting, difficulty with balance, slurred speech and general weakness. These symptoms cleared-up within 12 hours. The individual repeated the treatment one week later. After the second application, he lost consciousness three times but recovered after 24 hours (1090).

An interesting case of muscle degeneration involved a man who accidently ingested food seasoned with 15-30 mL lindane mistaken for monosodium glutamate. Thirty minutes later, he experienced grand mal seizures, nausea, vomiting and abdominal pain. Once in the hospital,

he continued to have generalized tonic-clonic seizures for 2 hours. Blood analysis revealed severe metabolic acidosis and a lindane concentration of 600 ng/mL. Albuminuria and intense myoglobin urea were also present. An electroencephalogram (EEG) revealed diffuse intermittent disturbances of cerebral activity. By day 4, the patient was drowsy, had photophobia and complained of headaches and vertigo. The serum concentration of lindane had decreased to 5 ng/mL at this time. Muscles in the arms and legs were tender and serum urea nitrogen, creatinine, LDH and SGOT concentrations were substantially elevated. These results are indicative of muscle necrosis. The muscle damage was thought to occur due to the direct action of lindane on the muscle tissue. Renal failure associated with mild hyperkalemia and hyperuricemia also developed at this time. By day 15 of hospitalization, the patient's condition was greatly improved, however, the limb muscles were still weak and atrophic. A biopsy of the left deltoid muscle revealed widespread areas of severe necrosis. Regeneration of muscle fibers was also present. The patient was released on the 24th day. Renal function, EEG and blood tests were all normal and muscular strength was improved. During the following year, the patient complained of difficulty with short-term memory, poor attention span, loss of libido and general weakness (1095).

47.3.2.2 Chronic Toxicologic Effects

Symptoms generally associated with prolonged use of a 1% lindane ointment include nausea, spasms, ataxia, and blood dyscrasia (1568). Occasional cases of aplastic anemia have also been reported following chronic lindane exposure (17).

Liver damage has been reported following long-term occupational exposure to lindane (1569). Eight workers heavily exposed to lindane, DDT or both for 5-13 years developed cirrhosis and chronic hepatitis.

Biochemical manifestations of toxic hepatitis were reported in 59 females and 29 males occupationally exposed to hexachlorocyclohexane (isomers not specified) over an 11-23 year period. The hepatobiliary system was effected in 55% of the workers while 33% developed chronic hepatitis. Chronic pancreatitis occurred in 5%. It was concluded that some form of biochemical abnormality occurred in at least 60% of those exposed (1398).

Tomczak et al. (1092) studied 54 male factory workers exposed for an average duration of 8 years to lindane during its production. Evaluation of sex hormones revealed a significant increase in serum luteinizing hormone (8.8 mIU/ml vs. 5.7 mIU/ml in the controls) while testosterone and follicle stimulating hormone levels remained normal. These results indicate an interference in sex hormone regulation. Further investigation is needed to establish if these alterations are of pathological significance.

Nervous system function was studied in this same group of factory workers by Baumann et al. (1093). Reflexes, forefinger tremor, electromyography and a manual skill tracking test were similar in the

test and control groups. Despite years of exposure to lindane, no signs of neurological impairment or peripheral motor nerve damage were found.

Hematological effects resulting from chronic lindane exposure was reported by West (1106). A young girl was diagnosed with an atypical blood count and anemia. Examination of her family revealed four other members suffering from mild anemia. All recovered once a lindane vaporizer, which had been operating for 1.5 years, was removed from the home.

An increased incidence of lung cancer was reported between 1970 and 1975 in 285 agricultural workers spraying various pesticides including hexachlorocyclohexane (isomer not specified). Based on the potential for exposure to pesticides in addition to hexachlorocyclohexane, no evaluation on carcinogenicity was made. However, it was concluded that the cancer incidence was too high to be attributed solely to smoking and further investigation was recommended (1432).

An unusual case of acute myeloblastic leukemia, secondary to aplastic anemia was associated with dermal exposure to a lindane pesticide mixture. A male patient was hospitalized due to left lobar pneumonia. Bone marrow aspiration and bone biopsy revealed marked hypoplastic anemia. It was discovered at this time that the patient worked in a small unventilated bookstore for the past 15 years where he frequently used large amounts of insecticide. The insecticide mixture contained lindane, piperonyl butoxide and pyrethrum in kerosene, xylene and toluene. The man was treated with antibiotics and leukocyte transfusions. His condition gradually improved. Three months later, his hemoglobin level dropped to 7.5 g/100 mL (13-18 g/100 mL is the normal range) and he was given blood transfusions. Bone marrow aspiration revealed aplastic anemia. The patient refused to follow warnings to discontinue use of the insecticide and within one month acute myeloblastic leukemia was diagnosed. The patient died soon after from septicemia. Even though the pesticide contained a variety of compounds, lindane was thought to be the main reason for the anemia and leukemia (1099).

47.3.3 Levels of Concern

Based on the induction of liver tumors in male CF1 mice fed 400 ppm lindane for 110 weeks, the USEPA has specified an ambient water quality criterion for this compound of zero. In that attaining a zero concentration level may be infeasible in some cases, the concentrations of lindane in water calculated to result in incremental lifetime cancer risks of 10^{-5}, 10^{-6}, and 10^{-7} from ingestion of both water and contaminated aquatic organisms were estimated to be 186, 18.6 and 1.86 ng/L, respectively (355). Risk estimates are expressed as a probability of cancer after a lifetime consumption of two liters of water per day and consumption of 6.5 g of fish per day containing a specified concentration of the contaminant. Thus, a risk of 10^{-5} implies that a lifetime daily consumption of two liters of drinking

water and 6.5 g of contaminated fish at the criterion level of 186 nanograms lindane per liter would be expected to produce one excess case of cancer above the normal background incidence for every 100,000 people exposed. It should be emphasized that these extrapolations are based on a number of assumptions and should be taken as crude estimates of human risk at best.

Under the National Primary Drinking Water Regulations (296), the maximum contaminant level for lindane in drinking water is 4 μg/L.

The WHO (666) recommends a health based guideline of 3 μg/L for lindane in drinking water.

OSHA (298) currently permits and the ACGIH (3) recommends exposure be limited to 0.5 mg/m^3 lindane averaged over an 8-hour work-shift.

IARC (803) lists lindane in category 2B (sufficient evidence in animals) in its weight-of-evidence ranking of potential carcinogens.

47.3.4 Hazard Assessment

Dietary administration of lindane induced liver tumors in male CF1 mice (1083); tests conducted with other mouse strains and rats were negative (1082,1100). Based on the findings in CF1 mice, the USEPA (667) calculated an upper-limit incremental unit cancer risk of 1.33 $(mg/kg/day)^{-1}$ for lindane.

Limited evidence exists to indicate potential mutagenic capability for lindane. Lindane did induce chromatid breaks in human lymphocytes and Chinese hamster fibroblasts in culture (1104,1103) but produced no sex-linked recessive lethal mutations in Drosophila (1102) or mutations in bacterial assays (1101).

No adverse effect were noted in a 3-generation study with rats fed lindane at a concentration of 100 ppm (1787). Other studies indicate no embryotoxic or teratogenic effects in either rats or rabbits administered 20 mg/kg by gavage during gestation (1079). Another study indicated possible embryotoxic effects in rats exposed to 25 mg/kg daily throughout gestation (1139).

The primary response to lindane is stimulation of the CNS, resulting in hyperexcitability and convulsions. Lindane is the most acutely toxic of the hexachlorocyclohexane isomers (12). The oral and dermal LD_{50} values for the rat are 76 mg/kg and 500 mg/kg, respectively (51). Long-term exposures result in pathological changes in liver and kidney; rats fed 800 ppm lindane in the diet for two weeks exhibited kidney damage (1084). The no-adverse-effect levels for both the rat (1082) and dog (1088) in 2 year dietary exposure studies were 50 ppm.

Effects of lindane intoxication in humans include repeated, clonic convulsions, respiratory difficulty and cyanosis. Fatalities have been documented (1566,1089,1099). Ingestion of large doses have led to

muscle and kidney necrosis (1095). Chronic exposure to lindane has been linked to anecdotal reports of aplastic anemia (17) and possible pancreatitis in workers exposed to an unspecified isomer of hexachlorocyclohexane (1398).

47.4 SAMPLING AND ANALYSIS CONSIDERATIONS

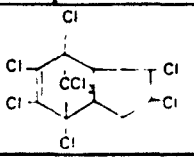
Determination of lindane concentrations in soil and water requires collection of a representative field sample and laboratory analysis. Care is required to prevent losses during sample collection and storage. Soil and water samples should be collected in glass containers; extraction of samples should be completed within 7 days of sampling and analysis completed within 40 days. In addition to the targeted samples, quality control samples such as field blanks, duplicates, and spiked matrices may be specified in the recommended methods.

EPA-approved procedures for the analysis of lindane, one of the EPA priority pollutants, in aqueous samples include EPA Methods 608, 625 (65), 8080, and 8250 (63). Prior to analysis, samples are extracted with methylene chloride as a solvent using a separatory funnel or a continuous liquid-liquid extractor. The concentrated sample extract is solvent exchanged into hexane and an aliquot of the hexane extract injected onto a gas chromatographic (GC) column using a solvent flush technique. The GC column is programmed to separate the semi-volatile organics; lindane is then detected with an electron capture detector (Methods 608 and 8080) or a mass spectrometer (Methods 625 and 8250).

The EPA procedures recommended for lindane analysis in soil and waste samples, Methods 8080 and 8250 (63), differ from the aqueous procedures primarily in the preparation of the sample extract. Solid samples are extracted with hexane/acetone using either soxhlet extraction or sonication methods. Neat and diluted organic liquids may be analyzed by direct injection.

Typical lindane detection limits that can be obtained in wastewaters and non-aqueous samples (wastes, soils, etc.) are shown below. The actual detection limit achieved in a given analysis will vary with instrument sensitivity and matrix effects. Detection limits for aqueous samples using Methods 625 and 8250 were not indicated; lindane is subject to decomposition during the extraction step. Methods 608 and 8080 are preferred methods for aqueous samples.

Aqueous Detection Limit	Non-Aqueous Detection Limit
0.004 µg/L (Method 608/8080)	1 µg/g (Method 8080)
	1 µg/g (Method 8250)

COMMON SYNONYMS:	CAS REG. NO.:	FORMULA:	AIR W/V CONVERSION FACTORS at 25°C (12)
1,2,4,5,6,7,8,8-Octachloro-2,3,3a,4,7,7a-hexahydro-4,7-methano-1H-indene Dichlorochlordene	57-74-9 NIOSH NO.: PB9800000	$C_{10}H_6Cl_8$	16.76 mg/m³ ≃ 1 ppm 0.0596 ppm ≃ 1 mg/m³
	STRUCTURE: 		MOLECULAR WEIGHT: 409.8

REACTIVITY	Chlordane is considered to be a halogenated organic compound for compatibility classification purposes. Halogenated organic compounds typically generate heat in reactions with cyanides, mercaptans, and other organic sulfides. Those with non-oxidizing mineral acids, amines, and strong oxidizing agents typically evolve heat and toxic gases, while those with caustics or nitrides evolve heat and flammable gases. Reactions with oxidizing mineral acids may generate heat, toxic gases, and fire, while those with azo or diazo compounds or hydrazines may evolve heat and usually innocuous gases. Certain elemental metals and alloys as sheets, rods, drops, etc., may evolve heat and fire in reactions with these compounds, while alkali and alkaline earth elemental metals and metals as powders, vapors, or sponges may evolve heat and initiate an explosion. Heat and explosion are also possible results of reactions with organic peroxides, organic hydroperoxides, or strong reducing agents (511).

*PHYSICO-CHEMICAL DATA	• Physical State (at 20°C): viscous liquid	(23)
	• Color: colorless to amber	(51)
	• Odor: slightly pungent, like chlorine	(60)
	• Odor Threshold: no data	( )
	• Liquid Density (g/ml at 25°C): 1.6	(60)
	• Freezing/Melting Point (°C): 103-108.8	(10)
	• Boiling Point (°C): 175 at 2 mm Hg	(38)
	• Flash Point (°C): not flammable	(38,60)
	• Flammable Limits in Air, % by Volume: not flammable	(38,60)
	• Autoignition Temperature (°C): not flammable	(38,60)
	• Vapor Pressure (mm Hg at 20°C): 0.00001	(38)
	• Saturated Concentration in Air (mg/m³ at 20°C): 0.22	(ADL estim)
	• Solubility in Water (mg/L at 25°C): 0.056	(33)
	• Viscosity (cp at 54°C): 58	(60)
	• Surface Tension (dyne/cm at 20°C): 25	(60)
	• Log (Octanol-Water Partition Coefficient), log K_{ow}: 5.48	(33)
	• Soil Adsorption Coefficient, K_{oc}: 38,000	(1210)
	• Henry's Law Constant (atm•m³/mol at 25°C): 2.2×10^{-4}	(1531)
	• Bioconcentration Factor: 14,100	(993)

*Properties refer to undiluted, technical-grade chlordane.

PERSISTENCE IN THE SOIL-WATER SYSTEM	Expected to be fairly immobile in the soil/ground-water system due to strong sorption and moderate volatilization. Data on degradation are limited; expected to be moderately persistent. Risk of ground-water contamination moderate; contamination of surface waters by surface runoff reported.

PATHWAYS OF EXPOSURE	Pathways of concern from the soil/ground-water system are migration to ground water drinking water supplies, uptake by crops from soil and bioaccumulation by aquatic organisms or domestic animals. Soil application of chlordane may also result in contamination of indoor air of slab-on-grade homes.

HEALTH HAZARD DATA	Signs and Symptoms of Short-term Human Exposure (38): Exposure may cause shaking, blurred vision, irritability, confusion, delirium, staggering, convulsions and death. Ingestion may cause nausea, vomiting and diarrhea. Absorption through the skin is rapid and has resulted in death.
	Toxicity Based on Animal Studies: LD_{50} (mg/kg): oral 283 [rat] (59); skin 780 [rabbit] (59) LC_{50} (mg/m^3): inhalation [cat] (59) 100•4 hr
	Long-Term Effects: Kidney and liver damage
	Pregnancy/Neonate Data: Decreased fertility
	Mutation Data: Generally negative
	Carcinogenicity Classification: IARC - 3; NTP - none assigned

HANDLING PRECAUTIONS (38,54,60)	Handle chemical only with adequate ventilation • Vapor concentrations of 0.5 to 5 mg/m^3: any supplied air respirator, self-contained breathing apparatus or chemical cartridge respirator with an organic vapor cartridge • 5-25 mg/m^3: any supplied air respirator or self-contained breathing apparatus with full facepiece; a chin-style or front- or backmounted pesticide protective mask; a chemical cartridge respirator with a full facepiece and organic vapor cartridge • Chemical goggles if there is probability of eye contact • Appropriate neoprene clothing to prevent repeated or prolonged skin contact.

EMERGENCY FIRST AID TREATMENT (38,59)	Ingestion: As many pesticides are combined with other toxicants and often dissolved in petroleum distillates, vomiting can lead to solvent aspiration and pneumonitis. If chlordane is in a petroleum-based carrier or in a mixture, do not induce vomiting. If chlordane is in water, induce vomiting. Contact physician immediately • Inhalation: Move victim to fresh air. If necessary, give artifcial respiration. Get medical attention • Skin: Remove contaminated clothing; wash skin with soap and water. If irritation persists, get medical attention • Eye: Irrigate for 15 min. with water. If irritation persists after washing, get medical attention.

ENVIRONMENTAL AND OCCUPATIONAL STANDARDS AND CRITERIA

AIR EXPOSURE LIMITS:

Standards
- OSHA PEL (8-hr TWA): 0.5 mg/m^3
- AFOSH PEL (8-hr TWA): 0.5 mg/m^3

Criteria
- NIOSH IDLH (30-min): 500 mg/m^3
- ACGIH TLV® (8-hr TWA): 0.5 mg/m^3 (skin)
- ACGIH STEL (15-min): 2 mg/m^3 (skin)

WATER EXPOSURE LIMITS:

Drinking Water Standards
None established

EPA Health Advisories
In the absence of formal drinking water standards, the EPA (992) has developed the following Health Advisories (formerly termed SNARLs) for noncarcinogenic risk for short- and long-term exposure to chlordane in drinking water:

- 1 day: none established
- 10 days: 0.22 mg/L
- long-term: none established

EPA Ambient Water Quality Criteria (355)
- Human Health
  - Based on ingestion of contaminated water and aquatic organisms, (10^{-5}, 10^{-6}, 10^{-7} cancer risk), 4.6 ng/L, 0.46 ng/L, 0.046 ng/L.
  - Based on ingestion of contaminated aquatic organisms only, (10^{-5}, 10^{-6}, 10^{-7} cancer risk), 4.8 ng/L, 0.48 ng/L, 0.048 ng/L.
- Aquatic Life
  - Freshwater species - The criterion to protect freshwater aquatic life as derived using the guidelines is 0.0043 µg/L as a 24-hour average and the concentration should not exceed 2.4 µg/L at any time.
  - Saltwater species - The criterion to protect saltwater aquatic life as derived using the guidelines is 0.0040 µg/L as a 24-hour average and the concentration should not exceed 0.09 µg/L at any time.

WHO Drinking Water Guideline (666)
A health-based guideline for drinking water of 0.3 µg/L is recommended for chlordane (total isomers). A daily per capita consumption of two liters of water was assumed.

REGULATORY STATUS (as of January 1, 1987)

Promulgated Regulations

- Federal Programs

Clean Water Act (CWA)

Chlordane is designated a hazardous substance. It has a reportable quantity (RQ) of 0.454 kg (347,985). It is also listed as a toxic pollutant (351). Water quality criteria have been set. No effluent limitations specific to this chemical have been set.

Safe Drinking Water Act (SDWA)

In states with an approved Underground Injection Control program, a permit is required for the injection of chlordane (technical)-containing wastes designated as hazardous under RCRA (295).

Resource Conservation and Recovery Act (RCRA)

Chlordane (technical) is identified as a hazardous waste (U036) and listed as a hazardous waste constituent (328,329). Waste streams from the following industry contain chlordane and are listed as specific sources of hazardous wastes: pesticides (chlordane production) (326,327).

Effective July 8, 1987, the land disposal of hazardous wastes containing halogenated organic compounds in total concentrations greater than or equal to 1000 mg/kg will be prohibited. The only exception will be underground injection (1755).

Comprehensive Environmental Response Compensation and Liability Act (CERCLA)

Chlordane is designated a hazardous substance under CERCLA. It has a reportable quantity (RQ) limit of 0.454 kg. Reportable quantities have also been issued for RCRA hazardous waste streams containing chlordane but these depend upon the concentrations of the chemicals in the waste stream (985).

Any facility at which chlordane is present in excess of its threshold planning quantity of 1000 pounds must notify state and local emergency planning officials. If chlordane is released from the facility in excess of its reportable quantity (RQ), local emergency planning officials must be notified (1751).

Federal Insecticide, Fungicide and Rodenticide Act (FIFRA)

Action levels for chlordane and its degradation products in agricultural commodities range from 0.1 to 0.3 ppm (973).

Marine Protection Research and Sanctuaries Act (MPRSA)
Ocean dumping of organohalogen compounds as well as the dumping of known or suspected carcinogens, mutagens or teratogens is prohibited except when they are present as trace contaminants. Permit applicants are exempt from these regulations if they can demonstrate that such chemical constituents are non-toxic and non-bioaccumulative in the marine environment or are rapidly rendered harmless by physical, chemical or biological processes in the sea (309).

Occupational Safety and Health Act (OSHA)
Employee exposure to chlordane shall not exceed an 8-hour time-weighted-average (TWA) of 0.5 mg/m^3 (298).

Hazardous Materials Transportation Act (HMTA)
The Department of Transportation has designated chlordane as a hazardous material which is subject to requirements for packaging, labeling and transportation (306).

- State Water Programs

  The following states have a criterion of 0.0043 µg/L for chlordane:

  New Jersey - in surface water
  West Virginia - in drinking water

  California has an action level of 0.055 ppb (731).

  Florida and Illinois have a criterion of 0.1 µg/L and 0.003 mg/L, respectively, for chlordane in the public water supply (731).

  Louisiana has a criterion of 2.4 µg/L and 4.6 ng/L for chlordane in fresh water and public water, respectively (731).

  Missouri does not allow chlordane to be present in state waters (731).

  New York has a ground water quality standard of 0.0001 mg/L (981).

  North Carolina has a criterion of 0.004 µg/L for chlordane in fresh water (731).

  Virginia has a ground water quality standard of 0.01 µg/L (981).

  Other states follow EPA Ambient Water Quality Criteria.

Proposed Regulations

- Federal Programs

  Safe Drinking Water Act (SDWA)
  EPA has proposed a Recommended Maximum Contaminant Level (RMCL) of zero for chlordane as part of the National Primary Drinking Water Regulations (992).

Resource Conservation and Recovery Act (RCRA)
EPA has proposed that solid wastes which contain a concentration equal to or greater than 0.03 mg/L chlordane be listed as hazardous in that they exhibit the characteristic defined as EP toxicity (1565).

EPA has proposed that non-liquid hazardous wastes containing halogenated organic compounds (HOCs) in total concentrations greater than or equal to 1000 mg/kg or liquid hazardous wastes containing HOCs in total concentrations greater than or equal to 1% HOCs must be incinerated in accordance with the requirements of 40CFR264.343 or 265.343 (1767).

EPA has also proposed that hazardous waste treatment, storage and disposal facilities monitor ground water for chlordane when EPA suspects the facilities of leaking contaminants (1754).

- State Water Programs
  No proposed regulations are pending.

EEC Directives

Directive on Drinking Water (533)
The mandatory values for total pesticides in surface water treatment categories A1, A2 and A3 used or intended for abstraction of drinking water are 0.001, 0.0025 and 0.005 mg/L, respectively. There are no guideline values.

Directive Relating to the Quality of Water for Human Consumption (540)
The maximum admissible concentration for chlordane is 0.1 µg/L. The total maximum allowable concentration for pesticides and related products is 0.5 µg/L.

Directive on Ground Water (538)
Direct discharge into ground water (i.e., without percolation through the ground or subsoil) of organophosphorous compounds, organohalogen compounds and substances which may form such compounds in the aquatic environment, substances which possess carcinogenic, mutagenic or teratogenic properties in or via the aquatic environment and mineral oils and hydrocarbons is prohibited. Appropriate measures deemed necessary to prevent indirect discharge into ground water (i.e., via percolation through ground or subsoil) of these substances shall be taken by member countries.

Directive on Bathing Water Quality (534)
When inspection of a bathing area shows that heavy metals, pesticides or cyanides may be present, concentrations should be checked by competent authorities.

Directive on the Quality Required of Shellfish Waters (537)
The mandatory specifications for organohalogenated substances specify that the concentration of each substance in the shellfish water or in shellfish flesh must not reach or exceed a level which has harmful effects on the shellfish and larvae. The guideline specifications for organohalogenated substances state that the concentration of each substance in shellfish flesh must be so limited that it contributes to the high quality of shellfish product.

Directive on the Discharge of Dangerous Substances (535)
Organohalogens, organophosphates, petroleum hydrocarbons, carcinogens or substances which have a deleterious effect on the taste and/or odor of human food derived from aquatic environments cannot be discharged into inland surface waters, territorial waters or internal coastal waters without prior authorization from member countries which issue emission standards. A system of zero-emission applies to discharge of these substances into ground water.

Directive on Marketing and Use of Dangerous Substances (541)
Chlordane may not be used in ornamental objects intended to produce light or color effects by means of different phases.

Directive on Classification, Packaging and Labeling of Pesticides (786)
Chlordane is listed as a Class II/b substance and is subject to packaging and labeling regulations.

Directive on the Classification, Packaging and Labeling of Dangerous Substances (787)
Chlordane is classified as a harmful substance and is subject to packaging and labeling regulations.

Directive on Plant Protection Products (1333)
Plant protection products containing chlordane may be neither placed on the market nor used. If it appears necessary, because of an unforeseeable danger threatening plant production which cannot be controlled by other means, such products may be permitted to be marketed and/or used for a maximum period of 120 days.

EEC Directives - Proposed

Proposal for a Council Directive on the Dumping of Waste at Sea (1793)
EEC has proposed that the dumping of pesticides at sea be forbidden without prior issue of a special permit.

Proposal for a Council Regulation Concerning Export From and Import Into the Community of Certain Dangerous Chemicals (1795)
EEC has proposed that any export of chlordane on its own or in preparations must be reported by the exporter to a designated authority in the state of export and the state of import. The product must be packaged and labeled in accordance with the Directive on Classification, Packaging and Labeling of Dangerous Substances.

48.1 MAJOR USES

Chlordane has been used extensively over the past 30 years for termite control, as an insecticide for homes and gardens and as a control for soil insects during crop production (54). Both the uses and production volume have decreased since the Environmental Protection Agency issued a registration suspension notice for all food crops and home and garden uses in 1978 (54). Its use is now restricted to subsurface ground insertion for termite control (994).

A general concern with the data available on chlordane is the purity of the material. Most often, technical-grade material has been used. Technical chlordane is composed of approximately 24% trans-chlordane, 19% cis-chlordane, 21.5% chlordene isomers, 10% heptachlor, 7% nonachlor, and 18.5% related chlorinated hydrocarbons (993). Improvements in manufacturing have resulted in products containing 75% trans- and 25% cis-chlordane and less than 1% heptachlor (59). Additionally, a certain degree of confusion exists due to the use of three different nomenclature systems: cis and trans chlordane are equivalent, respectively, to alpha and gamma chlordane as used by the manufacturer and beta and alpha chlordane as used by various investigators. The terms cis and trans have been used throughout this chapter whenever it was possible to identify the isomer in question.

48.2 ENVIRONMENTAL FATE AND EXPOSURE PATHWAYS

48.2.1 Transport in Soil/Ground-water Systems

48.2.1.1 Overview

Technical chlordane, commonly used as an insecticide, is a complex mixture of many chlorinated components, having different persistence patterns in the environment. The major components include cis-chlordane, trans-chlordane, heptachlor, and nonachlor. Most environmental studies have focused on the two major chlordane isomers and the persistence of technical chlordane is approximated by the behavior of these two components. After application of technical chlordane in soil, successive analyses for residues showed rapid disappearance of all minor components, leaving only cis-chlordane and trans-chlordane (1532). Other studies (1243,1498) have shown significant soil residues as well as residual indoor air concentrations after application of technical chlordane. In this chapter, discussion will be limited to the environmental fate of the cis- and trans-chlordane isomers.

Chlordane is expected to be relatively immobile in the soil/ground-water system when present at low concentrations. Bulk quantities of the liquid chemical (e.g., from a spill, heavy spray application, or improper disposal of excess formulations) could be transported through the unsaturated zone. However, most studies have shown that proper application of chlordane to soil surfaces does not result

TABLE 48-1

EQUILIBRIUM PARTITIONING CALCULATIONS FOR CHLORDANE IN MODEL ENVIRONMENTS[a]

Soil Environment	Estimated Percent of Total Mass of Chemical in Each Compartment		
	Soil	Soil-Water	Soil-Air
Unsaturated topsoil at 25°C[b,c]	99.9	0.01	10^{-4}
Saturated deep soil[d]	99.4	0.6	-

a) Calculations based on Mackay's equilibrium partitioning model (34,35,36); see Introduction in Volume 1 for description of model and environmental conditions chosen to represent an unsaturated topsoil and saturated deep soil. Calculated percentages should be considered as rough estimates and used only for general guidance.

b) Utilized estimated soil sorption coefficient (1210): K_{oc} = 38,000.

c) Henry's law constant taken as 2.2×10^{-4} atm•m³/mol at 25°C (1531).

d) Used sorption coefficient $K_p = 0.001\ K_{oc}$.

in rapid transport through the soil. Furthermore, as discussed later in this section, chlordane may be susceptible to degradation in the soil/ground-water system.

In general, transport pathways can be assessed by using an equilibrium partitioning model, as shown in Table 48-1. These calculations predict the partitioning of low soil concentrations of chlordane among soil particles, soil water and soil air. Portions of chlordane associated with the water and air phases of the soil have higher mobility than the adsorbed portion. Estimates for the unsaturated topsoil model indicate that almost all (99.9%) of the chlordane is expected to be associated with the stationary phase. Much less than 1% is expected to partition to the soil-water phase; therefore, only a small portion would be available to migrate by bulk transport (e.g., the downward movement of infiltrating water), dispersion and diffusion. An insignificant portion of the chlordane is expected in the gaseous phase of the soil; diffusion of vapors through the soil-air pores up to the ground surface is not expected to be important (other data shown below

indicate that volatilization at the surface may be enhanced by soil moisture). In saturated, deep soils (containing no soil air and negligible soil organic carbon), the percentage of the chlordane predicted to be present in the soil-water phase (Table 48-1) and available for transport with flowing ground water is expected to be fairly small. Based on this model, ground water underlying chlordane-contaminated soils with low organic content is not expected to be vulnerable to contamination.

Due to chlordane's extensive use as an insecticide, several groups have studied its persistence in soil (1210,1531,1532,994,1533). In general, these studies show that chlordane is quite persistent and transport with soil water (leaching) is low; volatilization - at least at the surface - may be important. The reported leaching index for chlordane suggests less than 10 cm movement through soil with rainfall of 150 cm per year (1539).

Half-lives of chlordane in soil have been reported to range from two years to eight years (1532,1211,1540,1541). Persistence data reported by other investigators (1542-1544) suggest that the longer half-lives are more probable. The lowest persistence (9% after 16 years) was reported in a study using very heavy application rates (112 kg/ha and 224 kg/ha) on sandy loam soil.

Soil monitoring studies have measured chlordane residues (ppb to ppm levels) in significant percentages of sampled farm lands, urban areas and residential areas. Uptake of chlordane by plants is generally thought to be limited to absorption by plant roots (1537) and has been shown to be related to soil type (994). No chlordane residues were detected in seeds from any crop (1533); however, one study (1538) reported translocation of chlordane into alfalfa foliage. In most temperate climates, only the cis- and trans-chlordane isomers persist after application of technical chlordane; however, in colder climates, the residues more closely resemble the technical chlordane mixture (994).

48.2.1.2 Sorption on Soils

Values of the equilibrium soil sorption constant, K_{OC}, for chlordane have been reported as 21,300 (812), 38,000 (1210), and 140,000 (33). These values indicate that chlordane will be fairly strongly sorbed onto soils with organic content > 0.1%. As with all neutral organic chemicals, the extent of sorption is proportional to the soil organic content. For low organic carbon soils (e.g., clays), the extent of sorption may also depend on properties such as surface area cation exchange capacity and degree of hydration.

Several investigators have examined the vertical and horizontal transport of chlordane applied to soil surfaces; most of the residue has been reported to be in the immediate vicinity of the treated area and migration below the surface was minimal. Examination of soil adjacent to the walls of a house treated with chlordane after

construction (1543) indicated that 99% to 100% of the residue was in the top 10 inches. The horizontal distribution showed that 40%, 19%, 20%, 17%, and 3% of the residue was found 0.5, 1, 2, 4, and 10 feet from the building, respectively; essentially, no residue was detected below the surface. In soil transport experiments using sand and loam soil columns to which 2.5 liters of water were added over 80 days, 99.5% to 100% of the applied chlordane was retained in the top 10 cm (1546). The same authors also examined soil core samples after chlordane application and found about 88% of the residue in the top 7.5 cm and another 10% of the residue 7.5-15 cm below the surface. Some leaching of chlordane from three treated surface soils to untreated sandy subsurface soil under field conditions has been reported (1547). Approximately 50% of the applied material in sand and loam leached into subsurface soil after 6-12 months, while 33% of the material in clay soils leached into subsurface soils during the same time periods.

Migration of chlordane bound to soil particles may occur under surface runoff conditions. In studies addressing pesticide loadings to two major river basins (1534), it was determined that greater inputs were originating from urban sources than from agricultural sources; surface runoff was suggested as the source. Translocation of chlordane from treated corn fields was also shown to occur via surface runoff (1558).

In summary, the available data suggest that sorption of chlordane onto soils of moderate to high organic content is strong. Under natural conditions, these is little vertical or horizontal movement in soil although surface runoff may cause some migration.

48.2.1.3 Volatilization from Soils

Transport of chlordane vapors through the air-filled pores of unsaturated soils is not expected to be a major transport pathway; modeling results indicate that a very small fraction of the chlordane loading will be present in the soil-air phase. However, due to its moderate vapor pressure (10^{-5} mm Hg), some volatilization may occur. The minor components of the technical chlordane mixture are expected to be more volatile than the trans- and cis-chlordane isomers discussed here (1536). Half-lives for the volatilization of chlordane from stirred aqueous solution have been reported to be approximately 30 hours (1548), while volatilization half-lives in natural waters are on the order of 6-12 weeks (10). Volatilization from soil is expected to be much slower.

Several authors (1510,1536,1511,1546) have described the effect of soil moisture content on the volatilization of chlordane. Laboratory and field studies have shown that relatively small amounts of moisture applied to a previously dry surface layer result in a marked increase in volatilization. The results of field experiments indicate that, with adequate moisture, pesticides applied to the surface of soil initially volatilize at rates proportional to the vapor density of the pure chemical. If the soil remains moist, volatilization appears to be

controlled by diffusion; the time required for the volatilization rate to decline to half the initial rate is similar for most pesticides and ranges from 6-9 hours (1510). When moisture on soil surfaces decreases to an amount approximately equal to one monomolecular layer, the effective vapor pressure of chlordane and thus its volatilization is greatly reduced (above one to three molecular layers of absorbed water, soil moisture changes have less influence on volatilization).

Field studies using two different application rates for chlordane showed 27% and 52% losses due to volatilization from damp, silty, clay loam over one month; no losses were observed over one month for chlordane applied to semi-arid sandy loam (1546). Similarly, a 10-fold decrease in chlordane volatilization was observed in experimental studies when a damp soil sample was allowed to dry out and the water-saturated air stream was replaced by dry air (1536). Glotfelty et al. (1511) presented volatilization data for chlordane applied to the surface of a moist silt loam soil and a drier sandy loam. Fairly rapid volatilization of chlordane from the surface of the moist silt loam was observed (50% lost in 2.5 days). By contrast, losses from the surface of the sandy soil were much lower (2% lost after 50 hours) probably due to the lack of capillary wetting which created a dry soil surface; losses remained low until moisture was applied. Another study (1510) reported 50% volatilization from moist soil after 11 days. Several studies (1243,1498) have documented the transport of soil-applied chlordane into the indoor air of residences. Most homes were slab-on-grade with sub-slab or intra-slab ventilation ducting. Vapor-phase transport or volatilization is the likely migration route.

Volatilization losses from environmental soils vary greatly with the extent of incorporation into the soil column and the manner of application. A comparative study of different chlordane formulations demonstrated that liquid formulations volatilize more easily than granular formulations (1535). In general, volatilization losses from environmental soils will be lower than those reported for experimental surface soils. However, heavy application to vegetation or other surfaces may yield extremely rapid volatilization and the persistence within the affected area may be on the order of days rather than the longer times required for dissipation after incorporation into soil.

48.2.2 Transformation Processes in Soil/Ground-water Systems

Chlordane has been reported to be susceptible to photolysis and biodegradation. Evidence for the photoisomerization of chlordane in the presence of photosensitizers has been summarized in References 10 and 806. In the presence of acetone, a thin film of technical chlordane exposed to sunlight was 85% degraded in 155 hours; under the same conditions, trans-chlordane was 60% degraded in 50 hours and cis-chlordane was 99% degraded in 27 hours (1549). The same authors reported that thin films of cis-chlordane exposed to sunlight for 460 hours exhibited 10% degradation. Rapid photolytic degradation of chlordane on bean leaves treated with rotenone (photochemical sensitizer) has been reported (1550); the authors observed 70 to 80%

loss of cis-chlordane and 15 to 20% loss of trans-chlordane in four hours. No loss was observed in the absence of rotenone. No information regarding the environmental photolysis of chlordane in the presence of natural substances was available.

Evidence of the microbial degradation of chlordane has been presented by several authors (1551-1553). However, data on microbial degradation in soil environments are very limited. Slow degradation in soils has been reported in several studies (1554,1555), and no significant degradation was reported in four soils over a three-month period under flooded and upland conditions (1556). Carter and Stringer (1557) reported that degradation was greater in the surface soil than in lower layers; 45% degradation in the upper 1-3 cm and 12.5% degradation in the lower layer was observed over 12 months. Another study examined degradation in sand, loam and clay soils; after 30 months, chlordane was reported to be 80-90% degraded in all systems (1547). The half-life for degradation of chlordane in natural soils is expected to be on the order of 2-4 years (1540).

48.2.3 Primary Routes of Exposure from Soil/Ground-water Systems

The above discussion of fate pathways suggests that chlordane is moderately volatile, is very strongly sorbed to soil, and has a high potential for bioaccumulation. These fate characteristics suggest several potential exposure pathways.

Volatilization of chlordane from a disposal site could result in inhalation exposure to workers or residents in the area under certain conditions as described in Section 48.2.2. The potential for ground water contamination is limited by the strong adsorptive characteristics of chlordane. However, the persistence of this chemical has allowed its transport to drinking water supplies. Mitre (83) reported that chlordane has been found at 7 of the 546 National Priority List (NPL) sites. It was detected at 5 sites in ground water, 4 sites in surface water, and 1 site in air. Chlordane has also been reported in ground water in the vicinity of houses treated for termite control. It has been detected in drinking water in five states. In New Jersey, five wells contained chlordane at 0.01 µg/L to 0.02 µg/L. One state reported chlordane in 49% of the 87 ground-water systems sampled (992). These data indicate that ground water contamination by chlordane can occur in some situations, even though it is strongly adsorbed to organic matter in soil.

The movement of chlordane in ground water or its movement with soil particles may result in discharge to surface water. As a result, ingestion exposures may occur resulting from the use of surface waters as drinking water supplies, and dermal exposures may result from the recreational use of surface waters. More importantly, however, is the potential for uptake of chlordane by aquatic organisms or domestic animals. The high bioconcentration factor and the persistence of chlordane suggest that these can be important exposure pathways from soil/ground-water systems.

Wood et al. (1545) reported the results of a study that suggested that fish contamination with chlordane in a Long Island, NY lake resulted from ground water discharges. The authors hypothesized that chlordane was passing through the sand-gravel substratum and accumulating in the lake sediment. Fish concentrations of 5.2 μg/g in carp filets and 0.38 μg/g in bass filets were found in this lake.

48.2.4 Other Sources of Human Exposure

Chlordane has been used as a pesticide in the United States for over 30 years for termite control, as an insecticide for homes and gardens, and as an insecticide for field crops. Although most uses of chlordane have now been cancelled, it is still commonly found in the environment.

Schafer et al. (1241) found that 20% of the 500 samples of finished drinking water from the Mississippi and Missouri River contained chlordane at concentrations up to 8 ppb. However, chlordane does not appear to be a common contaminant in drinking water nationwide. Data from the U.S. National Surface Water Monitoring Program show that chlordane has been detected in 1.1% of the surface water samples taken from 1976 to 1980, with a maximum value of 0.23 ppb. It was more commonly detected in the sediment (15.3%) up to a concentration of 2964 ppb (1242).

Similarly, air exposures to chlordane appear to be low (994). Carey and Kutz (1242) reported that 11.4% of 123 air samples at 10 U.S. locations contained chlordane. The mean concentration was 0.4 ng/m^3 and the maximum was 7.3 ng/m^3. Houses previously treated for termites may contain higher concentrations of chlordane in the air. Wright and Leidy (1243) found chlordane levels of 0.30 μg/m^3 in the air of homes before treatment, which was not readily explained. After treatment, concentrations up to about 5 μg/m^3 persisted to 12 months when sampling was discontinued. In addition, chlordane has been found in the air of slab houses that had been treated for termites below the slab. Livingston and Jones (1498) found that 77% of the apartments sampled that had been treated 2-16 years previously had detectable concentrations of chlordane up to 37.9 μg/m^3. Apartments that were sampled 1 year after treatment showed concentrations up to 263.5 μg/m^3. In further studies, Barnes (1500) found that houses treated prior to construction were much less likely to have detectable chlordane concentrations in the air (9% as compared to 74%). Again these houses were slab-on-grade with sub or intraslab ventilation ducting.

Food appears to be the most common source of human exposure to chlordane, although levels are generally low. Some crops are able to translocate chlordane from soil, where it is persistent, and it may concentrate in oils, meat, milk and eggs (994). Gartrell et al. (1244) reported dietary intakes of total chlordane as <0.001 to 0.01 μg/kg of body weight/day for infants during the years 1976 to 1979 and 0.0003 to 0.032 μg/kg/day for toddlers. Adult intakes ranged from

0.003-0.004 μg/kg/day over the same time period (1245). Dietary intake in Canada is similarly low. Over the period of 1976 - 1978, the average dietary intake was less than 0.001 μg/kg/day (1246).

48.3 HUMAN HEALTH CONSIDERATIONS

48.3.1 Animal Studies

48.3.1.1 Carcinogenicity

Chlordane produces dose-dependent incidence of liver neoplasms in mice following oral administration. Data concerning rats are inconclusive (25).

In an 80-week NCI study, B6C3F1 mice were fed analytical-grade chlordane, consisting of 94.8% chlordane (71.7% cis; 23.1% trans), 0.3% heptachlor, 0.6% nonachlor, 1.1% hexachlorocyclopentadiene, 0.25% chlordene isomers and other chlorinated compounds. All surviving mice were killed at 90-91 weeks. Time-weighted average dietary concentrations were 29.9 and 56.2 ppm for males and 30.1 and 63.8 ppm for females. A dose-related increase in the incidence of hepatocellular carcinomas was found in males and females in the high-dose group - 87.8% and 69.3%, respectively, compared to 11% and 0% in matched controls (1302).

In contrast to the findings in mice, Osborne-Mendel rats, fed time-weighted average dietary concentrations of 203.5 or 407 ppm (males) and 120.8 or 241.5 ppm (females) did not show a significant incidence of hepatocellular carcinoma. In treated male rats, there was an excess of follicular-cell thyroid neoplasms and malignant fibrous histiocytomas but these were discounted because the rates of incidence were low (9-13%) and/or are known to be variable in control rat populations. In this study, the incidence of these neoplasms in control animals ranged from 3.4 to 7.8% (1302).

A dose-related incidence of hepatocytomegaly was observed in both male and female CD-1 mice administered 4, 25 or 50 ppm of technical chlordane in their diet for 18 months study (1303). A dose-related increase in the incidence of nodules or nodular hyperplasia of the liver was also reported (based on gross pathology) in males and females in the 25 and 50 ppm groups. There was an increased incidence of hepatomas in males at the 5 and 25 ppm levels, but this was not statistically significant. Interpretation of these results was complicated by a high mortality rate (27-86%) and the large number of tissues lost from autolysis. Subsequent re-evaluations of the study by independent pathologists indicated that the majority of lesions diagnosed as nodular hyperplasia were more appropriately classified as hepatocellular carcinomas.

In a recent study, Williams and Numoto (1304) suggest that chlordane has the properties of a promoting agent. They found that groups of male B6C3F1 mice exposed to 20 ppm of the carcinogen diethylnitrosamine (DEN) in drinking water for 14 weeks followed by 25 weeks of a 25 or 50 ppm chlordane diet each had an 81% incidence of liver neoplasms. This is in contrast to a 40% incidence in animals given only DEN for 14 weeks and a 10.7% incidence in untreated controls.

48.3.1.2 Mutagenicity

Neither pure cis-chlordane nor trans-chlordane were mutagenic in the Ames Salmonella assay. Technical-grade chlordane was found to be mutagenic in three strains of Salmonella typhimurium but this may have been due to chemical impurities (996).

In mammalian systems, chlordane induced unscheduled DNA synthesis in SV-40 human fibroblasts without activation (997) but did not do so in cultured mouse, rat and hamster hepatocytes (25).

Negative results were obtained in dominant lethal assays in mice receiving either cis-chlordane (42, 58 or 290 mg/kg ip or 5 daily oral doses of 75 mg/kg) or trans-chlordane (5 daily oral doses of 50 mg/kg) (998). Similar negative results were reported in mice given oral or ip doses of 50 or 100 mg/kg technical-grade chlordane (999).

48.3.1.3 Teratogenicity, Embryotoxicity and Reproductive Effects

At high dosages (50-320 mg/kg diet), chlordane decreased the fertility of rats and mice and the viability of their offspring. Little or no effect was seen, however, in mice fed 25 mg/kg diet for six generations or in rats fed 30 mg/kg diet for three generations.

Mice fed diets containing 100 mg/kg diet for 6 generations showed decreased viability in the first and second generations. In the third generation, no offspring were produced. At 50 mg/kg diet, viability was reduced in the fourth and fifth generations and at 25 mg/kg diet, no statistically significant effects were observed after 6 generations (1000). Rats maintained from weaning on a diet containing a chlordane level of 320 mg/kg diet, showed reduced rates of mating and of viable litters and an increased rate in the death of progeny prior to weaning (1310). In a 3 generation study conducted in rats, dietary levels of up to 30 mg/kg did not have any effect on fertility, number of offspring or the weight, growth or mortality rate of the animals to weaning age (1301). No evidence of teratogenicity was found in any study.

48.3.1.4 Other Toxicologic Effects

48.3.1.4.1 Short-term Toxicity

The signs associated with acute chlordane poisoning are ataxia, convulsions, respiratory failure and cyanosis. Pathological manifestations include hemorrhage in the gastrointestinal tract, liver, kidneys,

lung and heart, pulmonary edema and congestion, and degenerative changes in the central nervous system (994).

The acute toxicities are difficult to interpret since they are dependent upon both the purity of the chlordane and the solvent used (2,12). Chlordane manufactured before 1951 was more toxic than that manufactured during and after 1951. The greater toxicity of the early product was partly due to the presence of hexachlorocyclopentadiene (12). In 1952, Ingle (1305) reported an oral LD_{50} value of 250 mg/kg for rats. Later reports of LD_{50} values for the rat ranged from 283 to 590 mg/kg (1306,1307). The cis- and trans-isomers have oral LD_{50} values of 392 and 327 mg/kg, respectively, while an equal mixture of both isomers resulted in an LD_{50} value of 371 mg/kg (1308).

Daily oral doses of 6.25 to 25 mg/kg administered in cottonseed oil for 15 days did not induce tremors or convulsions but daily doses of 50 mg/kg did induce toxic symptoms and death. Dose-related increases in cytoplasmic bodies were observed in the liver cells in all groups (1310).

The acute inhalation toxicity of chlordane was investigated in the early 1950's by Frings and O'Tousa (1312) and Ingle (1313). The former investigators exposed female mice to air saturated with chlordane for up to 4 days. The chlordane contained 25 to 40% unspecified related compounds. Most of the animals died within 4 days; the remainder died within the next 10 days. In contrast, Ingle exposed mice for 14 days and observed no deaths or adverse effects on the liver or central nervous system. However, when hexachlorocylclopentadiene was added, toxic effects and fatalities were observed. Ingle speculated that the toxicity seen by Frings and O'Tousa may have been caused by chlordane contaminated with hexachlorocyclopentadiene.

Dermal LD_{50} values in rats ranged from 590 to 840 mg/kg (2); however, Ingle (1309) reported that more purified chlordane raised the LD_{50} value to 1100-1200 mg/kg. A dermal dose of less than 780 mg/kg of "early" (i.e., less purified) chlordane was reported to cause severe skin irritation, tremors and convulsions in rabbits (1314). A purer product was only half as toxic to rabbits as the earlier chlordane formulation and did not cause any skin irritation or damage to the mucous membranes (994).

48.3.1.4.2 Chronic Toxicity

Chronic chlordane poisoning in animals produces degenerative changes in the liver, renal tubules, lungs, heart and intestinal submucosa (17). Chlordane is slowly metabolized to oxychlordane which is more toxic than chlordane itself (oral LD_{50} (rat) 19.1 mg/kg) (994). The alpha (cis) isomer is retained primarily in body fat but also in the kidney, muscle, liver, and brain in decreasing quantities. The highest concentrations of the gamma (trans) isomer are found in the kidney, followed by fat, liver, muscle and brain. Oxychlordane is found primarily in fat but at higher concentrations than chlordane

(12). Because of its storage in body fat, chlordane has a high degree of persistence and therefore a high potential for toxicity (17).

The Joint Meeting on Pesticide Residues has reviewed chronic oral toxicity data on chlordane and established the following no-observed adverse-effect-levels: in the rat, 5 mg/kg diet, equivalent to 0.25 mg/kg body weight; in the dog, 3 mg/kg diet, equivalent to 0.075 mg/kg body weight (1315).

Ingle (1316) in a two-year study, fed rats dietary levels of "early" technical chlordane ranging from 5 to 300 mg/kg. Convulsions and tremors were observed in animals receiving 150 mg/kg or more. Growth retardation and severe lung, liver and kidney damage were also observed at these levels. No lung or kidney damage was seen at the 5, 10 or 30 mg/kg levels. Liver damage was slight at 30 mg/kg, minimal at 10 mg/kg and absent at 5 mg/kg.

In a subsequent study on rats, technical chlordane containing fewer by-products was administered at levels of 2.5 to 300 mg/kg diet for 2 years. Cellular alterations were seen at 50 mg/kg and higher. Changes in food consumption, growth and mortality rate were seen only at the highest dose (1318).

In dogs fed dietary levels of 0.3 to 30 mg/kg for two years, no treatment-related changes were seen in behavior, food consumption, appearance, body weight, hematology or plasma biochemistry. Relative liver weights were increased and liver enzymes were altered at the 15 and 30 mg/kg levels (1317).

48.3.2 Human and Epidemiologic Studies

48.3.2.1 Short-term Toxicologic Effects

Acute chlordane poisoning produces CNS symptoms including headache, blurred vision, dizziness, slight involuntary muscle movements, tremor, sweating, insomnia, nausea and general malaise. More severe illness is characterized by muscular contractions and epileptiform convulsions, with loss of consciousness, urinary and fecal incontinence, disorientation, psychic disturbances and memory loss. These episodes may recur for 2 to 4 months following the cessation of exposure and are characterized by abnormal EEG patterns (995).

For adults, the estimated fatal oral dose is between 6 and 60 g, although convulsive symptoms have occurred with as little as 2.25 g (2,17). Olanoff et al. (1319) reported a case in which an individual ingested 215 g of chlordane in a liquid pesticide formulation which had been stored in a wine bottle. The rapid induction of emesis probably prevented this individual's death. Symptoms included vomiting, diarrhea, seizures, coma and respiratory failure. Whole blood chlordane concentration 3.5 hours after ingestion was 5 mg/L. The individual recovered after 13 days. Tissue samples obtained 58 days after ingestion revealed 5 ppm of chlordane metabolites (oxychlordane, heptachlor epoxide and trans-nonachlor) in the abdominal fat. This is

substantially higher than the 0.1 to 0.4 ppm measured in the subcutaneous fat of the general U.S. population. In another case, a person who ingested 6 g (104 mg/kg) in talc suffered burns of the mouth, severe gastritis, diffuse pneumonia, anuria, mania and convulsions. Death occurred after 9.5 days. Autopsy revealed severe necrotizing bronchopneumonia and degeneration of the renal tubules (1322).

Chlordane contamination of a public water system in Chattanooga, Tennessee resulted in symptoms of mild toxicity in 18% of the affected population. Chlordane concentrations in the tap water of the 42 houses that were affected ranged from 0.1 to 92,500 ppb. In 23 houses, the concentration exceeded 100 ppb and 11 of these had concentrations in excess of 1000 ppb. A survey of 71 affected residents revealed that 13 (18%) had symptoms compatible with mild chlordane poisoning. These included nausea, vomiting, abdominal pain, dizziness, blurred vision, headache or muscle dysfunction. None was hospitalized and all recovered within 48 hours after exposure with no apparent chronic sequelae (1321).

An inhalation exposure reported by Garrettson et al. (1320) is indicative of the persistance of chlordane. In this case, a woman was exposed to chlordane vapors over a 3 day period after spraying 16 gallons of the diluted insecticide through her home. Three days after the start of spraying she experienced numbness in her arm and around her nose and mouth which lasted from 3 to 4 weeks. She also experienced nausea and vomiting which persisted for 3 weeks and anorexia which persisted for 6 months. Severe headaches with a frequency of 2 per week lasted for 4 months. One month after exposure, myoclonic jerks began to occur. The reason for this time delay could not be explained. Anorexia and malaise induced the woman to seek treatment about 4 months after symptoms began. At this time, serum heptachlor was 30 ng/mL and fat heptachlor was 20 μg/g. After one week of treatment, the serum level dropped to 4 ng/mL. Treatment was continued on an out-patient basis and the patient reported symptomatic improvement.

Skin absorption of chlordane is rapid (46). A worker who spilled a 25% suspension on his clothing (which was not removed) began having convulsions 40 minutes later and died shortly thereafter (1322).

Technical grade chlordane is said to be irritating to the skin and mucous membranes but this may be due to the presence of contaminants (38). Presumably this is not a problem with the recently manufactured product (12). Chlordane may persist for long periods on the skin of persons using it. In one study, hexane rinsings of the hands of a former pest-control operator contained chlordane 2 years after his last known exposure (1323).

48.3.2.2 Chronic Toxicologic Effects

Limited studies of long-term human exposure to chlordane have revealed no consistent or significant detrimental effects.

There are anecdotal reports suggesting a correlation between chlordane exposure and the subsequent development of aplastic anemia, leukemia and neuroblastoma (1324). Five out of fourteen children with neuroblastoma were exposed either pre- or postnatally to chlordane. Only 2 of the 6 cases with anemia or leukemia were exposed to chlordane alone. The other cases were complicated by exposures to multiple chemicals. These case reports do not provide sufficient information to support a causal relationship.

In a 1981 case-control study, Wang and Gruffenman (1326) found no association between blood dyscrasias and occupational exposure to chlordane. Wang and MacMahon (1327) studied a cohort of 1403 workers employed for 3 months or longer in the production of chlordane or heptachlor between 1946 and 1975. The data indicated an excess of lung cancer which was not considered statistically significant (12 observed vs. 9 expected); however, there was a statistically significant excess in deaths from cerebrovascular disease (17 observed vs. 9.3 expected). These deaths all occurred after termination of employment and were not related to duration of exposure. Ditraglia et al. (1325) studied a cohort of these same workers who had achieved 6 months employment prior to December 31, 1964. This date was selected to allow for a sufficient latency period. These investigators found a deficit in observed deaths due to all malignant neoplasms. A slight excess of stomach cancer was observed, which was not statistically significant.

Other studies of long-term chlordane exposure have not revealed any abnormalities in the liver, kidneys, skin, nervous system and blood-forming organs. Princi and Spurbeck (1328) found no adverse effects in 34 men engaged in the production of insecticides, including chlordane and exposed through skin contact and inhalation for 11-36 months. Vapor concentrations were as high as 10 mg/m^3. In addition, no adverse effects were seen in 15 workers exposed to vapor levels of 0.0012 - 0.0017 mg/m^3 for periods of 1 to 15 years (1329) or in 24 men exposed to unspecified levels for 2 months to 5 years (1330).

48.3.3 Levels of Concern

The USEPA (355) has specified an ambient water quality criterion of zero for chlordane, based on the induction of liver carcinoma in mice. In that attainment of a zero concentration level may be infeasible in some cases, the concentrations of chlordane in water calculated to result in incremental lifetime cancer risks of 10^{-5}, 10^{-6}, and 10^{-7} from ingestion of both water and contaminated aquatic organisms were estimated to be 4.6, 0.46 and 0.046 ng/L, respectively. Risk estimates are expressed as a probability of cancer after a lifetime daily consumption of two liters of water and 6.5 g of fish that have bioaccumulated chlordane. Thus a risk of 10^{-5} implies that a lifetime daily consumption of two liters of drinking water and 6.5 g of contaminated fish at the criterion level of 4.6 ng/L of chlordane would be expected to produce one excess case of cancer above the normal background incidence for every 100,000 people exposed. It should be

emphasized that these extrapolations are based on a number of assumptions and should be taken as crude estimates of human risk at best.

IARC (803) lists chlordane in category 3 (cannot be classified as to its carcinogenicity to humans) in its weight-of-evidence ranking for carcinogens.

For noncarcinogenic risks, the USEPA (992) has issued a health advisory of 0.22 mg/L (10 days) for short-term exposure to chlordane in drinking water. The WHO (666) recommends a level of 0.3 μg/L for chlordane (total isomers) in drinking water. A temporary FAO/WHO ADI for humans of 0 to 1 μg/kg body weight was confirmed by FAO in 1977 (666).

Both OSHA (298) and the ACGIH (3) currently permit 8-hour time-weighted average exposures of 0.5 mg/m^3 for chlordane, with a notation of possible skin absorption.

48.3.4 Hazard Assessment

Chlordane is moderately toxic in acute exposures. Acute lethal values generally fall in the 200 to 1000 mg/kg range (59). Bioaccumulation, primarily in body fat, may result from continuous exposure. In humans, chlordane primarily affects the central nervous system, inducing irritability, tremors and convulsions. The fatal oral dose for adults is estimated to be between 6 and 60 g, with onset of symptoms occurring within 45 minutes to several hours after ingestion (2,17). Chlordane is readily absorbed through the skin (46).

The carcinogenicity of chlordane has been studied in both mice and rats (1302). Inclusion of up to 407 ppm analytical-grade chlordane in the diet of rats did not induce hepatocellular carcinoma. In the mouse, up to 56 ppm analytical-grade or 25 ppm technical-grade chlordane did induce a significant incidence of hepatocellular carcinoma. No significant carcinogenic effect was noted in mice fed 30 ppm analytical chlordane and no evidence of carcinoma was seen with 5 ppm technical chlordane. Thus, the carcinogenic activity noted at the 25 ppm level with technical chlordane may reflect the presence of heptachlor.

Considerable controversy exists concerning the interpretation of hepatic lesions observed in laboratory mice exposed to chlordane in the diet, especially with respect to the possible implications of these findings for man. In part, this situation arises from a lack of agreement among pathologists on diagnostic criteria for clasifying hepatic lesions as benign or malignant neoplasia. Another factor is the high background incidence of these tumors in untreated mice.

Several epidemiologic studies involving occupational exposure to chlordane do not provide any evidence of increased cancer mortality (1325,1326,1327) although anecdotal reports suggest a relationship

between exposure to chlordane and blood dyscrasias, acute leukemia and development of neuroblastomas in children (1324). Available human data, however, are insufficient to permit an evaluation of the potential carcinogenicity of chlordane for humans at this time.

Results in mutagenicity tests including an *in vivo* assay are generally negative and do not indicate a mutagenic hazard.

Little or no effect was seen in either mice or rats fed 25 and 30 mg/kg diet of chlordane over several generations. Higher doses resulted in decreased fertility and viability of offspring. No teratogenic effects were observed (1000,1301,1310).

Chronic animal studies suggest liver and kidney damage but these findings have not been observed with long-term human exposure.

48.4 SAMPLING AND ANALYSIS CONSIDERATIONS

Determination of chlordane concentrations in soil and water requires collection of a representative field sample and laboratory analysis. Care is required to prevent losses during sample collection and storage. Soil and water samples should be collected in glass containers; extraction of samples should be completed within 7 days of sampling and analysis completed within 40 days. In addition to the targeted samples, quality control samples such as field blanks, duplicates, and spiked matrices may be specified in the recommended methods.

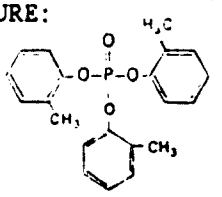
EPA-approved procedures for the analysis of chlordane, one of the EPA priority pollutants, in aqueous samples include EPA Methods 608, 625 (65), 8080, and 8250 (63). Prior to analysis, samples are extracted with methylene chloride as a solvent using a separatory funnel or a continuous liquid-liquid extractor. The concentrated sample extract is solvent exchanged into hexane and an aliquot of the hexane extract injected onto a gas chromatographic (GC) column using a solvent flush technique. The GC column is programmed to separate the semi-volatile organics; chlordane is then detected with an electron capture detector (Methods 608 and 8080) or a mass spectrometer (Methods 625 and 8250).

The EPA procedures recommended for chlordane analysis in soil and waste samples, Methods 8080 and 8250 (63), differ from the aqueous procedures primarily in the preparation of the sample extract. Solid samples are extracted with hexane/acetone using either soxhlet extraction or sonication methods. Neat and diluted organic liquids may be analyzed by direct injection.

Typical chlordane detection limits that can be obtained in wastewaters and non-aqueous samples (wastes, soils, etc.) are shown below. The

actual detection limit achieved in a given analysis will vary with instrument sensitivity and matrix effects. (Detection limits for aqueous samples using Methods 625 and 8250 were not indicated; chlordane is a mixture of isomers.)

Aqueous Detection Limit	Non-Aqueous Detection Limit
0.014 µg/L (Method 608/8080)	1 µg/g (Method 8080) 1 µg/g (Method 8250)

COMMON SYNONYMS:	CAS REG. NO.: FORMULA:	AIR W/V CONVERSION FACTORS at 25°C (12)
Phosphoric acid, tris (2-methyl-phenyl) ester Tri-o-tolyl phosphate TOCP TOTP	78-30-8 $C_{21}H_{21}O_4P$ NIOSH NO.: TD0350000 STRUCTURE: 	15.04 mg/m³ = 1 ppm 0.0665 ppm = 1 mg/m³ MOLECULAR WEIGHT: 368.37

REACTIVITY	Given its chemical structure, TOCP is likely to be considered in the reactivity group of organophosphates, phosphothioates, and phosphodithioates for compatibility classification purposes. Such substances typically generate heat in reactions with alkali or alkaline earth elemental metals; heat and toxic gases in reactions with mineral acids; and heat and possible explosion with caustics. Additionally reported are unknown but possibly hazardous reactions with azo or diazo compounds, hydrazines or organic peroxides or hydroperoxides. One specific source notes that TOCP can react with oxidizing agents. Another, however, states that TOCP has no hazardous incompatibilities (51,54,511).

PHYSICO-CHEMICAL DATA	• Physical State (at 20°C): liquid	(23)
	• Color: practically colorless	(23)
	• Odor: no data	( )
	• Odor Threshold: no data	( )
	• Liquid Density (g/ml at 20°C): 1.1955	(68)
	• Freezing/Melting Point (°C): 11, -33	(68,60)
	• Boiling Point (°C): 410	(68)
	• Flash Point (°C): 225	(12,506)
	• Flammable Limits in Air, % by Volume: no data	(506)
	• Autoignition Temperature (°C): 385	(506)
	• Vapor Pressure (mm Hg at 20°C): 1×10^{-7}	(1219)
	• Saturated Concentration in Air (mg/m³ at 20°C): 2×10^{-3}	(ADL estim)
	• Solubility in Water (mg/L at 20°C): 0.3	(38)
	• Viscosity (cp at 21.1°C): 102.2	(60)
	• Surface Tension (dyne/cm at 25°C): 44	(60)
	• Log (Octanol-Water Partition Coefficient), log K_{ow}: 5.11	(29)
	• Soil Adsorption Coefficient, K_{oc}: 62,000	(611)
	• Henry's Law Constant (atm·m³/mol at 20°C): 1.3×10^{-7}	(964)
	• Bioconcentration Factor: 170 (fathead minnow)	(806)

PERSISTENCE IN THE SOIL-WATER SYSTEM	Fairly immobile in soil water systems due to strong soil sorption, low water solubility and low vapor pressure. Resistant to photolysis and hydrolysis but easily biodegraded.

PATHWAYS OF EXPOSURE	The primary pathway from soil/ground-water systems is the migration of TOCP to ground water drinking water supplies, although it is expected to be relatively immobile. Bioaccumulation by aquatic organisms or domestic animals may be important exposure pathways in some instances. Inhalation is not expected to be a significant exposure route.

HEALTH HAZARD DATA	Signs and Symptoms of Short-term Human Exposure (54): The major effects of TOCP are on the spinal cord and peripheral nervous system. After acute exposure, nausea, vomiting, diarrhea and abdominal pain are seen followed by a latent period of 3 to 30 days. Next, muscle soreness and numbness of fingers, calf muscles, and toes occur, progressing to foot and wrist drop. These effects can be manifested after ingestion, inhalation or dermal absorption of TOCP.
	Toxicity Based on Animal Studies: LD_{50} (mg/kg) oral 1160 [rat] (47) skin 1500 [cat] (1352) LC_{50} (mg/m^3) inhalation -- no data
	Long-Term Effects: Peripheral neuropathy, paralysis of lower arms and legs
	Pregnancy/Neonate Data: Testicular toxicity in rats
	Mutation Data: No data
	Carcinogenicity: No data

HANDLING PRECAUTIONS (38,52)	Handle only with adequate ventilation • Vapor levels of 0.1-0.5 mg/m^3: any dust or mist respirator except single use • 0.5-1.0 mg/m^3: any supplied-air respirator, self-contained breathing apparatus, fume respirator, high efficiency particulate filter respirator or dust and mist respirator, except single-use or quarter mask • Chemical goggles if there is probability of eye contact • Neoprene, nitrile, PVC, PVA gloves/apron/boots to prevent repeated or prolonged contact with the liquid.

EMERGENCY FIRST AID TREATMENT (38,54)	Ingestion: As many pesticides are combined with other toxicants and often dissolved in petroleum distillates, vomiting can lead to solvent aspiration and pneumonitis. If TOCP is in a petroleum-based carrier or in a mixture, do not induce vomiting. If TOCP is in water, induce vomiting. Contact physician immediately • Inhalation: Move victim to fresh air. If necessary, give artifcial respiration. Get medical attention • Skin: Remove contaminated clothing; wash skin with soap and water. If pain or irritation persists, get medical attention • Eye: Irrigate for 15 min. with water. If pain or irritation persists after washing, get medical attention.

ENVIRONMENTAL AND OCCUPATIONAL STANDARDS AND CRITERIA

AIR EXPOSURE LIMITS:

Standards
- OSHA PEL (8-hr TWA): 0.1 mg/m^3
- AFOSH PEL (8-hr TWA): 0.1 mg/m^3

Criteria
- NIOSH IDLH (30-min): 40 mg/m^3
- ACGIH TLV® (8-hr TWA): 0.1 mg/m^3 (skin)
- ACGIH STEL (15-min): deleted

WATER EXPOSURE LIMITS:

Drinking Water Standards - None established

EPA Health Advisories - None established

EPA Ambient Water Quality Criteria (355)
- Human Health
  No criterion established; tri-ortho-cresyl phosphate is not a priority pollutant.
- Aquatic Life
  No criterion established; tri-ortho-cresyl phosphate is not a priority pollutant.

REGULATORY STATUS (as of January 1, 1987)

Promulgated Regulations

- Federal Programs

  Toxic Substances Control Act (TSCA)
  Manufacturers, processors or distributors of tri-o-cresyl phosphate must report production, usage and disposal information to EPA. They, as well as others who possess health and safety studies on tri-o-cresyl phosphate, must submit them to EPA (334,335).

  Marine Protection Research and Sanctuaries Act (MPRSA)
  Ocean dumping of organohalogen compounds as well as the dumping of known or suspected carcinogens, mutagens or teratogens is prohibited except when they are present as trace contaminants. Permit applicants are exempt from these regulations if they can demonstrate that such chemical constituents are non-toxic and non-bioaccumulative in the marine environment or are rapidly rendered harmless by physical, chemical or biological processes in the sea (309).

  Occupational Safety and Health Act (OSHA)
  Employee exposure to tri-o-cresyl phosphate shall not exceed an 8-hour time-weighted-average (TWA) of 0.1 mg/m^3 (298).

  Hazardous Materials Transportation Act (HMTA)
  The Department of Transportation has designated tri-o-cresyl phosphate as a hazardous material which is subject to requirements for packaging, labeling and transportation (306).

- State Water Programs
  There are no specific state regulations for tri-o-cresyl phosphate.

Proposed Regulations

- Federal Programs
  No proposed regulations are pending.

- State Water Programs
  No proposed regulations are pending.

EEC Directives

Directive Relating to the Quality of Water for Human Consumption (540)
The maximum admissible concentration for tri-o-cresyl phosphate is 0.1 µg/L. The total maximum allowable concentration for pesticides and related products is 0.5 µg/L.

Directive on Ground Water (538)
Direct discharge into ground water (i.e., without percolation through the ground or subsoil) of organophosphorous compounds, organohalogen compounds and substances which may form such compounds in the aquatic environment, substances which possess carcinogenic, mutagenic or teratogenic properties in or via the aquatic environment and mineral oils and hydrocarbons is prohibited. Appropriate measures deemed necessary to prevent indirect discharge into ground water (i.e., via percolation through ground or subsoil) of these substances shall be taken by member countries.

Directive on the Discharge of Dangerous Substances (535)
Organohalogens, organophosphates, petroleum hydrocarbons, carcinogens or substances which have a deleterious effect on the taste and/or odor of human food derived from aquatic environments cannot be discharged into inland surface waters, territorial waters or internal coastal waters without prior authorization from member countries which issue emission standards. A system of zero-emission applies to discharge of these substances into ground water.

Directive on Marketing and Use of Dangerous Substances (541)
Tri-o-cresyl phosphate may not be used in ornamental objects intended to produce light or color effects by means of different phases.

Directive on the Classification, Packaging and Labeling of Dangerous Substances (787)
Tri-o-cresyl phosphate is classified as toxic substance and is subject to packaging and labeling regulations.

Directive on Paints, Varnishes, Printing Inks, Adhesives and Similar Products (1334)
Tricresyl phosphate mixtures containing more than 1% esterified o-cresol are classified as toxic substances when present at concentrations greater than 1% and as harmful substances when present at concentrations ranging from 0.2 to 1%. Mixtures containing a maximum of 1% esterified o-cresol are classified as harmful substances when present at concentrations equal to or greater than 5%.

49.1 MAJOR USES

Tricresyl phosphate exists in three isomeric forms, the ortho-, meta- and para-isomers. Tri-ortho-cresyl phosphate (TOCP), a contaminant in commercial tricresyl phosphate, is the most toxic of the three isomers and is the only isomer of toxicologic importance. Modern mixtures contain less than 1% of the ortho isomer, although earlier formulations may have contained as much as 20% (17,54). Tricresyl phosphate is used as a plasticizer for chlorinated rubber, vinyl plastics, polystyrene, polyacrylic and polymethacrylic esters, as a solvent and binder in nitrocellulose and various natural resins, as an adjuvant in the milling of pigment pastes and as an additive to synthetic lubricants and gasoline. It is also used as a hydraulic fluid, a fire retardant, and in phenol recovery from coke oven waste waters (54).

49.2 ENVIRONMENTAL FATE AND EXPOSURE PATHWAYS

49.2.1 Transport in Soil/Ground-water Systems

49.2.1.1 Overview

Although U.S. production and use of tricresyl phosphate has been heavy in the past (30-40 million pounds per year in the period from 1964 to 1973 (1491)), there is relatively little information available on its fate and transport in the environment. Based on available information, TOCP is expected to be relatively immobile in the soil/ground-water environment when present at low concentrations (dissolved in water). However, bulk quantities of the liquid chemical (e.g., from a spill) could be transported down through the unsaturated zone. TOCP is expected to sorb strongly onto soils, especially those with significant organic carbon content. Although the chemical is susceptible to biodegradation, it appears to be resistant to degradation by hydrolysis or photolysis so that it may persist for long periods in the soil/ground-water environment.

Environmental transport pathways for TOCP can be generally assessed by using an equilibrium partitioning model as shown in Table 49-1. These calculations predict the partitioning of low soil concentrations of the chemical among soil particles, soil water and soil air. The estimates for the unsaturated topsoil model show that essentially all of the chemical (99.99%) is sorbed to the soil, and only a very small amount (0.008%) is in solution and available for downward percolation. The model predicts negligible amounts to be present in the soil air phase and thus volatilization losses should be negligible. In saturated deep soils (containing no air and negligible soil organic carbon), the model predicts that most of the chemical (99.6%) will be sorbed and only a small amount (0.4%) present in the mobile ground-water phase.

TABLE 49-1

EQUILIBRIUM PARTITIONING CALCULATIONS FOR TRI-O-CRESYL PHOSPHATE IN MODEL ENVIRONMENTS[a]

Soil Environment	Estimated Percent of Total Mass of Chemical in Each Compartment		
	Soil	Soil-Water	Soil-Air
Unsaturated topsoil at 20°C[b,c]	99.99	0.008	1.4×10^{-7}
Saturated deep soil[d]	99.6	0.4	-

a) Calculations based on Mackay's equilibrium partitioning model (34,35,36); see Introduction in Volume 1 for description of model and environmental conditions chosen to represent an unsaturated topsoil and saturated deep soil. Calculated percentages should be considered as rough estimates and used only for general guidance.

b) Utilized estimated soil sorption coefficient: K_{oc} = 62,000 (611).

c) Henry's law constant taken as 1.3×10^{-7} atm·m³/mol at 20°C (964).

d) Used sorption coefficient $K_p = 0.001\ K_{oc}$.

49.2.1.2 Sorption on Soils

A soil sorption constant (K_{oc}) of 62,000 has been estimated (611) based upon a measured value of the octanol-water partition coefficient (log K_{ow} = 5.11 (29)). This value of K_{oc} is indicative of relatively strong sorption to soils containing > 0.1% organic carbon. The extent of sorption will increase with increasing soil organic carbon content. No data were found on the sorption of TOCP to soils and sediments.

49.2.1.3 Volatilization from Soils

Based upon an estimated vapor pressure of 1×10^{-7} mm Hg (20°C) (1219) and a Henry's law constant of 1.3×10^{-7} atm·m³/mol (20°C) (964), volatilization from soil is expected to be an unimportant transport pathway except for near-surface dry soils.

49.2.2 Transformation Processes in Soil/Ground-water Systems

TOCP is expected to be resistant to direct photolysis based on the fact that there is no light absorption above 290 nm (806).

It is known that organophosphate chemicals can undergo hydrolysis, and that the reaction may be base-catalyzed (529,806,1493,1494,1495). However, the rate of hydrolysis in the environment is expected to be slow. One estimate gives the environmental hydrolysis half-life as 82 years at pH 7 and 30 days at pH 10 (806). The base-catalyzed reaction presumably results in initial clevage of a phosphorus-oxygen bond (1491).

A variety of data are available on the biodegradability of tri-p-cresyl phosphate (CAS No. 78-32-0) and the isomer mixture tricresyl phosphate (CAS No. 1330-78-5), as well as TOCP (806,1490,1496,1497). Most of these data show that tricresyl phosphates are significantly biodegraded by natural microorganisms obtained from sewage treatment plants and surface waters. Substantial or complete degradation took place within a few days in most tests. Examples of data from two tests using river and lake water are shown in Figures 49-1 and 49-2. In both cases, the disappearance of the chemical represents primary biodegradation.

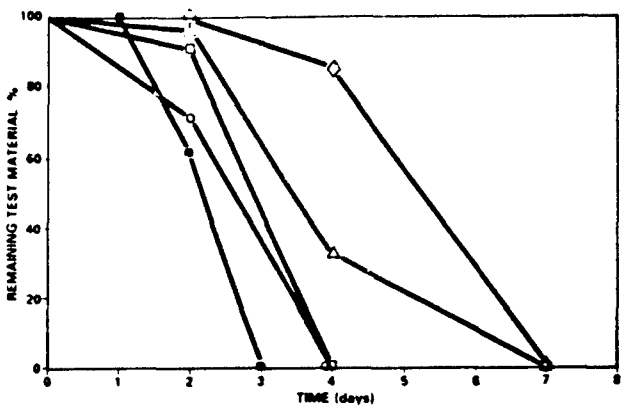


FIGURE 49-1

BIODEGRADATION OF TRICRESYL PHOSPHATE IN MISSISSIPPI RIVER WATER

Source: Saeger et al. (1490)

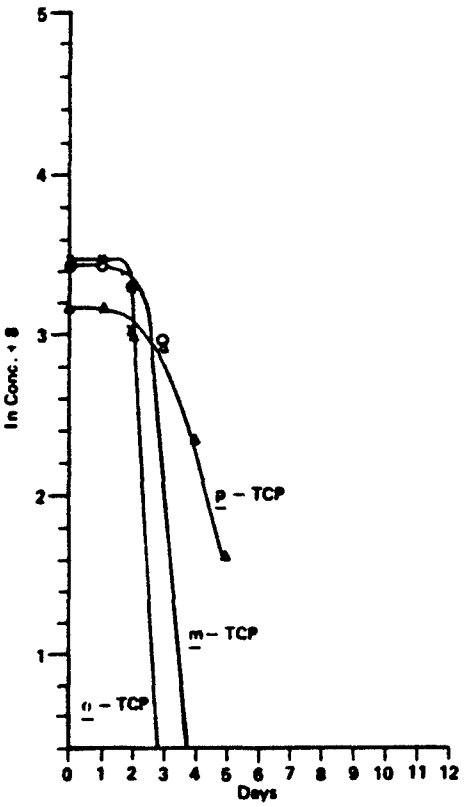


FIGURE 49-2

LOSS OF TRICRESYL PHOSPHATE ISOMERS IN LAKE ONTARIO WATER

Source: Howard and Deo (1496)

One initial metabolite of tri-p-cresyl phosphate is reported to be p-hydroxybenzoic acid (806). Based on CO_2 evolution studies for tri-cresyl phosphate (isomer mixture), Saeger et al. (1490) conclude that the chemical undergoes ultimate biodegradation (in which all carbon is converted to CO_2) fairly easily. In their test using acclimated bacterial seed, 79% of the ultimate CO_2 production was reached after 7 days, 82% after 28 days, and 86% after 48 days.

49.2.3 Primary Routes of Exposure from Soil/Ground-water Systems

The above discussion of fate pathways suggests that TOCP is of low volatility, is strongly sorbed to soil, and has a moderate potential for bioaccumulation. These fate characteristics provide some indication of potentially important exposure pathways.

Volatilization of TOCP from a disposal site is not likely to represent an important exposure pathway. The potential for ground-water contamination is limited by the strong adsorptive characteristics of TOCP. The presence of this compound in ground water drinking water supplies has not been reported in the literature.

As TOCP is expected to be relatively immobile in the soil/ground-water environment, discharges to surface water via this route are not expected to be significant. Any releases to surface water would be strongly sorbed to sediment and would not be likely to result in direct human exposure through drinking water. Uptake by aquatic organisms is possible, however, based on this compound's potential for bioaccumulation.

49.2.4 Other Sources of Human Exposure

The production of TOCP has declined dramatically in the last ten years. The primary source of exposure to this compound still appears to be in occupational settings (1788). To the extent that this compound is used in consumer products, direct consumer exposure is possible. However, environmental exposures to TOCP (through food, drinking water, and air) have not been reported (1788).

49.3 HUMAN HEALTH CONSIDERATIONS

49.3.1 Animal Studies

49.3.1.1 Carcinogenicity

No carcinogenicity data are available for TOCP. The NTP plans to conduct a two year study with TOCP (883).

49.3.1.2 Mutagenicity

No mutagenicity studies were found for TOCP.

49.3.1.3 Teratogenicity, Embryotoxicity and Reproductive Effects

The testicular toxicity of TOCP was evaluated in F344 rats by Somkuti et al. (1338,1339). Animals dosed orally with 10-150 mg/kg/day TOCP for 3-63 days had a time-dependent increase in the inhibition of sperm motility and an inhibition of testicular non-specific esterase. Pairfed controls showed no signs of testicular toxicity (1339).

Morphological testicular changes were evaluated by the same investigators after administering 150 mg/kg/day TOCP in corn oil for 3, 5, 7, 10, 14 or 21 days. A corn oil-treated group served as controls. By day 5 there were numerous detached spermatids. There was also a progressive decrease in sperm density in the seminiferous tubules (0 by day 14). Morphological findings indicate a possible selective effect of TOCP on the Sertoli cells (1338).

49.3.1.4 Other Toxicologic Effects

49.3.1.4.1 Short-term Toxicity

TOCP is a delayed onset neurotoxin which lacks the potent anticholinesterase properties exhibited by other organophosphorus compounds (200). Cats and chickens are the species most sensitive to the neurotoxic effects of TOCP and exhibit clinical and histopathological manifestations similar to humans. Rats and mice are less sensitive, apparently due to differences in pharmacokinetics and metabolism (1228). Species sensitivity also appears to be age-related with younger animals being more resistant to the toxic effects of TOCP (1227).

In TOCP-treated cats and chickens, extensive damage is observed in the spinal cord and sciatic nerves. Damage to the myelin sheath and Schwann cells is secondary to the lesions in the axon, which start at the distal end of the longer axons (46). Cholinergic signs appear up to 2 days after dosing and may persist for several days until weakness and ataxia develop in the lower limbs. This progresses to paralysis which, in severe cases, also affects the upper limbs (1227). This delayed polyneuropathy is known as organophosphorus-induced delayed neurotoxicity (OPIDN). It should be noted that OPIDN is not induced by all organophosphorus compounds. The ability of one compound but not another to cause OPIDN has not been fully elucidated (1348,1227,1228).

Johnson (1227) has hypothesized that this process is initiated by phosphorylation of a protein neurotoxic esterase (NTE) in the nervous system. This phosphoryl-enzyme complex must then undergo "aging", a process which involves loss of a group attached to the phosphorus, resulting in attachment of a negatively charged phosphoryl group to the protein. For compounds that age, if threshold levels of NTE inhibition are achieved, OPIDN occurs. The attainment of high levels of NTE inhibition (70-80%) in the brain, spinal cord or peripheral nerve tissue of experimental animals soon after dosing with an organophosphorus compound predicts the onset of clinical signs approximately two weeks later (1227,1348).

Support for the NTE hypothesis comes from the correlation between the inhibitory effect of many organophosphorus compounds on NTE and their ability to produce delayed neurotoxicity in hens. For example, TOCP, a known inducer of OPIDN, produces about 90% inhibition of NTE and 10% inhibition of acetylcholinesterase (AChE) in the hen brain. Parathion, another organophosphorus compound, does not induce OPIDN, has no significant effect on brain NTE activity, but does inhibit AChE activity upwards of 80% (1434). However, this correlation between high levels (> 70%) of NTE inhibition and development of OPIDN has not been consistently observed (1228). Several dimethyl phosphates produce a high level of NTE inhibition in hens but do not cause OPIDN (1229). Conversely, Olajos et al. (1230) have found that hens developed OPIDN with only a 32% level of NTE inhibition after being given cumulative doses of 2-5 mg/kg diisopropyl phosphorofluoridate, another delayed onset neurotoxin.

In rats, oral LD_{50} values for TOCP range from 1160 to 3000 mg/kg (47,59). In cats, dermal and oral LD_{50} values were determined to be 1500 and 3000 mg/kg, respectively (1352).

Chickens given oral doses of 100 mg/kg TOCP for 15 days had a 98% inhibition of NTE activity and experienced severe neurotoxic effects (1349). One oral dose of 750 mg/kg resulted in unsteady gait and ataxia within 21 days. In this case, NTE was inhibited by 87% (1350). On the other hand, CD-1 mice receiving 262 mg/kg by gavage for 30 days exhibited no signs of clinical neuropathy (1349) but rats given single oral doses of 3480 mg/kg had 90% NTE inhibition within 20 hours. They developed the neuropathology of OPIDN with severe central and peripheral nerve degeneration but remained resistant to ataxia (1351). In an unspecified species and route, 20-30 daily doses of 5 mg/kg TOCP were equivalent to a single dose of 120-200 mg/kg (1232).

Single dermal doses of 250-2000 mg/kg produce delayed neurotoxic effects in cats, the severity of which were dose-dependent. Animals treated with 1000-2000 mg/kg developed severe cholinergic effects despite treatment with drugs to prevent these effects such as atropine and pralidoxime immediately after dosing (1353). Among the cholinergic effects seen were vomiting, diarrhea and anorexia. Neurological effects included leg weakness, difficulty in standing and muscle fasciculation. Cats treated with 2000 mg/kg dermally died within 25 days. Extensive axonal degeneration was seen in all cats treated with 1000 or 1500 mg/kg. Two out of three cats given a 500 mg/kg dermal application and all three animals treated with 250 mg/kg showed histologic lesions indicative of OPIDN but did not exhibit any signs of toxicity. A single dermal dose of 100 mg/kg did not produce neurotoxicity in cats (1353).

49.3.1.4.2 Chronic Toxicity

Long-term administration of TOCP causes the same neurotoxic effects as acute administration provided that a threshold level of inhibition-aging of NTE is reached which triggers OPIDN. These threshold levels may be species-specific (1234).

In mice, daily oral dosing of 225 mg/kg for 270 days caused a decrease in body weight gain, muscle wasting, weakness and ataxia which progressed to severe hind limb paralysis. No cholinergic signs of toxicity were present even though acetylcholinesterase was inhibited 65%. Neurotoxic esterase was inhibited by 87%. Histologic examination revealed extensive degeneration of the axon and myelin of the spinal cord (1234).

Abou-Donia et al. (1353) examined the effect of long-term dermal application of 0.5-100 mg/kg to cats. The animals were treated for 90 days and observed for 30 days thereafter. Animals given 0.5 mg/kg did not show any signs of acute poisoning. Doses of 5-100 mg/kg produced signs of an acute effect; the onset, duration and severity of this effect were dose-dependent. Animals given 100 mg/kg had the most severe response which began 9 days after the first administration. They developed severe ataxia which progressed to paresis. All succumbed after a mean of 36 daily doses. Animals given 10 mg/kg developed acute poisoning after an average of 25 days. All developed severe ataxia and 1 of the 4 progressed to paresis. Cats given 5 mg/kg showed less severe acute effects (mild ataxia) after an average of 35 days. Cats given 1 mg/kg showed leg weakness after a mean of 74 doses. Histopathological changes in the spinal cord were seen in 2 of 3 cats given 100 mg/kg and in 5 of 6 given 10 mg/kg. Only 1 of 3 at the 5 mg/kg level had any spinal cord lesions. Spinal cords of those receiving 0.5 or 1 mg/kg were normal. A significant finding was that all surviving animals showed clinical improvement after TOCP was discontinued.

49.3.2 Human and Epidemiologic Studies

49.3.2.1 Short-term Toxicologic Effects

Most human intoxications with TOCP have involved accidental ingestion of adulterated alcoholic beverages and cooking oils (12). Fatalities are rare and occur primarily in individuals who have ingested large quantities in a short time. The lethal oral dose of TOCP for humans is about 1 g/kg; severe paralysis has resulted from ingestion of 6-7 mg/kg (46).

In each episode of TOCP-poisoning, the clinical picture has been consistent. Shortly after ingestion there may be nausea, vomiting, diarrhea and abdominal pain lasting from a few hours to 2 days depending on the quantity ingested. After a latent period of 5 to 28 days, sharp cramplike pains may occur in the calves with some numbness in the hands and feet. Within a few hours, there is increasing weakness of the legs and feet which may progress to bilateral foot drop. A few days later, weakness of the fingers and wrists may develop, but the paralysis is not usually as severe as that in the feet and legs. Sensory changes, if they occur, are minor. Muscular weakness may increase over a period of several weeks or months. Recovery may take months or years and in 25-30% of the cases, permanent residual effects

remain in the lower limbs. In milder cases, recovery appears to be complete but there may be minor, residual neurologic effects (12,46,200).

The most famous occurrence of TOCP poisoning was the "Jamaica ginger paralysis" which effected 50,000 Americans during the 1930's. "Jake", an ethanolic extract of ginger, was popular as tonic, particularly in the southern United States. The formula had originally contained castor oil but TOCP was substituted because of its lower cost. This led to an epidemic of partial paralysis among consumers of the beverage (1340). In a 47-year follow-up of eleven patients, 10 were found to be dicabled (1343).

Another epidemic poisoning occurred in Morocco in 1959. It involved 10,000 people who ingested olive oil adulterated with jet engine lubricating oil containing 3% TOCP. Ten to fifteen percent of those affected remained permanently disabled (1341).

In 1977, an outbreak of acute polyneuropathy affected 20 young women in Sri Lanka who consumed gingili oil contaminated with TOCP over a two week period. The total amount of TOCP ingested was estimated to be 2.8-5.6 g (70-140 mg/kg for a 40-kg female). Symptoms began with pain in the calves followed by weakness of feet and hands over a 1 to 3 day period. They had the characteristic high-stepping gait caused by bilateral foot drop. Other abnormal signs were wrist drop, bilateral claw hands and absent ankle jerks (1342).

TOCP is not a skin irritant. About 0.1 to 0.4% of a dose applied to human skin is absorbed (12).

Optic neuritis has been observed in cases of TOCP poisoning, but a link to TOCP as the causative agent has not been firmly established (19).

49.3.2.2 Chronic Toxicologic Effects

Little is known about the effects of chronic human exposure to low concentrations of TOCP. There have been only a few reports of occupational exposures (2).

A case of permanent paralysis was reported in a man engaged in the manufacture of the meta and para isomers of tricresyl phosphate. As much as 6-10% TOCP was present as a contaminant during manufacture. The man had worked for 5 months before symptoms of anorexia, nausea and leg pain had developed (59).

Hunter et al. (1344) described 3 cases of polyneuritis in workers manufacturing various aryl phosphates with the suspicion that TOCP was the causative factor. Vapor concentrations ranged from 0.55-2.5 mg/m^3, however, absorption through the skin was not ruled out. Length of exposure was not reported.

Inhibition of butyryl cholinesterase was reported in another group of workers engaged in the manufacture of aryl phosphates containing up to 20% TOCP. Vapor concentration of aryl phosphates ranged from 0.2 to 3.4 mg/m^3. No correlation was seen between the cholinesterase level and the degree of exposure or with minor gastrointestinal or neuromuscular symptoms. Length of exposure was not given (1345,1346).

A correlation between long-term TOCP exposure and chronic granulocytic leukemia was suggested by Duhrsen et al. (1347). The patient was an automobile mechanic who had worked with fuels, motor oil and lubricants for 32 years. Investigation revealed a tri-cresyl phosphate concentration of 0.6% in some of these products with 1-3% being the ortho isomer. The patient had initially been examined for chronic polyneuropathy, beginning spastic paraparesis and leuko- and thrombocytosis of unknown origin. A diagnosis of chronic granulocytic anemia was made. No medical history or follow-up information was reported.

49.3.3 Levels of Concern

No criteria or standards have been established in the U.S. for TOCP with regard to acceptable levels of exposure via drinking water. EEC countries require a maximum TOCP concentration of 0.1 μg/L for water used for human consumption (540).

Both OSHA (298) and ACGIH (3) have set an occupational exposure limit of 0.1 mg/m^3 for TOCP, with an indication of potential skin absorption. The TLV® was set to prevent neurotoxic effects (3).

49.3.4 Hazard Assessment

Tricresyl phosphate exists in three isomeric forms - ortho-, meta- and para-isomers. Only the ortho form (i.e., TOCP) is of toxicologic importance.

TOCP is moderately toxic via ingestion exposure and is readily absorbed through the skin without inducing local irritant effects; the oral and dermal LD_{50} values for the rat are 1160 and 300 mg/kg, respectively (47,1352). The lethal dose for human is about 1 g/kg body weight (46).

The major concern associated with TOCP exposure is a condition known as organophosphorus-induced delayed neurotoxicity (OPIDN). OPIDN has been observed in humans exposed to TOCP-adulterated food as well as experimentally in sensitive animal species. After a latent period of 3 to 30 days post-exposure, clinical signs of ataxia followed by paralysis of the lower extremities are exhibited. Neuronal lesions are characterized by degeneration of axons. Severe paralysis has resulted in humans from ingestion of 6 to 7 mg/kg (46). Recovery may take months to years; approximately 25-30% of the cases never recover.

There are no data presently available with regard to the carcinogenic and mutagenic potential of TOCP. Recent reports, however, have noted possible testicular toxicity in rats dosed with 10 to 150 mg/kg/day orally for periods ranging from 3 to 63 days (1338,1339).

The lack of data with respect to chronic human exposure to TOCP, carcinogenicity and mutagenicity when considered along with possible testicular toxicity and the well established neurotoxicity of TOCP suggest that due care be exercised to avoid exposure to TOCP.

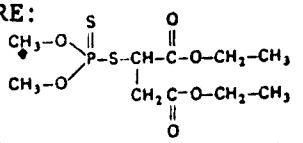
49.4 SAMPLING AND ANALYSIS CONSIDERATIONS

Determination of the concentration of TOCP in soil and water requires collection of a representative field sample and laboratory analysis. Care is required to prevent losses during sample collection and storage. Soil and water samples should be collected in glass containers; extraction of samples should be completed within 7 days of sampling and analysis completed within 30-40 days. In addition to the targeted samples, quality control samples such as field blanks, duplicates, and spiked matrices should be included in the analytical program.

TOCP is not included among the EPA-designated priority pollutants, and an EPA-approved procedure for the analysis of TOCP is not available. However, EPA Method 8140 is a recommended procedure for the analysis of organophosphorus pesticides in ground water and waste samples (63) and should be an appropriate method for the analysis of TOCP. In this method, aqueous samples are extracted at neutral pH with methylene chloride using a separatory funnel or a continuous liquid-liquid extractor. Solid samples are extracted using either soxhlet extraction or sonication methods; neat and dilute organic liquids may be analyzed by direct injection. An aliquot of the sample or concentrated sample extract is injected onto a gas chromatographic (GC) column for separation of the semi-volatile organics. Detection of the individual organophosphorus pesticides is then accomplished by either a nitrogen/phosphorus (N/P) detector operated in the phosphorus sensitive mode or a flame photometric detector (FPD). The FPD is more selective for phosphorus than the N/P.

In addition, a NIOSH-approved method for the analysis of levels of TOCP in air samples is available (40). Sampling and analysis is performed by collection of TOCP on a filter, followed by extraction with ether, and gas chromatographic analysis using a flame photometric detector.

A detection limit for TOCP using these methods was not determined but would be in the range of 1-10 $\mu g/L$ for aqueous samples, 1-10 $\mu g/g$ for non-aqueous samples which have been extracted and part-per-million (ppm) range for samples which have been directly injected.

COMMON SYNONYMS:	CAS REG. NO.:	FORMULA:	AIR W/V CONVERSION FACTORS at 25°C (1098)
Butanedioic acid, [(dimethoxyphosphinothioyl)-thio]-,diethyl ester Carbophos	121-75-5 NIOSH NO.: WM8400000	$C_{10}H_{19}O_6PS_2$	13.7 mg/m³ = 1 ppm 0.073 ppm = 1 mg/m³
	STRUCTURE: 		MOLECULAR WEIGHT: 330.36

REACTIVITY	For compatibility classification purposes, malathion is considered to be in the reactivity group of organophosphates, phosphothioates and phosphodithioates. Such substances typically generate heat in reactions with alkali or alkaline earth elemental metals, heat and toxic gases in reactions with mineral acids, and heat and possible explosion with caustics. Hazardous reactions with azo or diazo compounds, hydrazines or organic peroxides or hydroperoxides are also possible. More specific sources indicate that malathion may be incompatible with strong oxidizers, that it is hydrolyzed at various rates above a pH of 7, and that prolonged contact with iron or iron-bearing material may cause breakdown of the material. Reaction with a strong base may generate excessive heat, storage at 50-115°C leads to a non-hazardous decomposition reaction (that produces several toxic products), and heating above 150°C causes rapid decomposition (54,59,507,511).

PHYSICO-CHEMICAL DATA	• Physical State (at 20°C): liquid	(69)
	• Color: deep brown to yellow	(69)
	• Odor: skunk-like	(60)
	• Odor Threshold: no data	( )
	• Liquid Density (g/ml at 25°C): 1.2315	(23)
	• Freezing/Melting Point (°C): 2.9	(69)
	• Boiling Point (°C): 156-157 at 0.7 mm Hg	(69)
	• Flash Point (°C): > 162.8	(60,507)
	• Flammable Limits in Air, % by Volume: no data	( )
	• Autoignition Temperature (°C): no data	( )
	• Vapor Pressure (mm Hg at 20°C): 6.6×10^{-6}	(1219)
	• Saturated Concentration in Air (mg/m³ at 20°C): 1.2×10^{-1}	(ADL estim)
	• Solubility in Water (mg/L at 20°C): 145	(38)
	• Viscosity (cp at 20°C): no data	( )
	• Surface Tension (dyne/cm at 24°C): 37.1	(60)
	• Log (Octanol-Water Partition Coefficient), log K_{ow}: 2.84	(1488)
	• Soil Adsorption Coefficient, K_{oc}: 1800	(1211)
	• Henry's Law Constant (atm•m³/mol at 20°C): 2×10^{-8}	(1216)
	• Bioconcentration Factor: 33 (estim)	(37)

PERSISTENCE IN THE SOIL-WATER SYSTEM	Fairly immobile and non-persistent in soil water systems due to moderate sorption and relatively rapid degradation by hydrolysis (at pH > 7) and biodegradation. Photolytic degradation important for surface waters and soil.

PATHWAYS OF EXPOSURE	The primary pathway of concern from soil/ground-water systems is the migration of malathion to ground water drinking water supplies. However, the potential for adsorption and degradation make the contamination of water supplies with malathion less likely than with other chemicals. Exposures through inhalation or bioaccumulation are not generally expected to be significant.

HEALTH HAZARD DATA	Signs and Symptoms of Short-term Human Exposure (38): After ingestion of malathion, loss of appetite, nausea, vomiting, abdominal cramps and diarrhea may appear within 2 hours. Inhalation results in chest tightness, blurred vision, constricted pupils, headache and watering of the mouth. After skin absorption, sweating and twitching in the area of absorption may occur.
	Toxicity Based on Animal Studies: LD_{50} (mg/kg) oral 370 [rat] (47) skin 4444 [rat] (47) LC_{50} (mg/m^3) inhalation [mouse] (1374) > 15
	Long-Term Effects: Decreased cholinesterase levels
	Pregnancy/Neonate Data: Negative
	Mutation Data: Limited evidence
	Carcinogenicity Classification: IARC - 3; NTP - no evidence

HANDLING PRECAUTIONS (38)	Handle chemical only with adequate ventilation • Vapor concentrations of 15 mg/m^3-150 mg/m^3: any supplied-air respirator or self-contained breathing apparatus; any chemical cartridge respirator with organic vapor cartridge and dust fume and mist filters, including pesticide respirators which meet the requirements of this class • 150-750 mg/m^3: any supplied-air respirator or self-contained breathing apparatus with full facepiece • Chemical goggles if there is probability of eye contact • Full-body coveralls and impervious gloves.

EMERGENCY FIRST AID TREATMENT (38)	Ingestion: Because many pesticide formulations are combined with other pesticides, fungicides or insecticides and are frequently dissolved in petroleum distillates, vomiting involves a serious risk that solvent will be aspirated, leading to chemical pneumonitis. For these reasons, if the ingested malathion is dissolved in a petroleum-based carrier or a mixed formulation, do not induce vomiting. Contact physician or emergency medical facility immediately. If the ingested malathion is in an aqueous carrier, induce vomiting. Get medical attention immediately • Inhalation: Move victim to fresh air, give artificial respiration if necessary • Skin: Wash skin with soap and water. Remove contaminated clothing • Eye: Irrigate with large amounts of water.

ENVIRONMENTAL AND OCCUPATIONAL STANDARDS AND CRITERIA

AIR EXPOSURE LIMITS:

Standards
- OSHA PEL (8-hr TWA): 15 mg/m^3
- AFOSH PEL (8-hr TWA): 15 mg/m^3

Criteria
- NIOSH IDLH (30-min): 500 mg/m^3
- ACGIH TLV® (8-hr TWA): 10 mg/m^3 (skin)
- ACGIH STEL (15-min): none established

WATER EXPOSURE LIMITS:

Drinking Water Standards - None established

EPA Health Advisories - None established

EPA Ambient Water Quality Criteria (355)
- Human Health
  No criterion established; malathion is not a priority pollutant.
- Aquatic Life
  No criterion established; malathion is not a priority pollutant.

REGULATORY STATUS (as of January 1, 1987)

Promulgated Regulations

- Federal Programs

Clean Water Act (CWA)
Malathion is designated a hazardous substance. It has a reportable quantity (RQ) limit of 45.4 kg (347,985).

Comprehensive Environmental Response Compensation and Liability Act (CERCLA)
Malathion is designated a hazardous substance under CERCLA. It has a reportable quantity (RQ) limit of 45.4 kg. Reportable quantities have also been issued for RCRA hazardous waste streams containing malathion but these depend upon the concentrations of the chemicals in the waste stream (985).

Federal Insecticide, Fungicide and Rodenticide Act (FIFRA)
The combination of malathion in methyl eugenol is exempt from the requirement of a tolerance on all raw agricultural commodities when used in Oriental fruit fly eradication programs in accordance with the following specifications:

- One part technical malathion to three parts methyl eugenol;
- The combination must be impregnated on a carrier or mixed with a gel approved under 40CFR180.1001(d);
- The maximum actual dosage per application per acre shall be 28.35 g methyl eugenol and 9.45 g technical malathion (984).

Tolerances have been established for malathion residues in or on raw agricultural commodities. Levels range from 0.2 to 135 ppm (976).

Marine Protection Research and Sanctuaries Act (MPRSA)
Ocean dumping of organohalogen compounds as well as the dumping of known or suspected carcinogens, mutagens or teratogens is prohibited except when they are present as trace contaminants. Permit applicants are exempt from these regulations if they can demonstrate that such chemical constituents are non-toxic and non-bioaccumulative in the marine environment or are rapidly rendered harmless by physical, chemical or biological processes in the sea (309).

Occupational Safety and Health Act (OSHA)
Employee exposure to malathion shall not exceed an 8-hour time-weighted-average (TWA) of 15 mg/m^3 (298).

Hazardous Materials Transportation Act (HMTA)
The Department of Transportation has designated malathion as a hazardous material which is subject to requirements for packaging, labeling and transportation (306).

Food, Drug and Cosmetic Act (FDCA)
Malathion may be safely used in paper trays intended for use only in the drying of grapes. It may not exceed 100 mg per square foot. Total residues of malathion resulting from the drying of grapes on treated trays and from application to grapes before harvest shall not exceed 12 ppm on processed ready-to-eat raisins.

Residues of malathion in refined safflower oil from application to the growing safflower plant shall not exceed 0.6 ppm (886).

- State Water Programs
  California has an action level of 160 ppb (731).
  Florida has a criterion of 0.1 μg/L for malathion in the public water supply (731).
  Missouri has a ground water quality standard of 0.1 μg/L (981).
  New York has a ground water quality standard of 0.007 mg/L (981).

Proposed Regulations

- Federal Programs
  No proposed regulations are pending.

- State Water Programs
  No proposed regulations are pending.

EEC Directives

Directive on Drinking Water (533)
The mandatory values for total pesticides in surface water treatment categories A1, A2 and A3 used or intended for abstraction of drinking water are 0.001, 0.0025 and 0.005 mg/L, respectively. There are no guideline values.

Directive Relating to the Quality of Water for Human Consumption (540)
The maximum admissible concentration for malathion is 0.1 μg/L. The total maximum allowable concentration for pesticides and related products is 0.5 μg/L.

Directive on Ground Water (538)
Direct discharge into ground water (i.e., without percolation through the ground or subsoil) of organophosphorous compounds, organohalogen compounds and substances which may form such compounds in the aquatic environment, substances which possess carcinogenic, mutagenic or teratogenic properties in or via the aquatic environment and mineral oils and hydrocarbons is prohibited. Appropriate measures deemed necessary to prevent indirect discharge into ground water (i.e., via percolation through ground or subsoil) of these substances shall be taken by member countries.

Directive on Bathing Water Quality (534)
When inspection of a bathing area shows that heavy metals, pesticides or cyanides may be present, concentrations should be checked by competent authorities.

Directive on the Quality Required of Shellfish Waters (537)
The mandatory specifications for organohalogenated substances specify that the concentration of each substance in the shellfish water or in shellfish flesh must not reach or exceed a level which has harmful effects on the shellfish and larvae. The guideline specifications for organohalogenated substances state that the concentration of each substance in shellfish flesh must be so limited that it contributes to the high quality of shellfish product.

Directive on the Discharge of Dangerous Substances (535)
Organohalogens, organophosphates, petroleum hydrocarbons, carcinogens or substances which have a deleterious effect on the taste and/or odor of human food derived from aquatic environments cannot be discharged into inland surface waters, territorial waters or internal coastal waters without prior authorization from member countries which issue emission standards. A system of zero-emission applies to discharge of these substances into ground water.

Directive on Marketing and Use of Dangerous Substances (541)
Malathion may not be used in ornamental objects intended to produce light or color effects by means of different phases.

Directive on Classification, Packaging and Labeling of Pesticides (786)
Malathion containing more than 1.3% isomalathion is listed as a Class II/c substance and malathion containing less than 1.8% isomalathion is listed as a Class II/d substance. Both are subject to packaging and labeling regulations.

Directive on the Classification, Packaging and Labeling of Dangerous Substances (787)
Malathion is classified as a harmful substance and is subject to packaging and labeling regulations.

EEC Directives - Proposed

Proposal for a Council Directive on the Dumping of Waste at Sea (1793)
EEC has proposed that the dumping of pesticides at sea be forbidden without prior issue of a special permit.

50.1 MAJOR USES

Malathion, introduced in 1950, has a wide range of agricultural and horticultural uses, but is employed primarily as an insecticide and acaricide on fruits, vegetables and ornamental plants. It is also used to control animal ectoparasites, flies, lice and mosquitoes (1118, 1300). It is available in a variety of formulations, either alone, or combined with other insecticides or fungicides. Early samples were marketed as a technical-grade with a purity of 65-77%; with improved synthesis methods, the purity of malathion now exceeds 99% (17,1037).

50.2 ENVIRONMENTAL FATE AND EXPOSURE PATHWAYS

50.2.1 Transport in Soil/Ground-water Systems

50.2.1.1 Overview

Malathion is expected to be relatively immobile in the soil/-ground-water environment when present at low concentrations (dissolved in water). Bulk quantities of the liquid chemical (e.g., from a spill, heavy spray application or improper disposal of excess formulations) could be transported down through the unsaturated zone. However, most studies have shown that normal application of malathion sprays to soil surfaces do not result in transport of the chemical to any significant distance below the soil surface. Furthermore, malathion is readily susceptible to a number of degradation pathways (hydrolysis, photolysis, biodegradation) so that residuals from normal applications have fairly short half-lives (days to weeks) in the topsoil environment. The environmental persistence is strongly dependent upon temperature, soil pH, organic carbon content and microbiological activity, as well as other parameters. Under special conditions (e.g., no sunlight, low temperature, low soil pH, high soil organic carbon content), the half-life of malathion in the environment could be quite long (months to years). Such conditions, in combination with high infiltration rates, could allow ground water to be contaminated.

Environmental transport pathways for malathion can be generally assessed by using an equilibrium partitioning model as shown in Table 50-1. These calculations predict the partitioning of low soil concentrations of malathion among soil particles, soil water and soil air. The estimates for the unsaturated topsoil model show that while essentially all of the chemical (99.7%) is sorbed to the soil, a small amount (0.3%) is in solution and could be transported down with percolating waters. Negligible amounts of the chemical are predicted to be in the soil air and thus volatilization losses would be expected to be very small. In saturated, deep soils (containing no air and negligible soil organic carbon), the model predicts substantially more malathion (11.7%) to be in the mobile ground-water phase.

Many of the early studies on transport and fate of malathion in the soil/ground-water system are described in references 1374, 1203-1208 and 1216.

TABLE 50-1

EQUILIBRIUM PARTITIONING CALCULATIONS FOR MALATHION IN MODEL ENVIRONMENTS[a]

Soil Environment	Estimated Percent of Total Mass of Chemical in Each Compartment		
	Soil	Soil-Water	Soil-Air
Unsaturated topsoil at 25°C[b,c]	99.7	0.29	7.2×10^{-7}
Saturated deep soil[d]	88.3	11.7	-

a) Calculations based on Mackay's equilibrium partitioning model (34,35,36); see Introduction in Volume 1 for description of model and environmental conditions chosen to represent an unsaturated topsoil and saturated deep soil. Calculated percentages should be considered as rough estimates and used only for general guidance.

b) Utilized estimated soil sorption coefficient: K_{oc} = 1800 (1211).

c) Henry's law constant taken as 2.0×10^{-8} atm•m³/mol at 25°C (1216).

d) Used sorption coefficient $K_p = 0.001\ K_{oc}$.

50.2.1.2 Sorption on Soils

There appear to be relatively few studies focusing on the soil sorption properties of malathion. In part, this is because studies have shown malathion to be readily degraded and thus not problematic with regard to its soil leaching potential.

Values of the equilibrium soil sorption constant, K_{oc}, for malathion have been reported as 2300 (1209), 930 (1210) and 1797 (1211); the value, 1797, is an average of measurements for 2 soils and has a coefficient of variation of 66%. These values indicate that sorption of malathion on topsoils (containing > 0.1% organic carbon) is of moderate strength; i.e., most of the chemical will be sorbed to the soil, but not so strongly that leaching is prevented. As with all neutral organic chemicals, the extent of soil sorption is directly proportional to the soil organic carbon content. For low organic carbon soils (e.g., clays), the extent of sorption may also depend on

other properties of the soil such as surface area, cation exchange capacity and degree of hydration (1374). Under certain conditions, malathion can be sorbed into the interlayer spaces of montmorillonite clays (1374,1212).

Malathion sorption to four soils has been shown to decrease slightly with increasing temperature over the range of 15°C to 40°C (1213). For example, the Freundlich sorption constant, K, for malathion decreased 18% (average of 4 soils) when the temperature was raised from 15°C to 30°C (1213). By contrast, malathion sorption to natural and synthetic humic acids has been shown to increase slightly with increasing temperature, possibly due to an increase in the number of sorption sites on the humic acids at the higher temperatures (1214).

Other laboratory, field and modeling studies on the downward movement of soil-applied malathion tend to support the conclusion that sorption is strong enough (in conjunction with easy degradation) to prevent contamination of ground-water aquifers (1374,1215,1216). However, Bomberger et al. (1209) conclude from modeling studies - which modeled transport but not degradation - that "malathion is not strongly adsorbed and could leach deeply into the soil." In one calculation, assuming application of 305 cm rain water to a typical soil with a field capacity of 30%, they estimated the depth of maximum concentration of malathion to be 102 cm.

50.2.1.3 Volatilization from Soils

Malathion has a low vapor pressure (6.6×10^{-6} mm Hg at 20°C (1219)) and a low Henry's law constant (2.0×10^{-8} atm-m³/mol at 20°C (1216)). These values, coupled with malathion's moderate extent of soil and sediment sorption, imply that volatilization from soils (or surface waters) should not be an important transport pathway. The relative insignificance of volatilization has been demonstrated in a variety of laboratory or field tests (1216,1217,1218) and modeling studies (1209). Volatilization losses in these studies were typically less than one percent of the malathion present. Volatilization losses from the surfaces of foliage or structures (e.g., after spray applications) could be substantially larger.

50.2.2 Transformation Processes in Soil/Ground-water Systems

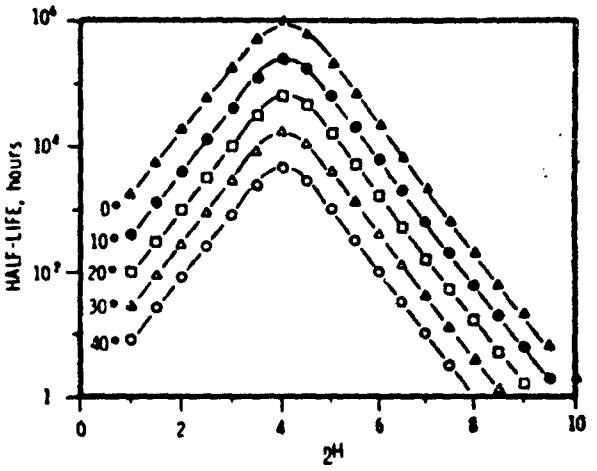
Malathion is susceptible to a number of degradation processes - including hydrolysis, biodegradation and photolysis - and is not considered to be persistent in the environment.

Evidence for the photolytic degradation of malathion (in surface waters or surfaces exposed to the light) has been reported (1204,1205,-1220,1222). Wolfe et al. (1205) concluded that the photolysis of malathion by sunlight is too slow to compete with chemical degradation in pure water. However, some naturally occurring substances in surface waters appear to catalyze the photolysis, and photolytic half-lives as

low as 16 hours (in Sawanee River water) have been estimated (1204,-1222). The photolytic half-life for malathion on glass plates exposed to artificial sunlight has been measured as 51 hours (1220).

Data on the importance of hydrolysis in the environmental degradation of malathion are provided in references 1374, 1203-1205, 1207, 1216-1218, 1221 and 1222. The 1976 review by [illegible] et al. (1205) concluded that hydrolysis of malathion was likely to be the major pathway for its transformation in basic natural waters (pH greater than 7). The hydrolysis products are a mixture of malathion acids, fumaric acid and its ethyl esters, and O,O-diethylphosphorodithioic acid (1205). The rate of hydrolysis, and subsequent environmental half-life, is strongly dependent on both pH and temperature as shown in Figure 50-1. The hydrolysis half-life at 20°C and pH 7, for example (from Figure 50-1), is seen to be about 200 hours (8.3 days). Chapman and Cole (1207) summarize hydrolysis half-life measurements from several investigations, including their own, as shown in Table 50-2.

Chapman and Cole (1207) conducted further experiments to see if the pH dependence of the hydrolysis of malathion observed in aqueous solution could also be observed in heterogeneous, mostly solid systems with low microbial activity. Using malathion concentrations of 1 and



Source: Wolf et al. (1221)

FIGURE 50-1

TEMPERATURE AND pH EFFECTS ON MALATHION DEGRADATION

TABLE 30-2

HYDROLYSIS HALF-LIVES FOR MALATHION IN AQUEOUS SOLUTIONS AT TEMPERATURES NEAR 20°C

pH	No. of Data Points	Hydrolysis Half-Life (weeks) Mean	Range
6	6	7.8	1 - 21
7	5	3.0	1 - 7
8	5	0.8	0.5 - 1.0

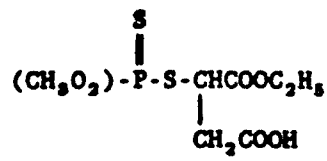
Source: Chapman and Cole (1207).

20 ppm on three types of alumina (acid, neutral, basic) containing 15% water, they found that the chemical was poorly recovered and/or rapidly degraded on these solids irrespective of pH. Subsequent tests were conducted with natural soils at different pH values. Malathion was again rapidly degraded although the results showed some anomalous pH dependence which suggested that other processes in addition to chemical degradation were involved.

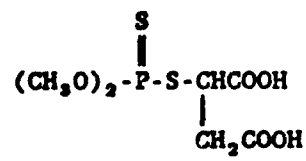
Chapman and Harris (1221) have shown that the hydrolysis of malathion is catalyzed by the cupric, Cu(II), ion over a range of pH values. They cite other studies indicating that the hydrolysis of organophosphorus compounds can be catalyzed by other types of chemicals including nitrogenous organic bases, metal ions (type unspecified) and metal chelates.

Studies on the biodegradation of malathion are reviewed in a number of reports (1374,1203,1206,1211,1216). The general conclusion is that under normal conditions, malathion is readily biodegradable and that biodegradation probably competes with hydrolysis as the most important environmental degradation pathway. Rao and Davidson (1211), using a variety of reported data from laboratory tests simulating aerobic conditions, estimate a mean biodegradation half-life of 0.8 days (87% coefficient of variation).

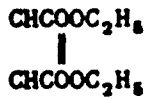
Malathion has been shown to be degradable by a variety of bacteria and fungi, and can be the sole source of carbon and/or phosphorus for some species (1374,1223,1224,1225). The major metabolite produced from bacterial action is β-malathion monoacid (I). Small amounts of malathion dicarboxylic acid (II), diethyl maleate (III), and O,O-dimethyl phosphorodithioic acid (IV) are also produced.



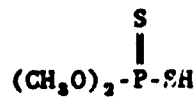
I



II



III



IV

Paris et al. (1226), using microorganisms from 14 natural surface waters, showed that malathion biodegradation can be described with a second order rate equation:

$$-\frac{d[S]}{dt} = k\,[B]\,[S]$$

where k is a second-order rate constant (with units of liters per organism per hour), [B] is the concentration of bacteria (organisms/-liter), [S] is the concentration of malathion (mg/L), and t is time (hr). The mean value of k for malathion was $(4.4 \pm 2.9) \times 10^{-11}$ liters per organism per hour; this is for the 14 surface waters whose average temperature was 21°C.

50.2.3 Primary Routes of Exposure from Soil/Ground-water Systems

The above discussion of fate pathways suggests that malathion is effectively nonvolatile, is moderately to strongly sorbed to soil, and has a low potential for bioaccumulation. These fate characteristics suggest several potential exposure pathways.

Volatilization of malathion from a disposal site is not likely to represent an important exposure pathway. There is some potential for drinking water contamination through the movement of this compound with ground water, particularly in sandy soils. This compound was not reported in Mitre's compilation (83) of compounds detected at the 546 National Priority List (NPL) sites. This may be partially due to the adsorption of malathion to soil, but is probably also due to its susceptibility to degradation.

Discharges of malathion to surface waters from soil/ground-water systems would probably not represent a significant source of exposure due to malathion's low potential for bioaccumulation and to degradability.

50.2.4 Other Sources of Human Exposure

Malathion has been registered for use as an insecticide for over 30 years. As a result of its wide use, there are a number of sources of exposure to malathion.

Malathion was detected in 30% of 123 air samples at 19 U.S. locations. The maximum concentration was 220 ng/m³ and the mean concentration was 7.3 ng/m³ (1242). These data suggest that inhalation may represent a source of exposure.

NRC (2113) reported that malathion had not been detected in drinking water at that time. In addition, Carey and Kutz (1247) reported finding malathion in 0.1% of the samples in the National Surface Water Monitoring Program from 1976-1980 with a maximum value of 0.18 µg/L. Malathion was not detected in the sediment in this monitoring program.

Malathion is commonly found in foods. It is included in the U.S. Food and Drug Total Diet Study to determine dietary intake. Over the years 1976-1978, the average dietary intake for adults ranged from 0.128-0.154 µg/kg body weight/day. In 1979, the average daily intake was 0.265 µg/kg/day. Average daily intakes for infants and toddlers over the same time period ranged from 0.044-0.259 µg/kg/day (1244,1249). In Canada, the average daily intake over the years 1976-1978 was 0.012 µg/kg/day (1244). The largest source of exposure appeared to be grain and cereal products, and oils and fats.

50.3 HUMAN HEALTH CONSIDERATIONS

Malathion is available in a variety of different formulations, including a number of formulations that contain malathion in combination with other insecticides and/or fungicides. The toxicity of commercial malathion formulations, therefore, is greatly dependent on ingredients; the content of impurities, particularly isomalathion which potentiates the toxicity of malathion; and the presence of toxic degradation products such as maloxon that may form during storage (1098,1374). Early samples of malathion were marketed as technical-grade, with a purity of 65-77%, the purity of currently produced malathion exceeds 99% (17,1037).

50.3.1 Animal Studies

50.3.1.1 Carcinogenicity

No evidence of carcinogenicity was found in mice and rats administered malathion (purity 95%) in the diet in either of two studies

carried out by the NCI. The initial study, done in 1978, was conducted in Osborne-Mendel rats and B6C3F1 mice. Mice were given doses of 8000 or 16,000 ppm and rats received 4700 or 8150 ppm over an 80 week period. The animals were observed for an additional period of 14 to 33 weeks. A significant increase in hepatocellular carcinoma in male mice was noted, but it was comparable to the historical incidence in the laboratory and not considered to be associated with malathion administration. There was no evidence of carcinogenicity in male or female Osborne-Mendel rats (1354).

In the second study, F344 rats were fed diets containing 2000 or 4000 ppm for 103 weeks and observed for an additional 2-3 weeks. No tumors were found in either sex that could be related to malathion administration; the females may not have received the maximum tolerated dose (1355). A recent NTP re-evaluation of the histopathology of these malathion studies found no substantive reason to warrant altering the original conclusion that malathion was not carcinogenic (1356). Reuber (1357) has published a dissenting view; he believes malathion to be carcinogenic in both rat species.

50.3.1.2 Mutagenicity

There is limited evidence for the mutagenicity of malathion. Negative results have been obtained in several strains of Salmonella typhimurium in the reverse mutation assay either in the presence or absence of rat liver microsomal activation (1358,1361,1363); however, a positive result with metabolic activation was reported in strain TA100 (1360). Weak mutagenic activity was also detected in a reverse mutation assay using B. subtilis TKJ6321 (1361).

Malathion (99%) caused an increase in sister chromatid exchange in human fetal lung fibroblasts after a single exposure to 40 μg/mL or two exposures to 20 μg/mL (1364). Similar results were obtained in Chinese hamster ovary cells exposed to 0.3 to 1 mM of 99% malathion and in Chinese hamster V79 cells exposed to concentrations up to 40 μg/mL of 94% malathion (1365,1366). In contrast, Degraeve et al. (1367) observed no dominant lethals and no chromosome damage in bone marrow cells, spermatogonia, and primary spermatocytes of Q strain mice receiving 8 ppm malathion in drinking water 5 days per week for 7 weeks. Negative mutagenic effects were also observed in a sex-linked recessive lethal mutation test in Drosophila melanogaster fed solutions containing 0.25 or 0.5 mg/L malathion (1362) and no dominant lethality was observed in mice fed 1200, 2500 or 5000 mg/kg diet for 7 weeks (1363).

50.3.1.3 Teratogenicity, Embryotoxicity and Reproductive Effects

No evidence of teratogenicity or embryotoxicity has been found in rats given maternally tolerated doses of malathion during pregnancy (1359). The effect of single intraperitoneal dose on rat fetuses was evaluated by Kimbrough and Gaines (1159) who injected dams with 600 or 900 mg/kg on the 11th day of pregnancy. The fetuses were removed after the 20th day. No adverse effects were seen.

No teratogenic effects were noted in the offspring of male and female rats fed dietary concentrations of 4000 mg/kg (approximately 240 mg/kg bw/day) for 2 generations. However, the survival of the progeny on days 7 and 21 after birth was found to be reduced with the survivors showing growth retardation (1369). No teratogenic or embryotoxic effects were observed in Wistar rats given doses of 50 to 300 mg/kg by gavage on days 6 through 15 of gestation (1370).

50.3.1.4 Other Toxicologic Effects

50.3.1.4.1 Short-term Toxicity

The acute toxicity and LD_{50} values of malathion depend upon the purity of the compound tested (1359). The oral LD_{50} values of 65% malathion in male mice and male rats were 1260 and 369 mg/kg, respectively, and those of 99% malathion were 4059 and 5843 mg/kg, respectively (1359). The oral LD_{50} value of 99.7% pure malathion in male rats was approximately 10,000 mg/kg, while malaoxon, the active metabolite, has an oral LD_{50} value of 23-158 mg/kg for the rat (1098). Sex differences in susceptibility to the effects of malathion are generally confined to rodents given malathion orally, with males found to be less sensitive to malathion than females. This difference has been attributed to differences in the rates of detoxification (1300).

The toxic effects of malathion in both animals and humans is due to inhibition of acetylcholinesterase, leading to an accumulation of endogenous acetylcholine (1359). Signs of malathion poisoning in both animals and men include headache, dizziness, weakness, tremor, nausea, abdominal cramps, diarrhea, and sweating. Blurred vision, chest tightness, wheezing cough, pulmonary edema, tearing, salivation, slow heart beat and toxic psychosis are common. In severe cases convulsions and unconsciousness may occur (1373).

In dogs, an intravenous dose of 100 mg/kg had no apparent effect, while 200 mg/kg produced signs of cholinesterase inhibition and 250 mg/kg was lethal (1371). A single oral dose of 300 mg/kg caused approximately the same inhibition of acetylcholinesterase as about 15-20 mg/kg inhaled by rabbits exposed to an aerosol containing 123 mg/m^3 for 6 hours (1372). Rats, mice and guinea pigs exposed to vapor concentrations up to 67 mg/m^3, 8 hours per day, 5 days per week for 4 weeks experienced no significant cholinesterase depression or any other toxic effects (1371).

Animal experiments indicate that dermal application of malathion can cause cholinergic effects and death. Single applications of 2460 to 6150 mg/kg (90% purity) produced some toxicity in rabbits (12). Dermal LD_{50} values in rats have been reported to be greater than 4400 mg/kg (1368).

Undiluted malathion dropped on a rabbit's eye caused slight immediate irritation with conjunctival hyperemia and edema of the lids, but the eye returned to normal within 24 hours (19).

50.3.1.4.2 Chronic Toxicity

Long-term oral toxicity studies of malathion have been conducted in rats for periods of up to 2 years. No signs of intoxication were observed in rats fed diets containing 4000 ppm for 5 months or 1000 ppm for 6 months (1369,1375). Exposure of rats to diets containing 500-20,000 ppm for two years caused significant depression of cholinesterase activity in red cells at all exposure levels with food intake and growth decreased at the 20,000 ppm level (1376). Hepatocyte degeneration as well as prolongation of the prothrombin time and partial thromboplastin time were seen in female Sprague-Dawley rats that received 1 ppm malathion in drinking water for 6 months (1113).

Intraperitoneal injection of malathion in rats for 60 days resulted in a no adverse effect level of 100 mg/kg while dosages of 200 and 300 mg/kg resulted in mortality rates of 60 and 100%, respectively (1377).

50.3.2 Human and Epidemiologic Studies

50.3.2.1 Short-term Toxicologic Effects

Malathion has a relatively low order of toxicity in comparison with other organophosphates (46). The apparent reason for this is the rapid detoxification of both malathion and malaoxon, a metabolite of malathion, by esterases in the liver and other organs. Malathion has only a slight inhibitory action on cholinesterase but malaoxon is an active inhibitor and therefore more toxic (46). Early reports of malathion toxicity described more severe toxic effects due to the presence of malaoxon and other impurities. The purity of the malathion currently used (99%) has resulted in a corresponding decrease in observed acute toxicity (17). The human oral lethal dose is estimated to range from 0.4-1 g/kg (1300).

Manifestations of acute poisoning in humans are similar to those in animals. The first symptoms to appear after inhalation are respiratory and ocular. These include tightness in the chest, wheezing, pinpoint pupils and blurred vision. Gastrointestinal effects, such as nausea, vomiting and diarrhea appear 15 minutes to 2 hours after ingestion while symptoms such as localized sweating will appear 15 minutes to 4 hours after percutaneous exposure (1378). There is a single anecdotal report of an association between a brief inhalation exposure to malathion and subsequent development of aplastic anemia (1379).

Almost all reports of fatalities from malathion have resulted from ingestion. The principal cause of death is respiratory failure (1380). Harris et al. (1381) described the case of a 45-year-old woman who ingested an unknown amount of malathion. Six hours later she was admitted to a hospital, unconscious, and in total cardiac and respiratory arrest. Seizures developed about 8 hours after admission. Hyperglycemia and moderate bradycardia were also noted. Two days after

admission, the woman showed slight voluntary movement and responded to external stimuli. However, ventricular fibrillation occurred 4 hours later. Cholinesterase activity was absent from both red cells and plasma. The woman died 5.5 days after ingestion. Autopsy revealed generalized edema, severe pulmonary edema and bronchopneumonia which were probably indirect effects of shock and respiratory failure. Ingestion of 0.5 mg/kg has resulted in cyanosis, incontinence, miosis, hypotension and respiratory distress (1382,1383), however, ingestion of 8 ounces has been survived (1393).

Intramuscular injection of 3 mL resulted in hypotonia of the limbs, excessive sweating, and convulsions with the individual recovering in 2 weeks (1385).

In a group of workers with an average exposure of 3.3 mg/m^3 for 5 hours (maximum of 56 mg/m^3), the cholinesterase levels in the blood were not significantly lowered and none exhibited signs of cholinesterase inhibition (46).

A 10% malathion solution applied to the skin as a dressing and retained in contact with the skin for 2 days produced sensitization. Solutions of 0.1 and 1.0% had no effect (1386). Application of 1.1% malathion dust for 8 hours daily for 3 weeks produced no significant depression of red cell cholinesterase (1387).

50.3.2.2 Chronic Toxicologic Effects

Long-term studies of malathion have been conducted in human volunteers by both the oral and inhalation routes. Golz (1388) exposed 12 men to a total of 84 one-hour exposures to malathion aerosol for 42 consecutive days. Initial concentrations were calculated to be 5.3, 21.2 or 84.8 mg/m^3. No cholinergic signs or symptoms were observed, however, there was moderate irritation of the nose and conjunctiva.

Moeller and Rider (1389) fed 10 men daily doses of malathion dissolved in corn oil to determine the amount that could be ingested over an extended time period without causing depression of cholinesterase activity. Five subjects each received 16 mg/day for 47 days and 5 others received 24 mg/day for 56 days. The observed decrease in cholinesterase activity reached a maximum 3 weeks after malathion was discontinued. Erythrocyte cholinesterase levels returned to baseline within 10 days and plasma cholinesterase leveled off at 93% of baseline within the same time period.

Hayes et al. (1390) found no decrease in blood cholinesterase following the dermal application of 28 g of 1.5% or 10% malathion dust 5 times weekly for 8-16 weeks. During the course of the experiment, burning and dermatitis were the only complaints noted. This study suggests that up to 2.5 g malathion/day can be safely applied to the skin. This is equal to an absorbed dose of 40 mg/kg for a 70 kg man.

Although depressive and schizophrenic behavior have been linked to exposure to organophosphate insecticides, including malathion (1391), no causal relationship has been established (1392).

50.3.3 Levels of Concern

The NAS (213) calculated a no-adverse-effect level for malathion in drinking water of 0.14 mg/L. An acceptable daily intake of 0.02 mg/kg body weight has also been established by the WHO for malathion (1668).

The NTP (1356) classifies malathion as presenting no evidence of carcinogenic activity in animals. IARC (1359) list malathion as a category 3 carcinogen (i.e., insufficient evidence).

OSHA (298) has set an 8-hour time-weighted-average of 15 mg/m^3 for this compound. The ACGIH (3) recommends a threshold limit value of 10 mg/m^3 for malathion.

50.3.4 Hazard Assessment

Malathion is an organophosphorus insecticide whose mode of action is the inhibition of cholinesterase enzymes. It is generally considered to be one of the least toxic to humans among this class of compounds. The major signs and symptoms of malathion intoxication include headaches, dizziness, weakness, tremors, sweating, blurred vision, chest tightness, diarrhea, salivation and lacrimation (1373).

Chronic toxicity information on this compound is surprisingly sparse. A two year study with rats indicated about 500 ppm malathion in the diet significantly decreased red-cell cholinesterase activity; reductions in growth and food intake were observed at 20,000 ppm (1376).

Two carcinogenicity studies conducted with both rats and mice were found to provide no evidence of carcinogenic activity (1354,1355). Tests in bacteria and with mammalian and human cells in culture provide limited evidence of mutagenic activity for malathion (1360,1361,1364-1366). However, other studies noted no activity with malathion in a mouse dominant lethal test or in mouse spermatogonia and marrow cells in vivo (1363,1367).

There is no evidence to suggest embryotoxic or teratogenic effects for malathion in studies conducted with rats (1159,1370) and no significant effects on reproduction were noted in a two-generation rat study (1369).

Studies with human volunteers indicate that ingestion of up to 16 mg of malathion daily for 47 days had no significant effect (1389). Available data suggest that relatively large quantities of malathion must be ingested for lethality. The human oral lethal dose is estimated to range from 400 to 1000 mg/kg (1300).

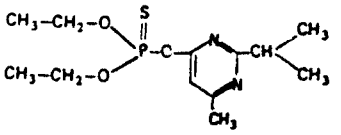
50.4 SAMPLING AND ANALYSIS CONSIDERATIONS

Determination of malathion concentrations in soil and water requires collection of a representative field sample and laboratory analysis. Care is required to prevent losses during sample collection and storage. Soil and water samples are collected in glass containers; extraction of samples should be completed within 7 days of sampling and analysis completed within 30-40 days. In addition to the targeted samples, quality control samples such as field blanks, duplicates, and spiked sample matrices may be specified.

EPA Method 8140 (63) is an approved procedure for the analysis of malathion in aqueous samples. Prior to analysis, samples are extracted at neutral pH with methylene chloride as the solvent using a separatory funnel or a continuous liquid-liquid extractor. An aliquot of the concentrated sample extract is injected onto a gas chromatographic (GC) column using a solvent flush technique. The GC column is programmed to separate the semi-volatile organics; malathion is then detected with either a nitrogen/phosphorus (N/P) detector operated in the phosphorus-sensitive mode or a flame photometric detector (FPD). The FPD is more selective for phosphorus than the N/P.

The same method is recommended for malathion analysis in soil and waste samples. The procedure for solid samples differs from the aqueous procedure primarily in the preparation of the sample extract. Solid samples are extracted using either soxhlet extraction or sonication methods. Neat and diluted organic liquids may be analyzed by direct injection.

A detection limit for malathion using this method was not determined but would be in the range of 0.1-1.5 $\mu g/L$ for aqueous samples, 1-10 $\mu g/g$ for non-aqueous samples which have been extracted and part-per-million (ppm) range for samples which have been directly injected.

COMMON SYNONYMS:	CAS REG. NO.:	FORMULA:	AIR W/V CONVERSION FACTORS at 25°C
O,O-Diethyl-O-(6-methyl-2-(1-methylethyl)-4-pyrimidinyl) phosphorothioate Diazide Dimpylate	333-41-5 NIOSH NO.: TF3325000	$C_{12}H_{21}N_2O_3PS$	12.44 mg/m³ ≈ 1 ppm 0.08 ppm ≈ 1 mg/m³
	STRUCTURE: 		MOLECULAR WEIGHT: 304.36

REACTIVITY	For compatibility classification purposes, Diazinon® is considered to be in the reactivity group of organophosphates, phosphothioates and phosphodithioates. Such substances typically generate heat in reactions with alkali or alkaline earth metals; heat and toxic gases in reactions with mineral acids; and heat and possible explosions with caustics. Additionally reported are unknown but possibly hazardous reactions with azo or diazo compounds, hydrazines or organic peroxides or hydroperoxides. A maker reports that temperature above 53°C and strong alkaline materials should be avoided. Also noted is that the compound decomposes gradually in alkaline media to carbon dioxide, carbon monoxide, monothionotepp and diazoxon (507,511).

PHYSICO-CHEMICAL DATA	• Physical State (at 20°C): liquid	(12)
	• Color: colorless	(12)
	• Odor: faint ester-like odor	(51)
	• Odor Threshold: no data	( )
	• Liquid Density (g/ml at 20°C): 1.116	(51)
	• Freezing/Melting Point (°C): not pertinent	( )
	• Boiling Point (°C): 84	(51)
	• Flash Point (°C): practically nonflammable; difficult to burn when pure	(13,60)
	• Flammable Limits in Air, % by Volume: not pertinent	(60)
	• Autoignition Temperature (°C): not pertinent	(60)
	• Vapor Pressure (mm Hg at 20°C): 1.4×10^{-4}	(2)
	• Saturated Concentration in Air (mg/m³ at 20°C): 2.3	(ADL estim)
	• Solubility in Water (mg/L at 20°C): 40	(1118)
	• Viscosity (cp at 20°C): 3.201	(60)
	• Surface Tension (dyne/cm at 20°C): 35 (est)	(60)
	• Log (Octanol-Water Partition Coefficient), log K_{ow}: 3.81	(1488)
	• Soil Adsorption Coefficient, K_{oc}: 440	(1489)
	• Henry's Law Constant (atm·m³/mol at 20°C): 8.2×10^{-7}	(964)
	• Bioconcentration Factor: 310 (est)	(37)

PERSISTENCE IN THE SOIL-WATER SYSTEM	Fairly immobile and non-persistent in soil water systems due to moderate sorption and moderate rate of degradation by hydrolysis and biodegradation. Typical half-life after soil application is 1-2 months. Photolytic degradation important for surface waters and soil surfaces.

PATHWAYS OF EXPOSURE	The primary pathway of concern from soil/ground-water systems is the migration of Diazinon® to ground water drinking water supplies. However, its potential for adsorption and degradation make the contamination of water supplies with Diazinon® less likely than other chemicals. Exposures through inhalation or bioaccumulation are not generally expected to be significant.

HEALTH HAZARD DATA	Signs and Symptoms of Short-term Human Exposure (2,45): Diazinon® is a cholinesterase inhibitor. Symptoms of exposure include weakness, headache, tightness in chest, blurred vision, non-reactive pinpoint pupils, salivation, sweating, nausea, vomiting, diarrhea, abdominal cramps and slurred speech. Convulsions and coma may also occur if poisoning is severe.
	Toxicity Based on Animal Studies: LD_{50} (mg/kg) oral 85 [mouse] (59) skin 2750 [mouse] (59) LC_{50} (mg/m^3) inhalation [mouse] (59) 1600•4 hr
	Long-Term Effects: Headache, mental confusion, insomnia muscular twitching
	Pregnancy/Neonate Data: Negative
	Mutation Data: Negative
	Carcinogenicity: Negative

HANDLING PRECAUTIONS (507)	Adequate ventilation • At 50 ppm: chemical cartridge respirator with organic vapor cartridge and full facepiece • Chemical goggles if there is probability of eye contact • Rubber, vinyl or nitrile gloves and protective clothing.

EMERGENCY FIRST AID TREATMENT (45)	Ingestion: Because many pesticide formulations are combined with other pesticides, fungicides or insecticides and are frequently dissolved in petroleum distillates, vomiting involves a serious risk that solvent will be aspirated, leading to chemical pneumonitis. For these reasons, if the ingested diazinon is dissolved in a petroleum-based carrier or a mixed formulation, do not induce vomiting. Contact physician or emergency medical facility immediately. If the ingested diazinon is in an aqueous carrier, induce vomiting. Get medical attention immediately • Inhalation: Move victim to fresh air. Perform artificial respiration if necessary. Get medical attention • Skin: Remove contaminated clothing and wash contaminated areas with soap and water. Get medical attention if symptoms develop • Eye: Irrigate eyes with water for at least 15 minutes. Get medical attention.

ENVIRONMENTAL AND OCCUPATIONAL STANDARDS AND CRITERIA

AIR EXPOSURE LIMITS:

Standards
- OSHA PEL (8-hr TWA): none established
- AFOSH PEL (8-hr TWA): none established

Criteria
- NIOSH IDLH (30-min): none established
- ACGIH TLV® (8-hr TWA): 0.1 mg/m^3 (skin)
- ACGIH STEL (15-min): deleted

WATER EXPOSURE LIMITS:

Drinking Water Standards - None established

EPA Health Advisories - None established

EPA Ambient Water Quality Criteria (355)
- Human Health
  No criterion established; Diazinon® is not a priority pollutant.
- Aquatic Life
  No criterion established; Diazinon® is not a priority pollutant.

REGULATORY STATUS (as of January 1, 1987)

Promulgated Regulations

- Federal Programs

  Clean Water Act (CWA)
  Diazinon® is designated a hazardous substance. It has a reportable quantity (RQ) limit of 0.454 kg (347,985).

  Comprehensive Environmental Response Compensation and Liability Act (CERCLA)
  Diazinon® is designated a hazardous substance under CERCLA. It has a reportable quantity (RQ) limit of 0.454 kg. Reportable quantities have also been issued for RCRA hazardous waste streams containing Diazinon® but these depend upon the concentrations of the chemicals in the waste stream (985).

  Federal Insecticide, Fungicide and Rodenticide Act (FIFRA)
  EPA is canceling registrations and denying applications for Diazinon® use on golf courses and sod farms (1336).

  Marine Protection Research and Sanctuaries Act (MPRSA)
  Ocean dumping of organohalogen compounds as well as the dumping of known or suspected carcinogens, mutagens or teratogens is prohibited except when they are present as trace contaminants. Permit applicants are exempt from these regulations if they can demonstrate that such chemical constituents are non-toxic and non-bioaccumulative in the marine environment or are rapidly rendered harmless by physical, chemical or biological processes in the sea (309).

  Hazardous Materials Transportation Act (HMTA)
  The Department of Transportation has designated Diazinon® as a hazardous material which is subject to requirements for packaging, labeling and transportation (306).

- State Water Programs

  California has an action level of 14 ppb (731).
  New York has a ground water quality standard of 0.0007 mg/L (981).

Proposed Regulations

- Federal Programs

  No proposed regulations are pending.

- State Water Programs

  No proposed regulations are pending.

EEC Directives

Directive on Drinking Water (533)
The mandatory values for total pesticides in surface water treatment categories A1, A2 and A3 used or intended for abstraction of drinking water are 0.001, 0.0025 and 0.005 mg/L, respectively. There are no guideline values.

Directive Relating to the Quality of Water for Human Consumption (540)
The maximum admissible concentration for Diazinon® is 0.1 µg/L. The total maximum allowable concentration for pesticides and related products is 0.5 µg/L.

Directive on Ground Water (538)
Direct discharge into ground water (i.e., without percolation through the ground or subsoil) of organophosphorous compounds, organohalogen compounds and substances which may form such compounds in the aquatic environment, substances which possess carcinogenic, mutagenic or teratogenic properties in or via the aquatic environment and mineral oils and hydrocarbons is prohibited. Appropriate measures deemed necessary to prevent indirect discharge into ground water (i.e., via percolation through ground or subsoil) of these substances shall be taken by member countries.

Directive on Bathing Water Quality (534)
When inspection of a bathing area shows that heavy metals, pesticides or cyanides may be present, concentrations should be checked by competent authorities.

Directive on the Quality Required of Shellfish Waters (537)
The mandatory specifications for organohalogenated substances specify that the concentration of each substance in the shellfish water or in shellfish flesh must not reach or exceed a level which has harmful effects on the shellfish and larvae. The guideline specifications for organohalogenated substances state that the concentration of each substance in shellfish flesh must be so limited that it contributes to the high quality of shellfish product.

Directive on the Discharge of Dangerous Substances (535)
Organohalogens, organophosphorous, petroleum hydrocarbons, carcinogens or substances which have a deleterious effect on the taste and/or odor of human food derived from aquatic environments cannot be discharged into inland surface waters, territorial waters or internal coastal waters without prior authorization from member countries which issue emission standards. A system of zero-emission applies to discharge of these substances into ground water.

Directive on Marketing and Use of Dangerous Substances (541)
Diazinon® may not be used in ornamental objects intended to produce light or color effects by means of different phases.

Directive on Classification, Packaging and Labeling of Pesticides (786)
Diazinon® is listed as a Class II/a substance and is subject to packaging and labeling regulations.

Directive on the Classification, Packaging and Labeling of Dangerous Substances (787)
Diazinon® is classified as a toxic substance and is subject to packaging and labeling regulations.

EEC Directives - Proposed

Proposal for a Council Directive on the Dumping of Waste at Sea (1793)
EEC has proposed that the dumping of pesticides at sea be forbidden without prior issue of a special permit.

51.1 MAJOR USES

Diazinon® is a popular insecticide among homeowners for its use in garden and lawn care. It is also widely used on fruits and vegetables and on forage and field crops. Diazinon® is used by professional exterminators to control cockroaches, silverfish, flies and fleas. It is also effective in the control of ticks and fleas on domestic animals and in the control of face fly larvae in livestock manure (54,59).

51.2 ENVIRONMENTAL FATE AND EXPOSURE PATHWAYS

51.2.1 Transport in the Soil/Ground-water Systems

51.2.1.1 Overview

Diazinon® is expected to be relatively immobile in the soil/ground water environment when present at low concentrations (dissolved in water). Bulk quantities of the liquid chemical (e.g., from a spill, heavy spray application, or improper disposal of excess formulations) could be transported down through the unsaturated zone. However, most studies have shown that normal application of Diazinon® sprays to soil surfaces do not result in transport of the chemical to any significant distance below the soil surface. Furthermore, as described later in this section, Diazinon® is readily susceptible to a number of degradation pathways (hydrolysis, photolysis, biodegradation) so that residuals from normal applications have fairly short half-lives (2-10 weeks) in the topsoil environment. The environmental persistence is strongly dependent upon temperature, soil pH, organic carbon content and microbiological activity, as well as other parameters. Under special conditions (e.g., no sunlight, low temperature, neutral soil pH, high soil organic carbon content), the half-life of Diazinon® in the environment could be quite long (months to years). Such conditions, in combination with high infiltration rates, could allow ground waters to be contaminated.

Diazinon® can act as a weak base, with protonation probably occurring first on the nitrogen in the '3' position (i.e., ortho to the ring methyl group). The value for pK_a(1) is estimated to be 2.4 (1219) indicating that 50% of the chemical would be protonated at pH = 2.4, and 9% would be protonated at pH = 3.4, etc. The increased protonation at these low pH values would tend to significantly increase the chemical's solubility and mobility in the soil/ground-water system.

Environmental transport pathways for Diazinon® can be generally assessed by using an equilibrium partitioning model as shown in Table 51-1. These calculations predict the partitioning of low soil concentrations of Diazinon® among soil particles, soil water and soil air. The estimates for the unsaturated topsoil model show that while essentially all of the chemical (98.8%) is sorbed to the soil, a small amount (1.2%) is in solution and could be transported down with percolating waters. Negligible amounts of the chemical are predicted to be

TABLE 51-1

EQUILIBRIUM PARTITIONING CALCULATIONS FOR DIAZINON® IN MODEL ENVIRONMENTS[a]

Soil Environment	Estimated Percent of Total Mass of Chemical in Each Compartment		
	Soil	Soil-Water	Soil-Air
Unsaturated topsoil at 20°C[b,c]	98.8	1.2	1.2×10^{-6}
Saturated deep soil[d]	6535	-	-

a) Calculations based on Mackay's equilibrium partitioning model (34,35,36); see Introduction in Volume 1 for description of model and environmental conditions chosen to represent an unsaturated topsoil and saturated deep soil. Calculated percentages should be considered as rough estimates and used only for general guidance.

b) Utilized estimated soil sorption coefficient: $K_{oc} = 440$.

c) Henry's law constant taken as 8.2×10^{-7} atm·m³/mol at 20°C (964).

d) Used sorption coefficient $K_p = 0.001\ K_{oc}$.

in the soil air and thus volatilization losses would be expected to be very small. In saturated, deep soils (containing no air and negligible soil organic carbon), the model predicts substantially more Diazinon® (35%) to be in the mobile ground-water phase.

Diazinon® has been used (in large quantities) as an insecticide for about 20 years. Many of the early studies on its transport and fate in the soil/ground-water system are described in references 1204-1208, 1211, 1216 and 1475.

51.2.1.2 Sorption on Soils

There appear to be relatively few studies focusing on the soil sorption properties of Diazinon®, in part because many studies have shown it to be readily degraded and thus not problematic with regard to its soil leaching potential.

Values of the equilibrium soil sorption constant, K_{oc}, for Diazinon® may be calculated from laboratory sorption data in two publications. An average K_{oc} of 445 is calculated from the data of Sharom et al. (1476) for three materials (a creek sediment, a sandy loam and a sand) while a value of 744 is obtained for an organic soil with 75.3% organic matter. A value of 417 is calculated from the data of Miles (1477) for a creek sediment. A K_{oc} value of 580 is cited by Laskowski et al. (1209) without any backup. All of these values are substantially lower (by a factor of 2 to 6) than would be predicted using correlations of K_{oc} with water solubility or with octanol-water partition coefficients. These values indicate that sorption of Diazinon® on topsoils (containing > 0.1% organic carbon) is of moderate strength; i.e., most of the chemical will be sorbed to the soil, but not so strongly that leaching is prevented. As with all neutral organic chemicals, the extent of soil sorption is directly proportional to the soil organic carbon content. For low organic carbon soils (e.g., clays), the extent of sorption may also depend on other properties of the soil such as surface area, cation exchange capacity, and degree of hydration. Under certain conditions, Diazinon® can be sorbed into the interlayer spaces of montmorillonite clays (1212,1478).

Other laboratory, field and modeling studies on the downward movement of soil-applied Diazinon® generally tend to support the conclusion that sorption is strong enough (in conjunction with degradation) to prevent contamination of ground-water aquifers (1215,1216, 1479,1480).

51.2.1.3 Volatilization from Soils

Diazinon® has a low vapor pressure (1.4×10^{-4} mm Hg at 20°C (1204)) and a low Henry's Law constant (8.2×10^{-7} atm m^3/mol at 20°C (1219)). These values, coupled with the moderate extent of soil and sediment sorption of Diazinon®, imply that volatilization from soils (or surface waters) should not be an important transport pathway if water is present However, experiments designed to measure Diazinon® losses from model soil pit and evaporation pond systems have shown that a significant fraction, and in some cases even a major fraction, of the chemical present may be lost to the air by volatilization (1217,1218). Branham and Wehner (1479), who conducted microecosystem tests simulating Diazinon® application to turfgrass, concluded that volatilization accounted for a small amount of the chemical lost from the site of application. Jenkins et al. (1215) also showed that volatilization losses were small in lysimeter studies simulating land disposal of wastewater by spray irrigation. Volatilization losses from the surfaces of foliage or structures (e.g., after spray applications) could be substantially larger. Volatilization accounted for the loss of 86 percent of the Diazinon® on watch glasses over a 90 day period at 35°C; loss of 77.5 percent occurred within the first 15 days (1204).

51.2.2 Transformation Processes in Soil/Ground-water Systems

Diazinon® is susceptible to a number of degradation processes - including hydrolysis, biodegradation and photolysis - so that the chemical is not considered to be persistent in the environment.

Evidence for the photolytic degradation of Diazinon® (in surface waters or surfaces exposed to the light) is provided in references 1204, 1205 and 1485. Wolfe et al. (1205) concluded that the photolysis of Diazinon® by sunlight is a slow process, due principally to weak absorption of sunlight. The susceptibility of Diazinon® to indirect photolysis or free radical oxidation has not been investigated.

Data on the importance of hydrolysis in the environmental degradation of Diazinon® are provided in references 1204, 1205, 1207, 1216, 1221, 1475 and 1481-1484. In their 1976 review, Wolfe et al. (1205) concluded that hydrolysis of Diazinon® is very slow at pH values normally found in lakes and rivers (minimum half-life one month at 20°C), but that hydrolysis rates did increase with decreasing pH. The rate of hydrolysis, and subsequent environmental half-life, is strongly dependant on both pH and temperature as shown in Figures 51-1 and 51-2. Chapman and Cole (1207) summarize hydrolysis half-life measurements from several investigations, including their own, as shown in Table 51-2. Note that Diazinon® actually is most resistant to hydrolysis near pH 7.

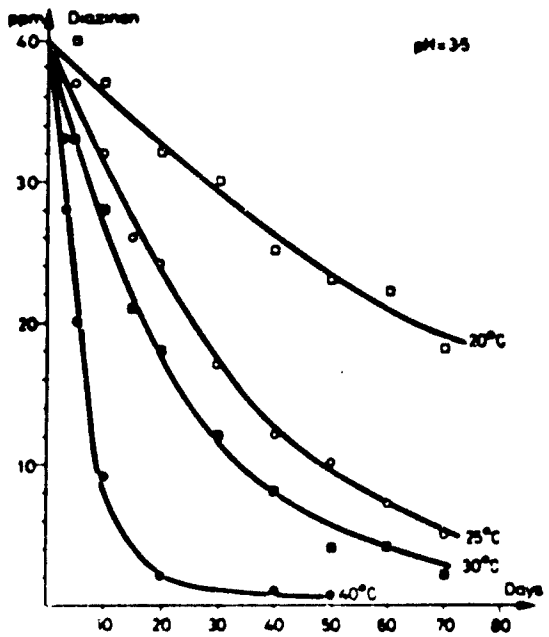


FIGURE 51-1

DECOMPOSITION OF DIAZINON® AS A FUNCTION OF TEMPERATURE

Source: Keckés et al. (1475)

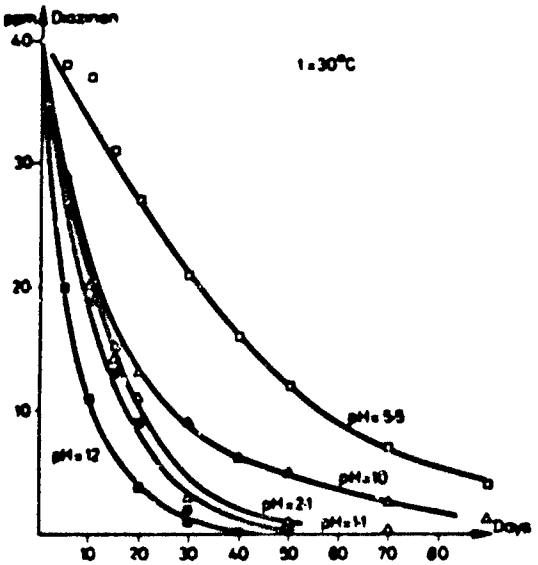


FIGURE 51-2

DECOMPOSITION OF DIAZINON® AS AS A FUNCTION OF pH

Source: Keckés et al. (1475)

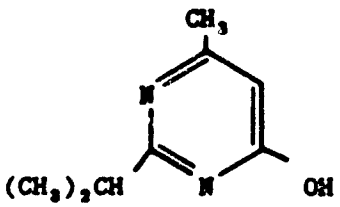
TABLE 51-2

HYDROLYSIS HALF-LIVES FOR DIAZINON® IN AQUEOUS SOLUTIONS AT TEMPERATURES NEAR 20°C

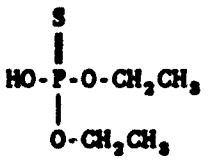
pH	No. of Data Points	Hydrolysis Half Life (weeks) Mean	Range
5	2	3	2 - 4
6	4	3.5	1 - 8
7	4	11	1 - 26
8	3	5	1 - 8

Source: Based on data in Chapman and Cole (1207); data are from 6 different publications.

From the above, it is clear that Diazinon® is subject to base- and acid-catalyzed hydrolysis. Second-order alkaline hydrolysis rate constants of 5.6×10^{-3} $M^{-1}s^{-1}$ (20°C) and 2.4×10^{-3} $M^{-1}s^{-1}$ (27°C), and acid hydrolysis rate constants of 2.3×10^{-2} $M^{-1}s^{-1}$ (20°C) and 7.3×10^{-2} $M^{-1}s^{-1}$ (27°C), have been reported (1205). The principal initial hydrolysis products are 2-isopropyl-4-methyl-6-hydroxy pyrimidine (I) and O,O-diethyl phosphorothionic acid (II) (1204,1205,1481).



I



II

The effect of the presence of solids (sand, alumina, soil), humic acids, and other materials (e.g., cupric ions) on the hydrolysis of Diazinon® at various pHs has been investigated in several studies (1207,1221,1475,1481,1482,1484) with some results being confusing or anomalous. To some extent the presence of solids may dampen the effect of pH on hydrolysis rates. It has been suggested that Diazinon® sorbed on soils is not susceptible to alkaline hydrolysis, but is susceptible to neutral hydrolysis (1484). The presence of cupric ions appears to catalyze the hydrolysis reaction (1205,1221). The rate of hydrolysis decreases for Diazinon® when it is mixed in various technical formulations (e.g., dusts, oil solutions, emulsifiable concentrates) used for spray application (1481,1482).

Studies on the biodegradation of Diazinon® are described in a number of reports (1204,1211,1216,1223,1224,1475,1479,1486). The general conclusion is that under normal conditions Diazinon® is moderately biodegradable. Rao and Davidson (1210), using a variety of literature data from laboratory tests simulating aerobic conditions, estimated a mean biodegradation half life of 32-48 days.

Diazinon® can be the sole source of phosphorus for some species of microorganisms (1223). Acclimation appears to be important for biodegradation. Many studies have not adequately distinguished between the roles of abiotic hydrolysis and biologically mediated hydrolysis in the initial degradation steps yielding the two hydrolysis products mentioned above.

51.2.3 Primary Routes of Exposure from Soil/Ground-water Systems

The above discussion of fate pathways suggests that Diazinon® has a low volatility, is moderately sorbed to soil, and based on the bioconcentration factor calculated from its K_{ow}, Diazinon® has a moderate potential for bioaccumulation. These fate characteristics suggest several potential exposure pathways.

Volatilization of Diazinon® from a disposal site is not likely to represent an important exposure pathway under most conditions. Drinking water contamination resulting from the migration of Diazinon® with ground water may occur, although it is relatively immobile in soil and appears to be susceptible to a number of degradation pathways. This compound was not reported in Mitre's (83) compilation of compounds detected at the 546 National Priority List (NPL) sites. In addition, it has not been detected in any of the national drinking water surveys of ground water.

Discharges of Diazinon® to surface water from soil/ground-water systems would probably not represent significant sources of exposure due to Diazinon® degradability.

51.2.4 Other Sources of Human Exposure

Diazinon® has been registered as an insecticide and used on a wide variety of agricultural crops, domestic animals, lawns and gardens and household pests. As a result, consumers may be exposed through product use as well as the environment.

Diazinon® was detected in 48% of 123 air samples at 10 U.S. locations. The maximum concentration was 23 ng/m^3 and the mean concentration was 2.1 ng/m^3 (1242). These data suggest that inhalation may represent a common source of exposure, although at low levels.

NRC (213) stated that little information was available on the presence of Diazinon® in drinking water. Carey and Kutz (1242) reported that Diazinon® was found in 1.2% of the samples in the

National Surface Water Monitoring Program from 1976-1980 with a maximum value of 2.38 µg/L. It was also detected infrequently in sediment over the same time period. It was found in 0.5% of the sediment samples with a maximum concentration of 7.1 µg/kg.

Due to its use on numerous agricultural crops, Diazinon® is commonly found in foods. It is included in the U.S. Food and Drug Administration's (FDA) Total Diet Study to determine the dietary intake of selected pesticides and other chemicals. The average daily intake for adults over the years 1976 - 1979 ranged from 0.004-0.010 µg/kg body weight/day. Average daily intakes for infants and toddlers over the same period ranged from 0.002-0.014 µg/kg/day. The largest source of exposure came from grain and cereal products, leafy vegetables and fruit.

The use of Diazinon® in home lawns and gardens can result in direct consumer exposure through both dermal and inhalation routes. Davis et al. (1559) examined the exposure to applicators of Diazinon®. They found that inhalation exposures ranged from 1.9-7.4 µg/hr over the period of application. Dermal exposures ranged from 5,500-29,000 µg/hr during the application period. The ranges were a function of the method of application, the area of application, and the amount of clothing worn. These data suggest that consumer exposures can be significant compared to other sources of exposure, although the frequency of exposure would be low.

51.3 HUMAN HEALTH CONSIDERATIONS

51.3.1 Animal Studies

51.3.1.1 Carcinogenicity

The National Cancer Institute (NCI) (1146) conducted a study of the carcinogenic effects of Diazinon® in F344 rats and B6C3F1 mice. Rats were fed a diet containing 0, 400 or 800 ppm Diazinon® while mice were fed 0, 100 or 200 ppm Diazinon®. All animals were treated for 103 weeks. Low- and high-dose male rats and high-dose female rats showed signs of hyperactivity and all treated female rats exhibited signs of bloating, vaginal bleeding and vaginal discharge. The only clinical sign of Diazinon® toxicity in mice was hyperactivity. No dose-related trend in tumors was present in any of the treated rats or mice of either sex at incidences that could be clearly related to the administration of Diazinon® in the diet. Based on the data provided in this bioassay, the NCI concluded that Diazinon® was not carcinogenic for F344 rats or B6C3F1 mice of either sex.

51.3.1.2 Mutagenicity

Diazinon® was not mutagenic when tested in strains TA1535, TA1537, TA1538, TA98 and TA100 of Salmonella typhimurium and strain WP_2 of Escherichia coli (1108,1143).

Strain D_3 of S. cerevisiae showed no recombinant activity of any kind when tested with Diazinon® (1143). Diazinon® also had no effect on unscheduled DNA synthesis in strain WI-38 of human lung fibroblast cells (1143) or on sister chromatid exchange in Chinese hamster V79 cells (1109,1144).

51.3.1.3 Teratogenicity, Embryotoxicity and Reproductive Effects

The teratogenic effect of Diazinon® in rats was studied by Kimbrough and Gaines (1159). Pregnant Sherman rats were given a single intraperitoneal injection of 0, 100, 150 or 200 mg/kg Diazinon® on the 11th day of gestation. Fetuses were examined on day 20. Two of five dams treated with 200 mg/kg Diazinon® died before the experiment was completed. A high incidence of resorption (11 vs. 0.8 in control animals) was observed in this group. Of the six surviving fetuses, one had hydrocephalus (enlarged head due to fluid accumulation in the cranial vault), one had the first distal phalanx missing and one had ectomelia (incomplete or lack of development of long bones of the limbs). Dams injected with 150 mg/kg Diazinon® had a significantly reduced net weight gain (47 g vs. 82 g for controls). Fetal weights were also significantly reduced (2.56 g vs. 3.14 g in controls). No malformations were noted in the 150 mg/kg group. The only detrimental effect of the 100 mg/kg treatment was that 6 out of 50 fetuses exhibited a dilated renal pelvis. These results indicate that Diazinon® when injected intraperitoneally on the 11th day of gestation may induce malformations but only at doses toxic to the dams.

Diazinon® was not teratogenic in rabbits orally administered 7 mg/kg or 30 mg/kg during organogenesis (59). Similarly, no teratogenic effects were reported in hamsters fed 0.125 or 0.25 mg/kg Diazinon® during organogenesis. Cholinergic signs were seen in rabbits ingesting the high dose of Diazinon® and in all treated hamsters (59).

Similar to many organophosphate insecticides, Diazinon® has been shown to have a profound effect on avian embryogenesis when injected directly into chick eggs. Malformations are primarily skeletal in nature (1110,1145). Organophosphate induced teratogenesis occurs exclusively in avian species and not in mammals (1145). It is unclear why this is so.

51.3.1.4 Other Toxicologic Effects

51.3.1.4.1 Short-term Toxicity

Diazinon® is a cholinesterase inhibitor and typical signs of toxicity include vomiting, salivation, diarrhea, trembling, respiratory depression, cyanosis, pulmonary edema, convulsions and coma (45). The oral LD_{50} in the mouse is 85 mg/kg (59), while the dermal LD_{50} for this species is 2750 mg/kg (59). The inhalation LC_{50} in the mouse is listed as 1600 mg/m^3 for 4 hours (59).

Goats were given 0.5 or 5 mg/kg Diazinon® by gavage daily for 7 days, or a single dose of 150 or 700 mg/kg Diazinon®. There were no clinical signs of Diazinon® toxicity in the 0.5 or 5 mg/kg treatment groups. The goat given the single 150 mg/kg dose developed mild toxicosis in the form of constricted pupils during the first 24 hours of testing. The goat given the single dose of 700 mg/kg was hypersalivating within 1.5 hours of administration. By the second hour, CNS depression and abdominal pain were observed. Ataxia, periodic muscle tremors, disorientation, colic and groaning persisted and by the tenth hour the goat was unable to stand. Within two hours of treatment with appropriate drugs, the goat could stand and muscle tremors and hypersalivation ceased. Signs of toxicity began to reoccur by the 24th hour and treatment was again administered. The animal appeared fully recovered 6 days after the initial dose of Diazinon® (1112).

Intraperitoneal injection of a single dose of 100 mg/kg Diazinon® into male Wistar rats significantly inhibited both plasma and erythrocyte cholinesterase activity. Erythrocyte cholinesterase was inhibited more than plasma cholinesterase (18% activity by the 24th hour after dosing vs. 61% activity in plasma). Also, the Diazinon® content in the kidney was much greater than in the liver and brain. At 8 hours after administration, the Diazinon® content of the kidney was 500 times the level found in the liver and 11 times greater than the level found in the brain.

51.3.1.4.2 Chronic Toxicity

Davis and Holub (1158) investigated the effects of Diazinon® in male and female Wistar rats fed 0 or 25 ppm Diazinon® for 30 days. No clinical signs of toxicity were observed in any of the treated animals. A significant reduction in plasma cholinesterase activity was present in both male and female rats fed 25 ppm Diazinon®. Enzyme activity was 22-30% lower in the treated females than in the treated males. Erythrocyte acetylcholinesterase activity was also 13-17% lower in treated females than in treated males. Brain acetylcholinesterase activity was decreased in treated females, though not significantly over controls. However, this reduction in enzyme activity was statistically significant when compared to corresponding male enzyme levels. Davies and Holub concluded that female rats were more susceptible to Diazinon® than male rats when administered in the diet for a 30 day period.

Rats fed up to 1000 ppm technical Diazinon® in the diet for 4 weeks or 1000 ppm active Diazinon® as a wettable powder for 72 weeks exhibited no apparent gross signs of toxicity (12). In dogs, exposure to 9.3 mg/kg/day orally produced signs of toxicity after 5 weeks as well as complete cholinesterase inhibition. The animals had returned to normal 2 weeks after withdrawal of Diazinon® from the diet (12).

Diazinon® (1750 ppm by gavage) was shown to significantly reduce clotting time in rats after a short-term exposure (1111), which led Lox and Davis (1113) to continue their investigation with an evaluation of clotting activity after long-term Diazinon® exposure. Female Sprague-Dawley rats were treated with 1 ppm Diazinon® in the drinking water for 6 months. Exposure to an extremely low level of Diazinon® continuously for 6 months produced no adverse effects on the blood clotting activity or hepatic morphology of female Sprague-Dawley rats.

51.3.2 Human and Epidemiologic Studies

51.3.2.1 Short-term Toxicologic Effects

The toxicity of Diazinon® is based on its ability to inhibit the activity of the cholinesterase enzymes (1115,1158,16). The resulting symptoms are similar to those found from excessive and continued stimulation of the CNS. Clinical signs include weakness, unsteadiness, blurred vision and a sense of constriction of the chest. This is usually followed by vomiting, abdominal cramps, diarrhea, salivation, profuse sweating, tremors of the extremities and difficulty breathing. Pinpoint and non-reactive pupils and cyanosis may occur as well as severe muscular fibrillations, convulsions and coma. Death primarily results from respiratory arrest due to the failure of the respiratory center, paralysis of the respiratory muscles or intense bronchoconstriction (5).

A fatal case of suicidal ingestion of Diazinon® was reported by Poklis et al. (1147). The victim was found dead along with a half empty bottle of pesticide containing 10% Diazinon® as the active ingredient. Post mortem examination revealed heavy, congested lungs and small intradermal and submucosal hemorrhages throughout the stomach and gastric mucosa and the grey and white matter of the brain. Diazinon® was detected in adipose tissue, bile, blood, brain, stomach contents, kidney and liver. It was estimated that the victim ingested 22 g of Diazinon® (i.e., 293 mg/kg bw). Plasma cholinesterase activity was found to be 0 Rappaport Units/ml (normal cholinesterase activity in adults is 40-80 Rappaport Units/ml plasma).

Another fatal Diazinon® suicide was reported by Heyndickx et al. (1148). Despite hospitalization, Diazinon® ingestion was not known to have occurred until the autopsy. The victim was admitted to the hospital with two severed radial veins. Despite seemingly successful treatment, the patient died a few hours later. Post mortem revealed edema of both lungs and an oily, green fluid in the stomach which analysis confirmed to be Diazinon®. The stomach and small intestines contained the majority of Diazinon® (756 mg% and 262 mg%, respectively). Brain, liver, kidney and lung tissue also revealed the presence of Diazinon®, but in much smaller amounts. Diazoxon, the more toxic metabolite, was not found in any tissue analyzed.

Wedin et al. (1114) reported an attempted case of suicide with renal involvement in addition to the general symptomatology usually observed. The patient was admitted to the hospital approximately one hour after ingesting 8 ounces of Diazinon® in water. The man was conscious and alert but was vomiting, had brachycardia (55 beats/minute) and hypoactive bowel sounds. Urine output, which was dark and cloudy, averaged 22 mL/hour. Urinalysis revealed moderate unidentifiable crystals. Treatment was administered and all symptoms subsided, however, crystalluria persisted until the 9th day of hospitalization. In a review of this case study, Albright (1152) suggested that since no other cases of renal involvement have been reported for Diazinon®, the low urine output was most likely related to volume depletion rather than a nephrotoxic effect.

Two cases of dermal and respiratory exposure to Diazinon® and its breakdown products were reported by Soliman et al. (1153). Both men were spraying a 60% diazinon-containing pesticide stored in tin containers without gloves or masks. By noon time, one man complained of nausea and vomiting. He became weaker, the muscles of his limbs twitched and he had difficulty breathing. At the hospital he was given atropine sulfate and released the following morning without incident. The second man reported nausea and vomiting later that afternoon, but went home as usual. He continued to vomit, had burning eyes and blurred vision and had difficulty breathing. He became weaker and developed a severe headache which persisted for 3 days. Cholinesterase activity in both men was depressed by 38-58%. Subsequent blood tests from both victims revealed a substantial increase in plasma cholinesterase activity two weeks after the poisoning. The erythrocyte cholinesterase activity showed minimal improvement up to 18 days post-exposure. Analysis of the pesticide revealed the Diazinon® to have broken down, primarily into the major hydrolytic product, 2-isopropyl-4-methyl-6-hydroxypyrimidine along with small amounts of other transformation products such as O,O,O',O'-tetraethyldithiopyrophosphate and monothionotetraethylpyrophosphate. These organopyrophosphate products are the only known components of Diazinon® decomposition which are extremely toxic to humans (with the exception of diazoxon). The catalytic decomposition was thought to be caused by the tin containers used for storing the Diazinon®. Use of aluminum containers resulted in no reports of poisoning (1153).

An unusual case of Diazinon® poisoning was reported by Conyers and Goldsmith (1286). After washing sheep by hand with Diazinon® to prevent parasite infestation, a farmhand developed psychosis. Symptoms began within 6 hours and included insomnia and restlessness. The next morning the farmhand was confused, forgetful and apathetic. He was admitted to the hospital where the serum cholinesterase level was 0.9 IU/ml (the normal adult male serum cholinesterase range is 2.6-5.53 IU/ml). The patient recovered completely within 2 days with no evidence of mental confusion or memory loss. Six days after the poisoning incident his serum cholinesterase level was shown to increase to 2.0 IU/ml. Conyers and Goldsmith concluded that the cause of the

farmhand's acute confusional psychosis was due to Diazinon® intoxication even though no other classical symptoms of Diazinon® toxicity manifested themselves.

51.3.2.2 Chronic Toxicologic Effects

Limited data are available on long-term human exposure to Diazinon® because, like other organophosphorous pesticides, it is an acutely poisonous agent and symptoms usually manifest between 1 and 24 hours post exposure.

Volunteers receiving 0.025-0.030 mg/kg Diazinon® for 32-34 days (route unspecified) showed no significant changes in plasma or erythrocyte cholinesterase activity (1150). A second study (1151) reported the results of 3 volunteers dosed (route unspecified) with 0.05 mg/kg Diazinon® daily for 5 days. After a 23-day period of no treatment, the subjects again received 0.05 mg/kg Diazinon® for 5 days. Plasma cholinesterase activity was inhibited by 60-65% compared with levels prior to testing. Three additional volunteers were then given 0.25 mg/kg Diazinon® daily for 43 days. Plasma cholinesterase activity was inhibited 15-20% (1151).

51.3.3 Levels of Concern

There are no OSHA standards for Diazinon®. The ACGIH (3) recommends an 8-hour time-weighted-average of 0.1 mg/m^3 with a notation of possible skin absorption.

The National Academy of Science calculated a no adverse effect level for Diazinon® in drinking water of 0.014 mg/L (54).

An acceptable daily intake of 0.002 mg/kg has been established for Diazinon® by WHO/FAO (54).

51.3.4 Hazard Assessment

The National Cancer Institute (1146) concluded Diazinon® was not carcinogenic for F344 rats fed up to 800 ppm in the diet or for B6C3F1 mice fed up to 200 ppm in the diet for two years. Mutagenicity tests with this compound are also negative.

A few malformed fetuses (3 of 6 survivors) were reported for rats injected with 200 mg/kg Diazinon® intraperitoneally during gestation; however, this dose was lethal to 2 of 5 dams. Studies in rabbits and hamsters administered Diazinon® orally gave no indications of teratogenic effects (59).

Diazinon® is a cholinesterase inhibitor. Typically signs of toxicity include vomiting, salivation, diarrhea, trambling, respiratory depression, cyanosis, pulmonary edema, convulsions and coma (45). Long-term exposure of laboratory animals produced no gross signs of

toxicity, alterations in growth or pathology at autopsy (12) but did result in significant reductions in plasma cholinesterase activity.

Limited data are available with regard to chronic human exposure to Diazinon® due to the acute toxic nature of Diazinon®. One report did note, however, that no adverse effects other than inhibition of plasma cholinesterase by 15-20% were recorded for human volunteers given 0.25 mg/kg Diazinon® daily for 43 days. The route of administration was not specified (1151).

51.4 SAMPLING AND ANALYSIS CONSIDERATIONS

Determination of Diazinon® concentrations in soil and water requires collection of a representative field sample and laboratory analysis. Care is required to prevent losses during sample collection and storage. Soil and water samples are collected in glass containers; extraction of samples should be completed within 7 days of sampling and analysis completed within 30-40 days. In addition to the targeted samples, quality control samples such as field blanks, duplicates, and spiked matrices may be specified.

EPA Method 8140 (63) is an approved procedure for the analysis of Diazinon® in aqueous samples. Prior to analysis, samples are extracted at neutral pH with methylene chloride as the solvent using a separatory funnel or a continuous liquid-liquid extractor. An aliquot of the concentrated sample extract is injected onto a gas chromatographic (GC) column using a solvent flush technique. The GC column is programmed to separate the semi-volatile organics; Diazinon® is then detected with either a nitrogen phosphorus (N/P) detector operated in the phosphorus sensitive mode or a flame photometric detector (FPD). The FPD is more selective for phosphorus than the N/P.

The same method is recommended for Diazinon® analysis in soil and waste samples. The procedure for solid samples differs from the aqueous procedure primarily in the preparation of the sample extract. Solid samples are extracted using either soxhlet extraction or sonication methods. Neat and diluted organic liquids may be analyzed by direct injection.

Typical Diazinon® detection limits that can be obtained in wastewaters and non-aqueous samples (wastes, soils, etc.) are shown below. The actual detection limit achieved in a given analysis will vary with instrument sensitivity and matrix effects.

Aqueous Detection Limit	Non-Aqueous Detection Limit
0.6 µg/L (Method 8140)	1 µg/g (Method 8140)

COMMON SYNONYMS:	FORMULA OF MAJOR COMPONENTS:	
Aroclor® 1016 Chlorodiphenyl (41% Cl) PCB	$C_{12}H_8Cl_2$ (20%) $C_{12}H_7Cl_3$ (57%) $C_{12}H_6Cl_4$ (21%)	CAS REG. NO.: 12674-11-2 NIOSH NO.: TQ1351000 MOLECULAR WEIGHT: 258 (average)
Aroclor® 1242 Chlorodiphenyl (42% Cl) PCB	$C_{12}H_8Cl_2$ (16%) $C_{12}H_7Cl_3$ (49%) $C_{12}H_6Cl_4$ (25%) $C_{12}H_5Cl_5$ (8%)	CAS REG. NO.: 53469-21-9 NIOSH NO.: TQ1356000 MOLECULAR WEIGHT: 266 (average)
Aroclor® 1254 Chlorodiphenyl (54% Cl) PCB	$C_{12}H_6Cl_4$ (21%) $C_{12}H_5Cl_5$ (48%) $C_{12}H_4Cl_6$ (23%) $C_{12}H_3Cl_7$ (6%)	CAS REG. NO.: 11097-69-1 NIOSH NO.: TQ1360000 MOLECULAR WEIGHT: 328 (average)
Aroclor® 1260 Chlorodiphenyl (60% Cl) Clophen A60 Phenoclor DP6 PCB	$C_{12}H_5Cl_5$ (12%) $C_{12}H_4Cl_6$ (38%) $C_{12}H_3Cl_7$ (41%) $C_{12}H_2Cl_8$ (8%)	CAS REG. NO.: 11096-82-5 NIOSH NO.: TQ1362000 MOLECULAR WEIGHT: 376 (average)

REACTIVITY	Aroclor® compounds are generally considered halogenated organic compounds for compatibility classification purposes. Reactions of such materials with cyanides, mercaptans or other organic sulfides typically generate heat, while those with non-oxidizing mineral acids, amines, azo compounds, hydrazines, caustics or nitrides commonly evolve heat and toxic or flammable gases. Reactions with oxidizing mineral acids may generate heat, toxic gases and fires. Reactions with alkali or alkaline earth metals, certain other chemically active elemental metals like aluminum, zinc or magnesium, organic peroxides or hydroperoxides, strong oxidizing agents or strong reducing agents typically result in heat generation and explosions and/or fires. PCBs are specifically known to react exothermally with liquid chlorine. Photolysis in sunlight causes various degradative reactions (12,505,511).

PHYSICOCHEMICAL DATA

	Aroclor® 1016	Aroclor® 1242	Aroclor® 1254	Aroclor® 1260
• Physical State (at 20°C):	oily liquid (1457)	liquid (46)	viscous liquid (38)	liquid (23)
• Color:	clear (1457)	straw-dark brown (46)	pale yellow	colorless (23)
• Odor:	mild hydro-carbon (1457)	mild hydro-carbon (2)	mild hydro-carbon (38)	no data
• Odor Threshold:	<——— no data ———>			
• Liquid Density (g/ml at 20°C):		1.38-1.39 (12)		
(g/ml at 30°C):	1.44 (54)			1.44 (54)
(g/ml at 90°C):			1.47-1.49 (12)	
• Freezing/Melting Point (°C):	-18.89 (2)	-19 (38)	10 (pour point) (38)	no data
• Boiling Point (°C):	340-375 (54)	325-366 (38)	365-390 (38)	340-375 (54)
• Flash Point (°C):	<——— relatively non-flammable (67,508) ———			
• Flammable Limits in Air, % by Volume:	<——— no data ———			
• Autoignition Temperature (°C):	<— can be incinerated at high temperatures —> (12,54)			
• Vapor Pressure (mmHg at 20°C):			6×10^{-5} (38)	
(mmHg at 25°C):	4×10^{-4} (10)	4×10^{-4} (10)		4×10^{-5} (10)

PHYSICOCHEMICAL DATA - Continued

	Aroclor® 1016	Aroclor® 1242	Aroclor® 1254	Aroclor® 1260
• Saturated Concentration in Air (mg/m³ at 20°C) (ADL estim)	5.6	5.8	1.1	0.8
• Solubility in Water (mg/L at 20°):			0.012-0.07 (10,1583)	0.0027 (10)
(mg/L at 25°):	0.22-0.91 (1536,1589,1583)	0.2-0.7		
• Log (Octanol-Water Partition Coefficient), log K_{ow}:	5.3-5.6 (29)	5.3-6.1 (29)	5.6-8 (29)	6.1-9.3 (29)
• Soil Adsorption Coefficient, K_{ow}:	~10^5 (611)	~10^5 (611)	10^6-10^7 (611)	10^6-10^9 (611)
• Henry's Law Constant (atm·m³/mol at 20°):	3.2×10^{-4} (31)	3.4×10^{-4} (1571)	2.8×10^{-4} (1571)	3.4×10^{-4} (1571)
• Bioconcentration Factor:	← 10^4-10^6 (10) →			

PERSISTENCE IN THE SOIL-WATER SYSTEM	Aroclor® 1016, 1242, 1254 and 1260 are expected to be highly immobile in the soil/ground-water system due to rapid and strong sorption. In the absence of organic solvents, leaching is minimal; the presence of organic solvents (e.g., chlorobenzenes) may significantly increase mobility. Volatilization is expected to be slow, but may be a significant long-term transport process. Photolytic and biological degradation of PCBs may occur in the soil/ground-water environment but are not expected to be rapid. In general, the higher chlorinated biphenyls are less mobile and more persistent than the lower chlorinated species.

PATHWAYS OF EXPOSURE	Although they are generally strongly sorbed, the primary pathway of concern from a soil/ground-water system is the migration of PCBs to ground-water drinking water supplies. Inhalation may be an important exposure pathway in some cases. Fish contamination and consumption may occur upon release to surface waters.

HEALTH HAZARD DATA

Signs and Symptoms of Short-term Human Exposure (46):
Systemic effects include anorexia, nausea, edema of the face and hands, and abdominal pain. A burning sensation to the skin and eyes as well as eye discharge are also common.

Toxicity Based on Animal Studies:

	Aroclor® 1016	Aroclor® 1242	Aroclor® 1254	Aroclor® 1260
LD_{50} (mg/kg) oral	no data	4250 [rat] (51)	1295 [rat] (51)	4000-10,000 [rat] (59)
skin	no data	no data	no data	1300-2000 [rabbit] (59)
LC_{50} (mg/m³) inhalation	<——— no data ———>			

Long-Term Effects (PCBs): Chloracne, liver injury

Pregnancy/Neonate Data (PCBs): Reduced reproductive capacity

Mutation Data (PCBs): Inadequate

Carcinogenicity Classification (PCBs): IARC - 2B

HANDLING PRECAUTIONS (38)	Aroclor® 1016 and 1242 Vapor concentrations of 1-10 mg/m³: any supplied-air respirator with a full facepiece, helmet or hood or any self-contained breathing apparatus with full facepiece • > 10 mg/m³: self-contained breathing apparatus with a full facepiece operated in the pressure-demand or other positive pressure mode or a combination respirator which includes a Type C supplied-air respirator with full facepiece operated in pressure-demand or other positive pressure or continuous flow mode and an auxiliary self-contained breathing apparatus operated in pressure-demand or other positive pressure mode • Impervious clothing, gloves, face shields (8-inch minimum) and other appropriate protective clothing to prevent possible skin contact • Splash-proof safety goggles if eye contact is possible. Aroclor® 1254 and 1260 Vapor concentrations of 0.5-5 mg/m³: any supplied-air respirator with a full facepiece, helmet or hood or any self-contained breathing apparatus with full facepeice • > 5 mg/m³: self-contained breathing apparatus with a full facepiece operated in the pressure-demand or other positive pressure mode or a combination respirator which includes a Type C supplied-air respirator with full facepiece operated in pressure-demand or other positive pressure or continuous flow mode and an auxiliary self-contained breathing apparatus operated in pressure-demand or other positive pressure mode • Impervious clothing, gloves, face shields (8-inch minimum) and other appropriate protective clothing to prevent possible skin contact • Splash-proof safety goggles if eye contact is possible.

EMERGENCY FIRST AID TREATMENT (54)	Ingestion: Induce vomiting if victim is conscious. Get medical attention • Inhalation: Move victim to fresh air immediately. Perform artificial respiration if necessary. Get medical attention • Skin: Remove contaminated clothing. Wash skin with soap and water immediately. Get medical attention • Eye: Irrigate immediately with large amounts of water. Get medical attention.

ENVIRONMENTAL AND OCCUPATIONAL STANDARDS AND CRITERIA

AIR EXPOSURE LIMITS:

Standards

- OSHA PEL (8-hr TWA): chlorodiphenyl 42% chlorine: 1 mg/m^3; 54% chlorine: 0.5 mg/m^3 (skin)
- AFOSH PEL (8-hr TWA): chlorodiphenyl 42% chlorine: 1 mg/m^3; 54% chlorine: 0.5 mg/m^3 (skin)

Criteria

- NIOSH IDLH (30-min): chlorodiphenyl 42% chlorine: 10 mg/m^3; 54% chlorine: 5 mg/m^3 (skin)
- ACGIH TLV® (8-hr TWA): chlorodiphenyl 42% chlorine: 1 mg/m^3; 54% chlorine: 0.5 mg/m^3 (skin)
- ACGIH STEL (15-min): chlorodiphenyl 42% chlorine: 2 mg/m^3; 54% chlorine: 1 mg/m^3 (skin)

WATER EXPOSURE LIMITS:

Drinking Water Standards - None established

EPA Health Advisories - None established

EPA Ambient Water Quality Criteria (355)

- Human Health
  - Based on ingestion of contaminated water and aquatic organisms, (10^{-5}, 10^{-6}, 10^{-7} cancer risk), 0.79 ng/L, 0.079 ng/L, 0.0079 ng/L total PCBs.
  - Based on ingestion of contaminated aquatic organism only, (10^{-5}, 10^{-6}, 10^{-7} cancer risk), 0.79 ng/L, 0.079 ng/L, 0.0079 ng/L total PCBs.
- Aquatic Life
  - Freshwater species
    To protect freshwater aquatic life the criterion is 0.014 µg/L total PCBs as a 24-hour average.
  - Saltwater species
    To protect saltwater aquatic life, the criterion is 0.030 µg/L total PCBs as a 24-hour average.

REGULATORY STATUS (as of January 1, 1987)

Promulgated Regulations

- Federal Programs

Clean Water Act (CWA)

Under the toxic pollutant effluent standards, PCBs are prohibited in any discharge from any manufacturer of PCBs, electrical capacitors or electrical transformers (850).

PCBs are designated hazardous substances. They have reportable quantity (RQ) of 4.54 kg (347,985). They are also listed as toxic pollutants (351). Water quality criteria have been set. No effluent limitations specific to this chemical group have been set.

Resource Conservation and Recovery Act (RCRA)

Polychlorinated biphenyls are listed as hazardous waste constituents (328). Solid wastes containing concentrations of PCBs equal to or greater than 10 mg/kg (dry weight) must be incorporated into soil when it is to be applied to land used for producing animal feed. Incorporation of the waste into the soil is not required if it is assured that the PCB content is less than 0.2 mg/kg (actual weight) in animal feed or less than 1.5 mg/kg (fat basis) in milk (1237).

Effective July 8, 1987, the land disposal of liquid hazardous wastes containing polychlorinated biphenyls at concentrations greater than or equal to 50 ppm will be prohibited. The only exception will be underground injection (1755).

Toxic Substances Control Act (TSCA)

The use of polychlorinated biphenyls is prohibited except when used in a totally enclosed manner which ensures that any exposure of human beings or the environment will be insignificant. EPA may authorize the use of PCBs in a manner other than totally enclosed if that use will not present an unreasonable risk of injury to health or the environment. PCBs at concentrations of 50 ppm or greater must be disposed of in an incinerator. Numerous exceptions to this disposal requirement are outlined in 40CFR761.60 (1769).

Comprehensive Environmental Response Compensation and Liability Act (CERCLA)

PCBs compounds are designated hazardous substances under CERCLA. They have a reportable quantity (RQ) limit of 4.54 kg. Reportable quantities have also been issued for RCRA hazardous waste streams containing PCBs but these depend upon the concentrations of the chemicals in the waste stream (985).

Marine Protection Research and Sanctuaries Act (MPRSA)
Ocean dumping of organohalogen compounds as well as the dumping of known or suspected carcinogens, mutagens or teratogens is prohibited except when they are present as trace contaminants. Permit applicants are exempt from these regulations if they can demonstrate that such chemical constituents are non-toxic and non-bioaccumulative in the marine environment or are rapidly rendered harmless by physical, chemical or biological processes in the sea (309).

Hazardous Materials Transportation Act (HMTA)
The Department of Transportation has designated PCBs as hazardous materials which are subject to requirements for packaging, labeling and transportation (306).

Food, Drug and Cosmetic Act (FDCA)
The temporary tolerance for PCB residues are as follows:

1.5 ppm in milk and manufactured dairy products (fat basis)
3 ppm in poultry (fat basis)
0.3 ppm in eggs
0.2 ppm in finished animal feed for food producing animals and in infant and junior foods
2 ppm in animal feed components of animal origin and in the edible portion of fish and shellfish
10 ppm in paper food-packaging material (1404)

- State Water Programs
  The following states have a criterion of 0.001 μg/L for PCBs (731):

  Florida - in the public water supply
  North Carolina - in fresh water
  West Virginia - in drinking water

  New Jersey has a criterion of 0.014 μg/L for PCBs in surface water (731) and a standard of 0.001 μg/L in ground water (981).

  New Mexico has a ground water quality standard of 0.001 mg/L (981).

  Louisiana has a criterion of 2 μg/L and 0.79 ng/L for PCBs in fresh water and public water, respectively (731).

  New York has a ground water quality standard of 0.0001 mg/L (981).

  Missouri does no allow PCBs to be present in state waters (731).

  Other states follow EPA Ambient Water Quality Criteria.

Proposed Regulations

- Federal Programs

  Clean Water Act (CWA)
  Effluent guidelines for Aroclor® 1242 have been proposed in the pulp, paper and paperboard point source category (1331).

  Safe Drinking Water Act (SDWA)
  EPA has proposed a Recommended Maximum Contaminant Level (RMCL) of zero for PCBs as part of the National Primary Drinking Water Regulations (992).

  Resource Conservation and Recovery Act (RCRA)
  EPA has proposed that hazardous waste treatment, storage and disposal facilities monitor ground water for PCBs when EPA suspects the facilities of leaking contaminants (1754).

  EPA has proposed that liquid hazardous wastes containing polychlorinated biphenyls in concentrations greater than or equal to 50 ppm or less than 500 ppm must be incinerated or burned in compliance with requirements outlined in 40CFR761.70 and 761.60. Liquid hazardous wastes with polychlorinated biphenyls in excess of 500 ppm must be incinerated (1767).

- State Water Programs
  No proposed regulations are pending.

EEC Directives

Directive Relating to the Quality of Water for Human Consumption (540)
The maximum admissible concentration for PCBs is 0.1 μg/L. The total maximum allowable concentration for pesticides and related products is 0.5 μg/L.

Directive on Ground Water (538)
Direct discharge into ground water (i.e., without percolation through the ground or subsoil) of organophosphorous compounds, organohalogen compounds and substances which may form such compounds in the aquatic environment, substances which possess carcinogenic, mutagenic or teratogenic properties in or via the aquatic environment and mineral oils and hydrocarbons is prohibited. Appropriate measures deemed necessary to prevent indirect discharge into ground water (i.e., via percolation through ground or subsoil) of these substances shall be taken by member countries.

Directive on the Quality Required of Shellfish Waters (537)
The mandatory specifications for organohalogenated substances specify that the concentration of each substance in the shellfish water or in shellfish flesh must not reach or exceed a level which has harmful effects on the shellfish and larvae. The guideline specifications for organohalogenated substances state that the concentration of each substance in shellfish flesh must be so limited that it contributes to the high quality of shellfish product.

Directive on the Discharge of Dangerous Substances (535)
Organohalogens, organophosphates, petroleum hydrocarbons, carcinogens or substances which have a deleterious effect on the taste and/or odor of human food derived from aquatic environments cannot be discharged into inland surface waters, territorial waters or internal coastal waters without prior authorization from member countries which issue emission standards. A system of zero-emission applies to discharge of these substances into ground water.

Directive on Marketing and Use of Dangerous Substances (541)
Polychlorinated biphenyls (except mono- and dichlorinated biphenyls) and preparations with a PCB content higher than 0.01% may not be used. Up to 30 June 1986 they were allowed for use under the following conditions:

- Closed system electrical equipment, transformers, resistors and inductors;
- Large condensers (≥ 1 kg total weight);
- Small condensers, provided that the chlorine content of the PCBs is no greater than 43% and does not contain more than 3-5% of penta- and higher chlorinated biphenyls;
- Heat transmitting fluids in closed-circuit heat-transfer installations, except in those used for processing foodstuffs, pharmaceuticals and veterinary products;
- Hydraulic fluids utilized in underground mining equipment;
- Primary and intermediate products for further processing into other products not prohibited under the Directive.

Equipment, plant and fluids which were in service after 30 June 1986 shall continue to be authorized until they are disposed of or reach the end of their service life. Member states may prohibit this continued use for reasons of health and the environment.

Member states may also authorize the use of PCBs when it is not possible to use substitute products.

Directive on Toxic and Dangerous Wastes (542)
Any installation, establishment, or undertaking which produces, holds and/or disposes of certain toxic and dangerous wastes including phenols and phenol compounds; organic-halogen compounds; chrome compounds; lead compounds; cyanides; ethers and aromatic polycylic compounds (with carcinogenic effects) shall keep a record of the quantity, nature, physical and chemical characteristics and origin of such waste, and of the methods and sites used for disposing of such waste.

Directive on the Classification, Packaging and Labeling of Dangerous Substances (787)
PCBs are classified as harmful substances and are subject to packaging and labeling regulations.

Directive on the Disposal of Polychlorinated Biphenyls and Polychlorinated Terphenyls (1239)
Member states must take measures to prohibit the uncontrolled discharge, dumping and tipping of PCBs or of objects containing PCBs. They must also take measures to make the disposal of PCB wastes compulsory and ensure that it is in a manner which does not endanger human health or the environment. Installations and establishments shall be authorized by member states for the purposes of disposing PCBs.

Directive on Transfrontier Shipment of Hazardous Waste (1433)
When the holder of a hazardous waste such as polychlorinated biphenyls intends to ship it to another member state, authorities of the member states concerned must be provided with information on the source and composition of the waste, measures to be taken to ensure safe transport, insurance against damage and the existence of a contractual agreement with the consignee of the waste. All transfrontier shipments must be properly packed and labeled and must be accompanied by instructions to be followed in the event of danger or accident.

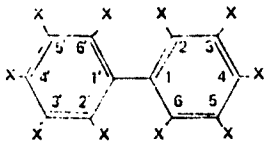
EEC Directives - Proposed

Proposal for a Council Directive on the Dumping of Waste at Sea (1793)
EEC has proposed that the dumping of organohalogen compounds at sea be prohibited.

Proposal for a Council Regulation Concerning Export From and Import Into the Community of Certain Dangerous Chemicals (1795)
EEC has proposed that any export of polychlorinated biphenyls on its own or in preparations must be reported by the exporter to a designated authority in the state of export and the state of import. The product must be packaged and labeled in accordance with the Directive on Classification, Packaging and Labeling of Dangerous Substances.

52.0 INTRODUCTION

This chapter encompasses a general review of the environmental fate, exposure and health effects of four commercial polychlorinated biphenyl (PCBs) mixtures marketed in the U.S. under the name Aroclor® (Aroclor® 1016, 1242, 1254 and 1260). The Aroclor® formulations are complex mixtures of PCBs produced by progressive chlorination of biphenyl with anhydrous chlorine. The composition of the end product is determined by the degree of chlorination. The structural formula of PCBs and convention numbering of substituent positions is shown in Figure 52-1.



X represents either a chlorine or a hydrogen atom

FIGURE 52-1

STRUCTURAL FORMULATION OF PCBs

A total of 209 different biphenyls are theoretically possible by replacement of from one to ten hydrogen atoms on the biphenyl ring system by chlorine.

The individual Aroclor® mixtures are identified by four digits: the first two digits of most Aroclor® formulations, 12, indicate that the preparation is a mixture; the second two digits denote the approximate chlorine content by weight percent. For example, Aroclor® 1242 is a mixture with 42% average chlorine content. Aroclor® 1016 is a relatively recent mixture and does not conform to the above notation; its composition is similar to Aroclor® 1242.

The behavior of Aroclor® products in the environment is largely dictated by the behavior of the individual components of PCBs. The Environmental Fate and Exposure Pathways Section, therefore, focuses on data for the PCB components; where available, data specific to the four Aroclor® formulations are also included. The data provided in Section 52.3, Human Health Considerations, in contrast, are specific to the Aroclor® mixtures since the toxicology data are generally specific to each mixture.

52.1 MAJOR USES

Aroclor® compounds are very inert, thermally and chemically stable compounds with dielectric properties. They have been used in nominally closed systems as heat transfer liquids, hydraulic fluids and lubricants, and in open-ended systems in which they came in direct contact with the environment as plasticizers, surface coatings, inks, adhesives, pesticide extenders and for microencapsulation of dyes for carbonless duplicating paper. In 1974, use of PCBs in the United

States was limited to closed systems, i.e., approximately 70% of PCBs produced were used in capacitors while the remaining 30% were utilized in transformers (1457).

52.2 ENVIRONMENTAL FATE AND EXPOSURE PATHWAYS

52.2.1 Transport in Soil/Ground-water Systems

52.2.1.1 Overview

The environmental behavior of the Aroclor® mixtures is a direct function of their relative composition with respect to the individual chlorinated biphenyl species. Table 52-1 summarizes the approximate composition of the four Aroclor® products considered in this chapter. It is important to remember that Aroclor® formulations are mixtures and the physical properties and chemical behavior of mixtures cannot be precisely defined. The individual PCBs in a pure state are generally solids at room temperature; however, due to melting point depression, Aroclor® mixtures are oily to resinous liquids at ambient temperatures.

Individual PCBs vary widely in their physical and chemical properties according to the degree of chlorination and position of the chlorines on the biphenyl structure. In general, as chlorine content increases, adsorption increases while transport and transformation processes decrease. The specific PCB distribution measured in environmental samples may be distorted and may not correspond to the specific Aroclor® mixture responsible for the contamination. For this reason, most of the fate and transport discussion will focus on the chlorinated biphenyl species rather than the Aroclor® mixtures.

In general, transport pathways can be assessed by using an equilibrium partitioning model, as shown in Table 52-2. These calculations predict the partitioning of low soil concentrations of the PCB mixtures among soil particles, soil water, and soil air; portions associated with the water and air phases of the soil have higher mobility than the adsorbed portion. Estimates for the unsaturated topsoil model indicate that almost all (> 99.99%) of the Aroclor® formulations are expected to be associated with the stationary phase. Much less than 1% is expected to partition to the soil-water phase; therefore, only a small portion would be available to migrate by bulk transport (e.g., the downward movement of infiltrating water), dispersion and diffusion. An insignificant portion of the Aroclor® formulations is expected in the gaseous phase of the soil; diffusion of vapors through the soil-air pores up to the ground surface is not expected to be important. In saturated, deep soils (containing no soil air and negligible soil organic carbon), sorption is still expected to be the most significant fate process. Overall, ground water underlying PCB-contaminated soils is not expected to be vulnerable to contamination.

TABLE 52-1

APPROXIMATE COMPOSITION (%) OF AROCLOR® FORMULATIONS

	1016	1242	1254	1260
$C_{12}H_9Cl$	1	1	<0.1	ND
$C_{12}H_8Cl_2$	20	16	0.5	ND
$C_{12}H_7Cl_3$	57	49	1	ND
$C_{12}H_6Cl_4$	21	25	21	1
$C_{12}H_5Cl_5$	1	8	48	12
$C_{12}H_4Cl_6$	<0.1	1	23	38
$C_{12}H_3Cl_7$	ND	<0.1	6	41
$C_{12}H_2Cl_8$	ND	ND	ND	8
$C_{12}H_1Cl_9$	ND	ND	ND	ND
Average M.W.	257.9	266.5	328.4	375.7

Source: Reference 10

The persistence of PCBs in water systems is well documented; however, data on persistence in soil systems are much more limited. The distribution of PCBs in the soil/ground-water system following two separate accidental spills of Aroclor® 1254 have been documented (1580,1588). In the first case, 6800 to 21,000 liters of transformer oil containing Aroclor® 1254 and chlorobenzenes were released after rupture of an underground pipe at a transformer manufacturing plant (1588). Large quantities of PCBs were found to have migrated both vertically (nine meters through granular fill and fractured clay) and horizontally at the site; Aroclor® 1254 distribution was found to be very heterogeneous. The authors postulated that due to the low organic content (<1%) of soil at the site, PCB contamination existed in three phases: dissolved aqueous phase, adsorbed phase, and an oily liquid phase (Aroclor®/solvent mixture). Movement of the oily liquid was probably responsible for the downward migration of large quantities of PCBs through the clay fractures, as well as lateral movement through

TABLE 52-2

EQUILIBRIUM PARTITIONING CALCULATIONS FOR AROCLOR® 1016, 1242, 1254, AND 1260 IN MODEL ENVIRONMENTS[a]

Soil Environment	Estimated Percent of Total Mass of Chemical in Each Compartment		
	Soil	Soil-Water	Soil-Air
Unsaturated topsoil at 25°C[b,c]	>99.99	<0.01	<0.001
Saturated deep soil[d]	>99.75	<0.25	-

a) Calculations based on Mackay's equilibrium partitioning model (34,35,36); see Introduction in Volume 1 for description of model and environmental conditions chosen to represent an unsaturated topsoil and saturated deep soil. Calculated percentages should be considered as rough estimates and used only for general guidance.

b) Utilized range of estimated (611) soil sorption coefficients representing the biphenyls present at greater than 4% of the Aroclor® mixtures.

Aroclor® 1016: $K_{oc} = 10^5$ to 2×10^5

Aroclor® 1242: $K_{oc} = 10^5$ to 6.3×10^5

Aroclor® 1254: $K_{oc} = 2 \times 10^5$ to 5×10^7

Aroclor® 1260: $K_{oc} = 6.3 \times 10^5$ to 10^9

c) Henry's law constant (atm·m³/mol at 25°C) taken as: 3.2×10^{-4} for Aroclor® 1016 (31), and 3.4×10^{-4}, 2.8×10^{-4} and 3.4×10^{-4} for Aroclor® 1242, 1254, and 1260, respectively (1571).

d) Used sorption coefficient $K_p = 0.001\ K_{oc}$.

the fill. The isomer distribution pattern of PCBs at the surface was different from that of Aroclor® 1254, reflecting the preferential loss of the lower chlorinated biphenyls due to weathering and degradation.

A second spill of 1500 gallons of askarel (Aroclor® 1254/chlorinated benzene solution) also resulted in extensive vertical and

horizontal soil contamination, as well as some ground-water contamination (1580). As in the other case, distribution in the soil/clay was non-uniform. Extensive rainfall following this particular spill also resulted in significant transport of Aroclor® 1254 with surface runoff. Both of these spills involved large quantities of askarel (Aroclor® 1254 in chlorobenzene solvent), and the observed contamination patterns may result from saturation conditions in the topsoil and migration of a separate oily liquid phase.

52.2.1.2 Sorption on Soils

Adsorption to soils and sediments is the major fate process affecting PCBs in the environment. PCB sorption has been studied and reviewed in a number of reports (10,1588,1589,1590,1534,1591,1592). In general, the rate of adsorption by soil materials was found to be rapid and conformed to the Freundich adsorption equation (1583,1596); adsorption capacity was highly correlated with organic content (1594,1596,1592), surface area (1596), and clay content (1594,1595) of the soil materials; PCBs were reported to be unable to penetrate into the inner surfaces of clay materials (1592). Desorption of sorbed PCB is not expected to be rapid (1593).

Distribution coefficients for PCBs on suspended solids in Saginaw Bay have been reported to range from 4×10^4 to 9×10^4 (1591). Representative partition coefficients for PCBs on actual soil materials are given in Table 52-3. In general, higher chlorinated isomers are more strongly sorbed; however, preferential adsorption is also dependent on ring position of the substituted chlorine (1592); values for K_{oc} range from approximately 10^5 for dichlorobiphenyl to 10^6 for octachlorobiphenyl (611).

Experimental studies (1583) on the mobility of Aroclor® 1242 and 1254 in soil materials indicate that these PCBs were adsorbed strongly and remained immobile when leached with water or aqueous leachate from a waste disposal site. However, they were found to be highly mobile when leached with carbon tetrachloride. The mobilities of the PCBs were highly correlated with their solubilities in the leaching solvent and the organic content of the soil material. PCB mobility data, expressed as the ratio of the distance the PCBs moved to the distance the solvent traveled (R_f), are presented in Table 52-4. It should be noted that even with carbon tetrachloride, a high percentage of the PCBs were retained on the soil while some moved with the solvent front.

Additional studies were performed by the same authors using different solvents and varying amounts of water; these data are presented in Table 52-5. Relatively small amounts of water (9%) in methanol were shown to significantly reduce the mobility of PCBs compared to the mobility in the pure solvent.

In summary, the available data indicate that sorption of PCBs, particularly the higher chlorinated biphenyls onto soil materials, will be rapid and strong. In the absence of organic solvents, leaching is

TABLE 52-3

EQUILIBRIUM PARTITION COEFFICIENTS FOR PCBs

Aroclor®	Matrix	K	Organic Content (%)	Ref.
1254	Illite	1.4×10^4	NA	1595
	Chlorite	1.0×10^4	NA	
1242	Sand	22	<0.01	1592
	Montmorillonite Clay	172	0.9	
	Silt loam	532	4.3	

not expected to be important, and PCBs are expected to be immobile in the soil/ground-water system; PCBs will be much more mobile in the presence of organic solvents. In the case of large spills of PCB/solvent mixtures, the soil and aqueous phases may become saturated resulting in a separate oily phase which may be more mobile.

52.2.1.3 Volatilization from Soils

Transport of PCB vapors through the air-filled pores of unsaturated soils is not expected to be a rapid transport pathway. Modeling results indicate that a very small fraction of PCB loading will be present in the soil-air phase. On the other hand, volatilization (mostly from aqueous systems) and atmospheric transport are thought to account for the widespread, almost ubiquitous, distribution of PCBs in the environment. Several studies (1589,1597,1598,1600) have shown that vapor phase transport can be a significant process for loss of PCBs from water bodies. Adsorption to organic matter, however, has been shown to compete strongly with volatilization. Adsorption onto suspended sediment has been presented as an explanation for the lower rates of volatilization exhibited for natural water bodies compared to estimated rates (10). Volatilization from soil was reported to be slow compared to volatilization from sand or PCB solution (1601).

Calculated half-lives for the volatilization of Aroclor® 1242, 1248, 1254, and 1260 from 1 mm water column have been reported to range from 9.5 hours to 12.1 hours (1602); other authors have reported half-lives on the order of 3-4 hours for di- and tetrachlorobiphenyls (1597). Volatilization of Aroclor® 1260 from river water was reported to be only 67% after 12 weeks; after addition of sediment, the loss dropped to 34% after 12 weeks (1599,1603). The Henry's law constants and volatilization half-lives do not vary widely with degree of chlorination of the PCBs.

TABLE 52-4

MOBILITY OF AROCLOR® 1242 AND AROCLOR® 1254 IN SEVERAL SOIL MATERIALS WITH VARIOUS LEACHING SOLVENTS

Soil Material	Organic Content (%)	R_f VALUES					
		H_2O		Du Page Leachate		CCl_4	
		1242	1254	1242	1254	1242	1254
Ava silty clay loam	1.2	.02	.02	.02	.02	1.00	.96
Bloomfield loamy sand	0.2	.03	.03	-	-	-	-
Catlin silt loam	4.7	.02	.02	.04	.04	1.00	1.00
Catlin loam	0.6	.02	.02	.03	.03	1.00	1.00
Cisne silt loam	1.3	.03	.02	.03	.02	1.00	1.00
Coal char (1200 F)	74	.03	.03	.04	.04	1.00	1.00
Drummer Silt loam	2.2	.03	.03	-	-	1.00	1.00
Flanagan silt loam	2.6	.02	.02	.06	.05	1.00	1.00
Ottawa silica sand	<0.01	.03	.03	.03	.03	1.00	1.00

Source: Griffin and Chian (1583)

TABLE 52-5

MOBILITY OF AROCLOR® 1242 AND AROCLOR® 1254 ON SILICA-GEL TLC PLATES USING VARIOUS LEACHING SOLVENTS

	R_f VALUES	
	Aroclor® 1242	Aroclor® 1254
D.I. H_2O	0.15	0.15
DuPage leachate	0.15	0.15
80% H_2O and 20% Acetone	0.09	0.06
Acetone	1.00	1.00
15% H_2O and 85% Methanol	0.79	0.79
9% H_2O and 91% Methanol	0.80	0.83
Methanol	1.00	1.00
Benzene	0.99	0.95
Carbon tetrachloride	1.00	1.00

Source: Griffin and Chian (1584)

The available data indicate that due to low water solubility, volatilization of water-borne PCBs not sorbed to sediment or suspended solids may be significant; when sorbed to soils/sediments, volatilization will be drastically reduced. However, since other fate and transport processes in the soil environment are relatively slow, volatilization of PCBs sorbed on surface soils may occur. Elevated airborne concentrations of PCBs have been measured near PCB disposal areas (1600).

52.2.2 Transformation Processes in Soil/Ground-water Systems

PCBs have been reported to be strongly resistant to chemical degradation by oxidation or hydrolysis. However, they have been shown to be susceptible to photolytic and biological degradation (10). Baxter and Sutherland (1572) have shown that successive biochemical and photochemical processes contribute to the degradation of PCBs in the

environment. Experimental results indicate that the highly chlorinated PCBs can be photolytically degraded, resulting in the formation of lower chlorinated species and substituted products, as well as potential formation of biphenylenes and chlorinated dibenzofurans (1573,1574,1575,1576); the presence of oxygen retards the photolytic degradation of PCBs.

There is some doubt as to the applicability of these photolysis experiments to environmental conditions, since they were generally carried out in organic solvents, often in the presence of other additives. However, since the rate of photolytic dechlorination is greatest for the highly chlorinated species (1576) (i.e., those species that are most resistant to biodegradation), photolytic degradation, although slow, may be a significant transformation process for these molecules. Furthermore, since they are rapidly adsorbed to soils, these highly chlorinated PCBs may be concentrated in the surface layers and their actual photolysis rates may be higher than expected.

Microbial degradation has been reported to be an important transformation process for PCBs (10,1577,1578,1579,1581,1582,1583,1584, 1585). In general, the lower chlorinated PCBs were more easily degraded than the higher chlorinated species. Position of chlorine substitution on the biphenyl molecule also affected the rate of PCB degradation. Biodegradability of PCBs has been reported to be a function of the number of carbon-hydrogen bonds available for hydroxylation by microbial oxidation; adjacent unchlorinated carbons have been shown to facilitate metabolism through formation of arene oxide intermediates (10). Both aerobic oxidative biodegradation and anaerobic dechlorination have been identified as PCB transformation processes in Hudson river sediments (1585). Composting studies (1582) indicate that aerobic systems exhibited greater PCB reductions than anaerobic systems (42 to 48% vs. 18 to 28% reduction after two weeks).

The biodegradation of Aroclor® 1016, 1242, 1254, and 1260 is a function of their relative content of the lower chlorinated biphenyls. Aroclor® 1016 and 1242 are largely comprised of di-, tri-, and tetrachloro biphenyls, which have been shown to be biodegraded in microbial cultures, aquatic systems, and soils at fairly rapid rates (1583,10,1584,1582,1577,1579). Aroclor® 1254 and 1260 are largely comprised of higher chlorinated species and are expected to be resistant to biodegradation. In fact, Liu (1579) reported that an increase of chlorination from monochlorobiphenyls to predominantly trichlorobiphenyls (Aroclor® 1016 and 1242) and pentachlorobiphenyls (Aroclor® 1254) resulted in a corresponding decrease in degradation from 100% to 29% and 19%, respectively; similar results were reported by other authors (1586). In an experiment with reservoir sediment, Aroclor® 1254 was degraded approximately 50% in six weeks (846). Using an acclimated semi-continuous activated sludge experiment with 48-hour exposure, degradation rates of 33%, 26%, and 19% were determined for Aroclor® 1016, 1242, and 1254, respectively (1586).

A study of the fate of Aroclor® 1254 in soil and ground water after an accidental spill showed essentially no reduction in Aroclor® 1254 concentration due to biodegradation after two years (1580). On the other hand, other authors (1584) reported moderate biodegradation of Aroclor® 1254 in soils (40% degraded in 112 days) and no degradation of Aroclor® 1260 (primarily hexa- and hepta-chlorobiphenyls). The presence of the lower chlorinated biphenyls has been shown to actually increase the rate of biodegradation of the higher PCBs through co-metabolism (1581,1579,1583,1587).

In summary, most studies have reported substantial PCB degradation in aqueous solutions; biodegradation rates are greatest for the lower chlorinated species. While adsorption of PCBs by soil and competition by native soil organisms may alter the degradation rate, several authors have reported substantial PCB degradation in soil systems (1582,1583,1584). Mixed cultures of PCB-degrading microbes have been isolated from PCB-contaminated soils (1583), suggesting that PCBs will be degraded to some extent in the environment.

52.2.3 Primary Routes of Exposure from Soil/Ground-water Systems

The above discussion of fate pathways suggests that PCBs in general have a low volatility, are very strongly sorbed to soil, and have a high potential for bioaccumulation. These fate characteristics suggest several potential exposure pathways.

Volatilization of PCBs from a disposal site is not likely to represent an important exposure pathway under most conditions. Tofflemire and Shen (1808) concluded, however, that volatilization of PCBs was of greater concern than ground-water contamination for a number of open PCB dump sites and dredge spoil sites along the upper Hudson River. Some control programs had been initiated to prevent ground-water contamination.

Drinking water contamination resulting from the migration of PCBs with ground water may occur, although PCBs are relatively immobile in soil. Mitre (83) reported that PCBs have been found at 58 of the 546 National Priority List (NPL) sites. They were detected in 32 sites in ground water, 48 sites in surface water and 4 sites in air. In the National Organics Monitoring Survey conducted in 1976-77, PCBs were found in 6% of the finished ground-water supplies at levels of 0.1 μg/L (992). One state also reported that PCBs were detected in 32 of the 163 ground-water supplies sampled, with concentrations as high as 1.27 μg/L (992). These data do indicate that ground-water contamination by PCBs can occur in some situations.

The movement of PCBs in ground water or, more likely, their movement with soil particles may result in discharges to surface waters. As a result, ingestion exposure may occur through the use of surface waters as drinking water supplies, and dermal exposures may result from the recreational use of surface waters. More importantly, however, is the potential for uptake of PCBs by aquatic organisms or

domestic animals. The high bioconcentration factor and the persistence of PCBs suggest that these can be important exposure pathways. In fact, such contamination has been documented in a number of cases. (1801).

52.2.4 Other Sources of Human Exposure

As a result of their widespread use over a number of years, PCBs are now considered ubiquitous pollutants. Results from the National Human Adipose Tissue Survey (NHATS) show that in 1981 greater than 99% of the U.S. population have measurable levels of PCBs in fatty tissues (1807).

Exposure sources for PCBs are numerous. As mentioned above, PCBs were found to some extent in ground-water drinking water supplies. They were also found in 2% of finished surface water systems at concentrations less than or equal to 1.4 μg/L (992).

PCBs are also commonly found in air, resulting in low level inhalation exposures in most locations. Eisenreich et al. (1810) reported ranges of concentrations for remote areas of 0.02-0.5 ng/m^3, 0.1-2 ng/m^3 for rural areas, and 0.5-30 ng/m^3 for urban areas. For the most part, the measurements most closely represent Aroclor® 1242, 1248, and 1254 (1806).

As for many other persistent organic compounds, PCBs in food can represent a significant source of exposure. Gartrell et al. (1244) reported average dietary intakes of PCBs ranging from ND to 0.099 μg/kg of body weight/day for infants and toddlers over the years 1976-1979. Adult intakes ranged from < 0.0001 to 0.027 μg/kg/day over the same time period (1245). The largest sources of exposure are meat, fish and poultry. Other specialized studies of the components of the diet have taken place. For example, Frank et al. (1247) reported 0.033 ppm PCBs in bovine milk fat and various authors have reported PCBs in mother's milk (1805,1802,1803). In addition, fish contamination problems have occurred in a number of locations. The National Fish Monitoring Program collected fish from 107 stations in major rivers around the U.S. and in the Great Lakes. A total of 315 composite samples were collected. PCBs were reported at 94% of the stations sampled; the wet-weight mean residue concentration reported was 0.53 μg/g total PCBs. Residues similar to Aroclor® 1260 were most prevalent, and Aroclor® 1254 and 1248 were less prevalent (1800).

Direct exposure to PCBs has occurred in the past. For example, Schecter (1804) reported the contamination of an office building by PCBs resulting from overheating of an electrical transformer.

52.3 HUMAN HEALTH CONSIDERATIONS

52.3.1 Animal Studies

52.3.1.1 Carcinogenicity

Among the PCB mixtures tested in chronic oral exposure studies with laboratory animals, two of interest were found to induce liver neoplasms; Aroclor® 1254 and Aroclor® 1260. There are no data available for Aroclor® 1016 or Aroclor® 1242.

IARC has determined that although there is insufficient evidence to confirm PCBs as human carcinogens, there is sufficient evidence of the carcinogenic effect of PCBs in animals. Based on the IARC rating system, PCBs were classified as Group 2B compounds (1250).

Aroclor® 1016 and Aroclor® 1242

No data on carcinogenicity are available.

Aroclor® 1254

Kimbrough and Linder (1240) fed 300 ppm Aroclor® 1254 to male BALB/cJ mice for 11 months or for 6 months followed by the control diet for the remaining 5 months of the study. In the mice fed Aroclor® 1254 for 11 months, hepatomas were observed in 9/22 (41%) survivors and adenofibrosis and enlarged livers in all 22 survivors. Examination of livers of mice treated for 6 months and then allowed to recover for 5 months showed slight-to-moderate diffuse, interstitial fibrosis. One mouse developed a small hepatoma. No hepatic lesions were observed in 58 control mice.

In a study conducted by the National Cancer Institute (NCI) (1283,1193), male and female F344 rats were administered 0, 25, 50 or 100 ppm Aroclor® 1254 daily for 104-105 weeks. Clinical signs of toxicity including alopecia, amber-colored urine, facial edema, exophthalmos and cyanosis were observed in the 50 or 100 ppm Aroclor® 1254 groups. An increased incidence of lymphoma and leukemia combined was seen in males (12.5% for control animals, 8.3% for the low dose animals, 20.8% for the 50 ppm group and 37.5% for the high dose group). However, comparisons of each treatment group with the matched controls were not statistically significant and the tumors could not clearly be related to Aroclor® 1254 treatment. Hepatocellular adenomas and carcinomas were found in Aroclor® 1254 treated animals but not in control animals. Furthermore, a dose-related incidence of nodular hyperplasia appeared in all animals treated with Aroclor® 1254 but this trend was not statistically significant. Adenocarcinomas of the stomach, jejunum or cecum were observed in 2 treated male and 2 treated female rats as well as a carcinoma in a treated male. These lesions, although not statistically significant, appear to be treatment-related since no control animals developed these types of tumors. NCI concluded that Aroclor® 1254 was not carcinogenic in F344 rats but that

the high incidence of hepatocellular proliferative lesions in both male and female rats was Aroclor® 1254-related. Also, the tumors found in the gastrointestinal tract may also have been due to Aroclor® 1254 administration.

Morgan et al. (1194) limited their investigation to the gastric effects of PCBs. Male and female F344 rats were fed a diet containing 0, 25, 50 or 100 ppm Aroclor® 1254 for 26 months. Rats fed 50 or 100 ppm Aroclor® 1254 had a lower body weight than the control animals and developed signs of PCB toxicity. The incidence of stomach lesions increased as the dietary intake of Aroclor® 1254 increased. In control animals, 6.4% developed lesions while in the 25, 50 and 100 ppm PCB-treated groups, 10.4%, 16.7% and 35.4% developed lesions, respectively. A total of 6 definite and 2 suspected, but not confirmed adenocarcinomas developed in Aroclor® 1254 fed rats. Adenocarcinomas rarely occur in F344 rats. Morgan et al. concluded that Aroclor® 1254 incorporated into the diet for 2 years induced intestinal metaplasia which resulted in the probable induction of adenocarcinomas in F344 rats.

Aroclor® 1260

Norback and Weltman (1169,1170) fed Sprague-Dawley rats Aroclor® 1260 in the diet at a level of 100 ppm for 16 months, followed by 50 ppm for 8 months and finally, a control diet for 5 months. Hepatocellular tumors developed in 95% of the female rats and 15% of the male rats. Seventy percent of the females also developed various forms of bile duct tumors; only 37% of the males developed such tumors. Norback and Weltman concluded that Aroclor® 1260 was a complete liver carcinogen acting as both an initiator and promotor.

Kimbrough et al. (1171) studied the effect of this Aroclor® congener in female Sherman rats fed 0 or 100 ppm Aroclor® 1260 for 21-22 months. Hepatocellular carcinomas developed in 14.13% of the treated rats and in only 0.58% of control animals. Treated rats also developed a high incidence of neoplastic liver nodules (79.5% vs. zero in control animals) and hepatocellular alterations (98.9% vs. 16.2% in control rats).

52.3.1.2 Mutagenicity

Aroclor® 1016

No data were found specific to the mutagenic activity of this congener.

Aroclor® 1242

No mutagenic activity was evident for Aroclor® 1242 in a mammalian cell assay using V79 Chinese hamster cells (1180). Green et al. (1181) studied the effect of Aroclor® 1242 on bone marrow cells in Osborne-Mendel rats. A single dose of 1250, 2000 or 5000 mg/kg or a

multiple dose of 500 mg/kg/day Aroclor® 1242 for 4 days was administered. No reduction of mitotic indices or increase in chromosomal abnormalities were observed. Cytogenic abnormalities were found in treated rats, however the increase was not statistically significant.

Green et al. (1182) also conducted a dominant lethal test on Osborne-Mendel rats. Male rats were treated with a single oral dose of 625, 1250 or 2500 mg/kg or multiple doses of 125 or 250 mg/kg/day Aroclor® 1242 for 5 days, then bred to untreated females. No significant effects were observed on embryo implantation or lethality in any of the treatment groups.

Aroclor® 1254

Doses in excess of 100 mg/kg Aroclor® 1254 did not produce any enhancement of mutagenic activity in strains TA98 and TA100 of Salmonella typhimurium (1251). Aroclor® 1254 also did not induce unscheduled DNA synthesis in cultured rat hepatocytes or chromosomal aberrations in cultured human lymphocytes (1457). Rats orally administered 75, 150 or 300 mg/kg Aroclor® 1254 daily for 5 days or fed 25 or 100 mg/kg Aroclor® 1254 for 70 days, did not show an increase in dominant lethal mutations (1457).

Aroclor® 1260

No evidence of mutagenic activity was shown in a dominant lethal assay (12).

52.3.1.3 Teratogenicity, Embryotoxicity and Reproductive Effects

Numerous publications have demonstrated the ability of PCBs to cross the placenta and accumulate in fetal tissues. However, indications of structural malformations, genetic changes or other teratogenic effects have been few; most oral exposure studies have been negative. Reproductive capacity, however, can be notably depressed with PCB exposure, particularly in females.

Aroclor® 1016

Adult female rhesus monkeys were fed diets containing 0, 0.25 or 1 ppm Aroclor® 1016 daily throughout gestation and throughout a 4-month nursing period (total exposure of 21-22 months) (1186). There was no significant difference in the number of breeding attempts between the control and and treated groups and all monkeys delivered viable offspring. Birth weights of the offspring born to the 1 ppm treated monkeys were significantly lower than the controls (422 g vs. 512 g for controls) but no other significant differences were noted between treated and control offspring. The PCB content in the skin of offspring at birth was 1.54 ppm for controls, 1.65 ppm for the 0.25 ppm treated group and 3.37 ppm for the 1 ppm treated group. After nursing for 4 months, mesenteric fat tissue of offspring of treated mothers

contained 10.3 and 27.5 ppm Aroclor® 1016 in the 0.25 and 1 ppm treated animals, respectively. Eight months post-weaning, mesenteric fat PCB levels had dropped to 1.96 and 3.75 ppm, respectively. This study indicates that Aroclor® 1016, even when administered at doses low enough not to cause toxicity in the adult, accumulates in the adipose tissue and subsequently is transferred to the offspring via the placenta and the milk.

Aroclor® 1242

No deleterious effects on reproduction resulted in rats fed 1 or 10 ppm Aroclor® 1242. However, rats fed 100 ppm had reduced mating indices in second generation animals (1460). In addition, Keplinger (1461) also observed a reduced survival rate in rats fed 100 ppm Aroclor® 1242.

Chickens fed 20 mg/kg Aroclor® 1242 in the diet showed reduced hatching. Abnormalities included edema and unabsorbed yolk (1458). Chickens fed 100 ppm Aroclor® 1242 had decreased egg production and reduced hatching (1460).

Aroclor® 1254

Severe reproductive failure occurred in female minks following oral administration of 1, 5 or 10 ppm of Aroclor® 1254 for 4 months. The rates of conception were 8/10, 3/12 and 0/6, respectively, compared to 11/11 in controls. Decreased fetal survival was also evident; the incidences of live births were 3/9 (33%), 33/43 (77%) and 56/66 (85%) for the 5 ppm, 1 ppm and control groups, respectively (1191,1187).

Truelove (1160) investigated the teratogenic and embryotoxic effects of ingested Aroclor® 1254 on cynomolgus monkeys. Beginning on day 60 of gestation, two pregnant monkeys were given 100 µg/kg/day, one monkey was given 400 µg/kg/day Aroclor® 1254 and one monkey served as a control. Treatments were administered daily throughout gestation and post-partum. Offspring of both monkeys fed 100 µg/kg Aroclor® 1254 were delivered still-born. The 400 µg/kg treated monkey delivered a live offspring, but both the birth weight and the weight gain for the next 130 days was significantly reduced. The offspring died on day 139 due to impaired immunological function. Autopsy revealed acute bronchopneumonia. The only maternal clinical sign of toxicity was the loss of fingernails in one of the 100 µg/kg treated monkeys and the 400 µg/kg treated monkey. All treated adult monkeys also showed signs of diminished immunologic capacity on day 50 post-partum (148 days of treatment). At autopsy, the PCB concentrations of the liver and kidney in the 400 µg/kg treated dam were 7.17 ppm and 1.88 ppm, respectively. The nursing infant of this dam had a liver PCB concentration of 47.94 ppm and a kidney concentration of 23.72 ppm. PCB content in the adipose tissue of the exposed infant increase from 35 ppm at 5 days of age to 483 ppm on day 139 when the infant died. These high accumulations of PCBs in the infant resulted from the transfer of PCBs from the mother to the infant via the milk.

Spencer (1196) fed female albino rats 0, 25, 50, 100, 200, 300, 600 or 900 ppm Aroclor® 1254 daily on days 6 through 15 of gestation. No embryonic resorption was observed by day 12 in females fed up to 900 ppm Aroclor® 1254. Maternal toxicity was seen at 600 and 900 ppm levels. Fetotoxic effects were present in the form of decreased fetal survival rates at levels of 300 ppm and above and reduced birth weights at 100 ppm or more.

Male and female Wistar rats were given drinking water containing 70 ppm Aroclor® 1254 for 9 weeks. After the first week of treatment, treated rats were allowed to mate with control rats. No adverse effects on the fertility of male rats exposed to Aroclor® 1254 were noted. Several treated females died during the 7th week and by the 9th week, fetal resorption was obvious. By the end of the 9th week, both the treated males and females were returned to ordinary tap water. Biochemical studies revealed that Aroclor® 1254 elevated the mixed function oxidase activity. This increase persisted even after exposure to Aroclor® 1254 was terminated and rats were given tap water (1197).

Watanabe and Sugahara (1277) examined the teratogenic effects of PCBs injected subcutaneously into pregnant ddY mice on days 6-16 of gestation. Mice received 1-5 mg Kaneclor® 500 (52-54% Cl) daily. The total dose was 10-50 mg of PCB per pregnant mouse. Examinations of fetuses on day 18 of gestation revealed a significant dose-related incidence of cleft palate. Of 1765 control fetuses, none developed cleft palate while 0.2, 0.9, 3.6, 3.9 and 5.8% of the fetuses in the 10, 20, 30, 40 and 50 mg/mouse treatment groups, respectively, did develop cleft palate. Mice given a total of 25 or 100 mg PCB over gestational days 6-11 also showed an increase in the incidence of cleft palate (1.2 and 17.9%, respectively). Since this particular defect has not been reported in feeding studies, the route of administration may play a role.

PCBs have the ability to induce the liver mixed function oxidase system which results in a faster than normal rate of metabolism of endogenous substrates such as steroid hormones. The decrease in steroid hormones is expected to affect reproduction. To investigate this effect, Brezner et al. (1162) orally administered 0 or 10 mg/kg Aroclor® 1254 daily for at least 30 days to female Wistar rats that had just delivered litters. The only PCB exposure to the pups was via the mother's milk. Over the 4-week dosing period, maternal rats experienced a significant weight loss. Rats exposed for 6 weeks exhibited a significantly prolonged estrous cycle (67.3% of the treated rats were affected vs. 6% in control rats). Receptivity of females was decreased in the treated rats, i.e., sperm was present in the vaginal smears of only 79.5% of the treated females vs. 100% in the control females. Among pregnant females, 89% of the treated females completed pregnancy vs. 100% of control females. Vaginal bleeding occurred in 71% of treated females on days 10-15 of gestation and 71% of the treated females delivered 1-3 days late while only 21% of controls showed vaginal bleeding and 10% delivered late. The average litter size of PCB-treated rats was smaller than normal (6.5 vs. 10 pups in

the control group) and an average of 1.5 pups/litter were dead in the treated group. Development of the pups from treated dams was slower and an increase in mortality was seen before weaning. In female offspring of the Aroclor® 1254-treated group, vaginal opening occurred at an earlier age (39 days vs. 43 days in control animals) and there was a significant delay in the appearance of first estrus (8 days vs. 4.4 days in the control animals). Other reproductive parameters were not affected. Once PCB exposure ceased, body weight reached control values within 2-3 months and a reversal of the adverse reproductive effects was seen.

Sager and Girard (1161) expanded the findings of Brezner et al. (1162) and reported the results of early postnatal exposure of rats to Aroclor® 1254 on reproductive performance later in life. Mothers of the test group were fed 0, 8, 32 or 65 mg/kg Aroclor® 1254 on days 1, 3, 5, 7 and 9 of lactation. Offspring were then allowed to mature to either young or mature adults. Vaginal opening and first estrus were delayed in offspring exposed to PCBs. In the mature adult group, the incidence of pseudopregnancy in animals exposed to 32 mg/kg early in life was markedly increased. In the high dose group, implantation was significantly inhibited. Also, mature adults in the 32 or 65 mg/kg exposure groups exhibited increased embryonic deaths. Sager and Girard concluded that rats exposed to PCBs early in life through mother's milk experienced reproductive dysfunction in adult life despite decreasing PCB levels in the body tissue.

Sager (1163) studied the early postnatal effect of PCBs on adult male reproduction in Holtzman rats. Lactating dams were orally administered 0, 8, 32 or 64 mg/kg Aroclor® 1254 on days 1, 2, 3, 5, 7 and 9. Males were weaned on day 23, allowed to mate beginning on day 130 and autopsied on day 165. Any pregnant females resulting from the mating period were autopsied on day 11-12 of gestation. Examination of the pregnant females revealed a decreased number of implanations and significantly fewer surviving fetuses. The resorption rate was significantly increased and significantly fewer females became pregnant after exposure to the treated males. Treated males showed a reluctance to mate. Prostate weight was significantly lower in treated male offspring. Seminal vesicle weight was also decreased in males exposed to the top 2 dosages while testes weight was significantly increased. Sager (1163) postulated that PCB exposure during the critical period of post-natal development could disrupt the normal hormonal environment which in turn, could affect reproductive functioning in the adult male.

Aroclor® 1260

Aroclor® 1260 was fed to rats at a concentration of 0, 1, 10 or 100 ppm. No effect was seen at the 1 or 10 ppm treatment level. Ingestion of 100 ppm Aroclor® 1260 resulted in an increased incidence of stillborns (1460).

52.3.1.4 Other Toxicologic Effects

A number of issues arise with regard to an assessment of the toxicity of various Aroclor® congeners. Studies have shown that the degree of toxicity depends on both the number and location of the halogen atoms. In addition, the relationship between dose and time must be considered since a lower dose may be able to produce a given level of intoxication if exposure is extended, due to the accumulative nature of these compounds. Finally, the type of toxic reaction or the dose required to elicit a reaction may vary considerably with different species. In general, non-human primates are more susceptible to PCB intoxication than rabbits and rats; females are generally more susceptible than males, and the young are generally more susceptible than adults.

52.3.1.4.1 Short-term Toxicity

In most species, the first sign of acute intoxication with PCBs is usually weight loss or reduced weight gain. Severely intoxicated rats have exhibited ataxia, diarrhea and lack of response to pain stimuli; histopathological changes are observed primarily in the liver and kidney. The median time to death is usually 2-3 weeks for small laboratory animals. Oral LD_{50} values in rats range from 4000 to 11,000 mg/kg, with toxicity generally decreasing with increased chlorination (1178).

Aroclor® 1016

Alvares et al. (1275) intraperitoneally administered 50 mg/kg Aroclor® 1016 to male Sprague-Dawley rats for 4 days. Rat livers were examined 24 hours after the last treatment. Aroclor® 1016 was shown to induce a significant increase in liver microsome protein. The cytochrome P-450 content was doubled and the ethylmorphine N-demethylase activitity was shown to triple while benzo(a)pyrene hydroxylase induction increased only 50% over control levels.

Aroclor® 1242

Bruckner et al. (1279) orally administered 2.5, 4 or 6 g/kg Aroclor® 1242 to male Sprague-Dawley rats. After 4 hours of dosing, animals in all treatment groups exhibited loose stools, diminished exploratory behavior and decreased response to pain stimuli. Animals also developed an unusual stance characterized by an arching of the back and an elevated posterior portion of the trunk. Within the next 24 hours, rats treated with 6 g/kg Aroclor® 1242 developed profuse diarrhea, adipsia (avoidance of drinking), oliguria, anorexia, erythema of the limbs, and weakness. Ataxia, coma and death followed. Progressive dehydration was evident as shown by a decreasing body weight and increasing packed cell volume. Animals in the 2.5 g/kg treatment group gradually improved and only showed slight signs of oliguria and anorexia 72 hours after dosing. Blood analysis of rats given 4 g/kg Aroclor® 1242 showed a greater proportion of poly-

morphonuclear leukocytes than in control rats. Also, many erythrocytes were crenated (scalloped or notched). Necropsy revealed minute, pale foci in the liver. Microsopic examination showed fatty deposits and necrotic foci of vacuolated hepatocytes. Widely scattered areas of vacuolated tubular epithelial cells similar to those observed in the hepatocytes were found in the kidney. All other tissues were normal.

Aroclor® 1254

Carter (1164) investigated the effect of Aroclor® 1254 on liver weight in male Fischer rats fed 0 or 20 ppm Aroclor® 1254 in the diet for either 1, 2, 4, 8 or 14 days. There was no significant difference in cumulative food consumption between the control group and the 20 ppm group regardless of the duration of treatment and body weights were comparable. However, a significant increase in liver weight was noted on day four of treatment which continued throughout the experiment. This increase in liver weight was due to the toxic effect of Aroclor® 1254 on centrilobular hepatocytes which resulted in hypertrophy of the cells.

Carter and Mercer (1198) examined the toxic effect of Aroclor® 1254 as distinguished from the effects of decreased food consumption associated with high PCB exposure. Male Fischer rats were fed 0, 150 or 350 ppm Aroclor® 1254 for 10 days. Based on the quantity of food consumed in each treatment group, additional groups of rats were fed the same amount of food minus Aroclor® 1254. No significant change in kidney weight was observed. Spleen weight was significantly decreased in both the 350 ppm treated rats and in the pair-fed controls, indicating that the depression in food consumption was responsible for the decreased spleen weight and not the PCB. Aroclor® 1254 did have an effect on liver weight. Animals in the 150 or 350 ppm group both showed a statistically significant increase in liver weight over both the control and pair-fed animals.

Carter (1165) also investigated whether low levels of Aroclor® 1254 administered over relatively short periods of time would induce the hypercholesterolemia usually observed after long term exposure to high levels of PCBs. Male Fischer rats were fed diets containing 0, 2, 4, 8, 16 or 32 ppm Aroclor® 1254 for 4 days. No effect on body weight gain, final body weight or the total food consumption was observed. Liver weights were significantly increased in the animals fed 16 or 32 ppm Aroclor® 1254 for the 4-day test period and serum cholesterol levels were significantly elevated in the 8, 16, 32 ppm treated animals. Serum high density lipoprotein cholesterol levels were elevated in all PCB treated groups but significantly elevated only in the 32 ppm treated group.

Aroclor® 1260

No compound specific data were found on acute toxic effects of Aroclor® 1260.

52.3.1.4.2 Chronic Toxicity

Aroclor® 1016

The effect of chronic exposure to Aroclor® 1016 on immunological function was studied by Silkworth and Loose (1188). C57BL/6 mice were fed a diet containing 167 ppm Aroclor® 1016 for 3, 6, 13, 24 or 40 weeks. Aroclor® 1016 did not consistently alter lymphocyte function but did produce transient alteration. Silkworth and Loose (1188) suggested that Aroclor® 1016 did not interfere with the effector phase of the cell-mediated immune response but implicated the B-cells as possible target cells in PCB-induced humoral immunotoxicity. The PCB-altered humoral immunity also may indicate that PCBs can express selective toxicity on different portions of the immune system, with a more profound influence exhibited by of antibody-mediated immunity than cell-mediated immunity.

Aroclor® 1242

McNulty (1183) reported results from feeding rhesus monkeys 3-800 ppm Aroclor® 1242 for 27-245 days. The first signs of toxicity were usually decreased activity and depressed appetite. The face became swollen and the eyelids were red and puffy. A fine papular roughening of the skin appeared on the face, trunk and extremities and body hair was lost in an irregular fashion. Overall weight loss was as much as 35% before animals became profoundly depressed and died. Autopsy revealed mucous metaplasia of the gastric mucosa and squamous metaplasia of the sebaceous glands. Atrophy of the thymus gland was also seen and in some cases the cortical thymocytes almost completely disappeared. The liver was enlarged, but hepatocytes appeared normal. Since these changes occurred 6-13 months after a short, high level exposure (level not specified) to Aroclor® 1242, McNulty speculated that the pathological effects of PCBs persist until the stored PCBs are finally metabolized and excreted. Thirteen months after a 40 day exposure to dietary Aroclor® 1242, cysts of the mandible and maxilla were still present. These cysts are thought to form when the specialized enamel-secreting epithelium investing the crowns of unerupted teeth is converted to nonkeratinizing desquamating oral epidermis. The castoff squamous cells then create the cysts around the unerupted teeth resulting in severe deformation of the jaw (1184).

Aroclor® 1254

An accidental case of Aroclor® 1254 poisoning occurred in a group of monkeys. Six weeks after being transferred to a newly constructed primate building, 53/249 monkeys died of an unusual form of gastropathy. Autopsies revealed diffuse mucinous gastric hyperplasia. Clinical signs in all affected animals were similar and included diarrhea, weakness, gingivitis, emaciation and dehydration. Alopecia and conjunctivitis were also frequently observed. An additional 32 monkeys exhibited these clinical signs before death, but no gastric hyperplasia. Anorexia and respiratory distress occurred frequently in

these animals. When gastric hyperplasia did occur, it usually lasted 4-8 weeks and did not respond to any type of treatment. Microscopic evaluation of the affected areas revealed glandular hyperplasia and cysts. Analysis of tissue revealed Aroclor® 1254 present in the liver and adipose tissues at up to 14 ppm. It was later discovered that paint and concrete samples from the primate housing unit contained 25 ppm Aroclor® 1254 and was the cause of the illness. Once the animals were removed from the PCB source, they began to recover (1167).

Miniats et al. (1168) studied the effects of Aroclor® 1254 in germ-free Yorkshire piglets fed 12.5, 25, 50 or 100 mg/kg Aroclor® 1254 daily until death. Clinical signs of toxicity included hepatitis, focal hepatic necrosis and cirrhosis, acute nephritis and nephrosis, erosion of the gastric mucosa, degeneration of the skeletal muscles and myocardium and lesions in the brain.

Aroclor® 1260

Vos and Beems (1278) studied the effects of Aroclor® 1260 applied to rabbit skin. One mL of 118 mg PCB-containing solution was dropped daily, 5 times a week for 38 days onto the shaved backs of female New Zealand rabbits. Microscopic examination of the Aroclor® 1260 treated animals revealed hyperplasia and hyperkeratosis of the follicular epithelium with the formation of comedo-like structures. These resulted from the plugging of the dilated hair follicles with keratin. Necroscopy of all animals that died or were killed on day 38 revealed a significant increase in liver and kidney weight. Liver lesions were present in all treated animals with periportal fibrosis being a common finding. Kidney damage was also found in all treated animals. Hydropic degeneration of the convoluted tubules was present in half of the animals while nuclear pycnosis (a thickening, structureless mass) and lyses of the tubular epithelial cells was present in all animals. There was a reduction in the number of germinal centers in the spleen and lymph nodes and atrophy of the thymus in the PCB-treated animals indicating an immunosuppressive effect. Vos and Beems concluded that PCBs are readily absorbed by the skin in quantities capable of causing similar systemic lesions of the liver, kidney and lymphoid tissue as seen during ingestion of PCBs.

52.3.2 Human and Epidemiologic Studies

52.3.2.1 Short-term Toxicologic Effects

PCBs are slowly metabolized compounds and toxic symptoms usually occur only after long-term exposure and bioaccumulation.

There are no data available on short-term human exposure to any of the Aroclor® congeners.

52.3.2.2 Chronic Toxicologic Effects

52.3.2.2.1 Yusho

The most notable example of the possible effects of PCB exposure in humans is the Yusho incident which occurred in Japan in 1968. Kaneclor® 400 (48% Cl) inadvertently leached into a commercial rice oil preparation. After a latent period of 5-6 months, symptoms began to manifest. It was initially estimated that the oil was contaminated with 1000-3000 ppm PCBs but re-analysis revealed the presence of 968 ppm PCBs and 8 ppm polychlorodibenzofuran (PCDF). The majority of people consumed about 200 μg/kg/day. Early symptoms of Yusho (literally "oil disease"), included enlargement and hypersecretion of the meibomian gland of the eye, swelling of the eyelids, pigmentation of the fingernails and mucous membranes, fatigue and nausea. These symptoms were followed by hyperkeratosis, darkening of the skin with follicular enlargement, acneform eruptions with secondary staphylococcal infection, edema of the arms and legs and bronchitis-like respiratory symptoms which persisted for years (1174).

As dermal and mucosal conditions improved after a few years post-exposure, evidence of various systemic disturbances became apparent. Most victims displayed neurological symptoms (e.g., headache, numbness in the limbs, hypoesthesia and neuralgic limbs). CNS damage was not apparent. A significant positive correlation was noted between PCB blood levels in Yusho victims and the severity of dermal lesions, ocular symptoms, elevated serum triglyceride concentrations, limb paresthesia and other symptoms (1178).

The majority of Yusho victims complained of persistent cough, sputum production and chronic bronchitis-like symptoms. Secondary respiratory infections were often noted, although no fever and little change in leucocyte count or erythrocyte sedimentation rate was seen (1280). Examination of 400 Yusho patients revealed respiratory symptoms including expectoration in 40% and wheezing in 2% of 289 non-smokers; the former (along with persistent coughing) appeared with the development of skin eruptions, while the latter appeared several months later. Other respiratory symptoms included bronchiolitis in many, and pneumonia or atelectasis in about 10% of the patients. The incidence and severity of the respiratory symptoms correlated well with the concentration of PCB in the blood and sputa. Viral or bacterial infection increased the severity of the respiratory symptoms and persisted in patients with blood PCB levels over 10 ppb.

Examination of organs of deceased Yusho victims revealed high levels of PCDF. Liver and adipose tissue samples of Yusho patients revealed 2-25 and 6-13 ppb PCDF, respectively, while no PCDFs were detected in unexposed volunteers. PCDFs were also shown to be retained in the body, particularly in the liver, much longer than PCBs. In fact, 2,3,4,7,8-penta-CDF was still present in the tissue of a patient 9 years after the poisoning incident (1174).

The ability of PCBs to cross the placenta and affect the fetus was evident in babies born to Yusho mothers. Of the 12 infants born in 1968 to 11 Yusho mothers and 2 non-Yusho women with Yusho husbands, 10 infants lived and 2 were stillborn. All infants had eye discharge. Nine of the ten live infants had dark greyish skin and 5 had greyish pigmentation of the gums and nails. One of the stillborn fetuses had marked hyperkeratosis, atrophy of the epidermis and cystic dilation of the hair follicles. Also, an increased melanin pigment was present in the blood cells and the epidermis. All newborns were small and the growth rate of the 10 infants was significantly slower than unaffected children. Teeth were erupted at birth and there was spotted calcification of the parieto-occipital skull, wide fontanels and sagittal suture along with facial edema and exophthalmic eyes (1192).

Miller (1199) also reviewed the effects of PCBs on infants of exposed mothers. A deep brown pigmentation of the skin (usually referred to as cola-colored skin) was the most prevalent symptom. Biopsy of the skin showed an increase in melanin and hyperkeratosis. The pigmentation cleared up within 2-5 months. Low birth weights were also a primary effect of PCB toxicity. The majority of infants had a thick white discharge from the eye and cysts of the meibomian gland. Some of the children exhibited severely swollen eyelids and facial edema. Gingival hyperplasia and teeth present at birth occurred in 16% of the infants investigated. The children with gum overgrowth and natal teeth eruption also had spotty calcification in the occipital region of the skull and a wide separation of the sagittal suture and large anterior and posterior fontanels (membrane covering the unossified space in the skull). These symptoms suggest an irregular calcification which may explain the large unossified areas of the brain and the reduced resistance of the mandible to erupting teeth.

52.3.2.2.2 Yu-Cheng

An incident similar to Yusho was reported in Taiwan in 1979 following consumption of rice oil contaminated with PCBs. The resulting disease was called Yu-Cheng (oil disease). Symptoms included acneform eruptions and follicular accentuation, pigmentation of the skin and nails, swelling of the eyelids and eye discharge, headache, nausea, and numbness of the limbs. Blood disorder included a decrease in red blood cells, an increase in white blood cells and a decrease in hemoglobin and γ-immunoglobin (1178).

Chang et al. (1281) measured B-cells to evaluate effects on humoral immunity and T-cells to test for effects on cell-mediated immunity in Yu-Cheng patients. Thirty patients were studied with an average blood PCB level of 45 ppb. PCB poisoning did not affect the total lymphocyte count or the number of B-cells. Suppressor T-cells were not affected, but helper T-cells were significantly decreased in Yu-Cheng patients (26.1% vs. 36.9% helper T-cells in control subjects) indicating a range in sensitivity of different lymphocytes to PCBs. Chang et al. concluded that cell-mediated immunity, as shown by decreased T-cell levels, was significantly correlated with PCB toxicity.

Chen et al. (1176) found that the severity of neuropathy was related to the concentration of PCB and PCB derivatives in the blood. The average blood level of PCB in 110 Yu-Cheng victims was 39 ppb. Sensory and motor nerve conduction velocities were shown to be significantly slower in PCB-intoxicated patients.

52.3.2.2.3 Occupational Exposure

Occupational exposure to PCBs presents a different clinical picture. The symptoms most commonly observed appear to be dermal and mucosal effects but no consistent disturbances in liver function. An investigation of former capacitor workers was presented by Lawton et al. (1175). Exposure to PCBs occurred between 1954-1977 when Aroclor® 1242 and 1016 were used extensively. Air levels were estimated to at least 690 $\mu g/m^3$; dermal contact also occurred. An 80% clearance of the lower chlorinated PCBs was noted in workers re-examined 29 months after exposure had ceased. Traces of highly chlorinated PCBs were found in the blood of long-time workers, particularly those exposed to Aroclor® 1254 before its use was discontinued in 1954. In 1976, blood levels of this compound were 8 ppm. By 1979, 25 years after exposure was discontinued, blood levels were 6 ppm. There was also a statistically significant association of log serum triglycerides and total cholesterol with every measure of log serum PCBs.

Smith et al. (1177) investigated cholesterol and triglyceride levels in PCB-exposed workers and the possible correlation to cardiovascular effects. Two-hundred twenty-eight employees of an electrical equipment manufacturing plant were evaluated. From 1959 to 1971, Aroclor® 1242 was used; Aroclor® 1016 was used thereafter. Forty-seven employees from a public utility plant were also evaluated, 14 of which worked in transformer maintenance. Another 46 employees of a private utility company, 15 working in transformer maintenance and 10 who worked in transformer overhaul, were included. Serum log PCBs correlated significantly with symptoms of mucous membrane and skin irritation, of systemic malaise and of altered peripheral sensation. Serum log PCBs was also correlated with serum (SGOT), plasma log (triglycerides) and log high density lipoprotein which indicate an effect on liver metabolism and possible development of cardiovascular disease.

Aroclor® 1016

Five employees (1275) of a capacitor manufacturing plant, exposed to Aroclor® 1016 for at least 2 years, were evaluated for possible effects of PCBs. Clinical examination revealed no signs suggestive of PCB toxicity except for occasional reports of skin or mucous membrane irritation upon direct contact with PCB oil or fumes. Blood, liver and kidney function tests were all normal.

Aroclor® 1242

The half-life of serum Aroclor® 1242 was investigated by Steele et al. (1172). Examination of 114 people tested for PCB levels in their blood in 1977 were retested in 1984. Results indicated a rapid decrease (of the lower chlorinated Aroclor® 1242) compared to the highly chlorinated PCBs. Assuming no further exposure after the 1977 testing, the half-life for Aroclor® 1242 was estimated to be 6-7 months. Since Aroclor® 1242 was still detected in 1984 at low levels, Steele et al. concluded that people were continuously exposed to low levels of PCBs through environmental background exposure.

An examination of workers occupationally exposed to Aroclor® 1242 was conducted by Ouw et al. (1185). One group of employees dipped capacitor casings directly into a vat of hot Aroclor® 1242. Exposure of this group was excessive with both inhalation and dermal absorption. A second group of employees assembled the Aroclor®-dipped capacitor components which resulted in skin absorption. A control group was included in the study and consisted of volunteers with no history of exposure to PCBs. Exposed workers complained of a burning sensation of the eyes, face and skin, and a persistent body odor. One worker developed chloracne while 5 others complained of eczematous rashes on the hands and legs. Workers dipping the capacitor casings in Aroclor® 1242 absorbed the more volatile compounds while workers exposed to PCBs during the assembly of the PCB dipped components absorbed the heavier compounds. Blood Aroclor® 1242 levels ranged from 313-602 ppb for the group of workers dipping the capacitor casings and 100-899 ppb for the group assembling the components. Some individual abnormal results occurred in the liver function test; however, overall the group was within normal limits. Aroclor® 1242 is known to penetrate human skin which results in a significant source of exposure. This would account for the high blood level seen in the group of workers dermally exposed during assembly of the capacitors.

Aroclor® 1254

A slight increase in the incidence of cancer, particularly melanoma of the skin, has been reported in a small group of men occupationally exposed to Aroclor® 1254. Eight cancers (in 7 workers) were reported between 1957 and 1975 in 92 workers exposed to Aroclor® 1254. Of these eight cancers, 3 were malignant melanoma and 2 were cancer of the pancreas. Data from the NCI estimate that 0.04 malignant melanomas should be expected to develop in this group. These data suggest a possible correlation between Aroclor® 1254 and the development of malignant melanomas. Exposure to other chemicals was not known (1457,1459).

Aroclor® 1260

The half-life of serum Aroclor® 1260 was investigated by Steele et al. (1172). Five men occupationally exposed to Aroclor® 1242 and Aroclor® 1260 in 1977 were reevaluated in 1984 to determine the status

of PCBs in the blood. Six participants not exposed to PCBs who served as controls in the 1977 study were also re-evaluated. Results showed a gradual decrease of the Aroclor® with a more rapid decrease of the less chlorinated Aroclor® 1242. The half-life of each PCB was determined based on the blood levels reported in the 1977 study and the present study. The estimated half-life of Aroclor® 1242 was 6-7 months while the estimated half-life of Aroclor® 1260 was 33-34 months.

52.3.3 Levels of Concern

Based on sufficient evidence that PCBs are carcinogens in experimental animals, the USEPA (355) has specified an ambient water quality criterion for these compounds of zero. In that attainment of a zero concentration level may be infeasible in some cases, the concentrations of PCBs in water calculated to result in incremental lifetime cancer risks of 10^{-5}, 10^{-6}, and 10^{-7} from ingestion of both water and contaminated aquatic organisms were estimated to be 0.79, 0.079 and 0.0079 nanograms/L, respectively. Risk estimates are expressed as a probability of cancer after a lifetime consumption of two liters of water per day and consumption of 6.5 g per day of fish that have bioaccumulated the compound. Thus, a risk of 10^{-5} implies that a lifetime daily consumption of two liters of drinking water and 6.5 g of fish at the criterion level of 0.79 nanograms/L PCBs would be expected to produce one excess case of cancer above the normal background incidence for every 100,000 people exposed. It should be emphasized that these extrapolations are based on a number of assumptions and should be taken as crude estimates of human risk at best.

IARC (3250) lists PCBs as category 2B carcinogens. i.e., sufficient evidence of carcinogenicity in animals.

OSHA (298) currently permits exposure to between 0.5 mg/m^3 (54% Cl) and 1 mg/m^3 (42% Cl) with a notation of potential skin absorption. The ACGIH (3) recommends identical exposure limits as OSHA and lists short-term exposure limits of between 1 mg/m^3 (54% Cl) to 2 mg/m^3 (42% Cl).

52.3.4 Hazard Assessment

In that commercial preparations of PCBs are complex mixtures of several isomers, assessment of hazard for the various congeners is confounded by a number of factors. Not only dose, but also the dose-time relationship are important determinants of effect; a lesser amount of PCBs may be able to produce a given level of intoxication, if exposure is extended. In addition, considerable species sensitivity to the same PCB formulation has also been noted.

In acute, relatively high-dose studies with most species, the first sign of intoxication is usually weight loss or reduced weight gain, which is only partially due to a decrease in food or water consumption. Severely poisoned rats have exhibited ataxia, diarrhea

and lack of response to pain stimuli. Death was most likely caused by progressive dehydration and central nervous depression (1279) The median time to death is usually 2 to 3 weeks for small laboratory animals. Oral LD_{50} values in rats range from 4000 to 11,000 mg/kg, with toxicity generally decreasing with increased chlorination (1178).

The most consistent pathological changes observed in most mammalian species after PCB exposure have been alterations in the liver. Liver enlargement has been noted even in those species in which actual liver lesions were minimal (such as monkeys) and at doses below which other effects, such as reduced thymus weights, were observed. Investigators suggest that the liver enlargement may be due to hepatocellular hypertrophy (1164).

Chronic oral exposure studies in rodents indicated Aroclor® 1254 to be carcinogenic in mice and Aroclor® 1260 to be carcinogenic in rats, inducing benign and malignant liver tumors (1283,1193,1194,1169, 1170,1171). There are no data for Aroclor® 1016 or Aroclor® 1242. There is also suggestive evidence of the development of malignant melanoma in humans exposed to PCBs (1457,1459).

Mutagenicity data are inadequate to establish a clear picture of mutagenic activity for these compounds. Negative findings have been reported for Aroclor® 1242 in mammalian cells (1180,1181) as well as in a dominant lethal test in rats (1182). Aroclor® 1254 gave negative results in cultured human lymphocytes (1457), in bacterial tests (1251) and in a rat dominant lethal study (1457). A single report on Aroclor® 1260 provided negative results in a dominant lethal test (2). No data were found for Aroclor® 1016.

A number of studies have indicated that PCB exposure has a notable depressive effect on reproductive capacity and fetal survival (1196,1197,1460,1160). Exposure of rats to PCBs during the prenatal period resulted in changes in sexual development in females (1162,1161) and reduced reproductive function in males (1163). Indications of structural malformations or other teratogenic effects, however, have been few (1016); most oral exposure studies have been negative.

Humans appear to be among the most sensitive species to PCBs. The most notable example is the Yusho incident which occurred in Japan in 1968. Initial symptoms of PCB poisoning were non-specific, including general fatigue, gastrointestinal disturbances, weakness, spasms and hearing and visual disturbances. The most common specific symptoms were dermal and mucosal effects, including acneform eruptions, hyperpigmentation (especially of the face, eyelids, nails and gingivae), cystic dilation of the hair follicles and hyperkeratosis. Severe ocular manifestations were also evident in the acute phase of the disease, the most notable being hypersecretion of the meibomian glands causing swelling of the upper eyelids and abnormal pigmentation of the conjunctiva (1174).

Developmental abnormalities were observed in several Yusho babies, including premature eruption of teeth, larger frontal and occipital fontanels and maintenance of an abnormally wide sagittal suture. Spotted and sporadic ossification of the skull and facial edema with exophthalmia were also reported. No other obvious malformations were evident (1192,1199).

The USEPA (667) has calculated an upper-limit incremental unit cancer risk of 4.34 $(mg/kg/day)^{-1}$ for PCBs.

52.4 SAMPLING AND ANALYSIS CONSIDERATIONS

Determination of the concentrations of the various Aroclor® congeners (1254, 1260, 1242 and 1016) in soil and water requires collection of a representative field sample and laboratory analysis. Care is required to prevent losses during sample collection and storage. Soil and water samples should be collected in glass containers; extraction of samples should be completed within 7 days of sampling and analysis completed within 40 days. In addition to the targeted samples, quality control samples such as field blanks, duplicates, and spiked matrices may be specified in the recommended methods.

EPA-approved procedures for the analysis of Aroclor® congeners, EPA priority pollutants, in aqueous samples include EPA Methods 608, 625 (65), 8080 and 8250 (63). Prior to analysis, samples are extracted with methylene chloride as a solvent using a separatory funnel or a continuous liquid-liquid extractor. The concentrated sample extract is solvent exchanged into hexane and an aliquot of the hexane extract injected onto a gas chromatographic (GC) column using a solvent flush technique. The GC column is programmed to separate the semi-volatile organics; Aroclor® congeners are then detected with an electron capture detector (Methods 608 and 8080) or a mass spectrometer (Methods 625 and 8250).

The EPA procedures recommended for Aroclor® analysis in soil and waste samples, Methods 8080 and 8250 (63), differ from the aqueous procedures primarily in the preparation of the sample extract. Solid samples are extracted with hexane/acetone (Method 8080) or methylene chloride (Method 8250) using either soxhlet extraction or sonication methods. Neat and diluted organic liquids may be analyzed by direct injection.

Typical detection limits that can be obtained for the Aroclor® congeners in waste waters and non-aqueous samples (wastes, soils, etc.) are shown below. The actual detection limit achieved in a given analysis for a given Aroclor® will vary with instrument sensitivity and matrix effects. (Aroclor® congeners are mixtures of isomers; multiple peaks are used for quantification.)

Aqueous Detection Limit	Non-Aqueous Detection Limit
0.065 µg/L (Method 608/8080)	1 µg/g (Method 8080)
36 µg/L (Method 625)	1 µg/g (Method 8250)

COMMON SYNONYMS:	CAS REG. NO.:	FORMULA:	AIR W/V CONVERSION FACTORS at 25°C
Chromic acid, disodium salt Chromate of soda Disodium chromate	7775-11-3 NIOSH NO.: GB2955000	$CrO_4 \cdot 2Na$	6.62 mg/m³ ≈ 1 ppm 0.15 ppm ≈ 1 mg/m³
	MOLECULAR WEIGHT: 161.97		

REACTIVITY	Sodium chromate is an oxidizing agent that may cause fire in contact with combustible materials. One source explains that it is mildly oxidizing in water solutions and highly oxidizing in strong acid solutions, thus requiring separation from organic materials, oils, greases, and any other oxidizing materials. Others list strong alkalies and strong acids as incompatible as well as combustible, organic, or other readily oxidizable materials such as paper, wood, sulfur, aluminum, plastics, etc. The NFPA notes that chromates in general may cause explosive decomposition of hydrazine. Compatibility charts indicate incompatibility with all types of organic or combustible materials (54,60,505,507,511).

PHYSICO-CHEMICAL DATA	• Physical State (at 20°C): crystals	(507)
	• Color: yellow	(507)
	• Odor: none	(507)
	• Odor Threshold: not pertinent	( )
	• Density (g/ml at 20°C): 2.723	(59)
	• Freezing/Melting Point (°C): 792	(59)
	• Boiling Point (°C): decomposes	(507)
	• Flash Point (°C): not flammable	(507)
	• Flammable Limits in Air, % by Volume: not flammable	(507)
	• Autoignition Temperature (°C): not flammable	(507)
	• Vapor Pressure (mm Hg at 20°C): not pertinent	( )
	• Saturated Concentration in Air (mg/m³ at 20°C): not pertinent	( )
	• Solubility in Water (30°C): 8.73×10^3	(59)
	• Viscosity (cp at 20°C): not pertinent	( )
	• Surface Tension (dyne/cm at 20°C): not pertinent	( )
	• Log (Octanol-Water Partition Coefficient), log K_{ow}: not pertinent	( )
	• Soil Adsorption Coefficient, K_{oc}: not pertinent	( )
	• Henry's Law Constant (atm•m³/mol at 20°C): not pertinent	( )
	• Bioconcentration Factor: not pertinent	( )

PERSISTENCE IN THE SOIL-WATER SYSTEM	Sodium chromate, as aqueous Na^+ and CrO_4^{-2}, is expected to be relatively mobile in soil. However, protonation of CrO_4^{-2} to $HCrO_4^-$ (the predominant species at pH < 6.5) decreases its mobility, and reduction to relatively immobile trivalent forms of chromium occurs readily in soils with sufficient organic matter.

PATHWAYS OF EXPOSURE	Exposure via ingestion of contaminated drinking water is the most likely route for chromate; volatilization from contaminated sources is not important. Other forms of chromium are found at trace levels in air and certain foods.

HEALTH HAZARD DATA	Signs and Symptoms of Short-term Human Exposure (54): Cr(VI) dust or mist may cause coughing and wheezing, headache, dyspnea, pain on deep inspiration, fever and loss of weight. Local contact can result in dermatitis, skin ulcers and perforated nasal septa.
	Toxicity Based on Animal Studies: LD_{50} (mg/kg) oral 50 [rat] (47) skin 1600 [rabbit] (507) LC_{50} (mg/m^3) inhalation [rat] (507) 104
	Long-Term Effects: Kidney damage, dermatitis
	Pregnancy/Neonate Data: Teratogenic and embryolethal
	Mutation Data: Sufficient evidence
	Carcinogenicity Classification: IARC-1; NTP-none assigned

HANDLING PRECAUTIONS (38)	Handle chemical only with adequate ventilation • Concentrations <5 mg/m^3: any dust and mist respirator • 5-10 mg/m^3: any dust and mist respirator, except single-use or quarter-mask respirator or any fume respirator or high efficiency particulate respirator or any supplied-air respirator or any self-contained breathing apparatus • 10-50 mg/m^3: a high efficiency particulate filter respirator with a full facepiece or any supplied-air respirator with full facepiece, helmet or hood or any self-contained breathing apparatus with a full facepiece • 50-500 mg/m^3: a powered air-purifying respirator with a high efficiency particulate filter or a Type C supplied-air respirator operated in pressure-demand or other positive pressure or continuous-flow mode • Chemical goggles if there is a probability of eye contact • Protective gloves, aprons and footwear.

EMERGENCY FIRST AID TREATMENT (54)	Ingestion: Give large quantities of water and induce vomiting. Get medical attention • Inhalation: Move the victim to fresh air immediately. Perform artificial respiration if necessary. Get medical attention • Skin: Remove contaminated clothing and wash skin with soap and water immediately. Get medical attention • Eye: Irrigate immediately with large amounts of water. Get medical attention.

ENVIRONMENTAL AND OCCUPATIONAL STANDARDS AND CRITERIA

AIR EXPOSURE LIMITS:

Standards

- OSHA PEL (8-hr TWA): soluble chromium salts - 0.5 mg/m³
  chromic acid and chromates - ceiling
  1 mg/10m³

- AFOSH PEL (8-hr TWA): soluble chromium salts - 0.5 mg/m³
  chromic acid and chromates ceiling
  1 mg/10m³

Criteria

- NIOSH IDLH (30-min): chromium metal and insoluble salts -
  500 mg/m³ (as Cr)

- ACGIH TLV® (8-hr TWA):
  Water soluble chromium (VI) compounds - 0.05 mg/m³ (as Cr)

  Certain water insoluble chromium (VI) compounds - 0.05 mg/m³ (as Cr). A1 - human carcinogen

  Other chromium compounds - 0.5 mg/m³ (as Cr)

- ACGIH STEL (15-min): none established

WATER EXPOSURE LIMITS:

Drinking Water Standards

Under the National Primary Drinking Water Regulations (296), the maximum contaminant level (MCL) for chromium is 0.05 mg/L. This MCL applies to community water systems which serve a population of 10,000 people or more and which add a disinfectant as part of their treatment process.

EPA Health Advisories

EPA (992) has developed the following Health Advisories (formerly termed SNARLs) for noncarcinogenic risk for short and long-term exposure to chromium (VI) in drinking water:

- 1 day: none established
- 10 days: 5 mg/L
- long-term: 0.84 mg/L

EPA Ambient Water Quality Criteria (355,1777)

- Human Health
  The ambient water quality criterion for total chromium (VI) is recommended to be identical to the drinking water standard of 0.05 mg/L of chromium.

- Aquatic Life
  - Freshwater species

    Freshwater aquatic organisms and their uses should not be affected unacceptably if the four-day average concentration of chromium (VI) does not exceed 11 μg/L more than once every 3 years on the average and if the 1 hour average concentration does not exceed 16 μg/L more than once every 3 years on the average.

    Freshwater aquatic organisms and their uses should not be affected unacceptably if the four-day average concentration (in μg/L) of chromium (III) does not exceed the numerical value given by e(0.8190[ln(hardness)]+1.561 more than once every 3 years on the average and if the 1 hour average concentration (in μg/L) does not exceed the numerical value given by e(0.8190[ln(hardness)]+3.688 more than once every 3 years on the average.

  - Saltwater species

    Saltwater aquatic organisms should not be affected unacceptably if the four-day average concentration of chromium (VI) does not exceed 50 μg/L more than once every 3 years on the average and if the 1 hour average concentration does not exceed 1100 μg/L more than once every 3 years on the average.

    No saltwater criterion can be derived for chromium (III), but 10,300 μg/L is the EC_{50} for eastern oyster embryos, whereas 50,400 μg/L did not affect a polycheate worm in a life-cycle test.

WHO Drinking Water Guideline (666)

A health-based guideline for drinking water of 5 μg/L is recommended for total chromium. A daily per capita consumption of two liters of water was assumed.

REGULATORY STATUS (as of January 1, 1987)

Promulgated Regulations

- Federal Programs

Clean Water Act (CWA)

Sodium chromate and sodium dichromate are designated as hazardous substances. They have a reportable quantity (RQ) limit of 454 kg (347,985). Chromium and chromium compounds are listed as toxic pollutants. Water quality criteria have been set. Guidelines exist for effluent containing hexavalent chromium in the petroleum refining and inorganic chemicals manufacturing point source categories (896,1436). Guidelines exist for total chromium in leather tanning and finishing, textile mills, petroleum refining and inorganic chemicals manufacturing point source categories (1437,893,896,1436) and in the steam electric power generating, ferroalloy manufacturing and nonferrous metals manufacturing point source categories (1438,895,894).

Safe Drinking Water Act (SDWA)

Under the National Primary Drinking Water Regulations (296), the maximum contaminant level (MCL) for chromium is 0.05 mg/L. This MCL applies to community water systems which serve a population of 10,000 people or more and which add a disinfectant as part of their treatment process.

In states with an approved Underground Injection Control program, a permit is required for the injection of chromium-containing wastes designated as hazardous under RCRA (295).

Resource Conservation and Recovery Act (RCRA)

Chromium compounds are listed as hazardous waste constituents (328). Non-specific sources of hexavalent chromium-containing wastes are wastewater treatment sludges from the chemical conversion coating of aluminum and from electroplating operations. Waste streams from the following industries contain hexavalent chromium and are listed as specific sources of hazardous wastes: inorganic pigments, petroleum refining, iron and steel and secondary lead (326,327).

Solid wastes which contain a concentration equal to or greater than 5 mg/L chromium are listed as hazardous in that they exhibit the characteristic defined as EP toxicity (988).

Effective July 8, 1987, land disposal of liquid hazardous wastes, including free liquids associated with any solid or sludge containing hexavalent chromium and/or its compounds at concentrations greater than or equal to 500 mg/L will be prohibited. The only exception will be underground injection (1755).

Used oil that is burned for energy recovery may not contain greater than 10 ppm chromium (1768).

Comprehensive Environmental Response Compensation and Liability Act (CERCLA)
Sodium chromate is designated a hazardous substance under CERCLA. It has a reportable quantity (RQ) limit of 454 kg. Reportable quantities have also been issued for RCRA hazardous waste streams containing sodium chromate but these depend upon the concentrations of the chemicals in the waste stream (985).

Marine Protection Research and Sanctuaries Act (MPRSA)
Ocean dumping of organohalogen compounds as well as the dumping of known or suspected carcinogens, mutagens or teratogens is prohibited except when they are present as trace contaminants. Permit applicants are exempt from these regulations if they can demonstrate that such chemical constituents are non-toxic and non-bioaccumulative in the marine environment or are rapidly rendered harmless by physical, chemical or biological processes in the sea (309).

Occupational Safety and Health Act (OSHA)
Employee exposure to soluble chromium salts shall not exceed an 8-hour time-weighted-average (TWA) of 0.5 mg/m^3. Chromic acid and chromates have a ceiling level of 1 mg/10 m^3 which should not be exceeded at any time during an 8-hour work shift (298).

Hazardous Materials Transportation Act (HMTA)
The Department of Transportation has designated sodium chromate as a hazardous material which is subject to requirements for packaging, labeling and transportation (306).

Food, Drug and Cosmetic Act (FDCA)
Sodium chromate is approved for use as an indirect food additive (362).

The level for chromium in bottled drinking water is 0.05 mg/L. This level is identical to the maximum contaminant level (MCL) given under the Safe Drinking Water Act (365).

- State Water Programs
  All states follow the National Primary Drinking Water Regulations under the Safe Drinking Water Act.

  States with additional regulations for chromium (731,981):

  Georgia - 20 µg/L in all waters
  Oregon - 20 µg/L in the public water supply
  Wyoming - 100 µg/L in Class 2 ground water
  Wisconsin - 5 µg/L preventive action limit in ground water

Proposed Regulations

- Federal Programs

  Clean Water Act (CWA)
  Effluent guidelines for chromium have been proposed in the organic chemicals, plastics and synthetic fibers category (357).

  Safe Drinking Water Act (SDWA)
  EPA has proposed a Recommended Maximum Contaminant Level (RMCL) of 0.12 mg/L for total chromium as part of the National Primary Drinking Water Regulations (992).

  Resource Conservation and Recovery Act (RCRA)
  EPA has proposed that hazardous waste treatment, storage and disposal facilities monitor ground water for total chromium when EPA suspects the facilities of leaking contaminants (1754).

  EPA has proposed listing used oil (including automotive, hydraulic, coolant, insulating and metalworking oils) as a non-specific source of chromium-containing waste (1566).

  EPA has proposed that solid wastes which contain a concentration equal to or greater than 5.0 mg/L hexavalent chromium be listed as hazardous in that they exhibit the characteristic defined as EP toxicity (1798).

  Clean Air Act (CAA)
  EPA intends to list chromium as a hazardous air pollutant. Emission standards (NESHAPS) will be proposed at a later date (1406).

- State Water Programs

  No proposed regulations are pending.

EEC Directives

Directive on Drinking Water (533)
The mandatory values for total chromium in surface water treatment categories A1, A2 or A3 are 0.05 mg/L. There are no guideline values.

Directive Relating to the Quality of Water for Human Consumption (540)
The maximum admissible concentration for chromium is 50 µg/L.

Directive on Ground Water (538)
Direct and indirect discharge of chrome into ground water shall be subject to prior review so as to limit such discharges.

Directive on Bathing Water Quality (534)
When inspection of a bathing area shows that heavy metals, pesticides or cyanides may be present, concentrations should be checked by competent authorities.

Directive on the Quality Required of Shellfish Waters (537)
The mandatory specifications for chromium specify that the concentration of each substance in the shellfish water or in shellfish flesh must not reach or exceed a level which has harmful effects on the shellfish and larvae. The synergistic effects of other metals must be taken into consideration. The guideline specifications state that the concentration of chromium in shellfish flesh must be so limited that it contributes to the high quality of shellfish product.

Directive on the Discharge of Dangerous Substances (535)
Chromium cannot be discharged into inland surface waters, territorial waters or internal coastal waters without prior authorization from member countries which issue emission standards. A system of zero-emission applies to discharge of these substances into ground water.

Directive on Toxic and Dangerous Wastes (542)
Any installation, establishment, or undertaking which produces, holds and/or disposes of certain toxic and dangerous wastes including phenols and phenol compounds; organic-halogen compounds; chrome compounds; lead compounds; cyanides; ethers and aromatic polycyclic compounds (with carcinogenic effects) shall keep a record of the quantity, nature, physical and chemical characteristics and origin of such waste, and of the methods and sites used for disposing of such waste.

Directive on the Classification, Packaging and Labeling of Dangerous Substances (787)
Sodium dichromate is classified as an irritant substance and is subject to packaging and labeling regulations.

Directive on Paints,Varnishes, Printing Inks, Adhesives and Similar Products (1334)
Sodium dichromate is classified as an irritant substance when present in concentrations greater than or equal to 0.5%.

Directive on Transfrontier Shipment of Hazardous Waste (1433)
When the holder of a hazardous waste such as chromium intends to ship it to another member state, authorities of the member states concerned must be provided with information on the source and composition of the waste, measures to be taken to ensure safe transport, insurance against damage and the existence of a contractual agreement with the consignee of the waste. All transfrontier shipments must be properly packed and labeled and must be accompanied by instructions to be followed in the event of danger or accident.

EEC Directives - Proposed

Proposal for a Council Directive on the Dumping of Waste at Sea (1793)
EEC has proposed that the dumping of chromium compounds at sea be forbidden without prior issue of a special permit.

Proposal for a Council Directive on Water Quality Objectives for Chromium (1428)
EEC has proposed that the concentration of dissolved chromium in fresh water be below 5-50 μg/L depending on water hardness. For sea water, the upper limit would be 15 μg/L. The proposal would not regulate chromium in ground water or drinking water. Implementation of the program would be completed by 15 September 1991.

53.1 MAJOR USES

Sodium chromate (Na_2CrO_4) is used in leather tanning, wood preservation, corrosion inhibition and pigment manufacturing. It is also used as a raw material for production of other chromium compounds such as sodium dichromate ($Na_2Cr_2O_7$) (1252).

53.2 ENVIRONMENTAL FATE AND EXPOSURE PATHWAYS

53.2.1 Transport in the Soil/Ground-water Systems

53.2.1.1 Overview

The high solubility of sodium chromate in water means that the mobility of sodium (Na^+) and chromate (CrO_4^{-2}) must be considered separately when assessing its mobility in the soil/ground-water environment. The sodium ion can be expected to be relatively mobile depending on the soil type and the concentration of other cations competing for soil ion exchange sites. However, the sodium ion is of little environmental significance compared to the chromate ion.

The chromate ion, as such, is expected to be relatively mobile in the soil/ground-water environment (1702). In protonated form ($HCrO_4^-$), the mobility of the ion is decreased. The organic matter in the soil readily reduces chromate (or dichromate) to a trivalent form, either Cr^{+3} or CrO_2^-, which form compounds of much lower solubility than the hexavalent chromates. In soils of low organic matter content, however, bulk quantities of chromate could be transported down through the unsaturated zone, if the sorbing capacity of the soil is exceeded.

The chromate ion can act as a weak base, with a strength close to that of the bicarbonate ion. The acid dissociation constant of $HCrO_4^-$ is $10^{-6.51}$ (25°C, zero ionic strength) (1704); this indicates that at pH 6.5 half the chromate in solution would exist as $HCrO_4^-$, at pH 5.5, 90% would exist in this form, and at pH 7.5, 9%.

Environmental transport pathways for sodium chromate cannot be assessed using an equilibrium partitioning model as is done for organic chemicals. Because it is an ionic species that readily dissolves into its component ions, sodium chromate is non-volatile. The susceptibility of hexavalent chromium to reduction by organic matter makes partitioning calculations virtually meaningless.

53.2.1.2 Sorption on Soils

The high solubility of sodium chromate in water (37.7 wt % at 15°C (1701)) indicates that reactions involving its precipitation on soils are expected to be relatively unimportant. Except in arid regions, solid Na_2CrO_4 that is deposited on soil will readily dissolve in atmospheric precipitation. Where this happens, or where spills of aqueous Na_2CrO_4 have occurred, the fate of Na^+ and CrO_4^{-2} must be

considered individually. Since the chromate ion is of much greater environmental concern than sodium, most of the discussion below focuses on it.

Sodium sorption on soils occurs primarily by ion exchange (1702). It is relatively weakly retained by soils. Among major monovalent cations (which tend to be less strongly held than multivalent cations), it is just slightly more strongly held than lithium, the most weakly retained ion (1703). The ion exchange of sodium is governed by the laws of mass action at exchange sites (1702) and thus the presence and concentration of other competing cations in the soil water determine its retention.

The transport of chromium introduced as chromate is strongly dependent on the transformations it undergoes, which are described in the following section. As noted above, sodium chromate is highly soluble in water, as are most other chromates. Exceptions are lead chromate ($PbCrO_4$), barium chromate ($BaCrO_4$), and silver chromate (Ag_2CrO_4), with pK_{sp} values, (at 25°C and zero ionic strength) of 12.60, 9.67, and 11.92, respectively (1704). Barium and silver concentrations are too low under environmental conditions to control chromate solubility; however, lead chromate may, under certain conditions, precipitate at pH < 8 if the Pb^{+2} concentration is controlled by $PbSO_4(s)$ (at pH < 6) and $PbCO_3(s)$ (at pH > 6) (1702).

The distribution of chromate between protonated and deprotonated form ($HCrO_4^-$ and CrO_4^{-2}) is dependent on pH. Both forms may be sorbed to soils, although their behavior differs. Chromate may be sorbed like SO_4^{-2} and HPO_4^{-2}, by forming binuclear bridged structures on geothite [Fe•OCr(OO)•Fe] or aluminum oxides and other soil colloids having positively charged surfaces, or it may be sorbed by ligand exchange (1705).

Chromium(VI) has also been found to sorb to activated carbon, primarily as $Cr_2O_7^{-2}$ and $HCrO_4^-$ (1708). Chromium(III) was found to be sorbed to a lesser extent. Bichromate, $HCrO_4^-$ (also called hydrochromate), may behave like HPO_4^- and be tightly held in soils or it may act like HCO_3^-, Cl^-, and NO_3^- and remain soluble (1705). In experiments using K_2CrO_4, James and Bartlett (1705) found an average of 36% of the Cr(VI) was removed by 38 soils having a mean pH of 5.4, while 13% was removed from limed soils having a pH of 7. Subsurface B horizon soils were found to remove somewhat more Cr(VI) than A horizon soils. The precise mechanism of chromate removal could not be determined, and thus the relative contributions of Cr(VI) precipitation, sorption and reduction to Cr(III) could not be assessed. Nevertheless, the finding of increased Cr(VI) removal at decreased pH is consistent with the observation that $HCrO_4^-$ is the predominant Cr(VI) species sorbed (1706) since it would be present in increasing concentrations at lower pH's.

Most data on CrO_4^{-2} sorption to soils have been obtained using pure soil minerals rather than actual soil samples (1702). The results of these studies indicate that minerals with high isoelectric points

(e.g., αAl_2O_3, $FeO_3 \cdot H_2O$(am), other iron oxides, and (to a lesser extent) clay minerals) adsorb Cr(VI) at pH's of roughly 2 to 7 (1702). The Langmuir adsorption maxima (μmol sorbed/gram of soil) for Cr(VI) on two soil minerals using K_2CrO_4 as the electrolyte are given in the following table.

TABLE 53-1

CHROMATE SORPTION

Soil Mineral	Solution pH	Langmuir Maxima μmol/g
Kaolinite	3	1.79
	4	0.85
	5	0.62
	7	0.29
Montmorillonite	3	3.64
	4	2.50
	5	2.22
	7	0.98

53.2.1.3 Volatilization from Soils

As an ionic species readily soluble in water, sodium chromate is non-volatile, and thus volatilization from soil is expected to be an insignificant transport pathway.

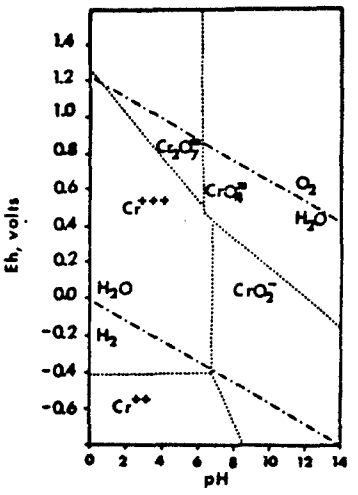
53.2.2 Transformation Processes in Soil/Ground-water Systems

As CrO_4^{-2} and $Cr_2O_7^{-2}$ are hydrolysis products of Cr(VI), neither is further hydrolyzed itself. Reduction of CrO_4^{-2} may be the most important reaction affecting its environmental transport. Its redox behavior is illustrated in Figure 53-1, which shows the predominant form of aqueous chromium over a range of pH and Eh (oxidation-reduction potential) conditions.

For water in equilibrium with air at pH 7, the theoretical value of Eh at 25°C is 0.80 volts, and the dependence of Eh on pH and the partial pressure of oxygen P_o can be expressed as (1706):

$$Eh = 1.234 - 0.058\ pH + 0.0145 \log P_o$$

Thus, in well oxygenated waters of intermediate pH, CrO_4^{-2} and $Cr_2O_7^{-2}$, both containing hexavalent chromium, are expected to predominate. At lower pH (and Eh) levels, Cr(VI) is reduced to Cr(III), either as Cr^{+3} or CrO_2^-.



Source: Bartlett and Kimble (1710)

FIGURE 53-1

Eh-pH DIAGRAM OF Cr SPECIES IN WATER AT 25°C

Figure 53-1 and the discussion above should be taken as descriptions of limiting conditions only. Often equilibrium conditions are not quickly reached in ground waters, as shown by the work of Lindberg and Runnells (1707).

Hexavalent chromium as $K_2Cr_2O_7$ was found to be spontaneously reduced to Cr(III) by soil organic matter even at pH levels above neutrality (1708). However in soils with very low organic matter content, reduction did not occur until an energy source was added. Thus, in deep saturated soils with little organic matter Cr(VI) would not be expected to be reduced despite a lack of air.

Trivalent chromium species have been found to be oxidized to the hexavalent form in the presence of oxidized forms of manganese (1711). Thermodynamic considerations, based on the addition of half cell reactions for Cr(III) oxidation and Mn reduction, generally favor the formation of Cr(VI) (1711). Chromate that has been reduced to the trivalent form but remains in solution may be reoxidized to hexavalent form if it moves to areas where manganese oxides are present.

The biological transformation of Cr(VI) species (CrO_4^{-2} or $Cr_2O_7^{-2}$) is one of reduction. Cr(VI) readily penetrates cell membranes and is then reduced, its toxicity probably resulting from the oxidation of cell components (1712). Because it is an essential nutrient, chromium is bioaccumulated in many organisms (10,1713,1714).

It has been suggested that chromium could be methylated in reducing environments but no evidence that this occurs in natural or experimental systems was found (10). It is also possible that CrO_4^{-2} could be used as an oxygen source for microorganisms under anaerobic conditions, although this process could not be distinguished from the chemical reduction of these species to Cr(III) with the loss of oxygen (10).

53.2.3 Primary Routes of Exposure from Soil/Ground-water Systems

The above discussion of fate pathways suggests that the mobility and potential exposure to sodium chromate is very dependent on the environmental conditions. This compound or its ions are considered to have a low volatility as are the various forms of chromium. The chromate ion is generally expected to be mobile in soils, although other forms of chromium may be less mobile under some conditions. Based upon experimental BCF values for fish, chromium has a moderate potential for bioaccumulation. These fate characteristics suggest several potential exposure pathways.

Volatilization of chromate or other forms of chromium from a disposal site is not likely to represent an important exposure pathway under most conditions. Drinking water contamination resulting from the migration of chromate or other forms of chromium may occur, although chromate is considered relatively immobile in soil. Mitre (83) reported that chromium (probably total) has been found at 53 of the 546 National Priority List (NPL) sites. It was detected at 33 sites in ground water, 33 sites in surface water, and one site in air. As chromium is a naturally occurring element, this prevalence is not necessarily an indication of widespread contamination. In addition, the presence of chromium in ground water drinking water supplies has been observed. In three national surveys of ground water supplies from 1969 to 1980, chromium was found at levels above 5 μg/L in 77 of 795 supplies sampled (9.7%). The mean of the positive values was 16 μg/L, with a maximum of 49 μg/L (1641). Again, however, it is unclear if these levels represent contamination from anthropogenic sources. It is clear, however, that chromium in some form could be and is found in ground water.

The movement of chromate in ground water or with soil particles may result in discharges to surface waters. As a result, ingestion exposures may occur through the use of surface waters as drinking water supplies, and dermal exposures may result from the recreational use of surface waters. In addition, various forms of chromium may be taken up by aquatic organisms or domestic animals. Again, environmental conditions affect the form and the extent of bioaccumulation of chromium by aquatic organisms. However, this pathway may be important in some situations.

53.2.4 Other Sources of Human Exposure

Chromium is a naturally occurring element and, as a result, there are numerous sources of exposure to chromium. Most reports of levels in the environment or in food are given as total chromium. These data are summarized briefly here.

As mentioned above, chromium was found to some extent in ground water drinking water supplies. It was also found at levels above 5 $\mu g/L$ in 24 of 142 surface water supplies (16.9%). The mean concentration at the positive values was 10 $\mu g/L$, and all concentrations were less than 25 $\mu g/L$ (992).

Chromium is also commonly found in air, although at low concentrations. EPA reports that data from 1977 to 1980 show a mean chromium concentration for the urban areas sampled (16 locations) of 0.0052 $\mu g/m^3$ to 0.1568 $\mu g/m^3$. The maximum 24 hour average concentration was 2.487 $\mu g/m^3$. The mean chromium concentrations in four non-urban background areas ranged from 0.0052 $\mu g/m^3$ to 0.0090 $\mu g/m^3$ (1641). Concentrations of chromium near sources can be greater, and levels as high as 13.5 $\mu g/m^3$ total chromium have been reported in the vicinity of a chromium pigment producer (1642).

Most foods contain chromium at levels ranging from about 0.01 to 0.5 mg/kg, but acidic foods may contain higher levels (1641). The dietary intake of chromium from typical American diets containing 43% fat was estimated to be 62 $\pm$ 28 μg/day. For diets consisting of 25% fat, the intake was estimated to be 89 $\pm$ 56 μg/day (1643). Smokers may have an additional source of chromium as tobaccos have been found to contain 0.24 to 0.63 mg/kg chromium (1252).

The above data clearly show that there are numerous sources of exposure to chromium. The exact form of chromium depends on the source and the media.

53.3 HUMAN HEALTH CONSIDERATIONS

Although chromium can exist in several valence states, the biologically significant forms of the element are the hexavalent and trivalent chromium compounds. However, due to their greatly differing abilities to penetrate cellular membranes and associated toxicity in biological systems, hexavalent (CrVI) chromium is recognized as a toxic substance while trivalent chromium (CrIII) is regarded as essential for nutrition and relatively non-toxic (1252).

Sodium chromate is a soluble (in water), hexavalent form of chromium. Other chromium compounds that are also categorized as soluble and hexavalent and therefore expected to exhibit similar toxicity, include potassium chromate, sodium or potassium dichromate and chromium trioxide (CrO_3) (1252).

53.3.1 Animal Studies

53.3.1.1 Carcinogenicity

Inconclusive findings have been reported for the carcinogenicity of hexavalent chromate in a variety of laboratory animals, tested by various routes (1252).

Levy et al. (1671) investigated the carcinogenicity of sodium chromate or sodium dichromate in 48 male and 52 female Porton-Wistar rats. Each rat received a steel pellet loaded with 2 mg of the test substance suspended in cholesterol. The pellet was implanted in the left bronchus. After 2 years, the lungs were examined. Both chromium compounds induced squamous metaplasia in the lungs of 18% (16/89) of the rats exposed to sodium chromate and 19.1% (17/89) of the rats exposed to sodium dichromate. Squamous metaplasia is regarded to be a preneoplastic lesion.

Steffee and Baetjer (1233) exposed guinea pigs by inhalation to a mixture of chromate dust, aerosols of potassium dichromate and sodium chromate, and pulverized residue dust obtained from roasted material from which soluble chromates had leached. The mixture was inhaled 4-5 hours/day, 4 days/week for the animals' life span. Pulmonary adenomas developed in 6% of the guinea pigs (vs. zero in the control group). Negative results were obtained in a separate experiment with eight rabbits exposed by inhalation to the same chromate mixture for 4-5 hours/day, 4 days/week for 50 months (1233).

Male Wistar rats were exposed in a chamber to 0, 25, 50 or 100 $\mu g/m^3$ sodium dichromate aerosol 22-23 hours/day for 18 months and observed for an additional 12 months. No clinical signs of irritation or toxicity were observed. One adenocarcinoma and 2 adenomas were present in the lungs of 19 surviving rats exposed to 100 $\mu g/m^3$ sodium dichromate. A squamous cell carcinoma in the pharynx region was also reported in the high exposure group. No lung tumors were found in the 25 or 50 $\mu g/m^3$ group (1809).

Heuper and Payne (1672) intramuscularly injected 39 Bethesda Black rats with 2 mg sodium dichromate in gelatin. Injections were administered monthly for 16 months and rats were observed for 24 months. By the 18th month, only 17 (43.6%) of the rats were alive. No tumors were observed at the injection site in any of the rats. Intrapleural injections of 2 mg sodium dichromate into 39 Bethesda Black rats once a month for 16 months gave similar results. One adenocarcinoma of the lung (0.025 incidence) was found in the chromium-treated rats. No tumors were found in control rats (1672).

The available data are inadequate to evaluate the carcinogenicity of sodium chromate. There is sufficient evidence of respiratory carcinogenicity in men occupationally exposed to chromate during chromate production but data on lung cancer risk for other chromium-associated occupations and for cancer at other sites are

insufficient (1252). These studies are discussed in the Human and Epidemiologic Studies section of this chapter. IARC (1250) has determined that there is sufficient evidence for certain insoluble hexavalent chromium compounds, such as calcium chromate, sintered calcium chromate, lead chromate, strontium chromate, sintered chromium trioxide and zinc chromate, to induce cancer in rats. In that the data do not allow evaluation of the relative risk of various valence states of chromium nor soluble versus nonsoluble chromium compounds, IARC has classified all chromium compounds as Group 1 compounds (i.e., sufficient evidence of carcinogenicity to humans).

53.3.1.2 Mutagenicity

Numerous studies utilizing a variety of test systems have demonstrated that hexavalent chromium salts are mutagenic while trivalent chromium compounds are generally inactive presumably because they bind to extracellular constituents and therefore do not enter the cell (1471,1252).

Sodium dichromate was tested in the Ames assay by Bennicelli et al. (1465) and was found to induce a strong mutagenic effect in the TA102 strain of Salmonella typhimurium. Sodium dichromate was also reported to have weak activity in strains TA1537, TA1538 and TA98 of Salmonella typhimurium (1466).

In other bacterial tests, including gene conversion in Schizosaccharomyces pombe, mitotic recombination in Saccharomyces cerevisiae, reverse mutation in Escherichia coli trp$^-$ and arg$^-$, and the DNA repair test in Bacillus subtilis and Escherichia coli, sodium dichromate was positive (1466).

Chromium platers occupationally exposed to hexavalent chromium and matched controls were studied by Nagaya (1467). No differences in sister-chromatid exchange frequency was noted in lymphocytes of these two groups. The urinary chromium levels in exposed workers ranged from 2.6 μg/L to 80.3 μg/L. However, Bianchi et al. (1469) observed a significant increase in the frequency of sister-chromatid exchange in 4 rodent cell systems treated in vitro with hexavalent chromium at levels up to 10^{-3} mM.

Nishio et al. (1468) reported irreversible inhibition of DNA synthesis in cultured mouse L cells at concentrations of 10 μM hexavalent chromium and Bigaliev (1470) found chromosome aberrations in lymphocyte cultures of individuals who came in contact with chromium.

Cupo et al. (1472) treated chick hepatocytes with 5 μM sodium chromate for 2 hours. DNA strand breaks, DNA interstrand cross-links, and DNA-protein cross-links were noted. After removal of the chromate, strand breaks and interstrand cross-links were completely repaired by 3 and 12 hours, respectively. A significant level of DNA-protein cross-links persisted 40 hours after chromate removal. DNA cross-links were also found in nuclei isolated from the liver and kidney of rats treated with chromate (1473).

The mutagenicity of hexavalent chromium can be decreased or eliminated by biological reducing agents such as rat liver microsomes (1252). Chemical reducing agents also appear to be effective. Gentile et al. (1471) found that chelants bind to the chromium compound and reduce or eliminate mutagenicity. Effective chelators included EDTA, salicylate and Tiron (disodium 1,2-dihydroxybenzene-3,5-disulfonate).

Thus, there is sufficient evidence that hexavalent chromium is capable of inducing DNA damage and to be mutagenic in at least three bacterial systems and mammalian cells, inducing chromosomal aberrations in a variety of mammalian cells in vitro and in vivo.

53.3.1.3 Teratogenicity, Embryotoxicity and Reproductive Effects

Little information is available on the effects of sodium chromate on reproduction. However, experimentation with other hexavalent forms of chromium have been documented in the literature. Gale (1274) intravenously administered 5, 7.5, 10 or 15 mg/kg hexavalent chromium trioxide to pregnant golden hamsters during the 8th day of gestation. Fetuses were taken on the 12th, 14th or 15th day of gestation. Lethality occurred in 75% of the dams treated with the 15 mg/kg dose and the rates of resorptions were increased for the 7.5 (29%) and 10 mg/kg (41%) groups vs. 2% for controls. The rate of malformations also increased with dose. The incidence of cleft palate was statistically significant in all treatment groups (34% in the 5 mg/kg group, 85% in the 7.5 mg/kg group, 84% in the 10.5 mg/kg group vs. 2% in control animals). Other malformations included exencephaly (brain outside skull), rib fusion, micrognathia (unusual smallness of the jaw), ventral body wall defect, abnormal hind limbs, encephalocele (hernia of the brain), tail abnormalities, renal agenesis and hydrocephalus.

The embryo permeability and potential embryotoxic effects of sodium dichromate in mice were investigated by Danielsson et al. (1462). Forty-two pregnant C57BL mice were intravenously administered a single dose of sodium dichromate (hexavalent state) or chromium trichloride (trivalent state) during gestation days 8 through 18. In the sodium dichromate treated mice, animals injected on day 13 of gestation had embryonic chromate concentrations of 12% one hour after injection while the chromium trichloride treated mice had a concentration of 0.4% at the same time period. From this point of gestation on (i.e., late gestation), both forms of chromate accumulated in the calcified areas of the fetal skeleton. The fetal concentration of both Cr III and Cr VI increased with gestational age.

53.3.1.4 Other Toxicologic Effects

53.3.1.4.1 Short-term Toxicity

Toxic effects of acute chromium (VI) exposure include skin ulcerations, rhinitis, gastritis, dyspnea, pulmonary edema and kidney damage (46). Unlike Cr (III) compounds, Cr (VI) compounds tend to

cross biological membranes quite readily and are somewhat more readily absorbed from the gut or through the skin (1464). The oral LD_{50} of sodium chromate in the rat is 50 mg/kg (59). The dermal LD_{50} for sodium chromate in the rabbit is 1600 mg/kg (59).

Hughes (1474) injected a 0.08 M solution of sodium dichromate into the corneal stroma of rabbits. The reaction produced was considered severe and was graded 70 on a scale of 1 to 100. A 0.08 M solution of sodium chromate produced a similar reaction when injected into the cornea of rabbits (1474). Application of sodium chromate crystals to intact rabbit cornea for 2.5 minutes resulted in localized endothelial injury and blue stromal edema (19). Crystals of sodium dichromate produced a similar, but more severe reaction along with gross bulging of the cornea (19).

Sodium dichromate is used as an additive in mud drilling in the oil industry and resulted in a rare case of acute chromate poisoning in cattle (1773). Two hundred sixty yearling heifers were turned out into a large pasture that contained an oil drilling operation. Several days later, 10 animals were found dead. Post-mortem examination showed gastroenteritis with a hemorrhagic abomasum and bloody ingesta in the small intestine, hemorrhages in the rectum and congested and swollen kidneys. Histopathological examination revealed degeneration of multiple individual hepatocytes, necrosis and tubular degeneration in the kidney. Chromium levels in the kidney of two animals were 67.4 and 71.8 ppm. No additional deaths were reported after clean-up of the area.

Cats exposed by inhalation to 11-23 mg/m^3 hexavalent chromium (as dichromate) for 2-3 hours/day for 5 days developed bronchitis and pneumonia but no effects were observed in similarly exposed rabbits (1464).

Kidney damage is a major deleterious effect of sodium chromate in mammals (1661,1662,1669,1670). Evan et al. (1661) investigated the sequence of structural changes in the kidneys of male Wistar rats injected intraperitoneally with 0, 10 or 20 mg/kg sodium chromate. Kidneys were examined 1, 6, 24 and 48 hours after treatment. Electron microscopy revealed that the structural changes were confined to the microvilli of the convoluted portion of the proximal tubule and were first seen 1 hour after the 20 mg/kg dose and 6 hours after the 10 mg/kg dose. The majority of nephrons appeared to be damaged resulting in a reduction in renal blood flow or ischemia.

Kirschbaum et al. (1662) continued the investigation of the effect of sodium chromate on the kidney by studying brush border alterations of the proximal tubule following chromium administration. Female Sprague-Dawley rats were subcutaneously injected with 20 mg/kg sodium chromate and observed for 4 hours. Excretion of N-Ac-glc ase, a lysosomal enzyme widely accepted as a sensitive indicator of cell damage, was significantly increased. Urine lysozyme excretion was also markedly elevated indicating either decreased reabsorption of filtered lysozyme or release of lysozyme from renal epithelium.

In another experiment, male Sprague-Dawley rats were given an intraperitoneal injection of 20 or 40 mg/kg sodium dichromate while control rats were given 0.5 ml of 0.9% NaCl solution. Rats were sacrificed by decapitation 0 to 40 hours post-injection. The nuclei from the right renal cortex of the kidney, the front hepatic lobe of the liver or the whole lung were examined for DNA damage. Results indicate that rat liver cells may be more efficient at repairing hexavalent-chromium induced DNA damage than kidney or lung cells and the lung and kidney are more sensitive than the liver to chromium-induced DNA damage (1669).

53.3.1.4.2 Chronic Toxicity

Hexavalent chromium can be tolerated by animals in low concentrations especially when administered in feed or drinking water, in which the degree of absorption is a factor. For example, dogs administered hexavalent chromium (as potassium chromate) in drinking water for 4 years at a level of 0.45 to 11.2 mg/L exhibited increased chromium concentrations in liver and spleen but no significant pathological changes (1464,1462). A similar study in rats indicated no adverse effects with exposure to 25 ppm in drinking water for one year (1463).

Nageswara-Rao et al. (1775) studied the effects of a diet of sodium chromate-treated, parboiled rice fed to Swiss mice and chicks for one year. The chromium content of the treated rice was 0.7 ppm. No effect on food intake, growth or organ weight was observed in any of the animals and histological evaluations were normal.

Accumulation of chromium in mammalian tissues begins to occur at levels of 5 mg/L or more hexavalent chromium in drinking water (1463). Rats exposed to 4 mg/L hexavalent chromium in drinking water exhibited no adverse effects on growth rate, food intake or blood chemistry but chromium was found in tissues; even levels of 25 mg/L hexavalent chromium in the drinking water of rats for 6 months produced no histopathology (1463).

53.3.2 Human and Epidemiologic Studies

53.3.2.1 Short-term Toxicologic Effects

The lethal human dose of various forms of hexavalent chromium compounds by ingestion is estimated to be in the range of 1.5 to 16 grams (1452). Hemorrhagic changes are normally seen in various organs, especially the gastrointestinal tract, in fatal poisoning cases, pathological changes in the kidneys are also observed (1452).

Ingestion of hexavalent chromium (as sodium dichromate) usually results in profuse vomiting and diarrhea with erosions, abdominal pain, bleeding and circulatory collapse. Symptoms, which may occur up to 72 hours after exposure, include thrombocytopenia with bleeding diathesis, anemia, intravascular hemolysis, acute tubular necrosis, hepatitis,

seizures and other CNS disturbances (1663). Mortality usually occurs in one of two phases: early multisystem involvement may occur resulting in shock as the most prominent cause of death; if the victim survives the initial phase, hepatic and renal failure may occur and result in death (1664).

A fatal case of sodium dichromate ingestion was reported by Ellis et al. (1664). A 22-month-old boy ingested an unknown quantity of sodium dichromate solution. Vomiting was immediately induced. Fifteen minutes post-ingestion the boy was admitted to the hospital for treatment. Twelve hours post-ingestion the boy suffered cardiopulmonary arrest but was resuscitated. A generalized seizure was noted 18 hours post-ingestion. The infant died 30 minutes later. Autopsy revealed gross edema with a 2 kg weight gain over the 18 hours of hospitalization. Bilateral pleural effusions and marked pulmonary edema with severe bronchitis and acute bronchopneumonia were also present. Microscopic examination of the heart revealed wavy fibers suggestive of early hypoxic changes. The liver was congested and necrotic hepatocytes were noted. Acute tubular necrosis was noted in the kidneys. Severe submucosal edema was present in the stomach. Necrosis of the mucosa and marked edema of the submucosa were observed in duodenal and jejunal tissue. The ileum and colon had minimal mucosal necrosis and severe submucosal edema. The lumens of the duodenum, jejunum and colon were filled with unclotted blood.

Recovery following ingestion of a lethal dose of sodium dichromate was described by Walpole et al. (1663). A 24-month-old boy began to cough and vomit profusely 2-3 minutes after ingesting 50 mL of 10% sodium dichromate solution. The boy became pale, sweaty, lethargic and drowsy. He recovered soon after treatment and was discharged from the hospital on day six. Three weeks later, he began to vomit and developed symptoms of probable dysphagia (difficulty in swallowing). Further progress was uneventful except for emotional disturbance and the onset of seizures 2 months after ingestion. Since the boy had ingested a lethal dose of sodium dichromate, Walpole speculated that the initial profuse vomiting saved the boy from lethal renal complications.

53.3.2.2 Chronic Toxicologic Effects

Chronic toxicity problems associated with chromium exposure are of concern primarily in an industrial environment. Such effects have been reviewed in detail elsewhere (1463,1252).

Hexavalent chromium causes ulceration of the skin and ulceration and perforation of the nasal septum. This is due to the reduced vascularity of the mucous membrane lining the nasal fossae which allows it to be easily destroyed. The destruction of this tissue cuts off the blood supply to the cartilage resulting in necrosis. This ulcerative process stops once it reaches the bone. At this point, healing takes place, usually with ecthymatous crust covering the mucus. The beginning of the process is characterized by sneezing and the ordinary

symptoms of nasal catarrh. Pain is not significant and the only apparent inconvenience is the formation of mucous plugs in the nasal passages (1463).

A study conducted by the United States Public Health Service investigated 897 workers in seven chromate-producing plants (1673). The time each employee worked in the chromate industry was compared with the incidence of nasal septum perforation. The incidence of nasal septum perforation increased significantly as duration of employment in the chromium industry increased (see Table 53-2).

Ulceration may also occur when chromium comes in contact with the skin. These ulcerations are referred to as "chromeholes" and are usually noted at the base of the finger nails, the knuckles, the eyelids, the edges of the nostrils, the toes and occasionally the throat. The ulceration is usually slow to occur, deep and not very painful (1463).

Allergenic contact dermatitis is a major problem faced by industries using chromium. Chromium dermatitis tends to persist, and to resist therapy due to its ability to remain in the dermis of the affected areas even after exposure has been discontinued. Hexavalent chromium which gets into the skin is reduced to the trivalent form and combines with skin proteins to form complete antigens capable of causing sensitization. Milner (1791) described a worker in a printing company who was constantly exposed to chromium. Dermatitis was controlled for 7 years by antihistamines and steroids, however, symptoms began to increase in severity. The worker experienced severe discomfort due to swelling, oozing, weeping and fissuring of the hands and wrists. A patch test to 0.25% potassium dichromate was strongly positive. Application of a 10% ascorbic acid solution to the hands hourly while at work resulted in complete elimination of the dermatitis within one month. Hexavalent chromium is reduced to the trivalent form, by ascorbic acid, which impedes passage into the skin and prevents dermatitis.

Dust or mist containing hexavalent chromium irritates mucous membranes and causes sneezing, rhinorrhea, irritation and redness of the throat and general bronchospasm. Sensitization may develop, resulting in typical asthmatic attacks which recur on later exposure. Exposure to high concentrations may produce coughing, headache, dyspnea and substernal pain (1463).

A case of a delayed anaphylactoid reaction to sodium chromate was reported by Moller et al. (1776). A 29-year-old welder with a 10 year chromate-exposure history experienced transient skin and eye irritation after an overexposure to chromic acid mist. Twelve hours later he developed periorbital pain, swelling, and a diffuse urticarial eruption. Upon return to work 5 months later, the reaction recurred and was associated with chest tightness and dyspnea. He experienced a third episode at home following several hours of arc welding. Intradermal and prick tests to sodium chromate were negative. However,

TABLE 53-2

PERFORATION OF NASAL SEPTUM IN CHROMATE WORKERS

Duration of Employment in the Chromate Industry	All Workers		
	Total Number	Workers with Perforation Number	%
less than 6 months	41	1	2.4
6 months to 3 years	117	46	39.3
3 to 10 years	370	205	55.4
over 10 years	369	257	69.6
TOTAL:	897	509	56.7

Source: 1673

four hours after a bronchial challenge with 29 $\mu g/m^3$ sodium chromate for 25 minutes, he developed generalized urticaria, facial angioedema and bronchospasm. Blood analysis revealed a three-fold increase in plasma histamine. Skin biopsy showed a perivascular mixed cellular infiltrate with edema. Moller concluded that a delayed anaphylactoid reaction in response to inhaled metal salt had occurred, possibly via cell-mediated immunity.

Several studies suggest a correlation between cancer mortality, and industrial chromate exposure (1665,1666,1250). Mortality was investigated in 178 male employees and retirees from 9 chromeplating plants. All subjects had worked with chromium for at least one year during the period of January 1, 1951 through December 31, 1981 (1665). The current air concentrations averaged 7 $\mu g/m^3$ as chromium trioxide near the chromium baths and 3 $\mu g/m^3$ in the middle of the room. However, investigations performed in the same plants prior to 1980 reported higher mean chromium trioxide concentrations, i.e., 109 $\mu g/m^3$ near the chromium baths and 35 $\mu g/m^3$ in the middle of the room (1665). A total of 15 deaths had occurred, fairly close to the expected number (15.4), however, mortalities from tumors significantly exceeded the expected number (8 vs. 4.2). Malignancies were almost entirely observed in the group of workers exposed to chromic acid in hard chromeplating plants. The incidence of death from lung cancer was significantly increased ($P = 0.03$) and a higher mortality from stomach tumors was seen in the chromeplating workers.

A retrospective study carried out by Becker et al. (1666) investigated the cancer risk of arc welders exposed to fumes containing chromium and nickel. The study consisted of 1224 male welders and 1694 male turners. The turners worked in the same environment as the welders but were not exposed to air-borne nickel and chromium. Becker noted that although not exposed to chromium, the turners were exposed to mineral cutting oils containing nitrosamines which may represent a cancer risk. The study noted 77 deaths in the welders (6.3%) and 163 deaths in the turners (9.6%). After an adjustment for age was made, a statistically significant incidence of malignant neoplasms was observed in welders exposed to nickel and chromium welding fumes for over 30 years.

Analysis of 11 cases of lung carcinoma in chromate factory workers was reported by Nishiyama et al. (1667). The average duration of exposure was 23.9 years. The age of onset ranged from 41 to 68 years. Ten of the eleven were heavy smokers; seven of the workers had perforation of the nasal septa. The primary sites of the cancers were the bronchi. A total of 9 squamous cell carcinomas and 3 small cell carcinomas were found.

53.3.3 Levels of Concern

The EPA (355) has set an ambient water quality criteria for total chromium (VI) of 0.05 mg/L. The drinking water standard for chromium is 0.05 mg/L (296). EPA (992) has also developed health advisories for noncarcinogenic risks from exposure to chromium (VI) in drinking water of 5 mg/L for up to 10 days and 0.84 mg/L for long-term exposure.

The WHO (666) recommends a drinking water level of 5 μg/L total chromium.

IARC (1250) list chromium and its compounds in category 1 (sufficient evidence of human carcinogenicity) in its weight-of-evidence ranking of potential carcinogens.

The OSHA (298) standard for soluble chromium salts such as sodium chromate is 0.5 mg/m^3. The ACGIH (3) also recommends a threshold limit value for both water soluble and certain insoluble chromium (VI) compounds of 0.5 mg/m^3 (as Cr) with an A1-human carcinogen notation for certain insoluble chromium (VI) compounds.

53.3.4 Hazard Assessment

Carcinogenicity findings for hexavalent chromium in a variety of laboratory animals tested by various routes have resulted in inconclusive results (1252). The data specific to sodium chromate are inadequate to evaluate its carcinogenic potential. However, sufficient evidence exists of the carcinogenicity of certain insoluble hexavalent chromium compounds. In addition, several epidemiologic studies indicate an increased risk of lung cancer among workers exposed to a mixture of chromium (VI) compounds in the chromate production industry

(1665,1666,1250). The chromium compound(s) responsible has not been established. In that available evidence does not permit a clear delineation of the relative contribution of chromium compounds of different oxidation states or solubilities, IARC (1250) classifies all chromium compounds as Group 1 (i.e., sufficient evidence of carcinogenicity to humans).

The USEPA (667) has calculated an upper-limit incremental unit cancer risk of 41 $(mg/kg/day)^{-1}$ for chromium based on human occupational data.

Hexavalent chromium salts are mutagenic in several bacterial systems, induce chromosomal aberrations in a variety of mammalian cells and are capable of inducing DNA damage (1465,1466,1469,1470,1472). Hexavalent chromium is also embryotoxic to mice and hamsters and induced malformations in surviving hamster fetuses, including cleft palate and skeletal defects (1274,1462).

Hexavalent chromium compounds readily cross biological membranes and can be absorbed from the gastrointestinal tract, the lungs and via the skin (1464). Toxic effects of chromium (VI) exposure include gastritis, rhinitis, dermatitis, skin ulcerations and kidney damage (1452,46).

Dusts of hexavalent chromium compounds are severe irritants of the nasopharynx, lungs and skin and have been linked to production of ulcerated nasal mucosa, perforated nasal septa and pulmonary edema (1463).

Ingestion of chromium (VI) compounds usually results in vomiting, abdominal pain, bleeding and diarrhea (1663); toxic levels induce hepatic and renal failure (1664). The lethal ingested dose for humans is estimated to be in the range of 1.5 to 1.6 grams (1452).

53.4 SAMPLING AND ANALYSIS CONSIDERATIONS

Determination of sodium chromate (as chromate) concentrations in soil and water requires collection of a representative field sample and laboratory analysis for hexavalent chromium [Cr(VI)]. For the determination of trace metals, care is required to prevent losses and avoid contamination during sample collection. Samples may be collected in either glass or plastic containers; for metals, polyethylene with a polypropylene cap (no liner) is preferred. Samples should be preserved by cooling and maintaining samples at 4°C until analysis. Samples should be analyzed as soon as possible after collection; maximum holding time is 24 hours. In addition to the targeted samples, quality control samples such as field blanks, duplicates, and spiked matrices may be specified in the recommended methods.

EPA-approved procedures for the analysis of hexavalent chromium in aqueous samples include Methods 218.4 and 218.5 (1420), 7195, 7196, and

7197 (65) and 303B (1422). Methods 218.4, 7197, and 303B are based on chelation of hexavalent chromium with ammonium pyrrolidine dithiocarbamate (APDC) and extraction with methyl isobutyl ketone (MIBK); the sample extract is aspirated into the flame of an atomic absorption spectrophotometer for determination of a hexavalent chromium concentration. Hexavalent chromium may also be chelated with pyrrolidine dithiocarbamic acid in chloroform; a colorimetric procedure using diphenylcarbazide may also be used to determine the hexavalent chromium concentration. Methods 218.5 and 7195 are based on the separation of hexavalent chromium from the sample by coprecipitation of lead chromate with lead sulfate in a solution of acetic acid. After separation, the supernate is drawn off and the Cr(VI) precipitate resolubilized in nitric acid as trivalent chromium and quantified by furnace (Methods 218.5 and 7195) or flame (Method 7195) atomic absorption. In addition, hexavalent chromium may be determined colorimetrically by reaction with diphenylcarbazide in acid solution using Method 7196; a red-violet color is produced whose absorbance may be measured spectrophotometrically.

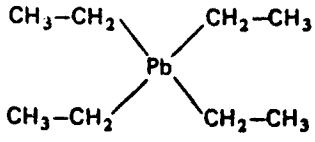
The EPA procedures recommended for determination of hexavalent chromium concentrations in aqueous samples may also be applicable to the determination of hexavalent chromium concentrations in soil and waste samples. These procedures differ primarily in the preparation of the sample for analysis; hexavalent chromium must be solubilized and separated from the sample matrix prior to analysis.

Hexavalent chromium in environmental systems is generally partially converted to trivalent chromium through reduction; there are several EPA-approved procedures for the determination of "total chromium" in both aqueous and non-aqueous samples. These methods include Methods 218.1, 218.2, and 218.3 (1420), 7190 and 7191 (63) and 303A, 303B, and 304 (1422). Samples for determination of total chromium may also be collected in either glass or plastic containers. Sample preservation involves adding concentrated nitric acid in the field until the pH of the sample is less than 2; maximum holding time is six months.

Typical detection limits for hexavalent chromium that can be obtained in wastewaters are shown below; detection limits were not indicated for non-aqueous samples. The actual detection limit achieved in a given analysis will vary with instrument sensitivity and matrix effects.

Aqueous Detection Limit

10 µg/L (Method 218.4)
5 µg/L (Method 218.5)
5 µg/L (Method 7195)
500 µg/L (Method 7196)
1 µg/L (Method 7197)

COMMON SYNONYMS:	CAS REG. NO.:	FORMULA:	AIR W/V CONVERSION FACTORS at 25°C
Tetraethyl plumbane TEL	78-00-2 NIOSH NO.: TP4550000	$C_8H_{20}Pb$	13.22 mg/m³ ≈ 1 ppm 0.075 ppm ≈ 1 mg/m³
	STRUCTURE: 		MOLECULAR WEIGHT: 323.45

REACTIVITY	Various sources indicate that reaction of tetraethyl lead with strong oxidizing agents such as potassium permanganate or sulfuryl chloride may cause a fire or explosion and that the compound is also incompatible with concentrated acids. Exposure to sunlight may cause decomposition to tri-, di-, and mono-ethyl lead compounds. Decomposition may also occur due to heating (with attendant pressure rise in closed containers) and reaction with rust and certain other metals. Chemical compatibility charts suggest other general incompatibilities with organic peroxides or hydroperoxides, epoxides, explosives, and polymerizable compounds (38,54,60,511,512).

PHYSICO-CHEMICAL DATA	• Physical State (at 20°C): oily liquid	(23)
	• Color: colorless (may be dyed red, orange or blue)	(23)
	• Odor: sweet	(60)
	• Odor Threshold: no data	( )
	• Liquid Density (g/ml at 20°C): 1.653	(14)
	• Freezing/Melting Point (°C): -137	(14)
	• Boiling Point (°C): 152 at 291 mm	(14)
	• Flash Point (°C): 93.3 (cc); 85.0 (oc)	(38,60,506)
	• Flammable Limits in Air, % by Volume: 1.8%-?	(506)
	• Autoignition Temperature (°C): decomposes first	(23,38,60)
	• Vapor Pressure (mm Hg at 20°C): 0.15	(67)
	• Saturated Concentration in Air (mg/m³ at 20°C): 2660	(ADL estim)
	• Solubility in Water (mg/L at 20°C): insoluble	(23)
	• Viscosity (cp at 20°C): 0.864	(21)
	• Surface Tension (dyne/cm at 20°C): 28.5	(60)
	• Log (Octanol-Water Partition Coefficient), log K_{ow}: no data	( )
	• Soil Adsorption Coefficient, K_{oc}: 22,900	(1716)
	• Henry's Law Constant (atm•m³/mol at 20°C): 0.90	(1715)
	• Bioconcentration Factor: no data	( )

PERSISTENCE IN THE SOIL-WATER SYSTEM	Tetraethyl lead is expected to be relatively immobile and non-persistent in soil due to degradation, sorption, and volatilization. Typical half-lives in water are on the order of one week, and degradation has generally been found to be enhanced in sunlight.

PATHWAYS OF EXPOSURE	The primary exposure pathway of concern from soil/groundwater systems is the migration of tetraethyl lead to groundwater drinking water supplies, although it is relatively immobile and may degrade under some conditions. Exposures through inhalation may also be important in some situations.

HEALTH HAZARD DATA	Signs and Symptoms of Short-term Human Exposure (38,51): Mild symptoms of tetraethyl lead intoxication include headache, anxiety, insomnia, nausea, appetite loss, low body temperature, slow heart beat and tremor. Skin contact may cause itching, burning and redness. The liquid and vapor may be irritating to the eyes.
	Toxicity Based on Animal Studies: LD_{50} (mg/kg) oral 14 [rat] (19) skin 200-1500 (1080) [rabbit] LC_{50} (mg/m^3) inhalation [rat] (59) 850-1 hr
	Long-Term Effects: CNS and neurologic effects
	Pregnancy/Neonate Data: Embryotoxic
	Mutation Data: Conflicting
	Carcinogenicity Classification: IARC - none assigned; NTP - none assigned

HANDLING PRECAUTIONS (38,1080)	Handle only with adequate ventilation • Vapor concentrations of 0.075-0.75 mg/m^3: any supplied-air respirator or self-contained breathing apparatus • 0.75-3.75 mg/m^3: any supplied-air respirator or self-contained breathing apparatus with full facepiece • 3.75-40 mg/m^3: a type-C supplied-air respirator operated in pressure demand or other positive pressure or continuous-flow mode • Chemical goggles if there is probability of eye contact • Neoprene or PVC protective clothing to prevent skin contact.

EMERGENCY FIRST AID TREATMENT (38,1080)	Ingestion: Induce vomiting if victim is conscious. Get medical attention • Inhalation: Move victim to fresh air; give artificial respiration if necessary. Get medical attention • Skin: Rinse contaminated area with kerosene or similar petroleum products, if readily available. Remove contaminated clothing and shoes, then wash skin with soap and water. Get medical attention • Eye: Irrigate with large amounts of water. Get medical attention.

ENVIRONMENTAL AND OCCUPATIONAL STANDARDS AND CRITERIA

AIR EXPOSURE LIMITS:

Standards

- OSHA PEL (8-hr TWA): 0.075 mg/m^3 (as Pb) (skin)
- AFOSH PEL (8-hr TWA): 0.075 mg/m^3 (as Pb) (skin)

Criteria

- NIOSH IDLH (30-min): 40 mg/m^3 (as Pb)
- ACGIH TLV® (8-hr TWA): 0.1 mg/m^3 (as Pb) (skin)
- ACGIH STEL (15-min): deleted

WATER EXPOSURE LIMITS:

Drinking Water Standards

Under the National Primary Drinking Water Regulations (296), the maximum contaminant level (MCL) for lead is 0.05 mg/L. This MCL applies to community water systems which serve a population of 10,000 people or more and which add a disinfectant as part of their treatment process (991).

EPA Health Advisories

The EPA (992) has developed a Health Advisory (formerly termed SNARL) for non-carcinogenic risk for long-term exposure to lead in drinking water of 0.02 mg/L.

EPA Ambient Water Quality Criteria (355,1777)

- Human Health

  The ambient water quality criterion for lead is recommended to be identical to the existing drinking water standard which is 0.05 mg/L.

- Aquatic Life
  - Freshwater

    Freshwater aquatic organisms and their uses should not be affected unacceptably if the 4-day average concentration (in μg/L) of lead does not exceed the numerical value given by e(1.266[ln(hardness)]-4.661) more than once every 3 years on the average and if the 1-hour average concentration (in μg/L) does not exceed the numerical value given by e(1.266[ln(hardness)]-4.616) more than once every 3 years on the average.

  - Saltwater species

    Saltwater aquatic organisms and their uses should not be affected unacceptably if the 4-day average concentration of lead does not exceed 5.6 μg/L more than once every 3 years on the average and if the 1-hour average concentration does not exceed 140 μg/L more than once every 3 years on the average.

WHO Drinking Water Guideline (666)

A health-based guideline for drinking water of 0.05 mg/L is recommended for lead. A daily per capita consumption of two liters of water was assumed.

REGULATORY STATUS (as of January 1, 1987)

Promulgated Regulations

- Federal Programs

Clean Water Act (CWA)

Tetraethyl lead is designated a hazardous substance. It has a reportable quantity (' of 4.54 kg (347,985). Lead and lead compounds are listed as toxic pollutants (351). Water quality criteria have been set. Guidelines exist for lead effluent in point source categories for the manufacture of glass, rubber, batteries, inorganic chemicals, iron and steel and non-ferrous metals (1449,1202,1439,1436,354,894). Guidelines also exist in point source categories for metal finishing, ore mining and dressing, porcelain enameling, copper forming and electroplating (1444,1560,1561,1562,1446) and also in point source categories for electrical and electronic components, metal molding and casting and non-ferrous metals forming (1563,1564,1443).

Safe Drinking Water Act (SDWA)

Under the National Primary Drinking Water Regulations (296), the maximum contaminant level (MCL) for lead is 0.05 mg/L. This MCL applies to community water systems which serve a population of 10,000 people or more and which add a disinfectant as part of their treatment process.

In states with an approved Underground Injection Control program, a permit is required for the injection of tetraethyl lead-containing wastes designated as hazardous under RCRA (295).

Resource Conservation and Recovery Act (RCRA)

Tetraethyl lead is identified as an acute hazardous waste (P110) and listed as a hazardous waste constituent (328,329). Lead compounds are also listed as hazardous waste constituents (328). Waste streams from the following industries contain lead and are listed as specific sources of hazardous waste: inorganic pigments, iron and steel, secondary lead, petroleum refining and explosives (326,327).

Used oil that is burned for energy recovery may not contain greater than 100 ppm lead (1768).

Effective July 8, 1987, land disposal of liquid hazardous wastes, including free liquids associated with any solid or sludge-containing lead and/or its compounds at concentrations greater than or equal to 500 mg/L will be prohibited. The only exception will be underground injection (1755).

Solid wastes which contain a concentration equal to or greater than 5.0 mg/L lead are listed as hazardous in that they exhibit the characteristic defined as EP toxicity (988).

Comprehensive Environmental Response Compensation and Liability Act (CERCLA)
Tetraethyl lead is designated a hazardous substance under CERCLA. It has a reportable quantity (RQ) limit of 4.54 kg. Reportable quantities have also been issued for RCRA hazardous waste streams containing tetraethyl lead but these depend upon the concentrations of the chemicals in the waste stream (985,1733).

Any facility at which tetraethyl lead is present in excess of its threshold planning quantity of 100 pounds must notify state and local emergency planning officials. If tetraethyl lead is released from the facility in excess of its reportable quantity (RQ), local emergency planning officials must be notified (1751).

Clean Air Act (CAA)
The national primary and secondary ambient air quality standards for lead and its compounds are 1.5 mg/m^3, maximum arithmetic mean averaged over a calendar quarter (1405).

As of January 1, 1986, it is prohibited to produce or import leaded gasoline with a lead content in excess of 0.10 g/gallon (1567).

Marine Protection Research and Sanctuaries Act (MPRSA)
Ocean dumping of organohalogen compounds as well as the dumping of known or suspected carcinogens, mutagens or teratogens is prohibited except when they are present as trace contaminants. Permit applicants are exempt from these regulations if they can demonstrate that such chemical constituents are non-toxic and non-bioaccumulative in the marine environment or are rapidly rendered harmless by physical, chemical or biological processes in the sea (309).

Occupational Safety and Health Act (OSHA)
Employee exposure to tetraethyl lead (as Pb) shall not exceed an 8-hour time-weighted-average (TWA) of 0.075 mg/m^3 (298).

Hazardous Materials Transportation Act (HMTA)
The Department of Transportation has designated tetraethyl lead as a hazardous material which is subject to requirements for packaging, labeling and transportation (306).

Food, Drug and Cosmetic Act (FDCA)
The level for lead in bottled drinking water is 0.05 mg/L. This level is identical to the maximum contaminant level (MCL) given under the Safe Drinking Water Act (365).

Consumer Product Safety Act (CPSA)
Under the Federal Hazardous Substances Act, any paint or surface coating material intended or suitable for household use and shipped in interstate commerce cannot contain lead compounds in which the lead content (calculated as the metal) is in excess of 0.06% of the total weight of the contained solids or dried paint film. This regulation also applies to any toy or other article intended for use by children (1236).

- State Water Programs

  All states follow the National Primary Drinking Water Regulations under the Safe Drinking Water Act.

  States with additional regulations for lead are (731,981):

  Arizona - 0.1 mg/L in non-community water systems.
  Florida - 30 µg/L in the public water supply.
  Illinois - 0.1 mg/L in general use water.
  North Carolina - 25 µg/L in fresh water.
  Wisconsin - 5 µg/L preventive action limit in ground water.
  Wyoming - 5 mg/L in Class 2 ground water;
  0.1 mg/L in Class 3 ground water.

Proposed Regulations

- Federal Programs

  Clean Water Act (CWA)
  Effluent guidelines for lead have been proposed in the organic chemicals, plastics and synthetic fibers category (357).

  Safe Drinking Water Act (SDWA)
  EPA has proposed a Recommended Maximum Contaminant Level (RMCL) of 0.020 mg/L for lead as part of the National Primary Drinking Water Regulations (992).

  Resource Conservation and Recovery Act (RCRA)
  EPA has proposed that hazardous waste treatment, storage and disposal facilities monitor ground water for total lead when EPA suspects the facilities of leaking contaminants (1754).

  EPA has proposed listing as hazardous, mixtures of acutely toxic wastes, such as tetraethyl lead (1396).

  EPA has proposed listing wastewater treatment sludges from the sodium-lead alloy alkyl lead process and washwater from the formulation of mixed alkyl leads as specific sources of tetraethyl lead-containing hazardous waste (1397).

  EPA has proposed listing used oil (including automotive, hydraulic, coolant, insulating and metalworking oils) as a non-specific source of lead-containing waste (1566).

- State Water Programs
  No proposed regulations are pending.

EEC Directives

Directive on Drinking Water (533)
The mandatory values for lead in surface water treatment categories A1, A2 or A3 are 0.05 mg/L. There are no guideline values.

Directive Relating to the Quality of Water for Human Consumption (540)
The maximum admissible concentration for lead is 50 µg/L in running water.

Directive on Ground Water (538)
Direct and indirect discharge of lead into ground water shall be subject to prior review so as to limit such discharges.

Directive on Bathing Water Quality (534)
When inspection of a bathing area shows that heavy metals, pesticides or cyanides may be present, concentrations should be checked by competent authorities.

Directive on the Quality Required of Shellfish Waters (537)
The mandatory specifications for lead specify that the concentration of each substance in the shellfish water or in shellfish flesh must not reach or exceed a level which has harmful effects on the shellfish and larvae. The synergistic effects of other metals must be taken into consideration. The guideline specifications state that the concentration of lead in shellfish flesh must be so limited that it contributes to the high quality of shellfish product.

Directive on the Discharge of Dangerous Substances (535)
Lead cannot be discharged into inland surface waters, territorial waters or internal coastal waters without prior authorization from member countries which issue emission standards. A system of zero-emission applies to discharge of these substances into ground water.

Directive on Marketing and Use of Dangerous Substances (541)
Tetraethyl lead may not be used in ornamental objects intended to produce light or color effects by means of different phases.

Directive on Toxic and Dangerous Wastes (542)
Any installation, establishment, or undertaking which produces, holds and/or disposes of certain toxic and dangerous wastes including phenols and phenol compounds; organic-halogen compounds; chrome compounds; lead compounds; cyanides; ethers and aromatic polycyclic compounds (with carcinogenic effects) shall keep a record of the quantity, nature, physical and chemical characteristics and origin of such waste, and of the methods and sites used for disposing of such waste.

Directive on the Classification, Packaging and Labeling of Danzerous Substances (787)
Tetraethyl lead is classified as a toxic substance and is subject to packaging and labeling regulations.

Directive on Transfrontier Shipment of Hazardous Waste (1433)
When the holder of a hazardous waste such as lead intends to ship it to another member state, authorities of the member states concerned must be provided with information on the source and composition of the waste, measures to be taken to ensure safe transport, insurance against damage and the existence of a contractual agreement with the consignee of the waste. All transfrontier shipments must be properly packed and labeled and must be accompanied by instructions to be followed in the event of danger or accident.

Directive on Paints, Varnishes, Printing Inks, Adhesives and Similar Products (1334)
Lead alkyls are classified as toxic substances when present in concentrations greater than 0.1% and as harmful substances when present in concentrations ranging from 0.05 to 0.1%. Other lead compounds are classified as harmful when present at concentrations greater than or equal to 1.0%.

Directive on the Lead Content of Petrol (1430)
The maximum permitted lead content of leaded petrol is 0.15 g/L. Until April 1, 1990, unleaded petrol may contain up to 0.020 g/L of lead compounds.

Directive on a Limit Value for Lead in the Air (1429)
The limit value for the concentration of lead in air is 2 $\mu g/m^3$ expressed as an annual mean concentration.

Directive on Major Accident Hazards of Certain Industrial Activities (1794)
Tetraethyl lead manufacturers are required to notify competent authorities if it is stored or processed in quantities in excess of 50 tons. If a major accident occurs, authorities must be provided with the circumstances of the accident, substances involved, emergency measures taken, and the data available for assessing the effects on man and the environment.

EEC Directives - Proposed

Proposal for a Council Directive on the Dumping of Waste at Sea (1793)
EEC has proposed that the dumping of lead compounds at sea be forbidden without prior issue of a special permit.

54.1 MAJOR USES

Tetraethyl lead (TEL) is the primary component of formulated anti-knock mixtures for gasoline. Anti-knock agents prevent pre-ignition in internal combustion engines. U.S. consumption of TEL reached a peak of 312 million kg in 1970, but has declined significantly since the Environmental Protection Agency issued regulations requiring a gradual reduction in the lead content of gasoline. EPA has estimated that 51.8 million kg of lead were used in 1983. This is equivalent to 13 million gallons of TEL assuming that 3 ml of TEL provides 3.17 g of elemental lead (1409). Tetraethyl lead has also been used as an intermediate in the production of organomercury fungicides but the agricultural use of these compounds is no longer permitted in the U.S. (21,1252).

54.2 ENVIRONMENTAL FATE AND EXPOSURE PATHWAYS

54.2.1 Transport in the Soil/Ground-water Systems

54.2.1.1 Overview

Tetraethyl lead is expected to be relatively immobile at low concentrations (dissolved in water). Bulk quantities of the liquid chemical (e.g., from a spill of the pure substance, a gasoline additive that contains it, or leaded gasoline) could be transported down through the unsaturated zone. However, as described later in this section, tetraethyl lead is volatile and susceptible to a number of degradation processes (photolysis, hydrolysis, oxidation).

Environmental transport pathways for TEL can generally be assessed by using an equilibrium partitioning model, as shown in Table 54-1. These calculations predict the partitioning of low soil concentrations of TEL among soil particles, soil water, and soil air. The estimates for the unsaturated topsoil model show that while almost all of the chemical (97.5%) is sorbed to the soil, a small portion (2.5%) is in the soil air, and thus is available to diffuse through the soil-air pores to the soil surface. Migration of tetraethyl lead by bulk transport (percolating water) or aqueous phase diffusion or dispersion is expected to be insignificant since such a small fraction partitions to the soil water. In saturated, deep soils (containing no air and negligible soil organic carbon) a much greater fraction is in the mobile ground-water phase (1%), but still a very small amount compared to that sorbed to the soil.

Tetraethyl lead has been used in large quantities as a gasoline octane enhancer for about 60 years. However, its use is decreasing because it cannot be used in most new cars as it poisons the catalyst used in catalytic converters. Its use in all motor fuels in the U.S. is being phased out by law.

TABLE 54-1

EQUILIBRIUM PARTITIONING CALCULATIONS FOR TETRAETHYL LEAD IN MODEL ENVIRONMENTS[a]

Soil Environment	Estimated Percent of Total Mass of Chemical in Each Compartment		
	Soil	Soil-Water	Soil-Air
Unsaturated topsoil at 25°C[b,c]	97.5	0.022	2.5
Saturated deep soil[d]	99.0	1.0	-

a) Calculations based on Mackay's equilibrium partitioning model (34,35,36); see Introduction in Volume 1 for description of model and environmental conditions chosen to represent an unsaturated topsoil and saturated deep soil. Calculated percentages should be considered as rough estimates and used only for general guidance.

b) Utilized estimated soil sorption coefficient (1716): K_{cc} = 22,900.

c) Henry's law constant taken as 0.90 atm·m³/mol at 25°C (estimated using data from (1715).

d) Used sorption coefficient $K_p = 0.001\ K_{oc}$.

54.2.1.2 Sorption on Soils

There appear to be few, if any, studies on the soil sorption behavior of TEL, perhaps because the largest spills of the compound have occurred at sea. The susceptibility of TEL to degradation by light and its high volatility complicate the assessment of its leaching potential as well.

No values for the equilibrium soil sorption constant, K_{oc}, for TEL were found in the literature. An average value of 22,900 has been estimated using four correlation equations and the solubility data of Feldhake and Stevens (1715). This value indicates that TEL sorbs strongly to topsoils (containing > 0.1% organic carbon), i.e., a very large percentage of the chemical will be sorbed to soil although some leaching is still possible. As with all neutral organic chemicals, the extent of soil sorption is directly proportional to the soil organic carbon content. For low organic carbon soils (e.g., clays), the extent of sorption may also depend on other properties of the soil such as surface area, cation exchange capacity, and degree of hydration.

54.2.1.3 Volatilization from Soils

Tetraethyl lead has a relatively high vapor pressure which has been given as a function of temperature by Feldbake and Stevens (1715) based on the data of Buckner and Norrish (1717) as log P = 9.34286 - 2908.43/T where P is the vapor pressure in torr and T the absolute temperature (°C + 273.16). This equation indicates a vapor pressure of 0.26 torr at 20°C while a slightly lower value of 0.15 torr has also been given (67). These values together with TEL's low aqueous solubility result in a high volatility (0.90 atm·m^3/mol at 25°C based on the solubility and vapor pressure data in Reference 1715). Therefore, volatilization from soils should be an important transport pathway, if water is present, despite the tendency of TEL to sorb strongly.

54.2.2 Transformation Processes in Soil/Ground-water Systems

Tetraethyl lead is susceptible to a number of degradation processes including hydrolysis, photolysis, and oxidation, and thus it is not considered persistent in the environment.

The half-life for aqueous hydrolysis of TEL in water of pH 7 at 40°C has been given as eight days, with $(C_2H_5)_3PbOH$ being the hydrolysis product (1718). Triethyl lead hydroxide is soluble in water, however, so the hydrolysis product appears to be $(C_2H_5)_3Pb^+$.

The rate of TEL degradation in seawater and fresh water was investigated by Grove (1720) who determined a minimum half-life for the dissolved compound by measuring its concentration and those of its degradation products over time in stirred, open tanks. The minimum half-life was found to be about half-a-day in sea water and two days in fresh water. Using completely filled syringes of fresh water which had not been de-aerated, a half-life of about seven days resulted. Diffused daylight did not appear to accelerate the rate of decomposition.

Other work (1721,1722) has shown accelerated degradation of TEL in sunlight, however, using a liter of treated ("permuted") water to which 165 mg of TEL had been added (well above the solubility limit). Charlou et al. (1721) found about 1%, 20%, and 97-100% degradation after four hours for samples kept in darkness, exposed to sunlight and irradiated with UV light, respectively. The values correspond to a half-life of approximately 11.5 days for the sample kept in darkness but only 1.5 days for the one exposed to sunlight.

In distilled water, Jarvie et al. (1722) found tetraethyl lead to be much more stable in the dark with only two percent of an initial 12-15 x 10^{-5} M "solution" degraded after 77 days, whereas in sunlight 99% degraded after 15 days. The decomposition in darkness was found to be catalyzed by Cu^{+2} and Fe^{+2} ions; the adsorption of TEL from solution onto silica also accelerated the degradation with 97% reacting in about a month.

The degradation of TEL is believed to proceed through successive dealkylations: Et_4Pb to Et_3Pb^+ to Et_2Pb^{+2} to Pb^{+2} (1719,1722,1723). It has also been suggested that lead alkyl ions and inorganic lead may undergo biological alkylation (e.g., 1723,1570). However, its significance in natural environments has been doubted (1722,1723), and other work has indicated an absence of biological methylation (1724).

54.2.3 Primary Routes of Exposure from Soil/Ground-water Systems

The above discussion of fate pathways suggests that the mobility and exposure to tetraethyl lead will depend on the environmental conditions. This compound is considered to have a moderate volatility and to be moderately to strongly sorbed to soils. These fate characteristics suggest some possible exposure pathways.

Volatilization of TEL from a disposal site presents a potential pathway of exposure, however, the adsorption of this compound to soil may limit this occurrence as shown in Table 54-1. Drinking water contamination resulting from the migration of TEL may occur although TEL is considered relatively immobile in soil. Mitre (83) reported that lead was one of the most commonly detected contaminants both in ground water and surface water at National Priority List (NPL) sites. Most analyses, however, are conducted for total lead and are probably not indicative of the presence of TEL. Little information appears to be available on the presence of TEL in surface water or ground water (1738).

The movement of TEL in ground water or with soil particles may result in discharges to surface waters. As a result, ingestion exposures may occur through the use of surface waters as drinking water supplies, and dermal exposures may result from the recreational use of surface waters. In addition, TEL may be taken up by aquatic organisms or domestic animals. The extent to which these exposure pathways are important depends upon the importance of transport pathways (volatilization and adsorption to sediment) and also on the transformation of TEL in surface water. The fact that TEL has not been commonly reported in surface waters (1738), although analyses have been limited, suggests that associated exposure pathways may not be as important for TEL as direct exposure through contaminated ground water or air releases.

54.2.4 Other Sources of Human Exposure

The use of TEL as an antiknock additive in gasoline has lead to the presence of this compound in the atmosphere, largely as a result of losses in filling, transport and storage. As a result, concentrations are higher in such locations as parking garages and filling stations. For example, a concentration of 2000 ng/m^3 TEL was reported in the air at the exit of a parking garage (1735). Vapor organo-lead concentrations in six U.S. cities ranged from < 100 to 800 ng(Pb)/m^3. The ratio

between vapor R_4Pb and particulate lead in urban and suburban areas ranges from about 0.05-0.1 (1737). The range for suburban areas appears to be about 1-110 ng/m^3 (1737).

As mentioned above, there is little information on the presence of TEL in water, particularly drinking water supplies. Tetraethyl lead compounds have, however, been found in fish. Chau et al. (1739) reported levels of TEL ranging from 0.3-9.3 ng/g wet weight in a variety of species of fish from Ontario.

54.3 HUMAN HEALTH CONSIDERATIONS

54.3.1 Animal Studies

54.3.1.1 Carcinogenicity

No adequate, well-controlled study of the carcinogenic effects of TEL has been conducted. A study by Epstein and Mantel (1253) found that subcutaneous injection of 0.6 mg of TEL given in 4 divided doses to Swiss mice between birth and 21 days of age resulted in 20% mortality. Among survivors, malignant lymphomas were observed in 1 of 26 males and 5 of 41 females within 36 to 51 weeks. The incidence in male and female controls was 1 of 39 and 0 of 48, respectively. Since this type of tumor occurs frequently and with variable prevalence in untreated mice of this strain, the significance of this 12% incidence in females is difficult to assess, particularly in the absence of other corroborating data.

54.3.1.2 Mutagenicity

Exposure of Drosophila melanogaster to TEL resulted in an increased occurrence of nondisjunction and chromatid breaks (1256,1257). Negative findings were reported in a dominant lethal study conducted in mice (1258).

54.3.1.3 Teratogenicity, Embryotoxicity and Reproductive Effects

TEL is not teratogenic to either rats or mice. McClain and Becker (1259) administered oral doses of 7.5, 15 or 30 mg/kg to rats as 3 divided doses during early or late organogenesis (days 9, 10 and 11 or 12, 13 and 14, respectively). There was 100% maternal mortality in the 30 mg/kg groups. In the remaining treatment groups, there were increased incidences of resorptions and incomplete ossification, but these effects were considered to be due to the maternal toxicity of TEL rather than its direct effect on the fetus.

Kennedy et al. (1260) administered 0.01, 0.1, 1 or 10 mg/kg TEL by gavage to mice and rats daily during the organogenesis. Treatment with 10 mg/kg was discontinued in both species after 3 doses because of its toxic effect and the number of pregnancies were sharply reduced in

these groups. An increase in fetal resorption and growth retardation occurred in both species at the 1 mg/kg level. Three fetuses from 1 litter in the group of mice receiving 0.1 mg/kg displayed torsion of the rear limbs.

Administration of TEL to 5-day-old chick embryos resulted in 100% mortality by the 11th day. When TEL was given on the 8th day, mortality was 47% by day 11. All chicks died on the 20th day, after the opening of the egg, due to the inability to breathe. The neuromuscular systems were found to be atrophied. The administered dose was not reported (1261).

54.3.1.4 Other Toxicologic Effects

54.3.1.4.1 Short-term Toxicity

Systemic organolead poisoning can result from inhalation of the vapor or ingestion. Because of their high degree of lipid solubility, organolead compounds such as TEL are also absorbed through the skin (17,1255). The toxicity of TEL is believed to be due to its metabolic conversion to triethyl and inorganic lead.

TEL is known to be slowly metabolized to triethyl lead by mixed function oxidases in the liver. The triethyl form accumulates in nonosseous tissues, particularly the liver, kidney and brain (1255). It is believed that the triethyl form is eventually converted to diethyl lead and finally to inorganic lead and largely excreted in the urine (1262,1263). One day after iv administration of 12 mg/kg TEL to rabbits, total lead in the urine consisted of 69% diethyl lead, 27% inorganic lead and 4% triethyl lead. Triethyl lead accounted for 84% of the total lead in the liver, 68% in the kidney and 59% in the blood. Diethyl lead accounted for 93% of the total lead in the bile and inorganic lead made up 90% in the colonic and rectal contents (1264).

Oral LD_{50} values for TEL for the rat have ranged from 12.3 to 29 mg/kg (47,1265). After single oral doses of 17 mg/kg, rats showed irritability, hypermobility, tremors and spasticity. No behavioral changes were seen after a single oral dose 1.7 mg/kg (1266).

Single ip doses of 10 mg/kg had no effect on male rats. Doses greater or equal to 20 mg/kg caused 80% mortality. Mean survival times ranged from 38.5 to 149.4 hours. Among the toxic signs seen were tremor, jumping, hyperexcitation and tetanic convulsions. No significant changes in spontaneous motor activity were observed in surviving rats in the 10 and 20 mg/kg groups; however, the motor activity of dying rats in the 20 and 40 mg/kg groups significantly increased 5-7 days after administration (1268).

Adult male rats treated with 7.88 mg/kg TEL subcutaneously at 7, 14 or 28 days prior to a single challenge with 35 mg/kg pentylenetetrazole, a seizure-inducing compound, had a significantly higher seizure rate than controls pretreated with saline. This

suggests the possible involvement of the limbic system in the CNS toxicity of TEL (1269). The precise manner in which TEL alters brain function is not clearly known, but it may involve inhibition of monoamine oxidase (MAO) (1254).

TEL caused an immunosuppressive effect in male mice exposed to 0.5-10 ppm in drinking water for 3 weeks. The maximal effect was produced at concentrations less than 2 ppm (1270).

The lowest lethal dose in rabbits after percutaneous administration is 830 mg/kg (47). When rabbits received a dermal application of 0.75 mg for 4 hours, tissue levels reached a peak after 18 hours, except in the spleen and bone where peak levels were reached after 7 and 30 days, respectively (1271).

Grant tasted TEL-containing gasoline in rabbit eyes and found it to cause immediate pain and blepharospasm which lasted for several minutes. When the application was repeated 10 times within a 5 minute period, it produced conjunctival hyperemia and moderate flocculent discharge, but no corneal or conjunctival damage (19).

54.3.1.4.2 Chronic Toxicity

Few long-term studies of TEL have been conducted in animals. "Repeated exposure" to oral doses of 1.7 mg/kg was associated with behavioral changes, peripheral hyperemia and excessive body weight gain in rats. No macroscopic changes were seen in most animals killed 21 weeks after the start of exposure. Cardiac hypertrophy, hyperemia and edema of the brain and changes in the liver, pancreas, thyroid, lungs and thymus were seen in a few rats. Microscopic changes seen in the liver and central nervous system were attributed to TEL exposure (1266).

No clinical manifestations of TEL toxicity were seen in rhesus monkeys given oral doses equivalent to 6 mg/kg/day of lead for 6 months. Minor elevations of blood and tissue lead were seen (1272).

54.3.2 Human and Epidemiologic Studies

54.3.2.1 Short-term Toxicologic Effects

The signs and symptoms of TEL intoxication differ from those of inorganic lead intoxication and are often vague and easily missed (46). The onset of symptoms may be delayed for up to 8 days after exposure. Acute exposure to TEL causes symptoms of CNS toxicity. Mild manifestations of intoxication include weakness, fatigue, headache, nausea, vomiting, diarrhea, anorexia, insomnia and weight loss. Peculiar symptoms are the sensation of hairs in the mouth and the feeling of insects crawling on the body. Ataxia, nystagmus or tremor may then develop. Vegetative disturbances known as the "TEL triad" begin to occur: hypotonia, hypothermia and bradycardia. As the

intoxication worsens, there is confusion, delirium, manic excitement, catatonia, tonic-clonic convulsions or "organic weakness." The vegetative disturbances then become more pronounced. Loss of consciousness and death may follow after several days (1570). Severe intoxication causes recurrent or continuous episodes of disorientation and intense hyperactivity which may rapidly convert to convulsions that may terminate in coma or death (46,1263). Absorption of only 1 g may be sufficient to cause death within 3-30 days due to its slow degradation to triethyl lead (1263). Unless death occurs, recovery is usually complete within approximately 1 week in mild cases and up to 3 months in severe cases (46).

Another distinguishing feature of TEL intoxication is the normal or only slightly elevated blood lead and an abnormally high urinary lead. In severe intoxication, the urine lead is rarely less than 350 μg/L urine, while blood lead is rarely greater than 50 μg/100 g of blood (46). In addition, organically bound lead does not interfere with iron incorporation into protoporphyrin or with other stages of heme synthesis as shown by normal urinary levels of coproporphyrin, porphobilinogen and δ-aminolevulinic acid (1273). Also, there is a total absence of morphological or chemical abnormalities in the erythrocytes. These effects are all in sharp contrast to those caused by inorganic lead (46).

Urinary lead is the most common means for detection of TEL overexposure, but diethyl lead may also be used as a specific indicator. Results obtained by Turlakiewicz and Chmielnicka (1274) showed a positive correlation between the concentration of TEL in the air and the amount of diethyl lead and total lead in the urine. These investigators suggested that permissible level of urinary diethyl lead in occupationally exposed workers should not exceed 8 μg/L.

The principal risk of TEL intoxication is in occupational exposure by inhalation or absorption through skin (1254). Absorption of a sufficient quantity of TEL either briefly at a high rate (100 mg/m^3 for 1 hour) or for prolonged periods at a lower rate causes acute intoxication (46).

Tetraethyl lead poisoning is usually the result of accidental or intentional exposure to gasoline (1263); however, in one case of "massive" ingestion of pure TEL, the victim survived 36 hours. Initial signs and symptoms were referable to increased intracranial pressure, but death was due to pulmonary edema (1288).

In the case of gasoline exposure, it is uncertain which neurologic and psychiatric symptoms are caused by TEL and which by hydrocarbons in the fuel, but because of its longer half-life in the CNS (7-8 days in the brain), the symptoms have been attributed to TEL (1255,1289). The person poisoned by intentional "gasoline sniffing" manifests signs of encephalopathy which include irritability, anorexia, pallor, tremor, nausea, vomiting and delirium. The gasoline itself may cause acute pneumonitis. Death may occur from a combination of CNS depression,

respiratory irritation and bronchiolar obstruction (1289). Neurologically, there are mixed choreoathetoid movements (i.e., ceaseless involuntary jerky or writhing movements) of the hands, arms, facial muscles and extensor tendons of the feet (1289).

Coulehan et al. (1290) studied lead toxicity secondary to gasoline sniffing in 23 Navajo adolescents. Sixty-five percent of the cases first presented with toxic encephalopathy. Out of 47 episodes, 31% involved asymptomatic lead overload, 31% involved tremor, ataxia and other neurologic signs and 38% involved encephalopathy, disorientation and hallucinations. Blood lead levels were all elevated with no value exceeding 40 μg/dL.

Liquid TEL may penetrate the skin without producing appreciable local injury. TEL decomposition products in dust form may cause itching, burning and transient redness when in contact with moist skin or ocular membranes. TEL itself may be irritating to the eyes (54).

54.3.2.2 Chronic Toxicologic Effects

Chronic exposure to TEL may result in symptoms of inorganic lead poisoning as well as the CNS effects of organic lead intoxication (1263). Symptoms are reported to include subtle behavioral alterations, such as reduction or absence of reactions to sound or light, hypotension, bradycardia, loss of ability to concentrate and reduction of memory. The long-term sequelae of these effects have not been assessed (1293). Chronic intoxication has mostly been diagnosed in workers exposed to aviation fuel or leaded gasoline.

In a mortality study of 592 workers with a mean TEL exposure of 17.9 years, the incidence of death was less than expected in the general population and there was no increased cancer rate in a 20-year follow-up. However, a 20-year latency period is insufficient to exclude carcinogenicity and may underestimate the true incidence of cancer (1291,1255). A comparison of 153 white male employees exposed to TEL for 20 or more years with a similar group of workers with no TEL exposure found skin cancer to be prevalent but the incidence in exposed workers was not significantly different from that of non-exposed workers (5% vs. 2.9%). IARC considers this study to be inadequate because workers who left employment for any reason were not included (1292,1252).

Sweeney et al. (1293) examined the cause-specific mortality of 2510 male employees who worked at least one day at an East Texas chemical plant between 1952-1977. From 1952 to 1959, TEL was the principal product. Among the 1350 workers exposed to TEL alone, total mortality was less than expected. Mortality from respiratory cancers was elevated by 34% (15 observed vs. 11.23 expected deaths). Mortality from primary brain tumors was elevated by 86% (3 observed vs. 1.61 expected). No excess was statistically significant. There was no increased risk of mortality with increasing length of employment. Risk was found to be highest in those with less than 10 years of employment.

54.3.3 Levels of Concern

Various drinking water standards and criteria have been established for lead. The maximum contaminant level for lead under the National Primary Drinking Water Regulations is 0.05 mg/L (296). This concentration is also recommended for drinking water by the WHO (666) and for ambient water by the USEPA (355,1777).

OSHA (296) has set a limit of 0.075 mg/m^3 (as Pb) as the 8-hour work-shift exposure limit for TEL. The ACGIH (3) recommends an exposure limit of 0.1 mg/m^3 (as Pb). Both groups include a notation of possible skin absorption.

54.3.4 Hazard Assessment

All lead compounds are considered toxic, especially the organolead compounds such as tetraethyl lead. The toxicity of TEL is believed to be due to its metabolic conversion to triethyl and inorganic lead. TEL can be absorbed through the skin, inhaled as a vapor or ingested (17,1255). Oral LD_{50} values for rats range from 12 to 29 mg/kg (47,1265); the dermal LD_{50} value is in the 200 to 100 mg/kg range for rabbits (1080).

Few long-term animal studies are available for TEL. Rats repeatedly exposed to oral doses of 1.7 mg/kg TEL exhibited behavioral changes, hyperemia and excessive body weight gain. Necropsy at 21 weeks indicated enlarged hearts, brain edema and changes in liver, pancreas, thyroid, lung and thymus in some animals (1266). Another study conducted with rhesus monkeys provided no indications of clinical effects subsequent to 6 months exposure to TEL (6 mg/kg/day as Pb) (1272).

The carcinogenic effects of TEL have not been evaluated adequately. An increase in malignant lymphomas was reported in female Swiss mice that survived four subcutaneous injections of TEL (total dose 0.6 mg) during the first three weeks of life (1253). The significance of this finding is difficult to assess due to the variable spontaneous incidence of this tumor in the strain of mice and the lack of other evidence supporting the carcinogenic activity of this compound.

Limited mutagenicity studies indicate no dominant lethal effects in mice exposed to TEL (1258). An increase in chromatid breaks was reported, however, in TEL-exposed Drosophila (1256,1257). TEL is not teratogenic in either rats or mice with oral administration but is embryotoxic (1259,1260).

In humans, TEL toxicity is characterized by insomnia, hallucinations, emotional instability and increased physical activity of an erratic nature. One should also not lose sight of the fact that TEL is ultimately metabolized to lead and is therefore capable of inducing the multitude of adverse effects associated with lead exposure.

54.4 SAMPLING AND ANALYSIS CONSIDERATIONS

Determination of the concentration of tetraethyl lead in soil and water requires collection of a representative field sample and laboratory analysis. Care is required to prevent losses during sample collection and storage. Soil and water samples should be collected in glass containers; extraction of samples should be completed within seven days of sampling and analysis completed within 30-40 days. In addition to the targeted samples, quality assurance samples such as field blanks, duplicates, and spiked matrices should be included in the analytical program.

Tetraethyl lead is not included among the EPA-designated priority pollutants, and an EPA-approved procedure for the analysis of tetraethyl lead is not available. However, the recommended analytical methods for semivolatile organics, EPA Methods 625 (65) and 8250 (63), would be appropriate methods of choice for the analysis of tetraethyl lead in aqueous (Method 625) or solid and waste (Methods 625 and 8250) samples. Prior to analysis, aqueous samples are extracted with methylene chloride using a separatory funnel or a continuous liquid-liquid extractor; solid samples are extracted with methylene chloride using soxhlet extraction or sonication methods. An aliquot of the concentrated sample extract is injected onto a gas chromatographic (GC) column using a solvent flush technique. The GC column is then programmed to separate the semivolatile organics; tetraethyl lead is detected with a mass spectrometer. Neat and diluted organic liquids may be analyzed by direct injection of the sample.

A detection limit for tetraethyl lead using these methods was not determined but would be in the range of 1-10 $\mu g/L$ for aqueous samples and 1-10 $\mu g/g$ for non-aqueous samples which have been extracted and part-per-million (ppm) range for samples which have been directly injected.

COMMON SYNONYMS:	CAS REG. NO.:	FORMULA:	AIR W/V CONVERSION FACTORS at 25°C
Hydrazine anhydrous Diamine Levoxine Hydrazine base Diamide	302-01-2 NIOSH NO.: MU7175000	H_4N_2	1.3 mg/m³ ≈ 1 ppm 0.769 ppm ≈ 1 mg/m³
	STRUCTURE: H_2N-NH_2		MOLECULAR WEIGHT: 32.05

REACTIVITY	Hydrazine is a strong reducing agent that is extremely reactive with many materials. Contact with strong oxidizers such as hydrogen peroxide, nitrogen tetroxide, chromates, chromic anhydride, chlorine, fluorine, halogen fluorides, fuming nitric acid, nitrous oxide, oxygen and potassium or sodium dichromate may result in immediate ignition or explosion. Contact with metal oxides of iron, copper, lead, manganese, or molybdenum may cause flaming decomposition. Copper salts promote decomposition of hydrazine and the catalytic decomposition caused by Ranay nickel at room temperatures is vigorous. One maker suggests avoidance of all catalytic metals (lead, copper, zinc, cadmium, cobalt, molybdenum, gold, silver) and certain alloys of these metals. Hydrazine may ignite spontaneously in air when in contact with organic materials with large or porous surfaces such as rags, cotton waste, sawdust, earth, or wood, and one source even adds asbestos to this list. Explosive metal hydrazides form when hydrazine and alkali metals are mixed in liquid ammonia. The blue precipitate formed when nickel perchlorate is mixed with hydrazine in water has been known to explode when a glass stirring rod was introduced. Contact with tetryl results in immediate ignition. Ethereal solutions of hydrazine with zinc diamide or diethyl zinc produce zinc hydrazine that explodes at 70°C. Chemical compatibility charts indicate potentially hazardous reactions with a wide variety of other materials (504,505,507,511).

PHYSICO-CHEMICAL DATA	• Physical State (at 20°C): oily liquid, fuming in air	(12)
	• Color: clear	(12)
	• Odor: fishy, ammonia type odor	(12)
	• Odor Threshold: 3-4 ppm	(59)
	• Liquid Density (g/ml at 20°C): 1.0036	(2)
	• Freezing/Melting Point (°C): 2	(12)
	• Boiling Point (°C): 113.5	(12)
	• Flash Point (°C): 100, closed and open cup	(60,504)
	• Flammable Limits in Air, % by Volume: 4.7-100	(60,504)
	• Autoignition Temperature (°C): varies; 270 on glass surface, 23.9 on rusty iron surface, 132 on black iron, and 156 on stainless steel	(60,504, 506)

PHYSICO-CHEMICAL DATA (Continued)	• Vapor Pressure (mm Hg at 20°C): 10.4 (2) • Saturated Concentration in Air (mg/m^3 at 20°C): 28,000 (67) • Solubility in Water (mg/L at 20°C): miscible (60) • Viscosity (cp at 20°C): 0.9 (21) • Surface Tension (dyne/cm at 20°C): 66.67 (21) • Log (Octanol-Water Partition Coefficient), log K_{ow}: not pertinent ( ) • Soil Adsorption Coefficient, K_{oc}: not pertinent ( ) • Henry's Law Constant ($atm \cdot m^3/mol$ at 20°C): 2×10^{-7} (ADL estim) • Bioconcentration Factor: not pertinent ( )
PERSISTENCE IN THE SOIL-WATER SYSTEM	Hydrazine is fairly mobile in soil water systems, but fairly non-persistent as well. Soil pH and organic carbon content have a large effect on its retention. Its degradation half-life in water is on the order of days, and in waters exposed to the atmosphere, volatilization losses may be significant.
PATHWAYS OF EXPOSURE	The primary exposure pathway of concern from soil/ground-water systems is the migration of hydrazine to ground water drinking water supplies. Exposures through inhalation may be important in some situations. However, the importance of these pathways is very dependent on the environmental conditions.
HEALTH HAZARD DATA	Signs and Symptoms of Short-term Human Exposure (46): Hydrazine vapor is immediately irritating to the nose and throat and causes dizziness, nausea, itching, burning and swelling of the eyes over a period of several hours. Temporary blindness may occur and last for up to 24 hours. Exposure to liquid can cause severe burns. Systemic effects include weight loss, weakness, vomiting and convulsions.
	Toxicity Based on Animal Studies: LD_{50} (mg/kg): oral 60 [rat] (59); skin 91 [rabbit] (59) LC_{50} (mg/m^3): inhalation [rat] (59) 741 ppm/4 hr
	Long-Term Effects: Liver and kidney damage
	Pregnancy/Neonate Data: Embryolethality
	Mutation Data: Limited evidence
	Carcinogenicity Classification: IARC - 2b; NTP - none assigned

HANDLING PRECAUTIONS (54)	Handle chemical only with adequate ventilation • Vapor concentrations up to 10 ppm: Any supplied-air respirator or any self-contained breathing apparatus • 10-50 ppm: Any supplied-air respirator with full facepiece, helmet or hood or any self-contained breathing apparatus with full facepiece • 50-80 ppm: Any type C supplied-air respirator with full facepiece operated in pressure-demand or other positive pressure mode or with full facepiece, helmet, or hood operated in continuous-flow mode • Chemical goggles to protect the eyes • Rubber aprons, gloves and boots.

EMERGENCY FIRST AID TREATMENT (54)	Ingestion: If victim is conscious, induce vomiting. Get medical attention • Inhalation: Move victim to fresh air immediately; if necessary perform artificial respiration. Get medical attention • Skin: Flush exposed area with water immediately. Get medical attention • Eye: Irrigate eye immediately. Get medical attention.

ENVIRONMENTAL AND OCCUPATIONAL STANDARDS AND CRITERIA

AIR EXPOSURE LIMITS:

Standards
- OSHA PEL (8-hr TWA): 1 ppm (skin)
- AFOSH PEL (8-hr TWA): 1 ppm (skin)

Criteria
- NIOSH IDLH (30-min): 80 ppm (skin)
- ACGIH TLV® (8-hr TWA): 0.1 ppm (skin) A2 - suspected human carcinogen
- ACGIH STEL (15-min): none established

WATER EXPOSURE LIMITS:

Drinking Water Standards - None established

EPA Health Advisories - None established

EPA Ambient Water Quality Criteria (355)
- Human Health
  None established as hydrazine is not a priority pollutant.

- Aquatic Life
  None established as hydrazine is not a priority pollutant.

REGULATORY STATUS (as of January 1, 1987)

Promulgated Regulations

- Federal Programs

  Safe Drinking Water Act (SDWA)
  In states with an approved Underground Injection Control program, a permit is required for the injection of hydrazine-containing wastes designated as hazardous under RCRA (295).

  Resource Conservation and Recovery Act (RCRA)
  Hydrazine is identified as a reactive, toxic hazardous waste (U133) and listed as a hazardous waste constituent (328,329).

  Comprehensive Environmental Response Compensation and Liability Act (CERCLA)
  Hydrazine is designated a hazardous substance under CERCLA. It has a reportable quantity (RQ) limit of 0.454 kg. Reportable quantities have also been issued for RCRA hazardous waste streams containing hydrazine but these depend upon the concentrations of the chemicals in the waste stream (985).

  Any facility at which hydrazine is present in excess of its threshold planning quantity of 1000 pounds must notify state and local emergency planning officials. If hydrazine is released from the facility in excess of its reportable quantity (RQ), local emergency planning officials must be notified (1751).

  Marine Protection Research and Sanctuaries Act (MPRSA)
  Ocean dumping of organohalogen compounds as well as the dumping of known or suspected carcinogens, mutagens or teratogens is prohibited except when they are present as trace contaminants. Permit applicants are exempt from these regulations if they can demonstrate that such chemical constituents are non-toxic and non-bioaccumulative in the marine environment or are rapidly rendered harmless by physical, chemical or biological processes in the sea (309).

  Occupational Safety and Health Act (OSHA)
  Employee exposure to hydrazine shall not exceed an 8-hour time-weighted-average (TWA) of 1 ppm (298).

  Hazardous Materials Transportation Act (HMTA)
  The Department of Transportation has designated hydrazine as a hazardous material which is subject to requirements for packaging, labeling and transportation (306).

- State Water Programs
  There are no specific state regulations for hydrazine.

Proposed Regulations

- Federal Programs
  No proposed regulations are pending.

- State Water Programs
  No proposed regulations are pending.

EEC Directives

Directive on Ground Water (538)
Direct discharge into ground water (i.e., without percolation through the ground or subsoil) of organophosphorous compounds, organohalogen compounds and substances which may form such compounds in the aquatic environment, substances which possess carcinogenic, mutagenic or teratogenic properties in or via the aquatic environment and mineral oils and hydrocarbons is prohibited. Appropriate measures deemed necessary to prevent indirect discharge into ground water (i.e., via percolation through ground or subsoil) of these substances shall be taken by member countries.

Directive on the Discharge of Dangerous Substances (535)
Organohalogens, organophosphates, petroleum hydrocarbons, carcinogens or substances which have a deleterious effect on the taste and/or odor of human food derived from aquatic environments cannot be discharged into inland surface waters, territorial waters or internal coastal waters without prior authorization from member countries which issue emission standards. A system of zero-emission applies to discharge of these substances into ground water.

Directive on Marketing and Use of Dangerous Substances (541)
Hydrazine may not be used in ornamental objects intended to produce light or color effects by means of different phases.

Directive on the Classification, Packaging and Labeling of Dangerous Substances (787)
Hydrazine is classified as a toxic substance and is subject to packaging and labeling regulations.

55.1 MAJOR USES

Hydrazine is used in industry as a chemical intermediate in the manufacture of pharmaceuticals, plastic blowing agents, as an oxygen scavenger in boiler feed water treatment and in fuel cells (1402,1403). It is also used as a missile propellant (1431), and in auxiliary power units of the space shuttle orbiter and solid rocket boosters (1608). Each F-16 aircraft carries 6.5 gallons of a 70% hydrazine/30% water solution used in an emergency power unit to supply electrical and hydraulic power (1403,1608). As a major user of hydrazine, the Air Force has sponsored much of the research on its environmental chemistry (1402-1431,1608-1615).

55.2 ENVIRONMENTAL FATE AND EXPOSURE PATHWAYS

55.2.1 Transport in Soil/Ground-water Systems

55.2.1.1 Overview

Hydrazine is expected to be relatively mobile in the soil/ground-water system when introduced either in aqueous solutions or in pure form. Hydrazine is a liquid at ambient temperature and is used alone, mixed with water or with unsymmetrical dimethylhydrazine (UDMH). Bulk quantities of hydrazine in any of these forms could be transported through the unsaturated zone, despite hydrazine's high reactivity. However, as discussed later in this section, hydrazine is susceptible to a number of degradation pathways in the soil/ground-water system.

The hydrazinium cation, $N_2H_5^+$, is a weak acid pK_a = 7.98 (25°C, zero ionic strength) (1703), thus hydrazine acts as a base in solution. At pH 7 (and low hydrazine concentrations), approximately 90% of the hydrazine will be protonated and 9% will exist as N_2H_4, while at pH 8 approximately half will be protonated and half unprotonated.

Transport pathways for hydrazine cannot be assessed using an equilibrium partitioning model. Although hydrazine undergoes volatilization, much of it exists in ionized form, as described above, which is non-volatile. As an inorganic compound, its sorption to soils and sediments is not directly proportional to the soil organic carbon content as is the case for organic species. In equilibrium models the basis for partitioning between soil-water and soil is the K_{oc} value (organic carbon partition coefficient) for the chemical, which does not apply to inorganic chemicals, such as hydrazine.

55.2.1.2 Sorption on Soils

The sorption behavior of hydrazine on soils has been investigated by two groups of researchers. Using four soils with the properties shown in Table 55-1, Braun and Zirrolli (1610) examined the leaching and sorption behavior of hydrazine and related fuels. Soil columns 20

TABLE 55-1

SOIL PROPERTIES AND PERCENT HYDRAZINE RECOVERY

NAME	MOISTURE CONTENT (%)	SAND (%)	CLAY (%)	ORGANIC (% CARBON)	pH	CEC[a] (meq/100g)	% HYDRAZINE RECOVERED
Sand	-	100.0	-	-	-	-	39.1
Clay	1.5	69.3	27.9	tr[b]	3.7	18.8	7.6[d]
Organic	0.2	96.1	1.0	1.0	6.4	20.4	1.3
VAFB[c]	0.4	99.1	0.4	tr[b]	6.1	7.3	1.6

a. Cation exchange capacity
b. Trace
c. Vandenberg Air Force Base soil
d. One part clay soil was mixed with nine parts pure sand to form a column which had good water percolation properties

Source: Braun and Zirrolli (1610)

cm high and 10 cm in diameter were saturated with distilled, deionized water and drained, and 10 mL of 0.1% v/v hydrazine was applied and allowed to equilibrate for 15 minutes. The columns were then leached with 2 liters of distilled, deionized water at 5 mL/minute. The percent hydrazine recovered is shown in Table 55-1. These results should be interpreted with caution since no distinction was made between degradation and retention. Nonetheless they do show the high mobility of hydrazine in pure sand compared with soil containing organic matter.

Using 3 grams of the same soils mixed with 30 mL of a 0.002% v/v aqueous hydrazine solution for 20 minutes, the sorption results in Table 55-2 were obtained (1610). The "adsorbed" hydrazine was calculated from the difference between the initial aqueous hydrazine concentration and the aqueous concentration after equilibration with soil. The extracted value is a measure of that actually removed from the soil; the difference between adsorbed and extracted amounts may represent degradation or sorption.

Hayes et al. (1612) have studied the interaction of hydrazine with various soil materials. The sorption of hydrazine on cation-exchanged montmorillonites was found to be highly pH dependent. Since cation exchange between $N_2H_5^+$ and Na^+ was the main sorption mechanism, 5-6 times as much hydrazine sorbed at pH 4 as at pH 8. For Al^{+3}- and Fe^{+3}-exchanged montmorillonite, the increase was ten-fold over the same pH range, but for Ca^{+2} montmorillonite only a slight increase in sorption was observed.

Hayes et al. (1612) also found a large interaction between hydrazine and geothite under neutral and acidic conditions. While the extent of sorption was not quantified, the formation of soluble hydrazine-iron (II) complexes was observed. The work reported by Isaacson and Hayes (1615) and Hayes et al. (1612) on the sorption of hydrazine to humic acids was performed at pH 4 and is thus not particularly relevant to environmental conditions. However, the authors note that pH had little influence on the sorbent molecules so it could be expected that at higher pH the importance of chemisorption would increase and that of ion exchange (of $N_2H_5^+$) would decrease.

55.2.1.3 Volatilization from Soils

Hydrazine has a high vapor pressure (14 mm Hg at 25°C). Since it is used in pure form or as a major component of mixtures, volatilization from soils or surface waters can be a significant transport pathway. However, hydrazine acts as a base in solution, and its tendency to volatilize from aqueous solutions will depend on the fraction of N_2H_4 that remains unprotonated, which is a function of pH. A pseudo-Henry's law constant of 1.0 mg m^{-3}/percent hydrazine (v/v) in solution can be inferred from the data of MacNaughton et al. (1613) for mixtures of pure hydrazine and water at low hydrazine concentrations (< 0.1%).

TABLE 55-2
HYDRAZINE[a] BEHAVIOR IN SOIL SORPTION STUDIES
(See Table 55-1 for information on soil compositions)

Soil	% Adsorbed[b]	% Extracted[c]	% Nonrecovered[d]
Sand	1	2	-
VAFB	58	44	14
Organic	53	25	28
Clay[e]	77	59	18

a. Initial solution was 0.002 percent (v/v) hydrazine in water.

b. Percentage of hydrazine either decomposed or sorbed during soil-fuel mixing.

c. Percentage of hydrazine extractable from soil with 0.1N HCl.

d. Difference between percent sorbed/decomposed and that extracted - may indicate amount of fuel decomposed.

e. Clay soil was not diluted with pure sand in these studies.

Source: Braun and Zirrolli (1610)

Evaporation rates for hydrazine from petri dishes were found to range from 16-100 mg/cm^2 hr under uncontrolled ambient conditions (1613). When mixed with water (or when pure hydrazine has absorbed water and CO_2 from the atmosphere) volatilization is substantially decreased. Mixtures of water and hydrazine containing 75% or less hydrazine in 9 cm diameter petri dishes were found to lose about 10% or less of the hydrazine after 5 hours at 21.5°C with an air velocity of 63.5 cm/s.

55.2.2 Transformation Processes in Soil/Ground-water Systems

Hydrazine is a strong reducing agent, and might be expected to be very reactive in the environment. However, in the absence of catalysts (certain metal ions), it is remarkably stable (1608,1610). Using distilled water, pond water, and sea water, the aqueous oxidation of 0.1 mmol hydrazine after 5 days was found to be < 2%, 20%, and 40% complete, respectively (1402). Under similar conditions using filtered and unfiltered pond water to which 4×10^{-6}M Cu (II) had been added, roughly 90% of the hydrazine had degraded after 5 hours. The rate of

oxidation was strongly dependent on temperature, increasing 40-fold from 5° to 30°C for an initial 1 mg/L hydrazine solution at pH 8 with 10 mg/L dissolved oxygen and 10^{-6} mol/L Cu.

The half-life for hydrazine degradation (without regard to reaction type) has been reported to be about 5 days in oxygenated aqueous solutions (1613) and about 8.3 days in filtered pond water (1610).

The degradation of hydrazine is enhanced by the presence of organic matter (1615) and by bacteria (1608,1609). However, the toxicity of hydrazine to microorganisms makes its biological treatment (e.g., of waste propellants) impractical. It has been found that for activated sludge plants, an influent concentration below 1 mg/L would be required to provide a "no effect" level for proper operation (1403). Hydrazine was found to have a more pronounced effect on ammonia nitrification (oxidation) than on carbon oxidation (1609).

55.2.3 Primary Routes of Exposure from Soil/Ground-water Systems

The above discussion of fate pathways suggests that mobility and potential exposure to hydrazine is very dependent on the environmental conditions. The compound is considered to have a high volatility, however the ionized form is non-volatile. Under neutral or acidic conditions, most of the hydrazine will be protonated. Adsorption is similarly dependent on pH. Hydrazine does appear to be mobile in sandy soils and under alkaline conditions. The potential for bioaccumulation of hydrazine is very low. These fate characteristics suggest several potential exposure pathways.

Volatilization of hydrazine from a disposal site may represent an important exposure pathway under some conditions. There is also some potential for drinking water contamination resulting from the migration of hydrazine with ground water. No observations of either pathways were found in the literature. Their importance may be diminished by the degradation of hydrazine either in soil/ground-water systems or in the atmosphere.

Discharges of hydrazine to surface waters from soil/ground-water systems would probably not represent significant sources of exposure due to the volatility of hydrazine, and its potential for biodegradation.

55.2.4 Other Sources of Human Exposure

Information on other sources of exposure to hydrazine is limited. The primary source of human exposure appears to be smoking, as hydrazine is a component of mainstream cigarette smoke (1418). No data were found on its presence in the ambient environment and its use in fuel cells and as a missile propellant suggest no potential for consumer exposure.

55.3 HUMAN HEALTH CONSIDERATIONS

55.3.1 Animal Studies

55.3.1.1 Carcinogenicity

Elevated incidences of lung and liver tumors have been reported in rodents exposed to hydrazine and its sulfate salt.

CBA/Cb/Se mice were administered 0, 0.14, 0.28, 0.56 or 1.13 mg hydrazine/mouse daily via a stomach tube, for 150 days (1698), then held until death. A dose-related trend in the incidence of hepatomas was found, i.e., 1.9%, 18%, 57.1% and 61.2%, respectively, in the 0.14, 0.28, 0.56 and 1.13 mg/day treatment groups. An incidence of 6.8% was observed in the control group. Tumors metastasized to the lung in 4 mice in the high dose group.

A second phase of the experiment involved the treatment of golden hamsters with hydrazine. Oral hydrazine doses were 2.8 mg/day for 20 weeks or 3 mg/day for 15 weeks. Animals were examined at death. Hepatic lesions were present in 82.8% of the hamsters given the 2.8 mg/day treatment and 60.8% of the animals treated with 3 mg/day. No liver lesions were found in the control animals. The most frequently seen lesions in hydrazine-treated hamsters were cirrhosis and reticulo-endothelial cell proliferation (1698).

Biancifiori (1699) postulated that excess estrogen production might enhance pulmonary tumors induced by hydrazine. Hydrazine sulfate, at a dose of 1.13 mg/day, was administered by stomach tube for 150 days to female BALB/c/Cb/Se mice in various hormonal states. Hydrazine treatment increased the incidence of pulmonary tumors to 90% in virgin, 100% in breeder and 60% in gonadectomized female mice (vs. 4, 8 and 27% in control groups, respectively). Both adenomas and carcinomas were present in all treated animals. Carcinomas in the breeders metastasized to the adrenal glands and myocardium. Biancifiori concluded that the greater ovarian hormone production present in breeders accentuated the existing susceptibility to pulmonary tumor induction in BALB/c mice.

Mice exposed to 0, 1, or 5 ppm hydrazine in a 6-month inhalation study were evaluated for carcinogenic effects one year after the last exposure (1700). A total of 5 alveologenic carcinomas, 2 lymphosarcomas and 1 hepatoma were found in 6 of 9 mice (67%) exposed continuously to 1 ppm hydrazine. Five of 6 mice (83%) exposed to 5 ppm hydrazine, 6 hours/day, 5 days/week developed alveologenic carcinomas. The incidence of alveologenic carcinoma was dose-related. Other tumors observed in experimental animals did not occur in the control mice.

Lung adenomas and adenocarcinomas were noted in 21% of male and 28% of female Cb/Se rats at 109 weeks following daily administration of 12-18 mg hydrazine sulfate by gavage for 68 weeks. Hepatic cell carcinomas or spindle cell sarcomas were also found in 31% of the male rats. There were no tumors in control rats (1678).

Hydrazine sulfate did not exhibit any tumor initiating activity when administered orally (283 mg daily for 4 weeks) to BALB/c/Cb/Se mice followed by skin application of croton oil for 30 weeks (1681).

IARC considers these and other data (1250) sufficient evidence of positive carcinogenic effects induced by hydrazine and hydrazine salts in laboratory animals. Epidemiological data are considered inadequate to determine the carcinogenic effect of hydrazine and hydrazine salts in humans. IARC has classified hydrazine as a Group 2B compound (1250).

55.3.1.2 Mutagenicity

Hydrazine is mutagenic in various microbial tests and in Drosophila but its mutagenicity in mammals in vivo is debatable. It has been shown to induce thymidine mutations without metabolic activation in L5178Y mouse lymphoma cells (1629) and was mutagenic in Escherichia coli strain WP2 (1628). Hydrazine was also positive in the Ames test with a broad range of activity towards the TA1535, TA100, TA1537, TA1538 and TA98 strains of Salmonella typhimurium (1632).

Parodi et al. (1632) found hydrazine induced significant DNA fragmentation in the liver and lung of male Swiss mice. Also, the frequency of sister chromatid exchange was increased 2- to 3-fold in Chinese hamster ovary cells following hydrazine treatment (1629) and was mutagenic to hamster V-79 cells (1631).

Hydrazine has induced both specific-locus and recessive lethal mutations in Drosophila (1633) and was positive in a mouse host-mediated assay (1679).

Unscheduled DNA synthesis was not induced by hydrazine in mice given 10 to 120 mg/kg hydrazine intraperitoneally. during the early stages of spermatogenesis (1630) and hydrazine was shown to be negative in mouse dominant-lethal tests (1633).

55.3.1.3 Teratogenicity, Embryotoxicity and Reproductive Effects

The effect of repeated injections of low doses of hydrazine on fetal development was studied by Lee and Aleyassine (1639). Pregnant Wistar rats were injected subcutaneously with 8 mg/kg hydrazine for 10 days (gestational days 11-21). A second group of pregnant rats were administered the same treatment in addition to a daily intramuscular injection of 200 mg/kg pyridoxine hydrochloride (Vitamin B_6). Since hydrazine inhibits some pyridoxal phosphate dependent enzymes (1778), administration of Vitamin B_6 might provide protection against hydrazine toxicity. Half of the rats were sacrificed and their fetuses examined on day 21 while the remaining animals were allowed to deliver to term. Three maternal deaths were reported in the group treated with hydrazine alone. These animals were extremely emaciated before death and post mortem examination revealed a loss of glycogen in the liver cells. Fetal examination revealed resorption of a large number of fetuses in

the hydrazine only group. Surviving fetuses were pale, edematous and studded with petechial hemorrhages. No gross malformations were seen. Injection of Vitamin B_6 improved the fetal survival rate from 37% to 70%. All newborns of dams treated with hydrazine died within the first 24 hours. In the group given hydrazine and Vitamin B_6, 50% delivered live newborns but these animals were pale and less active than saline controls. All pups were dehydrated the first 1-2 days but eventually recovered and all but 4 developed and grew normally through weaning.

Keller et al. (1634) continued the investigation of the embryotoxicity of hydrazine in Fischer 344 rats. Hydrazine intraperitoneally injected at a dose of 10 mg/kg/day on gestational days 7-9, 10-12 or 13-15 revealed that development during days 7-9 was most susceptible to the effects of hydrazine. The incidence of resorption was significantly higher in this treatment group (6.1 vs. 1.5 in controls). Fetal abnormalities were also significantly increased in this group with 50% of the fetuses examined exhibiting anomalies (super-numerary ribs, moderate hydronephrosis and moderate hydrocephalus). In a separate experiment, the incidence of resorption was significantly increased in rats treated percutaneously with 50 mg/kg hydrazine on gestational day 9 for 30 minute (9.4 vs. 0.3 in control animals). Ten of 12 litters were completely resorbed in this group. Maternal toxicity was evident in this group. It was concluded that hydrazine was embryotoxic to the rat and showed a dose-related embryolethality with early organogenesis being most susceptible to the toxic effects of hydrazine.

55.3.1.4 Other Toxicologic Effects

55.3.1.4.1 Short-term Toxicity

Hydrazine is a highly corrosive compound which can produce many toxic effects. CNS disturbances, hematological disturbances, and tissue damage resulting from fat deposition and cellular necrosis have all been reported (2,46). The oral LD_{50} of hydrazine for the rat is 60 mg/kg while the percutaneous LD_{50} is 91 mg/kg for the rabbit. Inhalation of hydrazine is also highly toxic and the LC_{50} is listed as 570 ppm for 4 hours for the rat (59).

Jacobson et al. (1640) reported the toxic effects of hydrazine on the central nervous system. Rodents exposed to hydrazine vapor (concentration not stated) were restless, had difficulty breathing, and experienced convulsions and exophthalmos. Death occurred within several hours of hydrazine exposure. The skin permeability constant for hydrazine vapor in rats is reported to be 6×10^{-5} cm/hr (1780).

The dermal toxicity of hydrazine is widely documented in laboratory animals. A cloth with 3 mL of hydrazine applied to the shaved bellies of 3 rabbits for one minute resulted in the death of 2 animals 60 and 90 minutes, respectively, after application. The rabbit which survived had been anesthetized prior to treatment and the area of application washed after the hydrazine cloth was removed. Within 2

hours of treatment, the affected skin reddened, turned blue, then brown with a dry, burned appearance. The area became dry, scaly, crusted and inflamed before healing (1627).

Keller et al. (1624) investigated the rate and extent of absorption of hydrazine in the rabbit. A direct correlation between the duration of hydrazine exposure and serum hydrazine concentrations was shown. Severe chemical burns were found in rabbits percutaneously exposed to 95% anhydrous hydrazine or 70% aqueous hydrazine solution. The lesions contained areas of trans-epidermal necrosis with varying degrees of dermal necrosis. No significant lesions were noted following percutaneous exposure to 15% or 2% anhydrous hydrazine. Data also indicate that a lag time exists between percutaneous exposure to hydrazine and the increase in serum hydrazine concentration. This delayed absorption supports the existence of an epidermal compartment.

Scales and Timbrell (1779) studied the pathogenesis of hydrazine-induced fat accumulation in male Sprague-Dawley rats within the first 4 hours of intraperitoneal injection with 60-200 mg/kg hydrazine hydrate. Control rats were injected with water. The LD_{50} value for hydrazine given intraperitoneally was between 80 and 100 mg/kg. Rats given the highest doses went into convulsions within 5 minutes and died within 3 hours of dosing. A dose of 60 mg/kg was well tolerated for 24 hours; the livers of these animals were pale, enlarged and showed marked hepatocyte vacuolation. Electron microscopy revealed numerous lipid vacuoles in the hepatocytes. The severity of the fatty liver was similar after a dose of 40 mg/kg hydrazine. Lipid vacuoles, an increased number of microbodies and swollen mitochondria were also detected in the proximal tubules of the kidney. Pretreatment with phenobarbital produced an induction of cytochrome P-450 which caused a decrease in the extent of fatty vacuolation. Animals pretreated with piperonyl butoxide, a microsomal enzyme inhibitor, showed greater fatty vacuolation after hydrazine treatment. Depletion of hepatic glutathione by pretreating animals with diethyl maleate produced no histological changes.

55.3.1.4.2 Chronic Toxicity

The majority of long-term studies reported in the literature deal with inhalation of very low levels of hydrazine vapor.

To examine the long-term effects of free base hydrazine inhalation, Vernot et al. (1635) exposed Fischer 344 rats and Golden Syrian hamsters to 0, 0.05, 0.25, 1 or 5 ppm hydrazine, C57BL/6 mice to 0, 0.05, 0.25 or 1 ppm hydrazine and beagle dogs to 0, 0.25 or 1 ppm hydrazine. All animals were exposed 6 hours/day, 5 days/week for one year. Hamsters were retained for 12 months, mice for 15 months, rats for 18 months and dogs for 38 months post-exposure.

In contrast to other studies, mice were the most resistant to hydrazine exposure, exhibiting a questionable borderline increase in benign lung tumors at the top exposure level. No deleterious effects

were observed in dogs at necropsy. Inflammation and squamous metaplasia were increased in the nose, larynx and trachea of rats exposed to 5 ppm hydrazine, indicative of the irritative effects of the higher concentration of hydrazine. Increased inflammatory and degenerative changes were also noted in the reproductive system of female rats exposed to 5 ppm. Hamsters developed generalized amyloidosis (pathologic change characteristic of degenerative disease) in the liver, kidney, thyroid and adrenal glands. Hemosiderosis in the liver, bile duct hyperplasia, and senile atrophy of the testes were increased in exposed hamsters. Neoplasms of the nasal epithelium increased in rats and hamsters with greater than 50% of the male rats exhibiting benign nasal tumors at the 5 ppm level. Adenomatous polyps were commonly observed at this dose level (86/193 vs. 0/291 in control rats and 16/160 vs. 1/181 in control hamsters). Neoplasms were also observed in the thyroid (4/137 vs. 0/145 in controls) and the digestive system (6/145 vs. 0/169 in controls) of hamsters, however, these values were not statistically significant. It was concluded that hydrazine was capable of inducing nasal tumors, primarily benign, in rats and hamsters after 1 year of intermittent inhalation. Colon, stomach and thyroid tumors in hamsters and bronchial adenomas in rats occurred in small numbers only at the highest level tested.

Results of animals involved in a 6-month hydrazine inhalation study were reported by Comstock et al. (1771). By the end of the experiment, 50% of the dogs, 76% of the rats, 75% of the mice and 80% of the guinea pigs exposed to 18 mg/m^3 hydrazine were dead. Necropsy of the surviving dogs revealed lipid deposition in the spleen and liver. Anemia was also evident. All animals exposed to 6 mg/m^3 hydrazine for 6 months survived. Signs of toxicity included loss of appetite, loss of body weight, vomiting, irregular breathing, fatigue and tremors.

Haun and Kinkead (1772) reported results of a low exposure inhalation study with hydrazine. Beagle dogs, Rhesus monkeys, Sprague-Dawley rats and ICR mice were exposed to 0.2 or 1 ppm hydrazine vapor continuously for 6 months or 1 or 5 ppm hydrazine vapor 6 hours/day, 5 days/week for 6 months. Following 8 weeks of exposure, hematocrit values were reduced 11%, hemoglobin concentrations were reduced 16-22% and erythrocyte counts were reduced 10-12% in dogs exposed to 1 ppm hydrazine continuously or 5 ppm intermittently. All values returned to normal 2 weeks after exposure ended. Reticulocytosis also occurred in dogs exposed to 1 ppm hydrazine continuously. Histological examination of all animals showed moderate to severe fatty liver changes. Death of 40% of the mice exposed to 1 ppm continuously and 35% of the mice exposed to 5 ppm hydrazine intermittently was attributed to these liver changes (1772).

55.3.2 Human and Epidemiologic Studies

55.3.2.1 Short-term Toxicologic Effects

The majority of reports on hydrazine toxicity involve industrial related exposure of chronic inhalation or dermal exposure. Very few acute case studies have been reported.

One case of accidental ingestion of hydrazine was reported by Reid (1636). After swallowing "between a mouthful to a cupful" of hydrazine the victim immediately vomited and lost consciousness. He was unconscious, flushed and afebrile with dilated pupils upon admission to the hospital. Twelve hours post-ingestion, he stopped vomiting, his pupils contracted and diverged to the right and he was sporadically violent. He was treated with Vitamin B_6 48 hours later. Following treatment, the man's memory and voluntary movement returned to normal. He was able to draw but could not write and he could not sense vibrations. He also experienced prickling of the skin on his arms and legs. His condition was reported to improve and he was discharged from the hospital 2 weeks post-ingestion.

NIOSH (1625) reported eye injury in a German factory worker exposed to hydrazine vapor. About ten hours after exposure, inflammation, swelling and a purulent discharge were observed. Temporary blindness ensued.

55.3.2.2 Chronic Toxicologic Effects

The majority of chronic toxicity data in humans are generated from long-term industrial exposure and mainly involved dermal or inhalation contact with hydrazine.

A fatality attributed to dermal hydrazine exposure was reported by Sotaniemi et al. (1648). The victim handled hydrazine once a week for six months. Usually after exposure he experienced lethargy, conjunctivitis and tremors. The day following his last exposure to hydrazine he developed fever, vomiting and diarrhea. He soon developed abdominal pain, black feces, and enlarged abdomen and liver. Fluid began to accumulate in the lungs. Following treatment, his condition improved only to worsen 12 days later. He died 20 days following the fatal exposure. Autopsy revealed severe tracheitis and bronchitis, and the lungs were filled with exudate. Microscopic examination of the kidneys revealed severe tubular necrosis, interstitial hemorrhages and inflammation indicative of toxic nephrosis. The heart was enlarged and the myocardium was discolored. Examination of the liver revealed focal areas of necrosis and degeneration. Sotaniemi et al. (1646) considered the damage to the lung, liver and kidneys to be due to hydrazine poisoning. Evans (1697) described the condition of a worker dermally exposed to hydrazine intermittently for about 5 months. A rash consisting of many small vesicles developed on the back of both hands and between the fingers of the worker. The vesicles began to rupture and form small crusts and fissures developed on the fingers. Following treatment, the worker had no further contact with hydrazine for 10 days and the rash completely disappeared. He then inadvertently came into contact with hydrazine hydrate and the rash reoccurred by the following day. Examination of his fingers at this time revealed the presence of hydrazine in spite of what was described as normal washing.

A case of hydrazine-induced inflammatory dermatitis was reported by Reidenberg et al. (1637). A female laboratory technician developed

lupus erythematosus-like symptoms following occupational exposure to hydrazine sulfate. Termination of exposure led to a remission of the symptoms. The technician and her identical twin (who had never been exposed to hydrazine) were subsequently challenged with hydrazine. Arthralgias and stiffness, rash, fatigue and low grade fever developed in the technician, but not the twin. Hydrazine, in vitro, blocked IgG production by the technician's cells but had no effect on the twin. Both women were slow acetylators, a genetic trait which has been shown to predispose to lupus.

A follow-up epidemiological study to a 1977 cluster of heart attacks in Olin Corporation workers exposed to hydrazine (data not available) was reported in Pesticide & Toxic Chemical News (1774). The study concluded that the cluster of myocardial infarctions reported in 1977 among hydrazine workers was a chance occurrence. No additional heart problems have been reported and no correlation was shown between hydrazine exposure and myocardial involvement.

The carcinogenic risk associated with occupational exposure to hydrazine was investigated by Wald et al. (1638). Plant records were obtained for 406 men who worked in hydrazine production for at least six months between 1945 and 1971. Records were analyzed for age, duration of employment and estimated extent of hydrazine exposure. The observed mortality was close to the expected values for lung cancer, other cancer and all causes of death, irrespective of the level of exposure (49 total deaths vs. 61.47 expected and 4 lung cancer deaths vs. 6.65 expected). Wald concluded that no obvious long-term hazard appears to be associated with hydrazine exposure. However, it should be noted that the sample size was small and only 78 men had substantial exposure (between 1 and 10 ppm hydrazine vapor in air).

55.3.3 Levels of Concern

The OSHA (298) standard is 1 ppm averaged over an 8-hour work-shift, with a notation of potential skin absorption. The ACGIH (3) classifies hydrazine as A2, suspect human carcinogen, and recommends exposure no higher than 0.1 ppm and warns of possible skin penetration.

IARC (1250) classifies hydrazine as a 2B carcinogen (i.e., sufficient evidence in animals).

55.3.4 Hazard Assessment

Hydrazine is a strong skin and mucous membrane irritant, a convulsant and a hepatotoxin. It is absorbed via the lungs, gastrointestinal tract and through intact skin. Signs of acute intoxication include anorexia, weight loss, weakness, vomiting, excitement and convulsions. The major histologic findings include fatty degeneration of the liver and nephritis. Chemical burns can result from skin contact with liquid hydrazine (1627,1624).

A number of studies have demonstrated that hydrazine, given mainly as hydrazine sulfate, produces a high incidence of pulmonary adenomas and adenocarcinomas in both mice and rats (1678,1698,1699). Hepatomas and hepatocarcinomas have been observed in mice treated orally with hydrazine sulfate (1698) and a significant incidence of nasal polyps were observed in hamsters exposed to 5 ppm hydrazine base by inhalation for one year (1635). Hydrazine is mutagenic in a variety of microbial tests (1628,1629,1632) and in Drosophila (1633) but its mutagenicity in mammals in vivo is debatable. Negative results have been reported for a dominant lethal study in mice (1633) but positive findings were noted in a mouse host-mediated assay (1679).

With regard to reproductive effects, subcutaneous injections of 8 mg/kg hydrazine during gestation resulted in 100% lethality among offspring of treated rats (1639). This was attributed, at least in part, to inhibition of fetal growth. Co-administration of Vitamin B_6 allowed the dams to maintain a steady gain in body weight but resulted in only partial protection of the fetuses. Intraperitoneal or dermal applications of hydrazine were also found to be embryolethal to rats, with increased susceptibility noted during early rather than late embryogenesis (1634).

55.4 SAMPLING AND ANALYSIS CONSIDERATIONS

Determination of the concentration of hydrazine in soil and water requires collection of a representative field sample and laboratory analysis. Due to the volatility of hydrazine, care is required to prevent losses during sample collection and storage. Soil and water samples should be collected in airtight containers with no headspace; analysis should be completed within 14 days of sampling. In addition to the targeted samples, quality assurance samples such as field blanks, duplicates, and spiked matrices should be included in the analytical program.

Hydrazine is not included among the EPA-designated priority pollutants, and an EPA-approved procedure for the analysis of hydrazine is not available. However, one analytical method (1142) recommended for the analysis of azo compounds, hydrazines and derivatives involves derivatization with either acetone or furfuraldehyde and analysis of the derivative by gas chromatography with a nitrogen-phosphorus detector, mass spectrometer or a flame ionization detector.

In addition, a NIOSH-approved method for the analysis of hydrazine compounds in air samples is available (40). Sampling and analysis is performed by drawing a measured volume of air through a tube containing sulfuric acid coated silica gel to trap the hydrazine compounds; the sorbent is then treated with distilled water to desorb the hydrazines. A reagent containing sodium acetate and 2-furaldehyde is added to the sample extract to derivatize the hydrazines; the resulting derivatives are extracted into ethyl acetate and analyzed by gas chromatography with a flame ionization detector.

A detection limit for hydrazine using these methods was not determined but might be in the range of μg/L for aqueous samples and μg/g for non-aqueous samples.

COMMON SYNONYMS:	FORMULA	CAS REG. NO.	NIOSH NO.	AIR W/V CONVERSION FACTORS at 25°C
Cyanide anior	CN	57-12-5	GS7175000	
Cyanide ion	HCN	74-90-8	MW6825000	
Hydrocyanic	NaCN	143-33-9	VZ7525000	1.06 mg/m^3 ≈ 1 ppm (CN)
acid, ion	KCN	151-50-8	TS8760000	0.94 ppm ≈ 1 mg/m^3 (CN)
				MOLECULAR WEIGHT: 26.02 (CN)

REACTIVITY	EPA compatibility charts indicate that reactions of cyanides with mineral acids or organic acids typically evolve toxic and flammable gases. Those with halogenated organics or ketones generally produce heat while those with nitrides or alkali or alkaline earth metals produce heat and flammable gases. Azo or diazo compounds or hydrazines generally evolve innocuous gases while isocyanates may additionally produce heat. Polymerizable compounds or epoxides may undergo violent exothermic polymerization. Reactions of cyanides with organic peroxides, organic hydroperoxides, or strong oxidizing agents may result in heat and toxic gas evolution as well as explosion. The NFPA indicates that violent explosions occur at 450°C if cyanide salts are melted with nitrite salt or a chlorate and further notes that a mixture of chlorates with cyanides may explode if subjected to heat, shock, or friction. Fluorine is said to attack cyanides vigorously in the cold. Magnesium reacts with incandescence when heated with cyanides of cadmium, cobalt, copper, lead, nickel or zinc. Addition of cyanides to a molten nitrate bath will result in an explosion, as may a mixture with nitric acid or potassium cyanide (505,511).

PHYSICO-CHEMICAL DATA	• Physical State (at 20°C): liquid (HCN)	(12)
	• Color: colorless (HCN)	(12)
	• Odor: bitter almonds (HCN)	(67)
	• Odor Threshold: 2-5 ppm (HCN)	(67)
	• Liquid Density (g/ml at 20°C): 0.687 (HCN)	(69)
	• Freezing/Melting Point (°C): -13.2 (HCN)	(12)
	• Boiling Point (°C): 25.7 (HCN)	(12)
	• Flash Point (°C): -17.8 closed cup (HCN); various salts are not combustible	(60,504, 506,507)
	• Flammable Limits in Air, % by Volume: 5.6-6 to 40-41 (HCN); various salts are not combustible	(60,504, 506,507)
	• Autoignition Temperature (°C): 538-540 (HCN); various salts are not combustible	(60,504, 506,507)
	• Vapor Pressure (mm Hg at 20°C): 620 (HCN)	(67)
	• Saturated Concentration in Air (mg/m^3 at 20°C): 918,783 (HCN)	(calc)
	• Solubility in Water (mg/L at 20°C): miscible (HCN)	(12)

PHYSICO-CHEMICAL DATA (Continued)	• Viscosity (cp at 20°C): not pertinent ( ) • Surface Tension (dyne/cm at 20°C): not pertinent ( ) • Log (Octanol-Water Partition Coefficient), log K_{ow}: not pertinent ( ) • Soil Adsorption Coefficient, K_{oc}: not pertinent ( ) • Henry's Law Constant ($atm \cdot m^3/mol$ at 25°C): 1.22×10^{-4} (1426) • Bioconcentration Factor: not pertinent ( )
PERSISTENCE IN THE SOIL-WATER SYSTEM	The cyanide ion is mobile in the soil/ground-water system due to the high solubility of most CN^- salts and the lack of anion retention by soils. At low concentrations however, the ion is biodegradable by almost all organisms, and in waters exposed to the atmosphere volatilization losses (as HCN) are expected to be significant.
PATHWAYS OF EXPOSURE	The primary exposure pathway of concern from soil/ground-water systems is the migration of cyanide to ground water drinking water supplies. Exposures through inhalation or the accumulation of cyanide by aquatic organisms or domestic animals are not likely to be significant exposure pathways.
HEALTH HAZARD DATA	Signs and Symptoms of Short-term Human Exposure (49): Exposure to hydrogen cyanide can result in symptoms within minutes which are characterized by constriction of the throat, nausea, vomiting, confusion, giddiness, staggering, headache, dilated pupils, hypotension, tachycardia and hyperpnea. This is followed by dyspnea, unconsciousness, convulsions and death.
	Toxicity Based on Animal Studies: LD_{50} (mg/kg): oral 8.5 [mouse] (HCN) (67); skin -- no data LC_{50} (mg/m^3): inhalation [rat] (67) 158 (HCN)•30 minutes
	Long-Term Effects: Fatigue, nausea, headache and goiter
	Pregnancy/Neonate Data: Malformations at near lethal levels in one study
	Mutation Data: Inadequate to assess
	Carcinogenicity: No data

HANDLING PRECAUTIONS (54)	Handle chemical only with adequate ventilation. Vapor concentrations up to 50 mg/m^3: Supplied-air respirator or self-contained breathing apparatus • Escape: Gas mask with canister providing protection against cyanide compounds (chin-style or front- or back-mounted canister) with particulate filter or self-contained breathing apparatus • Chemical goggles to prevent contact with the eyes • Protective clothing and rubber gloves to avoid contact with skin.

EMERGENCY FIRST AID TREATMENT (507)	Rapid onset - Get medical attention immediately • Ingestion: Induce vomiting if victim is conscious. Get medical attention immediately • Inhalation: Move victim to fresh air. Give artificial respiration if necessary. Avoid mouth-to-mouth resuscitation. Get medical attention immediately • Skin: Remove contaminated clothing and wash skin with soap and water. Get medical attention immediately • Eye: Flush eye with water for 15 minutes. Get medical attention immediately.

ENVIRONMENTAL AND OCCUPATIONAL STANDARDS AND CRITERIA

AIR EXPOSURE LIMITS:

Standards

- OSHA PEL (8-hr TWA): as CN 5 mg/m³ (skin); as HCN 11 mg/m³ (skin)
- AFOSH PEL (8-hr TWA): as CN 5 mg/m³ (skin); as HCN 11 mg/m³ (skin)

Criteria

- NIOSH IDLH (30-min): Cyanides (as CN) 50 mg/m³; HCN (as CN) 60 mg/m³
- ACGIH TLV® (8-hr TWA): Cyanides (as CN) 5 mg/m³ (skin)
- ACGIH STEL (15-min): None established

WATER EXPOSURE LIMITS:

Drinking Water Standards - None established

EPA Health Advisories

In the absence of formal drinking water standards, the EPA (992) has developed the following Health Advisories (formerly termed SNARLs) for noncarcinogenic risk for short- and long-term exposure to cyanide in drinking water:

- 1 day: 0.75 mg/L
- 10 days: 0.75 mg/L
- long-term: none established

EPA Ambient Water Quality Criteria (355,1777)

- Human Health
  - Based on ingestion of contaminated water and aquatic organisms, the criterion is 200 μg/L (cyanides).

- Aquatic Life
  - Freshwater species
    Freshwater aquatic organisms and their uses should not be affected unacceptably if the 4-day average concentration of cyanide does not exceed 5.2 μg/L more than once every 3 years on the average and if the one hour average concentration does not exceed 22 μg/L more than once every 3 years on the average.

  - Saltwater species
    Saltwater aquatic organisms and their uses should not be affected unacceptably if the one hour average concentration of cyanide does not exceed 1.0 μg/L more than once every 3 years on the average.

WHO Drinking Water Guideline (666)

A health-based guideline for drinking water of 10 $\mu g/L$ is recommended for cyanide. A daily per capita consumption of two liters of water was assumed.

REGULATORY STATUS (as of January 1, 1987)

Promulgated Regulations

- Federal Programs

Clean Water Act (CWA)

Hydrogen cyanide is designated a hazardous substance. It has a reportable quantity limit (RQ) of 4.54 kg (347,985). Cyanides are listed as toxic pollutants (351). Water quality criteria have been set. Guidelines exist for cyanide ion effluent in the battery manufacturing, coil coating, aluminum forming, photographic, non-ferrous metals forming and metal powders, and non-ferrous metals manufacturing point source categories (1439,1440, 1441,1442,1443,894). Guidelines exist for total cyanide in the pesticide chemicals, metal finishing, pharmaceutical manufacturing, electroplating, inorganic chemicals manufacturing, iron and steel manufacturing and ferroalloy manufacturing point source categories (1447,1444,1445,1446,1436,354,895).

Safe Drinking Water Act (SDWA)

In states with an approved Underground Injection Control program, a permit is required for the injection of cyanide-containing wastes designated as hazardous under RCRA (295).

Resource Conservation and Recovery Act (RCRA)

Hydrogen cyanide and other soluble cyanide salts are identified as acute hazardous wastes (P063,P030) and listed as hazardous waste constituents (328,329). Non-specific sources of cyanide-containing wastes are treatment sludges and spent solutions from electroplating and metal heat treating operations. Waste streams from the following industries contain cyanides and are listed as specific sources of hazardous wastes: inorganic pigments and coking (326,327).

Effective July 8, 1987, it will be prohibited to dispose of liquid hazardous wastes, including free liquids associated with any solid or sludge, which contains free cyanides at concentrations greater than or equal to 1000 mg/L. The only exception will be underground injection (1755).

Comprehensive Environmental Response Compensation and Liability Act (CERCLA)

Cyanides, including hydrogen cyanide are designated hazardous substances under CERCLA. They have a reportable quantity (RQ) limit of 4.54 kg. Reportable quantities have also been issued for RCPA hazardous waste streams containing cyanides but these depend upon the concentrations of the chemicals in the waste stream (985).

Any facility at which hydrogen cyanide is present in excess of its threshold planning quantity of 100 pounds must notify state and local emergency planning officials. If hydrogen cyanide is released from the facility in excess of its reportable quantity (RQ), local emergency planning officials must be notified (1751).

Federal Insecticide, Fungicide and Rodenticide Act (FIFRA)
Tolerances have been established for hydrogen cyanide residues from post-harvest fumigation. Levels range from 25 to 250 ppm (1448).

Marine Protection Research and Sanctuaries Act (MPRSA)
Ocean dumping of organohalogen compounds as well as the dumping of known or suspected carcinogens, mutagens or teratogens is prohibited except when they are present as trace contaminants. Permit applicants are exempt from these regulations if they can demonstrate that such chemical constituents are non-toxic and non-bioaccumulative in the marine environment or are rapidly rendered harmless by physical, chemical or biological processes in the sea (309).

Occupational Safety and Health Act (OSHA)
Employee exposure to cyanide (as CN) shall not exceed an 8-hour time-weighted-average (TWA) of 5 mg/m^3. Exposure to hydrogen cyanide shall not exceed an 8-hour time-weighted-average of 11 mg/m^3 (298).

Hazardous Materials Transportation Act (HMTA)
The Department of Transportation has designated cyanide solutions and anhydrous stabilized hydrogen cyanide as a hazardous material which is subject to requirements for packaging, labeling and transportation (306).

Food, Drug and Cosmetic Act (FDCA)
The following tolerances have been established for residues of hydrogen cyanide:

125 ppm in cereal flours;
50 ppm in cereals that are cooked before being eaten;
50 ppm in uncooked ham, bacon and sausage;
200 ppm in cocoa (1395)

Consumer Product Safety Act (CPSA)
Under the Federal Hazardous Substances Act, products containing soluble cyanide salts have been banned. Excluded from this regulation are unavoidable manufacturing residues of cyanide salts in other chemicals that under reasonable and foreseeable conditions of use will not result in a concentration of cyanide greater than 25 ppm (1236).

- State Water Programs

  The following states have a ground water quality standard of 0.2 mg/L for cyanide (981):

  New Jersey
  New Mexico
  New York
  Wyoming

  Other states with ground water quality standards for cyanide (981):

  Minnesota - 0.01 mg/L in Class 1 ground water
  Virginia - 0.005 mg/L
  Missouri - 0.05 mg/L
  Wisconsin - 0.46 mg/L enforcement standard
  0.092 mg/L preventive action limit

  The following states have a criterion of 5 µg/L for cyanide (731):

  Florida, Oregon - in the public water supply
  North Carolina - in fresh water
  West Virginia - in drinking water

  Other states with criteria for cyanide (731):

  Georgia - 3.5 µg/L in all waters
  Iowa - 0.02 mg/L in Class C drinking water
  Minnesota - 0.01 mg/L in water for domestic consumption
  Mississippi - 0.025 mg/L in the public water supply
  New York - 0.1 mg/L in Class AA drinking water
  Illinois - 0.025 mg/L in general use water
  Tennessee, Idaho - 0.2 mg/L in the domestic water supply

  California has an action level of 200 ppb (731).

  Other states follow EPA Ambient Water Quality Criteria.

Proposed Regulations

- Federal Programs

  Clean Water Act (CWA)

  Effluent guidelines for cyanide have been proposed in the organic chemicals, plastics and synthetic fibers category (357).

  Resource Conservation and Recovery Act (RCRA)

  EPA has proposed that hazardous waste treatment, storage and disposal facilities monitor ground water for cyanide when EPA suspects the facilities of leaking contaminants (1754).

  EPA has proposed listing as hazardous, mixtures of acutely toxic wastes, such as hydrogen cyanide (1396).

- State Water Programs
  No proposed regulations are pending

EEC Directives

Directive on Drinking Water (533)
The mandatory values for cyanide in surface water treatment categories A1, A2 or A3 are 0.05 mg/L. There are no guideline values.

Directive Relating to the Quality of Water for Human Consumption (540)
The maximum admissible concentration for cyanides is 50 µg/L.

Directive on Ground Water (538)
Direct discharge into ground water (i.e., without percolation through the ground or subsoil) of cyanides is prohibited. Appropriate measures deemed necessary to prevent indirect discharge into ground water (i.e., via percolation through ground or subsoil) of these substances shall be taken by member countries.

Directive on Bathing Water Quality (534)
When inspection of a bathing area shows that heavy metals, pesticides or cyanides may be present, concentrations should be checked by competent authorities.

Directive on the Discharge of Dangerous Substances (535)
Cyanides cannot be discharged into inland urface waters, territorial waters or internal coastal waters without prior authorization from member countries which issue emission standards. A system of zero-emission applies to discharge of these substances into ground water.

Directive on Marketing and Use of Dangerous Substances (541)
Hydrogen cyanide may not be used in ornamental objects intended to produce light or color effects by means of different phases.

Directive on Toxic and Dangerous Wastes (542)
Any installation, establishment, or undertaking which produces, holds and/or disposes of certain toxic and dangerous wastes including phenols and phenol compounds; organic-halogen compounds; chrome compounds; lead compounds; cyanides; ethers and aromatic polycyclic compounds (with carcinogenic effects) shall keep a record of the quantity, nature, physical and chemical characteristics and origin of such waste, and of the methods and sites used for disposing of such waste.

Directive on the Classification, Packaging and Labeling of Dangerous Substances (787)
Hydrogen cyanide is classified as a flammable, toxic substance and is subject to packaging and labeling regulations.

Directive on Transfrontier Shipment of Hazardous Waste (1433)
When the holder of a hazardous waste such as cyanide intends to ship it to another member state, authorities of the member states concerned must be provided with information on the source and composition of the waste, measures to be taken to ensure safe transport, insurance against damage and the existence of a contractual agreement with the consignee of the waste. All transfrontier shipments must be properly packed and labeled and must be accompanied by instructions to be followed in the case of danger or accident.

Directive on Major Accident Hazards of Certain Industrial Activities (1794)
Hydrogen cyanide manufacturers are required to notify competent authorities if it is stored or processed in quantities in excess of 20 tons. If a major accident occurs, authorities must be provided with the circumstances of the accident, substances involved, emergency measures taken, and the data available for assessing the effects on man and the environment.

EEC Directives - Proposed

Proposal for a Council Directive on the Dumping of Waste at Sea (1793)
EEC has proposed that the dumping of cyanides at sea be forbidden without prior issue of a special permit.

56.1 MAJOR USES

Cyanide (CN^-) is usually defined as hydrocyanic acid (HCN) and its salts. HCN and its alkali salts like sodium and potassium cyanide are primarily used as vermicidal fumigants, insecticides and rodenticides. They are also found in metal polishes (particularly silver polish), electroplating solutions and in various metallurgical and photographic processes (17).

56.2 ENVIRONMENTAL FATE AND EXPOSURE PATHWAYS

56.2.1 Transport in Soil/Ground-water Systems

56.2.1.1 Overview

The cyanide ion (CN^-) is expected to be relatively mobile in the soil/ground-water system when present at low dissolved concentrations. Bulk quantities of solutions containing the ion (e.g., from a spill or improper waste disposal) could be transported down through the unsaturated zone. However, as described below, at low concentrations and under aerobic conditions, cyanide is susceptible to biodegradation.

The cyanide ion acts as a weak base in solution, comparable in strength to ammonia. Its conjugate acid, HCN, has a pK_a of 9.21 (25°C, zero ionic strength) (1704). This means that below pH 9, most CN^- will be protonated, and in waters of environmental concern (pH < 8), over 90% will exist as HCN.

Transport pathways for the cyanide ion cannot be assessed as they are for organic species by using an equilibrium partitioning model. These models are based on the sorption and volatilization of non-ionized, neutral organic chemicals, and thus are not applicable to individual inorganic ions (or their parent salts).

Metallic cyanides such as AgCN, CuCN and $Zn(CN)_2$ are used commercially for electroplating their respective metal cation. Sodium and potassium cyanides are also used in plating solutions to increase the solubility of transition metal cyanides. Ferrocyanides and iron blue (a complex ferrocyanide salt) are added to road salts to prevent caking (1423), and thereby enter sewers and deposit on roadsides.

A review of the environmental effects of cyanide can be found in reference 1623, while its chemistry and uses are described in reference 1423.

56.2.1.2 Sorption on Soils

As an anion, the cyanide ion is expected to be only weakly retained by soils. Hydrogen cyanide is not strongly partitioned to suspended matter or sediments, due primarily to its high solubility in water (10). Cyanide salts tend to be highly soluble as well, exceptions being AgCN (pK_{sp} = 15.66), $Hg_2(CN)_2$ (pK_{sp} = 39.3) (1704) and $Zn(CN)_2$ (pK_{sp} = 15.9) (1424). Since neither silver, mercury nor zinc

is present in significant concentrations in the soil/ground-water environment, they will not control cyanide solubility, and pr cipitation of the cyanide salts from ground water can be expected to be insignificant.

The mobility of the cyanide ion in several soils (applied as KCN in deionized water) was studied by Fuller (1425). It was found to be most easily leached from a soil having a high pH and high free $CaCO_3$ concentration, although an acid soil had almost as poor retention. The ion was found to be most strongly held by soils having a high concencration of Mn and hydrous oxides of Fe. In landfill leachate, CN^- mobility consistently increased with decreasing soil pH. In general, CN^-, whose sorption behavior is similar to that of Cl^-, is very mobile in soils, with enhanced mobility in soils of low pH, low concentration of free iron oxides, and containing little kaolin, chlorite, and gibbsite-type clays (high positive charges) (1425).

Cyanide complexed as $Fe(CN)_6^{-3}$ (which, as described below, can form in soil) was also found to be very mobile in soil, with high pH and high free $CaCO_3$ enhancing its mobility (1425). Potassium cyanide added to landfill leachate was found to be less mobile than either $Fe(CN)_6^{-3}$ or CN^- in deionized water due to the precipitation of iron blue.

Sorption isotherm data for CN^-, like other mobile anions, are not available in the literature. In any case, the sorption behavior will depend upon the composition of the soil.

56.2.1.3 Volatilization from Soils

The cyanide ion is non-volatile. However, the weakness of HCN as an acid indicates that HCN will predominate over CN^- in solutions of pH up to about 9, and HCN is moderately volatile. It has a vapor pressure of 741 mm Hg at 25°C (14), and its Henry's law constant, H, has been given as a function of temperature, T, for HCN concentrations ranging from 0.01 to 0.5 M and temperatures from 20-95°C as (1426)

$$\log H = - \frac{1272.9}{T} + 6.238$$

where H is in mm Hg/moles/L and T in degrees Kelvin.

The volatilization of HCN has been found to be relatively rapid. with a half-life of HCN in natural water samples (8 liters in battery jars left outdoors in Minnesota) of roughly 10-50 hours (10). Thus, the volatilization of HCN can be expected to be an important loss pathway for CN^- in solutions exposed to the atmosphere.

56.2.2 Transformation Processes in Soil/Ground-water Systems

The cyanide ion undergoes a number of transformations in water. Hydrolysis rate constants for CN^- using sodium cyanide, potassium ferri-

cyanide, and cuprous cyanide in sterilized river water at pH 7-8 were found to be 0.002/hr and 0.0033/hr at 10 and 23°C, respectively (1423). These quasi first-order rate constants correspond to half-lives of approximately 15 and 9 days at 10°C and 23°C, respectively. Earlier studies have found HCN hydrolysis to be extremely slow except under very acidic conditions, with a half-life of over a year under alkaline conditions, at 33°C (10).

The cyanide ion forms complexes of varying stability with a number of metal ions, especially those of zinc, cadmium, mercury, and the transition metals. Under environmental conditions, the most important of these complexes are $Fe(CN)_6^{-4}$ and $Fe(CN)_6^{-3}$ with overall equilibrium constants of formation of $10^{35.4}$ and $10^{43.6}$, respectively (1704).

The formation of cyanide complexes removes free CN^- from solution, thereby increasing the dissociation of HCN to maintain the equilibrium between HCN and free CN^- and H^+. It also increases the mobility of the metal ion to which it is complexed, Zn^{+2} for example (1617), by preventing the sorptions of the metal to clays.

Iron cyanide complexes are considered stable, but susceptible to photodecomposition by sunlight, releasing free CN^- as they dissociate, but possibly reforming at night (982). The rate of photodegradation has been found to be rapid; Broderius and Smith (1401) report mid-day half-lives (in St. Paul, Minnesota in surface waters under full sunlight conditions) of 20 to 50 minutes for 100 μg CN^-/L of hexacyanoferrate (II) solutions and 60 to 160 minutes for 100 μg CN^-/L of hexacyanoferrate (III) solutions, depending on the time of year.

The hexacyanoferrate III ion complex has been found by Cherryholmes et al. (1620) to undergo biological dissociation in the dark, releasing free CN^-. A 3293 mg/L $K_3Fe(CN)_6$ solution prepared with sterilized and inoculated water showed a free CN^- concentration of 1460 $\mu g/L$ within 25 days compared to only 16 $\mu g/L$ for the control (not inoculated); with a larger bacterial population, a free CN^- concentration of 3952 $\mu g/L$ was achieved during the same period.

The rate of cyanide complexation with iron has been found to be very slow for free CN^- concentrations less than 3 mg/L, and even at an initial CN^- concentration of 10 mg/L (and CN/Fe = 1 at 23°C) the reaction rate was less than 0.01 mg/L hr (1423). Thus, CN^- formed by photodegradation or biodegradation will tend to remain as CN^- or HCN.

The cyanide ion, itself, has been found to undergo oxidation to CNO^- in the presence of titanium dioxide powder and sunlight (1618). Quartz sample tubes containing 1 mmol/L CN^- exposed to sunlight for two days showed over 99% removal when TiO_2 was present, but almost no removal (< 1%) in the absence of TiO_2.

Both hydrogen cyanide and metallocyanide complexes are susceptible to biodegradation by almost all microorganisms (10). Cyanide has been found to be degraded in aerobic microbial systems (1619,1622) such as

are found in sewage treatment plants, although volatilization can be an important loss pathway in these plants as well (1619). Other lower species such as the mucoraceous fungus Rhizopus orzae have been found to degrade cyanides (1621) as can higher plants and animals.

The rate of biodegradation is dependent upon environmental conditions such as temperature and the concentrations of microorganisms and cyanide. Half-lives for cyanide biodegradation in river water spiked with NaCN and acclimated microorganisms were found to range from 10 and 60 hours (1423).

At high cyanide concentrations and under aerobic conditions, cyanide toxicity inhibits microbial growth until the microorganisms become acclimated. Under anaerobic conditions, biodegradation may hardly occur since anaerobics are very sensitive to high cyanide concentrations. A limit of 2 mg/L of cyanide has been reported for effective anaerobic degradation (1425).

56.2.3 Primary Routes of Exposure from Soil/Ground-water Systems

The above discussion of fate pathways suggests that the mobility and potential exposure to cyanide is somewhat dependent on the environmental conditions. The cyanide ion is considered to be non-volatile, although HCN is highly volatile. Most forms of cyanide are expected to be relatively mobile in soil/ground-water systems. Cyanide is expected to have a low potential for bioaccumulation, as it can be metabolized. These fate characteristics suggest several potential exposure pathways.

Volatilization of cyanide from a disposal site is not likely to represent an important exposure pathway under most conditions. At lower pH values, the volatilization of HCN may represent an important exposure pathway.

Drinking water contamination resulting from the migration of cyanide is likely to occur, although it is susceptible to both chemical and biological degradation. Mitre (83) reported that cyanide salts have been found at 29 of the 546 National Priority List sites. It was detected at 17 sites in ground water, 15 sites in surface water, and 2 sites in air. These data indicate that cyanide is mobile in soil systems and ground water contamination may result.

The movement of cyanide in ground water may result in discharges to surface waters. As a result, ingestion exposures may occur through the use of surface waters as drinking water supplies, and dermal exposures may result from the recreational use of surface waters. The bioaccumulation of cyanide by domestic animals or fish from surface waters is not expected to be an important exposure pathway as cyanide has a low potential for bioaccumulation and may be degraded in surface waters.

56.2.4 Other Sources of Human Exposure

Although cyanide has been used in this country extensively, other sources of exposure appear to be limited. Cyanogenic glycosides are naturally occurring in some plant species and produce HCN upon hydrolysis (1423). These compounds are not generally thought to be part of the U.S. diet (1419). Both HCN and $Ca(CN)_2$ are registered as fumigants and tolerances have been established for these uses on some grains, citrus fruits, nuts, cucumbers, lettuce, radishes and tomatoes (1604). The extent to which cyanide is actually found in these foods is unknown.

Although cyanide has been found in ground water, the prevalence and levels of cyanide in drinking water are low (1419). A survey of 969 water supplies in 1970 showed an average concentration 0.09 µg/L and a maximum concentration of 8 µg/L (1419). Apparently, no nationwide monitoring for cyanide has taken place since that time.

Inhalation of cyanide may result from a variety of sources. It is produced in fires from burning urethanes, acrylonitriles, or polyamides in plastics. It is also released in automobile emissions (1423). Probably the most important source of exposure, however, is in cigarette smoke. Smokers may be exposed to from 0.01 - 40 mg/day in mainstream smoke depending on the type of cigarette smoked, the amount inhaled, and the number of cigarettes smoked (1423).

56.3 HUMAN HEALTH CONSIDERATIONS

56.3.1 Animal Studies

56.3.1.1 Carcinogenicity

No definitive data on the carcinogenicity of cyanide are available. Rats fed a diet fumigated with 300 µg/L HCN exhibited no indications of any carcinogenic effect after two years (1781). However, dietary levels varied and histopathology was conducted only for a limited number of animals. Therefore, no definitive conclusion can be drawn regarding the carcinogenicity of HCN.

An early experiment by Perry (1687) found that prolonged inhalation of cyanide arrested body growth in young rats and retarded the growth of Jensen sarcoma implants. However, the effective dose (not specified) was concluded to be too close to the lethal dose to be practical.

56.3.1.2 Mutagenicity

No definitive studies on the mutagenic effects of cyanide have been reported.

The cytotoxicity of cyanide was tested in Chlorella pyrenoidosa by Broda and Dombrowicz (1785). Cyanide in concentrations of 1.96-3.76 mμg/mL had minimal inhibitory effect.

These data on the mutagenicity of cyanide are inadequate to assess the mutagenic potential of cyanide.

56.3.1.3 Teratogenicity, Embryotoxicity and Reproductive Effects

Due to its acutely toxic effects, little data are available on the effects of cyanide in reproduction and fetal development.

The teratogenic potential of sodium cyanide was evaluated in the golden hamster by Doherty et al. (1782). Cyanide was administered continuously by slow infusion at a rate of 0, 0.126, 0.1275 or 0.1295 mmol/kg/hr on gestational days 6 through 9. A total dose equivalent to 30-40 times the acute sc LD_{50} dose was administered. A high incidence of malformations and resorptions were observed in offspring of all treatment groups with neural tube defects consisting of exencephaly (brain outside scull) and encephalocoele (hernia of the brain) being the most common. Hydropericardium and crooked tail were also observed, but to a lesser extent. Fetal crown rump length was also decreased. Administration of cyanide and sodium thiocyanate simultaneously protected against both the toxic and teratogenic effects of sodium cyanide. The significance of these findings in view of the high level, continuous exposure is unclear, and preclude extrapolation to human exposure situations.

Thiocyanate, (SCN) the primary metabolic product of cyanide detoxification, produced inhibitory effects at high concentrations on mesodermal and endodermal development of the chick embryo (1685). In view of the high dose and the large number of false positives generated in this closed system, little confidence can be placed on this finding. Furthermore, Kreutler et al. (1786) reported no indications of adverse effects in rat pups born to dams administered 160 μg SCN/mL in their drinking water (~6.4 mg SCN/rat/day), beginning on day 2 of pregnancy.

56.3.1.4 Other Toxicologic Effects

56.3.1.4.1 Short-term Toxicity

Death due to cyanide poisoning is attributed to an interference with the cytochrome oxidase system which prevents oxygen from reaching vital tissues resulting in tissue hypoxia and death. The oral LD_{50} value for HCN in the mouse is 8.5 mg/kg (67) while the LC_{50} in the rat is 142 ppm (HCN) for 30 minutes (67). Once absorbed, cyanide readily reacts with the trivalent iron of cytochrome oxidase in mitochondria. Respiration is stimulated in an attempt to bring oxygen to the tissue. A transient state of CNS stimulation with hyperpnea occurs. Hypoxic convulsions and death due to respiratory arrest result if treatment is not rapidly administered (16).

Inhalation of cyanide can lead to rapid acute toxicity and death (1691,1684). Sato (1691) placed groups of 10 mice in airtight chambers containing HCN gas in various concentrations. At 20 ppm, approximately 20% of the mice died after 4.5 hours. Death also occurred after 4 hours in the 15 ppm exposed group. Mobility became hindered and respiration was labored when mice were exposed to 10 ppm for 2 hours. And, at 5 ppm, a marked decrease in food intake was observed.

Haymaker et al. (1684) exposed six dogs to 165, 590, 620, 690, 700 and 700 mg/m^3 for 10, 2, 2, 2, 1.75 and 1.75 minutes, respectively. Four of the six dogs had convulsive seizures. Autopsy of the dog exposed to 620 mg/m^3 for 2 minutes revealed marked proliferation of histiocytes in the leptomeninges (membranes covering the brain) and in the perivascular spaces of the molecular layer of the cerebellum. Purkinje cells were barely visible. Some of the dogs suffered necrosis of gray matter. It is unclear if these lesions are related directly to cyanide, thiocyanate or general cytotoxic anoxia.

Cyanide is also readily absorbed through the skin. Guinea pigs, with their abdomens shaved, were fastened belly side down to a board with a one inch diameter circle through which the abdomen was exposed to 97% HCN vapor. Only percutaneous absorption was permitted. Within a few minutes, rapid respiration followed by twitching of muscles, convulsions, and death was observed (1692).

Vick and Froehlick (1456) have suggested that early death due to cyanide poisoning is due in part to cardiovascular-respiratory failure in addition to a block of the cytochrome oxidase system. This conclusion was based on the observation in dogs that artificial respiration with or without 100% oxygen was ineffective and treatment with amyl nitrite did not produce any appreciable increase in methemoglobin until after restoration of cardiovascular function.

Johnson et al. (1682) investigated the effect of cyanide on the accumulation of calcium in the brain and the relationship of changes in brain calcium levels to the CNS-mediated signs of toxicity. Male Swiss-Webster mice were subcutaneously injected with 10 mg/kg potassium cyanide. A significant decrease in whole-brain total calcium was seen within 5 minutes of the injection, which was followed by a significant increase within 15 minutes. The cyanide-induced rise in brain calcium levels corresponded to the induction of tremors. Subtremor doses (0.5-7 mg/kg KCN) were ineffective in altering the whole-brain total calcium concentrations. The initial drop in whole-brain calcium levels during the first 5 minutes of the study was thought to be due to a cyanide-induced release of calcium from intra-cellular organelles. The sudden increase in whole-brain total calcium within 15 minutes suggested that calcium accumulation occurred.

55.3.1.4.2 Chronic Toxicity

Howard and Hanzal (1781) conducted a 2-year-feeding study to determine chronic effects of cyanide in rats. Groups of 10 male and 10

female Carworth Farm rats were fed a diet fumigated with 0, 100 or 300 ppm hydrogen cyanide. The level of exposure, however, varied throughout the study and may have dropped to 80 ppm at intervals. No signs of toxicity were noted. Food consumption, growth rate, and survival of the treated animals were comparable with the controls. No pathological or histological abnormalities were observed in a representative number of rats that were examined. Elevated thiocyanate levels were noted in the plasma, liver and kidney of the cyanide treated rats at termination. In view of the limited data and the uncertainties with regard to exact dosage, the only conclusion that can be drawn is that 80 to 300 ppm HCN in the diet presented no apparent hazard to rats.

Hertting et al. (1689) administered 0.5 to 2 mg/kg sodium cyanide to dogs once or twice a day for 15 months. Acute toxic signs were usually observed following ingestion with complete recovery occurring within half an hour. No evidence of physiological changes in organ function or permanent alterations in intermediary metabolism were observed.

Beagle dogs were fed 150 ppm sodium cyanide in the diet for 30 days with no effect on food consumption, hematologic parameters, behavioral characteristics or microscopic changes in organs or tissues (1690). These data indicate that substantial but sublethal doses of cyanide can be tolerated for long periods of time without any permanent damage.

Occasionally blindness has been reported in cyanide intoxicated laboratory animals due to optic tract demyelination. Lessell (1680) injected rats subcutaneously with increasing doses of sodium cyanide (0.4-1.7 mg/100 g) three times a week for 3 months. Seventy percent of the treated rats developed demyelinative and necrotic lesions in the corpus callosum and 20% of the animals had lesions in the optic nerve. All rats with a demyelinative optic neuropathy had a marked corpus callosal lesion. The vulnerability of both these tracts is most likely due to the low cytochrome oxidase levels in these tissues. Impairment of this already low level by cyanide results in histotoxic anoxia and the observed damage to the corpus callosal and the optic nerve.

56.3.2 Human and Epidemiologic Studies

56.3.2.1 Short-term Toxicologic Effects

Acute intoxication from HCN results in a sense of suffocation, tachycardia with palpitations, vertigo, buzzing in the ear, headache, epigastric burning, vomiting, general weakness, tremors, sensory obtusion, dyspnea and loss of consciousness (1683). Cyanide binds to metallic cofactors and inhibits 42 enzyme systems with cytochrome oxidase being especially sensitive; concentration of 3.3×10^{-8} moles/mL of cyanide completely inhibits cytochrome oxidase (1423).

Cyanide is a fast-acting poison which can be inhaled, ingested and/or absorbed through the skin (1683). The human lethal dose of ingested HCN is believed to be 50-90 mg; this corresponds to about 1 mg/kg for a 70-kg person. The toxicity of cyanide salts is somewhat lower because of slower absorption, i.e., 200-250 mg or about 3 mg/kg for 70-kg man (1423). Death may be delayed for an hour.

Recoveries, however, from ingestion of up to 3-5 g KCN without therapy and up to 6 g KCN with therapy have been documented (1423,1799,1675). Results of oral intoxication with cyanide, however, must be interpreted with caution in that the presence of food in the digestive tract may retard absorption.

Cyanide is also readily absorbed through the skin and can be fatal by this route. Raestrup (1784) described a case in which a man accidentally dropped fused KCN into a puddle of water. The water-cyanide solution splashed into his face and he immediately lost consciousness. He died 3 hours later. Muller-Hess (1677) also reported a fatal accident in which a worker was splashed on the head and shoulders with an 80% NaCN solution. He died in less than one hour.

Numerous cases of acute cyanide intoxication via inhalation have been cited in the literature (1423,1683,1688). Inhalation of HCN concentrations above 90 $\mu g/L$ (~100 mg/m^3) is lethal in humans (1423).

Three men in protective masks, but no additional protective clothing, entered a 2% HCN atmosphere. All 3 men were overcome in 8 to 10 minutes but managed to escape before they collapsed. Symptoms of acute cyanide exposure were manifested followed by complete recovery within 3 days (1676).

Wexler et al. (1695) examined the cardiac function of four men executed by HCN inhalation (concentrations not reported). Within the first three minutes of exposure, all subjects had a marked decrease in heart rate accompanied by sinus irregularity and the complete disappearance of P waves. All subjects showed A-V dissociation with a secondary decrease in rates during the fifth minute. Death occurred by 13 to 14 minutes. These data indicate that cyanide exerts no specific effect on the myocardium but induces effects typical of hypoxia.

56.3.2.2 Chronic Toxicologic Effects

Few reports of ill effects associated with long-term exposure to small quantities of cyanide are cited in the literature. Some investigators (1693,1683) have observed weakness, vertigo, nausea, rapid pulse, headache, flushing of the face and gastric distress in individuals suspected of having chronic cyanide poisoning.

A goldsmith apprentice suspected of having chronic cyanide toxicity was described by Sandberg (1783). Five months after returning from a 13-month leave of absence, the individual developed headache,

general malaise, paresis of the left arm and left leg, grey skin, dilated left pupil, blindness in the left half of the visual field, and an altered EEG showing diffuse frontal theta activity. It was revealed that in addition to dermal exposure from the 1.5% aqueous KCN solution used to clean the gold, the man inhaled HCN which evolved from the solution when heated. Blood analysis showed CN levels at 10-12 μg/100 mL. All symptoms disappeared within 4 months and blood CN levels dropped to 2-3 μg/mL.

Permanent disability resulting from chronic dermal exposure to cyanide was reported by Collins and Martland (1686). Cyanide was absorbed through the skin of a 38-year-old hotel worker who polished silver for 2 years by dropping the silver into KCN solution and wiping it off without gloves. The workers hands and arms turned a brownish-red and his fingernails turned black. Itching, diarrhea, headache, pain and stiffness in the back, weakness in the arms and legs and urine retention developed. Eventually, clinical manifestations resembling acute anterior poliomyelitis developed. After six months of incapacitation, the patient could walk with braces and crutches. The role of cyanide in this case remains unclear.

Chronic cyanide toxicity bear a striking similarity to thiocyanate intoxication, and it has been suggested that the symptoms ascribed to chronic cyanide poisoning may, in fact, be due to the toxicity of its metabolic product, thiocynate. Heavy smoking and eating cabbage-type vegetables can exacerbate the symptoms of occupational cyanide exposure due to additional formation of thiocynate (1683).

Wuthrich (1693) described a clinical case involving a man exposed sporadically to cyanide vapor for six years. Symptoms included loss of appetite, nervousness, vertigo, headache, nausea and vomiting. After exposure to cyanide had ceased for 14 days, the patient was given a placebo of NaCl, iv, for 3 days. The man's condition improved dramatically. On the fourth day, 1.4 g of sodium thiocynate was substituted for the NaCl injection. Nausea, lack of appetite and nervousness returned. After 3 days of sodium thiocynate injections, the man's condition worsened and he stated that he felt exactly as he had in his work place. Injections with NaCl resulted in the disappearance of symptoms within 2 days.

An increased urinary excretion of thiocynate was observed in case hardeners exposed to 4-6 ppm cyanide vapor and possibly to cyanide salts over the years (1694). No signs of toxicity were reported. However, El Ghawabi et al. (1696) reported 20 cases of mild to moderate thyroid enlargement among 36 male electroplating workers exposed to an average of 6.5-10.4 ppm cyanide for up to 15 years. Blood thiocyanates resulting from chronic cyanide exposure compete with iodide for uptake by the thyroid gland resulting in the appearance of goiters.

Chronic cyanide toxicity has been implicated in various neuropathic disorders. These diseases include Nigerian nutritional neuropathy, Leber's optical atrophy, retrobulbar neuritis, pernicious

anemia, cretinism and ataxic tropical neuropathy. A common contributing factor found in each of these conditions was a diet high in cyanogenic glycosides (1683)

56.3.3 Levels of Concern

The USEPA (355) has established an ambient water quality criterion for cyanides of 200 μg/L for the protection of human health from the toxic properties of cyanide ingested through water and contaminated aquatic organisms.

For noncarcinogenic risk, the USEPA (992) has issued health advisories of 0.75 mg/L (1-10 days) for exposure to cyanide in drinking water. The WHO (666) recommends a level of 10 μg/L for drinking water.

Both OSHA (298) and the ACGIH (3) have set an occupational exposure limit of 5 mg/m^3 (as CN^-) for cyanide, with a notation of possible skin absorption.

Neither IARC nor NTP have classified this compound with regard to carcinogenic activity.

56.3.4 Hazard Assessment

Cyanide is a rapidly acting, chemical asphyxiant, which is readily absorbed from the alveolar membrane, intestinal mucosa and/or skin, and rapidly appears in the blood. The more quickly a critical concentration of cyanide is attained in the tissues, the more severe the effects. In sufficient doses, cyanide produces rapid death by inhibiting key respiratory enzymes and thereby preventing the body from utilizing available oxygen. At nonlethal doses, cyanide is detoxified to the relatively nontoxic thiocyanate ion. Thus, exposure to small but continuous doses of cyanide may produce no visible effects, while high doses of cyanide over a short time interval saturate normal detoxification mechanisms, which results in acute lethality. Minimum lethal doses of HCN for humans are approximately 50-90 mg by ingestion and approximately 100-150 mg/m^3 by inhalation (1423). With the ingestion of simple cyanide salts such as KCN, death may be delayed as long as an hour due to poor absorption (1423).

No indications of adverse effects were noted in long-term feeding studies available for cyanide (1781,1689). No data were available on the carcinogenic and mutagenic effects of cyanide. A single report noted malformations in hamsters exposed continuously to NaCN by infusion during gestation (1782). The significance of this study to the human situation is questionable.

The majority of available data deal with the effects of acute exposure to high levels of cyanide which leads either to death or complete recovery. Symptoms of cyanide exposure in humans include weakness, headache, confusion, nausea, vomiting, increased rate of respiration or slow, gasping respiration and eye and skin irritation. This is followed by collapse, coma, convulsions and death. Little is known about the effects of chronic exposure to low levels of cyanide

(1683). Studies have circumstantially implicated cyanide exposure as a factor in several neurological disorders such as Nigerian nutritional neuropathy, but the evidence is not conclusive. The ability of humans to detoxify cyanide rapidly at low exposure levels suggests that the risk of chronic low-level exposure to cyanide are minimal.

56.4 SAMPLING AND ANALYSIS CONSIDERATIONS

Determination of cyanide ion (as total cyanide) concentrations in soil and water requires collection of a representative field sample and laboratory analysis. Care is required to prevent losses and avoid contamination during sample collection. Samples may be collected in either glass or plastic containers of one liter or larger size. Sample preservation involves cooling and maintaining samples at 4°C with the addition of sodium hydroxide in the field until the pH of the sample is > 12; ascorbic acid should be added in the presence of residual chlorine. Samples should be analyzed as soon as possible after collection; maximum holding time is 14 days (24 hours when sulfide is present). In addition to the targeted samples, quality control samples such as field blanks, duplicates, and spiked matrices may be specified in the recommended methods.

EPA-approved procedures for the analysis of cyanide in aqueous samples include Methods 335.2 and 335.3 (1420), 9010 (63) and 412 (1422). In Methods 335.2, 9010, and 412B, the cyanide as hydrocyanic acid (HCN) is released from cyanide complexes by a reflux-distillation operation and absorbed in a scrubber containing a sodium hydroxide solution; the cyanide ion in the absorbing solution is then determined by volumetric titration (Methods 335.2, 9010, and 412C), colorimetrically (Method 335.2 and 412D) or potentiometrically (Method 412E). In Method 335.3, cyanide (as HCN) is released from cyanide complexes by UV digestion and distillation; cyanides are converted to cyanogen chloride by reactions with chloramine-T which subsequently reacts with pyridine and barbituric acid to yield a red-colored complex.

The EPA procedures recommended for determination of total cyanide concentrations in aqueous samples may also be applicable to the determination of cyanide in soil and waste samples. These procedures differ primarily in the preparation of the sample for analysis; cyanide ion must be solubilized and separated from the sample matrix prior to analysis.

Typical detections limits for cyanide that can be obtained in wastewaters are shown below; detection limits were not indicated for non-aqueous samples. The actual detection limit achieved in a given analysis will vary with instrument sensitivity and matrix effects.

Non-Aqueous Detection Limit

1 mg/L (Method 335.2/titration procedure)
0.02 mg/L (Method 335.2/colorimetric procedure)
5 µg/L (Method 335.3)
1 mg/L (Method 9010)
1 mg/L (Method 412C)
0.02 mg/L (Method 412D)
0.05 mg/L (Method 412E)

806. Syracuse Research Corporation, 1985, Environmental Fate Data Bases (CHEMFATE, DATALOG, BIOLOG). Computerized numeric and bibliographic database prepared and maintained by Syracuse Research Corp, Merrill Lane, Syracuse, NY 13210.

807. Figge, K.; Klahn, J.; Koch, J., 1983, Testing of chemicals by evaluation of their distribution and degradation patterns in an environmental standard system. Regulatory Toxicol. Pharmacol. 3:199-215.

808. Jury, W.A.; Spencer, W.F.; Farmer, W.J., 1984, Behavior assessment model for trace organics in soil: III Application of screening model. J. Environ. Qual. 13:573-579.

809. Pollard, J.E.; Hern, S.C., 1985, A field test of the EXAMS model in the Monongahela River. Environ. Toxicol. Chem. 4:361-369.

810. Goerlitz, D.F.; Troutman, D.E.; Godsy, E.M.; Franks, B.J., 1985, Migration of wood-preserving chemicals in contaminated groundwater in a sand aquifer at Pensacola, Florida. Environ. Sci. Technol. 19:955-961.

811. Reinhard, M.; Goodman, N.L.; Barker, J.F., 1984, Occurrence and distribution of organic chemicals in two landfill leachate plumes. Environ. Sci. Technol. 18:953-961.

812. Kenaga, E.E., 1980, Predicted bioconcentration factors and soil sorption coefficients of pesticides and other chemicals. Ecotoxicol. Environ. Safety 4:26-38. (As cited in 806)

813. Briggs, G.G., 1981, Theoretical and experimental relationships between soil adsorption, octanol-water partition coefficients, water solubilities, bioconcentration factors and the parachor. J. Agric. Food Chem. 29:1050-1059. (As cited in 806)

814. Artiola-Fortuny, J.; Fuller, W.H., 1982, Adsorption of some monohydroxybenzene derivatives by soils. Soil Sci. 133:18-26. (As cited in 806)

815. Scott, H.D.; Wolf, D.C.; Lavy, T.L., 1982, Apparent adsorption and microbial degradation of phenol by soil. J. Environ. Qual. 11:107-111. (As cited in 806)

816. Boyd, S.A., 1982, Adsorption of substituted phenols by soil. Soil Science 134:337-343. (As cited in 806)

NOTE: References 1 through 805 can be found in the Reference List included in Volume 1 of the Guide.

817. Scott, H.D.; Wolf, D.C.; Lavy, T.L., 1983, Adsorption and degradation of phenol at low concentrations in soil. J. Environ. Qual. 12:91-95. (As cited in 806)

818. Isaacson, P.J.; Frink, C.R., 1984, [No citation given]. (As cited in 806)

819. Hemphill, L.; Swanson, W.S., 1964, Sorption of organic acids by pure clay minerals in aqueous solution. Proc. 18th Industrial Waste Conf., Eng. Bull. Purdue U., Lafayette, IN 18:204-217. (As cited in 806)

820. Donaldson, E.C.; Crocker, M.E.; Manning, F.S., 1975, Adsorption of organic compounds on Cottage Grove sandstone. BERC/RI-75/4, Bartlesville, OK; Bartlesville Energy Research Center. (As cited in 806)

821. Greskovich, E.J., 1974, Equilibrium data for various compounds between water and mud. AIChE J. 20:1024-1025. (As cited in 806)

822. Luh, M.D.; Baker, R.A., 1970, Organic sorption from aqueous solutions by two clays. Proc. 25th Industrial Waste Conf., Purdue U., Eng. Bull., Ext. Series 25:534-542. (As cited in 806)

823. Yost, E.C., Anderson, M.A., 1984, Absence of phenol adsorption on geothite. Environ. Sci. Technol. 18:101-106. (As cited in 806)

824. Shetiya, R.S.; Rao, K.N.; Shatnar, J., 1976, OH radical rate constants of phenols using p-nitrosodimethylaniline. Ind. J. Chem. 14A:575-578. (As cited in 939)

825. Conrad, R.; Seiler, W., 1985, Characteristics of abiological carbon monoxide formation from soil organic matter, humic acids, and phenolic compounds. Environ. Sci. Technol. 19:1165-1169.

826. Baker, M.D.; Mayfield, C.I., 1980, Microbial and nonbiological decomposition of chlorophenols and phenols in soil. Water, Air and Soil Pollut. 13:411-424.

827. Kawaguchi, H., 1984, Photocatalytic decomposition of phenol in the presence of titanium dioxide. Environ. Technol. Lett. 5:471-474.

828. Chesney, R.H.; Sollitti, P.; Rubin, H.E., 1985, Incorporation of phenol carbon at trace concentrations by phenol-mineralizing microorganisms in fresh water. Appl. Environ. Microbiol. 49:15-18.

829. Deeley, G.M.; Skierkowski, P.; Robertson, J.M., 1985, Biodegradation of [^{14}C] phenol in secondary sewage and landfill leachate measured by double-vial radiorespirometry. Appl. Environ. Microbiol. 49:867-869.

830. Boyd, S.A.; Shelton, D.R.; Berry, D.; Tiedje, J.M., 1983, Anaerobic biodegradation of phenolic compounds in digested sludge. Appl. Environ. Microbiol. 46:50-54.

831. Newfield, R.D.; Mack, J.D.; Strakey, J.P., 1980, Anaerobic phenol biokinetics. J. Water Pollut. Control. Fed. 52:2367-2377.

832. Lustre, A.O.; Issenberg, P., 1970, Phenolic components of smoked meat products. J. Food Chem. 18:1056.

833 Osipoff, R.J.; Hutzler, N.J.; Crittenden, J.C., 1981, Interaction of specific toxic organic chemicals percolating through a soil. Proceed. Industrial Waste Conf. 1980:17-23.

834. Boyd, S.A.; Shelton, D.R., 1984, Anaerobic biodegradation of chlorophenols in fresh and acclimated sludge. Appl. Environ. Microbiol. 47:272-277.

835. Baker, M.D.; Mayfield, C.I.; Innis, W.E., 1980, Degradation of chlorophenols in soil, sediment and water at low temperatures. Water Res. 14:1765-1771.

836. Haider, K.; Jagnow, G.; Kohnen, R.; Lim, S.U., 1974, Degradation of chlorinated benzenes, phenols and cyclohexane derivatives by benzene and phenol utilizing soil bacteria under anerobic conditions. Arch. Microbiol. 96:183-200.

837. Seidler, J.J.; Landau, M.; Dieberg, F.E.; Pierce, R.H., 1986, Persistence of pentachlorophenol in a wastewater-estuarine aquaculture system. Bull. Environ. Contam. Toxicol. 36:101-108.

838. Sugiura, K.; Aoki, M.; Kaneko, S.; Daisaku, I.; Komatsu, Y.; Shibuya, H.; Suzuki, H.; Goto, M., 1984, Fate of 2,4,6-trichlorophenol, pentachlorophenol, p-chlorobiphenyl, and hexachlorobenzene in an outdoor experimental pond: Comparison between observations and predictions based on laboratory data. Arch. Environ. Contam. Toxicol. 13:745-758.

839. Knowlton, M.F.; Huckins, J.N., 1983, Fate of radiolabeled sodium pentachlorophenate in littoral microcosms. Bull. Environ. Contam. Toxicol. 30:206-213.

840. Boyle, T.P.; Robinson-Wilson, E.F.; Petty, J.D.; Weber, W., 1980, Degradation of pentachlorophenol in simulated lentic environment. Bull. Environ. Contam. Toxicol. 24:177-184.

841. Crossland N.O.; Wolff, C.J.M., 1985, Fate and biologic effects of pentachlorophenol in outdoor ponds. Environ. Toxicol. Chem. 4:73-86.

842. Weiss, V.M.; Scheunert, I.; Klein, W.; Korte, F., 1982, Fate of pentachlorophenol - ^{14}C in soil under controlled conditions. J. Agric. Food Chem. 30:1191-1194.

843. Gile, J.D.; Collins, J.C.; Gilbert, J.W., 1982, Fate and impact of wood preservatives in a terrestrial microcosm. J. Agric. Food Chem. 30:295-301.

844. Brockway, D.L.; Smith, P.D.; Stancil, F.E., 1984, Fate and effects of pentachlorophenol in hard- and soft-water microcosms. Chemisphere 13:1363-1377.

845. DeLaune, R.D.; Gambrell, R.P.; Reddy, K.S., 1983, Fate of pentachlorophenol in estuarine sediment. Environmental Pollution (Ser. B) 6:297-308.

846. Gambrell, R.B.; Taylor, B.A.; Reddy, K.S.; Patrick, W.J. Jr., 1984, Fate of selected toxic compounds under controlled redox potential and pH conditions in soil and sediment-water systems. Report No. EPA-600/3-83-018, U.S. Environmental Protection Agency, Environmental Research Laboratory, Athens, GA. NTIS PB 84-140169.

847. Branson, D.R.; Blau, G.E., 1979, The materials balance to estimating environmental concentrations. Unpublished material presented at the workshop on "Biotransformation and Fate of Chemicals in the Aquatic Environment", The University of Michigan's Biological Station, Pelstron, MI, August 19-24 (1979). (As cited in 909)

848. Choi, J.; Aomine, S., 1974, Adsorption of pentachlorophenol by soils. Soil Sci. Plant Nutr. 20:135-144. (As cited in 909)

849. Kilzer, J.; Scheunert, I.; Geyer, H.; Klein, W.; Korte, F., 1979, Laboratory screening of the volatilization rates of organic chemicals from water and soil. Chemosphere 8:751-761. (As cited in 806)

850. Gile, J.D.; Gillette, J.W., 1979, Fate of selected fungicides in a terrestrial laboratory ecosystem. J. Agric. Food Chem. 17:1159-1164. (As cited in 806)

851. Metcalf, R.L.; Cole, L.K.; Wood, S.G.; Mandel, D.J.; Milbrath, M.L., 1979, Design and evaluation of a terrestrial model ecosystem for evaluation of substitute pesticide chemicals. Report No. EPA/600/3-79-004, U.S. Environmental Protection Agency, Environmental Research Laboratory, Corvallis, OR. (As cited in 806)

852. Choudhry, G.G.; van der Wielen, F.W.M.; Webster, C.R.B.; Hutzinger, O., 1985, Photochemistry of halogenated benzene derivatives. Part VI. Photo-reactions of tetra- and pentachlorophenols in water-acetonitrile mixtures. Can. J. Chem. 63:469-475.

853. Ahlborg, V.G.; Thunberg, T.M., 1980, Chlorinated phenols: occurrence, toxicity, metabolism, and environmental impact. CRC Critical Reviews in Toxicol. 7:1-35.

854. Valo, R.; Apajalahti, J.; Salkinoja-Salonen, K., 1985, Studies on the physiology of microbial degradation of pentachlorophenol. Appl. Microbiol. Biotechnol. 21:313-319.

855. Moos, L.P.; Kirsch, E.J.; Wukasch, R.F.; Grady, C.P.L. Jr., 1983, Pentachlorophenol biodegradation - I: Aerobic. Water Res. 17:1575-1584.

856. Serjeant, E.P.; Dempsey, B., 1979, Ionization Constants of Organic Acids in Aqueous Solution. IUPAC Chemical Data Series, Pergamon Press, NY. (As cited in 806)

857. Boule, P.; Guyon, C.; Lemaire, J., 1982, Photochemistry and environment IV - Photochemical behavior of monochlorophenols in dilute aqueous solution. Chemosphere 11:1179-1188.

858. Kallman, M.J.; Coleman, E.A.; Borzelleca, J.F., 1982, Behavioral toxicity of 2-chlorophenol in adult mice. Fed. Proc. 41:Abstract 7654.

859. Fincher, E.L.; Payne, W.J., 1962, Bacterial Utilization of Ether Glycols. Appl. Microbiol. 10:542-547. (As cited in 806)

860. Dow Chemical Co., 1981, The Glycol Ethers Handbook, Midland, MI: Dow Chemical Company.

861. Ellis, L.F.; Samuel-Maharajah, R.; Mendelin, L.M.; Ruth, L.; Pivnick, H., 1956, Oxidation components of soluble oils. Appl. Microbiol. 5:345-348.

862. Lokke, H., 1984, Leaching of ethylene glycol and ethanol in subsoils. Water, Air and Soil Pollution 22:373-387.

863. Conway, R.A.; Waggy, G.T.; Spiegel, M.H.; Berglund, R.L., 1983, Environmental fate and effects on ethylene oxide. Environ. Sci. Tech. 17:107-112.

864. Dwyer, D.F.; Tiedje, J.M., 1983, Degradation of ethylene glycol and polyethylene glycols of methanogenic consortia. Appl. Environ. Microbiol. 46:185-190.

865. Schink, B.; Stieb, M., 1983, Fermentative degradation of polyethylene glycol by a strictly anaerobic, gram-negative, nonsporeforming bacterium, Pelobacter venetianus sp. nov. Appl. Environ. Microbiol. 45:1905-1913.

866. Rossiter, W.J.; Brown, P.W.; Godette, M., 1983, The determination of acidic degradation products in aqueous ethylene glycol and propylene glycol solution using ion chromatography.

867. Kersters, K.; Deley, J., 1963, The oxidation of glycols by acetic acid bacteria. Biochim. Biophys. Acta. 71:311-331. (As cited in 806)

868. Gaston, L.W.; Stadtman, E.R., 1963, Fermentation of ethylene glycol by Clostridium glycolium. J. Bacteriol. 85:356-362. (As cited in 806)

869. Jones, N.; Watson, G.K., 1976, Ethylene glycol and polyethylene glycol catabolism by sewage bacterium. Biochem. Soc. Trans. 4:891-892. (As cited in 806)

870. Tsukamura, M., 1966, Utilization of glycols and certain other carbohydrates as sole carbon sources. Amer. Rev. Resp. Dis. 94:796-798. (As cited in 806)

871. Harada, T.; Nagashima, Y., 1975, Utilization of alkylether compounds by soil bacteria. J. Ferment. Technol. 53:218-222. (As cited in 806)

872. Jensen, H.L., 1964, Studies on soil bacteria (Arthrobacter globiformis) capable of decomposing the herbicide Endothal. Acta. Agric. Scand. 14:193-207. (As cited in 806)

873. Matsui, S.; Murakami, T.; Sasaki, T.; Hirose, Y.; Iguma, Y., 1975, Activated sludge degradability of organic substances in the waste water of the Kashima petroleum and petrochemical industrial complex in Japan. Prog. Water Technol. 7:645-659. (As cited in 806)

874. Evans, W.H.; David, E.J., 1974, Biodegradation of mono-, di- and triethylene glycols in river waters under controlled laboratory conditions. Water Res. 8:97-100. (As cited in 806)

875. Haines, J.R.; Alexander, M., 1975, Microbial degradation of polyethylene glycols. Appl. Microbiol. 29:621-625. (As cited in 806)

876. Zahn, R.; Wellens, H., 1980, [Examination of biological degradability through the batch method - further experience and new possibilities of usage]. Z. Wasser Abwasser Forsch. 13:1-7. (As cited in 806)

877. Means, J.L.; Anderson, S.J., 1981, Comparison of five different methods for measuring biodegradability in aqueous environments. Water, Air and Soil Poll. 16:301-315. (As cited in 806)

878. Slave, T.; Mihail, A.; Burmaz, N., 1974, Degradation of some organic impurities in residual waters. Rev. Chim. 25:666-670. (As cited in 806)

879. Daughertl, L.C., 1980, The growth of Pseudomonas aeruginosa on glycols of industrial importance. Lubrication Engin. 36:718-723. (As cited in 806)

880. Bridie, A.L.; Wolff, C.J.M.; Winter, M., 1979, BOD and COD of some petrochemicals. Water Res. 13:627-630. (As cited in 806)

881. Price, K.S.; Waggy, G.T.; Conway, R.A., 1974, Brine shrimp bioassay and seawater BOD of petrochemicals. J. Water Pollut. Contr. Fed. 46:63-77. (As cited in 806)

882. Heukelekian, H.; Rand, M.C., 1955, Biochemical oxygen demand of pure organic compounds. J. Water Pollut. Contr. Assoc. 29:1040-1053. (As cited in 806)

883. National Toxicology Program (NTP), 1986, Management status report. Produced from NTP Chemtrack System.

884. U.S. Food and Drug Administration (USFDA), 1977, Compliance program evaluation FY1974. Total diet studies, Bureau of Foods.

885. Federal Register, 1978, Wood preservation pesticides, initiation of schedule for review and notices of rebuttable presumption against registration of certain pesticides; pentachlorophenol, position document 1. 43:48446-48447.

886. 21CFR193.260 and 193.520 Food additives permitted in food for human consumption; malathion.

887. 21CFR193.100 Food additives permitted in food for human consumption; 2,4-D.

888. Federal Register, 1986, Revocation of DDT and TDE food and feed additive regulations. 51:46616.

889. Federal Register, 1986, Revocation of DDT and TDE tolerances. 51:46658.

890. U.S. Environmental Protection Agency (USEPA), 1985, "Draft Health Advisories on 50 chemicals sent to states by EPA". Pesticide and Toxic Chemical News, Oct. 23, 1985:20-22.

891. Federal Register, 1985, Pesticide chemicals category effluent limitations guidelines, pretreatment standards, and new source performance standards. 50:40672.

892. Federal Register, 1985, Metal molding and casting industry point source category effluent limitations guidelines, pretreatment standards and new source performance standards. 50:45212.

893. 40CFR410 Textile mills point source category.

894. 40CFR421 Non-ferrous metals manufacturing point source category.

895. 40CFR424 Ferroalloy manufacturing point source category.

896. 40CFR419 Petroleum refining point source category.

897. 40CFR426 Glass manufacturing point source category.

898. 40CFR430 Pulp, paper and paperboard point source category.

899. 40CFR429 Timber products processing point source category.

900. U.S. Environmental Protection Agency (USEPA), 1980, Ambient water quality criteria for 2-chlorophenol. EPA Report No. 440/5-80-034. Washington, D.C.: U.S. Environmental Protection Agency, Office of Water Regulations and Standards. PB81-117459.

901. Scow, K.; Goyer, M.; Perwak, J.; Woodruff, C.; Saterson, K.; Payne, E.; Wood, M., 1981, An exposure and risk assessment for chlorinated phenols. Washington, D.C.: U.S. Environmental Protection Agency, Office of Water Regulations and Standards. PB85-211951.

902. Boutwell, R.K.; Bosch, D.K., 1959, The tumor-promoting action of phenol and related compounds for mouse skin. Cancer Res. 19:413-424. (As cited in 900, 901 and 939)

903. Chung, Y., 1978, Studies on cytochemical toxicities of chlorophenols to rat. Yakhak Hoe Chi 22:175-192. (As cited in 901)

904. Exon, J.H.; Koller, L.D., 1982, Effects of transplacental exposure to chlorinated phenols. Env. Health Persp. 46:137-140.

905. Farquharson, M.E.; Gage, J.C.; Northover, J., 1958, The biological action of chlorophenols. Brit. J. Pharmacol. 13:20-24. (As cited in 900)

906. Hijazi, N.; Chai, R.; Amster, M.; Duffee, R., 1983, Indoor organic contaminants in energy efficient bldgs. In: Specialty Conference On: Measurement and Monitoring of Non-Criteria

(Toxic) Contaminants in Air. Frederick, E.R., ed. Air Pollution Control Assoc. (APCA): Pittsburg, PA pp 471-477.

907. U.S. Environmental Protection Agency (USEPA), 1980, Ambient water quality criteria for chlorinated phenols. EPA Report No. 440/5-80-032. Washington, D.C.: U.S. Environmental Protection Agency, Office of Water Regulations and Standards. PB81-117434.

908. Exon, J.D., 1984, A review of chlorinated phenols. Vet. Hum. Toxicol. 26:508-520.

909. Scow, K.; Goyer, M.; Perwak, J.; Payne, E.; Thomas, R.; Wallace, D.; Walker, P.; Wood, M.; Delpire, L., 1980, An exposure and risk assessment for pentachlorophenol. Washington, D.C.: U.S. Environmental Protection Agency, Office of Water Regulations and Standards. PB85-211944.

910. U.S. Environmental Protection Agency (USEPA), 1980, Ambient water quality criteria for pentachlorophenol. EPA Report No. 440/5-80-065. Washington, D.C.: Criteria and Standards Division, Office of Water Regulations and Standards. PB81-117764.

911. Innes, J.R.M.; Ulland, B.M.; Valerio, M.G.; Petrucelli, L.; Fishbein, L.; Hart, E.R.; Pallota, A.J.; Bates, R.R.; Falk, H.L.; Gart, J.J.; Klein, M.; Mitchell, I.; Peters, J., 1969, Bioassay of pesticides and industrial chemicals for tumorigenicity in mice. A preliminary note. J.N.C.I. 42:1101-1114. (As cited in 909)

912. Schwetz, B.A.; Keller, P.A.; Gehring, P.J., 1974, The effect of purified and commercial grade pentachlorophenol on rat embryonal and fetal development. Toxicol. Appl. Pharmacol. 28:151-161.

913. Fahrig, R.; Nilsson, C.A.; Rappe, C., 1978, Genetic activity of chlorophenols and chlorophenol impurities. Rao, K.A., ed. Pentachlorophenol: Chemistry, Pharmacology and Environmental Toxicology. New York: Plenum Press. pp 325-338. (As cited in 909 and 914)

914. Williams, P.L., 1982, Pentachlorophenol, an assessment of the occupational hazard. J. Am. Ind. Hyg. Assoc. 43:799-810.

915. Andersen, K.J.; Leighty, E.G.; Takahashi, M.T., 1972, Evaluation of herbicides for possible mutagenic properties. J. Agr. Food Chem. 20:649-656. (As cited in 909)

916. Buselmaier, W.; Roehrborn, G.; Propping, P., 1973, Comparative investigations on the mutagenicity of pesticides in mammalian test systems. Mutat. Res. 21:25-26. (As cited in 909 and 2005)

917. Vogel, E.; Chandler, J., 1974, Mutagenicity testing of cyclamate and some pesticides in Drosophila melanogaster. Experientia 30:621-623. (As cited in 909)

918. Bauchinger, M.; Dresp, J.; Schmid, E.; Hauf, R., 1982, Chromosome changes in lymphocytes after occupational exposure to pentachlorophenol (PCP). Mutat. Res. 102:83-88.

919. Schwetz, B.A.; Quast, J.F.; Keeler, P.A.; Humiston, C.G.; Kociba, R.J., 1978, Results of two-year toxicity and reproduction studies on pentachlorophenol in rats. Rao, K.R., ed. Pentachlorophenol: Chemistry, Pharmacology and Environmental Toxicology. New York: Plenum Press. pp 301-309. (As cited in 25, 909 and 910)

920. Williams, P.L., 1983, Commercial PCP: Toxic impurities. Occup. Health Saf. 52:14-16.

921. McGavack, T.; Boyd, L.; Piccione, F.; Terranova, R., 1941, Acute and chronic intoxications with sodium pentachlorophenate in rabbits. J. Ind. Hyg. Toxicol. June 1941:239-251. (As cited in 920)

922. Johnson, R.; Gehring, P.J.; Kociba, R.; Schwetz, B., 1973, Chlorinated dibenzodioxins and pentachlorophenol. Environ. Health Persp. 5:87-99. (As cited in 914)

923. Dow Chemical Company, 1969, Toxicity summary for Dowicide 7. Report of the Ad Hoc Study Group on Pentachlorophenol Contaminants - 1978. (As cited in 909)

924. Fielder, R.J.; Sorrie, G.S.; Bishop, C.M.; Jones, R.B.; VanDenHeuvel, M.J., 1982, Pentachlorophenol. Toxic. Rev. 5.

925. Goldstein, J.A.; Friesen, M.; Linder, R.E.; Hickman, P.; Haas, J.R.; Bergman, H., 1977, Effect of pentachlorophenol on hepatic drug metabolizing enzymes and porphyria related to contamination with chlorinated dibenzo-p-dioxins and dibenzofurans. Biochem. Pharmacol. 26:1549-1557. (As cited in 910)

926. Kociba, R.J. et al., 1971, Results of 90-day toxicological study in male rats maintained on diets containing production grade or purified pentachlorophenol. Dow Chemical Company, Midland, Michigan. (As cited in 910)

927. Kerkvliet, N.I.; Baecher-Steppan, L.; Schmitz, J.A., 1982, Immunotoxicity of pentachlorophenol (PCP): Increased susceptibility to tumor growth in adult mice fed technical PCP-contaminated diets. Toxicol. Appl. Pharmacol. 62:55-64.

928. Bevenue, A.; Haley, T.J.; Klemmer, H.W., 1967, A note on the effects of a temporary exposure of an individual to

pentachlorophenol. Bull. Environ. Contam. Toxicol. 2:293-296. (As cited in 909)

929. Sungster, B.; Wegman, R.C.C.; Hofstee, A.W.M., 1982, Non-occupational exposure to pentachlorophenol: Clinical findings and plasma-PCP-concentrations in three families. Human Toxicol. 1:123-133.

930. Chapman, J.B.; Robinson, P., 1965, Pentachlorophenol poisoning from bath-water. Lancet 7398:2366-2367. (As cited in 909)

931. Knudsen, I.; Verschuuren, H.G.; DenTonkelaar, E.M.; Kroes, R.; Helleman, P.F.W., 1974, Short-term toxicity of pentachlorophenol in rats. Toxicology 2:141-152. (As cited in 909)

932. Gray, R.E.; Gilliland, R.D.; Smith, E.E.; Lockard, V.G.; Hume, A.S., 1985, Pentachlorophenol intoxication: report of a fatal case, with comments on the clinical course and pathologic anatomy. Arch. Environ. Health 40:161-164.

933. Baader, E.W.; Bauer, H.J., 1951, Industrial intoxication due to pentachlorophenol. Ind. Med. Surg. 20:286-290. (As cited in 46)

934. Roberts, H.J., 1963, Aplastic anemia due to pentachlorophenol and tetrachlorophenol. Southern Med. J. 56:632. (As cited in 909)

935. Begley, J.; Reichert, E.L.; Rashad, M.N.; Klemmer, H.W.; Siemsen, A.W., 1977, Association between renal function tests and pentachlorophenol exposure. Clin. Toxicol. 11:97-106. (As cited in 909)

936. Klemmer, H.W., 1972, Human health and pesticides - community pesticide studies. Residue Rev. 41:55-63. (As cited in 910)

937. Triebig, G.; Krekeler, H.; Gossler, K.; Valentin, H., 1981, Investigations into neurotoxicity of work related materials. Int. Arch. Occup. Environ. Health 48:357-367. (As cited in 924)

938. Klemmer, H.W.; Wong, L.; Sato, M.M.; Reichert, E.L.; Korsak, R.J.; Rashad, M.N., 1980, Clinical findings in workers exposed to pentachlorophenol. Arch. Environ. Contam. Toxicol. 9:715-725. (As cited in 927)

939. Scow, K.; Goyer, M.; Payne, E.; Perwak, J.; Thomas, R.; Wallace, D.; Wood, M., 1980, An exposure and risk assessment for phenol. Washington, D.C.: U.S. Environmental Protection Agency, Office of Water Regulations and Standards. PB85-221695/AS.

940. U.S. Environmental Protection Agency (USEPA), 1980, Ambient water quality criteria for phenol. EPA Report No. 440/5-80-066.

Washington, D.C.: U.S. Environmental Protection Agency, Office of Water Regulations and Standards. PB81-117772.

941. National Cancer Institute (NCI), 1980, Bioassay of phenol for possible carcinogenicity. NCI Carcinogenesis Technical Report Series No. 203, NCI-CG-TR-203, DHHS Publications No. (NIH) 80-1759 PB80-217346.

942. Gocke, E.; King, M.T.; Eckhart, K.; Wild, D., 1981, Mutagenicity of cosmetic ingredients licensed by the European communities. Mutat. Res. 90:91-109.

943. Haworth, S.; Lawler, T.; Mortelsmans, K.; Speck, W.; Zeiger, E., 1983, Salmonella mutagenicity test results for 250 chemicals. Environ. Mutagen. 5:3-142. (As cited in 800)

944. Cotruvo, J.A.; Simmon, V.F.; Spanggord, R.J., 1977, Investigation of mutagenic effects of products of ozonation reactions in water. Ann. N.Y. Acad. Sci. 298:124-140.

945. Erexson, G.L.; Wilmer, J.L.; Kligerman, A.D., 1985, Sister chromatid exchange induction in human lymphocytes exposed to benzene and its metabolites in vitro. Cancer Res. 45:2471-2477.

946. Hadorn, E.; Niggli, H., 1946, Mutations in Drosophila after chemical treatment of gonads in vitro. Nature 157:162-163. (As cited in 939)

947. Minor, J.L.; Becker, B.A., 1971, A comparison of the teratogenic properties of sodium salicylate, sodium benzoate, and phenol. Toxicol. Appl. Pharmacol. 19:373. (As cited in 939)

948. Price-Jones, C.; Ledoux, T.A.; Reel, J.R.; Langhoff-Paschke, L.; Marr, M.C.; Kimmel, C.A., 1984, Teratologic evaluation of phenol in CD-1 mice, September 18, 1980 to January 12, 1981. Research Triangle Institute. Research Triangle Park, North Carolina. PB85-104461.

949. National Institute for Occupational Safety and Health (NIOSH), 1976, Criteria for a recommended standard. Occupational exposure to phenol. DHEW Publication No. (NIOSH) 76-196.

950. Macht, D.I., 1915, An experimental study of lavage in acute carbolic acid poisoning. Johns Hopkins Hosp. Bull. 26:98-104. (As cited in 949)

951. Deichmann, W.B.; Kitzmiller, K.V.; Witherup, B.S., 1944, Phenol studies - VII. Chronic phenol poisoning, with special reference to the effects upon experimental animals of the inhalation of phenol vapor. Am. J. Clin. Pathol. 14:273-277. (As cited in 949)

952. Cosgrove, K.W.; Hubbard, W.B., 1928, Acid and alkali burns of the eye. Ann. Surg. 87:89-91. (As cited in 949)

953. Murphy, J.C.; Osterberg, R.E.; Seabaugh, V.M.; Bierbower, G.W., 1982, Ocular irritancy responses to various pHs of acids and bases with and without irritation. Toxicology 23:281-291.

954. Conning, D.M.; Hayes, M.J., 1970, The dermal toxicity of phenol - An investigation of the most effective first-aid measures. Br. J. Ind. Med. 27:155-159. (As cited in 949).

955. Deichmann, W.; Oesper, P., 1940, Ingestion of phenol-effects on the albino rat. Ind. Med. 9:296. (As cited in 940)

956. Johnstone, R.T.; Miller, S.E., 1960, The aromatic hydrocarbons and derivatives. Occupational Diseases and Industrial Medicine. Philadelphia: Saunders Co. pp 195-196. (As cited in 949)

957. Lewin, J.F.; Cleary, W.T., 1982, An accidental death caused by the absorption of phenol through skin. A case report. Forensic Sci. Int. 19:177-179.

958. Warner, M.A.; Harper, J.V., 1985, Cardiac dysrhythmias associated with chemical peeling with phenol. Anesthesiology 62:366-367.

959. Stajduhar-Caric, Z., 1968, Acute phenol poisoning. J. Forensic Med. 15:41-42. (As cited in 949)

960. Piotrowski, J.K., 1971, Evaluation of exposure to phenol - Absorption of phenol vapor in the lungs and through the skin and excretion of phenol in urine. Brit. J. Ind. Med. 28:172-178. (As cited in 949)

961. Baker, E.L.; Landrigan, P.J.; Bertozzi, P.E.; Field, P.H.; Basteyns, B.J.; Skinner, H.G., 1978, Phenol poisoning due to contaminated drinking water. Arch. Environ. Health 33:89-94.

962. Merliss, R.R., 1972, Phenol marasmus. J. Occup. Med. 14:55-56. (As cited in 12)

963. Bulsiewicz, H., 1977, The influence of phenol on chromosomes of mice Mus musculus in the process of spermatogenesis. Folia Morphol. 36:13-22. (As cited in 939)

964. Values were estimated by Arthur D. Little, Inc., from ratio of vapor pressure to water solubility.

965. Values were estimated by Arthur D. Little, Inc., using "group" method described by Hine and Mookerjee (966).

966. Hine, J.; Mookerjee, P.K., 1975, The intrinsic hydrophobic character of organic compounds. Correlations in terms of structural contributions. J. Org. Chem. 40:292-298.

967. Values were estimated by Arthur D. Little, Inc., using Method 1: Acids. (As cited in 968)

968. Lyman, W.J.; Potts, R.G., 1985, CHEMEST - A Program for Chemical Property Estimation. The CHEMEST program was created (and is maintained) by Arthur D. Little, Inc., Acorn Park, Cambridge, MA 02140.

969. Values were estimated by Arthur D. Little, Inc., using Method 2: Liquids and Solids. (As cited in 968)

970. Rasanen, L.; Hattula, M.L., 1977, The mutagenicity of MCPA and its soil metabolites, chlorinated phenols, catechols and some widely used slimicides in Finland. Bull. Environ. Contam. Toxicol. 18:565-571. (As cited in 900 and 907)

971. U.S. Environmental Protection Agency (USEPA), April 30, 1980, 2,6-Dichlorophenol, health and environmental effects. Profile No. 76. Washington, D.C.: Office of Solid Wastes.

972. Lenga, R.E., ed., 1985, The Sigma-Aldrich Library of Chemical Safety Data. 1st ed.

973. Federal Register, 1986, Revocation of chlordane tolerances. 51:46665.

974. Federal Register, 1986, Pesticide products containing pentachlorophenol for non-wood preservative uses; availability and transmittal of draft notice of intent to cancel registrations. 51:1843.

975. Federal Register, 1986, Creosote, pentachlorophenol and inorganic arsenicals; Amendment of notice of intent to cancel registrations. 51:1334.

976. 40CFR180.111 Malathion; tolerances for residues.

977. 40CFR180.126 Inorganic bromides resulting from soil treatment with ethylene dibromide; tolerances for residues.

978. 40CFR180.133 Lindane; tolerances for residues.

979. 40CFR180.142 2,4-D; tolerances for residues.

980. 40CFR180.340 Silvex; tolerances for residues.

981. American Petroleum Institute, 1985, Guide to State Groundwater Programs and Standards. API Publication No. 4416. Health and

Environmental Sciences Department. Washington, DC: American Petroleum Institute.

982. U.S. Environmental Protection Agency, 1976, Quality Criteria for Water. Washington D.C.: U.S. Environmental Protection Agency.

983. 40CFR180.1062 Butyl benzyl phthalate; exemption from the requirement of a tolerance.

984. 40CFR180.1067 Methyl eugenol and malathion combination; exemption from the requirement of a tolerance.

985. 40CFR302 Designation, reportable quantities, and notification.

986. Federal Register, 1985, Butyl benzyl phthalate; proposed test rule. 50:36446.

987. Federal Register, 1985, Hazardous waste management system; Identification and listing of hazardous waste. 50:53315.

988. 40CFR261.24 Characteristic of EP toxicity.

989. 40CFR264.96 Concentration limits.

990. Federal Register, 1986, Hazardous waste management system; Identification and listing of hazardous waste. 51:5327.

991. 40CFR141.12(a)(b) Maximum contaminant levels for organic chemicals - chlorinated hydrocarbons, chlorophenoxys.

992. Federal Register, 1985, National primary drinking water regulations; synthetic organic chemicals, inorganic chemicals and microorganisms. 50:46936.

993. U.S. Environmental Protection Agency (USEPA), 1980, Ambient water quality criteria for chlordane. EPA Report No. 440/5-80-027. Washington, D.C.: U.S. Environmental Protection Agency, Office of Water Regulations and Standards. PB81-117384.

994. World Health Organization (WHO), 1984, Environmental Health Criteria 34. Chlordane. Geneva: World Health Organization.

995. National Research Council (NRC), 1982, An Assessment of the Health Risks of Seven Pesticides Used for Termite Control, Washington, D.C.: National Academy Press. PB83-136374.

996. Simmon, V.F.; Kauhanen, K.; Tardiff, R.G., 1977, Mutagenic activity of chemicals identified in drinking water. Presented at Second International Conference of Environmental Mutagens, Edinburgh, Scotland, July 1977. (As cited in 993)

997. Ahmed, F.E.; Hart, R.W.; Lewis, N.J., 1977, Pesticide induced DNA damage and its repair in cultured human cells. Mutat. Res. 42:161-174.

998. Epstein, S.S.; Arnold, E.; Andrea, J.; Bass, W.; Bishop, Y., 1972, Detection of chemical mutagens by the dominant lethal assay in the mouse. Toxicol. Appl. Pharmacol. 23:288-325.

999. Arnold, D.W.; Kennedy, G.L., Jr.; Kepplinger, M.L.; Calandra, J.C.; Calo, C.J., 1977, Dominant lethal studies with technical chlordane, HCS-3260, and heptachlor:heptachlor epoxide. J. Toxicol. Environ. Health 2:547-555.

1000. Keplinger, M.L.; Deichmann, W.B.; Sala, F., 1968, Effects of pesticides on reproduction in mice. Ind. Med. Surg. 37:525. (As cited in 994)

1001. Marnett, L.J.; Hurd, H.K.; Hollstein, M.C.; Levin, D.E.; Esterbauer, H.; Ames, B.N., 1985, Naturally occurring carbonyl compounds are mutagens in Salmonella tester strain TA104. Mutat. Res. 148:25-34.

1002. Altenkirch, H.; Stoltenburg, G.; Wagner, H.M., 1978, Experimental studies on hydrocarbon neuropathies induced by methyl ethyl ketone (MEK). J. Neurol. 219:159-170.

1003. American Conference of Governmental Industrial Hygienists (ACGIH), 1986, TLVs-Threshold Limit Values for Chemical Substances in the Work Environment Adopted by ACGIH for 1985-86. Cincinnati, Ohio: ACGIH.

1004. Altenkirch, H.; Wagner, H.M.; Stoltenburg-Didinger, G.; Steppat, R., 1982, Potentiation of hexacarbon-neurotoxicity by methyl-ethyl-ketone (MEK) and other substances: clinical and experimental aspects. Neurobehav. Toxicol. Teratol. 4:623-627.

1005. Deacon, M.M.; Pilny, M.D.; John, J.A.; Schwetz, B.A.; Murray, F.J.; Yakel, H.O.; Kuna, R.A., 1981, Embryo- and fetotoxicity of inhaled methyl ethyl ketone in rats. Toxicol. Appl. Pharmacol. 59:620-622.

1006. Tham, R.; Bunnfors, I.; Eriksson, B.; Larsby, B.; Lindgen, S.; Odkvist, L.M., 1984, Vestibulo-ocular disturbances in rats exposed to organic solvents. Acta. Pharmacol. et Toxicol. 54:58-63.

1007. Vallat, J.M.; Leboutet, M.J.; Loubet, A.; Piva, C.; Dumas, M., 1981, N-hexane- and methyl ethyl ketone-induced polyneuropathy abnormal accumulation of glycogen in unmyelinated axons: Report of a case. Acta. Neuropathol. 55:275-279.

1008. Cavender, F.L.; Casey, H.W.; Gralla, E.J.; Swenberg, J.A., 1984, The subchronic inhalation toxicity of n-hexane and methyl ethyl ketone. In: Advances in Modern Environmental Toxicology, Vol. 6, McFarland et al. eds.

1009. Wahlberg, J.E., 1984, Erythema-inducing effects of solvents following epicutaneous administration to man-studied by laser doppler flowmetry. Scand. J. Work. Environ. Health 10:159-162.

1010. Barlow, S.M.; Sullivan, F.M., 1982, Reproductive Hazards of Industrial Chemicals: An Evaluation of Animal and Human Data, London: Academic Press.

1011. Zimmermann, F.K.; Mayer, V.W.; Scheel, I.; Resnick, M.A., 1985, Acetone, methyl ethyl ketone, ethyl acetate, acetonitrile and other polar aprotic solvents are strong inducers of aneuploidy in Saccharomyces cerevisiae. Mutat. Res. 149:339-351.

1012. Geller, I.; Gause, H.; Kaplan, H.; Hartmann, R.J., 1979, Effects of acetone, methyl ethyl ketone and methyl isobutyl ketone on a match-to-sample task in the baboon. Pharmacol. Biochem. Behav. 11:401-406.

1013. Chen, T.H.; Kavanagh, T.J.; Chang, C.C.; Trosko, J.E., 1984, Inhibition of metabolic cooperation in Chinese hamster V79 cells by various organic solvents and simple compounds. Cell Biol. Toxicol. 1:155-171.

1014. DiVincenzo, G.D.; Kaplan, C.J.; Dedinas, J., 1976, Characterization of the metabolites of methyl n-butyl ketone, methyl iso-butyl ketone and methyl ethyl ketone in guinea pig serum and their clearance. Toxicol. Appl. Pharmacol. 36:511-522.

1015. Couri, D.; Hetland, L.B.; Abdel-Rahman, M.S.; Weiss, H., 1977, The influence of inhaled ketone solvent vapors on hepatic microsomal biotransformation activities. Toxicol. Appl. Pharmacol. 41:285-289.

1016. Berg, E.F., 1971, Retrobulbar neuritis -- A case report of presumed solvent toxicity. Ann. Opthalmol. 3:1351-1353. (As cited in 1029)

1017. McCann, J.; Choi, E.; Yamasaki, E.; Ames, B.N., 1975, Detection of carcinogens as mutagens in the Salmonella/microsome test: assay of 300 chemicals. Proc. Nat. Acad. Sci. 72(12):5135-5139.

1018. Maronpot, R.R.; Zelenak, J.P.; Weaver, E.V.; Smith, N.J., 1983, Teratogenicity study of ethylene glycol in rats. Drug Chem. Toxicol. 6:579-594.

1019. Lamb, J.C.; Maronpot, R.R.; Gulati, D.K.; Russell, V.S.; Hommel-Barnes, L.; Subharwal, P.S., 1985, Reproductive and developmental toxicity of ethylene glycol in the mouse. Toxicol. Appl. Pharmacol. 81:100-112.

1020. Price, C.J.; Kimmel, C.A. Tyl, R.W.; Marr, M.C., 1985, The developmental toxicity of ethylene glycol in rats and mice. Toxicol. Appl. Pharmacol. 81:113-127.

1021. Anonymous, Ethylene glycol, polypropenoates studies submitted as "FYI" reports. Pesticide and Toxic Chemical News. October 23, 1985. pp 11-12.

1022. Murphy, M.J.; Ray, A.C.; Jones, L.P.; Reagor, J.C., 1984, 1,3-butanediol treatment of ethylene glycol toxicosis in dogs. Am. J. Vet. Res. 45:2293-2295.

1023. Graver, G.F.; Thrall, M.A.; Henre, B.A.; Grauer, R.M.; Hamar, D.W., 1984, Early clinicopathologic findings in dogs ingesting ethylene glycol. Am. J. Vet. Res. 45:2299-2303.

1024. Rajagopal, G.; Rameshi, N.; Ramakrishnan, S., 1981, Effect of acute ethylene glycol toxicity on blood ammonia and brain amino acids in male albino rats. Indian J. Exp. Biol. 19:538-540.

1025. Catchings, T.T.; Beamer, W.C.; Lundy, L.; Prough, D.S., 1985, Adult respiratory distress syndrome secondary to ethylene glycol ingestion. Ann. Emerg. Med. 14:594-596.

1026. Cieciura, L.; Kidawa, Z.; Orkisz, S.; Trznadel, K., 1983, Ultrastructural appearances of nephron damage in acute poisoning with ethylene glycol. Proceed. Eur. Dialysis and Transpl. Assoc. 20:636-640.

1027. Edelhauser, H.F.; Antoine, M.E.; Pederson, H.J.; Hiddeman, J.W.; Harris, R.G., 1983, Intraocular safety evaluation of ethylene oxide and sterilant residues. J. Toxicol. Cutaneous and Ocular Toxicol. 2:7-39.

1028. Patty, F.A.; Schrenk, H.H.; Yant, W.P., 1935, Acute response of guinea pigs to vapors of some new commercial organic compounds -- VIII. Butanone. U.S. Public Health Rep. 50:1217-1228. (As cited in 19 and 1029)

1029. National Institute for Occupational Safety and Health (NIOSH), 1978, Criteria for a recommended standard . . . Occupational exposure to ketones. DHEW Publ. No. (NIOSH) 78-173.

1030. Saida, K.; Mendell, J.R.; Weiss, H.S., 1976, Peripheral nerve changes induced by methyl n-butyl ketone and potentiation by methyl ethyl ketone. J. Neuropathol. Exp. Neurol. 35:207-225.

1031. Munies, R.; Wurster, D.E., 1965, Investigation of some factors influencing percutaneous absorption III. Absorption of methyl ethyl ketone. J. Pharm. Sci. 54:1281-1284.

1032. Smith, A.R.; Mayers, M.R., 1944, Study of poisoning and fire hazards of butanone and acetones. N.Y. State Ind. Bull. 23:174-176. (As cited in 1029)

1033. Altenkirch, H., 1979, Dt. Med. Wschr. 104:935. (As cited in 49)

1034. Homburger, F., 1968, U.S. Clearinghouse Fed. Sci. Tech. Inform., P.B. Rep. No. 183027. (As cited in 13)

1035. Derse, P.H., 1969, U.S. Clearinghouse Fed. Sci. Tech. Inform., P.B. Rep. No. 195153. (As cited in 13)

1036. Mason, M.M.; Cate, C.C.; Baker, J., 1971, Clin. Toxicol. 4:185. (As cited in 13)

1037. Blood, F.R., 1965, Food Cosmet. Toxicol. 3:229. (As cited in 13)

1038. Pfeiffer; Dunkelberg, 1980, Mutagenicity of ethylene oxide and propylene oxide and of the glycols and halohydrins formed from them during the fumigation of food. Food Cosmet. Toxicol. 18:115.

1039. Morris, H.J.; Nelson, A.A.; Calvery, H.O., 1942, J. Pharmacol. Exp. Therap. 74:266. (As cited in 13)

1040. Troisi, F.M., 1950, Chronic intoxication by ethylene glycol vapor. Br. J. Ind. Med. 7:65-69. (As cited in 13 and 19)

1041. Specht, H.; Miller, J.W.; Valaer, P.J.; Sayers, R.R., 1940, Acute response of guinea pigs to the inhalation of ketone vapors, NIH bulletin No. 176. Federal Security Agency, Public Health Service, National Institute of Health. (As cited in 1029)

1042. McLaughlin, J.; Marliac, J.P.; Verrett, J.; Mutchler, M.K.; Fitzhugh, O.G., 1964, Toxicity of fourteen volatile chemicals as measured by the chick embryo method. Am. Ind. Hyg. Assoc. J. 25:282-284.

1043. Van Duuren, B.L.; Sivak, A.; Katz, C.; Melchionne, S., 1971, Cigarette smoke carcinogenesis: Importance of tumor promoters. J. Nat. Cancer Inst. 47:235-240.

1044. Ross, D.S., 1973, Acute acetone intoxication involving eight male workers. Ann. Occup. Hyg. 16:73-75.

1045. Rengstorff, R.H.; Petrali, J.P.; Sim, V.M., 1972, Cataracts induced in guinea pigs by acetone, cyclohexane and dimethylsulfoxide. Am. J. Optom. Arch. Am. Acad. Optom. 49:308-319.

1046. McDonald, T.O.; Roberts, M.D.; Borgmann, A.R., 1972, Ocular toxicity of ethylene chlorohydrin and ethylene glycol in rabbit eyes. Toxicol. Appl. Pharmacol. 21:143-150.

1047. Roberts, J.A.; Seibold, H.R., 1969, Ethylene glycol toxicity in the monkey. Toxicol. Appl. Pharmacol. 15:624-631.

1048. Gitelson, S.; Werczberger, A.; Herman, J.B., 1966, Coma and hyperglycemia following drinking of acetone. Diabetes 15:810-811. (As cited in 1029)

1049. Casazza, J.P.; Felver, M.E.; Veech, R.L., 1984, The metabolism of acetone in rats. J. Biol. Chem. 259:231-236.

1050. Vigliani, E.C.; Zurlo, N., 1955, [Experiences of the Clinics Del Lavoro with some maximum concentrations of poisons of industry at the place of work (MAK).] Arch. Gewerbepathol. Gewerbehyg. 13:528-534. (As cited in 1029)

1051. Goldberg, M.E.; Johnson, H.E.; Pozzani, U.C.; Smyth, H.F., Jr., 1964, Effects of repeated inhalation of vapors of industrial solvent on animal behavior. Am. Ind. Hyg. Assoc. J. 25:369-375. (As cited in 1029)

1052. Matsushita, T.; Yoshimune, A.; Inoue, T.; Yamaka, S.; Suzuki, H., 1969, [Experimental studies for determining the maximum permissible concentrations of acetone -- 1. Biological reactions in one-day exposure to acetone.] Jpn. J. Ind. Health 11:477-485. (As cited in 1029)

1053. Lupulescu, A.P.; Birmingham, D.J., 1976, Effect of protective agents against lipid-solvent-induced damages. Arch. Environ. Health 31:33-36.

1054. DeFlora, S.; Zanacchi, P.; Camoirano, A.; Bennicelli, C.; Badolati, G.S., 1984, Genotoxic activity and potency of 135 compounds in the Ames reversion test and in bacterial DNA-repair test. Mutat. Res. 133:161-198.

1055. Parmeggiani L.; Sassi, C., 1954, [Occupational poisoning with acetone -- Clinical disturbances, investigations in work rooms and physiopathological research.] Med. Lav. 45:431-468. (As cited in 1029)

1056. Rao, K.S.; Cobel-Geard, S.R.; Young, J.T.; Hanley, T.R., Jr.; Hayes, W.C.; John, J.A.; Miller, R.R., 1983, Ethylene glycol

monomethyl ether II: Reproductive and dominant lethal studies in rats. Fundam. Appl. Toxicol. 3:80-85.

1057. Chapin, R.E.; Lamb, J.C., IV, 1984, Effect of ethylene glycol monomethyl ether on various parameters of testicular function in the F344 rat. Environ. Health Perspect. 57:219-224.

1058. Foster, P.M.D.; Creasy, D.M.; Foster, J.R.; Gray, T.J.B., 1984, Testicular toxicity produced by ethylene glycol monomethyl and monoethyl ethers in the rat. Environ. Health Perspect. 54:207-217.

1059. Nelson, B.K,; Setzer, J.V.; Brightwell, W.S.; Mathinos, P.R.; Kuczuk, M.H.; Weaver, T.E.; Goad, P.T., 1984, Comparative inhalation teratogenicity of four glycol ether solvents and amino derivatives in rats. Environ. Health Perspect. 57:261-271.

1060. National Institute for Occupational Safety and Health (NIOSH), 1983, The glycol ethers, with particular reference to 2-methoxyethanol and 2-ethoxyethanol: Evidence of adverse reproductive effects. Current Intelligence Bulletin #39. DHHS (NIOSH) Publication No. 83-112.

1061. Loch-Caruso, R.; Trosko, J.E.; Corcos, I.A., 1984, Interruption of cell-cell communication in Chinese hamster V79 cells by various alkyl glycol ethers: Implications for teratogenicity. Environ. Health Perspect. 57:119-129.

1062. Hanley, T.R.; Yano, B.L.; Nitschke, K.D.; John, J.A.; 1984, Comparison of the teratogenic potential of inhaled ethylene glycol monomethyl ethers in rats, mice and rabbits. Toxicol. and Appl. Pharmacol. 75:409-422.

1063. Nagano, K.; Nakayama, E.; Dobayashi, H.; Yamada, T.; Adachi, H.; Nishizawa, T.; Ozama, H.; Nakaichi, M.; Okuda, H.; Minami, K.; Yamazaki, K., 1981, Embryotoxic effects of ethylene glycol monomethyl ether in mice. Toxicology 20:335-343.

1064. Nelson, B.K.; Brightwell, W.S.; Bury, J.R.; Massari, V.J., 1984, Behavioral and neurochemical alterations in the offspring of rats after maternal or paternal inhalation exposure to the industrial solvent 2-methoxyethanol. Pharmacol. Biochem. Behav. 20:269-279.

1065. Heinonen, T.; Vainio, H., 1981, Dose-dependent toxicity of ethylene glycol monomethyl ether vapor in the rat. Eur. J. Drug Metab. Pharmacokinet. 6:275-280.

1066. Miller, R.R.; Ayres, J.A.; Calhoun, L.L.; Young, J.T.; McKenna, M.J., 1981. Comparative short-term inhalation toxicity of

ethylene glycol monomethyl ether and propylene glycol monomethyl ether in rats and mice. Toxicol. Appl. Pharmacol. 61:368-377.

1067. Miller, R.R.; Ayres, J.A.; Young, J.T.; McKenna, M.J., 1983, Ethylene glycol monomethyl ether. I. Subchronic vapor inhalation study with rats and rabbits. Fundam. Appl. Toxicol. 3:49-54.

1068. Nitter-Hauge, S., 1970, Poisoning with ethylene glycol monomethyl ether, report of two cases. Acta. Med. Scand. 188:277-280.

1069. Young, E.G.; Woolner, L.B., 1946, A case of fatal poisoning from 2-methoxyethanol. J. Industr. Hyg. 28:267. (As cited in 12)

1070. Romer, K.G.; Balge, F.; Freundt, K.J., 1985, Ethanol-induced accumulation of ethylene glycol monomethyl ethers in rats. Drug Chem. Toxicol. 8:255-264.

1071. Cook, R.R.; Bodner, K.M.; Kolesar, R.C.; Van Peenan, P.F.D.; Dickson, G.S.; Flanagon, K., 1982, A cross-sectional study of ethylene glycol monomethyl ether process employees. Arch. Environ. Health 37:346-351.

1072. Zavon, M.R., 1963, Methyl cellosolve intoxication. Am Ind. Hyg. Assoc. J. 24:36-41.

1073. Ohi, G.; Wegman, D.H., 1978, Transcutaneous ethylene glycol monomethyl ether poisoning in the work setting. J. Occup. Med. 20:675-676.

1074. Cohen, R., 1984, Reversible subacute ethylene glycol monomethyl ether toxicity associated with microfilm production: A case report. Am. J. Ind. Med. 6:441-446.

1075. Nakaaki, K.; Fukabori, S.; Osamu, T., 1980, An experimental study on percutaneous absorption of some organic solvents. J. Sci. Labour 56:1. (As cited in 1076)

1076. European Chemical Industry Ecology and Toxicology Center (ECETOC), 1985, Technical Report No. 17, The toxicology of glycol ethers and its relevance to man: An up-dating of ECETOC technical report no. 4. European Chemical Industry Ecology and Toxicology Centre. Brussels, Belgium.

1077. Probst, G.S.; McMahon, R.E.; Hill, L.E.; Thompson, C.Z.; Epp, J.K.; Neal, S.B., 1981, Chemically-induced unscheduled DNA synthesis in primary rat hepatocyte cultures: A comparison with bacterial mutagenicity using 218 compounds. Environ. Mutagen. 3:11-32.

1078. Bruckner, J.V.; Peterson, R.G., 1981, Evaluation of toluene and acetone inhalant abuse II. Model development and toxicology. Toxicol. Appl. Pharmacol. 61:302-312.

1079. Palmer, A.K.; Bottomley, A.M.; Worden, A.N.; Frohberg, H.; Bauer, A., 1978, Effects of lindane on pregnancy in the rabbit and rat. Toxicology 9:239-247.

1080. E. I. du Pont de Nemours and Company, 1985, Material Safety Data Sheet, Motor Fuel Anti-knock Compound.

1081. Rocchi, P.; Perocco, P.; Alberghini, W.; Fini, A.; Prodi, G., 1980, Effect of pesticides on scheduled and unscheduled DNA synthesis of rat thymocytes and human lymphocytes. Arch. Toxicol. 45:101-108.

1082. Weisse, I.; Herbst, M., 1977, Carcinogenicity study of lindane in the mouse. Toxicology 7:233-238.

1083. Thorpe, E.; Walker, A.I.T., 1973, The toxicology of dieldrin (HEOD). II. Comparative long-term oral toxicity studies in mice with dieldrin, DDT, phenobarbitone, β-BCH and γ-BCH. Food Cosmet. Toxicol. 11:433-442.

1084. Srinivasan, K.; Ramesh, H.P.; Radhakrishnamurty, R., 1984, Renal tubular dysfunction caused by dietary hexachlorocyclohexane (HCH) isomers. J. Environ. Sci. Health B19:453-466.

1085. Frank, R.; Braun, H.E., 1984, Lindane toxicity to four-month-old calves. Bull. Environ. Contam. Toxicol. 32:533-536.

1086. Srinivasan, K.; Radhakrishnamurty, R., 1983, Effect of dietary intake on hexachlorocyclohexane isomers on some haematological parameters. J. Food Sci. Technol. 20:322-324.

1087. Cattabeni, F.; Pastorello, M.C.; Eli, M., 1983, Convulsions induced by lindane and the involvement of the GABAergic system. Toxicology in the use, misuse and abuse of food, drugs and chemicals. Arch. Toxicol. Suppl. 6:244-249.

1088. Rivett, K.F.; Chesterman, H.; Kellett, D.N.; Newman, A.J.; Worden, A.N., 1978, Effects of feeding lindane to dogs for periods of up to 2 years. Toxicology 9:273-289.

1089. Davies, J.E.; Dedhia, H.V.; Morgade, C.; Barquet, A.; Maibach, H.I., 1983, Lindane poisonings. Arch. Dermatol. 119:142-144.

1090. Etherington, J.D., 1984, Major epileptic seizures and topical gamma benzene hexachloride. Br. Med. J. 289:228.

1091. Telch, J.; Jarvis, D.A., 1982, Acute intoxication with lindane (gamma benzene hexachloride). Can. Med. Assoc. J. 126:662-663.

1092. Tomczak, S.; Baumann, K.; Lehnert, G., 1981, Occupational exposure to hexachlorocyclohexane IV. Sex hormone alteration in HCH-exposed workers. Int. Arch. Occup. Environ. Health 48:283-287.

1093. Baumann, K.; Behling, K.; Brassow, H.L.; Stapel, L., 1981, Occupational exposure to hexachlorocyclohexane III. Neurophysiological findings and neuromuscular function in chronically exposed workers. Int. Arch. Occup. Environ. Health 48:165-172.

1094. Ray, A.C.; Norris, J.D.; Reagor, J.C., 1975, Benzene hexachloride poisoning in cattle. J. Am. Vet. Med. Assoc. 166:1180-1182.

1095. Munk, Z.M.; Nantel, A., 1977, Acute lindane poisoning with development of muscle necrosis. Can. Med. Assoc. J. 117:1050-1054.

1096. Solomon, L.M.; Fahrner, L.; West, D.P., 1977, Gamma-benzene hexachloride toxicity - a review. Arch. Dermatol. 113:353-357.

1097. Oesch, F.; Friedberg, T.; Herbst, M.; Paul, W.; Wilhelm, N.; Bentley, P., 1982, Effects of lindane treatment on drug metabolizing enzymes and liver weight of CF1 mice in which it evoked hepatomas and in non-susceptible rodents. Chem. Biol. Interact. 40:1-14.

1098. World Health Organization (WHO), 1982, Recommended health-based limits in occupational exposure to pesticides. Technical Report No. 677. Geneva: World Health Organization.

1099. Sidi, Y.; Kiltchevsky, E.; Shaklai, M.; Pinkhas, 1983, Acute myeloblastic leukemia and insecticide. N.Y. State J. Med. 83:161.

1100. National Cancer Institute (NCI), 1977, Bioassay of lindane for possible carcinogenicity. NCI Carcinogenesis Technical Report Series Number 14, NCI-CG-TR-14, DHEW Publication No. (NIH) 77-814.

1101. Buselmaier, W.; Rohrborn, G.; Propping, P., 1972, Mutagenicity investigations with pesticides in the host-mediated assay and the dominant lethal test in mice. Biol. Zbl. 91:311-325. (As cited in 25)

1102. Benes, V.; Sram, R., 1969, Mutagenic activity of some pesticides in Drosophila melanogaster. Ind. Med. 38:442-444. (As cited in 25)

1103. Ishidate, M., Jr.; Odashima, S., 1977, Chromosome tests with 134 compounds on Chinese hamster cells in vitro - A screening for chemical carcinogens. Mutat. Res. 48:337-354.

1104. Tzoneva-Maneva, M.T.; Kaloianova, F.; Georgieva, V., 1971, Influence of diazinon and lindane on the mitotic activity and the caryotype of human lymphocytes, cultivated in vitro. In: Proceedings of the XII International Congress of the Society of Blood Transfusion, Moscow, 1969, Bibl. Haemat., Basel, Karger 38:344-347. (As cited in 25)

1105. Ahmed, F.E.; Hart, R.W.; Lewis, N.J., 1977, Pesticide induced DNA damage and its repair in cultured human cells. Mutat. Res. 42:161-174.

1106. West, I., 1967, Lindane and hematologic reactions. Arch. Environ. Health 15:97-101. (As cited in 1107)

1107. National Institute for Occupational Safety and Health (NIOSH), 1978, Criteria for a recommended standard . . . Occupational exposure during the manufacture and formulation of pesticides. DHEW Publication No. (NIOSH) 78-174.

1108. Moriya, M.; Ohta, T.; Watanabe, K.; Miyazawa, T.; Kato, K.; Shirasu, G., 1983, Further mutagenicity studies on pesticides in bacterial reversion assay systems. Mutat. Res. 116:185-216.

1109. Chen, H.H.; Hsueh,J.L.; Sirianni, S.R.; Huang, C.C., 1981, Induction of sister-chromatid exchanges and cell cycle delay in cultured mammalian cells treated with eight organophosphorus pesticides. Mutat. Res. 88:307-316.

1110. Misawa, M.; Doull, J.; Uyeki, E.M., 1982, Teratogenic effects of cholinergic insecticides in chick embryos. III. Development of cartilage and bone. J. Toxicol. Environ. Health 10:551-563.

1111. Lox, C.D., 1983, Effects of acute pesticide poisoning on blood clotting in the rat. Ecotoxicol. Environ. Saf. 7:451-454.

1112. Mount, M.E., 1984, Diagnostic value of urinary dialkyl phosphate measurement in goats exposed to diazinon. Am. J. Vet. Res. 45:817-824.

1113. Lox, C.D.; Davis, J.R., 1983, The effects of long-term malathion or diazinon ingestion on the activity of hepatic synthesized clotting factors. Ecotoxicol. Environ. Saf. 7:546-551.

1114. Wedin, G.P.; Pennente, C.M.; Sachdev, S.S., 1984, Renal involvement in organophosphate poisoning. J.A.M.A. 252:1408 (letter).

1115. Van Der Meer, M.J.; Hundt, H.K.L.; Muller, F.O., 1983, Inhibition of atropine metabolism by organophosphate pesticides. Human Toxicol. 2:637-640.

1116. Tomokuni, K.; Tohru, H., 1985, Diazinon concentrations and blood cholinesterase activities in rats exposed to diazinon. Toxicol. Letters 25:7-10.

1117. Morrissey, R.L.; Wolff, G.L., 1986, Lindane-induced alveolar bronchiolization and alveolar cell tumors in yellow and pseudoagouti $A^{vy/a}$ mice. Abstract #327. (As cited in 1337)

1118. The British Crop Protection Council, 1983, The Pesticide Manual: A World Compendium, 7th edition, Worthing, C.R.; Walker, S.B., eds, London, England.

1119. Rathbun, R.E.; Stephans, D.W.; Schultz, D.I.; Tai, D.Y., 1982, Fate of acetone in water. Chemosphere 11:1097-1114.

1120. Gardner, E.P.; Wijayaratne, R.D.; Calvert, J.G., 1984, Primary quantum yields of photodecomposition of acetone in air under tropospheric conditions. J. Phys. Chem. 88:5069-5076.

1121. Rathbun, R.E.; Tai, D.Y., 1982, Volatilization of ketones from water. Water Air Soil Pollut. 17:281-293.

1122. Green, W.J.; Lee, G.F.; Jones, R.A., 1981, Clay-soils permeability and hazardous waste storage. J. Water Pollut. Contr. Fed. 53:1347-1354.

1123. Abrams, E.F., et al., 1975, Identification of organic compounds in effuents from industrial sources. EPA Report No. 560/3-75-002. (As cited in 1119)

1124. Helfgott, T.F.; Hart, F.L.; Bedard, R.G., 1977, An index of refractory organics. EPA Report No. 600/2-77-174; PB-272 438. (As cited in 31)

1125. Lyman, W.L.; Nelson, L.; Partridge, L.; Kalelkar, A.; Everett, J.; Allen, D.; Goodies, L.L.; Pollock, G., 1974, Survey study to select a limited number of hazardous materials to define amelioration requirements. U.S. Coast Guard, CG-0-46-75. (As cited in 31)

1126. Chou, W.L.; Speece, R.E.; Siddiqi, R.H., 1979, Acclimation and degradation of petrochemical wastewater components by methane fermentation. Biotechnol. Bioeng. Symp. 8:391-414. (As cited in 806)

1127. Dore, M.; Brunet, N.; Legube, B., 1975, Participation of various organic compounds in the evaluation of global pollution criteria. Trib. Cebedeau 28:3-11. (As cited in 806)

1128. Gerhold, R.M.; Malaney, G.W., 1966, Structural determinants in the oxidation of aliphatic compounds by activated sludge. J. Water Pollut. Contr. Fed. 38:562-579. (As cited in 806)

1129. Hatfield, R., 1957, Biological oxidation of some organic compounds. Ind. Eng. Chem. 49:192-196. (As cited in 806)

1130. Liu, D., 1979, A novel selective enrichment technique for use in biodegradation studies. In: Microbial degradation of pollutants in the marine environments. EPA Report No. 600/9-79-012. (As cited in 806)

1131. Lowery, C.E., Jr.; Foster, J.W.; Jurtshuk, P., 1968, The growth of various filamentous fungi and yeasts on n-alkanes and ketones. Studies of substrate specificity. Arch. Microbiol. 60:246-254. (As cited in 806)

1132. Lukins, H.B.; Foster, J.W., 1963, Methyl ketone metabolism in hydrocarbon-utilizing mycobacteria. J. Bacteriol. 85:1074-1087. (As cited in 806)

1133. Perry, J.J., 1968, Substrate specificity in hydrocarbon utilizing microorganisms. Antonie Van Leewuenhoek J. Microb. Serol. 34:27-36. (As cited in 806)

1134. Young, R.H.F.; Ryckman, D.W.; Buzzell, J.C., Jr., 1968, An improved tool for measuring biodegradability. J. Water Pollut. Contr. Fed. 40:354-368. (As cited in 806)

1135. Dojlido, J.R., 1979, Investigations of biodegradability and toxicity of organic compounds; Final report 1975-79. EPA 600/2-79-163, Cincinnati, OH: Municipal Environmental Research Lab 118 pp. (As cited in 806)

1136. Kato, T.; Akiyama, K.; Kawano, T., 1980, Origin of organic pollutants in the lake of Shinsei-ko. Yokohama Kokuritsu Daigaku Kankyo Kagaku Kenkyu Senta Kiyo 6:11-20. (As cited in 806)

1137. Lande, S.S.; Durkin, P.R.; Christopher, D.H.; Howard, P.H.; Saxena, J., 1976, Investigation of selected potential environmental contaminants: Ketonic solvents. EPA 560/2-76-003, Washington, D.C.: U.S. Environmental Protection Agency, Office of Toxic Substances.

1138. Mackay, D.; Shiu, W.Y.; Bobra, A.; Billington, J.; Chau, E.; Yeun, A.; NG, C.; Szeto, F., 1982, Volatilization of organic pollutants from water. EPA 600/53-82-019. Athens, GA: U.S. Environmental Protection Agency. NTIS PB82-230939.

1139. Mametkuliev, C.H., 1978, [Study of embryotoxic and teratogenic properties of the gamma isomer of HCH in experiments with rats]. Zdravookhr. Turkm. 20:28. (As cited in 1154)

1140. Inoue, T.; Takeuchi, Y., Hisanaga, N.; One, Y.; Iwata, M.; Ogata, M.; Saito, K.; Sakurai, H.; Hara, I.; Matsushita, T.; Ikeda, M., 1983, A nationwide survey on organic solvent components in various solvent products: Part 1. Homogeneous products such as thinners, depressers and reagants. Ind. Health 21:175-183.

1141. Kumai, M.; Koizumi, A.; Saito, K.; Sakurai, H.; Inove, T.; Takevchi, Y.; Hara, I.; Ogata, M.; Matsushita, T.; Ikeda, M., 1983, A nationwide survey on organic solvent components in various solvent products: Part 2. Heterogeneous products such as paints, inks, and adhesives. Ind. Health 21:185-197.

1142. U.S. Environmental Protection Agency (USEPA), 1980, Methods for level 2 analysis by organic compound category. EPA 600/10-80-104. USEPA Process Measurements Branch IERL, RTP, NC.

1143. Waters, M.D.; Sandhu, S.S.; Simmons, V.F.; Mortelmans, K.E.; Mitchell, A.D.; Jorgenson, T.A.; Jones, D.C.L.; Valencia, R.; Garrett, N.E., 1982, Study of pesticide genotoxicity. Basic Life Sci. Genet. Toxicol. 21:275-326.

1144. Chen, H.H.; Sirianni, S.R.; Huang, C.C., 1982, Sister chromatid exchanges in Chinese hamster cells treated with seventeen organophosphorus compounds in the presence of metabolic activation system. Environ. Mutagen. 4:621-624.

1145. Misawa, M.; Doull, J.; Kitos, P.A.; Uyeki, E.M., 1981, Teratogenic effects of cholinergic insecticides in chick embryos I. Diazinon treatment on acetylcholinesterase and choline acetyltransferase activities. Toxicol. Appl. Pharmacol. 57:20-29.

1146. National Cancer Institute (NCI), 1979, Bioassay of diazinon for possible carcinogenicity. NCI Carcinogenesis Technical Report Series No. 137, NCI-CG-TR-137, DHEW Publication No. (NIH) 79-1392.

1147. Poklis, A.; Kutz, F.W.; Sperling, J.F.; Morgan, D.P., 1980, A fatal diazinon poisoning. Forensic Sci. Int. 15:135-140.

1148. Heyndrickx, A.; Van Hoof, F.; DeWolf, L.; Van Peteghem, C., 1974, Fatal diazinon poisoning in man. J. Forensic Sci. Soc. 14:131-133.

1149. Derache, R., 1977, Orgarophosphorus Pesticides. Criteria (Dose/Effect Relationships) for Organophosphorus Pesticides. Pergamon Press: New York.

1150. Anonymous (1966) Untitled, Unpublished report from Industrial Bio-Test Labs., Inc. submitted to the World Health Organization by GEIGY Chemical Co. Summary In: WHO/FAO, 1967b pp. 229-230. (As cited in 1149)

1151. Industrial Biotest Laboratories Inc., 1966, Diazinon. Unpublished report submitted by GEIGY Chemical Co. Summary in: WHO/FAO 1967. p. 239. (As cited in 1149)

1152. Albright, R.K., 1984, Renal involvement in organophosphate poisoning. J.A.M.A. 252:1408 (letter).

1153. Soliman, S.A.; Sovocool, G.W.; Curley, A.; Ahmed, N.S.; El-Fiki, S.; El-Sabae, A.K., 1982, Two acute human poisoning cases resulting from exposure to diazinon transformation products in Egypt. Arch. Environ. Health 37:207-212.

1154. U.S. Environmental Protection Agency (USEPA), 1980, Ambient water quality criteria for hexachlorocyclohexane. EPA Report No. 440/S-80-054. Washington D.C.: U.S. Environmental Protection Agency, Office of Water Regulations and Standards. PB81-117657.

1155. Heyroth, F.F., 1952, In: S.J. Leland, ed., Chem. Spec. Manuf. Assoc. Proc. 6:110. (As cited in 1154)

1156. Frawley, J.P.; Fitzhugh, O.G., 1949, Rate of disappearance of isomers of benzene hexachloride from fat deposits in rats. Fed. Proc. 8:292. (As cited in 1154)

1157. Kitamura, S., et al., 1970, Japan J. Pub. Health 17:108. (As cited in 1154)

1158. Davies, D.B.; Holub, B.J., 1980, Comparative subacute toxicity of dietary diazinon in the male and female rat. Toxicol. Appl. Pharmacol. 54:359-367.

1159. Kimbrough, R.D.; Gaines, T.B., 1969, Effect of organic phosphorus compounds and alkylating agents on the rat fetus. Arch. Environ. Health 16:805-808.

1160. Truelove, J.; Grant, D.; Mes, J.; Tryphonas, H.; Tryphonas, L.; Zawidzka, Z., 1982, Polychlorinated biphenyl toxicity in the pregnant cynomolgus monkey: A pilot study. Arch. Environ. Contam. Toxicol. 11:583-588.

1161. Sager, D.; Girard, D., 1983, Early postnatal exposure to PCBs and reproductive function in young and mature adult female rats. Fed. Proc. 42:355. Abstract No. 372.

1162. Brezner, E.; Terkel, J.; Perry, A.S., 1984, The effect of Aroclor 1254 (PCB) on the physiology of reproduction in the female rat - I. Comp. Biochem. Physiol. 77C:65-70.

1163. Sager, D.B., 1983, Effect of postnatal exposure to polychlorinated biphenyls on adult male reproductive function. Environ. Res. 3:76-94.

1164. Carter, J.W., 1983, Onset of hepatomegaly in PCB (Aroclor 1254)-treated rats. Bull. Environ. Contam. Toxicol. 31:183-187.

1165. Carter, J.W., 1984, Hypercholesterolemia induced by dietary PCBs (Aroclor 1254) in Fischer rats. Bull. Environ. Contam. Toxicol. 33:78-83.

1166. Iverson, F.; Truelove, J.; Hierlihy, S.L., 1982, Hepatic microsomal enzyme induction by Aroclors 1248 and 1254 in cynomolgus monkeys. Food Chem. Toxicol. 20:307-310.

1167. Geistfeld, J.G.; Bond, M.G.; Bullock, B.C.; Varian, M.C., 1982, Mucinous gastric hyperplasia in a colony of rhesus monkeys (Macaca mulatta) induced by polychlorinated biphenyl (Aroclor 1254). Lab. Anim. Sci. 32:83-86.

1168. Miniats, O.P.; Platonow, N.S.; Geissinger, H.D., 1978, Experimental polychlorinated biphenyl toxicosis in germ free pigs. Can. J. Comp. Med. 42:192-199.

1169. Weltman, R.H.; Norback, D.H., 1982, Development of hepatocellular and cholangiocellular neoplasms in the livers of male and female Sprague-Dawley rats after chronic administration of Aroclor 1260. Fed. Proc. 41:446. Abstract No. 1029.

1170. Norback, D.H.; Weltman, R.H., 1985, Polychlorinated biphenyl induction of hepatocellular carcinoma in the Sprague-Dawley rat. Environ. Health Perspect. 6:97-105.

1171. Kimbrough, R.D.; Squire, R.A.; Linder, R.E.; Strandberg, J.D.; Montali, R.J.; Burse, V.W., 1975, Induction of liver tumors in Sherman strain female rats by polychlorinated biphenyl (Aroclor 1260). J. Nat. Cancer Instit. 55(6):1453-1456.

1172. Steele, G.; Stehr-Green, P.; Welty, E., 1986, Estimates of the biologic half-life of polychlorinated biphenyls in human serum. The N.E.J. Med. 314:926-927.

1173. Thomas, P.T.; Hinsdill, R.D., 1978, Effect of polychlorinated biphenyls on the immune responses of rhesus monkeys and mice. Toxicol. Appl. Pharmacol. 44:41-51.

1174. Masuda, Y.; Yoshimura, H., 1984, Polychlorinated biphenyls and dibenzofurans in patients with Yusho and their toxicological significance: A review. Am. J. Ind. Med. 5:31-44.

1175. Lawton, R.W.; Ross, M.R.; Feingold, J.; Brown, J.F., Jr., 1985, Effects of PCB exposure on biochemical and hematological findings in capacitor workers. Environ. Health Perspect. 60:165-184.

1176. Chen, R.C.; Tang, S.Y.; Miyata, H.; Kashimoto, T.; Chang, Y.C.; Chang, K.J.; Tung, T.C., 1985, Polychlorinated biphenyl poisoning: Correlation of sensory and motor nerve conduction, neurologic symptoms, and blood levels of polychlorinated biphenyls, quaterphenyls and dibenzofurans. Environ. Res. 37:340-348.

1177. Smith, A.B.; Schloemer, J.; Lowry, L.K.; Smallwood, A.W.; Ligo, R.N.; Tanaka, S.; Stringer, W.; Jones, M.; Hervin, R.; Glueck, C.J., 1982, Metabolic and health consequences of occupational exposure to polychlorinated biphenyls. Br. J. Ind. Med. 39:361-369.

1178. U.S. Environmental Protection Agency (USEPA), 1980, Ambient water quality criteria for polychlorinated biphenyls. EPA Report No. 440/5-80-068. Washington, D.C.: U.S. Environmental Protection Agency, Office of Water Regulations and Standards. PB81-117798.

1179. World Health Organization (WHO), 1976, Environmental Health Criteria 2. Polychlorinated biphenyls and terphenyls. Geneva: World Health Organization.

1180. E.I. duPont de Nemours & Co., Inc. 1985, Material Safety Data Sheet, Motor Fuel Antiknock Compound.

1181. Green, S., et al., 1975a, Lack of cytogenetic effects in bone marrow and spermatogonial cells in rats treated with polychlorinated biphenyls-Aroclors 1242 and 1254. Bull. Environ. Contam. Toxicol. 13:14. (As cited in 1178)

1182. Green, S.; Saure, F.M.; Friedman, L., 1975b, Lack of dominant lethality in rats treated with polychlorinated biphenyls (Aroclor 1242 and 1254). Food Cosmet. Toxicol. 13:507-510. (As cited in 1178)

1183. McNulty, W., 1977, PCB poisoning in rhesus monkeys. Primate News 15:3-7.

1184. McNulty, W.P., 1985, Toxicity and fetotoxicity of TCDD, TCDF and PCB isomers in rhesus macaques (Macaca mulatta). Environ. Health Perspect. 60:77-88.

1185. Ouw, H.K.; Simpson, G.R.; Siyali, D.S., 1976, Use and health effects of Aroclor 1242, a polychlorinated biphenyl, in an electrical industry Arch. Environ. Health 31:189-194.

1186. Barsotti, D.A.; VanMiller, J.P., 1984, Accumulation of a commercial polychlorinated biphenyl mixture (Aroclor 1016) in adult rhesus monkeys and their nursing infants. Toxicology 30:31-44.

1187. Aulerich, R.J.; Ringer, R.K.; Seagram, H.L.; Yoriatt, W.G., 1971, Effects of feeding coho salmon and other Great Lakes fish on mink reproduction. Can. J. Zool. 49:611-616. (As cited in 1178)

1188. Silkworth, J.B.; Loose,L.D., 1981, Assessment of environmental contaminant-induced lymphocyte dysfunction. Environ. Health Perspect. 39:105-128.

1189. Matthews, H.B.; Anderson, M.W., 1975b, Effect of chlorination on the distribution and excretion of polychlorinated biphenyls. Drug Metab. Dispos. 3:371. (As cited in 1178)

1190. Allen, J.R.; Norback, D.H., 1977, Carcinogenic potential of the polychlorinated biphenyls. Hiatt, H.H., et al., ed. Origins of Human Cancer. Cold Spring Harbor Conf. Cell Prolif. Cold Spring Harbor Lab., Cold Spring Harbor, N.Y. 4:173. (As cited in 1178)

1191. Ringer, R.K.; Aulerich, R.J.; Zabik, M., 1972, Effect of dietary polychlorinated biphenyls on growth and reproduction of mink. 164th Natl. Meet. Am. Chem. Soc. 12:149. (As cited in 1178)

1192. Yamashita, F., 1977, Clinical features of polychlorbiphenyls (PCB)-induced fetopathy. Paediatrician 6:20. (As cited in 1178)

1193. Ward, J.M., 1985, Proliferative lesions of the glandular stomach and liver in F344 rats fed diets containing Aroclor 1254. Environ. Health Perspect. 60:89-95.

1194. Morgan, R.W.; Ward J.M.; Hartman, P.E., 1981, Aroclor 1254-induced intestinal metaplasia and adenocarcinoma in the glandular stomach of F344 rats. Cancer Res. 41:5052-5059.

1195. Garthoff, L.H.; Cerra, F.E.; Marks, E.M., 1981, Blood chemistry alterations in rats after single and multiple gavage administration of polychlorinated biphenyls. Toxicol. Appl. Pharmacol. 60:33-44.

1196. Spencer, F., 1982, An assessment of the reproductive toxic potential of Aroclor 1254 in female Sprague-Dawley rats. Bull. Environ. Contam. Toxicol. 28:290-297.

1197. Baker, F.D.; Bush, B.; Tumasonis, C.F.; Lo, F.C., 1977, Toxicity and persistence of low-level PCB in adult Wistar rats, fetuses and young. Arch. Environ. Contam. Toxicol. 5:143-156.

1198. Carter, J.W.; Mercer, L.P., 1983, Pair-feeding study of PCB (Aroclor 1254) toxicity in rats. Bull. Environ. Contam. Toxicol. 31:686-691.

1199. Miller, R.W., 1985, Congenital PCB poisoning: A reevaluation. Environ. Health Perspect. 60:211-214.

1200. Wyllie, J.A.; Gabica, J.; Benson, W.W.; Yoder, J., 1975, Exposure and contamination of the air and employees of a pentachlorophenol plant, Idaho - 1972. Pestic. Monit. J. 9:150-153. (As cited in 25 and 918)

1201. Hinkle, D.K., 1973, Fetotoxic effects of pentachlorophenol in the golden Syrian hamster. Toxicol. Appl. Pharmacol. 25:455. Abstract No. 42.

1202. 40CFR428 Rubber manufacturing point source category.

1203. Mannecke, D.M.; Johnson, L.M.; Talbot, H.W.; Barik, S., 1982, Microbial metabolism and enzymology of selected pesticides. In: Biodegradation and Detoxification of Environmental Pollutants, Boca Raton, FL: CRC Press.

1204. Sanborn, J.R.; Metcalf, R.L.; Francis, B.M., 1977, The degradation of selected pesticides in soil: A review of the published literature. Report No. EPA-600/9-77-022, U.S. Environmental Protection Agency, Office of Research and Development, Cincinnati, OH.

1205. Wolfe, N.L.; Zepp, R.G.; Baughman, G.L.; Fincher, R.C.; Gordon, J.A., 1976, Chemical and photochemical transformation of selected pesticides in aquatic systems. Report No. EPA-600/3-76-067, U.S. Environmental Protection Agency, Environmental Research Laboratory, Athens, GA.

1206. Nelken, L.H.; Broome, M.; Lyman, W.J.; Scow, K.M.; Steber, W.D.; Berkowitz, J.B.; Noss, C.I., 1981, Fate and effects of five pesticides of military importance on secondary biological wastewater treatment plants. Final Report on Task Order No. 6 under Contract No. DAMD 17-79-C-9139, U.S. Army Medical Bioengineering Research and Development Laboratory, Fort Detrick, Frederick, MD.

1207. Chapman, R.A.; Cole, C.M., 1982, Observations on the influence of water and soil pH on the persistence of insecticides. J. Environ. Sci. Health B17:487-504.

1208. Guenzi, W.D., ed., 1974, Pesticides in Soil and Water. Madison, WI: Soil Science Society of America, Inc.

1209. Bomberger, D.C.; Gwinn, J.L.; Maybey, W.R.; Tusé, D.; Chou, T.W., 1983, Environmental fate and transport at the terrestrial-atmospheric interface. In: ACS Symp. Ser. 225: Fate of Chemicals in the Environment, Swann, R.L.; Eschenroeder. A., eds. pp. 197-214, Washington, D.C.: American Che 1 Society.

1210. Laskowski, D.A.; Goring, C.A.I.; McCall, P.J.; Swann, R.L., 1982, Terrestrial environment. Conway, R.A., ed. Environmental Risk Analysis for Chemicals, New York: Van Nostrand Reinhold Co.

1211. Rao, P.S.C.; Davidson, J.M., 1982, Retention and transformation of selected pesticides and phosphorus in soil-water systems: A critical review. Report No. EPA 600/3-82-060, U.S. Environmental Protection Agency, Environmental Research Laboratory, Athens, GA.

1212. Camazano, M.S.; Martin, M.J.S., 1983, Factors influencing interactions of organophosphorus pesticides with montmorillonite. Geoderma 29:107-118.

1213. Misra, S.G.; Joshi, H.C., 1980, Influence of temperature on adsorption of three organophosphorus pesticides by soil. Nat. Acad. Sci. Letters 3:301-304.

1214. Adhikari, J.; Sen, P.; Das, P.K., 1980, Studies on adsorption of malathion on humic substances. Indian Agric. 24:83-88.

1215. Jenkins, D.; Klein, S.A.; Yang, M.S.; Wagenet, R.J.; Biggar, J.W., 1978, The accumulation, translocation and degradation of biocides at land wastewater disposal sites: the fate of malathion, carbaryl, diazinon and 2,4-D butoxyethyl ester. Water Res. 12:713-723.

1216. Klein, S.A.; Jenkins, D.; Wagenet, R.J.; Biggar, J.W.; Yang, M.S., 1974, An evaluation of the accumulation, translocation, and degradation of pesticides at land wastewater disposal sites. Final Report on Contract No. USA-DADA-17-73-C-3109 for the U.S. Army Medical Research and Development Command, Washington, D.C.

1217. Sanders, P.F.; Seiber, J.N., 1983, A chamber for measuring volatilization of pesticides from model soil and water disposal system. Chemosphere 12:999-1012.

1218. Sanders, P.F.; Seiber, J.N., 1984, Organophosphorus pesticide volatilization; model soil pits and evaporation ponds. In: ACS Symp. Ser. 259, Treatment and Disposal of Pesticide Wastes, pp. 279-295, Washington, D.C.: American Chemical Society.

1243. Wright, C.G.; Leidy, R.B., 1982, Chlordane and heptachlor in the ambient air of houses treated for termites. Bull. Environ. Contam. Toxicol. 28:617-623.

1244. Cartrell, M.J.; Craun, J.C.; Podrebarac, D.S.; Gunderson, E.L., 1985a, Pesticides, selected elements and other chemicals in infant and toddler total diet samples. October 1978 - September 1979. J. Assoc. Off. Anal. Chem. 68:842-861.

1245. Cartrell, M.J.; Craun, J.C.; Podrebarac, D.S.; Gunderson, E.L., 1985b, Pesticides, selected element, and other chemicals in adult total diet samples. October 1978 - September 1979. J. Assoc. Off. Anal. Chem. 68:826-875.

1246. McLeod, H.A., 1980, Pesticide residues in the total diet in Canada, V:1976 to 1978. J. Food Safety 2:141-164.

1247. Frank, R.; Braun, H.E.; Holdrinet, M.; Sirons, G.J. et al., 1979, Organochlorine insecticides and industrial pollutants in the milk supply of southern Ontario, Canada, 1977. J. Food Prot. 42:31-37.

1248. Frank, R.; Braun, H.E.; Fleming, G., 1983, Organochlorine and organophosphorus residues in fat of bovine and porcine carcasses marketed in Ontario, Canada from 1969 to 1981. J. Food Prot. 46:893-900.

1249. Jonsson, V.; Liu, G.J.K.; Armbruster, J.; Kettelhut, L.L.; Drucker, B., 1977, Chlorohydrocarbon pesticide residues in human milk in Greater St. Louis, Missouri 1977. Am. J. Clin. Nutri. 30:1106-1109.

1250. International Agency of Research on Cancer (IARC), 1982, Working Group on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Supp. 4. Geneva: World Health Organization.

1251. Thompson, C.Z.; Gunnoe, M.D.; vanLier, R.B.L.; Probst, G.S., 1985, The effect of Aroclor 1254 dose on the metabolic activity of rat or mouse liver S9 in the Salmonella mutagenicity test. Environ. Mutagen. 7:22A.

1252. International Agency for Research on Cancer (IARC), 1980, Working Group on the Evaluation of the Carcinogenic Risk of Chemicals to Man. IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Volume 23. Geneva: World Health Organization.

1253. Epstein, S.S.; Mantel, N., 1968, Carcinogenicity of tetraethyl lead. Experientia 24:580-581. (As cited in 1254)

1254. World Health Organization (WHO), 1977, Environmental Health Criteria 3, Lead. Geneva: World Health Organization.

1255. Perwak, J.; Goyer, M.; Nelken, L.; Payne, E.; Wallace, D., 1981, An exposure and risk assessment for lead. Washington, D.C.: U.S. Environmental Protection Agency, Office of Water Regulation and Standards. PB85-220606.

1256. Ahlberg, J.; Ramel, C.; Wachtemeister, C.A., 1972, Organolead compounds shown to be genetically active. Ambio 1:29. (As cited in 1255)

1257. Ramel, C., 1973, The effect of metal compounds on chromosome segregation. Mutat. Res. 21:45.

1258. Kennedy, G.L.; Arnold, D.W., 1971, Absence of mutagenic effects after treatment of mice with lead compounds. Environ. Mutagen. Soc. Newsl. 5:37. (As cited in 1252)

1259. McClain, R.M.; Becker, B.A., 1972, Effects of organolead compounds on rat embryonic and fetal development. Toxicol. Appl. Pharmacol. 21:265-274.

1260. Kennedy, G.L.; Arnold, D.W.; Calandra, J.C., 1975, Teratogenic evaluation of lead compounds in mice and rats. Fd. Cosmet. Toxicol. 13:629-632.

1261. Torre, C.; DeGiorgis, P.L., 1982, Effects of tetraethyl lead on embryonic development. Studi Sassar. Sez. 60:14-17. Abstract. (As cited in 58)

1262. Turlakiewicz, Z.; Chmielnicka, J., 1985, Diethyl lead as a specific indicator of occupational exposure to tetraethyl lead. Br. J. Ind. Med. 42:682-685.

1263. Baselt, R.C., 1982, Disposition of Toxic Drugs and Chemicals in Man, 2nd ed. California: Biomedical Publications.

1264. Arai, F., 1981, Excretion of triethyl lead, diethyl lead and inorganic lead after injection of tetraethyl lead in rabbits. Sangyo Igaku 23:465-504. (As cited in 59)

1265. Dashiell, G.L.; Kennedy, G.L., 1984, The effects of fasting on the acute oral toxicity of nine chemicals in the rat. J. Appl. Toxicol. 4:320-325.

1266. Schepers, G.W.H., 1964, Tetraethyl lead and tetramethyl lead, comparative experimental toxicology, Part 1. Lead absorption and pathology. Arch. Environ. Health 8:277-295. (As cited in 1267)

1267. International Agency for Research on Cancer (IARC), 1973, Working Group on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. IARC Monographs on the Evaluation of the Carcirogenic Risk of Chemicals to Man. Vol 2. Geneva: World Health Organization.

1268. Kawamori, M.; Matsumoto, K.; Matsui, T., 1983, Acute intoxication by tetraethyl lead. I. Toxic symptoms of the central nervous system and spontaneous motor activity. Kyorin Igakkai Zasshi 14:3-11. Abstract. (As cited in 58)

1269. Swartzwelder, H.S., 1985, Central neurotoxicity after exposure to organic lead: Susceptibility to seizures. Neurosci. Lett. 58:225-228.

1270. Blakley, B.R.; Sisodia, C.S.; Mukkar, T.K., 1980, The effect of methylmercury, tetraethyl lead and sodium arsenite on the humoral immune response in mice. Toxicol. Appl. Pharmacol. 52:245-254.

1271. Kehoe, R.A.; Thaman, F., 1931, The behavior of lead in the animal organism. II. Tetraethyl lead. Amer. J. Hyg. 13:478. (As cited in 1267)

1272. Heywood, R., et al., 1979, Chronic oral administration of alkyl lead solutions to the rhesus monkey. Toxicol. Lett. 4:119-125. (As cited in 59)

1273. Gutniak, O.; Koziolowa, H.; Kowalski, E., 1964, Free protoporphyrin content of erythrocytes in chronic tetraethyl lead poisoning. Lancet 1:1137. (As cited in 1267)

1274. Gale, T.F., 1978, Embryotoxic effects of chromium trioxide in hamsters. Environ. Res. 16:101-109.

1275. Alvares, A.P.; Fischbein, A.; Anderson, K.E.; Kappas, A., 1977, Alterations in drug metabolism in workers exposed to polychlorinated biphenyls. Clin. Pharmacol. Therap. 22:140-146.

1276. Vos, J.G.; DeRoij, T.H., 1972, Immunosuppressive activity of a polychlorinated biphenyl preparation on the humoral immune response in guinea pigs. Toxicol. Appl. Pharmacol. 21:549-555.

1277. Watanabe, M.; Sugahara, T., 1981, Experimental formation of cleft palate in mice with polychlorinated biphenyls (PCB). Toxicology 19:49-53.

1278. Vos, J.G.; Beems, R.B., 1971, Dermal toxicity studies of technical polychlorinated biphenyls and fractions thereof in rabbits. Toxicol. Appl. Pharmacol. 19:617-633.

1279. Bruckner, J.V.; Khanna, K.L.; Cornish, H.H., 1973, Biological responses of the rat to polychlorinated biphenyls. Toxicol. Appl. Pharmacol. 24:434-448.

1280. Shigematsu, N.; Ishimaru, S.; Saito, R.; Ikeda, T.; Matsuba, K.; Sugiyama, K.; Masuda, Y., 1978, Respiratory involvement in polychlorinated biphenyls poisoning. Environ. Res. 16:92-100.

1281. Chang, K.J.; Hsieh, K.H.; Lee, T.P.; Tang, S.Y.; Tung, T.C., 1981, Immunologic evaluation of patients with polychlorinated biphenyl poisoning: Determination of lymphocyte subpopulations. Toxicol. Appl. Pharmacol. 61:58-63.

1282. Warshaw, R.; Fischbein, A.; Thornton, J.; Miller, A.; Selikoff, I.J., 1979, Decrease in vital capacity in PCB-exposed workers in a capacitor manufacturing facility. Ann. N.Y. Acad. Sci. 320:277-283.

1283. National Cancer Institute (NCI), 1978, Bioassay of Aroclor® 1254 for possible carcinogenicity. NCI Carcinogenesis Technical Report Series Number 38, NCI-CG-TR-38, DHEW Publication No. (NIH) 78-838.

1284. European Chemical Industry Ecology and Toxicology Centre (ECETOC), 1982, The toxicology of ethylene glycol monoalkylethers and its relevance to man. Technical Report No. 4. Brussels, Belgium.

1285. McGregor, D.B.; Willins, M.J.; McDonald, P.; Holmstrom, D.; McDonald, D.; Niemeier, 1981, Bis(2-methoxyethyl)ether and 2-methoxyethanol: Results from multiple assay for genotoxic potential. 5th Ann. Meeting UKEMS, University of Kent. (As cited in 1284)

1286. Conyers, R.A.J.; Goldsmith, L.E., 1971, A case of organophosphorus-induced psychosis. Med. J. Aust. 1:27-29.

1287. Rawlings, S.J.; Shuker, D.E.G.; Webb, M.; Brown, N.A., 1986, Embryotoxicity of alkoxy acids in postimplantation rat embryo culture: Structure-activity relations. Human Toxicol. 5:146.

1288. Stasik, M.; Byczkowska, Z.; Szendzikowski, S.; Fiedorczuk, Z., 1969, Acute tetraethyl lead poisoning. Arch. Toxicol. 24:283-291. (As cited in 17)

1289. Ross, C.A., 1982, Gasoline sniffing and lead encephalopathy. Can. Med. Assoc. J. 127:1195-1197.

1290. Coulehan, M.D., Hirsch, W.; Brillman, J.; Sanandria, J.; Welty, T.K.; Colaiaco, P.; Koros, A.; Lober, A., 1983, Gasoline sniffing and lead toxicity in Navajo adolescents. Pediatrics 71:113-117.

1291. Robinson, T.R., 1974, Twenty year mortality of tetraethyl lead workers. J. Occup. Med. 16:601-605. (As cited in 46)

1292. Robinson, T.R., 1976, The health of long service tetraethyl lead workers. J. Occup. Med. 18:31-40. (As cited in 1252)

1293. Sweeney, M.H.; Beaumont, J.J.; Waxweiler, R.J.; Halperin, W.E., 1984, An investigation of mortality from cancer and other causes of death among workers employed at an east Texas chemical plant. PB85-220945.

1294. Simmon, V.F.; Kauhanen, K.; Tardiff, R.G., 1977, Mutagenic activity of chemicals identified in drinking water. Dev. Toxicol. Environ. Sci. 2:249-258. (As cited in 1296)

1295. Dow Chemical Company, Unpublished data. (As cited in 12)

1296. Papa, P.A.; Fay, J.R.; Perry, L.R.; Atkinson, D.L.; Sigman, C.C.; Helmes, C.T., 1984, Survey of organic drinking water contaminants: Carcinogens, mutagens, and tumor promotors. Final Report. NCI contract No. 1-CP-95607. PB86-106499.

1297. Svirbely, J.L.; Highman, B.; Alford, W.C.; VonOettingen, W.F., 1947, The toxicity and narcotic action of monochloromonobromomethane, with special reference to inorganic and volatile bromide in blood, urine and brain. J. Ind. Hyg. Toxicol. 29:382. (As cited in 2, 12)

1298. Comstock, C.C.; Oberst, F.W.; Fogelman, R.W., 1953, Acute narcotic effects of monochloromonobromomethane vapor in rats. A.M.A. Arch. Ind. Hyg. Occup. Med 7:526. (As cited in 12)

1299. McDougall, J.N.; Jepson, G.W.; Clewell, H.J.; Andersen, M.E., 1985, Dermal absorption of dihalomethane vapors. Toxicol. Appl. Pharmacol. 79:150-158.

1300. National Institute for Occupational Safety and Health (NIOSH), 1976, Criteria for a recommended standard. . . Occupational exposure to malathion. DHEW (NIOSH) Publication No. 76-205.

1301. Ingle, L., 1967, Unpublished data. (As cited in 994)

1302. National Cancer Institute (NCI), 1977, Bioassay of chlordane for possible carcinogenicity. NCI Carcinogenesis Technical Report Series Number 8, NCI-CG-TR-8, DHEW Publication No. (NIH) 77-808.

1303. Epstein, S.S., 1976, Carcinogenicity of heptachlor and chlordane. Sci. Total Environ. 6:103-154. (As cited in 994)

1304. Williams, G.M.; Numoto, S., 1984, Promotion of mouse liver neoplasms by the organochlorine pesticides chlordane and

heptachlor in comparison to dichlorodiphenyltrichloroethane. Carcinogenesis 5:1689-1696.

1305. Ingle, L., 1952, Arch. Ind. Hyg. Occup. Med. 6:354. (As cited in 12)

1306. Ben-Dyke, R. et al., 1980, Acute toxicity data pesticides. Wildl. Rev. Pestic. Control 9:119. (As cited in 993)

1307. Ambrose, A.M.; Christensen, H.C.; Robbins, D.J., 1953, Pharmacological observations on chlordane. Red. Proc. Am. Soc. Exp. Biol. 12:298. (As cited in 993)

1308. Wazeter, F.X., et al., 1968, Alpha chlordane, gamma chlordane, alpha-gamma chlordane. Comparative acute oral toxicity (LD_{50}) in male albino rats. In: 1970 Evaluation of Some Pesticide Residues in Food. Food Agric. Org. United Naitons/WHO. (As cited in 993)

1309. Ingle, L., 1965, Monograph on chlordane-toxicological and pharmacological properties. University of Illinois, Food and Drug Library. Library of Congress Card No. 65-28686A. (As cited in 993)

1310. Ambrose, A.M.; Christensen, H.E.; Robbins,D. J.; Rather, L.J., 1953, Toxicology and pharmacological studies on chlordane. Arch. Ind. Hyg. Occ. Med. 1:197-210. (As cited in 994)

1311. Stewart, C.F., 1985, Chemical skin burns. Am. Fam. Physician 31:149-157.

1312. Frings, H.; O'Tousa, J.E., 1950, Toxicity to mice of chlordane vapor and solutions administered cutaneously. Science 111:568-660. (As cited in 995)

1313. Ingle, L., 1953, The toxicity of chlordane vapors. Science 118:213-214. (As cited in 995)

1314. Lehman, A.J., 1952, Chemicals in foods: A report to the Association of Food and Drug Officials on current developments Part II. Pesticides Section II: Dermal toxicity. Assoc. Food Drug Off. Q. Bull. 16:3-9. (As cited in 994)

1315. FAO/WHO, 1978, 1977 Evaluations of some pesticide residues in food. Rome: Food and Agriculture Organization of the United Nations. (As cited in 994).

1316. Ingle, L., 1952, Chronic oral toxicity of chlordane to rats. Arch. Ind. Hyg. Occup. Med. 6:357-367. (As cited in 994)

1317. International Research and Development Corporation (IRDC), 1967, Chlordane - two-year chronic feeding study in the beagle dog. Report 163-001. (As cited in 994)

1318. Ingle, L., 1965, Effects of 1-hydroxychlordene when incorporated into the diets of rats for 224 days. University of Illinois, Department of Zoology. Report for Velsicol Chemical Corporation. (As cited in 994)

1319. Olanoff, L.S.; Bristow, W.J.; Colcolough, J.,; Reigart, J.R., 1983, Acute chlordane intoxication. J. Toxicol. Clin. Toxicol. 20:291-306.

1320. Garrettson, L.K.; Guzelian, P.S.; Blanke, R.V., 1985, Subacute chlordane poisoning. Clin. Toxicol. 22:565-571.

1321. Harrington, J.M.; Baker, E.L., Jr.; Folland, D.S.; Saucier, J.W.; Sandifer, S.H., 1978, Chlordane contamination of a municipal water system. Environ. Res. 15:155-159.

1322. Derbes, J.V.; Dent, H.J.; Forest, W.W.; Johnson, M.F., 1955, Fatal chlordane poisoning. J.A.M.A. 158:1367-1369. (As cited in 46)

1323. Kazen, C.; Bloomer, A.; Welch, R.; Oudbier, A.; Price, H., 1974, Persistence of pesticides on the hands of some occupationally exposed people. Arch. Environ. Health 29:315-318. (As cited in 995)

1324. Infante,P.F.; Epstein, S.S.; Newton, W.A., Jr., 1978, Blood dyscrasias and childhood tumors and exposure to chlordane and heptachlor. Scand. J. Work Environ. Health 4:137-150.

1325. Ditraglia, D.; Brown, D.P.; Namekata, T.; Iverson, N., 1981, Mortality study of workers employed at organochlorine pesticide manufacturing plants. Scand. J. Work Environ. Health Suppl. 4 7:140-146.

1326. Wang, H.H.; Gruffenman, S., 1981, Aplastic anemia and occupational pesticide exposure: A case-control study. J.Occup. Med. 23:364-366.

1327. Wang, H.H.; MacMahon, B., 1979, Mortality of workers employed in the manufacture of chlordane and heptachlor. J. Occup. Med. 21:745-748. (As cited in 995)

1328. Princi, F.; Spurbeck, G.H., 1951, A study of workers exposed to the insecticides chlordane, aldrin and dieldrin. A.M.A. Arch. Ind. Hyg. Occup. Med. 3:64-72. (As cited in 995)

1329. Fishbein, W.J.; White, J.V.; Isaacs, H.J., 1964, Survey of workers exposed to chlordane. Ind. Med. Surg. 33:726-727. (As cited in 995)

1330. Alvarez, W.C.; Hyman, S., 1953, Absence of toxic manifestations in workers exposed to chlordane. A.M.A. Arch. Ind. Hyg. Occup. Med. 8:480-483. (As cited in 995)

1331. Federal Register, 1982, Pulp, paper and paperboard point source category effluent limitations guidelines and new source performance standards. 47:52066.

1332. Council of European Communities Directive on Hexachlorocyclohexane, 9 October 1984. (84/491/EEC-OJL274, 17 October 1984.)

1333. Council of European Communities Directive on Plant Protection Products, 21 December 1978. (79/117/EEC-OJL33, 8 February 1979.)

1334. Council of European Communities Directive on Paints, Varnishes, Printing Inks, Adhesives and Similar Products, 7 November 1977. (77/728/EEC-OJL303, 28 November 1977; as amended by 79/831/EEC, 15 October 1979 and 81/916/EEC, 28 November 1981.)

1335. Federal Register, 1983, Intent to cancel pesticide products containing lindane. 48:48512.

1336. Federal Register, 1986, Intent to cancel registrations of denial of applications for registration of pesticide products containing diazinon; conclusion of special review. 51:35034.

1337. Society of Toxicology, 1986, The Toxicologist Abstracts of 25th Anniversary Meeting. Vol. 6, No. 1, March 1986.

1338. Somkuti, S.G.; Lapadula, D.M.; Chapin, R.E.; Lamb, J.C. IV; Abou-Donia, M.B., 1986, The morphogenesis and ultrastructural changes of the tri-o-cresyl phosphate (TOCP)-induced testicular lesions in F344 rats. Abstract 1164. (As cited in 1337)

1339. Somkuti, S.G.; Lapadula, D.M.; Chapin, R.E.; Lamb, J.C. IV; Abou-Donia, M.B., 1986, Testicular toxicity of tri-o-cresyl phosphate (TOCP) in F344 rats. Abstract 1165. (As cited in 1337)

1340. Morgan, J.P., 1982, The Jamaica ginger paralysis. J.A.M.A 248:1864-1867.

1341. Albertini, A.V.; Gross, D.; Zinn, W.M., 1968, Triaryl phosphate poisoning in Morocco 1959. Georg Thieme Verlag, Stuttgart. (As cited in 12, 200)

1342. Senanayake, N.; Jeyarathnam, J., 1981, Toxic polyneuropathy due to gingili oil contaminated with tri-cresylphosphate affecting adolescent girls in Sri Lanka. Lancet 8211:88-89.

1343. Morgan, J.P.; Penovich, P., 1978, Jamaica ginger paralysis: Forty-seven year follow-up. Arch. Neurol. 35:530-532. (As cited in 1340)

1344. Hunter, D.; Perry, K.M.A.; Evans, R.B., 1944, Toxic polyneuritis arising during the manufacture of tricresyl phosphate. Br. J. Ind. Med. 1:227-231. (As cited in 2, 12)

1345. Tabershaw, I.R.; Kleinfeld, M.K., 1957, Manufacture of tricresyl phosphate and other alkyl phenyl phosphates: an industrial hygiene study. II. Clinical effects of tricresyl phosphate. A.M.A. Arch. Ind. Health 15:541-544. (As cited in 46)

1346. Tabershaw, I.R.; Kleinfeld, M.K.; Feiner, B., 1957, Manufacture of tricresyl phosphate and other alkyl phenyl phosphates: an industrial hygiene study. I. Environmental factors. A.M.A. Arch. Ind. Health 15:537-540. (As cited in 46)

1347. Duhrsen, U.; Meusers, P.; Engelhard, M.; Brittenger, G., 1984, Chronic granulocytic leukemia and chronic polyneuromyelopathy after 32 years exposure to tri-ortho-cresyl phosphate. Blut. 49:230.

1348. Lotti, M.; Becker, C.E.; Aminoff, M.J., 1984, Organophosphate polyneuropathy: pathogenesis and prevention. Neurology 34:658-662.

1349. Soliman, S.; Linder, R.; Farmer, J.; Curley, A., 1982, Species suseptibility to delayed toxic neuropathy in relation to <u>in vivo</u> inhibition of neurotoxic esterase by neurotoxic organophosphorous esters. J. Toxicol. Environ. Health 9:189-197.

1350. Robertson, D.G.; Schwab, B.W.; Richardson, R.J.; Anderson, R.J., 1986, Electrophysiologic correlates of OPIDN in hen. Abstract 485. (As cited in 1337)

1351. Padilla, S.; Veronesi, B., 1985, The relationship between neurological damage and neurotoxic esterase inhibition in rats acutely exposed to tri-ortho-cresyl phosphate. Toxicol. Appl. Pharmacol. 78:78-87.

1352. Abou-Donia, M.B.; Jensen, D.N.; Lapadula, D.M., 1983, Neurologic manifestations of tri-o-cresyl phosphate delayed neurotoxicity in cats. Neurobehav. Toxicol. Teratol. 5:431-442.

1353. Abou-Donia, M.B.; Trofatter, L.P.; Graham, D.G.; Lapadula, D.M., 1986, Electromyographic, neuropathologic, and functional

correlates in the cat as the result of tri-o-cresyl phosphate delayed neurotoxicity. Toxicol. Appl. Pharmacol. 83:126-141.

1354. National Cancer Institute (NCI), 1978, Carcinogenesis bioassay of malathion for possible carcinogenicity. NCI Carcinogenesis Technical Report Series No. 24, NCI-CG-TR-24. DHEW Publications No. (NIH) 78-824.

1355. National Cancer Institute (NCI), 1979. Carcinogenesis bioassay of malathion for possible carcinogenicity. NCI Carcinogenesis Technical Report Series No. 192, NCI-CG-TR-192. DHEW Publications No. (NIH) 79-1748.

1356. Huff, J.E.; Bates, R.; Eustis, S.L.; Haseman, J.K.; McConnell, E.E., 1985, Malathion and malaoxon: histopathology reexamination of the National Cancer Institute's carcinogenesis studies. Environ. Res. 37:154-173.

1357. Reuber, M.D., 1985, Carcinogenicity and toxicity of malathion and malaoxon. Environ. Res. 37:119-153.

1358. Shirasu, Y.; Moriya, M.; Kato, K.; Furuhashi, A.; Kada, T., 1976, Mutagenicity screening of pesticides in the microbial system. Mutat. Res. 40:19-30. (As cited in 1359)

1359. International Agency for Research on Cancer (IARC), 1982, Working Group on the Evaluation of the Carcinogenic Risk of Chemicals to Man. IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Vol. 29. Geneva: World Health Organization.

1360. Kawachi, T.; Yahagi, T.; Kada, T.; Tazima, Y.; Ishidate, M.; Sasaki, M.; Sugiyama, T., 1980, Cooperative programme on short-term assays for carcinogenicity in Japan. Montesano, R.; Bartsch, H.; Tomatis, L., eds. Molecular and Cellular Aspects of Carcinogen Screening Tests. IARC Scientific Publication No. 27., p. 323-330.

1361. Shiau, S.Y.; Huff, R.A.; Wells, B.C.; Felkner, I.C., 1980, Mutagenicity and DNA-damaging activity for several pesticides tested with Bacillus subtilis mutants. Mutat. Res. 71:169-179. (As cited in 1359)

1362. Waters, M.D.; Simmon, V.F.; Mitchell, A.D.; Jorgenson, T.A.; Valencia, R., 1980, An overview of short-term tests for the mutagenic and carcinogenic potential of pesticide. J. Environ. Sci. Health B15:867-906. (As cited in 1359)

1363. Simmon, V.F.; Mitchell, A.D.; Jorgenson, T.A., 1977, Evaluation of selected pesticides as chemical mutagens. In vitro and in vivo studies. EPA Report 600/1-77-028, p. 143. (As cited in 1359)

1364. Nicholas, A.H.; Vienne, M.; Van den Berghe, H., 1979, Induction of sister chromatid exchanges in cultured human cells by an organophosphorous insecticide: malathion. Mutat. Res. 67:167-172.

1365. Nishio, A.; Uyeki, E.M., 1981, Induction of sister chromatid exchanges in Chinese hamster ovary cells by organophosphate insecticides and their oxygen analogs. J. Toxicol. Environ. Health 8:939-946.

1366. Chen, H.H.; Hsueh, J.L.; Sirianni, S.R.; Huang, C.C., 1981, Induction of sister chromatid exchanges and cell cycle delay in cultured mammalian cells treated with eight organophosphorous pesticides. Mutat. Res. 88:307-316.

1367. Degraeve, N.; Chollet, M.; Moutschen, J., 1984, Cytogenetic and genetic effects of subchronic treatments with organophosphorous insecticides. Arch. Toxicol. 56:66-67.

1368. Gaines, T.B., 1969, Acute toxicity of pesticides. Toxicol. Appl. Pharmacol. 14:515-534.

1369. Kalow, W.; Marton, A., 1961, Second generation toxicity of malathion in rats. Nature 192:464-465. (As cited in 1300 and 1359)

1370. Khera, K.S.; Whalen, C.; Trivett, G., 1978, Teratogenicity studies on linuron, malathion, and methoxychlor in rats. Toxicol. App. Pharmacol. 45:435-444.

1371. Golz, H.H., 1955, Malathion: summary of pharmacology and toxicology. American Cyanamid Company, Agricultural Chemicals Division. (As cited in 1098 and 1300)

1372. Weeks, M.H.; Angerhoffer, R.A.; Davenport, C.D., 1975, Preliminary assessment of the acute toxicity of malathion in animals. Report No. 99-002-74/76. U.S. Army Environmental Hygiene Agency, Aberdeen Proving Ground, MD, p. 1-25. (As cited in 1300)

1373. Morgan, D.P., 1982, Recognition and Management of Pesticide Poisonings. 3rd ed., EPA Report No. 540/9-80-005.

1374. U.S. Environmental Protection Agency (USEPA), 1975, Initial scientific and minieconomic review of malathion. EPA Report No. 540/1-75-005. Washington, D.C.: Criteria and Evaluation Division, Office of Pesticide Programs.

1375. Holland, E.G.; Hazleton, L.W.; Hanzal, D.L., 1952, Toxicity of malathion (o,o-dimethyl dithiophosphate of diethyl mercaptosuccinate). Fed. Proc. 11:357. (As cited in 1374)

1376. Golz, H.H.; Shaffer, C.B., 1956, Malathion: summary of pharmacology and toxicology. American Cyanamid Company. (As cited in 1374)

1377. DuBois, K.P.; Doull, J.; Deroin, J.; Cummings, O.K., 1953, Studies on the toxicity and mechanism of action of some new insecticidal thionophosphates. A.M.A. Arch. Ind. Hyg. Occup. Med. 8:350-358. (As cited in 43)

1378. Grob, D., 1963, Anticholinesterase intoxication in man and its treatment. Koelle, G.B., ed. Handbuch der Experimentellen Pharmakologie, Berlin: Springer-Verlag, Vol. 15, p. 989-1027.

1379. Reeves, J.D.; Driggers, D.A.; Kiley, V.A., 1981, Household insecticide associated aplastic anemia and acute leukemia in children. Lancet 8241:300-301.

1380. Namba, T.; Greenfield, M.; Grob, D., 1970, Malathion poisoning - a fatal case with cardiac manifestations. Arch. Environ. Health 21:533-541.

1381. Harris, C.J.; Kemberling, S.R.; Williford, E.A.; Morgan, D.P., 1969, Pesticide intoxications in Arizona. Ariz. Med. 20:872-876. (As cited in 1300)

1382. Richards, A.G., 1964, Malathion poisoning successfully treated with large doses of atropine. Can. Med. Assoc, J. 91:82-83. (As cited in 1300)

1383. Mathewson, I.; Hardy, E.A., 1970, Treatment of malathion poisoning - Experience of two cases in Sarawak. Anaesthesia 25:265-271. (As cited in 1300)

1384. Culver, D.; Caplan, P.; Batchelor, G.S., 1956, Studies of human exposure during aerosol application of malathion and chlorthion. A.M.A. Arch. Ind. Health 13:37. (As cited in 46)

1385. Sridevi, S.H., Thomas, M.J., 1982, Intramuscular injection of malathion in attempted suicide. J. Assoc. Phys. India 30:121-122.

1386. Milby, T.H.; Epstein, W.L., 1964, Allergic contact sensitivity to malathion. Arch. Environ. Health 9:434-437. (As cited in 1300)

1387. Gutentag, P.J., 1959, Cutaneous application of 1.1% malathion powder to volunteers, CWLR 2290. U.S. Army Chemical Center, Research and Development Command, Chemical Warfare Laboratories.

1388. Golz, H.H., 1959, Controlled human exposures to malathion aerosols. Arch. Ind. Health 19:516-523. (As cited in 1300)

1389. Moeller, H.C.; Rider, J.A., 1962, Plasma and red blood cell cholinesterase activity as indications of the threshold of the incipient toxicity of ethyl-p-nitrophenyl thionobenzene and malathion in human beings. Toxicol. Appl. Pharmacol. 4:123-130. (As cited in 1300)

1390. Hayes, W.J., Jr.; Mattson, A.M.; Short, J.G.; Witter, R.F., 1960, Safety of malathion dusting powder for louse control. Bull. WHO 22:503-514. (As cited in 1300)

1391. Gershorn, S.; Shaw, F.H., 1961, Psychiatric sequelae of chronic exposure to organophosphorous insecticides. Lancet 1371-1374.

1392. Clark, G., 1971, Organophosphate insecticides and behavior, a review. Aerospace Med. 42:735-740.

1393. Hanna, W.J.; Choo-Kang, E., 1983, Malathion poisoning: a report of 2 cases. W.I. Med. J. 32:109-111.

1394. Federal Register, 1983, Occupational exposure to ethylene dibromide. 48:45956.

1395. 21CFR193.240 Food additives permitted in food for human consumption; hydrogen cyanide.

1396. Federal Register, 1986, Hazardous waste management system; Identification and listing of hazardous waste; Commercial chemical products. 51:5472.

1397. Federal Register, 1986, Hazardous waste managaement system; Identification and listing of hazardous waste. 51:7455.

1398. Sasinovich, L.M., 1974, Toxic hepatitis due to prolonged exposure to BHC. Vrach. Delo. 10:33. (As cited in 1154)

1399. 40CFR180.397 Ethylene dibromide; tolerances for residues.

1400. Federal Register, 1984, Effective date for action levels for ethylene dibromide in processed grain products. 49:18624.

1401. Broderius, S.J.; Smith, L.L., 1980, Direct photolysis of hexacyanoferrate complexes: proposed applications to the aquatic environment. EPA Report No. EPA 600/3-80-003. Washington D.C.: U.S. Environmental Protection Agency.

1402. MacNaughton, M.G.; Urda, G.A.; Bowen, S.E., 1978, Oxidation of hydrazine in aqueous solutions. Report No. CEEDO-TR-78-11. Tyndall Air Force Base, Florida: Civil and Environmental Development Office. NTIS AD-A058239.

1403. MacNaughton, M.G.; Farmwald, J.A., 1979, The effects of amine based missile fuels on the activated sludge process. Report No.

ESL-TR-79-39. Tyndall Air Force Base, Florida: Engineering and Service Laboratory. Air Force Engineering and Services Center. NTIS AD-A085186.

1404. 21CFR109.30 Tolerances for polychlorinated biphenyls (PCB's).

1405. 40CFR50.12 National primary and secondary ambient air quality standards for lead.

1406. Federal Register, 1985, Intent to list chromium of hexavalent chromium as a hazardous air pollutant. 50:24317.

1407. Torkelson, T.R.; Oyen, F.; Rowe, V.K., 1960, The toxicity of bromochloromethane (methylene chlorobromide) as determined on laboratory animals. Am. Ind. Hyg. Assoc. J. 21:275. (As cited in 12)

1408. Rutstein, H.R., 1963, Acute chlorobromomethane toxicity. Arch. Environ. Health 7:440-444. (As cited in 2 and 12)

1409. Mueller Associates Inc., 1985, Gasoline octane enhancement: technology, economics, and environmental, health and safety considerations. Prepared for U.S. Dept. of Energy. Assistant Secretary for Environment, Safety and Health. Office of Environmental Analysis. DE85-014694.

1410. National Toxicology Program (NTP), 1982, Carcinogenesis bioassay of butyl benzyl phthalate. NTP Technical Report Series No. 213, NTP-80-25. NIH Publication No. 82-1769.

1411. Theiss, J.C.; Stoner, G.D.; Shimkin, M.B.; Weisburger, E.K., 1977, Test for carcinogenicity of organic contaminants of United States drinking waters by pulmonary tumor response in strain A mice. Cancer Res. 37:2717-2720. (As cited in 202 and 403)

1412. Zeiger, E.; Haworth, S.; Mortelmans, K.; Speck, W., 1985, Mutagenicity testing of di(2-ethylhexyl)phthalate and related chemicals in Salmonella. Environ. Mut. 7:213-232.

1413. Agarwal, D.K.; Maronpot, R.R.; Lamb, J.C., Kluwe, W.M., 1985, Adverse effects of butyl benzyl pthalate on the reproductive and hematopoietic systems of male rats. Toxicology 35:189-206.

1414. Haberman, S.; Guess, W.L.; Rowan, D.F.; Bowman, R.O., Bower, R.K., 1968, Effects of plastics and their additives on human serum proteins, antibodies and developing chick embryos. Soc. Plastic Eng. J. 24:62-69. (As cited in 403)

1415. Bower, R.K.; Haberman, S.; Minton, P.D., 1970, Teratogenic effects in the chick embryo caused by esters of phthalic acid. J. Pharmacol. Exp. Ther. 171:314-324. (As cited in 403)

1416. Mallette, F.S.; Von Haam, E., 1952, The toxicity and skin effects of compounds used in the rubber and plastics industries. II. Plasticizers. Arch. Ind. Hyg. Occup. Med. 6:231. (As cited in 399)

1417. Staples, C.A.; Werner, F.; Hoogheem, T.J., 1985, Assessment of Priority pollutant concentrations in the United States using STORET database. Env. Toxicol. Chem. 4:131-142.

1418. Sonnenfeld, G.; Hudgens, R.W., 1983, Effect of carcinogenic components of cigarette smoke in in vivo production of murine interferon. Cancer Research 43:4720-4722.

1419. U.S. Environmental Protection Agency (USEPA), 1985, Drinking water criteria document for ethylene dibromide (EDB). EPA Report No. 600/X-84-181. Cincinnati, OH: Environmental Criteria and Assessment Office. Prepared for USEPA Office of Drinking Water. PB86-118247.

1420. U.S. Environmental Protection Agency (USEPA), 1983, Methods for chemical analysis of water and wastes. EPA Report No. 600/479/020. Cincinnati, OH: Environmental Monitoring and Support Laboratory.

1421. U.S. Environmental Protection Agency (USEPA), 1982, The determination of chlorinated herbicides in industrial and municipal wastewater: Method 615. Cincinnati, OH: Environmental Monitoring and Support Laboratory. PB82-155995.

1422. American Public Health Association (APHA), 1985, Standard Methods for the Examination of Water and Wastewater, 16th ed. Washington, D.C.: APHA.

1423. Fiksel, J., Cooper, C.,; Fschenroeder, A.; Goyer, M.; Perwak, J.; Scow, K.; Thomas, R.; Tucker, W.; Wood, M., 1981, An exposure and risk assessment for cyanide. EPA Report No. 440/4-85-008. Washington, D.C.: Environmental Protection Agency, Office of Water Regulations and Standards. PB85-220572.

1424. Morel, F.M.M., 1983, Principles of Aquatic Chemistry. New York: John Wiley & Sons.

1425. Fuller, W.H., 1978, Investigation of landfill leachate pollutant attenuation by soils. EPA Report 600/2-78-158 Cincinnati, OH: Environmental Protection Agency, Municipal Environmental Research Laboratory.

1426. Kotlik, S.B.; Lebedeva, G.N., 1974, Equilibrium pressures of HCN and NH_3 over aqueous solutions. Zh Prikladnoi Khinii 47:44-446 (English translation by Consultants Bureau, New York: Plenum Publishing Co.)

1427. European Community Commission Proposal for a council Directive Amending Directive 79/117/EEC Prohibiting the Placing on the Market and Use of Plant Protection Products Containing Certain Active Substances. Com (86) 237 Final, 30 April 1986.

1428. European Community Commission Proposal for a Council Directive on Water Quality Objectives for Chromium. Com (85) Final, 18 December 1985.

1429. Council of European Communities Directive on a Limit Value for Lead in the Air (82/885/EEC-OJL 378, 31 December 1982).

1430. Council of European Communities Directive on the Lead Content of Petrol, 20 March 1985 (85/210/EEC-OJL 96/25, 3 April 1985).

1431. Pitts, J.N., Jr.; Tuazon, E.C.; Carter, W.P.; Winer, A.M., Harris, G.W.; Atkinson, R.; Graham, R.A., 1980, Atmospheric chemistry of hydrazines: gas phase kinetics and mechanistic studies. Report No. ESL-TR-80-39. Tyndall Air Force Base Florida: Engineering and Services Laboratory, Air Force Engineering and Services Center. NTIS AD-A093486.

1432. Barthel, E., 1976, [High incidence of lung cancer in persons with chronic professional exposure to pesticides in agriculture]. Z. Erkrank. Atm.-Org. 146:266-274. (As cited in 25)

1433. Council of European Communities Directive on Transfrontier Shipment of Hazardous Waste, 6 December 1984 (84/631/EEC-OJ No. L 326; as amended by Directive 85/469/EEC).

1434. Soliman, S.A.; Farmer, J.; Curley A., 1982, Is delayed neurotoxicity a property of all organophosphorous compounds? A study with a model compound: parathion. Toxicology 23:267-279.

1435. Federal Register, 1986, Polyhalogenated dibenzo-p-dioxins/dibenzofurans; testing and reporting requirements. 50:51794.

1436. 40CFR415 Inorganic chemicals manufacturing point source category.

1437. 40CFR425 Leather tanning and finishing point source category.

1438. 40CFR423 Steam electric power generating point source category.

1439. 40CFR461 Battery manufacturing point source category.

1440. 40CFR465 Coil coating point source category.

1441. 40CFR467 Aluminum forming point source category.

1442. 40CFR459 Photographic point source category.

1443. 40CFR471 Non-ferrous metals forming and metal powders point source category.

1444. 40CFR433 Metal finishing point source category.

1445. 40CFR439 Pharmaceutical manufacturing point source category.

1446. 40CFR413 Electroplating point source category.

1447. 40CFR455 Pesticide chemicals point source category.

1448. 40CFR180.30 Hydrogen cyanide; tolerances for residues.

1449. 40CFR426 Glass manufacturing point source category.

1450. Mathias, C.G.T., 1982, Contact dermatitis from cyanide plating solutions. Arch. Dermatol. 118:420-422.

1451. Blanc, P.; Hogan, M.; Mallin, K.; Hryhorczuk, D.; Hessl, S.; Bernard, B., 1985, Cyanide intoxiciation among silver-reclaiming workers. J. Am. Med. Assoc. 253:367-371.

1452. Okoh, P.N.; Pitt, G.A.J., 1982, The metabolism of cyanide and the gastrointestinal circulation of the resulting thiocynate under conditions of chronic cyanide intake in the rat. Can. J. Physiol. Pharmacol. 60:381-386.

1453. U.S. Environmental Protection Agency (USEPA), 1978, Review of the environmental effects of pollutants: V. Cyanide. EPA-600/1-78-027. Cincinnati, Ohio, Office of Research and Development, Health Effects Research Laboratory. PB 289920.

1454. Rutkowski, J.V.; Roebuck, B.D.; Smith, R.P., 1986, Liver damage does not increase the sensitivity of mice to cyanide given acutely. Toxicology 38:305-314.

1455. Yamamoto, K.; Yamamoto, Y., 1977, A comparison between cyanide poisoning by oral route and that by inhalation, with special reference to the blood cyanide levels and blood gases. An experimental study. Jap. J. Legal Med. 31:140-145.

1456. Vick, J.A.; Froehlich, H.L., 1985, Studies of cyanide poisoning. Arch. Int. Pharmacodyn. 273:314-322.

1457. International Agency for Research on Cancer (IARC), 1978, Working Group on the Evaluation of the Carcinogenic Risk of Chemicals to Man. IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans. Vol. 18. Geneva: World Health Organization.

1458. Cecil, H.C.; Bitman, J.; Lillie, R.J.; Fries, G.F.; Verrett, J., 1974, Embryotoxic and teratogenic effects in unhatched fertile

eggs from hens fed PCBs. Bull. Environ. Contam. Toxicol. 11:489-495. (As cited in 1457)

1459. National Institute for Occupational Safety and Health (NIOSH), 1975, Current Intelligence Bulletin 7, Polychlorinated Biphenyls (PCBs).

1460. Burke, J.; Fitzhugh, O.G., 1970, Suppl. No. 1, States Report of Chemistry and Toxicology of PCBs. Food and Drug Administration, Washington, D.C. (As cited in 12)

1461. Keplinger, M.L.; Fancher, O.E.; Calandra, J.C., 1971, Toxicol. Appl. Pharmacol. 19:402. (As cited in 12)

1462. Danielsson, B.R.G.; Hassoun, E.; Dencker, L., 1982, Embryotoxicity of chromium: distribution in pregnant mice and effects on embryonic cells in vitro. Arch. Toxicol. 51:233-245.

1463. National Academy of Science (NAS), 1974, Medical and Biological Effects of Environmental Pollutants: Chromium. Committee on Biological Effects of Atmospheric Pollutants, Washington, D.C.

1464. U.S. Environmental Protection Agency (USEPA), 1980, Ambient water quality criteria for chromium. EPA Report No. 440/5-80-035. Washington, D.C.: Office of Water Regulations and Standards Criteria Division. PB81-117467.

1465. Bennicelli, C.; Camoirano, A.; Petruzzelli, S.; Zanacchi, P.; DeFlora, S., 1983, High sensitivity of Salmonella TA102 in detecting hexavalent chromium mutagenicity and its reversal by liver and lung preparations. Mutat. Res. 122:1-5.

1466. Petrilli, F.L.; DeFlora, S., 1981, Mutagenicity of chromium compounds. 2nd Proc. Chromates Symp., 1980. Ind. Health Found. pp 76-99.

1467. Nagaya, T., 1986, No increase in sister-chromatid exchange frequence in lymphocytes of chromium platers. Mutat. Res. 170:129-132.

1468. Nishio, A.; Uyeki, E.M., 1985, Inhibition of DNA synthesis by chromium compounds. J. Toxicol. Environ. Health 15:237-244.

1469. Bianchi, V.; Celotti, L.; Lanfranchi, G.; Majone, F.; Martin, G.; Montaldi, A.; Sponza, G.; Tamino, G.; Venier, P.; Zantedeschi, A.; Levis, A.G., 1983, Genetic effects of chromium compounds. Mut. Res. 117:279-300.

1470. Bigaliev, A.B., 1981, Chromosome aberrations in a lymphocyte culture of persons who come in contact with chromium. Cytol. Genet. 15:58-62.

1471. Gentile, J.M.; Hyde, K.; Schubert, J., 1981, Chromium genotoxicity as influenced by complexation and rate effects. Toxicol. Letters 7:439-448.

1472. Cupo, D.Y.; Wetterhahn, K.E., 1984, Repair of chromate-induced DNA damage in chick embryo hepatocytes. Carcinogenesis 5:1705-1708.

1473. Tsapakos, M.J.; Hampton, T.H.; Wetterhahn-Jennette, K., 1981, The carcinogen chromate induces DNA cross-links in rat liver and kidney. J. Biological Chem. 256:3623-3626.

1474. Hughes, W.F., Jr., 1948, The tolerance of rabbit cornea for various chemical substances. Appendix I. Bull. Johns Hopkins Hosp. 82:338-349. (As cited in 19)

1475. Kecskés, M.; Hargital, L.; Farkas, E. Tóth, Á., 1977, Decomposition of diazinon in different soil types. Soil Biol. Conserv. Biosphere, (Proc. Mtg.) 7th, Mtg. Date 1975; pp. 59-71; ed. by J. Szegi.

1476. Sharom, M.S.; Miles, J.R.W.; Harris, C.R.; McEwen, F.L., 1980, Behaviour of 12 insecticides in soil and aqueous suspensions of soil and sediment. Water Res. 14:1095-1100.

1477. Miles, J.R.W., 1978, Adsorption of insecticide residues -- importance in environmental sampling and analysis. Environ. Sci. Res. (Hydrocarbons, Halogenated Hydrocar. Aquat. Environ.) 16:81-90.

1478. Dios Cancela, G.; Gonzalez Garcia, S.; Aguilar, M.M., 1984, Adsorption of diazinon by montmorillonite. I. Effect of the exchangeable cation. An. Edafol. Agrobiol. 43:387-398. Abstract.

1479. Branham, B.E.; Wehner, D.J., 1985, The fate of diazinon applied to thatched turf. Agron. J. 77:101-104.

1480. Leistra, M., 1985, Computer simulations of the transport of pesticides with nonuniform water flow in greenhouse soil. Soil Sci. 140.161-169.

1481. Dennis, W.H., Jr.; Rosencrance, A.B.; Randall, W.F.; Meier, E.P., 1980, Acid hydrolysis of military standard formulations of diazinon. J. Environ. Sci. Health B15:47-60.

1482. Meier, E.P.; Warner, M.C.; Dennis, W.H., Jr.; Randall, W.F.; Miller, T.A., 1976, Chemical degradation of military standard formulations of organophosphate and carbamate pesticides. I. Chemical hydrolysis of diazinon. Tech. Rpt. 7611, U.S. Army Medical Bioengineering Research and Development Laboratory, Fort Detrick, Frederick, MD ADA036051.

1483. Petrova, T.M., 1985, Hydrolytic degradation of insecticides. Agrokhimiya 8:93-99. Abstract.

1484. Macalady, D.L.; Wolfe, N.L., 1985, Effects of sediment sorption and abiotic hydrolyses. 1. Organophosphorothioate esters. J. Agric. Food Chem. 33:167-173.

1485. Burkhard, N.; Guth, J.A., 1979, Photolysis of organophosphorus insecticides on soil surfaces. Pestic. Sci. 10:313-319.

1486. Forrest, M.; Lord, K.A.; Walker, N.; Woodville, H.C., 1981, The influence of soil treatments on the bacterial degradation of diazinon and other organophosphorus insecticides. Environ. Pollut. (Series A) 24:93-104.

1487. Bowman, B.T.; Sans, W.W., 1983, Further water solubility determinations of insecticidal compounds. J. Environ. Sci. Health B18:221-227.

1488. Bowman, B.T.; Sans, W.W., 1983, Determination of octanol-water partitioning coefficients (K_{ow}) of 61 organophosphorus and carbamate insecticides and their relationship to respective water solubility (S) values. J. Environ. Sci. Health B18:667-683.

1489. Weighted average of measured values cited in text of report.

1490. Saeger, V.W.; Hicks, O.; Michael, P.R.; Tucker, S.E., 1979, Environmental fate of selected phosphate esters. Environ. Sci. Technol. 13:840-844.

1491. Lapp, T.W., 1976, The manufacture and use of selected aryl and alkyl aryl phosphate esters. Report No. EPA 560/6-76-008, U.S. Environmental Protection Agency, Office of Toxic Substances, Washington, D.C. (N.T.I.S. PB-251678).

1492. OHMTADS data base entry for Tricresyl phosphate (CAS No. 1330-78-5) which is a mixture of ortho and para isomers; data base available via Chemical Information Systems, Inc., Baltimore, MD.

1493. Wolfe, N.L., 1980, Organophosphate and organophosphorothioate esters: application of linear free energy relationships to estimate hydrolysis rate constants for use in environmental fate assessments. Chemosphere 9:571-79.

1494. Kormachev, V.V.; Sanatullin, V.S.; Ganina, O.N.; Gefter, E.L.; Kukhtin, V.A., 1975, Study of thermal oxidative and hydrolytic stability of tris (.beta.-chloroethyl) phosphate. Deposited document, VINITI 2685-75. (Abstract: CA87(13):101601y)

1495. Waeschke, H.; Mitzner, R., 1980, Substituent effects in the alkaline hydrolysis of tertiary phosphates. Z. Chem. 20:381. Abstract.

1496. Howard, P.H.; Deo, P.G., 1979, Degradation of aryl phosphates in aquatic environments. Bull. Environ. Contam. Toxicol. 22:337-344.

1497. Ku, Y.; Alvarez, G.H., 1982, Biodegradation of (14C) tri-p-cresyl phosphate in a laboratory activated sludge system. Appl. Environ. Microbiol. 43:619-622.

1498. Livingston, J.M.; Jones, C.R., 1981, Living area contamination by chlordane used for termite treatment. Bull. Environ. Contam. Toxicol. 27:406-411.

1499. Sieper, H., 1972, Residues and metabolism. In: Lindane - Monograph of an Insecticide. E. Ulmann, ed., FGR: Verlag K. Schillinger.

1500. Barnes, E.S., 1983, Chlordane in Air Force family housing: a study of slab-on-grade houses. USAF Occupational and Environmental Health Laboratory, Brooks, AFB, TX. USAF OEHL Report 83-129EH111DPB.

1501. Karanth, N.G.K.; Jayaram, M.; Majumder, S.K., 1982, Insecticidal residue in vegetables obtained from soil treated with hexachlorocyclohexane. J. Food Sci. Tech. 19:14-19.

1502. Kushwaha, K.S.; Yodav, P.R.; Kathpal, T.S.; Kavadia, V.S., 1980, Persistence of aldrin and BHC in sandy loam soil under the cover of root crops. Sym. on Environmental Pollution and Toxicology. p. 251-261.

1503. Kathpal, T.S.; Dewan, R.S.; Jotwani, M.G., 1976, Persistence of BHC residues in/on sorghum. Indian J. Pl. Prot. 4:1-5. (As cited in 1502)

1504. Agnihotri, H.P.; Pandey, S.Y.; Jain, H.K., 1974, Persistence of BHC and aldrin in soil and translocation in Mung (Phaseolus aureus L.) and Lobia (Vigna sinensis siva). Indian J. Ent. 36(4):261-267. (As cited in 1502)

1505. Sharom, M.S.; Miles, J.R.W.; Harris, C.R.; McEwen, F.L., 1980, Behavior of 12 insecticides in soil and aqueous suspensions of soil and sediment. Water Research 14:1095-1100.

1506. El Beit, I.O.D.; Wheelock, J.V.; Cotton, D.E., 1981, Factors involved in the dynamics of pesticides in soils: the effect of pesticide concentration on leachability and adsorption. Intern. J. Environ. Studies 16:181-187.

1507. El Beit, I.O.D.; Wheelock, J.V.; Cotton, D.E., 1981, Factors involved in the dynamics of pesticides in soils: the effect of temperature and period of contact on leachability and adsorption of pesticides by soils. Intern. J. Environ. Studies 16:189-196.

1508. Chiou, C.T.; Shoup, T.D.; Porter, P.E., 1985, Mechanistic roles of soil humus and minerals in the sorption of nonionic organic compounds from aqueous and organic solutions. Org. Geochem. 8:9-14.

1509. Boucher, F.R.; Lee, G.F., 1972, Adsorption of lindane and dieldrin pesticides on unconsolidated aquifer sands. Environ. Sci. Tech. 6:539-543. (As cited in 10)

1510. Nash, R.G., 1983, Comparative volatilization and dissipation rates of several pesticides from soil. J. Agric. Food Chem. 31:210-217.

1511. Glotfelty, D.E.; Taylor, A.W.; Turner, B.C.; Zoller, W.H., 1984, Volatilization of surface-applied pesticides from fallow soil. J. Agric. Food Chem. 32:638-643.

1512. Spencer, W.F.; Cliath, M.M., 1973, Pesticide volatilization as related to water loss from soil. J. Environ. Qual. 2:284-289.

1513. Harper, L.A., White, A.W.; Bruce, R.R.; Thomas, A.W.; Leonard, R.A., 1976, Soil and microclimate effects on trifluralin volatilization. J. Environ. Qual. 5:236-242.

1514. Siddaramappa, R.; Sethunanthan, N., 1975, Persistence of gamma-BHC and beta-BHC in Indian rice soil under flooded conditions. Pestic. Sci. 6:395-403. (As cited in 10)

1515. Saleh, F.Y.; Dickson, K.L.; Rodgers, J.H., 1982, Fate of lindane in the aquatic environment: rate constants of physical and chemical processes. Environ. Tox. Chem. 1:289-297.

1516. Eichelberger, J.W.; Lichtenberg, J.J., 1971, Persistence of pesticides in river water. Environ. Sci. Tech. 5:541-544. (As cited in 10)

1517. Gunther, F.A., 1971, Halogen derivatives of aliphatic hydrocarbons. Residue Rev. 36:34-77. (As cited in 10)

1518. El Beit, I.O.D.; Cotton, D.E.; Wheelock, I.V., 1983, Persistence of pesticides in soil leachates: effect of pH, ultra-violet irradiation and temperature. Intern. J. Environmental Studies 21:251-259.

1519. Malaiyandi, M.; Shah, S.M.; Lee, P., 1982, Fate of α- and δ-hexachlorocyclohexane isomers under simulated environmental conditions. J. Environ. Sci. Health. A17:283-297.

1520. El Beit, I.O.D.; Wheelock, J.V.; Cotton, D.E., 1981, Pesticide - microbial interaction in the soil. Intern. J. Environ. Studies 16:171-180.

1521. Flores-Ruegg, E.; DeAndrea, M.M.; Helene, C.G.; Hirata, R., 1980, Persistence of pesticide residues in Brazilian soil samples related to organic matter and microbiological activity. In: Agrochem. Residue - Biota Interact. Soil Aquat. Ecosys., Proc. Rep. Comb. Advis. Group Meet., Vienna, Austria: IAEA. pp 181-187.

1522. Vogtmann, H.; Fragstein, P.; Draeger, P., 1984, The degradation of agrichemicals during composting. In: Prec. Int'l. Symp. "Peat Agric. Hortic.". 2nd ed. K.M. Schallinger, ed. Bet Dagan, Israel: Volcani Center, Inst. Soils Water.

1523. Tu, C.M., 1976, Utilization and degradation of lindane by soil microorganisms. Arch. Microbial. 108:259-263. (As cited in 10)

1524. Matsumura, F.; Benezet, H.J.; Patil, K.C., 1976, Factors affecting microbial metabolism of γ-BHC. Nippon Noyaku Gakkaishi. 1:3-8. (As cited in 10)

1525. Hill, D.W.; McCarty, P.L., 1967, Anaerobic degradation of selected chlorinated hydrocarbon pesticides. J. Water Pollut. Control. Fed. 39:1259-1277. (As cited in 10)

1526. Newland, L.W.; Chesters, G.; Lee, G.B., 1969, Degradation of γ-BHC in simulated lake impoundments as affected by aeration. J. Water Pollut. Control Fed. 41(5 Pt. II):R174-R188. (As cited in 10)

1527. Mathur, S.P.; Saha, J.G., 1975, Microbial degradation of carbon -14-labelled lindane in a flooded sandy loam soil. Soil Sci. 120:301-307. (As cited in 10)

1528. Beland, F.A.; Farwell, S.O.; Robocker, A.E.; Geer, R.D., 1976, Electrochemical reduction and anaerobic degradation of lindane. J. Agri. Food Chem. 24:753-756. (As cited in 10)

1529. Haider, K.; Jagnow, G., 1975, Degradation of carbon -14-, tritium-, and chlorine-36-labelled hexachlorocyclohexane by anaerobic soil microorganisms. Arch. Microbiol. 104:113-121. (As cited in 10)

1530. Tarasov, M.N.; Korotova, L.G.; Demchenko, A.S.; Brazhnikova, L.V., 1978, Hexachlorocyclohexane, metaphos, and chlorophos decomposition in soil and their migration with the waters of surface runoff. Symp. Environ. Transp. Transform. Pestic., U.S. Environmental Protection Agency. EPA-600/9-78-003:108-116.

1531. Rao, R.S.C.; Hornsby, A.G.; Jessup, R.E., 1985, Indices for ranking the potential for pesticide contamination of groundwater. Proceed. Soil Crop Sci. Soc. Fla. 44:1-8.

1532. Rosenblatt, D.H.; Miller, T.A.; Dacre, J.C.; Muul, I.; Cogley, D.R., 1975, Problem Definition Studies on Potential Environmental Pollutants II. Physical, Chemical, Toxicological, and Biological Properties of 16 Substances. Fort Detrick, Fredrick, MD: U.S. Army Medical Bioengineering Research and Development Laboratory.

1533. Nash, R.G.; Harris, W.G., 1973, Chlorinated hydrocarbon insecticide residues in crops and soil. J. Environ. Quality. 2:269-273.

1534. Frank, R., 1981, Pesticides and PCBs in the Grand and Saugeen river basins. J. Great Lakes Res. 7:440-454

1535. Atallah, Y.H.; Whitacre, D.M.; Hoo, E.L., 1979, Comparative volatility of liquid and granular formulations of chlordane and heptachlor from soil. Bull. Environ. Contam. Toxicol. 22:570-574.

1536. Stauffer, T.B., 1977, Chlordane Volatility. Tyndall AFB, Florida: Civil and Environmental Engineering Development Office; CEEDO-TR-77-9.

1537. Nash, R.G., 1974, Plant uptake of insecticides, fungicides, and fumigants from soils. In: Pesticides in Soil and Water. Guenzi, W.D.; Ahlrichs, J.L.; Chester, G.; Bloodworth, M.E.; Nash, R.G.; Dinauer, R.C.; Davis, M.E.; Eisele, L., eds. Madison, WI: Soil Society of America. (As cited in 1532)

1538. Wilson, D.M.; Oloffs, P.C., 1973, Residues in alfalfa following soil treatment with high purity chlordane (Velsicol HCS-3260). Bull. Environ. Contam. Toxicol. 9:337-344. (As cited in 1532)

1539. Haque, R.; Freed, V.H., 1974, Behavior of pesticides in the environment: Environmental chemodynamics. Residue Reviews 52:89-116. (As cited in 1532)

1540. Menzie, C.M., 1972, Fate of pesticides in the environment. Annual Review of Entomology 17:199-222. (As cited in 806)

1541. Nash, R.G.; Woolson, E.A., 1967, Persistence of chlorinated hydrocarbon insectides in soils. Science 157:924-927. (As cited in 806)

1542. Nash, R.G.; Woolson, E.A., 1968, Distribution of chlorinated insecticides in cultivated soil. Soil Sci. Amer. Proc. 32:525-527. (As cited in 1532)

1543. Bennett, G.W.; Ballee, D.L.; Hall. R.C.; Fahey, J.E.; Butts, W.L.; Osmun, J.V., 1974, Persistence and distribution of chlordane and dieldrin applied as termiticides. Bull. Environ. Contam. Toxicol. 11:64. (As cited in 806)

1544. Stewart, D.K.R.; Chisholm, D., 1971, Long-term persistence of BHC, DDT, and chlordane in a sandy loam soil. Can. J. Soil Sci. 61:379-383. (As cited in 806)

1545. Wood, L.W.; Jones, P.A.; Richards, A., 1986, Possible sediment scavenging of chlordane and contamination of the aquatic biota in Belmont Lake, New York. Bull. Environ. Contam. Toxicol. 36:159-167.

1546. Wilson, D.M.; Oloffs, P.C., 1973, Persistence and movement of alpha and gamma chlordane in soils following treatment with high purity chlordane (Velsicol HCS-3260). Can. J. Soil Sci. 53:465. (As cited in 806)

1547. Wiese, I.H.; Basson, N.C.J., 1966, The degradation of some persistent chlorinated hydrocarbon insecticides applied to different soil types. S. Afr. J. Agr. Sci. 9:945-969. (As cited in 806)

1548. Atlas, E.; Foster, R.; Girin, C.S., 1982, Air-sea exchange of high molecular weight organic pollutants: Laboratory studies. Environ. Sci. Tech. 16:283-286. (As cited in 806)

1549. Benson, W.R.; Lombardo, P.; Egry, I.J.; Ross, R.D., Jr.; Barron, R.P.; Mastbrook, D.W.; Hansen, E.A., 1971, Chlordane photoalteration products: Their preparation and identification. J. Agric. Food Chem. 19:857-862. (As cited in 806)

1550. Ivie, G.W.; Knox, J.R.; Khalifa, S.; Yamamoto, I.; Casida, J.E., 1972, Novel photoproducts of heptachlor epoxide, trans-chlordane and trans-nonachlor. Bull. Environ. Contam. Toxicol. 7:376-382. (As cited in 10)

1551. Iyengar, L.; Rao, A.V.S.P., 1973, Metabolism of chlordane and heptachlor by Aspergillis niger. J. Gen. Appl. Microbiol. 19:321-324. (As cited in 806)

1552. Beeman, R.W.; Matsumura, F., 1981, Metabolism of cis- and trans-chlordane by a soil microorganism. J. Agric. Food Chem. 29:84. (As cited in 806)

1553. Speidel, H.K.; Bourquin, A.W.; Mann, J.E.; Fair, J.F.; Bennett, E.O., 1972, Microbiological removal of pesticide from aqueous environments. Dev. Ind. Microbial. 13:277-282. (As cited in 806)

1554. Sanborn, J.R.; Francis, B.M.; Metcalf, R.L., 1977, The degradation of selected pesticides in soil: A review of published literature. Report No. 600/9-77-022, U.S. Environmental Protection Agency, Cincinnati, OH. (As cited in 806)

1555. Kearney, P.C.; Woolson, E.A.· Plimmer, J.R.; Isensee, A.R., 1969, Decontamination of pesticides in soil. Res. Rev. 29:137. (As cited in 806)

1556. Castro, T.F.; Yoshida, T., 1971, Degradation of organochlorine insecticides in flooded soils in the Philippines. J. Agr. Food Chem. 19:1168-1170. (As cited in 806)

1557. Carter, F.L.; Stringer, C.A., 1971, Soil persistence of termite insecticides. Pest. Contr. 39:13. (As cited in 806)

1558. U.S. Environmental Protection Agency (USEPA), 1975, Translocation of heptachlor and chlordane from Indiana cornfields. Report No. EPA/330/9-75/002. Denver, CO: National Enforcement Investigations Center.

1559. Davis, J.E.; Stevens, E.R.; Staiff, D.C.; Butler, L.C., 1983, Potential exposure to diazinon during yard application. Environ. Monit. Assess. 3:23-28.

1560. 40CFR440 Ore mining and dressing point source category.

1561. 40CFR466 Porcelin enameling point source category.

1562. 40CFR468 Copper forming point source category.

1563. 40CFR469 Electrical and electronic components point source category.

1564. 40CFR464 Metal molding and casting industry point source category.

1565. Federal Register, 1986, Hazardous waste management system; identification and listing of hazardous waste; notification requirements; reportable quantity adjustments; proposed rule. 51:21648.

1566. Danapoulos, E.; Mellisino, K.; Katsas, G., 1953, Serious poisoning by hexachlorocyclohexane. Arch. Industr. Hyg. Chicago 8:582-587. (As cited in 19 and 1096)

1567. 40CFR80 Regulation of fuels and fuel additives.

1568. Lee, B., 1976, Suspected reactions of gamma benzene hexachloride. JAMA 236:2346. (As cited in 1154)

1569. Schuttmann, W., 1968, [Chronic liver disease after occupational exposure to dichloro diphenyltrichlorethane (DDT) and hexachlorocyclohexane (HCH).]. Int. Arch. Gewerbepath. Gewerbehyg. 24:193-210. (As cited in 25)

1570. Grandjean, P.; Grandjean, E.C., eds., 1984, Biological Effects of Organolead Compounds. Boca Raton: CRC Press.

1571. Burkhard, L.P.; Armstrong, D.E.; Andren, A.W., 1985, Henry's law constants for the polychlorinated biphenyls. Environ. Sci. Technol. 19:590-596.

1572. Baxter, R.M.; Sutherland, D.A., 1984, Biochemical and photochemical processes in the degradation of chlorinated biphenyls. Environ. Sci. Tech. 18:608-610.

1573. Safe, S.; Bunce, N.J.; Chittin, B.; Hutzinger, O.; Ruzo, L.O., 1976, Photodecomposition of halogenated aromatic compounds. In: Identification and Analysis of Pollutants in Water; L.H. Kieth, ed., Ann Arbor, MI: Ann Arbor Sci. (As cited in 10)

1574. Valentine, R.S., 1981, LARC-light activated reduction of chemicals. Pollution Engineering 13:35-37.

1575. Chaudhary, S.K.; Mitchell, R.H.; West, P.R., 1984, Photodechlorination of polychlorinated biphenyls in the presence of hydroquinone in aqueous alcoholic media. Chemosphere. 13:1113-1131.

1576. Bunce, N.H.; Kumar, Y., 1978, An assessment of the impact of solar degradation of PCBs in the aquatic environment. Chemosphere. 7:155-164. (As cited in 10)

1577. Liu, D., 1982, Assessment of continuous biodegradation of commercial PCB formulations. Bull. Environ. Contam. Toxicol. 29:200-207.

1578. Erickson, M.D., 1986, Analytical Chemistry of PCBs. Boston, MA: Butterworth Publishers.

1579. Liu, D., 1980, Enhancement of PCBs biodegradation by sodium ligninsulfonate. Water Research. 14:1467-1475.

1580. Moein, G.J.; Smith, A.J.; Stewart, P.L., 1976, Follow-up study of the distribution and fate of polychlorinated biphenyls and benzenes in soil and groundwater samples after an accidental spill of transformer fluid. In: Proc. 1976 National Conf. on Control of Hazardous Materials Spills.

1581. Brunner, W.; Sutherland, F.H.; Focht, D.D., 1985, Enhanced biodegradation of polychlorinated biphenyls in soil by analog

enrichment and bacterial inoculation. J. Environ. Qual. 14:324-328.

1582. Isbister, J.D.; Anspach, G.L.; Kitchens, J.F., 1984, Composting for degradation of PCBs in soils. In: 1984 Hazardous Material Spills Conference Proceedings, Nashville, TN, April 9-12, 1984.

1583. Griffin, R.A.; Chian, E.S.K., 1980, Attenuation of water-soluble polychlorinated biphenyls by earth materials. EPA 600/2-80-027. Cincinnati, OH: U.S. Environmental Protection Agency, NTIS PB80-219652.

1584. Hankin, L.; Sawhney, B.L., 1984, Microbial degradation of polychlorinated biphenyls in soil. Soil Science. 137:401-407.

1585. Brown, J.F.; Warner, R.E.; Bedard, D.L.; Brennan, M.J.; Carnahan, J.C.; May, R.J.; Tofflemire, T.J., 1984, PCB transformers in upper Hudson sediments. Northeastern Environmental Science 3:166-178.

1586. Tucker, E.S.; Saeger, V.W.; Hicks, O., 1975, Activated sludge primary biodegradation of polychlorinated biphenyls. Bull. Environ. Contamin. Toxic. 14:705-713. (As cited in 1579)

1587. Baxter, R.A.; Gilbert, P.E.; Lidgett, R.A.; Mainprize, J.H.; Vodden, H.A., 1975, The degradation of polychlorinated biphenyls by microorganisms. Sci. Total Environ. 4:53-61. (As cited in 1579)

1588. Roberts, J.R.; Cherry, J.A.; Schwartz, F.W., 1982, A case study of a chemical spill: polychlorinated biphenyls (PCBs). 1. History distribution and surface translocation. Water Resources Research 18:525-534.

1589. Paris, D.F.; Steen, W.C.; Baughman, G.L., 1978, Role of physico-chemical properties of Aroclors 1016 and 1242 in determining their fate and transport in aquatic environments. Chemosphere. 4:319-325.

1590. Wilson, A.J.; Forester, J., 1978, Persistence of Aroclor 1254 in a contaminated estuary. Bull. Environ. Contam. Toxic. 19:637-640.

1591. Richardson, W.L.; Smith, V.E.; Wethington, R., 1983, Dynamic mass balance of PCB and suspended solids in Saginaw Bay - a case study. In: Physical Behavior of PCBs in the Great Lakes; D. Mackay et al., eds. Ann Arbor, MI: Ann Arbor Science.

1592. Lee, M.C.; Griffin, R.A.; Miller, M.L.; Chian, E.S.K., 1979, Adsorption of water-soluble polychlorinated biphenyl Aroclor 1242 and used capacitor fluid by soil materials and coal chars. J. Environ. Sci. Health. A14:415-442.

1593. Wildish, D.J.; Metcalfe, C.D.; Akagi, H.M.; McLeese, D.W., 1980, Flux of Aroclor 1254 between estuarine sediments and water. Bull. Environm. Contam. Toxciol. 24:20-26.

1594. Sawhney, B.L.; Frink, C.R.; Glowa, W., 1981, PCBs in the Housatonic River: determination and distribution. J. Environ. Qual. 10:444-448.

1595. Nau-Ritter, G.M.; Wurster, C.F., 1983, Sorption of polychlorinated biphenyls (PCB) to clay particulates and effects of desorption on phytoplankton. Water Res. 17:383-387.

1596. Griffin, R.; Clark, R.; Lee, M.; Chian, E., 1978, Disposal and removal of polychlorinated biphenyls in soil. In: Land Disposal of Hazardous Wastes, Proceedings of the Fourth Annual Research Symposium. EPA-600/9-78-016, Cincinnati, OH: U.S. Environmental Protection Agency, NTIS PB-286956.

1597. Chiou, C.T.; Freed, V.H.; Peters, L.J.; Kohnert, R.L., 1980, Evaporation of solutes from water. Environment International. 3:231-236.

1598. Murphy, T.J.; Pokojowczyk, J.C.; Mullin, M.D., 1983, Vapor exchange of PCBs with Lake Michigan: the atmosphere as a sink for PCBs. In: Physical Behavior of PCBs in the Great Lakes; D. Mackay et al., eds. Ann Arbor, MI: Ann Arbor Science.

1599. Oloffs, P.C.; Albright, L.J.; Szeto, S.Y., 1972, Fate and behavior of five chlorinated hydrocarbons in three natural waters. Can. J. Microbial. 18:1393-1398. (As cited in 10)

1600. Bidleman, T.F.; Burdick, N.F.; Wescott, J.W.; Billings, W.N., 1983, Influence of volatility on the collection of airborne PCB and pesticides with filter-solid adsorbent samplers. In: Physical Behavior of PCBs in the Great Lakes; D. Mackay et al., eds. Ann Arbor, MI: Ann Arbor Science.

1601. Haque, R.; Schmedding, D.W.; Freed, V.H., 1974, Aqueous solubility, adsorption and vapor behavior of polychlorinated biphenyl Aroclor 1254. Environ. Sci. Technol. 8:139-142. (As cited in 10)

1602. Mackay, D.; Leinonen, P.J., 1975, Rate of evaporation of low-solubility contaminants from water bodies to atmosphere. Environ. Sci. Technol. 7:611-614. (As cited in 10.)

1603. Oloffs, P.C.; Albright, L.J.; Szeto, S.Y.; Lau, J., 1973, Factors affecting the behavior of five chlorinated hydrocarbons in three natural waters and their sediments. J. Fish Res. Board, Canada 30:1619. (As cited in 10)

1604. Ouelette, R.P.; King, J.A., 1977, Chemical Week Pesticide Register. McGraw-Hill Book Co., New York, NY.

1605. Syracuse Research Corporation, 1985, Monograph on human exposure to chemicals in the workplace: Ethylene dibromide. PB86-133162.

1606. National Cancer Institute (NCI), 1978, Bioassay of 1,2-dibromoethane for possible carcinogenicity. NCI Carcinogenesis Technical Report Series No. 86, NCI-CG-TR-86, DHEW Publications No. (NIH) 78-1336.

1607. International Agency for Research of Cancer (IARC), 1977, Working Group on the Evaluation of the Carcinogenic Risk of Chemicals to Man. IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans. Vol. 15. Geneva: World Health Organization.

1608. Christensen, W.D.; Hudson, R.F.; Lewis, S.; et al., 1979, the second conference on the environmental chemistry of hydrazine fuels: 15 February, 1979. Report No. ESL-TR-82-22. Tyndall Air Force Base, Florida: Engineering and Services Laboratory, Air Force Engineering and Services Center. NTIS AD-A121324.

1609. MacNaughton, M.G.; Farmwald, J.A.; McDaniels, L; Urda, G., 1979, Biological degradation of hydrazine. Report No. ESL-TR-79-38 (CEEDO-TR-78-13). Tyndall Air Force Base, Florida: Engineering and Services Laboratory, Air Force Engineering and Services Center. NTIS AD-A084426.

1610. Braun, B.A.; Zirrolli, J.A., 1983, Environmental fate of hydrazine fuels in aqueous and soil environments. Report No. ESL-TR-82-45. Tyndall Air Force Base, Florida: Engineering and Services Laboratory, Air Force Engineering and Services Center. NTIS AD-A125813.

1611. MacNaughton, M.G.; Zirrolli, J.; Stauffer, B.; Stone, D.A., 1979, Environmental chemistry of hydrazine fuels, in Proceedings of 9th conference on environmental toxicology, 28, 29, and 30 March 1979. Report No. AMRL-TR-79-68. Wright Patterson Air Force Base, Ohio: Aerospace Medical Research Laboratory, Aerospace Medical Division, Air Force Systems Command.

1612. Hayes, M.H.B.; Isaacson, P.J.; Chiu, K.Y.; Lees, A.M.; Yormah, B.R., 1984, Interaction of hydrazine and of hydrazine derivatives with soil constituents and with soils. Report No. AFOSR-TR-84-1118. Washington, D.C.: USAF office of Scientific Research. NTIS AD-148475.

1613. MacNaughton, M.G.; Stauffer, T.B.; Stone, D.A., 1981, Environmental chemistry and management of hydrazine. Aviation, Space Environ. Med. 52: 149-153.

1614. Slonim, A.R.; Gisclard, J.B., 1976, Hydrazine degradation in aquatic systems. Bull. Environ. Contam, Toxicol. 16: 301-309.

1615. Isaacson, P.J.; Hayes, M.H.B., 1984, The interaction of hydrazine hydrate with humic acid preparations at pH 4, J. Soil Sci. 35:79-92.

1616. Bauer, D.; Gaillochet, P., 1978, Anhydrous hydrazine and water-hydrazine mixtures. Lagowski, J.J., ed., Chemistry of Non-Aqueous Solvents, Vol 5A: 251-275. New York: Academic Press.

1617. Farrah, H.; Pickering, W.F., 1979, The effect of pH and complex formation on the uptake of heavy metal ions by clays in sediments. Aggett, J.; Kjellstroem, T.; Crowe, D., eds., Proc. N.Z. Semin. Trace Elem. Health, 2nd., Aukland, New Zealand: University of Aukland, Department of Community Health.

1618. Frank, S.N.; Bard, A.J. 1977, Heterogeneous photocatalytic oxidation of cyanide ion in aqueous solutions at TiO_2 powder. J. Am. Chem. Soc. 99: 303-304.

1619. Raef, S.F.; Characklis, W.G.; Kessick, M.A.; Ward, C.H., 1977, Fate of cyanide and related compounds in aerobic microbial systems - I chemical reaction with substrate and physical removal. Water Res. 11: 477-483.

1620. Cherryholmes, K.L.; Cornils, W.J.; McDonald, D.B.; Splinter, R.C., 1985, Biological degradation of complex iron cyanides in natural aquatic systems. Cardwell, R.D.; Purdy, R.; Bahner, R.C., eds., Aquatic Toxicology and Hazard Assessment: Seventh Symposium, ASTM STM 854, R.D. Philadelphia: American Society for Testing and Materials.

1621. Padmaja, G.; Balagopal, C., 1985, Cyanide degradation by Rhizopus oryzae. Can. J. Microbiol. 31: 663-669.

1622. Shivaraman, N.; Parhad, N.M., 1984, Biodegradation of cyanide in a continuously fed aerobic system. J. Environ. Biol. 5: 273-284.

1623. Towill, L.E.; Drury, J.S.; Whitfield, B.L.; Lewis, E.B.; Galyan, E.L.; Hammons, A.S., 1978, Review of the environmental effects of pollutants: V. Cyanides. EPA Report No. EPA-600/1-78-027. Cincinnati, Ohio: U.S. Environmental Protection Agency, Health Effects Research Laboratory.

1624. Keller, W.C.; Murphy, J.P.F.; Bruner, R.H.; Andersen, M.E.; Olson, C.T., 1984, Toxicokinetics of hydrazine administered percutaneously to the rabbit. Air Force Aerospace Medical Research Laboratory, Aerospace Medical Division, Air Force

systems command, Wright-Patterson Air Force Base, OH. AFAMRL-TR-84-035. NTIS AD-A143-122.

1625. National Institute for Occupational Safety and Health (NIOSH), 1978, Criteria for a recommended standard... Occupational exposure to Hydrazines. U.S. Dept. of Health, Education and Welfare. DHEW (NIOSH) Pub. No. 78-172.

1626. Federal Register, 1986, Water quality criteria; availability of documents 51:43665.

1627. Thienes, C.H.; Roth, H.P.; Swenson, E.A.; Morgan, V.C.; Lombard, C.F., 1948, Final report on acute and chronic toxicity of hydrazine. Los Angeles, University Park, University of Southern California School of Medicine, Dept. of Pharmacology and Toxicology. (As cited in 1625)

1628. Noda, A.; Ishizawa, M.; Ohno, K.; Sendo, T.; Noda, H., 1986, Relationship between oxidative metabolites of hydrazine and hydrazine-induced mutagenicity. Toxicology Letters 31:131-137.

1629. Rogers, A.M.; Back, K.C., 1981, Comparative mutagenicity of hydrazine and 3 methylated derivatives in L51784 mouse lymphoma cells. Mutat. Res. 89:321-328.

1630. Sotomayor, R.E.; Chauhan, P.S.; Ehling, U.H., 1982, Induction of unscheduled DNA synthesis in the germ cells of male mice after treatment with hydrazine or procarbazine. Toxicology 25:201-211.

1631. Kuszynski, C.; Langenbach, R.; Malick, L.; Tompa, A.; Toth, B., 1981, Liver cell-mediated mutagenesis of V-79 cells by hydrazine and related compounds. Environ. Mut. 3:232. Abstract.

1632. Parodi, S.; DeFlora, S.; Cavanna, M.; Pino, A.; Robbiano, L.; Bennicelli, C.; Brambilla, G., 1981, DNA-damaging activity in vivo and bacterial mutagenicity of sixteen hydrazine derivatives as related quantitatively to their carcinogenicity. Cancer Research 41:1469-1482.

1633. Kimball, R.F., 1977, The mutagenicity of hydrazine and some of its derivatives. Mutat. Res. 39:111-126.

1634. Keller, W.C.; Olson, C.T.; Back, K.; Gaworski, C.L., 1982, Evaluation of the embryotoxicity of hydrazine in rats. AFAMRL-TR-82-29. Air Force Aerospace Medical Research Laboratory, Aerospace Medical Division, Air Force Systems Command, Wright-Patterson Air Force Base, OH.

1635. Vernot, E.H.; MacEwen, J.D.; Bruner, R.H.; Haun, C.C.; Kinkead, E.R.; Prentice, D.E.; Hall, A., III; Schmidt, R.E.; Eason, R.D.;

Hubbard, G.B.; Young, J.T., 1985, Long-term inhalation toxicity of hydrazine. Fundam. Appl. Toxicol. 5:1050-1064.

1636. Reid, F.J., 1965, Hydrazine poisoning. Br. Med. J. 5472:1246. (As cited in 1625)

1637. Reidenberg, M.M.; Durant, P.J.; Harris, R.A.; DeBoccardo, G.; Lahita, R.; Stenzel, K., 1981, A case of lupus erythematosus-like illness due to hydrazine. Fed. Proc. 40:739. Abstract.

1638. Wald, N.; Borehan, J.; Doll, R.; Bonsall, J., 1984, Occupational exposure to hydrazine and subsequent risk of cancer. Br. J. Ind. Med. 41:31-34.

1639. Lee, S.H.; Aleyassine, H., 1970, Hydrazine toxicity in pregnant rats. Arch. Environ. Health 21:615-169.

1640. Jacobson, K.H.; Clem, J.H.; Wheelwright, H.J.; Rinehart, W.E.; Mayes, N., 1955, The acute toxicity of the vapors of some methylated hydrazine derivatives. Arch. Ind. Health 12:609-616. (As cited in 1625).

1641. U.S. EPA, 1983, Health assessment document for chromium. Environmental Criteria and Assessment Office, Research Triangle Park, NC. EPA 600/8-83-014A.

1642. Snyder, A.D.; DeAngelis, D.G.; Eimutis, E.C.; Haik, D.M.; Ochsner, J. C.; Reznik, R.B.; Toy, H.D., 1977, Environmental monitoring near industrial sites: Chromium. Prepared for the Office of Toxic Substances, U.S. Environmental Protection Agency, NTIS, PB-271 881.

1643. Kumpulainen, J.T.; Wolf, W.R.; Veillin, C.; Mertz, W., 1979, Determination of chromium in selected United States diets. J. Agric. Food Chem. 27:490-494.

1644. Kaiser, K.L.E.; Comba, M.E., 1983, Volatile contaminants in the Welland River watershed. J. Great Lakes Res. 9:274-280.

1645. Rogers, R.D.; McFarlane, J.C., 1981, Sorption of carbon tetrachloride, ethylene dibromide, and trichloroethylene on soil and clay. Environ. Monit. Assess. 1:155-162.

1646. Chiou, C.T.; Peters, L.J.; Freed, V.H., 1979, A physical concept of soil-water equilibria for nonionic organic compounds. Science 206:831-832.

1647. Harkov, R.; Gianti, S.J., Jr.; Bozzelli, J.W.; LaRegina, J.E., 1985, Monitoring volatile organic compounds at hazardous and sanitary landfills in New Jersey. J. Environ. Sci. Health A20:491-501.

1648. Sotaniemi, E.; Hirvonen, J.; Isomaki, H.; Takkunen, J.; Kaila, J., 1971, Hydrazine toxicity in the human -- Report of a fatal case. Ann. Clin. Res. 3:30-33. (As cited in 1625)

1649. Mackay, D.; Yeun, A.T.K., 1983, Mass transfer coefficient correlations for volatilization of organic solutes from water. Environ. Sci. Technol. 17:211-217. (As cited in 806)

1650. Johns, R., 1976, Air pollution assessment of ethylene dibromide. Gov. Rep. Announce. Index 76:131. (As cited in 806)

1651. Ehrenberg, L.; Oster-Golkar, S.; Singh, D.; Lundquist, U., 1974, On the reaction kinetics and mutagenic activity of methylating and beta-halogenoethylating gasoline additives. Radiat. Bot. 15:185-194. (As cited in 806)

1652. Castro, C.E.; Belser, N.O., 1985, Photohydrolysis of ethylene dibromide. J. Agric. Food Chem. 33:536-538.

1653. Bouwer, E.J.; McCarty, P.L., 1983, Transformations of halogenated organic compounds under denitrification conditions. Appl. Environ. Microbiol. 45:1295-1299. (As cited in 806)

1654. Bouwer, E.J.; McCarty, P.L., 1984, Modeling of trace organics biotransformation in the subsurface. Groundwater 22:433-440. (As cited in 806)

1655. Castro, C.E.; Belser, N.O., 1968, Biodehalogenation, reductive dehalogenation of the biocides ethylene dibromide, 1,2-dibromo-3-chloropropane, and 2,3-dibromobutane in soil. Environ. Sci. Technol. 2:779-783. (As cited in 806)

1656. Howard, P.H.; Banerjee, S.; Robillard, K.H., 1985, Measurement of water solubilities, octanol/water partition coefficients and vapor pressures of commercial phthalate esters. Environmental Toxicology and Chemistry. 4:653-661.

1657. Gledhill, W.E.; Kaley, R.G.; Adams, W.J.; Hicks, O.; Michael, P.R.; Saeger, V.W.; LeBlanc, G.A., 1980, An environmental safety assessment of butyl benzyl phthalate. Environ. Sci. Technol. 14:301-305.

1658. Saeger, V.W.; Tucker, E.S., 1976, Biodegradation of phthalic acid esters in river water and activated sludge. Appl. and Environ. Microbiol. 31:29-34.

1659. Shelton, D.R.; Boyd, S.A.; Tiedje, J.M., 1984, Anaerobic biodegradation of phthalic acid esters in sludge. Environ. Sci. Technol. 18:93-97.

1660. Saeger, V.W.; Hicks, O.; Kaley, R.G.; Michael, P.R.; Mieure, J.P.; Tucker, E.S., 1979. Environ. Sci. Technol. 13:840-844. (As cited in 1657)

1661. Evans, A.P.; Dail, W.G., Jr., 1974, The effects of sodium chromate on the proximal tubules of the rat kidney: Fine structural damage and lysozymuria. Lab. Invest. 30:704-715.

1662. Kirschbaum, B.B.; Sprinkel, F.M.; Oken, D.E., 1981, Proximal tubule brush border alterations during the course of chromate nephropathy. Toxicol. Appl. Pharmacol. 58:19-30.

1663. Walpole, I.R.; Johnston, K.; Clarkson, R.; Wilson, G.; Bowers, G., 1985, Acute chromium poisoning in a 2-year old child. Aust. Paediatr. J. 21:65-67.

1664. Ellis, E.N.; Brouhard, B.H.; Lynch, R.E.; Dawson, E.B.; Tisdell, R.; Nichols, M.M.; Ramirez, F., 1982, Effects of hemodialysis and dimercaprol in acute dichromate poisoning. J. Toxicol.: Clin. Toxicol. 19:249-258.

1665. Franchini, I.; Magnani, F.; Mutti, A., 1983, Mortality experience among chromeplating workers - Initial findings. Scand. J. Work Environ. Health 9:247-252.

1666. Becker, N.; Claude, J.; Frentzel-Beyme, R., 1985, Cancer risk of arc welders exposed to fumes containing chromium and nickel. Scand. J. Work Environ. Health 11:75-82.

1667. Nishiyama, H.; Yano, H.; Nishiwaki, Y.; Kitaya, T.; Matsuyama, T.; Kodama, T.; Suemasu, K.; Tamai, S.; Takemoto, K., 1985, Lung cancer in chromate workers - analysis of 11 cases. Jpn. J. Clin. Oncol. 15:489-497.

1668. WHO, 1965, Evaluation of the Toxicity of Pesticide Residues in Food. Geneva: WHO/Food Add./27.65, pp 136-141. (As cited in 1359).

1669. Tsapakos, M.J.; Hampton, T.H.; Wetterhahn, K.E., 1983, Chromium (VI)-induced DNA lesions and chromium distribution in rat kidney, liver and lung. Cancer Res. 43:5662-5667.

1670. Cupo, D.Y.; Wetterhahn, K.E., 1985, Binding of chromium to chromatin and DNA from liver and kidney of rats treated with sodium dichromate and chromium (III) chloride in vivo. Cancer Res. 45:1146-1151.

1671. Levy, L.S.; Venitt, S., 1986, Carcinogenicity and mutagenicity of chromium compounds: the association between bronchial metaplasia and neoplasia. Carcinogenesis 7:831-835.

1672. Hueper, W.C ; Payne, W.W., 1962, Experimental studies in metal carcinogenesis. Chromium, nickel, iron, arsenic. Arch. Environ. Health 5:445-462. (As ciated in 1252)

1673. Federal Security Agency, 1953, Health of workers in chromate producing industry - A study. U.S. Public Health Service Publication No. 192. Washington, D.C.: U.S. Government Printing Office. (As cited in 1463).

1674. International Agency For Research on Cancer (IARC), 1973, IARC Monograph on the Evaluation of Carcinogenic Risk of Chemicals to Humans. Vol. 4. Geneva: World Health Organization.

1675. Uitti, R.J.; Rajput, A.H.; Ashenhurst, E.M.; Rozdilsky, B., 1985, Cyanide-induced parkinsonism: a clinicopathologic report. Neurology 35:921-925.

1676. Drinker, P., 1932, Hydrocyanic acid gas poisoning by absorption through the skin. J. Ind. Hyg. 14:1-2. (As cited in 1683)

1677. Muller-Hess, B., 1942, [Intoxication caused by absorption of hydrocyanic acid through the skin.] Muerch. Med. Wochecchr. 89:492. (As cited in 1683)

1678. Severi, L.; Biancifiori, C., 1968, Hepatic carcinogenesis in CBA/Cb/Se mice and Cb/Se rats by isonicotinic acid hydrazine and hydrazine sulfate. J. Natl. Cancer Inst. 41:331. (As cited in 1674)

1679. Rohrborn, G.; Propping, P.; Buselmaier, W., 1972, Mutagenic activity of isoniazid and hydrazine in mammalian test systems. Mutat. Res. 16:189-194.

1680. Lessell, S., 1971, Experimental cyanide optic neuropathy. Arch. Ophthal. 86:194-204.

1681. Biancifiori, C.; Bucciarelli, E.; Clayson, D.B.; Santilli, F.E., 1964, Induction of hepatomas in CBA/Cb/Se mice by hydrazine sulphate and the lack of effect of croton oil on tumor induction in BALB/C/Cb/Se mice. Brit. J. Cancer 18:543-550.

1682. Johnson, J.D.; Meisenheimer, T.L.; Isom, G.E., 1986, Cyanide-induced neurotoxicity: Role of neuronal calcium. Toxicol. Appl. Pharmacol. 84:464-469.

1683. National Institute for Occupational Safety and Health (NIOSH), 1976, Criteria for a recommended standard - Occupational exposure to hydrogen cyanide and cyanide salts. DHEW. Publ. No. (NIOSH) 77-108.

1684. Haymaker, W.; Ginzler,A.M.; Ferguson, R.L., 1952, Residual neuropathological effects of cyanide poisoning -- a study of the

central nervous system of 23 dogs exposed to cyanide compounds. Mil. Surg. 111:231-246. (As cited in 1683)

1685. Nowinski, W.W.; Pandra, J., 1946, Influence of sodium thiocyanate on the development of the chick embryo. Nature 157:414. (As cited in 1683)

1686. Collins, J.; Martland, H.S., 1908, Disease of the primary motor neurones causing the clinical picture of acute poliomyelitis: the result of poisoning by cyanide of potassium -- a clinical and experimental contribution to the toxic effects of cyanide of potassium upon the peripheral motor neurones. J. Nerv. Ment. Dis. 35:417-426. (As cited in 1683)

1687. Perry, I.H., 1935, The effect of prolonged cyanide treatment on body and tumor growth in rats. Am. J. Cancer 25:592-598. (As cited in 1683)

1688. U.S. Environmental Protection Agency (USEPA), 1980, Ambient water quality criteria for cyanides. EPA Report No. 440/5-80-037. Washingtor, D.C.: U.S. Environmental Protection Agency, Office of Water Regulations and Standards. PB81-117483.

1689. Hertting, G., et al., 1960, [Untersuchungen uber die folgen einer chronishen verabreichung akut toxicher dosen von natriumcyamid an hunden.] Acta. Pharmacol. Toxicol. 17:27. (As cited in 1688)

1690. American Cyanamid Co., 1959, Report on sodium cyanide: 30-day repeated feedings to dogs. Central Med. Dept. (As cited in 1688)

1691. Sato, T.; Fukyama, T.; Yamada, M., 1955, The allowable concentration of hydrogen cyanide in air. Bull. Inst. Public Health (Tokyo) 4:3-5. (As cited in 1683)

1692. Walton, D.C.; Witherspoon, M.G., 1926, Skin absorption of certain gases. J. Pharmacol. Exp. Ther. 26:315-324. (As cited in 1683)

1693. Wuthrich, F., 1954, [Chronic cyanide poisoning as industrial intoxicant.] Schweiz Med Wochenschr 84:105-107. (As cited in 1683)

1694. Hardy, H.L.; Jeffries, W.M.; Wasserman, M.M.; Waddell, W.R., 1950, Thiocyanate effect following industrial cyanide exposure -- report of two cases. N.E.J.M. 242:968-972. (As cited in 1683)

1695. Wexler, J.; Whittenberger, J.L.; Dumke, P.R., 1957, The effect of cyanide on the electro cardiogram of man. Am. Heart J. 34:163-183. (As cited in 1423)

1696. ElGhawabi, S.H.; Gaafar, M.A.; El-Saharti, A.A.; Ahmed, S.H.; Malash, K.K.; Fanes, R., 1975, Chronic cyanide exposure: A clinical, radioisotope, and laboratory study. Br. J. Ind. Med. 32:215-219.

1697. Evans, D.M., 1959, Two cases of hydrazine hydrate dermatitis without systemic intoxication. Br. J. Ind. Med. 16:126-127. (As cited in 1625)

1698. Biancifiori, C., 1970, Hematomas in CBA/Cb/Se mice and liver lesions in golden hamsters induced by hydrazine sulfate. J. Nat. Cancer Inst. 44:943-953.

1699. Biancifiori, C., 1970, Ovarian influence on pulmonary carcinogenesis by hydrazine sulfate in BALB/C/Cb/Se mice. J. Nat. Cancer Inst. 45:965-970.

1700. MacEwen, J.D., 1974, The effects of 6-month chronic low level inhalation exposures to hydrazine on animals. Springfield VA., U.S. Dept. of Commerce, National Technical Information Service. NTIS AD A011 865. (As cited in 1625)

1701. Seidell, A., 1970, Solubilities of Inorganic and Metal Organic Compounds, 4th ed., American Chemical Society, Washington, D.C.

1702. Rai, D.; Zachara, J.; Schwab, A.; Schmidt, D.; Girvin, D.; Rogers, J., 1984, Chemical Attenuation Rates, Coefficients and Constants in Leachate Migration. Vol. I: A Critical Review, Report EA-3356 to EPRI, Richland, Washington: Pacific Northwest Laboratories (Batelle Institute).

1703. Bohn, H.L.; McNeal, B.L.; O'Connor, G.A., 1979, Soil Chemistry. New York: John Wiley & Sons.

1704. Martell, A.,E.; Smith, R.M., 1976 and 1982, Critical Stability Constants, Vol. 4, Inorganic Complexes and Vol. 5, First Supplement. New York: Plenum Press.

1705. James, B.R.; Bartlett, R.J.; 1983. Behavior of chromium in soils: VII. Adsorption and reduction of hexavalent forms. J. Environ. Qual. 12:177-181.

1706. Hutchinson, G.E., 1975, A Treatise on Limnology, Volume 1, Part 2 Chemistry of Lakes. New York: John Wiley & Sons.

1707. Lindberg R.D.; Runnells, D.D., 1984, Ground water redox reactions; an analysis of equilibrium state applied to Eh measurements and geochemical modeling. Science 225:925-927.

1708. Bartlett, R.J.; Kimble, J.M., 1976, Behavior of chromium in soils: II hexavalent forms. J. Environ. Qual. 5:383-386.

1709. Huang, C.P.; Wu, M.H., 1977, The removal of chromium (VI) from dilute aqueous solutions by activated carbon. Water Res. 11:673-679.

1710. Bartlett, R.J.; Kimble, J.M., 1976, Behavior of chromium in soils: I. trivalent forms. J. Environ Qual. 5:379-383.

1711. Bartlett, R.; James, B., 1979, Behavior of chromium in soils: III oxidation. J. Environ. Qual. 8:31-35.

1712. Ross, D.S.; Sjogren, R.E.; Bartlett, R.J., 1981, Behavior of chromium in soils: IV. toxicity to microorganisms. J. Environ. Qual. 10:145-148.

1713. Ecological Analysts, Inc., 1981, "The sources, chemistry, fate and effects of chromium in aquatic environments." Washington, D.C.: American Petroleum Institute.

1714. Moore, J.W.; Ramamoorthy, S., 1984, Heavy Metals in Natural Waters. New York: Springer-Verlag.

1715. Feldhake, C.J.; Stevens, C.D., 1963, The solubility of tetraethyl lead in water. J. Chem. Eng. Data 8:196-197.

1716. Geometric near of 4 log K_{oc} values estimated by ADL, using solubility data from 1701.

1717. Buckler, E.J.; Norrish, R.G.W., 1936. J. Chem. Soc., 1567. (As cited in 1715)

1718. Brown, S.L.; Chan, F.Y.; Jones, J.L.; Liv, P.H.; McCaleb, K.E., 1975, Research program on hazard priority ranking of manufactured chemicals (chemicals 1-20). NTIS, PB 253161. (As cited in 806)

1719. Blanchard, G.; Martin, G; Charlou, J.L., 1983, Fate and behavior of TEL in natural environment. Heavy Met. Environ, Int. Conf., 4th, 2:1254-1257.

1720. Grove, J.R.; 1980, Investigation into the formation and behavior of aqueous solutions of lead alkyls. Branica, M.; Konrad, Z., eds., Lead in the Marine Environment. Oxford, U.K.: Pergamon Press.

1721. Charlou, J.L.; Caprais, M.P., Blanchard, G.; Martin, G., 1982, Degradation of TEL in seawater. Environmental Technology Letters, 3:415-424.

1722. Jarvie, A.W.P.; Markall, R.N.; Potter, H.R., 1981, Decomposition of organolead compounds in aqueous systems. Env. Res., 25:241-249

1723. Roderer, G.; 1981, Fate and toxicity of tetraalkyl lead and its derivatives in aquatic environments. Heavy Met. Environ. Int. Conf., 3rd, Edinburgh, U.K.: CEP Consultants.

1724. Reisinger, K.; Stoeppler, M.; Nurnberg, H.W., 1981, Evidence for the absence of biological methylation of lead in the environment. Nature 291:228-230.

1725. Shiau, S.Y.; Huff, R.A.; Wells, B.C.; Felkner, I.C., 1980, Mutagenicity and DNA-damaging activity for several pesticides tested with Bacillus subtilis mutants. Mutat. Res. 71:169-180. (As cited in 1605)

1726. Principe, R.; Dogliotti, E.; Bignami, M., 1981, Mutagenicity of chemicals of industrial and agricultural relevance in Salmonella, Streptomyces and Aspergillus. J. Sci. Food Agric. 32:826-832. (As cited in 1605)

1727. Kale, P.G.; Baum, J.W., 1979, Sensitivity of Drosophila melanogaster to low concentrations of gaseous mutagens. II. Chronic exposures. Mutat. Res. 68:59-68.

1728. Tezuka, H.; Ando,N.; Suzuki, R.; Terahata, M.; Moriya, M.; Shirasu, Y., 1980, Sister chromatid exchanges and chromosomal aberrations in cultured Chinese hamster cells treated with pesticides positive in microbial reversion assays. Mutat. Res. 78:177-191.

1729. Geddes, A.D., 1982, Sister chromatid exchange (SCE) induction in human lymphocytes in vitro by 1,2-dibromoethane with and without metabolic activation. Mutat. Res. 97:188-189. Abstract.

1730. Crespi, C.L.; Seixas, G.M.; Turner, T.R.; Ryan, C.G.; Penman, B.W., 1985, Mutagenicity of 1,2-dichloroethane and 1,2-dibromoethane in two human lymphoblastoid cell lines. Mutat. Res. 142:133-140.

1731. Steenland, K.; Carrano, A.; Clapp, D.; Ratcliffe, J.; Ashworth, L.; Meinhardt, T., 1985, Cytogenetic studies in humans after short-term exposure to ethylene dibromide. J. Occup. Med. 27:729-732.

1732. Steenland, K.; Carrano, A.; Ratcliffe, J.; Clapp, D.; Ashworth, L.; Meinhardt, T., 1986, A cytogenetic study of papaya workers exposed to ethylene dibromide. Mutat. Res. 171:151-160.

1733. Federal Register, 1986, Superfund programs; reportable quantity adjustments 51:34534.

1734. "Manual for Spills of Hazardous Materials," Technical Services Branch, Environmental Protection Service, Environment Canada,

Ottawa, Ontario, March 1984. (Cat. No. En40-320/1984E, ISBN 0-662-13186-X)

1735. Allvin, B.; Berg, S., 1977, Analysis of tetra alkyl lead in street air, SNV PM907. Swedish Environmental Protection Agency, Stockholm. (As cited in 1737)

1736. Purdue, L.J.; Enrione, R.E.; Thompson, R.J.; Bonfield, B.A., 1973, Determination of organic as total lead in the atmosphere by atomic absorption spectrometry. Anal. Chem. 45:527.

1737. Nielson, T., 1984, Atmospheric occurrence of organolead compounds. Biological Effects of Organolead Compounds. P. Grandjean and E.C. Grandjean, eds. CRC Press, Inc.

1738. Chau, Y.K.; Wong, P.T.S., 1984, Organic lead in the aquatic environment. Biological Effects of Organolead Compounds. P. Grandjean and E.C. Grandjean, eds. CRC Press, Inc.

1739. Chau, Y.K.; Wong, P.T.S.; Krammar, O.; Bengert, G.A.; Cruz, R.B.; Kinrade, J.O.; Lye, J.; Van Loon, J.C., 1980, Occurrence of tetroalkylled compounds in the aquatic environment. Bull. Environ. Contam. Toxicol. 24:265-269.

1740. Edwards, K.; Jackson, H.; Jones, A.R., 1970, Studies with alkylating esters - II. A chemical interpretation through metabolic studies of the antifertility effects of ethylene dimethane sulphonate and ethylene dibromide. Biochem. Pharmacol. 19:1783-1789. (As cited in 1741)

1741. National Institute for Occupational Safety and Health (NIOSH), 1977, Criteria for a recommended standard...Occupational exposure to ethylene dibromide. DHEW Publication No. (NIOSH) 77-221. PB276621.

1742. Short, R.D.; Minor, J.L.; Winston, J.M.; Seifter, J.; Lee, C.C., 1978, Inhalation of ethylene dibromide during gestation by rats and mice. Toxicol. Appl. Pharmacol. 46:173-182.

1743. National Toxicology Program (NTP), 1983, Carcinogenesis bioassay of 1,2-dibromoethane in F344 rats and B6CBF1 mice (inhalation study). NTP Carcinogenesis Technical Report Series No. 210, NTP 80-28, DHHS Publication No. (NIH) 82-1766. PB82-181710.

1744. Wong, L.C.K.; Winston, J.M.; Hong, C.B.; Plotnick, H., 1982, Carcinogenicity and toxicity of 1,2-dibromoethane in the rat. Toxicol. Appl. Pharmacol. 63:155-165.

1745. National Research Council (NRC), 1986, Drinking Water and Health, Volume 6. Washington, D.C.: National Academy Press.

1746. Olmstead, E.V., 1960, Pathological changes in ethylene dibromide poisoning. A.M.A. Arch. Ind. Hyg. Occup. Med. 21:45-49. (As cited in 1741)

1747. Letz, G.A., Pond, S.M.; Osterloh, J.D.; Wade, R.L.; Becker, C.E. 1984, Two fatalities after acute exposure to ethylene dibromide. JAMA 252:2428-2431.

1748. Reesal, M.R.; Shnitka, T.K.; Culver, D.B., 1985, Clostridia: an alternative cause of 'ethylene dibromide' fatalities (letter). JAMA 254:3181-3182.

1749. Letz, G.A.; Pond, S.M.; Becker, C.E., 1985, Clostridia: an alternative cause of ethylene dibromide fatalities - reply (letter). JAMA 254:3182.

1750. Pflesser, G., 1938, [Skin damaging effect of ethylene dibromide - A constituent of the liquid from remote water gauges.] Arch. Gewerbepathol. Gewerbehyg. 8:591-600. (As cited in 1741)

1751. Federal Register, 1986, Emergency planning and community right to know programs. 51:41570.

1752. Federal Register, 1986, Emergency planning and community right to know programs. 51:41593.

1753. Federal Register, 1986, Health and safety data reporting; submission of lists and copies of health and safety studies on certain substances. 51:27562.

1754. Federal Register, 1986, Hazardous waste management system; ground-water monitoring. 51:26632.

1755. Federal Register, 1986, Hazardous waste management system; land disposal restrictions. 51:40572.

1756. Ott, M.G.; Scharnweber, H.C.; Lamgner, R.R., 1980, Mortality experience of 161 employees exposed to ethylene dibromide in two production units. Br. J. Ind. Med. 37:163-168.

1757. TerHaar, G., 1980, An investigation of possible sterility and health effects from exposure to ethylene dibromide. Ames, B.; Infante, P.; Reitz, R., eds. Ethylene Dichloride: A Potential Health Risk. Banbury Report Volume 5. Cold Spring: Harbor, NY. (As cited in Current Int. Bull, SRI)

1758. Chemical Regulation Reporter, Sept. 26, 1986, Increased risk of reproductive effects found in workers exposed below OSHA limit. p. 791.

1759. Rowe, V.K.; Spencer, H.C.; McCollister, D.D.; Hollingsworth, R.L.; Adams, E.M., 1952, Toxicity of ethylene dibromide

determined on experimental animals. Arch. Ind. Hyg. Occup. Med. 6:158-173. (As cited in 12 and 1741)

1760. Kochman, M., 1928, [Possible industrial poisonings with ethylene dibromide.] Arch. Gewerbepathol. Gewerbehyg. 8:591-600. (As cited in 1741)

1761. Krishna, G.; Xu, J.; Nath, J.; Petersen, M.; Ong, T., 1985, In Vivo cytogenetic studies on mice exposed to ethylene dibromide. Mutat. Res. 158:81-87.

1762. Working, P.K.; Smith-Oliver, T.; White, R.D.; Butterworth, B.E., 1986, induction of DNA repair in rat spermatocytes and hepatocytes by 1,2-dibromoethane: the role of glutathione conjugation. Carcinogenesis 7:467-472.

1763. Kowalski, B.; Brittebo, E.B.; Brandt, I., 1985, Epithelial binding of 1,2-dibromoethane in the respiratory and upper alimentary tracts of mice and rats. Cancer Res. 45:2616-2625.

1764. Reznik, G.; Stinson, S.F.; Ward, J.M., 1980, Respiratory pathology in rats and mice after inhalation of 1,2-dibromo-3-chloropropane or 1,2-dibromoethane for 13 weeks. Arch. Toxicol. 46:233-240. (As cited in 1745)

1765. National Institute for Occupational Safety and Health (NIOSH), 1981, Current Intelligence Bulletin 37. Ethylene Dibromide (EDB) (Revised) DHHS (NIOSH) Publication No. 82-105. PB83-101774.

1766. SRI International, 1982, Quantitative cancer risk assessment for occupational exposure to ethylene dibromide. PB83-184325.

1767. Federal Register, 1986, Hazardous waste management system; land disposal restrictions. 51:44714.

1768. Federal Register, 1985, Hazardous waste management system; burning of waste fuel and used oil fuel in boilers and industrial furnaces. 50:49164.

1769. 40CFR761 Polychlorinated biphenyls (PCBs) manufacturing, processing, distribution in commerce, and use prohibitions.

1770. U.S. Environmental Protection Agency, 1985, Health Advisory - Methyl Ethyl Ketone. Draft. September 30, 1985.

1771. Comstock, C.C.; Lawson, L.H.; Greene, E.A.; Oberst, F.W., 1954, Inhalation toxicity of hydrazine vapor. AMA Arch. Ind. Hyg. Occup. Med. 10:476-490. (As cited in 1625)

1772. Haun, C.C.; Kinkead, E.R., 1973, Chronic inhalation toxicity of hydrazine, in proceedings of the 4th Annual Conference on

Environmental Toxicology. Springfield, VA, U.S. Dept. of Commerce, National Technical Information Service. NTIS AD 781 031. (As cited in 1625)

1773. Reagor, J.C., 1981, Chromate poisoning in cattle. The Southwestern Veterinarian 34:94.

1774. Anonymous, 1986, TSCA "FYI" Reports include epidemiology, mutagenicity studies. Pesticide and Toxic Chemical News. February 19, 1986, pp 28-29.

1775. NageswaraRao, C.; Vijayaraghavan, M.; NarasingaRao, B.S., 1983, Effect of long term feeding of chromate treated parboiled rice in chicks and mice. Indian J. Med. Res. 77:353-358.

1776. Moller, D.R.; Cassedy, K.; Brooks, S.M.; Bernstein, D.I.; Berstein, I.L., 1984, Delayed anaphylactoid reaction to inhaled sodium chromate. J. Allergy Clin. Immunol. 73:111.

1777. Federal Register, 1985, Water quality criteria; availability of documents. 50:30784.

1778. Prough, R.A.; Moloney, S.J., 1985, Hydrazines. In: Bioactivation of Foreign Compounds. Academic Press, Inc. ISBM 0-12-059480-3. Chapter 15, pp 443-449.

1779. Scales, M.D.C.; Timbrell, J.A., 1982, Studies on hydrazine hepatotoxicity. 1. Pathological findings. J. Toxicol. Environ. Health 10:941-953.

1780. McDougal, J.N.; George, M.E.; Clewell, H.J., III; Pollard, D.L.; Anderson, M.E., 1986, Dermal absorption of hydrazine vapor in rats. (As cited in 1337 abstract 979)

1781. Howard, J.M.; Hanzal, R.F., 1955, Chronic toxicity for rats of food treated with hydrogen cyanide. J. Arg. Food Chem. 3:325. (As cited in 1683)

1782. Doherty, P.A.; Ferm, V.H.; Smith, R.P., 1982, Congenital malformations induced by infusion of sodium cyanide in the golden hamster. Toxicol. Appl. Pharmacol. 64:456-464. (As cited in 11)

1783. Sandberg, C.G., 1967, A case of chronic poisoning with potassium cyanide? Acta. Med. Scand. 181:233-236. (As cited in 1683)

1784. Raestrup, 1926, [On cutaneous damage caused by potassium cyanide.] Zeutralbl. Gewerbehyg. 3:103-106. (As cited in 1683)

1785. Broda, B.; Dombrowicz, E., 1982, Use of a Chlorella test to determine toxicity of chemical compounds. Herba Pol. 28:45-50. (As cited in 58)

1786. Kreutler, P.A.; Varbanov, V.; Goodman, W.; Claya, G.; Stanbury, J.B., 1978, Interactions of protein deficiency, cyanide and thiocyanate on thyroid function in neonatal and adult rats. Am. J. Clin. Nutr. 31:282-289.

1787. Palmer, A.K.; Cozens, D.D.; Spicer, E.J.F.; Worden, A.N., 1978, Effects of lindane upon reproductive function in a 3-generation study in rats. Toxicology 10:45-54.

1788. Federal Register, 1983, Aryl phosphates response to intraagency testing committee. 48:57452.

1789. Hobson, D.W.; D'Addario, A.P.; Bruner, R.H.; Uddin, D.E., 1986, A subchronic dermal exposure study of diethylene glycol monomethyl ether and ethylene glycol monomethyl ether in the male guinea pig. Fund. Appl. Toxicol. 6:339-348.

1790. Mertz, W., 1975, Effects and metabolism of glucose tolerance factor. Nutrition Reviews 33:129-135.

1791. Milner, J.E., 1980, Ascorbic acid in the prevention of chromium dermatitis. J. Occup. Med. 22:51-52.

1792. Council of European Communities Directive on Limit Values and Quality Objectives for Discharges of Certain Dangerous Substances Included in List I of the Annex to Directive 76/464/EEC, 12 June 1986 (86/280/EEC-OJ L 181, 4 July 1986).

1793. Proposal for a Council Directive on the Dumping of Waste at Sea. Com (85) 373 Final, 4 July 1985.

1794. Council Directive on Major Accident Hazards of Certain Industrial Activities. June 24, 1982; 82/501/EEC. Official Journal No. L 230/1.

1795. Pankow, J.F.; Isabelle, L.M.; Asher, W.E., 1984, Trace organic compounds in rain. 1. Samplerdesign and analysis by adsorption/thermal desorption. Environ. Sci. Technol. 18:310-318.

1796. U.S. Environmental Protection Agency (USEPA), 1983, Ethylene dibromide (EDB) Position Document 4. Office of Pesticide Programs, USEPA, Sept. 27, 1983.

1797. Anonymous, 1985, Results of EPA groundwater monitoring. Chemical Regulation Reporter, Dec. 13, 1985, p. 1099.

1798. Federal Register, 1980, Hazardous waste management system; identification and listing of hazardous wastes. 45:72029.

1799. Graham, D.L.; Laman, D.; Theodore, J.; Rubin, E.D., 1977, Acute cyanide poisoning complicated by lactic acidosis and pulmonary edema. Arch. Intern. Med. 137:1051-1055. (As cited in 1423)

1800. Schmitt, C.J.; Zajicek, J.L.; Ribick, M.A., 1985, National Pesticide Monitoring Program: Residues of organochlorine chemicals in freshwater fish, 1980-81. Arch. Environ. Contam. Toxicol. 14:225-260.

1801. Brinkman, M.; Fogelmar, K.; Hoeflein, J.; Lindh, T.; Pastel, M.; Trench, W.C.; Aikens, D.A., 1981, Levels of polychlorinated biphenyls in the Fort Edward, New York, water system. Lawrence, L.H., ed. Adv. Identif. Anal. Org. Pollut. Water, Vol. 2. Ann Arbor, Michigan: Ann Arbor Science.

1802. Bush, B.; Snow, J.; Connor, S.; Koblintz, R., 1985, Polychlorinated biphenyl congeners (PCBs), p,p'-DDE and hexachlorobenzene in human milk in three areas of upstate New York. Arch. Environ. Contam. Toxicol. 14:443-450.

1803. Tessari, J.D.; Savage, E.P., 1980, Gass-liquid chromatographic determination of organochlorine pesticides and polychlorinated biphenyls in human milk. J. Assoc. Anal. Chem. 63:736-741.

1804. Schecter, A., 1983, Contamination of an office building in Binghamton, New York by PCBs, dioxins, furans and biphenyls after an electrical panel and electrical transformer incident. Chemosphere 12:669-680.

1805. Fytianos, K.; Vasilikiotis, G.; Weil, L.; Laskaridis, N., 1985, Preliminary study of organochlorine compounds in milk products, human milk, and vegetables. Bull. Environ. Contam. Toxicol. 34:504-508.

1806. Andren, A.W.; Doskey, P.V.; Strand, J.W., 1980, Atmospheric chemistry of PCBs and PAHs. Volume 9. EPA Report EPA-905/4-79-029-I, NTIS Report No. PB81-196487. 126 p.

1807. U.S. Environmental Protection Agency (USEPA), 1983, Environmental News. PCBs in humans shows decrease. Washington, D.C.: Office of Public Affairs.

1808. Tofflemire, T.; Shen, T., 1979, Volatilization of PCB from sediment and water: experimental and filed data. Mid-Atlantic Ind. Waste Conf. (Proc.) 11:100-109.

1809. Glaser, U.; Hochrainer, D.; Klöppel, H.; Oldiges, H., 1986, Carcinogenicity of sodium dichromate and chromium (VI/III) oxide aerosols inhaled by male Wistar rats. Toxicology 42:219-232.

1810. Eisenreich, S.J.; Johnson, T.C., 1983, PCBs in the Great Lakes: Sources, sinks, burdens. In: PCBs: Hum. Environ. Hazards, Woburn, MA: Butterworth. pp 49-75.

INDEX 1

CROSS INDEX OF CHEMICAL, COMMON AND TRIVIAL NAMES

The order of chemical, common and trivial names included in this index is strictly alphabetical; numerical and alphabetical prefixes signifying positions in a chemical name or stereochemistry have been ignored.

1,2,4,5,6,7,8,8-Octachloro-2,3,3a,4,7,7a-hexahydro-4,7-methano-1H-indene
See Chlordane, Chapter 48.

1,2-Benzenedicarboxylic acid, butyl phenylmethyl ester
See Butyl Benzyl Phthalate, Chapter 46.

1,2-Dibromoethane
See Ethylene Dibromide, Chapter 45.

1,2-Ethanediol
See Ethylene Glycol, Chapter 43.

2-Butanone
See Methyl Ethyl Ketone, Chapter 41.

2-Chloro-1-hydroxybenzene
See O-Chlorophenol, Chapter 37.

2-Chlorophenol
See O-Chlorophenol, Chapter 37.

2-Hydroxychlorobenzene
See O-Chlorophenol, Chapter 37.

2-Methoxyethanol
See Methyl Cellosolve®, Chapter 42.

2-Propanone
See Acetone, Chapter 40.

BBP
See Butyl Benzyl Phthalate, Chapter 46.

Benzenol
See Phenol, Chapter 36.

Benzyl butyl phthalate
See Butyl Benzyl Phthalate, Chapter 46.

Butanedioic acid, [(dimethoxyphosphinothioyl)-thio]-,diethyl ester
See Malathion, Chapter 50.

Carbolic acid
See Phenol, Chapter 38.

Carbophos
See Malathion, Chapter 50.

CBM
See Bromochloromethane, Chapter 44.

Chlorobromomethane
See Bromochloromethane, Chapter 44.

Chlorodiphenyl (41% Cl)
See Aroclor® 1016, Chapter 52.

Chlorodiphenyl (42% Cl)
See Aroclor® 1242, Chapter 52.

Chlorodiphenyl (54% Cl)
See Aroclor® 1254, Chapter 52.

Chlorodiphenyl (60% Cl)
See Aroclor® 1260, Chapter 52.

Chloromethyl bromide
See Bromochloromethane, Chapter 44.

Chlorophen
See Pentachlorophenol, Chapter 39.

Chromate of soda
See Sodium Chromate, Chapter 53.

Chromic acid, disodium salt
See Sodium Chromate, Chapter 53.

Ciophen A60
See Aroclor® 1260, Chapter 52.

Cyanide anion
See Cyanide, Chapter 56.

Cyanide ion
See Cyanide, Chapter 56.

Cyclohexane,1,2,3,4,5,6-hexachloro-,gamma isomer
See Lindane, Chapter 47.

Diamide
See Hydrazine, Chapter 55.

Diamine
See Hydrazine, Chapter 55.

Diazide
See Diazinon®, Chapter 51.

Dichlorochlordene
See Chlordane, Chapter 48.

Dimethyl ketone
See Acetone, Chapter 40.

Dimpylate
See Diazinon®, Chapter 51.

Disodium chromate
See Sodium Chromate, Chapter 53.

EDB
See Ethylene Dibromide, Chapter 45.

EG
See Ethylene Glycol, Chapter 43.

EGME
See Methyl Cellosolve®, Chapter 42.

Ethyl methyl ketone
See Methyl Ethyl Ketone, Chapter 41.

Ethylene glycol methyl ether
See Methyl Cellosolve®, Chapter 42.

Ethylene glycol monomethyl ether
See Methyl Cellosolve®, Chapter 42.

Fluorocarbon 1011
See Bromochloromethane, Chapter 44.

Gamma-benzene hexachloride
See Lindane, Chapter 47.

Gamma-BHC
See Lindane, Chapter 47.

Gamma-HCH
See Lindane, Chapter 47.

Glycol alcohol
See Ethylene Glycol, Chapter 43.

Glycol dibromide
See Ethylene Dibromide, Chapter 45.

Hydrazine base
See Hydrazine, Chapter 55.

Hydrazine, anhydrous
See Hydrazine, Chapter 55.

Hydrocyanic acid, ion
See Cyanide, Chapter 56.

Hydroxybenzene
See Phenol, Chapter 36.

Levoxine
See Hydrazine, Chapter 55.

MEK
See Methyl Ethyl Ketone, Chapter 41.

Methyl acetal
See Acetone, Chapter 40.

Methyl acetone
See Methyl Ethyl Ketone, Chapter 41.

Methyl glycol
See Methyl Cellosolve®, Chapter 42.

Methyl ketone
See Acetone, Chapter 40.

Methylene chlorobromide
See Bromochloromethane, Chapter 44.

O,O-Diethyl-O-(6-methyl-2-(1-methyethyl)-4-pyrimidinyl)phosphorothioate
See Diazinon®, Chapter 51.

PCB
See Aroclor®, Chapter 52.

PCP
See Pentachlorophenol, Chapter 39.

Penchlorol
See Pentachlorophenol, Chapter 39.

Penta
See Pentachlorophenol, Chapter 39.

Pentachlorophenate
See Pentachlorophenol, Chapter 39.

Permanent anti-freeze
See Ethylene Glycol, Chapter 43.

Phenic acid
See Phenol, Chapter 36.

Phenoclor DP6
See Aroclor® 1260, Chapter 52.

Phenyl hydrox[illegible]
See Pheno[illegible] Chapter 36.

Phenylic acid
See Phenol, Chapter 36.

Phosphoric acid, tris (2-methylphenyl) ester
See Tri-o-cresyl Phosphate, Chapter 49.

Phthalic acid, butyl benzyl ester
See Butyl Benzyl Phthalate, Chapter 46.

Pyroacetic acid
See Acetone, Chapter 40.

Pyroacetic ether
See Acetone, Chapter 40.

RCRA Waste Number U082
See 2,6-Dichlorophenol, Chapter 38.

TEL
See Tetraethyl Lead, Chapter 54.

Tetraethyl plumbane
See Tetraethyl Lead, Chapter 54.

TOCP
See Tri-o-cresyl Phosphate, Chapter 49.

TOTP
See Tri-o-cresyl Phosphate, Chapter 49.

Tri-o-tolyl phosphate
See Tri-o-cresyl Phosphate, Chapter 49.

INDEX 2

MOLECULAR FORMULA INDEX

The arrangement used in this index is based on the general molecular formula:

$$C_x H_y \text{ Element}_z$$

where the order of elements is alphabetical. Inorganics precede carbon-containing compounds. Organics lacking hydrogen are listed before any CH's. Compounds without known molecular formulas are listed at the end of the index.

$CrO_4 \cdot 2Na$

Sodium chromate. See Chapter 53.

H_4N_2

Hydrazine. See Chapter 55.

CN

Cyanide. See Chapter 56.

CH_2BrCl

Bromochloromethane. See Chapter 44.

$C_2H_4Br_2$

Ethylene dibromide. See Chapter 45.

$C_2H_6O_2$

Ethylene glycol. See Chapter 43.

C_3H_6O

Acetone. See Chapter 40.

$C_3H_8O_2$

Methyl Cellosolve®. See Chapter 42.

C_4H_8O

Methyl ethyl ketone. See Chapter 41.

C_6HCl_5O

Pentachlorophenol. See Chapter 39.

$C_6H_4Cl_2O$

2,6-Dichlorophenol. See Chapter 38.

C_6H_5ClO

O-Chlorophenol. See Chapter 37.

$C_6H_6Cl_6$
Lindane. See Chapter 47.

C_6H_6O
Phenol. See Chapter 36.

$C_8H_{20}Pb$
Tetraethyl lead. See Chapter 54.

$C_{10}H_6Cl_8$
Chlordane. See Chapter 48.

$C_{10}H_{19}O_6PS_2$
Malathion. See Chapter 50.

$C_{12}H_{21}N_2O_3PS$
Diazinon®. See Chapter 51.

$C_{19}H_{20}O_4$
Butyl benzyl phthalate. See Chapter 46.

$C_{21}H_{21}O_4P$
Tri-o-cresyl phosphate. See Chapter 49.

Molecular Formula Unknown

$C_{12}H_{10}Cl_x$
Aroclor® congeners. See Chapter 52.

INDEX 3

CAS NUMBER INDEX

CAS Number*	See Chapter
57-12-5	56
57-74-9	48
58-89-9	47
67-64-1	40
74-90-8	56
74-97-5	44
78-00-2	54
78-30-8	49
78-93-3	41
85-68-7	46
87-65-0	38
87-86-5	39
95-57-8	37
106-93-4	45
107-21-1	43
108-95-2	36
109-86-4	42
121-75-5	50
143-33-9	56
151-50-8	56
302-01-2	55
333-41-5	51
7775-11-3	53
11096-82-5	52
11097-69-1	52
12674-11-2	52
53469-21-9	52

*Numeric designation assigned by the American Chemical Society's Chemical Abstract Service which uniquely identifies a specific chemical compound.

INDEX 4

NIOSH NUMBER INDEX

NIOSH Number*	See Chapter
AL3150000	40
EL6475000	41
GB2955000	53
GS7175000	56
GV4900000	47
KH9275000	45
KL5775000	42
KW2975000	43
MU7175000	55
MW6825000	56
PA5250000	44
PB9800000	48
SJ3325000	36
SK2625000	37
SK8750000	38
SM6300000	39
TD0350000	49
TF3325000	51
TH9990000	46
TP4550000	54
TQ1351000	52
TQ1356000	52
TQ1360000	52
TQ1362000	52
TS8760000	56
VZ7525000	56
WM8400000	50

*A unique nine-position accession number (two letters and seven numerals) assigned alphabaetically to each substance in the Registry of Toxic Effects of Chemical Substances published by the National Institute for Occupational Safety and Health (Reference 47).

END

DATE

FILMED

5-88

DTIC