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The Installation Restoration Program Toxicology Guide

Volume 4

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Harry G. Armstrong Aerospace Medical Research Laboratory
Aerospace Medical Division
Air Force Systems Command
Wright-Patterson Air Force Base, Ohio
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THE INSTALLATION RESTORATION PROGRAM TOXICOLOGY GUIDE

Volume 4

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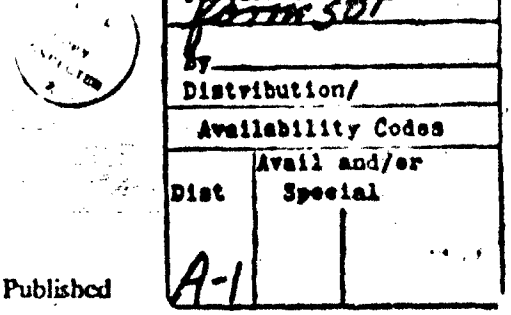

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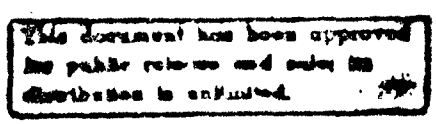

PREFACE

One of the objectives of the U.S. Air Force Installation Restoration Program (IRP) is to provide individuals responsible for the management and implementation of the 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. This IRP Toxicology Guide consists of four volumes which were initially issued in 1985-1987. The original Toxicology Guide was 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. The updated volumes of the Toxicology Guide include new regulatory requirements and recently published toxicology information. The updated Toxicology Guide was produced under an Interagency Agreement with the U.S. Department of Energy, Oak Ridge National Laboratory (87-TH-0002) for the Hazard Assessment Branch, Toxic Hazards Division, AAMRL, Wright-Patterson AFB, OH.

For each chemical in the IRP Toxicology Guide, the environmental fate, exposure pathways, toxicity, sampling and analysis methods and state and federal regulatory status are outlined. The material provided is intended as an overview of key topic areas; no attempt was made to provide a comprehensive review. Users are encouraged to read the Introduction to Volume 1 of the IRP Toxicology Guide before applying chemical-specific information.

Candidate chemicals for inclusion in subsequent Toxicology Guide updates should be forwarded through MAJCOM bioenvironmental engineers to HQ USAF/SGPA. Consultant service for current toxicological information should be obtained from the USAF OFHL/ECO, Brooks AFB, TX 78235-5000.

Substantial effort was made to assure that the information contained in the Toxicology Guide was current and reliable at the time of publication. Users are encouraged to report apparent discrepancies or errors to AAMRL/THA, Wright-Patterson AFB, OH 45433-6573. Copies of this document are available from: National Technical Information Services, 5285 Port Royal Road, Springfield, VA 22161. Federal Government agencies and their contractors registered with Defense Technical Information Center should direct requests for copies to: Defense Technical Information Center, Cameron Station, Alexandria, VA 22314.

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THE INSTALLATION RESTORATION PROGRAM TOXICOLOGY GUIDE
TABLE OF CONTENTS

Volume 1

Page

Preface i
Acknowledgements ii
List of Tables ix
List of Figures xviii
Introduction 1

1.1 Installation Restoration Program 1
1.1.1 Overview 1
1.1.2 The Installation Restoration Program Toxicology Guide 3

1.2 Factors That Impact Water Quality and Water Quality Regulations 6
1.2.1 Environmental Fate of Contaminants 6
1.2.2 Exposure Pathways 14
1.2.3 Human Health Considerations 18
1.2.4 Sampling and Analysis 26

1.3 Aspects of Risk Assessment/Risk Management Implementation 28
1.3.1 Specific Approaches to Risk Assessment 29
1.3.2 Uncertainties and Assumption of Risk Assessment Processes 33
1.3.3 Risk Management 35

1.4 U.S. Regulatory Status 36

1.5 European Community Directives 52

List of Abbreviations, Acronyms, Terms and Symbols AB-1

Chemical Records

1 Methylene Chloride 1-1
2 Dibromomethane 2-1
3 Dibromochloromethane 3-1
4 Chloroform 4-1
5 Trichlorofluoromethane 5-1
6 Carbon Tetrachloride 6-1
7 Chloroethane 7-1
8 1,1-Dichloroethane 8-1
9 1,2-Dichloroethane 9-1
10 1,1,1-Trichloroethane 10-1
11 1,1,2,2-Tetrachloroethane 11-1
12 1,2-Dichloropropane 12-1
13 Vinyl Chloride 13-1
14 1,1-Dichloroethylene 14-1
15 1,2-Dichloroethylene 15-1
16 Trichloroethylene 16-1

Volume 1 (Cont.)

Appendix 1 Useful Handbooks, Databooks, Response Guides and Air Force Documents A-1

Appendix 2 U.S. Air Force Points of Contact for the Installation Restoration Program A-17

Appendix 3 Math, Conversions, and Equivalents A-20

Appendix 4 State Water Quality Agencies and Contacts A-22

Index 1 Cross Index of Chemical, Common and Trivial Names I-1

Index 2 Molecular Formula Index I-24

Index 3 CAS Number Index I-29

Index 4 NIOSH Number Index I-31

Index 5 Quick Index I-34

Volume 2

Acknowledgements ii
List of Tables x
List of Abbreviations, Acronyms, Terms and Symbols AB-1

Chemical Records

17 Tetrachloroethylene 17-1
18 Benzene 18-1
19 Toluene 19-1
20 Ethyl Benzene 20-1
21 Xylene 21-1
22 2,4-Dimethylphenol 22-1
23 2,6-Dinitrotoluene 23-1
24 Chlorobenzene 24-1
25 1,2-Dichlorobenzene 25-1
26 1,3-Dichlorobenzene 26-1
27 1,4-Dichlorobenzene 27-1

Volume 2 (Cont.)

28 1,2,4-Trichlorobenzene 28-1
29 Diethyl Phthalate 29-1
30 Di-n-Butyl Phthalate 30-1
31 Di(2-ethylhexyl)phthalate 31-1
32 Naphthalene 32-1
33 Bis(2-chloroethyl)ether 33-1
34 N-Nitrosodimethylamine 34-1
35 N-Nitrosodiphenylamine 35-1
36 Phenol 36-1

Appendix 1 Useful Handbooks, Databooks, Response Guides and Air Force Documents A-1

Appendix 2 U.S. Air Force Points of Contact for the Installation Restoration Program A-17

Appendix 3 Math, Conversions, and Equivalents A-20

Appendix 4 State Water Quality Agencies and Contacts A-22

Index 1 Cross Index of Chemical, Common and Trivial Names I-1

Index 2 Molecular Formula Index I-24

Index 3 CAS Number Index I-29

Index 4 NIOSH Number Index I-31

Index 5 Quick Index I-34

Volume 3

Acknowledgements ii
List of Tables xii
List of Figures xviii
List of Abbreviations, Acronyms, Terms and Symbols AB-1

Chemical Records

37 O-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 Diazinon® 51-1
52 Aroclor® 1016, 1242, 1254, 1260 52-1
53 Sodium Chromate 53-1
54 Tetraethyl Lead 54-1

Appendix 1 Useful Handbooks, Databooks, Response Guides and Air Force Documents A-1

Appendix 2 U.S. Air Force Points of Contact for the Installation Restoration Program A-17

Appendix 3 Math, Conversions, and Equivalents A-20

Appendix 4 State Water Quality Agencies and Contacts A-22

Index 1 Cross Index of Chemical, Common and Trivial Names I-1

Index 2 Molecular Formula Index I-24

Index 3 CAS Number Index I-29

Index 4 NIOSH Number Index I-31

Index 5 Quick Index I-34

Volume 4

Acknowledgements ii
List of Tables xiv
List of Figures xix
List of Abbreviations, Acronyms, Terms and Symbols AB-1

Chemical Records

55 Hydrazine 55-1
56 Cyanide 56-1
57 DDT 57-1
58 DDD 58-1

59 DDE 59-1
60 2,4-D 60-1
61 2,4,5-T 61-1
62 2,4,5-TP 62-1
63 2,3,7,8-Tetrachlorodibenzo-p-dioxin 63-1
64 JP-4 (Jet Fuel 4) 64-1
65 Automotive Gasoline 65-1
66 Fuel Oils 66-1
67 Stoddard Solvent 67-1
68 Hydraulic Fluid 68-1
69 Mineral Base Crankcase Oil 69-1
70 Synthetic Crankcase Oil 70-1

Appendix 1 Useful Handbooks, Databooks, Response Guides and Air Force Documents A-1

Appendix 2 U.S. Air Force Points of Contact for the Installation Restoration Program A-17

Appendix 3 Math, Conversions, and Equivalents A-20

Appendix 4 State Water Quality Agencies and Contacts A-22

Index 1 Cross Index of Chemical, Common and Trivial Names I-1

Index 2 Molecular Formula Index I-24

Index 3 CAS Number Index I-29

Index 4 NIOSH Number Index I-31

Index 5 Quick Index I-34

LIST OF TABLES

Volume 1

Table		Page
1	Chemical Property Classifications and Relevant Exposure Pathways	15
1-1	Equilibrium Partitioning Calculations for Methylene Chloride in Model Environments	1-13
2-1	Equilibrium Partitioning Calculations for Dibromomethane in Model Environments	2-9
3-1	Equilibrium Partitioning Calculations for Dibromochloromethane in Model Environments	3-10
4-1	Equilibrium Partitioning Calculations for Chloroform in Model Environments	4-13
4-2	Equilibrium Partitioning Calculations for Sediments and Soils	4-15
5-1	Equilibrium Partitioning Calculations for Trichlorofluoromethane in Model Environments	5-12
6-1	Equilibrium Partitioning Calculations for Carbon Tetrachloride in Model Environments	6-14
7-1	Equilibrium Partitioning Calculations for Chloroethane in Model Environments	7-10
8-1	Equilibrium Partitioning Calculations for 1,1-Dichloroethane in Model Environments	8-11
9-1	Equilibrium Partitioning Calculations for 1,2-Dichloroethane in Model Environments	9-13
10-1	Equilibrium Partitioning Calculations for 1,1,1-Trichloroethane in Model Environments	10-12

LIST OF TABLES

Volume 1 (Cont.)

Table		Page
10-2	Retardation Factors for 1,1,1-Trichloroethane in River Sediments and Soils	10-13
11-1	Equilibrium Partitioning Calculations for 1,1,2,2-Tetrachloroethane in Model Environments	11-11
12-1	Equilibrium Partitioning Calculations for 1,2-Dichloropropane in Model Environments	12-11
13-1	Equilibrium Partitioning Calculations for Vinyl Chloride in Model Environments	13-13
13-2	Summary of Vinyl Chloride-Correlated Tumors in Sprague-Dawley Rats at the Lowest Effective Dose	13-18
14-1	Equilibrium Partitioning Calculations for 1,1-Dichloroethylene in Model Environments	14-11
15-1	Equilibrium Partitioning Calculations for Cis and Trans 1,2-Dichloroethylene in Model Environments	15-14
16-1	Equilibrium Partitioning Calculations for Trichloroethylene in Model Environments	16-12

Volume 2

17-1	Equilibrium Partitioning Calculations for Tetrachloroethylene in Model Environments	17-13
18-1	Equilibrium Partitioning Calculations for Benzene in Model Environment	18-12
19-1	Equilibrium Partitioning Calculations for Toluene in Model Environments	19-11
20-1	Equilibrium Partitioning Calculations for Ethyl Benzene in Model Environments	20-10
21-1	Equilibrium Partitioning Calculations for Xylene in Model Environments	21-15

LIST OF TABLES

Volume 2 (Cont.)

Table		Page
21-2	Xylene Isomers in Ground Water	21-18
22-1	Equilibrium Partitioning Calculations for 2,4-Dimethylphenol in Model Environments	22-8
23-1	Equilibrium Partitioning Calculations for 2,6-Dinitrotoluene in Model Environments	23-9
24-1	Equilibrium Partitioning Calculations for Chlorobenzene in Model Environments	24-13
25-1	Equilibrium Partitioning Calculations for 1,2-Dichlorobenzene in Model Environments	25-12
26-1	Equilibrium Partitioning Calculations for 1,3-Dichlorobenzene in Model Environments	26-11
27-1	Equilibrium Partitioning Calculations for 1,4-Dichlorobenzene in Model Environments	27-12
27-2	Retardation Factors for 1,4-Dichlorobenzene in River Sediments and Aquifer Materials	27-14
28-1	Equilibrium Partitioning Calculations for 1,2,4-Trichlorobenzene in Model Environments	28-11
29-1	Equilibrium Partitioning Calculations for Diethyl Phthalate in Model Environments	29-10
30-1	Equilibrium Partitioning Calculations for Di-n-Butyl Phthalate in Model Environments	30-10

LIST OF TABLES

Volume 2 (Cont.)

Table		Page
31-1	Equilibrium Partitioning Calculations for Di(2-ethylhexyl)phthalate in Model Environments	31-11
32-1	Equilibrium Partitioning Calculations for Naphthalene in Model Environments	32-10
33-1	Equilibrium Partitioning Calculations for Bis(2-chloroethyl)ether in Model Environments	33-11
34-1	Equilibrium Partitioning Calculations for N-Nitrosodimethylamine in Model Environments	34-9
35-1	Equilibrium Partitioning Calculations for N-Nitrosodiphenylamine in Model Environments	35-9
35-2	Carcinogenicity Data for N-Nitrosodiphenylamine in Experimental Animals	35-13
36-1	Equilibrium Partitioning Calculations for Phenol in Model Environments	36-15
36-2	Soil Adsorption Constants Reported for Phenol	36-17

Volume 3

Table		Page
37-1	Equilibrium Partitioning Calculations for O-Chlorophenol in Model Environments	37-13
38-1	Equilibrium Partitioning Calculations for 2,6-Dichlorophenol in Model Environments	38-13
39-1	Equilibrium Partitioning Calculations for Pentachlorophenol in Model Environments	39-19
40-1	Equilibrium Partitioning Calculations for Acetone in Model Environments	40-9
40-2	Permeability of Acetone in Three Clay-sites	40-11

LIST OF TABLES

Volume 3 (Cont.)

Table		Page
41-1	Equilibrium Partitioning Calculations for Methyl Ethyl Ketone in Model Environments	41-11
42-1	Equilibrium Partitioning Calculations for Methyl Cellosolve® in Model Environments	42-9
43-1	Equilibrium Partitioning Calculations for Ethylene Glycol in Model Environments	43-2
44-1	Equilibrium Partitioning Calculations for Bromochloromethane in Model Environments	44-9
45-1	Equilibrium Partitioning Calculations for Ethylene Dibromide in Model Environments	45-12
46-1	Equilibrium Partitioning Calculations for Butyl Benzyl Phthalate in Model Environments	46-9
46-2	Biodegradation of Butyl Benzyl Phthalate	46-11
47-1	Equilibrium Partitioning Calculations for Lindane in Model Environments	47-13
47-2	Freundlich Sorption Constants for Lindane	47-15
48-1	Equilibrium Partitioning Calculations for Chlordane in Model Environments	48-14
49-1	Equilibrium Partitioning Calculations for TOCP in Model Environments	49-9
50-1	Equilibrium Partitioning Calculations for Malathion in Model Environments	50-10
50-2	Hydrolysis Half-lives for Malathion in Aqueous Solutions at Temperatures near 20°C	50-13

Volume 3 (Cont.)

Table		Page
51-1	Equilibrium Partitioning Calculations for Diazinon® in Model Environments	51-10
51-2	Hydrolysis Half-lives for Diazinon in Aqueous Solutions at Temperatures Near 20°C	51-13
52-1	Approximate Composition (%) of Aroclor® Formulations	52-20
52-2	Equilibrium Partitioning Calculations for Aroclor® 1016, 1242, 1254 and 1260 Model Environments	52-21
52-3	Equilibrium Partitioning Coefficients for PCBs	52-23
52-4	Mobility of Aroclor® 1242 and Aroclor® 1254 in Several Soil Materials with Various Leaching Solvents	52-24
52-5	Mobility of Aroclor® 1252 and Aroclor® 1254 in Silica-gel TLC Plates Using Various Leaching Solvents	52-25
53-1	Chromate Sorption	53-13
53-2	Perforation of Nasal Septum in Chromate Workers	53-25
54-1	Equilibrium Partitioning Calculations for Tetraethyl Lead in Model Environments	54-14

Volume 4

Table		Page
55-1	Soil Properties and Percent Hydrazine Recovery	55-9
55-2	Hydrazine Behavior in Soil Sorption Studies	55-11
57-1	Equilibrium Partitioning Calculations for DDT in Model Environments	57-12
58-1	Equilibrium Partitioning Calculations for DDD in Model Environments	58-11
59-1	Equilibrium Partitioning Calculations for DDE in Model Environments	59-9

LIST OF TABLES

Volume 4 (Cont.)

Table		Page
60-1	Equilibrium Partitioning Calculations for 2,4-D in Model Environments	60-12
60-2	Freundlich Adsorption Constants for 2,4-D on Soils	60-15
61-1	Equilibrium Partitioning Calculations for 2,4,5-T in Model Environments	61-12
62-1	Equilibrium Partitioning Calculations for 2,4,5-TP in Model Environments	62-11
63-1	Equilibrium Partitioning Calculations for 2,3,7,8-TCDD in Model Environments	63-11
64-1	Major Components of One JP-4 Sample	64-10
64-2	Content of Trace Elements in One Sample of Petroleum-Derived JP-4	64-13
64-3	Additive Compounds Approved for Use in Military JP-4 Fuel	64-14
64-4	Equilibrium Partitioning of Select JP-4 Hydrocarbons in Model Environments	64-15
64-5	JP-4 Fuel-Water Partition Coefficients (K_w) for Selected Hydrocarbons	64-20
64-6	Acute Toxicity of Components of JP-4[1]	64-29
65-1	Composition Data (% W/W) for Various Gasolines	65-10
65-2	Gasoline Additives	65-11
65-3	Equilibrium Partitioning of Select Gasoline Hydrocarbons in Model Environments	65-14
65-4	Acute Toxicity of Components of Automotive Gasoline	65-28

LIST OF TABLES

Volume 4 (Cont.)

Table		Page
66-1	Trace Element Content in Petroleum - Derived Fuel Oils	66-18
66-2	Common Additives in Diesel Fuels	66-19
66-3	Equilibrium Partitioning of Potential Diesel Fuel Hydrocarbons in Model Environments	66-21
66-4	Potencies of Two Blended Fuel Oils for the Skin of C3H Mice	66-27
66-5	Acute Toxicity of Components of Fuel Oils	66-37
67-1	Composition Data for Stoddard Solvent	67-10
67-2	Equilibrium Partitioning of Potential Stoddard Solvent Hydrocarbons in Model Environments	67-11
68-1	Hydraulic Oils	68-9
68-2	Some Reported Mineral Oil and Synthetic Oil Bases for Hydraulic Oil/Lubricating Oil	68-16
68-3	Some Chemical Additives Used in Mineral and Synthetic Base Hydraulic Oil Lubricating Oil	68-18
68-4	Acute Toxicity of Selected Components of Hydraulic Fluid	68-26
68-5	Acute Toxicity of Selected Additives of Hydraulic Fluid	68-30
69-1	Ranges and Most Frequent Concentrations of Polynuclear Aromatic Compounds in Various Motor Oils (Fresh and Used) (mg/kg)	69-10
69-2	Compositional Information for Various Blended Mineral Base Oils	69-12

LIST OF TABLES

Volume 4 (Cont.)

Table		Page
69-3	Chemical Additives	69-15
69-4	Acute Toxicity of Components of Mineral Base Crankcase Oil	69-29
69-5	Acute Toxicity of Selected Additives of Mineral Base Crankcase Oil	69-37
70-1	Compositional and Structural Information and Characteristics of Common Synthetic Crankcase Oils	70-9
70-2	Some Synthetic Oil Bases	70-15
70-3	Some Chemical Additives Used in Synthetic Crankcase Oil	70-17
70-4	Acute Toxicity of Selected Components of Synthetic Crankcase Oil	70-24
70-5	Acute Toxicity of Selected Additives of Synthetic Crankcase Oil	70-27

LIST OF FIGURES

Volume 1

Figure		Page
1	Air Force Installation Restoration Program (IRP)	2
2	Representation of Chemical Partitioning in Model Topsoil by IRP Chemicals	9
3	Partitioning of Selected Chemicals in Modeled Deep Soil System	11
4	Exposure Pathways From a Hazardous Waste Disposal Site	16
5	Estimates of Incremental Risk Over Background Based on Three Extrapolation Models	31
6	Quantitative Health Risk Management	37
7	Comparison Between EPA's Superfund and USAF Installation Restoration Program (IRP)	46

Volume 3

39-1	Relation of the Apparent Adsorption to the pH of the Supernatant Liquid	39-18
49-1	Biodegradation of Tricresyl Phosphate in Mississippi River Water	49-10
49-2	Loss of Tricresyl Phosphate Isomers in Lake Ontario Water	49-10
50-1	Temperature and pH Effects on Malathion Degradation	50-12
51-1	Decomposition of Diazinon® as a Function of Temperature	50-12
51-2	Decomposition of Diazinon® as a Function of Temperature	51-12
52-1	Structural Formula of PCBs	52-18
53-1	Eh-pH Diagram of Cr Species in Water at 25°C	53-14

Volume 4

69-1 Typical Structures in Mineral Base Lubricating Oil 69-9

69-2 Composition of Heavy End Distillates of Crude Oil 69-11

LIST OF ABBREVIATIONS, ACRONYMS, TERMS AND SYMBOLS

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 a chapter and those that may help clarify some of the definitions themselves. Not listed are chemical synonyms which can be found in the chemical index and words adequately defined at the point of use.

A	Acre
AA	Atomic absorption spectroscopy
ACGIH	American Conference of Governmental Industrial Hygienists
Active metals	This refers to metals such as aluminium, calcium, magnesium, potassium, sodium, tin, zinc, and their alloys.
ADI	Acceptable daily intake
ADL	Arthur D. Little, Inc.
Adenocarcinoma	A malignant tumor originating in glandular or ductal epithelium.
Adenoma	A benign growth of glandular tissue.
ae	Acid equivalent
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 1A of the Periodic Table,) such as lithium, sodium, potassium, rubidium, cesium, and francium. The alkali metals react vigorously, 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 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.
API	American Petroleum Institute
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 relative 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
BUN	Blood urea nitrogen
bw	Body weight
C	Celsius (Centigrade)
CAA	Clean Air Act
CAG	Cancer Assessment Group of the U.S. Environmental Protection Agency
Calc	A number calculated by Arthur D. Little, Inc.
Carcinogen	Any cancer-producing substance.
Carcinoma	A malignant epithelial tumor.
CAS REG NO	Numeric designation assigned by the American Chemical Society's Chemical Abstract Service which uniquely identifies chemical compound.
cc	Cubic centimeter(s)
CERCLA	Comprehensive Environmental Response Compensation and Liability Act
CFR	Code of Federal Regulations
CL	Ceiling limit value
cm	Centimeter(s) (1E-02 meter)
Chemically active metals	This phrase generally refers to metals such as, calcium, magnesium, potassium, sodium, tin, zinc, and their alloys.

CNS	Central nervous system which consists of the brain and spinal cord. The CNS controls mental activity plus voluntary muscular activity. It also coordinates the parasympathetic and sympathetic nervous systems, which command the body's involuntary functions.
CO	Carbon monoxide
CO_2	Carbon dioxide
Cp	Centipoise
CPSA	Consumer Product Safety Act
C*t	Product of concentration multiplied by time of exposure
CWA	Clean Water Act
d	Density
da	Day(s)
°	Degrees, as in 37°C
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: O / \ -C - C- This group, commonly called "epoxy", characterizes the epoxy resins. Epichlorohydrin and ethylene oxide are well-known epoxides.
estim	Estimated value
F	Fahrenheit
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	Tap 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 upper explosive limit (UEL).
f_{oc}	Fraction organic carbon in soil ($0 \leq f_{oc} \leq 1$)
FR	Federal Register
ft	Foot
g	Gram(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 · 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.
Hemangiosarcoma	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)
HSDB	Hazardous Substances Data Bank
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 occurs within a living organism.
ip	Intraperitoneal
IR	Infrared spectroscopy
IRP	Installation Restoration Program
IU	International units
iv	Intravenous
K_s (or K_p)	Soil sorption coefficient
kg	kilogram(s) (1E+03 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.
LC_{Lo}	Lowest reported lethal concentration.

LC^*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.
LD_{Lo}	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) (10E-3 gram)
mg%	The concentration of a solution expressed in milligrams per 100 mL.
min	Minute(s)
Mineral acids (non-oxiding)	Examples include boric, disulfuric, fluosilicic, hydriodic, hydrobromic, hydrochloric, hydrocyanic, hyfluoric, 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 as well as oleum.

mL	Milliliter (1E-03 liter)
MLD	Minimum lethal dose
mm	Millimeter(s) (1E-03 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.
NIPDWR	National interim primary drinking water regulation
Nitride	Compounds of nitrogen with $N^{\equiv}$ 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) (1E-09 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 include 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
pg	picogram(s) (1E-12 grams)
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
Raw	Applied 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, hydrides, hydroborates, hyposulfites, iodides, phosphides, selenides, 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.
REL	Recommended exposure limit
Rf	Retardation factor, i.e., the ratio of the velocity of the interstitial water to the velocity of a pollutant in soil.
RfD	Reference dose
RMCL	Recommended maximum contaminant level
RNA	Ribonucleic acid
RQ	Reportable quantities
SAE	Society of Automotive Engineers
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 clean 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
STP	Standard temperature and pressure
Subcutaneous	Beneath the skin
Surface water	That water contained on the exterior or upper portion of the earth's surface; it does not include ground water.
Sym	Symmetrical
$t_{1/2}$	Half-life
TD_{Lo}	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 of a substance 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
ug	Microgram(s) (1E-06 gram)
µL	Microliter(s) (1E-06 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
Vol.%	The number of milliliters of a substance in 100 milliliters of the medium.
Water quality standard	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
w/w	Weight per unit weight
%	Percent
>	Greater than
≥	Greater than or equal to
<	Less than
≤	Less than or equal to
~	Approximately
->	Yields or causes
+	Plus

COMMON SYNONYMS:	CAS REG.NO.: 302-01-2 FORMULA: H_4N_2 NIOSH NO: MU7175000 STRUCTURE: $H_2N\text{-}NH_2$	AIR W/V CONVERSION FACTOR at 25 °C (12) 1.3 mg/m³ ≈ 1 ppm; 0.764 ppm ≈ 1 mg/m³. MOLECULAR WEIGHT: 32.05

Diamide
Diamine
Hydrazine
Hydrazine anhydrous
Hydrazine base
Levoxine

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 Raney 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: Liquid, oily, fuming in air (at 20°C)	(12)
	• Color: Clear	(12)
	• Odor: Fishy, ammonia type odor	(12)
	• Odor Threshold: 3.000 to 4.000 ppm	(59)
	• Density: 1.0036 g/mL; (HCN) (at 20°C)	(2)

PHYSICO-CHEMICAL DATA (Cont.)	• Freeze/Melt Point: 2.00°C	(12)
	• Boiling Point: 113.50°C	(12)
	• Flash Point: 100.00°C closed and open cup	(60,504)
	• Flammable Limits: 4.70 to 100.00% by volume	(60,504)
	• Autoignition Temp.: 23.9 to 270.0°C varies; 270 on glass, 23.9 rusty iron, 132 black iron, 156 stainless steel	(60,504,506)
	• Vapor Pressure: 1.04E+01 mm Hg (at 20°C)	(2)
	• Satd. Conc. in Air: 2.8000E+04 mg/m^3 (at 20°C)	(67)
	• Solubility in Water: Miscible (hygroscopic)	(60)
	• Viscosity: 0.900 cp (at 20°C)	(21)
	• Surface Tension: 6.6670E+01 dyne/cm (at 20°C)	(21)
	• Log (Octanol-Water Partition Coeff.): Not pertinent	
	• Soil Adsorp. Coeff.: Not pertinent	
	• Henry's Law Const.: 2.00E-07 atm · m^3/mol (at 20°C)	(1219)
	• Bioconc. 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 up to 24 hours. Exposure to liquid can cause severe burns. Systemic effects include weight loss, weakness, vomiting and convulsions. Acute Toxicity Studies: INHALATION: LC_{50} 741 ppm · 4 hr — Rat (59) LC_{50} 252 ppm · 4 hr — Mouse (3504) LC_{50} 570 ppm · 4 hr — Rat (3504) ORAL: LD_{50} 60 mg/kg — Rat (59) SKIN: LD_{50} 91 mg/kg — Rabbit (59) LD_{50} 190 mg/kg — Guinea pig (3504) Long-Term Effects: Liver and kidney damage Pregnancy/Neonate Data: Embryolethality. Slight teratogenic and fetotoxic in rats at dose levels also maternally toxic. Genotoxicity Data: Conflicting evidence. Carcinogenicity Classification: IARC - Group 2B (possibly carcinogenic to humans) NTP - No data EPA - Group B2 (probable human carcinogen)
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, 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.

ENVIRONMENTAL AND OCCUPATIONAL STANDARDS AND CRITERIA

AIR EXPOSURE LIMITS:

Standards
- OSHA TWA (8-hr): 0.1 ppm (skin)
- AFOSH PEL (8-hr): 0.1 ppm; Ceiling Limit (15-min): 0.3 ppm (skin)

Criteria
- NIOSH IDLH (30 min): NIOSH has recommended that the substance be treated as a potential carcinogen
- NIOSH Ceiling Limit (120 min.): 0.04 mg/m³
- 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 and Cancer Risk Levels (3744)
- No Health Advisories
- 1E-04 cancer risk: 1 μg/L

WHO Drinking Water Guideline
No information available.

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

REFERENCE DOSES:

No reference dose available.

REGULATORY STATUS (as of 01-MAR-89)

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 (3783, 3784).

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 (3766). Hydrazine is designated an extremely hazardous substance under SARA Title III Section 302. 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 annually. If hydrazine is released from the facility in excess of its reportable quantity (RQ), local emergency planning officials must be notified (3766). Under SARA Title III Section 313, manufacturers, processors, importers, and users of hydrazine must report annually to EPA and state officials their releases of this chemical to the environment (3787).

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 0.1 ppm. Employee skin exposure to hydrazine shall be prevented/reduced through the use of protective clothing and practices (3539).

Hazardous Materials Transportation Act (HMTA)
The Department of Transportation has designated hydrazine as a hazardous material with a reportable quantity of 0.454 kg, subject to requirements for packaging, labeling and transportation (3180).

Food, Drug and Cosmetic Act (FDCA)
Hydrazine may not be used as a boiler water additive in any amount in the preparation of steam that will contact food (361).

- State Water Programs

ALL STATES
All states have adopted EPA Ambient Water Quality Criteria and NDPWRs (see Water Exposure Limits section) as their promulgated state regulations, either by narrative reference or by relisting the specific numeric criteria. These states have promulgated additional or more stringent criteria:

NEW YORK
New York has an ambient water quality standard of 5 µg/L at less than 50 ppm hardness and 10 µg/L at greater than or equal to 50 ppm hardness for Class A, A-S, AA, AA-S, B, and C surface waters. New York also has an ambient water quality standard of 50 µg/L at less than 50 ppm hardness and 100 µg/L at greater than or equal to 50 ppm hardness for Class D surface waters (3500).

Proposed Regulations

- Federal Programs

No proposed regulations are pending.

- State Water Programs

No proposed regulations are pending. Most states are in the process of revising their water programs and proposing changes in their regulations which will follow EPA's changes when they become final. Contact with the state officer is advised. Changes are projected for 1989-90 (3683).

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.

Directive on the Approximation of the Laws, Regulations and Administrative Provisions Relating to the Classification, Packaging and Labeling of Dangerous Preparations (3991)
The labels on packages containing preparations classified as very toxic, toxic or corrosive must bear the safety advise S1/S2 and S46 in addition to the specific safety advice. If it is physically impossible to give such information, the package must be accompanied by precise and easily understood instructions.

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 (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 (pKa = 7.98, 25°C, at 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. 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,

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	-	-	-	-	89.1
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)

Braun and Zirrolli (1610) examined the leaching and sorptionbehavior of hydrazine and related fuels. Soil columns 20 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 $mg/cm^2 \cdot hr$ 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 4E-06M 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 1E-06 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 four 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).

Bosan et al. (3078) administered hydrazine sulfate (170, 340, or 510 mg/L in drinking water) to male Syrian golden hamsters for 2 years. Dimethylnitrosamine was used as a positive control. Negative control animals received distilled water only. Hepatocellular carcinomas were observed in animals treated at the highest dose after 78 weeks of exposure. The incidence of liver cancer was dose-related: 32% for hamsters exposed to 510 mg hydrazine sulfate/L, 12% for 340 mg/L, and none at 170 mg/L. In the positive controls, the incidence of cholangiocellular carcinomas was 73% and of hepatocellular carcinomas, 27%. There were no hepatocellular or cholangiocellular carcinomas in the negative control animals. (These results demonstrated for the first time that hydrazine was a liver carcinogen in the hamster).

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 mice, 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 Genotoxicity

Hydrazine is mutagenic in various microbial tests but its genotoxicity in mammals in vivo is debatable. Hydrazine was positive in the Ames test with a broad range of activity towards the TA1535, TA100, TA1537, TA1538 and TA98 strains of Salmonella typhimurium (1632) and was mutagenic in Escherichia coli strain WP2 (1628).

Shukla (3652) tested it in the sex-linked recessive lethal assay in Drosophila but "the data are too few for a test of significance." In an in vivo somatic cell assay with Drosophila, Negishi et al. (3490) treated larvae with hydrazine and did not observe any increase above controls in the wing-spot assay.

Speit et al. (3676) observed a dose-dependent increase in sister chromatid exchanges in cultured Chinese hamster V79 cells following hydrazine treatment, and Kuszynski et al. (1631) determined that hydrazine was a weak mutagen in detecting mutations to ouabain resistance in V79 cells. Hydrazine has been shown to induce thymidine mutations without metabolic activation in L5178Y mouse lymphoma cells (1629)

Sina et al. (3657), using alkaline elution as a means of observing DNA damage, observed that treatment with 3.0 mM hydrazine induced DNA breaks in freshly perfused rat hepatocytes treated in culture for 3 hr. Parodi et al. (1632) found a

significant increase in DNA breaks in the liver and lung of male Swiss mice injected intraperitoneally with hydrazine. Rohrborn et al. (1679) found it positive in a mouse host-mediated assay using Salmonella typhimurium hisG46 as the indicator organism, indicating that hydrazine was metabolized to a mutagen.

Unscheduled DNA synthesis was not induced by hydrazine in the germ cells of mice given 10 to 120 mg/kg hydrazine intraperitoneally during the early stages of spermatogenesis (1630) and hydrazine was shown to be negative in a mouse dominant-lethal test (3202).

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 6E-05 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 two 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.

Wakabayashi et al. (3822) studied the changes in physicochemical properties of mitochondrial membranes induced by hydrazine. It was found that hepatic mitochondria obtained from male Wistar rats placed on a 1% hydrazine diet for 3 days became slightly enlarged and sometimes elongated, while they became gigantic (megamitochondria) after 7 days of hydrazine treatment. The total amount of phospholipids (per mg protein) and the content of Ca^{2+} were increased in mitochondria after 3 days of hydrazine treatment, but were almost normal in megamitochondria after 7 days of hydrazine treatment.

Haghighi and Honarjou (3258) investigated the effects of hydrazine on phosphatidate phosphohydrolase (PAP) activity in the liver of adult male Wistar rats. The injection of 0.7 mmole/kg of hydrazine in fasting rats caused an increase in PAP activity in the soluble fraction of the liver up to 24 hr, after which time it declined. Increased activity of this enzyme was parallel with a rise in liver triacylglycerol (3.5-fold), and in the catecholamine concentration (3.4-fold) in adrenal glands. Hydrazine also caused an increase in serum glucose.

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 species, 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).

In an Air Force Systems Command document (3012), an inhalation study on male Rhesus monkeys, Sprague-Dawley albino rats, and ICR Swiss albino mice was described. Continuous exposure to hydrazine in concentrations of 0.78 (0.25-1.38) ppm for 90 days resulted in 20, 98, and 99% mortality of the monkeys, rats, and mice, respectively. In monkeys, fatty degeneration of the liver was common, and renal and myocardial involvement were seen occasionally. Both rats and mice showed macrophage and/or polymorphonuclear leukocyte infiltration in the lung and fatty degeneration of the liver.

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. (1648) 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 (3539) standard is 0.1 ppm averaged over an 8-hour work-shift, with a notation of potential skin absorption. The ACGIH (3005) 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) and the USEPA (3744) has given hydrazine a B2 classification indicating a "probable human carcinogen."

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 was 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) but its mutagenicity in mammals in vivo is debatable. Negative results have been reported for a dominant lethal study in mice (3202) 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 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 ug/g for non-aqueous samples.

Various spectrophotometric methods have also been used to determine hydrazine in water or waste waters (3426, 3547, 3118, 3024). The complexing agents include 2-hydroxy-1-naphthaldehyde, silver nitrate and gelatin, 4-dimethylaminobenzaldehyde, and vanillin. Detection limits vary from sub-ppm to ppm concentrations.

55.5 REFERENCES

Note: The nonsequential numbers of the references reflect the order of references as they appear in the master bibliography.

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COMMON SYNONYMS:	FORMULA / CAS REG NO	AIR W/V CONVERSION FACTOR at 25 °C
Cyanide Cyanide anion Cyanide ion Hydrocyanic acid, ion	CN 57-12-5 HCN 74-90-8 NaCN 143-33-9 KCN 151-50-8 NIOSH NO GS7175000 (CN) MW6825000 (HCN) VZ7525000 (NaCN) TS8760000 (KCN)	1.06 mg/m³ ≈ 1 ppm; 0.94 ppm ≈ 1 mg/m³. MOLECULAR WEIGHT: 26.02

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: Liquid (HCN) (at 20°C)	(12)
	• Color: Colorless (HCN)	(12)
	• Odor: Bitter almonds (HCN)	(67)
	• Odor Threshold: 2.000 to 5.000 ppm (HCN)	(67)
	• Density: 0.6870 g/mL; (HCN) (at 20°C)	(69)
	• Freeze/Melt Point: 13.20°C (HCN)	(12)

PHYSICO-CHEMICAL DATA (Cont.)	• Boiling Point: 25.70°C (HCN) • Flash Point: 17.80°C closed cup (HCN); various salts are not combustible. • Flammable Limits: 5.60 to 41.00 % by volume; 5.6-6 to 40-41 (HCN); various salts are not combustible. • Autoignition Temp.: 538.0 to 540.0°C (HCN), various salts are not combustible. • Vapor Pressure: 6.20E+02 mm Hg, (HCN) (at 20°C) • Satd. Conc. in Air: 9.1878E+05 mg/m³, (HCN), (calc) (at 20°C) • Solubility in Water: miscible (HCN) • Viscosity: not pertinent • Surface Tension: not pertinent • Log (Octanol-Water • Partition Coeff.): 0.66 • Soil Adsorp. Coeff.: not pertinent • Henry's Law Const.: 1.22E-04 atm · m³/mol (at 25°C) • Bioconc. Factor: 7.20E+01	(12) (60,504, 506,507) (60,504, (506,507) (60,504, 506,507) (67) (12) (1426)

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 hypernea. This is foliowed by dyspnea, unconsciousness, convulsions and death. Acute Toxicity Studies: INHALATION: LC_{50} 158 mg/m^3 · 30 min (HCN value) — Rat (67) ORAL: LD_{50} 8.5 mg/kg (HCN value) — Mouse (67) Long-Term Effects: Fatigue, nausea, headache, and goiter Pregnancy/Neonate Data: Malformations at near lethal levels in one study Genotoxicity Data: Inadequate data Carcinogenicity Classification: IARC - No data NTP - No data EPA - Group D (not classifiable as to human carcinogenicity)

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.

ENVIRONMENTAL AND OCCUPATIONAL STANDARDS AND CRITERIA

AIR EXPOSURE LIMITS:

Standards
- OSHA TWA (8-hr): as CN, 5 mg/m³; STEL (15-min): as HCN, 5 mg/m³ (skin)
- AFOSH PEL (8-hr TWA): as CN, 5 mg/m³; STEL (15-min): as HCN, 5 mg/m³ (skin)

Criteria
- NIOSH IDLH (30-min): Cyanides (as CN) 50 mg/m³; HCN (as CN) 50 ppm
- NIOSH CL (10-min): Cyanides as CN, 5 mg/m³; HCN as CN, 5 mg/m³
- NIOSH REL: None established
- ACGIH TLV® (8-hr TWA): Cyanides (as CN) 5 mg/m³ (skin); HCN 10 ppm (ceiling) (skin)
- ACGIH STEL (15-min): None established

WATER EXPOSURE LIMITS: (3742)

Drinking Water Standards
MCLG: 200 μg/L (tentative)

EPA Health Advisories and Cancer Risk Levels
The EPA has developed the following Health Advisories which provide specific advice on the levels of contaminants in drinking water at which adverse health effects would not be anticipated.

- 1-day (child): 200 μg/L
- 10-day (child): 200 μg/L
- longer-term (child): 200 μg/L
- longer-term (adult): 800 μg/L
- lifetime (adult): 200 μg/L

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

EPA Ambient Water Quality Criteria
- Human Health (355, 1777)
  - Based on ingestion of contaminated water and aquatic organisms, the criterion is 200 μg/L (cyanides).

ENVIRONMENTAL AND OCCUPATIONAL STANDARDS AND CRITERIA (Cont.)

- Aquatic Life (355, 1777)
  - 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.

REFERENCE DOSES:
ORAL: 2.200E+01 μg/kg/day (3744)

REGULATORY STATUS (as of 01-MAR-89)

Promulgated Regulations
- Federal Programs
  Clean Water Act (CWA)
  Hydrogen cyanide, sodium cyanide, and potassium cyanide are designated hazardous substances. All have a reportable quantity limit (RQ) of 4.54 kg (347, 3764). Cyanides are listed as toxic pollutants, subject to general pretreatment standards for new and existing sources, and effluent standards and guidelines (351, 3763). Effluent limitations have been set for cyanide ion effluent in the battery manufacturing, coil coating, aluminum forming, photographic, non-ferrous metals forming and metal powders, and nonferrous metals manufacturing point source categories (1439, 1440, 1441, 1442, 1443, 894). Effluent limitations have been set for total cyanide in the pesticide chemicals, metal finishing, pharmaceutical manufacturing, electroplating, inorganic chemicals manufacturing, iron and steel manufacturing, organice chemicals, plastics, and synthetic fibers, and ferroalloy manufacturing point source categories (1447, 1444, 1445, 1446, 1436, 354, 895, 3777). Limitations vary depending on the type of plant and industry.

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, sodium cyanide, potassium cyanide, and other soluble cyanide salts are identified as acute hazardous wastes (P063, P106, P098, P030) and listed as hazardous waste constituents (3783, 3784). Non-specific sources of cyanide-containing wastes are treatment sludges and spent solutions from electroplating and metal heat treating operations, and wastewater treatment sludges from the chemical conversion coating of aluminum (325,3765). Waste streams from the following industries contain cyanides and are listed as specific sources of hazardous wastes: inorganic pigments, coking operations, petroleum refining, and organic chemicals (nitrobenzene/aniline production) (3774, 3765). Cyanide is on EPA's ground-water monitoring list. EPA requires that all hazardous waste treatment, storage, and disposal facilities monitor their ground-water for chemicals on this list when suspected contamination is first detected and annually thereafter (3775). Effective July 8, 1987, it is 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. Effective August 8, 1988, underground injection into deep wells is prohibited. Certain variances exist until May, 1990, for land and injection well disposal of some wastewaters, nonwastewaters, and soil for which Best Demonstrated Available Technology (BDAT) treatment standards have not been promulgated by EPA (3786).

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 RCRA hazardous waste streams containing cyanides but these depend upon the concentrations of the chemicals in the waste stream (3766). Sodium, potassium, and hydrogen cyanide are all designated extremely hazardous substances under SARA Title III Section 302. Any facility

at which these chemicals are present in excess of their 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 (3766). Under SARA Title III Section 313, manufacturers, processors, importers, and users of hydrogen cyanide must report annually to EPA and state officials their releases of this chemical to the environment (3787).

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. For hydrogen cyanide an employee's 15-minute short-term exposure limit (STEL) of 5 mg/m^3 shall not be exceeded at any time during the work day. An employee's skin exposure to hydrogen cyanide shall be prevented/reduced through the use of protective clothing and practices (3539).

Hazardous Materials Transportation Act (HMTA)
The Department of Transportation has designated cyanide solutions and anhydrous stabilized hydrogen cyanide as hazardous materials with reportable quantities of 4.54 kg, subject to requirements for packaging, labeling and transportation (3180).

Food, Drug and Cosmetic Act (FDCA)
The following tolerances have been established for residues of hydrogen cyanide:

- 125 ppm in cereal flours;
- 90 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 (.236).

- State Water Programs

ALL STATES
All states have adopted EPA Ambient Water Quality Criteria and NPDWRs (see Water Exposure Limits section) as their promulgated state regulations, either by narrative reference or by relisting the specific numeric criteria. These states have promulgated additional or more stringent criteria:

CALIFORNIA
California has a drinking water quality standard of 200 µg/L for Municipal Regions 1, 2, 5, and 8, and three surface water quality standards: 20 µg/L for Ocean Plan waters, 5.2 µg/L for Region 2 waters for the protection of freshwater life, and 5 µg/L (one-hour-average) for Region 2 waters for the protection of marine life (3097).

CONNECTICUT
Connecticut has an MCL of 0.2 mg/L for drinking water (3137).

FLORIDA
Florida has a water quality criterion of 5 µg/L for all classes of surface water (3220).

ILLINOIS
Illinois has a finished water quality standard of 0.2 mg/L (3322).

IOWA
Iowa has water quality standards of 5 µg/L for Class B (wildlife aquatic) waters and 20 µg/L for Class C (drinking) waters (3327).

KANSAS
Kansas has an action level of 154 µg/L for ground-water (3213).

NEW YORK
New York has a ground-water quality standard of 0.2 mg/L and a water quality criterion of 0.1 mg/L for surface waters used for drinking water supplies (3500).

NORTH DAKOTA
North Dakota has a surface water quality standard of 0.1 mg/L for Class III streams (3512).

SOUTH DAKOTA
South Dakota has a water quality standard of 0.75 mg/L for ground-water (3671).

TEXAS
Texas has the following surface water quality criteria for the protection of aquatic life: 45.78 µg/L (fresh acute), 10.69 µg/L (fresh chronic), 5.6 µg/L (marine acute and chronic) (3112).

VERMONT
Vermont has a preventive action limit of 77 µg/L and an enforcement standard of 154 µg/L for ground-water (3682).

WISCONSIN
Wisconsin has a human threshold criterion of 0.6 mg/L for PublicWater Supply surface waters (3842). Wisconsin also has a preventive action limit of 40 µg/L and an enforcement standard of 200 µg/L for ground-water (3840).

Proposed Regulations

- Federal Programs

Safe Drinking Water Act (SDWA)
Under the National Primary Drinking Water Regulations, EPA will propose MCLs and MCLGs for cyanide in drinking water in March, 1990, with final promulgation planned for March, 1991 (3751).

Resource Conservation and Recovery Act (RCRA)
EPA has proposed BDAT treatment standards for certain cyanide wastewaters and nonwastewaters. Final promulgation is expected in June, 1989 (3795). EPA has proposed listing as hazardous, mixtures of acutely toxic wastes, such as hydrogen cyanide (1396).

- State Water Programs

MOST STATES

Most states are in the process of revising their water programs and proposing changes in their regulations which will follow EPA's changes when they become final. Contact with the state officer is advised. Changes are expected in 1989-90 (3683).

ILLINOIS

Illinois has proposed general use water quality standards: 22 μg/L acute standard, 5.2 μg/L chronic standard (3321).

IOWA

Iowa has proposed acute criteria of 20 μg/L for Class B (cold water aquatic) waters and Class C (drinking) waters and 45 μg/L for all other Class B waters. Iowa has also proposed chronic criteria of 5 μg/L for Class B (cold water aquatic) waters and 10 μg/L for all other Class B waters. These criteria are for the protection of aquatic life (3326).

MINNESOTA

Minnesota has proposed a Recommended Allowable Limit (RAL) of 154 μg/L for cyanide in drinking water (3451). Minnesota has also proposed a Sensitive Acute Limit (SAL) of 45 μg/L for designated surface waters, and a chronic criterion of 154 μg/L for ground-water, for the protection of human health (3452).

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 μg/1. The total maximum allowable concentration is 50 μg/1.

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.

Directive on the Approximation of the Laws, Regulations and Administrative Provisions Relating to the Classification, Packaging and Labeling of Dangerous Preparations (3991)
The labels on packages containing preparations classified as very toxic, toxic or corrosive must bear the safety advise S1/S2 and S46 in addition to the specific safety advice. If it is physically impossible to give such information, the package must be accompanied by precise and easily understood instructions.

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.

Resolution on a Revised List of Second-Category Pollutants (545)
Cyanide is one of the second-category pollutants to be studied by the Commission in the programme of action of the European Communities on Environment in order to reduce pollution and nuisances in the air and water. Risk to human health and the environment, limits of pollutant levels in the environment, and determination of quality standards to be applied will be assessed.

56.1 MAJOR USES

Cyanide (CN^-) usually occurs as hydrocyanic acid (HCN) and its salts. The annual U.S. consumption of HCN in 1983 was 947 million pounds (mp). The major end use of HCN in the U.S. in 1983 was in the production of adiponitrile (461 mp) and acetone cyanhydrin (282 mp), followed by cyanuric chloride (63 mp), sodium cyanide (44 mp), chelating agents (35 mp), nitrilotriacetic acid and salts (20 mp), and other uses (44 mp) (3242). Other major industrial uses of cyanides are in electroplating, photography, extraction of precious metals, case hardening of steels, and fumigation (1781).

56.2 ENVIRONMENTAL FATE AND EXPOSURE PATHWAYS

56.2.1 Transport in Soil/Groundwater Systems

56.2.1.1 Overview

The cyanide ion (CN^-) is expected to be relatively mobile in the soil/groundwater 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 pKa of 9.21 (25°C, zero ionic strength) (1704). This means that at pH 7.21, 99% of CN^- will be protonated and in waters of environmental concern (pH <7), cyanide will exist mostly 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 nonionized, 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/groundwater environment, they will not control cyanide solubility, and precipitation of the cyanide salts from groundwater 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 concentration 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.

The principal sinks of HCN in the atmosphere are attack by UV photons in the stratosphere and complicated and unresolved reactions with atmospheric OH and O(1D) (3129). Precipitation appears to be a negligible sink since the equilibrium concentration of HCN in water is very low at low partial pressures. Its atmospheric residence time has been calculated by the authors to be 2.5 y (range 1-5 y). This is in contrast with the surmise 'Physical transfer mechanisms, such as wet and dry deposition, may dominate the fate of cyanide in the atmosphere' (3739).

56.2.2 Transformation Processes in Soil/Groundwater Systems

The cyanide ion undergoes a number of transformations in water. Hydrolysis rate constants for CN^- using sodium cyanide, potassium ferricyanide, 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 photo-decomposition by sunlight, releasing free CN^- as they dissociate, but possibly reforming at nigl : (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 μg/L within 25 days compared to only 16 μg/L for the

control (not inoculated); with a larger bacterial population, a free CN^- concentration of 3952 µg/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. It can also be oxidized to CNO^- during chlorination of water supplies under alkaline conditions (3736).

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).

A combination of hot alkali digestion and chemical coagulation followed by a two-stage biological extended aeration system can reduce the cyanide level in waste from acrylonitrile plants 85-90 percent (3151).

56.2.3 Primary Routes of Exposure from Soil/Groundwater 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/groundwater 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 groundwater, 15 sites in surface water, and 2 sites in air. These data indicate that cyanide is mobile in soil systems and groundwater contamination may result.

The disposal of cyanide is still a problem in many industries as indicated in recent reports: (1) The U.S. Environmental Protertion Agency has successfully prosecuted the ARMCO Steen Company for discharging cyanide-laden effluents into the Houston shipping channels (3829); (2) J.C. Rhodes, Division of the USM Corporation has been indicted under the Clean Water Act for discharging 44,000 gallons of untreated wastewater (presumably containing cyanide since it involves electroplating and metal finishing operation) into the New Bedford Harbor (3708); (3) seventeen Michigan firms including General Motors, Chrysler Corporation, and Ford Motor Company have agreed to pay $1.5 million for discharging industrial solid wastes including cyanide (3709). The movement of cyanide in groundwater 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

Hydrogen cyanide is ubiquitous in nature arising from both natural and anthropogenic sources. Its presence in the atmosphere was first detected by Coffey et al. (3132) and confirmed by others (3596, 3100). According to Cicerone and Zellner (3129) HCN is present in the stratosphere and the northern hemisphere's non-urban troposphere at the 150-170 ppt level. To maintain the atmospheric burden of HCN at this level, it has been calculated that about 2E+11 g of nitrogen as HCN is required. The issue of whether atmospheric HCN is mostly natural or anthropogenic is still unresolved. Contribution from jet aircraft, volcanoes, lightning, and automotive emissions to the atmospheric burden of HCN is probably negligible. Cyanide has been reported to be a normal constituent of human blood, usually present at concentrations below 12 μmolar (3668).

Inhalation of cyanide may result from a variety of sources. It is produced in fires from burning urethanes, acrylonitriles, or polyamides in plastics. A survey of fire deaths in Glasgow showed toxic levels of CN in 31 percent of the cases. It has been suggested that more lives might be saved if a cyanide antidote were administered to unconscious victims by fire and ambulance crews (3116). However, doubts about the

efficacy of this treatment have been reported (3117). 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).

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). The ADI of cyanide from food has been set at 3.5 mg/day for a 70-kg adult male by the Food and Agriculture Association/World Health Organization (3813). The cyanide in soybean meal or soybean products (0.1 to 1.5 mg/kg) in the diet is the major source of dietary exposure to the general population in the U.S. The daily intake of cyanide has been calculated to be 0.3 to 4.5 μg/person/day assuming a consumption of <3 g/person/day in the U.S. (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 groundwater, 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.

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 Genotoxicity

Only a few studies on the genotoxic effects of cyanide have been reported, most of them negative. Kushi et al. (3384) demonstrated that HCN was mutagenic in strain TA100 of Salmonella typhimurium without metabolic activation, but not with S9, while strain TA98 in this study was not induced to revert with or without

metabolic activation. Other investigators using Escherichia coli and as many as seven strains in the Salmonella/microsome assay did not observe a genotoxic effect with another cyanide salt, potassium cyanide (3159, 3158). Owais et al. using strain TA1530, did not observe any genotoxic effects of sodium cyanide or its metabolites (3990). Cyanide inhibits DNA binding of genotoxicants, and Bodenner et al. were able to show that sodium cyanide reverses the crosslinking of DNA in cells previously treated with cisplatin (3072). 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

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 skull) 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.

In another Syrian Golden hamster study, Frakes et al. (3226) exposed females to cyanogenic glycosides through diets containing cassava meal. The low cyanide cassava contained approximately 0.6 mmol/kg and the high cyanide cassava approximately 7.9 mmol/kg (600 ppm) of cyanide. These diets were fed on days 3-14 of gestation. Cassava fed dams gained less weight than the controls. The offsprings showed reduced fetal weight and reduced ossification. The high cyanide diet was associated with a significant increase in the number of runts compared to the low protein control group. Olusi et al. observed that adult female rats fed diets containing 5 or 10 g/100 g of laboratory feed for two weeks or more before mating never became pregnant (3536). When females were given a diet of raw cassava (containing 0.36-2.5% hydrogen cyanide) only 4 of 10 exposed females became pregnant. The average litter size (5 vs. 6 for controls) and birth weight (5 vs. 7.5 g) was also reduced with this treatment. Kreutler et al. (1786) reported no indications of adverse effects in rat pups born to dams administered 160 μg thiocyanate(SCN)/mL in their drinking water (approx 6.4 mg SCN/rat/day), beginning on day 2 of pregnancy.

Pregnant sheep were exposed by gavage to increasingly frequent doses of potassium cyanide for 135 days in a study by Rudert and Lewis (3605). The doses started at 155 mg/dose once a day and increased to a maximum of 105 mg/dose nine times a day. When ewes showed toxicity at 155 mg/dose 4 times a day, dosing was changed to 105 mg/dose 6 times daily. One ewe died after 945 mg KCN had been administer for 22 days. Although the mean birth weight and growth rate of the exposed lambs did not differ from those of the controls, nearly 70% developed

symptoms of nutritional muscle degeneration (NM) and usually died within 7 days after showing symptoms. This condition was observed in only one control lamb that developed NM but recovered after 14 days.

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.

56.3.1.4.2 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

Physiological responses of various animals and humans exposed to varying concentration of HCN vapor have been reported (3482). Relative sensitivity of various animals to HCN vapor has been found to be: dog > mouse, cat, rabbit > rat, guinea pig > goat, monkey. Humans are thought to be similar to goats and monkeys in their susceptibility of HCN vapor. 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 3.3E-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. The LCt50's ($mg/m^3/min$) for man have been estimated by McNamara (3441) using the relationship, Man LCt50 = 4 X Mouse LCt50 at various exposure times: 2032 (0.5 min), 3404 (1 min), 4400 (3 min), 6072 (10 min), 20,632 (30 min).

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. Recently Bonsall (3075) reported a case of human survival without sequelae following exposure to 500 mg/m^3 of HCN for 6 minutes. This is not surprising since McNamara (3441) suggested that an exposure to 607 mg/m^3 for 10 minutes could be survived by 50 percent humans (3082).

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 $\mu g/100$ mL. All symptoms disappeared within 4 months and blood CN levels dropped to 2-3 $\mu g/mL$.

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, thiocyanate. Heavy smoking and eating cabbage-type vegetables can exacerbate the symptoms of occupational cyanide exposure due to additional formation of thiocyanate (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 thiocyanate was substituted for the NaCl injection. Nausea, lack of appetite and nervousness returned. After 3 days of sodium thiocyanate 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 thiocyanate 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 0.2 mg/L (1-day, 10-day, longer term) for children and 0.8 mg/L (longer term) and 0.2 mg/L (lifetime) for adults. The WHO (666) recommends a level of 10 μg/L for drinking water.

Both OSHA (3539) and the ACGIH (3005) have set an occupational exposure limit of 5 mg/m^3 (as CN^-) for cyanide, with a notation of possible skin absorption listed by ACGIH. For hydrogen cyanide, OSHA has established a STEL of 5 mg/m^3 (skin) (3539).

The Health and Safety Commission of Great Britain has introduced a new control limit for HCN, effective January 31, 1987: 10 mg/m^3, 10-min TWA. No recommendation has been made for a long-term exposure limit (3115).

Neither IARC nor NTP have classified this compound with regard to carcinogenic activity. USEPA (3749) lists it in carcinogenicity Group D (not classifiable as to human carcinogenicity).

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, and 9012 (63). In Methods 335.2, 9010, and 9012, the cyanide as hydrocyanic acid (HCN) is released from cyanide complexes by a reflux-distillation operation and absorbed in a scrubber containing sodium hydroxide solution; the cyanide ion in the absorbing solution is then determined colorimetrically. The cyanide is converted to cyanogen chloride by reaction with Chloramine-T, which is subsequently reacted with a pyridine-barbituric acid reagent to form a colored complex. If the samples contain hydrogen sulfide, metal sulfides, or compounds that may form hydrogen sulfide during distillation, they should be treated with bismuth nitrate prior to distillation. Nitrate and/or nitrite may also interfere in the analysis and samples containing these species should be pretreated with sulfamic acid.

The colorimetric procedure is used to determine concentrations below 1 mg/L. Above this concentration a titration procedure using silver nitrate and a rhodamine indicator is used (Method 335.2). In method 335.3 cyanide (as HCN) is released from cyanide complexes by UV digestion and distillation. The cyanide is then converted to cyanogen chloride and determined as described above. Methods 335.3 and 9012 are used for automated measurement of the 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. Pyrolysis GC with mass spectrometry has also been used to screen sediment/soil samples for cyanides (3160).

Typical detections limits for cyanide that can be obtained in waste waters are shown below; detection limits were not indicated for Methods 9010 and 9012 or for nonaqueous samples. The actual detection limit achieved in a given analysis will vary with instrument sensitivity and matrix effects.

Nonaqueous 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)

56.5 REFERENCES

Note: The nonsequential numbers of the references reflect the order of references as they appear in the master bibliography.

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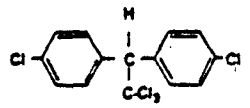
COMMON SYNONYMS:	CAS REG.NO.: 50-29-3 FORMULA: $C_{14}H_9Cl_5$ NIOSH NO: KJ3325000 STRUCTURE: 	AIP W/V CONVERSION FACTOR at 25°C (12) 14.5 mg/m³ ≈ 1 ppm; 0.0689 ppm ≈ 1 mg/m³. MOLECULAR WEIGHT: 354.50
1,1'-(2,2,2-trichloroethylidene)bis(4-chlorobenzene) 1,1,1-trichloro-2,2-bis(p-chlorophenyl)ethane DDT p,p'-DDT		

REACTIVITY	DDT is considered incompatible with strong oxidizers by one source and incompatible with alkaline materials by another. For general compatibility classification purposes, the compound is considered to be a halogenated organic. Reactions of halogenated organic materials with cyanides, mercaptans or other organic sulfides typically generate heat, while those with 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 (23, 54, 511).

PHYSICO-CHEMICAL DATA	• Physical State: Solid, crystalline or powder (at 20°C)	(12)
	• Color: Colorless to slight off-white	(12)
	• Odor: Odorless or slightly aromatic	(12)
	• Odor Threshold: 0.350 ppm	(59)
	• Density: 0.9800 to 0.9900 g/mL (at 20°C)	(12)
	• Freeze/Melt Point: 108.50°C	(59)
	• Boiling Point: 260.00°C	(59)
	• Flash Point: Combustible solid	(60)
	• Flammable Limits: No data	
	• Autoignition Temp.: No data	
	• Vapor Pressure: 1.50E-07 mm Hg (at 20°C)	(12)
	• Satd. Conc. in Air: 2.9000E-03 mg/m³ (at 20°C)	(1219)
	• Solubility in Water: 3.10E-03 to 3.40E-03 mg/L (at 25°C)	(67)
	• Viscosity: No data	
	• Surface Tension: No data	

PHYSICO-CHEMICAL DATA (Cont.)	• Log (Octanol-Water Partition Coeff.): 6.36 (2162) • Soil Adsorp. Coeff.: 3.02E+05 (2147) • Henry's Law Const.: 2.80E-05 atm · m^3/mol (at 25°C) (2146) • Bioconc. Factor: 3.8E+04 (rainbow trout), 1.1E+05 (estim) (2001,659)
PERSISTENCE IN THE SOIL-WATER SYSTEM	DDT is expected to be relatively immobile in the soil/ground-water system due to its strong sorption properties. Volatilization may be an important loss pathway from aquatic systems but is much slower in soils. Translocation of sorbed DDT with soil particles may be important. Biodegradation is expected to be the predominant fate process in soils, but occurs slowly under aerobic conditions. Photolysis can also contribute to DDT degradation in soils exposed to sunlight.
PATHWAYS OF EXPOSURE	The primary pathway of concern from the soil/ground-water system is the migration of DDT to ground water drinking water supplies, although this is not likely to occur in most situations. 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: (54) DDT is of moderate acute toxicity to man. Symptoms of exposure include paresthesia of the tongue, lips and face; tremors, apprehension, dizziness, confusion, malaise, headaches, convulsions, paresis of the hands, vomiting, irritation of the eyes and skin. Acute Toxicity Studies: ORAL: LD_{50} 87 mg/kg — Rat (47) LD_{50} 200 mg/kg — Mouse (3504) LD_{50} 135 mg/kg — Rat (3504) LD_{50} 150 mg/kg — Mouse (3504) LD_{50} 150 mg/kg — Rat (3504) LD_{50} 250 mg/kg — Mouse (3504) SKIN: LD_{50} 1931 mg/kg — Rat (47) LD_{50} 1000 mg/kg — Guinea pig (3504) LD_{50} 309 mg/kg — Rabbit (3504) Long-Term Effects: Liver and kidney damage Pregnancy/Neonate Data: Fetotoxic, not teratogenic Genotoxicity Data: Conflicting data Carcinogenicity Classification: IARC - Group 2B (possibly carcinogenic to humans) NTP - None assigned EPA - Group B2 (probable human carcinogen; sufficient evidence in animals and inadequate evidence in humans)
HANDLING PRECAUTIONS (54)	Handle chemical only with adequate ventilation • Concentrations of 10 mg/m³: chemical cartridge respirator with organic vapor cartridge with dust or mist filter, including pesticide respirator meeting these requirements or supplied-air respirator or self-contained breathing apparatus • 10-100 mg/m³: supplied-air respirator with full facepiece or self-contained breathing apparatus with full facepiece • 100-500 mg/m³: Type C supplied-air respirator operated in pressure demand, continuous flow mode or other positive pressure mode • Chemical goggles if there is probability of eye contact • Appropriate clothing and gloves to prevent repeated or prolonged skin contact.

ENVIRONMENTAL AND OCCUPATIONAL STANDARDS AND CRITERIA

AIR EXPOSURE LIMITS:

Standards
- OSHA TWA (8-hr): 1 mg/m³ (skin)
- AFOSH PEL (8-hr TWA): 1 mg/m³ (skin); STEL (15-min): 3 mg/m³

Criteria
- NIOSH IDLH (30-min): NIOSH has recommended that the substance be treated as a potential human carcinogen.
- NIOSH REL: no data
- ACGIH TLV® (8-hr TWA): 1 mg/m³

WATER EXPOSURE LIMITS:

Drinking Water Standards
None established

EPA Health Advisories and Cancer Risk Levels
None established

WHO Drinking Water Guideline (666)
A health-based guideline for drinking water of 1 µg/L is recommended for DDT. A daily per capita consumption of two liters of water was assumed.

EPA Ambient Water Quality Criteria
- Human Health (355)
  - Based on ingestion of contaminated water and aquatic organisms, (1E-05, 1E-06, 1E-7 cancer risk), 0.24 ng/L, 0.024 ng/L, 0.0024 ng/L.
  - Based on ingestion of contaminated aquatic organisms only, (1E-05, 1E-06, 1E-07 cancer risk), 0.24 ng/L, 0.024 ng/L, 0.0024 ng/L.
  - Based on ingestion of drinking water only (1E-05, 1E-06, 1E-07), 42 ng/L, 4.2 ng/L, 0.42 ng/L.

- Aquatic Life (355)
  - Freshwater species
    For DDT and its metabolites, the criterion is 0.0010 µg/L as a 24-hour average. The concentration should not exceed 1.1 µg/L at any time.

  - Saltwater species
    For DDT and its metabolites, the criterion is 0.0010 µg/L as a 24 hour average. The concentration should not exceed 0.13 µg/L at any time.

REFERENCE DOSES: (3744)
5E-04 mg/kg/day

REGULATORY STATUS (as of 01-MAR-89)

Promulgated Regulations

- Federal Programs

Clean Water Act (CWA)

Under the toxic pollutant effluent standards, DDT is prohibited in any discharge from DDT manufacturers or formulators. The ambient water criterion for DDT in navigable waters is 0.001 µg/L. This standard applies to all discharges of process wastes from manufacturing and storage areas subject to direct contamination by DDT through stormwater runoff or routine cleanup, and cleanup of spills (805). DDT is designated a hazardous substance. It has a reportable quantity (RQ) of 0.454 kg (347,3764). It is also listed as a toxic pollutant, subject to general pretreatment regulations for new and existing sources, and effluent standards and guidelines (351, 3763). Effluent limitations for DDT metabolites have been set in the following point source categories: electroplating (3767), steam electric power generating (3802), and metal finishing (3768). The limitations set are for the amount of total toxic organics (TTO) discharge permitted per day. DDT metabolites are included in calculating the TTO. Effluent limitations in the pesticide chemicals manufacturing point source category are set at 0.010 kg/1000 kg of organic pesticide chemicals (including DDT) maximum for any one day (891).

Safe Drinking Water Act (SDWA)

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

Resource Conservation and Recovery Act (RCRA)

DDT is identified as a toxic hazardous waste (U061) and listed as a hazardous waste constituent (3783, 3784). DDT is included on EPA's ground-water monitoring list. EPA requires that all hazardous waste treatment, storage, and disposal facilities monitor their ground-water for chemicals on this list when suspected contamination is first detected and annually thereafter (3775). Effective July 8, 1987, the land disposal of untreated hazardous wastes containing halogenated organic compounds in total concentrations greater than or equal to 1000 mg/kg will be prohibited. Effective August 8, 1988, the underground injection into deep wells of these wastes is prohibited. Certain variances exist until May, 1990 for land and injection well disposal of some wastewaters and nonwastewaters for which Best Demonstrated Available Technology (BDAT) treatment standards have not been promulgated by EPA (3786). EPA requires 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 (3782).

Comprehensive Environmental Response Compensation and Liability Act (CERCLA)
DDT 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 DDT but these depend upon the concentrations of the chemicals in the waste stream (3766).

Federal Insecticide, Fungicide and Rodenticide Act (FIFRA)
Action levels for the sum of DDT, DDE and DDD residues in agricultural commodities range from 0.05 to 0.5 ppm (889). As of January 1, 1989, EPA is cancelling registrations and denying applications of all dicofol products containing greater than 0.1% of DDT and related impurities (2268).

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 DDT shall not exceed an 8-hour time-weighted average (TWA) of 1 mg/m^3. An employee's skin exposure to DDT should be prevented/reduced through the use of protective clothing and practices (3539).

Hazardous Materials Transportation Act (HMTA)
The Department of Transportation has designated DDT a hazardous substance with a reportable quantity of 0.454 kg, subject to requirements for packaging, labeling, and transportation (3180).

Food, Drug and Cosmetic Act (FDCA)
The following action levels are recommended for the sum of DDT, DDE and DDD residues:

- 0.1 ppm in dried hops
- 1.25 ppm in manufactured dairy products
- 1.0 ppm in peppermint oil, spearmint oil and in crude soybean oil (888)

- State Water Programs
  ALL STATES
  All states have adopted EPA Ambient Water Quality Criteria and NPDWRs (see Water Exposure Limits section) as their promulgated state regulations, either by narrative reference or by relisting the specific numeric criteria. These states have promulgated additional or more stringent criteria:

ARKANSAS
Arkansas has set a chronic toxicity standard of 0.001 µg/L (24-hr average) for DDT in surface waters, and an acute toxicity standard of 1.1 µg/L (never to exceed this). This is for the protection of aquatic life (3587).

CALIFORNIA
California has drinking water standards of 42 µg/L for Municipal Region 1 and 5 waters and 4.0 µg/L for Ocean Plan waters (3097).

DISTRICT OF COLUMBIA
The District of Columbia has set a human health criterion of 0 µg/L for DDT and its isomers in the public water supply (3828).

ILLINOIS
Illinois has a water quality criterion of 0.05 mg/L for DDT in the public water supply (3322).

KANSAS
Kansas has an action level of 0.42 µg/L for ground-water (3213).

NEW YORK
New York has an MCL of 5 µg/L for drinking water, an ambient water quality standard of 0.01 µg/L for surface water classed for drinking water supply, and requires DDT to be nondetectable in ground-water (3501).

OKLAHOMA
Oklahoma requires the instream concentration of DDT never to exceed 0.2 µg/L for surface waters classed for fish and wildlife propagation (3534).

WEST VIRGINIA
West Virginia currently has a water quality criterion of 1 ng/L for Public A waters, but has proposed new criteria the same as the federal criteria. Final promulgation is expected by late spring 1989 (3835).

Proposed Regulations
- Federal Programs

  No proposed regulations are pending.

- State Water Programs

  MOST STATES

  Most states are in the process of revising their water programs and proposing changes in their regulations which will follow EPA's changes when they become final. Contact with the state officer is advised. Changes are projected for 1989-90 (3683).

  MINNESOTA

  Minnesota has proposed a Recommended Allowable Limit (RAL) of 1 μg/L for DDT in drinking water (3451). Minnesota has also proposed a Sensitive Acute Limit (SAL) of 1 μg/L for surface waters, and chronic criteria of 0.00013 μg/L for cold surface waters, 0.00026 μg/L for other designated surface waters, and 1 μg/L for designated ground-waters. These criteria are for the protection of human health (3452).

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 DDT is 0.1 μg/L. The total maximum allowable concentration for pesticides and related products is 0.5 μg/1.

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

Directive on Plant Protection Products (1333)
Plant protection products containing DDT 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. DDT may also be placed on the market or used in other specified cases.

Directive on the 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 p,p'-DDT is 10 μg/L. For total DDT (including isomers) the quality objective is 25 μg/L. The emission standard of DDT and isomers for DDT production is 0.7 mg/L water discharged as a monthly average and 1.3 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.

Proposal for a Council Regulation Concerning Export From and Import Into the Community of Certain Dangerous Chemicals (3993)
EEC has proposed that any export of DDT 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.

Resolution on a Revised List of Second-Category Pollutants (545)
DDT is one of the second-category pollutants to be studied by the Commission in the programme of action of the European Communities on Environment in order to reduce pollution and nuisances in the air and water. Risk to human health and the environment, limits of pollutant levels in the environment, and determination of quality standards to be applied will be assessed.

57.1 MAJOR USES

From 1946 to 1972, DDT was one of the most widely used agricultural insecticides in the world (12). During this time, DDT played an important role in many phases of agriculture and in the eradication of malaria, typhus and plague. As of January 1, 1973, all uses of DDT were cancelled with the exception of emergency public health uses; however, it is still used extensively in some tropical countries (59, 2000).

Technical DDT is a mixture consisting primarily of p,p'-DDT (65-80%), o,p'-DDT (15-21%), p,p'-DDE (>4%), and up to a dozen other components (2145). Most studies of DDT have examined either the p,p' isomer, the o,p' isomer, or the technical product. The discussion that follows also focuses on the technical DDT mixture, for it has received the most study. However, data for specific isomers are included whenever possible.

57.2 ENVIRONMENTAL FATE AND EXPOSURE PATHWAYS

57.2.1 Transport in Soil/Ground-water Systems

57.2.1.1 Overview

DDT is expected to be highly immobile in the soil/ground-water environment when present at low dissolved concentrations. Bulk quantities of DDT dissolved in an organic solvent could be transported through the unsaturated zone as the result of a spill or improper disposal of excess formulations. However, the extremely low solubility of DDT and its strong tendency to sorb to soils results in a very slow transport rate in soils.

In general, transport pathways can be assessed by using an equilibrium-partitioning model as shown in Table 57-1. These calculations predict the partitioning of low soil concentrations of DDT among soil particles, soil:water, and soil air. Due to its strong tendency to sorb to soil, virtually all of the DDT partitions to the soil particles of unsaturated top soil, with negligible amounts associated with the soil water or air. Even in saturated deep soil, which is assumed to contain no soil air and a smaller organic carbon fraction, almost all of the DDT is retained on the soil.

57.2.1.2 Sorption on Soils

DDT is characterized by a strong tendency to sorb to organic carbon. Kadeg et al. (2147) reported an arithmetic mean K_{oc} of 670, 200 for 17 reported values; the corresponding geometric mean was log K_{oc} = 5.48. As with all neutral organic chemicals, the extent of sorption is proportional to the soil organic carbon content.

TABLE 57-1
EQUILIBRIUM PARTITIONING CALCULATIONS FOR DDT
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]	100.0	1.7E-03	6.0E-06
Saturated deep soil[d]	99.9	7.9E-02	-

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 coefficient: K_{oc} = 302,000 (2147).
c) Henry's law constant taken as 2.8E-05 atm · m^3/mol at 25°C (2146).
d) Used sorption coefficient K_p = 0.001 x K_{oc}

In soils with little organic carbon (e.g., clays) the extent of sorption may also depend upon soil properties such as surface area, cation exchange capacity and degree of hydration.

The apparent sorption of DDT to soils and sediments is lessened, and thus its mobility is enhanced by the presence of dissolved organic matter in solution. Caron et al. (2148) found the sorption of DDT to a natural freshwater sediment to be reduced by 75% in the presence of 6.95 mg/L of dissolved organic carbon (in the form of humic acid extracted from another sediment). Using p,p'-DDT, Chiou et al. (2149) observed the apparent water solubility to be significantly enhanced (roughly 2-5 times) in the presence of 100 mg/L of humic and fulvic acids. (Sorption will decrease with increasing water solubility.) The partitioning of p,p'-DDT between soil-derived humic acid and water was approximately 4 times greater than with soil fulvic acids and 5-7 times greater than with aquatic (freshwater) humic and fulvic acids. These findings indicate that the mobility of DDT in natural waters may be several times greater than predicted (though probably still small) when the effect of dissolved organic matter is present. In waters containing large concentrations of dissolved organic material, such as swamps and bogs, this may be especially important.

57.2.1.3 Volatilization from Soils

The vapor pressure of DDT at 25°C has been given as 2.6E-10 atm (2150) with estimates of its Henry's law constant at 25°C ranging from 2.8E-05 to 2.0E-06 atm · m³/mol (2146). Volatilization is expected to be an important loss process in aquatic environments with the half-life for DDT on the order of several hours to several days (10). The presence of sediment particles, which would adsorb DDT from solution, would significantly reduce volatilization losses.

In soils, volatilization is much slower. Jury et al. (808), using soil of 1.25% organic carbon, to which DDT was applied uniformly to a depth of 1 cm at the rate of 1 kg/hectare, calculated volatilization half-lives of 497 and 432 days when water evaporation rates were 0.0 and 5.0 mm/day, respectively. The corresponding figures when the same quantity of DDT was mixed to a depth of 10 cm were 2300 and 2069 days.

Similar results were obtained by Lichtenstein et al. (2151) who studied the persistence of technical DDT (84% p,p'-DDT, 15% o,p'-DDT) in agricultural loam soil with crops over a 15 year period. Calculated half-lives for both isomers fell between 4.0 and 4.7 years for DDT applied at 10 pounds/acre; somewhat longer half-lives were measured for applications of 100 pounds/acre. These half-lives should be taken as upper limits of the volatilization rate, because other processes such as leaching and degradation contribute to the DDT loss.

In tropical soils, the loss of DDT has been found to be much more rapid. El Zorgani (2152) found a half-life of less than three weeks for DDT applied at an initial concentration of 6.65 ppm to the soil surface beneath a cotton crop in the Sudan. The loss of the o,p' isomer was several times greater than for the p,p' isomer; an insignificant fraction of the loss could be accounted for by conversion to p,p'-DDE. A half-life 110 days has been reported for DDT in Kenya (2153) where it was found to sublime directly into the atmosphere without conversion to DDE.

57.2.2 Transformation Processes in Soil/Ground-water Systems

The rate at which DDT degrades in the soil/ground-water environment is dependent on the conditions under which it is present. The pH strongly affects the rate of aqueous hydrolysis. Over the pH range typical of natural waters (pH 5-9), Wolfe et al. (2154) found the pseudo-first-order rate constant (k_{obs}) at 27°C could be expressed as:

$$k_{obs} = 1.9E\text{-}09 + 9.9E\text{-}03 \cdot [OH^-]$$

where k_{oh} is in s^{-1}, and [OH], the concentration of the hydroxide ion is in moles/liter. Hydrolysis half-lives of roughly 81 days, 8 years and 12 years at pH 9, 7, and 5, respectively, result from the rate constant obtained from this equation. The hydrolysis product of p,p'-DDT is p,p'-DDE (2145).

A photolysis half-life of 5 days was measured for DDT when it was present in natural water exposed to summer sunlight, although no photolysis was observed when the chemical was present in pure water (2155). Again, p,p'-DDE is a degradation product (2145). Chen et al. (1220) observed a similar half-life of 8 days for p,p'-DDT applied as a thin film (0.67 $\mu g/cm^2$) to glass plates and exposed to light of environmentally important wavelengths (maximum intensity at 300 nm). The degradation of DDT by ultraviolet light was found to be more effective when the DDT was present in humus-free soil than in soil containing humus (2156).

DDT has been found to undergo abiotic, reductive dehalogenation to DDD in the presence of Fe(II) porphyrin (2157). It has been suggested that the Fe(III) porphyrin, which results from the oxidation of the Fe(II) porphyrin in this process, is reconverted to the Fe(II) porphyrin in the presence of reduced organic material (2158). Dehydrochlorination of DDT to DDE (removal of a hydrogen and chlorine atom to form a double bond) has also been observed in model systems containing reduced porphyrins and in the natural environment (2157).

Gambrell et al. (2159) found the degradation of DDT to be little affected by pH but greatly affected by redox conditions. Under strongly reducing conditions (Eh = -150 mv), over 90% of the DDT was degraded within a few days. The authors note that this is an unusually rapid rate.

The half-life for the decomposition of DDT in aerobic soils has been reported to be in the range of 10 to 14 years compared with half-lives of 28 to 33 days in moist soils incubated under anaerobic conditions (2160). DDE is the major degradation product in aerobic soil, and it is believed to be produced predominantly by chemical processes. Under anaerobic conditions DDD is the major metabolite (10).

The bacterial and fungal cometabolism of DDT has been observed in the laboratory and has been suggested to be potentially important in the field as well (2161). In these reactions, bacteria which are not able to use DDT as their sole carbon source grow on non-chlorinated analogues of DDT, but degrade DDT in the process.

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

The above discussion of fate pathways suggests that DDT has low volatility, is very strongly sorbed to soil, and has a high potential for bioaccumulation. These fate characteristics suggest several potential exposure pathways.

The volatilization of DDT from a disposal site and the consequent exposure to workers and residents in the area is expected to be minimal. The potential for ground-water contamination is limited by DDT's strong sorption to soil. However, the persistence of DDT (and its degradation products DDD and DDE) has allowed its transport to drinking water supplies. Mitre (83) reported that DDT was found at 4 of 546 National Priority List sites. In each case, it was detected in surface water, but not in ground-water or air.

The movement of DDT in ground-water or its movement with soil particles may result in discharge to surface water. As a result, ingestion exposures may occur from the use of surface waters as drinking water supplies, and dermal exposures may result from the recreational use of surface waters. More important, however, is the potential for uptake of DDT by aquatic organisms or domestic animals. The high bioconcentration factor and the persistence of DDT (or its metabolites) suggest that ingestion of these organisms can be important exposure pathways from soil/ground-water systems. According to the USEPA more than 99% of DDT exposure is attributed to ingestion of contaminated aquatic organisms, with the remaining 1% attributed to ingestion of contaminated drinking water (2001).

57.2.4 Other Sources of Human Exposure

Peak usage of DDT occurred in the United States in 1963; on January 1, 1973 it was banned for all but essential public-health use (213). It is also banned in Canada, but is used in Mexico and many other countries (2163). DDT may be found in food products imported from these countries, and residuals are still commonly found in the domestic environment. Dicofol, a miticide that contains DDT as an impurity (found at concentrations up to 1.7% of the active ingredient in one study), is still in use in the U.S. -- primarily on cotton, citrus fruits, dry beans, apples and field corn (2164). Nevertheless, there has been a clear decline in the measured concentration of DDT in the environment since it was banned (with a shift towards a larger proportion of DDT breakdown products). Thus, the year in which studies of DDT in the environment or in diet were conducted should always be considered.

Schafer et al. (1241) found in 1969 that more than 33% of over 500 finished drinking water samples from the Mississippi and Missouri Rivers contained DDT, DDE or DDD. DDT was detected in 44% of 5718 ambient water samples taken across the U.S. in the early 1980's; the median concentration was 0.001 μg/L (1417).

Concentrations of DDT in ambient air over the continental U.S. have been low since its use was banned. For measurements taken between 1973 and 1979, the highest reported value was 16 ng/m^3 (mean of monthly average levels for 1972) in the Mississippi Delta, whereas at five other sites across the southern U.S., the highest measured concentration was 0.8 ng/m^3 (2001). By comparison, p,p'-DDT was detected in over 98% of the samples in a 1970-72 survey of 16 states, which had a mean concentration of 5.7 ng/m^3 (2167). Measurements of DDT deposition from the atmosphere indicate that fluxes are 10 to 20% of their peak values in the 1960's.

This suggests that DDT transport from Mexico and Central America is occurring, because DDT in dicofol is insufficient to explain the amounts observed (2163).

The total dietary intake of DDT was estimated to be 0.004 μg/kg body weight for adults in the U.S. in 1979 (1245). For toddlers (2 years old) and infants (6 months old), the total intake was estimated at 0.003 and 0.013 μg/kg body weight, respectively, in 1978. No DDT was detected in diets of either toddlers or infants in 1979 (1244). The major sources of DDT in the adult diet were meat, fish and poultry (>85%), with leafy vegetables, potatoes, and root vegetables making up the rest (1245).

In addition to total diet surveys, many studies of DDT contamination of individual food sources have been conducted. In a 1980-81 national survey of organochlorine residues in freshwater fish, p,p'-DDT was detected in fish from 79.4% of the 107 stations sampled (1800). The maximum wet-weight concentration was 2.69 μg/g and the geometric mean 0.05 μg/g.

DDT is also found in animal fats. In a 1981 study of DDT and related isomers (o,p- and p,p'-DDT, DDE, and DDD) in Ontario, mean concentrations of 12 μg/kg for bovine abdominal fat (197 composite samples from 990 carcasses) and 5 μg/kg for porcine abdominal fat (38 composite samples from 190 carcasses) were found (1248).

Milk is another source of human exposure to DDT. A 1981 survey of bovine milk in Illinois found 13.6% of the samples contained DDT and its analogues at concentrations above the detection limit (1 ppb) with the average concentration being 0.01 ppm (2166). Human milk can also be a source of exposure. A Canadian study of 26 women during the early 1980's found p,p'-DDT concentrations ranging from 3.8 to 5.5 ng/g whole milk over a 98-day lactation period (2165).

57.3 HUMAN HEALTH CONSIDERATIONS

57.3.1 Animal Studies

57.3.1.1 Carcinogenicity

The carcinogenicity of DDT has been extensively studied. IARC (13, 3838) concluded that the evidence for carcinogenicity of DDT is sufficient in animals and inadequate in humans and classified DDT as a 2B carcinogen.

The hepatocarcinogenicity of orally administered DDT has been demonstrated in several strains of mice and shows a dose-response relationship. Tomatis et al. (1944) conducted a two-generation feeding study in CF1 mice. A total of 881 animals were treated with dietary concentrations of 2, 10, 50, or 250 ppm technical DDT for their lifetime. A total of 224 mice were in the control groups. In both the parent and offspring generations there was an excess of mortality from week 60 onwards among

animals receiving 250 ppm. In treated males, the incidence of liver cell tumors ranged from 46 to 80% with 22% in controls. In females, all tumors were found after 100 weeks of age. The excess over controls was significant only in the groups receiving 50 or 250 ppm (13% and 67%, respectively, compared with 3% in controls). In another two-generation study conducted in BALB/c mice, a total of 515 females and 431 males were administered dietary concentrations of 0, 2, 20, or 250 ppm of technical DDT for their lifetime. In males, there was a large number of early deaths due to toxicity and fighting. Liver cell tumors were found in 48% of the high dose group, 5% of the 2 ppm group, none in the 20 ppm group and 2% of controls that survived more than 60 weeks. In females, the survival rates were comparable in all groups. Liver cell tumors were found in none of the control or 2 ppm groups, 0.8% in the 20 ppm group and 59% in the 250 ppm group. No metastases were found (1943). In a study of p,p'-DDT, CF-1 mice were fed diets containing 100 ppm for 110 weeks. Within 26 months, 79% of the males and 96% of the females developed liver tumors compared with 24% and 23% of the male and female controls, respectively (1083).

In the 2-year study, male B6C3F1 mice were administered dietary DDT at time-weighted-average (TWA) doses 22 or 44 ppm, and female mice were administered dietary doses of 87 or 175 ppm for 78 weeks and observed for an additional 15 weeks (2005). Under the conditions of this study, DDT was not carcinogenic in mice.

Rossi et al. (1942) administered to Wistar rats 500 ppm of technical DDT in the diet for their lifetime. The incidence of liver tumors was 35% in males and 56% in females compared with 0% in controls. Tumors were not induced in Osborne-Mendel rats given dietary DDT at doses of 321 or 642 ppm (males) and 210 or 420 ppm (females) for 78 weeks, followed by 35 weeks of observation (2005).

Feeding studies conducted in dogs and monkeys are inconclusive because of the small number of animals used and the inadequate duration of treatment (2002). The bioassays conducted in hamsters were negative. The animals were fed up to 1000 ppm in their diets over their lifetimes (1991, 1941). The reasons for the species differences were investigated by Gingell (1940). The difference between hamsters and mice is probably due to DDE, the principal metabolite of DDT. When both species are maintained on similar DDT-containing diets for a similar time, the levels of DDE in mice is approximately 100 times higher than those in the hamsters, with the rate of formation being much less in the hamster.

Inbred Swiss mice (60 per group; 30 per sex) were treated with technical grade DDT for 80 weeks as follows: Group O was given no DDT (controls); Group A was given 100 ppm of DDT in the diet; Group B was given a dose of 10 mg/kg in olive oil by intubation (treatment interval not given); Group C was given 0.25 mg in olive oil by subcutaneous injection twice per month; Group D was treated topically with 0.25 mg in 0.1 mL of olive oil twice per week (3348). Almost 50% of animals in all groups survived until 80 weeks; therefore sufficient animals survived for analysis of

late-developing lesion. The total number of animals with tumors was significantly increased in the groups treated by dietary administration, intubation, and subcutaneous injection, but the number was not significantly increased in those treated topically. The incidence of lung tumors (tubular papillary adenomas) and lymphomas were significantly increased in mice given DDT in the diet and by intubation; the incidence of liver cell carcinomas were not increased in any group. Other tumors were found, but the incidences were not increased above those of controls.

Several studies have addressed the tumor-promoting effects of DDT. In these studies DDT is administered after a subthreshold dose of a known carcinogen. These studies are summarized below:

Male and female Syrian golden hamsters (48 animals per sex) receiving 1000 ppm of technical-grade DDT (75% p,p'-DDT, 20% o,p'-DDT) in their diets for life did not show evidence of carcinogenicity at any site (3601). Adrenal tumors were found, but the incidence of these tumors, which were also found in high frequency in controls, were not significantly increased.

Hepatocarcinogenesis was studied in male $B_6C_3F_1$ mice treated with DEN and DDT (3839). Groups of mice were given 20 ppm of DEN in their drinking water for 14 weeks, allowed to rest for 4 weeks, and then given 50 ppm of DDT (97.6% purity) in their diet for 25 weeks (total study duration 43 weeks). Controls included untreated mice, mice given DEN without subsequent DDT treatment, mice only given 50 ppm of DDT for 25 weeks without prior DEN treatment, and mice given DDT prior to DEN. Interim sacrificed were conducted at 14, 18, 26, and 34 weeks, with the remaining animals sacrificed at 43 weeks. Liver lesions were quantitated by the number of altered foci, adenomas, and carcinomas. The number of foci in mice receiving DEN alone showed a progressive decrease during the course of the study (4.5 foci/sq.cm. at 26 weeks; 1.27 at 43 weeks); the number of tumors increased such that the final incidence was 8/20 (40%), 2 of which were carcinomas. The incidence of liver tumors was 10.7% in mice receiving no treatment. An insignificant increase in the number of altered foci were found in mice receiving DEN followed by DDT (3.08 at 43 weeks); the incidence of liver tumors was 14/21 (66.7%) at 43 weeks, 10 of which were carcinomas. No liver tumors were found in mice receiving DDT only, and 12.0% of animals receiving DDT prior to DEN developed liver tumors.

DDT was tested for its ability to enhance (or promote) the production of liver tumors in rats given a subcarcinogenic dose of diethylnitrosamine (DEN) (3506). Male Wistar rats were given 500 ppm of DEN in their drinking water for 2 weeks. A dose of 0.1 mL of 1.25% DDT in olive oil was given by gastric intubation, twice weekly for 12 weeks. One-half the animals were killed after 40 weeks and the other half after 52 weeks. No liver tumors were found in the group given DEN alone. One liver tumor was found in one of six rats sacrificed at 40 weeks, and three liver tumors were found in three of eight rats sacrificed at 52 weeks. According to the authors this incidence was not significant. DDT also did not affect the incidence of

liver tumors when given in combination with either phenobarbital and/or polychlorinated biphenyls.

Male Donryu rats were administered 600 ppm of dietary 3'-methyl-4-(dimethyl-amino)-azobenzene for 3 weeks starting at 21 days of age (3361). The animals then received 0, 5, 10, 20, 50, 100, or 500 ppm of dietary DDT continuously until they were sacrificed at 12 or 24 weeks of age. Another group of male Fisher rats were simultaneously administered 100 ppm of the carcinogen and 0, 50, or 100 ppm of DDT in their diet. Potential for hepatocarcinogenesis was measured by the number and size of altered hepatic foci. DDT administered after the carcinogen resulted in a dose-dependent increase in both the numbers and sizes of foci measured at 24 weeks. Only the numbers of foci were measured at 12 weeks and found to be increased.

Male Sprague-Dawley rats were given a control diet or a diet containing 0.02% 2-acetamidophenanthrene (AAP) for 3 weeks starting at 3 weeks of age (3631). After a 10-day rest period, the animals were given a diet containing 0.05% DDT for 45 weeks. The three treatment groups were as follows: AAP followed by DDT, AAP only, and DDT only. The total tumor incidence (all sites combined) was significantly increased from 21% (AAP only) to 68% (AAP plus DDT). The incidence of mammary tumors were increased in DDT-treated animals. The latencies for induction of ear duct gland tumors, which are known to be induced by AAP, and mammary tumors were decreased by as much as 15 and 20 weeks, respectively, in animals receiving DDT after AAP. This study showed that early latency for mammary tumors and possibly ear duct gland tumors is promoted by DDT.

57.3.1.2 Mutagenicity

The genotoxicity of DDT has been extensively studied. DDT has not shown genotoxic activity in any of the bacterial test systems studied. No increased frequency of reversions was observed in the five standard Salmonella typhimurium strains with or without metabolic activation. DDT was also negative in the rec-assay with Bacillus subtilis as well as the host-mediated assay with S. typhimurium and S. marcescens as indicators (2001, 916). Tests with eukaryotic yeast cells, such as Saccharomyces cerevisiae were also negative (2001).

DDT is not genotoxic in the test for sex-linked recessive lethal mutations in Drosophila melanogaster, although DDA, the principle urinary metabolite of DDT in mammals, gave positive results in this test system (1948). Clark (1947) fed DDT to Drosophila adult males and observed an increase in nondisjunction correlated with spermatocyte stages. Conversely, Woodruff et al. (3847) treated Drosophila melanogaster males for 3 days with 25 ppm DDT and did not observe any significant increase in partial or whole sex chromosome loss when these males were mated to repair-deficient females, a strain sensitive to agents that cause genetic perturbations.

In mammalian systems, reported studies are negative or marginally positive. DDT did not interact with DNA and did not produce unscheduled DNA synthesis in

cultured human fibroblasts or in rat, mouse, or hamster hepatocytes (1077, 1946, 1250). In the V79 Chinese hamster cell line, DDT was ineffective in inducing chromosome aberrations and 8-azaguanine forward mutations. Exposure was 30 or 35 μg/mL/24 hr (1996). Both chromosome breaks and exchanges were observed in rat-kangaroo cells treated with p,p'-DDT at 10 μg/mL/24 hr. The p,p'-isomer accounts for most of the toxicity attributed to technical DDT (1999).

Markaryan (3428) reported that DDT injected ip into male mice (0.01 mg/g body weight) induced chromosomal aberrations in bone marrow cells examined 21 hr after treatment. In the rodent dominant lethal assay, Clark (1947) and Epstein et al. (998) reported conflicting results. Clark administered two 50-mg/kg doses of technical DDT orally to male Swiss mice and found that it induced dominant lethal mutations in early spermatid and spermatocyte stages. This was reflected in a reduction in the number of implants per female and an increase in the number of dead implants. The difference was most pronounced 3 to 6 weeks after exposure. Oral doses of 100 mg/kg twice a week for 10 weeks caused a persistent increase in the number of mutations. This treatment caused changes in the morphology of the seminiferous tubules and degeneration of B-type spermatogonia. In contrast to these positive results, Epstein et al. (998) found no significant dominant lethal effects in ICR/Ha mice. The animals were given either single ip doses of 105 or 130 mg/kg or oral doses of 10 to 100 mg/kg daily for 2 days or 15 to 30 mg/kg/day for 5 days.

Palmer et al. (1945) reported weak positive effects using p,p'-DDT in a dominant lethal assay in rats. There was a statistically significant increase in the proportion of females having one or more dead implants after mating during week 3 with males given a single oral dose of 100 mg/kg. No significant effects were found in females mated with males given the same ip dose of DDT Krause et al. (3381) studied spermatogenesis and fetal wastage in male Wistar rats treated with DDT by gavage and observed significant adverse effects on spermatogenesis; fetal wastage was significantly higher in the treated group compared with controls.

57.3.1.3 Teratogenicity, Embryotoxicity and Reproductive Effects

DDT has been reported to exhibit estrogenic properties following in vivo administration to a number of mammalian species. The estrogenic action of technical DDT resides in the o,p'-isomer. To establish whether o,p'-DDT is a typical estrogen, its activity was compared with that of estradiol with respect to a variety of parameters. Welch et al. (1989) found that an ip injection of 1 or 5 mg/kg of technical grade DDT or o,p'-DDT caused a significant increase in the uterine wet weight in immature female rats. Single ip injections of 50 mg/kg of purified o,p'-DDT or technical DDT increased uterine wet weight by 49% and 43%, respectively, 6 hr after the injection. A similar dose of p,p'-DDT caused an increase of 28%, which, although statistically significant, is considered weak activity. Additional parameters used to measure estrogenic activity in vivo include elevation of uterine glycogen and ornithine decarboxylase activity. The minimum dose of o,p'-DDT required to cause an elevation of uterine glycogen in rats was 2.5 mg/kg

while the minimum dose causing induction of ornithine decarboxylase activity was 5 mg/kg (1980).

Although o,p'-DDT exhibits weak estrogenic activity in comparison with estradiol (approximately one-ten thousandth), this effect is significant, because it is known that exposure of female rats to exogenous estrogens may result in long-term toxic effects on the fertility of the mature animal. These effects include polycystic ovaries, anovulation, persistent vaginal estrus, and absence of mating behavior (1981). Gellert et al. (1982) found that female rats given 0.1 mg of o,p'-DDT (no route specified) on the second, third or fourth days of life showed precocious puberty, persistent vaginal estrus and anovulation. It also led to the development of polycystic ovaries and uterine histopathology, including patches of stratified squamous epithelium in the endometrium after puberty. Male neonates were unaffected by similar treatment, but other investigators have reported reproductive effects in male rats exposed to o,p'-DDT. Lee and Visek (1978) reported that male rats injected subcutaneously with 3 mg of o,p'-DDT 1 to 3 hr after birth subsequently showed an abnormal pattern of sexual brain differentiation that was attributed to inhibition of normal action of testosterone on the developing brain. In addition, male rats exposed to technical DDT (no route reported) at 500 mg/kg on the 4th and 5th days of life or at 200 mg/kg/day on days 4 to 23 showed lower fertility than controls. This was associated with degeneration of spermatogenic cells, and a decrease in the number of Leydig's cells. There was also damage to the seminiferous epithelium which was attributed to a reduction in testosterone (1966).

Exposure to DDT through maternal milk has been found to have lasting effects on mice and rats. The reproductive capacity of mice was found to be impaired when their mothers had been given four weekly doses of 50 mg/kg during lactation (1965). Preweaning exposure of neonatal male rats to milk from dams injected with 50 mg of o,p'-DDT daily during postnatal days 1 to 25 caused statistically significant alterations in body weight and in the weights of the testes and ventral prostate (1966).

There is no evidence that DDT is teratogenic at doses ranging from 1 to 50 mg/kg (1991). Embryotoxic and fetotoxic effects have been seen after single or repeated doses. Mice given doses of 1 mg/kg of p,p'-DDT on days 10, 12 and 17 of gestation had morphologic changes in their gonads and a decrease in the fertility of female offspring (1962). A single dose of 25 mg/kg or repeated doses of DDT at 2.5 mg/kg/day (duration not specified) were reported to cause significant blastotoxic, embryotoxic and fetotoxic effects in mice. No additional details were given (1964). Similarly, in rabbits, doses of 50 mg/kg on days 7, 8, and 9 of gestation caused premature delivery, increased resorption and decreased intrauterine growth but no teratogenic effect (1963). Fabro et al. (3206) administered 1 mg/kg/day of DDT orally on gestational days 4, 5, 6, and 7 to rabbits. They observed a slight increase in litter size, but statistically significant decreases in fetal weights and fetal organ weights on gestation day 28.

Multigenerational reproductive studies have been conducted in mice, rats, and dogs. In a six-generation study of mice fed a dietary level of 25 mg/kg, there was no effect on fertility, gestation, viability, lactation, or survival. A dietary level of 100 mg/kg produced a slight reduction in lactation and survival in some generations, but the effect was not progressive. A level of 250 mg/kg caused a high rate of fatalities and was discontinued after the second generation (1961). Ottoboni (1960) found no reproductive disturbances in two generations of Sprague-Dawley rats fed technical DDT at levels as high as 200 ppm but did report a significant increase of ringtail disease (a constriction of the tail followed by spontaneous amputation). No reproductive effects were reported in three generations of dogs fed from weaning at rates of 1, 5, or 10 mg/kg/day (1959).

57.3.1.4 Other Toxicologic Effects

57.3.1.4.1 Short-term Toxicity

DDT acts primarily on the central nervous system. Single large doses or repeated doses can produce hyperexcitability, tremors, ataxia, and epileptiform convulsions. Death from DDT poisoning is usually the result of respiratory arrest. In some species, DDT sensitizes the heart to epinephrine and these animals die from ventricular fibrillation (2000).

After oral administration, there is a latent period of several hours before toxic effects appear; death occurs in about 24 to 72 hr. The latent period after intravenous administration is approximately 5 min. Signs of poisoning reach a maximum level in about 30 minutes. Animals that survive, recover completely and are symptom-free in 18 to 24 hr (2000). There are marked species differences in susceptibility to acute poisoning by the oral route but when given by the intravenous route, the dose and time required for poisoning are similar for a variety of species (59). The oral LD_{50}s in rats, rabbits, and monkeys are 87, 250, and 200 mg/kg, respectively (47); the intravenous LD_{50}s for rats, rabbits, and monkeys are 47, 30 to 41, and 55 mg/kg, respectively (1991). The vehicle in which DDT is administered plays a role in its toxicity. In general, DDT appears to be more toxic when given as a solution in vegetable oil or animal fat than when given in some petroleum fraction (2000). For example, Clayton and Clayton (12) report the following LD_{50}s in Wistar rats (route unspecified): 240 mg/kg in olive oil, 420 mg/kg in corn oil, and 940 mg/kg in propylene glycol or mineral oil.

DDT is retained preferentially in fat. Its retention in other tissues and organs is proportional to the fat content of those organs. After repeated doses, DDT in adipose tissue increases rapidly at first and then more gradually until a steady state is reached. Less DDT is retained at higher doses, because the rate of excretion is relatively greater (2000). Rats with large amounts of DDT in their fat may suffer toxic effects if they are starved or if the DDT in the fat is mobilized. Conversely, increased protein in the diet decreases toxicity due to an increase in the activity of degradative enzymes (2000,1991).

In mammals, including man, DDT is metabolized by two pathways. It is converted to a slight extent to DDE, which does not undergo further biotransformation, but is stored indefinitely in adipose tissues. The major detoxification pathway is via dechlorination to DDD, which is readily degraded to a water soluble metabolite, DDA and is rapidly excreted into the urine (2000).

The acute toxicity of technical DDT appears to be due almost exclusively to the p,p'-isomer. In rats, an oral dose at 150 mg/kg of p,p'-DDT caused severe effects and 50% mortality, whereas o,p'-DDT at the same dose did not cause effects, although the concentrations of both compounds in the brain were about the same at various intervals after dosing. A dose of 3000 mg/kg of o,p'-DDT caused mild to moderate effects and the concentration in the brain was 5 to 9 times greater than that at which p,p'-DDT caused similar effects (1991).

The signs of acute DDT poisoning are similar at oral doses ranging from 100 to 600 mg/kg, but the time onset is delayed, the time-course is extended, and the severity less at low doses (1958). In Wistar rats, a 100 mg/kg dose of p,p'-DDT in corn oil caused no apparent signs of neurotoxicity during a 5-hr observation period. Administration of 200 mg/kg resulted in fine tremors in the 5th hour without any change in body temperature. When a dose of 600 mg/kg was administered, the first signs of intoxication were hyperresponsiveness to sound and tactile stimuli. These effects were observed about 2 hr after dosing. Between 2 and 3 hr, fine tremors were seen in the head and then progressing through the whole body. The tremors gradually became more intense between 4 and 5 hr. At the 5th hour, 50% of the animals had episodes of clonic seizures. Between 5 and 7.5 hr, clonic convulsions lasting 5 seconds occurred in all rats. All animals died 5.5 to 7.5 hr after a series of clonic convulsions or very violent tremors. Four of six animals had paralysis of their hind legs. A dose of 400 mg/kg caused similar effects but the neurotoxic signs were less pronounced (1958). In addition, marked hyperthermia and sympathetic discharge were observed to accompany the tremors and convulsions.

Tilson et al. (3718) demonstrated that adult male Fischer-344 rats given p,p'-DDT (0, 25, 50, or 100 mg/kg body weight) by gavage 3 hr prior to testing in a two-way shuttle box did not affect the number of passive avoidance responses, but 100 mg/kg did increase the latency required to make the response and significantly decreased the number of responses during the 10- to 20-sec intratrial period. In tests on passive avoidance DDT given prior to training did not significantly affect learning nor did it have an affect on retention of passive avoidance when the animals were again tested 7 days after dosing. The response of animals receiving DDT immediately after training and tested 7 days later was also not significantly affected by DDT. Tilson et al. (3718) reported that their results were in agreement with those of Uppal et al. (3758) who demonstrated that DDT did not affect the response to a pole-climb avoidance to electric shock, but it did tend to increase the avoidance latencies. Rats trained in a step-through passive avoidance after administering DDT had learning impairment when tested 24 or 48 hr after treatment (dose not reported); retention

was impaired in animals trained 24 hr after treatment with 95 mg/kg body weight of DDT and tested 48 hr later (3757)

Kitchen and Brown (3362) reported that two doses of p,p'-DDT (99 plus% purity) given 22, 66, 132, or 195 mg/kg body weight given orally (corn oil vehicle) to rats 21 and 4 hr prior to sacrifice did not cause significant DNA damage, changes in ornithine decarboxylase activity, or hepatic glutathione content or serum alanine aminotransferase activity (indicative of liver damage). The hepatic microsomal cytochrome P-450 content was significantly increased (28%) in rats given 66 mg/kg, but not at the other doses. The same parameters measured in mice treated with doses of 22 or 175 mg/kg body weight were not significantly affected.

Low doses of dietary DDT for 1 to 2 weeks caused induction of liver microsomal enzymes. A single oral dose of 1 mg/kg DDT or 0.5 mg/kg/day for 14 days caused the same effect (1991).

Few DDT inhalation studies have been conducted. "Several species" of animals exposed to levels of approximately 1000 ppm w/v in air for 2 hr daily showed signs of intoxication, and deaths occurred after 4-10 exposures (12). After two 7-hr exposure periods of 0.13 mg/L DDT (Neocid®) on day 1 and 0.4 mg/L on day 2, a rhesus monkey showed no signs of intoxication. Six rats exposed concurrently on the first day showed mild tremors. Six other rats exposed on the second day experienced tremors which lasted for 3 days. All rats survived. No ill effects were seen in a rabbit, a cat or a guinea pig exposed to levels of 0.2, 0.3 and 0.45 mg/L, 7 hr/day for 3 days (12).

The dermal toxicity of DDT is greatly dependent on the vehicle in which it is dispersed. In rats, DDT powder or a suspension in water has been reported to have an LD_{50} of 1,000,000 mg/kg. The dermal LD_{50} of DDT in an oil solution ranges from 250 to 3000 mg/kg (1991).

DDT has not been shown to cause ocular damage to animals. A 4% solution of pure DDT dissolved in purified kerosene tested on rabbit eyes had no effect (19).

57.3.1.4.2 Chronic Toxicity

In animals given repeated doses of DDT, pathological lesions are seen in the liver and kidneys (17).

Histopathologic changes were observed in the livers of rats exposed to dietary levels as low as 5 ppm for 4 to 6 months (1991). When rats were fed a diet containing 600 to 800 ppm DDT for 2 years, there was an increase in kidney weight, and the animals had moderately severe tremors, particularly during the early months. Concentrations of 400 ppm or above produced an abnormally high mortality rate and an increase in liver weight. Some animals had tremors. Tremors were rarely seen at

200 ppm but moderate liver damage was seen at concentrations of 200 ppm and above. At 100 ppm there were slight indications of liver damage (12).

In a study conducted by NCI (2005), female Osborne-Mendel rats receiving 630 ppm of dietary technical-grade p,p'-DDT exhibited CNS stimulation characterized by hyperactivity, body tremors, and a hunched appearance starting at week 5 of treatment. By week 26, 90% of the females, 40% of males receiving 840 to 1000 ppm of DDT, and 8% of females receiving 315 ppm showed signs of neurotoxicity. A decrease in dosage resulted in a decrease in neurotoxicity, but the signs reappeared as DDT intake was continued, presumably due to accumulation of DDT in the body.

Male and female Syrian golden hamsters receiving 1000 ppm of dietary technical-grade DDT, containing 70 to 75% p,p'-DDT and 20% o,p'-DDT, for life did not exhibit neurotoxic signs during the course of treatment (3601). These results indicated that hamsters are more resistant to both acute and chronic toxic effects of DDT. Rossi et al. (3601) reported that amyloidosis of the liver, kidney, and adrenals observed in 90% of control females and 64% of control males was reduced to 24% in female hamsters receiving DDT.

Monkeys develop liver histopathology only with exposure to relatively high dosage levels. No liver changes occurred in monkeys fed dietary levels of 200 ppm or less for periods of up to 7.5 years. One of six animals fed 5000 ppm developed the cytoplasmic inclusions that are characteristic of chlorinated hydrocarbon poisoning (1991). This lack of toxicity may be due to the inability of monkeys to convert DDT to DDE since no DDE was detected in the fat of these animals (1991,2001).

Mild to moderate morphological changes have been reported in the kidneys of animals given repeated doses of DDT. These include fatty degeneration, necrosis, calcification or slight brown pigmentation of the convoluted tubular epithelium, but a complete absence of kidney effects has been reported in other studies conducted in the same laboratories (2000).

No-effect-levels which have been reported are: 12.5 ppm diet in rats exposed for 18 to 24 months and 30 ppm diet in dogs exposed for a period of 15.7 months (12).

57.3.2 Human and Epidemiologic Studies

57.3.2.1 Short-term Toxicologic Effects

Signs of DDT poisoning in man are similar to those observed in animals. The earliest symptom of poisoning is hyperesthesia (i.e., abnormally increased sensitivity) of the mouth and lower part of the face which is followed by paresthesia (i.e., burning or prickling sensation) and tremor of the extremities, confusion, malaise, headache, fatigue and delayed vomiting. Human poisoning has been reported to have occurred only by ingestion. In general, symptoms occur as soon as 30 minutes after a large dose or as late as 6 hr after a small dose. In acute exposures, recovery is

usually complete or well advanced in 24 hr. In severe cases, recovery may take a week of more (1991,2001).

The human oral LD_{50} has been estimated to be approximately 250 mg/kg (1991). A single dose of 10 mg/kg produced illness in some subjects but no vomiting or convulsions occurred. When the dosage was 16 mg/kg or greater, convulsions occurred frequently. Generally, smaller doses did not produce illness, although a dose of 6 mg/kg produced perspiration, headache and nausea in one man. In rare cases, a dosage as high as 20 mg/kg might be taken without effect and doses as high as 285 mg/kg have been taken without fatal result; however, doses as high as those in the latter case lead to immediate vomiting so that the amount actually retained cannot accurately be determined (2000).

Uncomplicated DDT poisoning has been fatal in some cases but none of these has been reported in detail. Death has been caused more frequently by DDT solutions, but in most cases the symptoms were predominantly those of the solvent. NIOSH cites four deaths after suicidal ingestion of DDT but no details as to dose, vehicle or symptoms were reported (1991).

Hepatic and cardiac involvement are mentioned in only a small portion of the reported cases. In three men who ingested 5000 to 6000 mg (about 71 to 86 mg/kg), slight jaundice appeared after 4 to 5 days and lasted from 3 to 4 days. Palpitations, tachycardia, and "irregular heart action" have been noted in some cases. It is not known whether cardiac arrhythmia might be a possible cause of death in acute poisoning, as it is in some species of laboratory animals (59,1991).

The kinetics of DDT in humans has been extensively studied by Morgan and Roan (1994). DDT is stored in fat at about ten times the concentration of intake. Conversion of DDT to DDE is very slow, occurring at a rate of 20% over 3 years. DDT is eliminated from the body through reduction to DDD and conversion to DDA with a biologic half-life of about 1 year. DDE is eliminated more slowly with a biologic half-life of about 8 years.

Dermal exposure to DDT has not been associated with any illness or irritation. When small pads impregnated with either powdered DDT or 50% DDT solution were applied to the inner surface of the forearm, no effects were seen (2000).

DDT has not been demonstrated to have a selective toxic effect on the eye. Pure DDT dissolved in purified kerosene, which was tested in a concentration of 0.01%, caused no discomfort or irritation. Ocular irritation has followed contamination of the eye by powders containing DDT (19).

57.3.2.2 Chronic Toxicologic Effects

No clinical syndrome of chronic DDT intoxication is recognized in man (17). A number of small-scale studies involving controlled exposure of volunteers to technical DDT have been conducted.

Hayes et al. (1950, 1951) conducted two chronic exposure studies with volunteers given DDT orally. In the first study, 51 volunteers received 0, 3.5, or 35 mg of DDT per person daily for periods ranging up to 18 months. None complained of any symptoms or showed signs of illness in any of the physical or laboratory tests that were conducted. In a second study, 24 volunteers ingesting the same doses for 21.5 months were observed for an additional 25.5 months, and 6 were followed for 5 years. There was no clinical evidence of adverse effects in any of the volunteers.

In another study reported by Morgan and Roan (1994), four volunteers were given oral doses of technical DDT at 10 or 20 mg/day for 81 to 183 days. A battery of hematologic and biochemical tests conducted before, during, and after exposure detected no abnormalities.

DDT has been used on an experimental basis in an attempt to decrease serum bilirubin levels in patients with jaundice due to liver cirrhosis. Doses ranging from 0.3 to 3.0 mg/kg/day of p,p'-DDT have been administered for periods of up to 7 months with no evidence of adverse effects (1949).

Rabello et al. (1954) suggested that exposure to DDT may cause chromatid lesions. When they studied the lymphocytes of 33 workers in 3 plants in direct contact with DDT, they found that the frequency of chromatid aberrations was not significantly higher than that in 10 control subjects, or in 25 workers in the same plants indirectly exposed to DDT. However, five of the subjects exposed indirectly to DDT showed significant levels of DDT in the blood. When these workers were included in the directly exposed group, there was a significant increase in chromatid aberrations compared to the controls. The frequency of aberrations was 12% in the exposed group, 8.8% in the indirectly exposed group, and 2.2% in a general population control group. Corresponding blood plasma levels were 0.993 μg/mL, 0.275 μg/mL, and 0.03 μg/mL, respectively.

Occupational exposure to DDT is almost exclusively through the respiratory and dermal routes. In some cases when the particles of insecticidal dusts, wettable powders, and sprays are too large to reach the lower respiratory tract, the inhaled particles are carried to the pharynx and eventually swallowed. Dermal exposure to DDT may be high in some occupational situations, but the effect is minimal because the compound is so poorly absorbed (2000).

Early studies of workers exposed to DDT did not reveal any illness attributable to DDT or their formulations. Ortelee (1956) carried out clinical and laboratory examinations of 40 workers, all of whom were exposed to DDT. Some were also

exposed to other pesticides. The men had heavy exposure to DDT for 0.4 to 6.5 years. The average amounts of DDT absorbed were estimated to range from 14 to 42 mg/man/day. Upon completion of neurologic examinations and liver function tests, no abnormalities were found that could be attributed to DDT exposure. There were a few cases of minor eye and skin irritation. Another study of occupationally exposed workers also found no effects in those employed 11 to 19 years. Daily intake was estimated to be 17.5 to 18 mg/man (1955).

The largest study of occupationally exposed workers was conducted by the World Health Organization on DDT spraymen in Brazil and India. In Brazil, periodic clinical examinations were made of 279 spraymen exposed from 6 to 13 years and 406 controls. In the first examination, some minor neurological changes were seen in the spraymen but these were not confirmed in subsequent examinations. During the 3-year study period, a survey of illnesses requiring medical care during the 6 months preceding each periodic medical examination failed to demonstrate any differences between control and exposed groups. The blood level of DDT in the spraymen was about three times that of the control group. In India, the blood levels of 144 spraymen were 7.5 to 15 times higher than those of the controls. In the spraymen, knee reflexes were brisker, slight tremors were present and a timed Romberg test (differentiates between peripheral and cerebellar ataxia) was more poorly performed by spraymen. Twenty men were then examined by a neurologist who concluded that the initial differences were not real or that the tests had returned to normal in the few months between examinations. The signs were not dose-related since they showed no correlation with DDT serum levels (1953).

There are some epidemiology studies on the carcinogenicity of DDT, but IARC concluded that there is inadequate evidence for carcinogenicity in humans (1250). In three studies cited by NIOSH (1991) residue levels of DDT and DDE were significantly higher in tissues taken at autopsy from persons dying of cancer than those dying of other causes. No association was found in four other studies. Both Laws (1955) and Ortelee (1956) reported no evidence of cancer in the workers in their studies. Ditraglia et al. (1325) found no excess in overall mortality among workers exposed to DDT. They found a consistent increase in cancer mortality with an increase in the latency period; however, the numbers involved in the analysis were small. Four of six malignant neoplasms were in the respiratory system.

Wong et al. (1952) conducted a prospective mortality study on 3579 white male workers with potential exposures to various chemicals including DDT. There were 112 deaths among 740 employees identified as having DDT exposure. No significant increases in standard mortality ratios (SMRs) were noted for cause-specific mortalities among those exposed to DDT. A nonsignificant increase in the SMR for respiratory cancer was observed. A case-control study, including 111 individuals with chronic lymphatic leukemia and 431 controls, was conducted to identify risk factors (various types of exposures including chemicals) (3218). Exposure to DDT was associated with a crude odds ratio of 6.1 (range = 1.9 to 19.0). Cases and controls were not matched for ages (cases were older) or sex distribution (cases had a higher proportion

of males). Analysis of the data involving application of the Miettinen confounder score technique, based on multiple linear regression showed that DDT was still a strong determinant of risk (Mantel-Haenzel rate ratio = 6.0; range = 1.5 to 23). Another case-control study showed an increased risk for non-Hodgkins lymphoma associated with occupational exposure to organochlorine insecticides, such as DDT (3221). The odds ratio was 1.82 (range = 1.04 to 3.02). No increase in risk was noted for soft-tissue sarcomas, which had an odds ratio of 1.10 (range = 0.4 to 3.2). Eriksson et al. (3204), also conducted a case-control study and showed that the risk of developing soft-tissue sarcomas was not associated with exposure to DDT.

Grant (19) reported 1 case of chronic superficial punctate keratitis associated with fatal poisoning from long exposure to DDT dust but it is probable that it was a hypersensitivity reaction or that other constituents of the dust were responsible.

57.3.3 Levels of Concern

The USEPA (355) specified an ambient water quality criterion of zero for DDT, based on induction of liver carcinoma in mice. The concentrations of DDT in water associated with incremental lifetime cancer risks of 10^{-5}, 10^{-6}, 10^{-7} are 0.24, 0.024, and 0.0024 ng/L, respectively, for ingesting both water and contaminated aquatic organisms. 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 DDT. 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 0.24 ng/L of DDT would be expected to cause no more than one case of cancer above the normal background incidence for every 100,000 people exposed. The incremental lifetime cancer risks for consumption of aquatic organisms only are the same, 0.24, 0.024, and 0.0024 ng/L, because of the extremely high bioconcentration factor (2001).

Based on the geometric mean of the potency factors derived from several studies, a oral potency factor of 0.34 $(mg/kg/day)^{-1}$ was derived for DDT (3744). These studies were conducted in both rats and mice using both male and females, and the end point for each study was benign liver tumors. The drinking water unit risk was reported as $9.7 \times 10^{-6}/\mu g/L$. The inhalation potency factor was also 0.34 $(mg/kg/day)^{-1}$ and the inhalation unit risk was $9.7 \times 10^{-5}/\mu g/m^3$ (3328).

IARC (1250) lists DDT in category 2B (sufficient evidence of animal carcinogenicity and inadequate evidence for carcinogenicity in humans) in its weight-of-evidence ranking for potential carcinogens.

The WHO (666) recommends a level of 1 $\mu g/L$ for DDT in drinking water.

OSHA (3539) currently permits an 8-hr time-weighted average of 1 mg/m^3 for DDT with a notation of possible skin absorption. The ACGIH (3005) also has set 1 mg/m^3 as a TWA for DDT.

57.3.4 Hazard Assessment

Numerous carcinogenicity studies have been conducted for DDT in various animal species and, including mice, rats, hamsters, dogs, and monkeys. Some of these studies showed positive results and some showed negative results. The overall qualitative assessment of DDT in animals studies is that there is sufficient evidence that DDT is carcinogenic in animals, and it is classified as a B2 carcinogen by the USEPA (3328). IARC (1250) considers DDT carcinogenic in animals and classifies it as a group 2B compound.

Data on the activity of DDT are inadequate to define its genotoxic capabilities. There are conflicting data regarding DDT-induced sex-linked recessive lethal mutations in Drosophila melanogaster (1948, 1947, 3847), but DDT was not mutagenic in bacterial or yeast systems (2001, 916) or in the majority of mammalian systems tested (1077, 1946, 1250, 1966). Chromosome breaks and exchanges were reported in rat-kangaroo cells treated in culture with p,p'-DDT (1999), whereas conflicting results were reported in mice in the dominant lethal assay (1947, 998, 1945, 3381).

DDT is not teratogenic (1991); however it is embryotoxic and fetotoxic in rats, mice and rabbits (1962, 1964, 1963). Multigeneration reproductive studies showed no significant adverse effects in mice, rats and dogs (1961, 1960, 1959). DDT exhibits weak estrogenic activity that can result in long-term effects on fertility (1981, 1982, 1966).

Marked species-variability exists in animals acutely exposed to DDT. Oral LD_{50} values in the rat, mouse, dog, guinea pig, monkey, and rabbit range from 87 to 250 mg/kg (3933). DDT appears to be more toxic as a solution in vegetable oil or animal fat than when given in petroleum fractions (2000). When ingested, DDT acts primarily on the CNS causing hyperexcitability, tremors, ataxia, and epileptiform convulsions (1958, 1957, 2000). Death usually results from respiratory arrest or ventricular fibrillation (2000). Short-term low level inhalation of DDT cause no ill effects in rabbits, cats, guinea pigs or monkeys; exposed rats showed mild tremor activity (12). The dermal toxicity of DDT is dependent upon the vehicle in which it is suspended. In rats, the dermal LD_{50} of DDT powder suspended in water is 1,000,000 mg/kg, while the dermal LD_{50} values of DDT suspended in oil solutions ranges from 250 to 3000 mg/kg (1991). No ocular damage has been reported in animal studies (19).

Long-term dietary exposure to DDT resulted in liver and kidney damage in a number of animals (12,17). The no-effect level for the rat is 1.5 ppm in the diet for 18-24 months and for the dog is 30 ppm in the diet for 15.7 months (12).

In man, poisoning generally produces perspiration, headache, and nausea at low levels, followed by vomiting and convulsions at higher doses (2000). The human oral LD_{50} value has been estimated to be 250 mg/kg (1991). Liver and heart involvement

may result in jaundice, palpitations, tachycardia and "irregular heart action" (59,1991).

Dermal contact with DDT does not appear to cause irritation or systemic effects (2000). Ocular irritation has been reported following contamination of the eye with powders containing DDT; however, 0.01% solution of pure DDT instilled into the eye produced no effect (19).

No chronic toxicity was noted in humans after long-term ingestion of low doses of DDT (1950, 1951, 1994, 1949). Conflicting reports exist on the correlation of high tissue DDT and DDE levels and the incidence of cancer, particularly respiratory cancer (1991, 1955, 1956, 1325, 1952), but there is no evidence that DDT is a significant carcinogenic risk to humans.

One study reported that long-term occupational exposure may lead to chromosome lesions (1954). The only other long-term effects associated with occupational exposure to DDT were minor skin and eye irritation (1955, 1953). One questionable case of chronic superficial punctate keratitis was associated with fatal DDT poisoning (19).

57.4 SAMPLING AND ANALYSIS CONSIDERATIONS

Determination of DDT 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 DDT, 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; DDT is then detected with an electron capture detector or halogen specific detector (Methods 608 and 8080) or a mass spectrometer (Methods 625 and 8250).

Method 8080 has been recently evaluated (3405) for the simultaneous determination of chlorinated pesticides (CPs) and polychlorinated biphenyls (PCBs). It was determined that CPs and PCBs were not separated using the recommended column adsorption cleanup step which could lead to inaccurate results. Replacing the florosil column with silica gel and the packed analytical column with a capillary column eliminated the problem. Trapping and thermal desorption methods using

Tenax cartridges have also been used to determine pesticides in aqueous samples (3832). The accuracy and precision of automated interpretation of mass spectral data have been evaluated (3017).

It should be noted that it may be necessary to cleanup sample extracts to remove impurities that interfer with the final analysis. Gel permeation chromatography (GPC) (Method 3640) (63), column adsorption chroamtography (Method 3620 (63), or various techniques for removing sulfur (Method 3660) (63) may be used in this case prior to GC/electron capture or GC/mass spectrometric analysis. Interferences from phthalates may be minimized by avoiding sample contact with all plastic materials. The microcoulometric and electrolytic conductivity detectors which are more selective may also be used for determinations and will eliminate interferences from phthalate esters.

The EPA procedures recommended for DDT 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 DDT detection limits that can be obtained in wastewaters and nonaqueous 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	Nonaqueous Detection Limit
0.12 µg/L (Method 8080)	8 µg/kg (Method 8080 with GPC cleanup)
47 µg/L (Method 8250)	3.1 µg/g (Method 8250 with GPC cleanup)
0.012 µg/L (Method 608)	
4.7 µg/L (Method 8250)	

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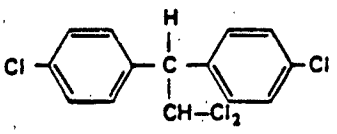
3993. Council of European Communities Directive. Proposal for a Council Regulation Concerning Export from an Import into the Community of Certain Dangerous Chemicals (amended 22 June 1988. OJ L 155).

COMMON SYNONYMS:	CAS REG.NO.: 72-54-8 FORMULA: $C_{14}H_{10}Cl_4$ NIOSH NO: KI0700000 STRUCTURE: 	AIR W/V CONVERSION FACTOR at 25°C 13.08 mg/m³ ≈ 1 ppm; 0.076 ppm ≈ 1 mg/m³. MOLECULAR WEIGHT: 320.05
1,1'-(2,2-dichloro ethylidene)bis (4-chloro)benzene DDD dichlorodiphenyl-dichloroethane TDE tetrachloro diphenylethane p p'-DDD		

REACTIVITY	One source simply reports that DDD is incompatible with alkalies. For general compatibility classification purposes, DDD is considered to be a halogenated organic compound. Reactions of halogenated organic materials with cyanides, mercaptans or other organic sulfides typically generate heat, while those with 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 aluminium, zinc or magnesium, organic peroxides or hydroperoxides, strong oxidizing agents, or strong reducing agents typically result in heat generation and explosions and/or fires (23, 511).

PHYSICO-CHEMICAL DATA	• Physical State: Solid, crystalline (at 20°C)	(23)
	• Color: Colorless	(23)
	• Odor: No data	
	• Odor Threshold: No data	
	• Density: No data	
	• Freeze/Melt Point: 112.00°C	(67)
	• Boiling Point: 109.00°C	(59)
	• Flash Point: Combustible solid	(23,60)
	• Flammable Limits: No data	
	• Autoignition Temp.: No data	
	• Vapor Pressure: 1.30E-09 to 2.50E-09 mm Hg (at 30°C)	(10)

PHYSICO-CHEMICAL DATA (Cont.)	• Satd. Conc. in Air: 2.30E-05 to 4.4000E-05 mg/m³ (at 20°C) (1219) • Solubility in Water: 1.60E-01 mg/L (at 24°C) (67) • Viscosity: No data • Surface Tension: No data • Log (Octanol-Water Partition Coeff.): 5.56 (2147) • Soil Adsorp. Coeff.: 2.40E+05 (2147) • Henry's Law Const.: 3.10E-05 atm · m³/mol (at 25°C) (2269) • Bioconc. Factor: 1.74E+04 (estim) (659)
PERSISTENCE IN THE SOIL-WATER SYSTEM	DDD is expected to be relatively immobile in the soil/ground-water system due to its strong sorption properties. Volatilization may be an important loss pathway from aquatic systems but is much slower in soils. Biodegradation is expected to be the predominant fate process in soils, as DDD is considered to be more easily degradable than DDT or DDE.
PATHWAYS OF EXPOSURE	The primary pathway of concern from the soil/ground-water system is the migration of DDD to ground water drinking water supplies. However, this is not likely to occur in most situations because of DDD's low solubility and strong tendency to sorb to soil. Uptake by crops from soil or bioaccumulation by aquatic organisms may be important exposure pathways in some instances.

HEALTH HAZARD DATA	Signs and Symptoms of Short-term Human Exposure: (1990) Adverse effects associated with o,p'-DDD ingestion include nausea, vomiting, CNS depression, skin rash and blurred vision. Acute Toxicity Studies: (3504) SKIN: LD_{50} 1200 mg/kg Rabbit ORAL: LD_{50} 113 mg/kg Rat Long-Term Effects: Direct or indirect effect on adrenal steroid hormone metabolism in humans. Pregnancy/Neonate Data: Not teratogenic in mice, o,p'-DDD fetotoxic, but p,p'-DDD is not. Genotoxicity Data: Limited conflicting data Carcinogenicity Classification: IARC - None assigned NTP - Negative evidence in mice and female rats, equivocal in male rats EPA - Group B2 (probable human carcinogen; sufficient evidence in animals and inadequate evidence in humans)

HANDLING PRECAUTIONS	There are no specific handling precautions for DDD. Handle in the same manner as DDT (see Record 57).

ENVIRONMENTAL AND OCCUPATIONAL STANDARDS AND CRITERIA

AIR EXPOSURE LIMITS:

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

Criteria
- NIOSH IDLH (30-min): None established
- NIOSH REL: No data
- ACGIH TLV® (8-hr TWA): None established
- ACGIH STEL (15-min TWA): None established

WATER EXPOSURE LIMITS:

Drinking Water Standards
None established

EPA Health Advisories and Cancer Risk Levels (3744)
No Health Advisories
- 1E-04 Cancer risk: 10 μg/L

WHO Drinking Water Guideline
No information available.

EPA Ambient Water Quality Criteria
- Human Health (355)
  - No criterion established due to insufficient data.

- Aquatic Life (355)
  - Freshwater species
    acute toxicity:
    no criterion, but lowest effect level occurs at 0.6 μg/L.

    chronic toxicity:
    no criterion established due to insufficient data.

  - Saltwater species
    acute toxicity:
    no criterion, but lowest effect level occurs at 3.6 μg/L.

    chronic toxicity:
    no criterion established due to insufficient data.

REFERENCE DOSES:
No reference dose available.

REGULATORY STATUS (as of 01-MAR-89)

Promulgated Regulations

- Federal Programs

Clean Water Act (CWA)

DDD is designated a hazardous substance. It has a reportable quantity (RQ) of 0.454 kg (347, 3764). It is also listed as a toxic pollutant, subject to general pretreatment standards for new and existing sources, and effluent standards and guidelines (351, 3763). Under the toxic pollutant effluent standards, DDD (a DDT metabolite) is prohibited in any discharge from DDT manufacturers or formulaters. The ambient water criterion for DDT and its isomers in navigable waters is 0.001 µg/L. This standard applies to all discharges of process wastes from manufacturing and storage areas subject to direct contamination by DDT and its isomers through stormwater runoff or routine cleanup, and cleanup of spills (805). Effluent limitations specific to this chemical have been set in the following point source categories: electroplating (3767), steam electric power generating (3802), and metal finishing (3768). The limitations set are for the amount of total toxic organics (TTO) discharge permitted per day. DDD is included when calculating the TTO. Effluent limitations in the pesticide chemicals manufacturing point source category are set at 0.010 kg/1000 kg of organic pesticide chemicals (including DDD) maximum for any one day (891).

Safe Drinking Water Act (SDWA)

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

Resource Conservation and Recovery Act (RCRA)

DDD is identified as a hazardous waste (U060) and listed as a hazardous waste constituent (3783, 3784). DDD is included on EPA's ground-water monitoring list. EPA requires that all hazardous waste treatment, storage, and disposal facilities monitor their ground-water for chemicals on this list when suspected contamination is first detected and annually thereafter (3775). Effective July 8, 1987, the land disposal of untreated hazardous wastes that contain halogenated organic compounds in total concentrations greater than or equal to 1000 mg/kg will be prohibited. Effective August 8, 1988, underground injection into deep wells of these wastes is prohibited. Certain variances exist until May, 1990 for land and injection well disposal of some wastewaters and nonwastewaters for which Best Demonstrated Available Technology (BDAT) treatment standards have not been promulgated by EPA (3786). EPA requires 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 (3782).

Comprehensive Environmental Response Compensation and Liability Act (CERCLA)
DDD is designated a hazardous substance under CERCLA. It has a reportable quantity limit of 0.454 kg. Reportable quantities have also been issued for RCRA hazardous waste streams containing DDD but these depend upon the concentrations of the chemicals in the waste stream (3766).

Federal Insecticide, Fungicide and Rodenticide (FIFRA)
Action levels for the sum of DDT, DDE and DDD residues in agricultural commodities range from 0.05 to 0.5 ppm (889). As of January 1, 1989, EPA is canceling registrations and denying applications of all dicofol products containing greater than 0.1% of DDT and related impurities (2268).

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 DDT shall not exceed an 8-hour time-weighted average (TWA) of 1 mg/m^3. DDD is a DDT metabolite (3539).

Hazardous Materials Transportation Act (HMTA)
The Department of Transportation has designated DDT a hazardous substance with a reportable quantity of 0.454 kg, subject to requirements for packaging, labeling, and transportation (3180).

Food, Drug and Cosmetic Act (FDCA)
The following action levels are recommended for the sum of DDT, DDE and DDD residues:

- 0.1 ppm in dried hops
- 1.25 ppm in manufactured dairy products
- 1.0 ppm in peppermint oil, spearmint oil and in crude soybean oil (888)

- State Water Programs

  ALL STATES

  All states have adopted EPA Ambient Water Quality Criteria and NPDWRs (see Water Exposure Limits section) as their promulgated state regulations, either by narrative reference or by relisting the specific numeric criteria. These states have promulgated additional or more stringent criteria:

  DISTRICT OF COLUMBIA

  The District of Columbia has set a human health criterion of 0 μg/L for DDT and its isomers in the public water supplies (3828).

  LOUISIANA

  Louisiana has a water quality criterion of 0.6 μg/L for DDD in fresh waters and 3.6 μg/L in marine waters (3406).

  NEW YORK

  New York has an MCL of 5 μg/L for DDD in drinking water, an ambient water quality standard of 0.01 μg/L for surface waters classed for drinking water supply, and requires DDD to be nondetectable in ground-water (3501).

Proposed Regulations

- Federal Programs

  No proposed regulations are pending.

- State Water Programs

  No proposed regulations are pending. Most states are in the process of revising their water programs and proposing changes in their regulations which will follow EPA's changes when they become final. Contact with the state officer is advised. Changes are projected for 1989-90 (3683).

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 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, oganohalogen 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 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 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 p,p'-DDT is 10 μg/L. For total DDT (including isomers) the quality objective is 25 μg/L. The emission standard of DDT and isomers for DDT production is 0.7 mg/L water discharged as a monthly average and 1.3 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.

58.1 MAJOR USES

DDD is not produced commercially in the U.S. and no longer has any registered uses (1118). It was formerly used for controlling pests on vegetables and tobacco (59). The pure o,p′-DDD isomer, specially synthesized, has been used for the treatment of adrenocortical carcinomas and for the over production of adrenal cortical steroids under the generic name, mitotane (2002).

58.2 ENVIRONMENTAL FATE AND EXPOSURE PATHWAYS

58.2.1 Transport in Soil/Ground-water Systems

58.2.1.1 Overview

Although it is no longer manufactured commercially, DDD is still found as an impurity in the pesticide DDT and the miticide dicofol. It is also the major breakdown product of DDT under anaerobic conditions. The p,p′ isomer of DDD is the third largest component of the technical DDT product after the two DDT isomers, accounting for >4% of the mixture (2145). It is present in somewhat lower concentrations in dicofol. In one study of several dicofol products (2164), DDD was present in amounts ranging from 0.1 to 2.5% of the amount of dicofol. Like DDT, DDD is expected to be highly immobile in the soil/ground-water environment when present at low dissolved concentrations. Bulk quantities of DDD dissolved in an organic solvent could be transported through the unsaturated zone as a result of a spill or the improper disposal of excess formulations. However, the extremely low solubility of DDD and its strong tendency to sorb to soil organic carbon results in a very slow transport rate in soils. In general, transport pathways can be assessed by using an equilibrium partitioning model as shown in Table 58-1. These calculations predict the partitioning of low soil concentrations of DDD among soil particles, soil water, and soil air. Due to its strong sorption to soil, virtually all of the DDD partitions to the soil particles of unsaturated top soil and negligible amounts to the soil air or water. Even in saturated deep soil, which is assumed to contain no soil air, and a smaller organic carbon fraction, almost all of the DDD is retained on the soil.

58.2.1.2 Sorption on Soils

DDD, like DDT, is characterized by a strong tendency to sorb to soil organic carbon. Although only one measured K_{oc} value for DDD was found (log K_{oc} = 5.38) (2147), it is consistent with the value obtained for DDT, as would be expected based on the similarity of their structures and their octanol:water partition coefficients (DDD log K_{ow} = 5.56) (2147). As with all neutral organic chemicals, the extent of DDD sorption is proportional to the soil organic carbon content. In soils with little

TABLE 58-1
EQUILIBRIUM PARTITIONING CALCULATIONS FOR DDD
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]	100	2.2E-03	8.3E-06
Saturated deep soil[d]	99.9	9.9E-02	-

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) Soil sorption coefficient: K_{oc} = 240,000 (2147).
c) Henry's law constant taken as 3.1E-05 atm · m³/mol at 25°C (2269).
d) Used sorption coefficient $K_p = 0.001 \times K_{oc}$.

organic carbon (e.g., clays) the extent of sorption may also depend upon such soil properties as surface area, cation exchange capacity, and degree of hydration.

The sorption of DDD to soils is lessened; thus, its mobility is enhanced by the presence of dissolved organic matter in solution. As described in Chapter 57, Section 57.2, the apparent solubility of DDT was increased several times in solutions containing humic and fulvic acids. Because the sorption behavior of DDD is expected to be much like that of DDT, its mobility in natural waters may be several times greater than predicted (though probably still small) if dissolved organic matter is present. This may be especially important in waters containing large concentrations of dissolved organic matter, such as swamps and bogs.

58.2.1.3 Volatilization from Soils

The vapor pressures of the p,p′- and o,p′-isomers of DDD at 30°C have been measured as 1.3E-09 and 2.5E-09 atm, respectively (10). The Henry's law constant estimated by use of the average vapor pressure of the two isomers and an aqueous solubility of 20 ppb (10) is 3.1E-05 atm · m³/mol (2269). This value is almost identical to that for DDT and roughly an order of magnitude less than that for DDE.

Experimental evidence indicates that DDD volatilization from water occurs at about one-third the rate for DDT (10), which may seem at odds with the similar estimates for the Henry's law constants for these two compounds. Given the uncertainties involved in measuring both the aqueous solubilities and the vapor pressures of these compounds, from which H is estimated, the findings cannot be considered inconsistent. Using a factor of one-third for the difference in the rate of volatilization of DDD and DDT, a volatilization half-life for DDD ranging from a day to less than a month has been estimated (10).

Volatilization of DDD from soils can be expected to be much slower than from water, because of the strong tendency of DDD to sorb to soil. Using wet river bed quartz sand in 15 mm deep petri dishes, Ware et al. (2270) measured volatilization losses of p,p′-DDD (present initially at 10 ppm) corresponding to a volatilization half-life of roughly 170 days, which is slightly more than twice that for p,p′-DDT under the same conditions. Because these experiments were conducted with a relatively thin layer of soil with a small organic carbon fraction, the actual volatilization rate of DDD in the field would be expected to be lower. If the relative volatilization rates of DDD and DDT in the field were the same as those observed by Ware et al., the volatilization half-life of DDD from soil could be assumed to be double the value of one to several years for DDT (808, 2151).

64.2.2 Transformation Processes in Soil/Ground-water Systems

Hydrolysis of DDD can be expected to be extremely slow under environmental conditions. Over the pH range typical of natural waters (pH 5-9), Wolfe et al. (2154) found the pseudo-first-order rate constant (k_{obs}) at 27°C could be expressed as:

$$k_{obs} = 1.1E\text{-}10 + 1.4E\text{-}03 \cdot [OH^-],$$

where k_{obs} is in s^{-1} and $[OH^-]$, the concentration of the hydroxide ion, in moles/liter. Hydrolysis half-lives of roughly 1.6, 88, and 190 years at pH 9, 7, and 5, respectively, correspond to the rate constant estimated from this equation. These estimates are consistent with the observations of Eichelberger and Lichtenberg (2274) that DDD, initially present in river water at 20 ppb, was not degraded over an eight week period (within 2.5%).

No information was found on the photolysis of DDD in natural waters. Direct photolysis of DDD (i.e., in pure water) is believed to be slower than that for DDT, which is estimated to have a half-life of over 150 years (10). However, DDT in natural water has been estimated to have a photolysis half-life of 5 days when exposed to sunlight in mid-June (2155), and DDD might be expected to have a similar half-life based on the similar structure of the two chemicals.

Data on the biodegradation of DDD are limited. In aquatic systems, biotransformation is believed to be slow (10), although a model ecosystem study has shown DDD to be more biodegradable than either DDT or DDE (2303). The

ketone analogue of DDD (i.e., p,p′-dichlorobenzophenone) has been suggested as the end product of the biodegradation of DDD in the environment (10, 213). DDD undergoes dehydrochlorination to 2,2-bis-(p-chlorophenyl)-1-chloroethylene, reduction to 2,2-bis-(p-chlorophenyl)-1-chlorethane, dehydrochlorination to 2,2-bis-(p-chlorophenyl)-ethylene, reduction to 1,1-bis-(p-chlorophenyl)-ethane, and eventual oxidation to bis-(p-chlorophenyl)- acetic acid (DDA), the ultimate excretory product of higher animals (213). DDD has also been observed to degrade in anaerobic sewage sludge (2157).

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

The above discussion of fate pathways suggests that DDD is moderately volatile, very strongly sorbed to soil, and has a high potential for bioaccumulation. These fate characteristics suggest several potential exposure pathways.

The volatilization of DDD from a disposal site and the consequent exposure to workers and residents in the area is possible due to the volatility of DDD. Its strong sorption to soil will tend to minimize this exposure pathway, as well as limiting its concentration in ground water. DDD was not among a list of 230 chemicals or groups of 546 National Priority List sites (83). It would not be expected to be found at disposal sites unless such pesticides as DDT or DDD had been disposed of there.

The movement of DDD in ground water or its movement with soil particles may result in the discharge to surface waters. As a result, exposure by ingestion may occur from surface waters used as drinking water supplies, and dermal exposures may result from the recreational use of surface waters. More important, however, is the potential for uptake of DDD by aquatic organisms or domestic animals. The high bioconcentration factor and persistence of DDD suggest that ingestion of these organisms can be an important exposure pathway from soil/ground-water systems.

58.2.4 Other Sources of Human Exposure

The use of pesticide products containing DDD has been prohibited in the U.S. since the early 1970's (2305), and the widespread use of DDT was banned as of January 1, 1973 (213). Because DDD is both a contaminant of technical DDT, as well as a breakdown product of DDT, its concentration in the environment has decreased since that time. DDT is still used in Mexico and other countries (2163), and DDD can be expected to be found in foods imported from those countries. The miticide dicofol, which contains DDD and DDT as an impurity, is still in use in the U.S., but as of January 1, 1989 contamination by DDT-related compounds will be limited to 0.1% of the dicofol content (2268). Because less DDD and DDT are now being introduced into the environment, the year in which exposure studies were conducted should always be noted.

No data on the ambient air concentrations of DDD were found in the literature. However, p,p′-DDD was detected in rain samples collected over Lake Superior in

1983 at a volume-weighted concentration of 0.11 ng/L (2304). Rapaport et al. (2163) suggested that atmospheric transport of DDT from Central America and Mexico and its subsequent deposition in eastern North America makes up 10 to 20% of the peak fluxes (around 1960). Because DDD is a contaminant of technical DDT, similar transport of it is likely.

Dietary intake of DDD is expected to be small. The total daily dietary intake for adults in the U.S. was estimated to be <0.001 μg/kg body weight in 1979, whereas none was detected for the three previous years (1245). This compares to an average daily intake of roughly 0.16 μg/kg between 1965 and 1970 (213). For toddlers (2 years old) and infants (6 months old), the total daily intake was estimated to be 0.001 and 0.003 μg/kg, respectively, in 1979 (1244). Vegetables were the sole source of DDD in the diets of infants and toddlers, whereas meat, fish, poultry and leafy vegetables accounted for all of the DDD in adult diets.

58.3 HUMAN HEALTH CONSIDERATIONS

58.3.1 Animal Studies

58.3.1.1 Carcinogenicity

Carcinogenicity studies of DDD have been conducted in rats and mice. The NCI administered technical-grade DDD in feed to Osborne-Mendel rats and B6C3F$_1$ mice. Time-weighted-average concentrations were 1647 or 3294 ppm for male rats, 850 or 1700 ppm for female rats and 411 or 822 ppm for male and female mice. Animals were dosed for 78 weeks with an additional observation period of 35 weeks for rats and 15 weeks for mice. No evidence of carcinogenicity was found in female rats or mice of either sex. Male rats had a significantly increased incidence of follicular-cell adenomas and carcinomas (combined) of the thyroid (33% in the low-dose group and 22% in the high-dose group compared with 5% in controls), suggesting a possible carcinogenic effect of DDD in male rats (2005).

Tomatis et al. (2003) observed lung and liver tumors in CF-1 mice fed diets containing 250 ppm p,p′-DDD for their lifetime. Adenomas and adenocarcinomas of the lung were seen in 86% and 73% of the treated males and females, respectively, compared with 54% in control males and 41% in control females.

58.3.1.2 Mutagenicity

DDD was not genotoxic in bacterial reversion assay systems with five strains of Salmonella typhimurium (TA98, TA100, TA1535, TA1537, TA1538) and one strain of E. coli (WP2 HCR) (1108). Mortelmans et al. (3469) also found it negative in four of the above strains tested with and without two different sources of metabolic activation. Highly significant increases in reverse mutation rates were observed in two strains of Serratia marcescens in a mouse host-mediated assay, whereas no increase in

reversion was observed in a spot test using these bacteria, suggesting that DDD is activated to a mutagenic agent by the host organism (916).

In a cultured rat-kangaroo cell line, p,p′-DDD produced a twofold increase in chromosome abnormalities as compared with the o,p′-isomer. At a concentration of 10 μg/L, p,p′-DDD caused chromosome damage in 15.5% of the cells. Damage consisted of single and multiple chromatid breaks and abnormal metaphases (1999). Mahr and Miltenburger (3419) treated B14FAF28 Chinese hamster cells in culture and observed significant increases in chromosome breaks and gaps. Maslansky and Williams (3431) did not observe an increase in unscheduled DNA synthesis in cultured hepatocytes of rat, mouse and Syrian hamster. DDD also caused transformations in mouse embryo cells, with a frequency of 2.2% at a concentration of 28.4 μM. These transformed cells, however, were not tumorigenic when inoculated into mice (1998). No human cell culture studies were found in the literature published to date.

58.3.1.3 Teratogenicity, Embryotoxicity and Reproductive Effects

DDD does not exhibit the same estrogenic effects that are exhibited by DDT. Welch et al. (1989) showed that a single ip injection of 50 mg/kg produced little or no effect on the uterine weight of Sprague-Dawley rats. An increase in uterine weight is an in vivo test for estrogenic activity.

DDD may permanently alter neuroendocrine differentiation in female rats. The minimal effective dose for inducing persistent vaginal estrus and anovulation was 0.1 mg on days 2, 3, and 4 of life. As the dose increased, the syndrome appeared earlier in life. Uterine histology was markedly changed in adult rats that grew from neonates treated with high doses (59).

The two isomers of DDD, p,p′-DDD and o,p-DDD, gave different results when tested in mice in a NCI teratogenicity study (3030). Offsprings of dams exposed subcutaneously to 46.4 or 100 mg/kg of p,p′-DDD on days 6 to 14 of gestation showed no evidence of fetotoxicity or teratogenicity. With the same exposure conditions, dams exposed to 100 or 215 mg/kg of o,p-DDD produced a reduced number of live neonates per litter and an increase in mortality of pups from day 1 to day 8. No consistent increase in teratogenic effects was observed in any group.

58.3.1.4 Other Toxicologic Effects

58.3.1.4.1 Short-term Toxicity

In animals, DDD is less toxic than DDT. Poisonings have a slower onset and a longer duration. In contrast to DDT poisonings, lethargy is more prominent and convulsions are less frequent (19).

DDD is present in tissues, because it is a primary metabolite of DDT. It is further broken down to DDA which is readily excreted in the urine either unchanged

or as various metabolites. The main action of DDD, especially the o,p'-isomer, is on the liver, where it stimulates the hepatic microsomal oxygenation of drugs and corticosteroids. This may explain much of its action on steroid metabolism in a wide variety of species, but it does not explain why DDD is unique in its ability to affect the adrenal gland. Its ability to induce adrenocortical atrophy in dogs was the original basis for its use in the treatment of adrenal cortical carcinomas in man.

In dogs, DDD caused gross atrophy of the adrenal gland and degeneration of the cells of its inner cortex. A dose as low as 4 mg/kg/day of the o,p'-isomer produced gross atrophy, whereas the dose of technical grade DDD required to produce the same effect was 50 to 200 mg/kg/day (duration of exposure was not given). Progressive hypotensive failure was seen in dogs given 50 mg/kg/day for 14 days when they were injected with epinephrine or norepinephrine. The hypotensive failure was associated with weakening of the contractile force of the heart and with a reduction in plasma volume (2000).

DDD causes no detectable histological damage to the adrenal gland of rats, mice, rabbits, monkeys, or humans, but may affect steroid production by the adrenal gland (3279). Kupfer (1993) suggested that the adrenal effects observed in these species may be caused by a direct or indirect effect on steroid production.

Other effects noted in rats were changes in the indicators of metabolic rate, such as food intake and oxygen consumption. Dosages of 1000 ppm caused an increased thyroid gland weight, and dosages of 3000 ppm also caused reduction in food intake, oxygen consumption, and body weight gain and an increased rate of cooling upon exposure to cold air leading the authors to conclude that DDD resulted in hypothyroidism in the rat (1992). Length of exposure was not reported.

RTECS reports an oral LD_{50} of 113 mg/kg in rats and a dermal LD_{50} of 1200 mg/kg in rabbits (3504).

There were no reports on the effects of ocular or dermal exposure in animals.

58.3.1.4.2 Chronic Toxicity

Chronic feeding of DDD resulted in liver, lung and thyroid tumors in mice and rats. These studies are discussed in Section 58.3.1.1. No other information was available.

58.3.1.1 No other information is available.

58.3.2 Human and Epidemiologic Studies

58.3.2.1 Short-term Toxicologic Effects

A human LDLo of 5000 mg/kg has been reported for DDD (51). The only human data that are available for DDD are related to its use (as the drug mitotane) in the treatment of adrenal cortical carcinomas and Cushing's syndrome due to adrenal hyperplasia (3279). Its pharmacological effect in man is caused by an alteration in peripheral cortisol metabolism leading to a reduction in 17-hydroxycorticosteroids and an increased formation of 6-B-hydroxycortisol. Stimulation of cortisol metabolism appears to be related to the induction of liver microsomal enzymes (1995). According to Southern et al. (3673, 3674) the effect of DDD is not due, predominately, to a direct effect on the adrenal gland, but continued treatment may directly affect the adrenals. The large doses (usually 8 to 10 g) required to produce clinical benefit often cause some toxic effects (1990). Toxic symptoms have been observed in 87% of patients ingesting DDD. These include nausea, vomiting, CNS depression and skin rash (1995). Infrequently occurring side effects on the eyes are blurring, diplopia, lens opacity and toxic retinopathy (1990). The toxic effects are reversible after discontinuation of the drug (1995). Dosages between 110 and 140 mg/kg/day did not produce any detectable injury to the liver, kidney, or bone marrow (2000).

58.3.2.2 Chronic Toxicologic Effects

"Long-term" administration of o,p'-DDD at doses higher than 3 g/day results in adrenal cortical atrophy (1995). Morgan and Roan (1994) reported that no abnormalities or harmful effects were detected in a man ingesting 5 mg p,p'-DDD for 81 days. DDD given to a 10-year girl at a dose of 7.5 g/day for a total of 9 kg did not cause side effects (3284, as cited in 3279). The therapeutic use of DDD, whether short-term or long-term, is related to its effect on adrenal steroid hormone metabolism (3279)

58.3.3 Levels of Concern

No standards have been established for human exposure to DDD. The USEPA has calculated a 1E-04 cancer risk level of 10 μg/L (3744).

58.3.4 Hazard Assessment

DDD may be carcinogenic in male Osborne-Mendel rats, as evidenced by an increased incidence of thyroid tumors after feeding 1647 and 3294 ppm (2005). No carcinogenic effect was observed in female rats fed levels up to 1700 ppm or B6C3F_1 mice of either sex fed up to 822 ppm for 78 weeks (2005). Another experiment

conducted with CF-1 mice resulted in an increase in the incidence of lung tumors in both sexes exposed to 250 ppm DDD in the diet for their lifetime.

Genotoxicity data provide conflicting results. A bacterial reversion test in a mouse host-mediated assay indicated a mutagenic effect for DDD (916), and chromosome aberrations were induced in rat kangaroo cells in culture (1999) and in cultured Chinese hamster cells (3419). DDD also caused transformations of mouse embryo cells; however, these transformed cells were not tumorigenic when injected into mice (1998). Bacterial assays were also negative (1108, 3469). Therefore, the mutagenic potential of DDD is unclear based on available data. DDD does not exhibit the estrogenic effects exhibited by DDT and DDE (1989). DDD may induce persistent vaginal estrus and anovulation in female rats at doses as low as 0.1 mg (59). DDD was not teratogenic in studies conducted by NTP (3030), but it did cause some fetotoxicity.

DDD appears to be less toxic than DDT, with a slower onset of toxic effects; lethargy is prominent, but convulsions occur less frequently than after DDT exposure (19). Gross atrophy of the adrenals was observed in dogs at levels as low as 4 mg/kg/day of the o,p'-isomer or 50 to 200 mg/kg/day of technical grade DDD (2000). No detectable histological damage to the adrenals was noted in rats, mice, rabbits, monkeys or humans (3279), but effects resulting in altered steroid production were noted.

A purified form of DDD used at rather high levels (usually 8-10 g) therapeutically in humans to treat adrenal cortical carcinomas and Cushing's syndrome, produce some toxic side effects (1990, 1995). The effects were reversed upon removal from DDD exposure (1995). Dosages between 110-140 mg/kg/day did not produce any detectable injury to the liver, kidney or bone marrow (2000), but doses as high as 7.5 g/kg/day may also be tolerated without discernable side effects.

58.4 SAMPLING AND ANALYSIS CONSIDERATIONS

Determination of DDD 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 DDD, one of the EPA priority pollutants, in aqueous samples include EPA Methods 608, 625 (63), 8080, and 8250 (63). Prior to analysis, samples are extracted with methylene chloride as a solvent in 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 is injected onto a gas chromatographic (GC) column using a solvent flush technique. The GC column is programmed to separate the semi-volatile organics; DDD 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 DDD 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 DDD 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
0.011 µg/L (Method 608)	1 µg/g (Method 8080)
0.012 µg/L (Method 8080)	1 µg/g (Method 8250)
2.8 µg/L (Method 625/8250)	

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Note: The nonsequential numbers of the references reflect the order of references as they appear in the master bibliography.

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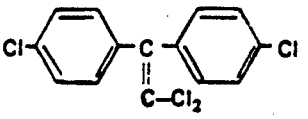
COMMON SYNONYMS:	CAS REG.NO.: FORMULA:	AIR W/V CONVERSION FACTOR at 25 °C
1,1'-(dichloro ethenylidene) bis(4-chloro benzene) DDE Dichlorodiphenyl-dichloroethylene	72-55-9 $C_{14}H_8Cl_4$ NIOSH NC: KV9450000 STRUCTURE: 	12.99 mg/m³ ≈ 1 ppm; 0.077 ppm ≈ 1 mg/m³. MOLECULAR WEIGHT: 318.02

REACTIVITY	DDE is an impurity in DDT residues and is of similar molecular structure to DDT. Its reactivity with other compounds is therefore also expected to be similar (see Chapter 57).

PHYSICO-CHEMICAL DATA	• Physical State: Solid, crystalline (at 20°C)	(59)
	• Color: White	(59)
	• Odor: No data	
	• Odor Threshold: No data	
	• Density: No data	
	• Freeze/Melt Point: 88.40°C	(59)
	• Boiling Point: No data	
	• Flash Point: Combustible solid	(60)
	• Flammable Limits: No data	
	• Autoignition Temp.: No data	
	• Vapor Pressure: 6.2 to 6.60E-06 mm Hg (at 20°C)	(10)
	• Satd. Conc. in Air: 1.1E-01 mg/m³ (at 20°C)	(1219)
	• Solubility in Water: 4E-02 mg/L (at 20°C)	(67)
	• Viscosity: No data	
	• Surface Tension: No data	
	• Log (Octanol-Water Partition Coeff.): 5.69 (p,p′ isomer), 5.78 (o,p′ isomer)	(10)
	• Soil Adsorp. Coeff.: 2.57E+05	(652)
	• Henry's Law Const.: 1.90E-04 atm · m³/mol (at 25°C)	(2269)
	• Bioconc. Factor: 1.10E+05 (bluegill)	(2001)

PERSISTENCE IN THE SOIL-WATER SYSTEM	DDE is expected to be relatively immobile in the soil/ground-water system due to its strong sorption properties. Volatilization may be an important loss pathway from aquatic systems but is much slower in soils. Translocation of sorbed DDE with soil particles may be important. Biodegradation is expected to be the predominant fate process in soils not exposed to sunlight, but occurs extremely slowly. Photolysis is expected to be the dominant degradation process in soils exposed to sunlight.
PATHWAYS OF EXPOSURE	The primary pathway of concern from the soil/ground-water system is the migration of DDE to ground water drinking water supplies. However, this is not likely to occur in most situations because of DDE's low solubility and strong tendency to sorb to soil. 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: There are no reports of acute human exposure to DDE. Acute Toxicity Studies: ORAL: LD_{50} 880 mg/kg Rat (3504) Long-Term Effects: Liver damage Pregnancy/Neonate Data: Not teratogenic, fetotoxic or embryotoxic in rats. Genotoxicity Data: Limited evidence but only in culture and at high concentrations Carcinogenicity Classification: IARC - None assigned NTP - Positive evidence mice, negative rats EPA - Group B2 (probable human carcinogen)
HANDLING PRECAUTIONS	There are no specific handling precautions for DDE. Handle in the same manner as DDT (see Record 57).

ENVIRONMENTAL AND OCCUPATIONAL STANDARDS AND CRITERIA

AIR EXPOSURE LIMITS:

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

Criteria
- NIOSH IDLH (30-min): None established
- NIOSH REL: no data
- ACGIH TLV® (8-hr TWA): None established
- ACGIH STEL (15-min): None established

WATER EXPOSURE LIMITS:

Drinking Water Standards
None established

EPA Health Advisories and Cancer Risk Levels (3744)
No Health Advisories
- 1E-04 Cancer risk: 10 µg/L

WHO Drinking Water Guideline
No information available.

EPA Ambient Water Quality Criteria
- Human Health (355)
  - No criterion established due to insufficient data.

- Aquatic Life (355)
  - Freshwater species
    acute toxicity:
    no criterion, but lowest effect level occurs at 1050 µg/L.

    chronic toxicity:
    no criterion established due to insufficient data.

  - Saltwater species
    acute toxicity:
    no criterion, but lowest effect level occurs at 14 µg/L.

    chronic toxicity:
    no criterion established due to insufficient data.

REFERENCE DOSES:
No reference dose available.

REGULATORY STATUS (as of 01-MAR-89)

Promulgated Regulations

- Federal Programs

Clean Water Act (CWA)

DDE is listed as a toxic pollutant, subject to general pretreatment standards for new and existing sources, and effluent standards and guidelines (351, 3763). Under the toxic pollutant effluent standards, DDE (DDT metabolite) is prohibited in any discharge from DDT manufacturers or formulators. The ambient water criterion for DDT and its isomers in navigable waters is 0.001 µg/L. This standard applies to all discharges of process wastes from manufacturing and storage areas subject to direct contamination by DDT and its isomers through stormwater runoff or routine cleanup, and cleanup of spills (805). Effluent limitations specific to this chemical have been set in the following point source categories: electroplating (3767), steam electric power generating (3802) and metal finishing (3768). The limitations set are for the amount of total toxic organics (TTO) discharge permitted per day. DDE is included when calculating the TTO. Effluent limitations in the pesticide chemicals manufacturing point source category are set at 0.010 kg/1000 kg of organic pesticide chemicals (including DDE) maximum for any one day (891).

Resource Conservation and Recovery Act (RCRA)

DDE is listed as a hazardous waste constituent (3783). DDE is included on EPA's ground-water monitoring list. EPA requires that all hazardous waste treatment, storage, and disposal facilities monitor their ground-water for chemicals on this list when suspected contamination is first detected and annually thereafter (3775). Effective July 8, 1987, the land disposal of untreated hazardous wastes containing halogenated organic compounds in total concentrations greater than or equal to 1000 mg/kg will be prohibited. Effective August 8, 1988, underground injection into deep wells of these wastes is prohibited. Certain variances exist until May, 1990 for land and injection well disposal of some wastewaters, nonwastewaters, and soils for which Best Demonstrated Available Technology (BDAT) treatment standards have not been promulgated by EPA (3786). EPA requires 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 (3782).

Comprehensive Environmental Response Compensation and Liability Act (CERCLA)

DDE is designated a hazardous substance under CERCLA. It has a reportable quantity limit of 0.454 kg. Reportable quantities have also been issued for RCRA hazardous waste streams containing DDE but these depend upon the concentrations of the chemicals in the waste stream (3766).

Federal Insecticide, Fungicide and Rodenticide Act (FIFRA)
Action levels for the sum of DDT, DDE and DDD residues in agricultural commodities range from 0.05 to 0.5 ppm (889). As of January 1, 1989, EPA is cancelling registrations and denying applications of all dicofol products containing greater than 0.1% of DDT and related impurities (2268).

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 DDT shall not exceed an 8-hour time-weighted average (TWA) of 1 mg/m³. DDD is a metabolite of DDT (3539).

Hazardous Materials Transportation Act (HMTA)
The Department of Transportation has designated DDD a hazardous substance with a reportable quantity of 0.454 kg, subject to requirements for packaging, labeling, and transportation (3180).

Food, Drug and Cosmetic Act (FDCA)
The following action levels are recommended for the sum of DDT, DDE and DDD residues: 0.1 ppm in dried hops, 1.25 ppm in manufactured dairy products, 1.0 ppm in peppermint oil, spearmint oil and in crude soybean oil (888)

- State Water Programs

ALL STATES
All states have adopted EPA Ambient Water Quality Criteria and NPDWRs (see Water Exposure Limits section) as their promulgated state regulations, either by narrative reference or by relisting the specific numeric criteria. These states have promulgated additional or more stringent criteria:

DISTRICT OF COLUMBIA
The District of Columbia has a human health criterion of 0 µg/L for DDT and its isomers in surface water classed for public water supply (3828).

NEW YORK
New York has an MCL of 5 µg/L for DDE in drinking water, an ambient water quality standard of 0.01 µg/L for surface water classed for drinking water supply, and requires DDE to be nondetectable in ground-water (3501).

Proposed Regulations

- Federal Programs

  No proposed regulations are pending.

- State Water Programs

  No proposed regulations are pending. Most states are in the process of revising their water programs and proposing changes in their regulations which will follow EPA's changes when they become final. Contact with the state officer is advised. Changes are projected for 1989-90 (3683).

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 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 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 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 p,p'-DDT is 10 μg/L. For total DDT (including isomers) the quality objective is 25 μg/L. The emission standard of DDT and isomers for DDT production is 0.7 mg/L water discharged as a monthly average and 1.3 mg/L water discharged as a daily average. These regulations must be complied to 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.

59.1 MAJOR USES

DDE is neither produced nor used commercially in the United States (59). It is a degradation product of DDT (see Chapter 57) and is found as a contaminant in technical grade DDT. DDE is also present in mammalian systems as a DDT metabolite (59, 2001).

59.2 ENVIRONMENTAL FATE AND EXPOSURE PATHWAYS

59.2.1 Transport in Soil/Ground-water Systems

59.2.1.1 Overview

The presence of DDE in the environment is primarily the result of the use of the insecticide DDT and the miticide dicofol. DDE is the principal degradation product of DDT under aerobic conditions, and it has been found to equal roughly 1-3% of the weight of dicofol in the technical mixture (2164).

Like DDT, DDE exists as both an o,p' and a p,p' isomer, with the o,p' and the p,p' isomers of DDT degrading to the respective DDE isomer. Because technical DDT consists of 65-80% p,p'-DDT and 15-21% o,p'-DDT, (2145), the p,p'-DDE isomer might be expected to predominate in the environment. In dicofol, however, the o,p' isomer typically makes up 80-90% of the DDE present (2164). The two isomers of DDE are considered individually below where data are available.

Like DDT, DDE is expected to be highly immobile in the soil/ground-water environment when present at low dissolved concentrations. Bulk quantities of DDE dissolved in an organic solvent (e.g., as a contaminant in dicofol) could be transported through the unsaturated zone as a result of a spill or improper disposal of excess formulations. However, the extremely low solubility of DDE and its strong tendency to sorb to soils would result in a very slow transport rate in soils.

In general, transport pathways can be assessed by using an equilibrium partitioning model, as shown in Table 59-1. These calculations predict the partitioning of low soil concentrations of DDE among soil particles, soil water and soil air. Due to its strong tendency to sorb to soil, virtually all of the DDE partitions to the soil particles of unsaturated topsoil, with negligible amounts associated with the soil water or air. Even in saturated deep soil, which is assumed to contain no soil air and a smaller organic carbon fraction, almost all of the DDE is retained on the soil.

TABLE 59-1
EQUILIBRIUM PARTITIONING CALCULATIONS FOR DDE[a]
IN MODEL ENVIRONMENTS

Soil Environment	Estimated Percent of Total Mass of Chemical in Each Compartment		
	Soil	Soil-Water	Soil-Air
Unsaturated topsoil at 25°C[b,c]	100	2.0E-03	4.8E-05
Saturated deep soil[d]	99.9	9.3E-02	-

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) Estimated soil sorption coefficient: K_{oc} = 257,000 (652).
c) Henry's law constant taken as 1.9E-04 atm · m³/mol at 25°C (2269).
d) Used sorption coefficient K_p = 0.001 K_{oc}.

59.2.1.2 Sorption on Soils

DDE is characterized by a strong tendency to sorb to organic matter in soils and in sediments. Only one value, log K_{oc} = 5.17 (2147), was found in the literature for the soil organic carbon partition coefficient. A log K_{oc} value of roughly 5 has been suggested based on log K_{ow} measurements of 5.69 for the p,p' isomer and 5.78 for the o,p' isomer (10). Using the geometric mean of these K_{ow} values and the regression equation of Means et al. (611), a log K_{oc} value of 5.41 is estimated. As with all neutral organic chemicals, the extent of sorption is proportional to the soil organic carbon content. In soils with little organic carbon (e.g., clays), the extent of sorption may also depend upon soil properties such as surface area, cation exchange capacity, and degree of hydration.

The apparent sorption of DDE to soils and sediments (like that of DDT), is lessened, and thus its mobility is enhanced by the presence of dissolved organic matter. As described in Chapter 57, Section 57.2, DDT concentrations were found to be higher in aqueous solutions containing humic and fulvic acids. Because the sorption behavior of DDE is expected to be much like that of DDT, its mobility in natural waters may be several times greater than predicted (though probably still small) if dissolved organic matter is present. In waters containing large concentrations of dissolved organic matter, such as swamps and bogs, this may be especially important.

59.2.1.3 Volatilization from Soils

The vapor pressure of p,p'-isomer of DDE at 20°C has been given as 8.7E-09 atm and that of the o,p' isomer as 8.2E-09 atm (10). A somewhat lower value of roughly eight times the vapor pressure of DDT has been suggested by Sleicher and Hopcraft (2153). Using the average vapor pressures for the two isomers to estimate the Henry's law constant, a value of 1.9E-04 atm.m³/mol is obtained (2269).

This estimate is roughly an order of magnitude larger than the Henry's law constant for DDT. Because volatilization losses for DDT are expected to be important, the same is also true for DDE. DDE has been found to volatilize from distilled and natural waters five times faster than DDT (10). Since the volatilization half-life for DDT has been reported to range from several hours to several days (see Section 57.2.1.3), proportionately shorter half-lives would be expected for DDE.

In soils, volatilization of DDE is much slower. Using wet river bed, quartz sand in 15 mm deep petri dishes, Ware et al. (2270) measured volatilization losses of p,p'-DDE (present initially at 10 ppm) that corresponded to a half-life of roughly 40 days. This value may be more indicative of an upper limit of the volatilization rate because soils of higher organic matter content would tend to sorb more of the DDE, and the rate of volatilization would be expected to be lower from thicker layers of soil. In the same study and under the same conditions, the o,p' isomer of DDT took 50% longer to reach half its initial concentration; p,p'-DDT took twice as long. This suggests that the volatilization of DDE in the field may occur at a rate somewhat greater than that for DDT, which has been found to have a volatilization half-life of one to several years (808, 2151). The observation that the volatilization rate of DDE from soil is not several times the rate for DDT, given that it has an order of magnitude larger Henry's law constant, may be explained by its strong sorption to soil, which tends to impede volatilization.

59.2.2 Transformation Processes in Soil/Ground-water Systems

DDE is the hydrolysis product of DDT and is quite resistant to further hydrolysis. A hydrolysis half-life of over 120 years at pH 5 and 27°C has been given (10). Thus, hydrolysis is not expected to be an environmentally significant process.

Several studies have examined the aqueous photolysis of DDE. Zepp and Schlotzhauer (2271) found that DDE in the aqueous phase of sediment suspensions exposed to ultraviolet light of wavelength >300 nm had a half-life of roughly 13 to 17 hours. Under the same conditions, DDE equilibrated with sediment for 60 days (i.e., sorbed to the sediment) photodegraded much more slowly. To reach 25% of its initial concentration, roughly seven half-lives were needed instead of the expected two, and little further degradation occurred. The authors suggested that over time, part of the DDE diffused into the sediment particles and became unavailable for photolysis. Chen et al. (1220) found the thin film photodegradation rate of p,p'-DDE to be about 90% of that for p,p'-DDT, and the half-life of DDE in aquatic systems at 40°N latitude has been estimated to range from one day in summer to six days in

winter (10). These findings suggest that photolysis of DDE may be an important loss process, as it is for DDT. However, for photolysis to occur, the chemical must be exposed to sunlight, which often is not the case for a large fraction of the amount sorbed to soils or deep sediments.

The biological degradation of DDE in aquatic environments is believed to occur very slowly if at all (10). In modeling the fate of DDE in a quarry, Di Toro and Paquin (2272) considered biodegradation to be insignificant compared to loss by photolysis and volatilization. The half-life for biodegradation in sediments has also been found to be extremely slow. Using radiolabeled p,p'-DDE mixed with river sediment, Lee and Ryan (2273) measured a half-life of 1100 days based on the evolution of CO_2. In short, photolysis appears to be the only degradation process that affects DDE significantly under environmental conditions.

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

The above discussion of fate pathways suggests that DDE is moderately volatile, very strongly sorbed to soil, and has a high potential for bioaccumulation. These fate characteristics suggest several potential exposure pathways.

The volatilization of DDE from a disposal site and the consequent exposure to workers and residents in the area is possible due to the volatility of DDE. However, its strong sorption to soil will tend to minimize this exposure pathway as well as limiting its concentration in ground-water. Mitre (83) reported that DDE was detected at one of 546 National Priority List sites. In that case, it was found only in surface water, not in ground-water or air.

The movement of DDE in ground-water or its movement with soil particles may result in the discharge to surface water. As a result, ingestion exposures may occur from the use of surface waters as drinking water supplies. Dermal exposures may result from the recreational use of surface waters. More important, however, is the potential for uptake of DDE by aquatic organisms or domestic animals. The high bioconcentration factor and the persistence of DDE suggest that ingestion of these organisms can be an important exposure pathway from soil/ground-water systems.

59.2.4 Other Sources of Human Exposure

The widespread use of DDT was banned as of January 1, 1973 (213). Since DDE is the principal degradation product of DDT under aerobic conditions, its concentration in the environment, like that of DDT, has decreased since then. DDT is still used in Mexico and other countries (2163), and DDE can be expected to be found in food imported from these countries. The miticide dicofol, which contains both DDT and DDE as impurities, is still in use in the U.S., but as of January 1, 1989, contamination by DDT-related compounds will be limited to 0.1% of the dicofol content (2268).

Schafer et al. (1241) found that more than 30% of over 450 finished drinking water samples collected between 1964 and 1967 from the Mississippi and Missouri Rivers contained p,p'-DDE. DDE was detected in 48% of 5333 ambient water samples taken across the U.S. during the early 1960's; the median concentration was 0.001 µg/L (1417). It was also found in 60% of 1087 surface water sediments sampled at median concentration of 0.1 µg/kg.

DDE is also present in the air. Mean concentrations of 0.093 ng/m³ p,p'-DDE were measured in Columbia, South Carolina between 1977 and 1980, and in 1980, the mean concentration over Denver was 0.021 ng/m³ (1600). Between 1970 and 1972, p,p'-DDE was detected in over 95% of the air samples in 16 states at a mean concentration of 1.8 ng/m³ (76). The deposition of DDT in eastern North America has been estimated to equal 10-20% of that occurring during peak usage of DDT in the 1960's (2163). This suggests that atmospheric concentrations of DDE may also be about 10-20% of their past peaks because agricultural use of DDT (today in Mexico and Central America) is still the primary source of DDE.

Human exposure to DDE in water and air is expected to be small compared to dietary intake. The total daily dietary intake for adults in the U.S. was estimated to be 0.087 µg/kg body weight in 1979 (1245). This compares to an average intake of roughly 0.24 µg/kg/day between 1965 and 1970 (213). For toddlers (2-years old) and infants (6-months old), the total daily intake was estimated to be 0.089 and 0.110 µg/kg body weight, respectively, in 1979 (1244). Dairy products and meat, fish, and poultry were the major sources of DDE in the diets of all three age groups.

59.3 HUMAN HEALTH CONSIDERATIONS

59.3.1 Animal Studies

59.3.1.1 Carcinogenicity

DDE induces liver tumors in mice and hamsters but not in rats (2003, 2004, 2005).

The National Cancer Institute (NCI) administered time-weighted- average doses of 148 or 261 ppm p,p'-DDE suspended in corn oil and incorporated into the diet of $B6C3F_1$ mice for a 78 week period with an additional observation period of 15 weeks. Among both sexes there was a statistically significant association between the concentration of DDE administered and the incidence of hepatocellular carcinomas. No carcinomas were observed in the control groups. In low-dose males and females, the incidence was 17% and 40%, respectively. In high-dose animals there was a 36% incidence in males and a 71% incidence in females (2005). Tomatis et al. (2003) found that lifetime exposure of CF-1 mice to 250 ppm p,p'-DDE suspended in olive oil and incorporated in the diet resulted in a high incidence and early appearance of liver tumors. Hepatomas were found in 74% of the males and 98% of the females compared with 34% of control males and 1% of control females. In animals dying

before the 90th week of age, liver tumors were observed in 40.7% of the males and 81.5% of the females.

p,p'-DDE suspended in olive oil also had a neoplastic effect in Syrian golden hamsters fed diets containing 500 or 1000 ppm for life. Hepatocellular tumors classified as neoplastic nodules were observed in the low-dose group in 15% of the females and 47% of the males and in the high-dose group in 21% of the females and 33% of the males. None of the control animals had these tumors. In addition, adrenocortical adenomas, which have a high spontaneous incidence in this strain, were more frequent in treated animals than in controls (2004).

The NCI found no evidence of carcinogenicity of p,p'-DDE in Osborne-Mendel rats although hepatotoxic effects were observed. Males were administered time-weighted-average doses of 437 or 839 ppm and females received time-weighted-average doses of 242 or 462 ppm. The animals all received the DDE suspended in corn oil and mixed in their feed and were dosed for 78 weeks followed by a 35-week observation period. Hepatotoxic effects which were observed included centrilobular necrosis (12% in low-dose animals and 18% in high-dose animals) and fatty metamorphosis in the hepatocytes (38% in low-dose animals and 41% in high-dose animals) (2005).

59.3.1.2 Genotoxicity

DDE has given only negative results when tested in bacterial systems. There was no increased frequency of histidine reversions in all strains of Salmonella typhimurium tested both with and without metabolic activation (2001, 3469, 3159, 3424), no increase in tryptophane reversions (3159), and no significant difference in the rec-assay using Escherichia coli (3159, 3424).

Vogel (3817) did not observe an increase in sex-linked recessive lethals when Drosophila were fed DDE, but Valencia et al. (3810) fed males 10,000 ppm and found it to be positive.

DDE induces point mutations and chromosomal aberrations in some lines of mammalian cells treated in vitro. Clive et al. (3989) observed an increase in mutants at the thymidine kinase locus as did McGregor et al. (3439) using concentrations as low as 25 μg/mL. DDE produced a significant increase in the mutation frequency at the HPRT locus in Chinese hamster ovary cells (3021) and in V79 Chinese hamster cells at a dose of 25-35 μg/mL, and an increase in chromosome aberrations when the cells were exposed to 35-40 μg/mL for 24 hours (1996). Conversely, Galloway et al. (3235) did not observe an increase in aberrations in Chinese hamster ovary cells treated in culture, and only a slight increase in sister chromatid exchanges. Mahr and Miltenburger (3419) observed significant increases in chromosomal aberrations in another strain of Chinese hamster cells treated with a dose of 44 ppm for 4 hrs. DDE also produced chromosomal abnormalities in a cultured rat-kangaroo cell line (1999). At a concentration of 10 μg/mL, the p,p' isomer caused chromatid breaks and exchanges in 13.7% of the cells.

In an in vitro mouse embryo cell culture system, DDE showed a slight increase in transformation frequency at high concentrations. Transformed cells, however, were not tumorigenic when inoculated into mice. Concentrations of DDE ranged from 2.8 to 42.6 μM (1998).

DDE also gave negative results in an in vivo mouse host-mediated bioassay with Salmonella typhimurium and in two strains of Serratia marcescens (916, 3092).

59.3.1.3 Teratogenicity, Embryotoxicity and Reproductive Effects

DDE exhibits some estrogenic effect with the o,p'-isomer being more potent. Forster et al. (1983) tested both DDE isomers for their ability to inhibit specific binding of estradiol to uterine cytosol and nuclear fractions. The o,p'-isomer inhibited the binding indicating estrogenic activity. The p,p'-isomer was inactive. The test species was not reported. Intraperitoneal injection of 50 mg/kg of p,p-DDE to rats did not increase uterine weight nor did it inhibit the uptake of estradiol-17B by the uterus (1989). The o,p'-isomer was not tested. When evaluated for the ability to increase uterine glycogen, another indicator of estrogenic activity, the o,p'-isomer was found to be active while the p,p'-isomer was inactive (1980, 1991).

The effect of p,p'-DDE on lactation in rats was studied by Kornbrust et al. (3376). DDE was administered in doses of 10 mg/kg to female rats 5 days/week for 5 weeks prior to mating and throughout gestation. No effect was observed on coital behavior, fertility, length of gestation, sex distribution, or viability of the offsprings. These results are in agreement with Bleyl et al. (3071) who treated rats with 50 ppm of DDE in diet for 10 weeks. The treatment was halted for 2 weeks before mating. In this study no effects on pre- or postimplantation embryo loss, litter size, or birth weight were observed. Ossification of the thorax of the DDE-treated offsprings was similar to that of the control pups on gestation day 20. No teratogenic or embryotoxic effects were observed in either of the above studies.

59.3.1.4 Other Toxicologic Effects

59.3.1.4.1 Short-term Toxicity

DDE has an oral LD_{50} value of 880 mg/kg in male rats (59) and 1240 mg/kg in female rats (2001). LD_{50} values reported in mice were 700 and 1000 mg/kg; sex was not specified (2000). Signs of acute exposure were not reported.

In mammalian species, DDE is formed by the dehydrochlorination of the trichloroethane moiety of DDT. The p,p'-isomer of DDE is the most stable and is retained most strongly in mammalian tissues whereas the o,p'-isomer is less persistent. DDE comprises about 20% of all DDT-derived residues in the livers of rats and mice fed DDT versus 2% in hamsters. In contrast, rhesus monkeys fed DDT did not store DDE at detectable amounts in the fat or liver. They metabolize DDT almost

exclusively by the DDD pathway. Also, when fed DDE, they stored high levels of DDE, a further indication of their inability to convert DDT to DDE (2001, 1994).

Acute toxic effects of DDE administration other than the induction of liver enzymes in rodents (2000, 2001) have not been reported.

59.3.1.4.2 Chronic Toxicity

Effects of long-term DDE exposure were evaluated during the carcinogenicity studies conducted by the NCI and Rossi et al. In the NCI bioassay (2005), DDE caused toxic hepatopathy in rats which was manifested by centrilobular necrosis and fatty metamorphosis in the hepatocytes. There were isolated instances of tremors, ataxia and loss of equilibrium. Rossi et al. (2004) observed no convulsions or tremors in treated hamsters.

Tomatis et al. (2003) reported a reduced lifespan in both male and female CF-1 mice treated with 250 ppm p,p'-DDE in the diet for 130 weeks. Myocardial necrosis and diffuse hemorrhages, leukocytic infiltration, and fibroblastic reaction developed in 36.6% of the treated males.

59.3.2 Human and Epidemiologic Studies

59.3.2.1 Short-term Toxicologic Effects

DDE, the metabolite of DDT, does not undergo any additional biotransformation, but is stored for an indefinite period of time in the adipose tissue (1263). The conversion of DDT to DDE occurs slowly. The biological half-life of DDE is approximately 8 years (59). Morgan and Roan (1994) estimated the conversion rate to be less than 20% over 3 years. This is in sharp contrast to the efficiency of absorption and storage of p,p'-DDE itself. DDE ingestion increases serum DDE levels 30 times as fast per unit dose as does DDT ingestion. Similarly, DDE in adipose tissue increases 13 times as fast in response to DDE ingestion as it does during DDT ingestion. The distribution of DDE into other organs generally parallels their fat content. Other areas where DDE tends to concentrate are the bone marrow and the lymph nodes (1991). Other than these metabolic studies, there are no reports of acute human exposure to DDE.

59.3.2.2 Chronic Toxicologic Effects

Morgan and Roan (1994) conducted the only study on the effects of chronic DDE administration. They administered 5 mg p,p'-DDE orally to one subject for 92 days. Hematologic and clinical biochemical tests were conducted before, during and after exposure. No abnormalities were detected.

Storage of DDE in man may be affected by enzyme inducers such as phenobarbital and diphenylhydantoin. Volunteers given diphenylhydantoin at a rate of 300 mg/day for 9 months showed a 61% reduction in DDE storage. Epileptics on

"maintenance doses" of diphenylhydantoin or phenobarbital stored little or no DDE in their fat or blood (1991).

Rashad et al. (1991) reported a significant association between serum cholesterol and p,p'-DDE. Details of the study were not given, but the investigators attributed an increase in cholesterol to liver stimulation by p,p'-DDE.

59.3.3 Levels of Concern

No standards have been established to date for DDE. The EPA has derived a 1E-04 cancer risk level of 10 μg/L (3744).

59.3.4 Hazard Assessment

Liver tumors were induced in mice fed 148-261 ppm DDE and hamsters fed 500-1000 ppm (2003, 2004, 2005) but no carcinogenic effect was observed in rats fed levels up to 839 ppm of p,p'-DDE for 78 weeks (2005).

There is no evidence that DDE is capable of inducing genotoxic effects in bacterial cells, and there is conflicting evidence that it causes point mutations and chromosomal aberrations in mammalian cells in culture (1996-1999, 3419, 3021, 3439). Negative in vivo results were reported, for host-mediated assays in mice (916, 3092), and transformed mouse embryo cells failed to induce a tumorigenic response when inoculated into mice (1998). The mutagenic potential of DDE is therefore unclear based on available data. No teratogenicity studies have been conducted with DDE. The o,p'-isomer does exhibit some estrogenic effects (1983, 1980).

Males appear to be more susceptible to the acute toxic effects of DDE with oral LD_{50} values reported as 880 and 1240 mg/kg for the male and female rat, respectively (59, 2001). Signs of acute exposure to DDE have not been reported.

In addition to tremors, ataxia and a loss of equilibrium, hepatotoxicity, characterized by centrilobular necrosis and fatty metamorphosis, has been reported following chronic ingestion of DDE by rats (2005). Reduced lifespan, leukocytic infiltration, and fibroblastic reaction have been reported for CF-1 mice (2003).

The only reports of DDE exposure in humans are from metabolic trials in controlled laboratory settings (1263, 1994, 1991). DDE is stored primarily in fat, bone marrow and lymph nodes (1991) with a biological half-life of approximately 8 years in man (59).

Oral administration of 5 mg of p,p'-DDE to one human volunteer for 92 days produced no observed adverse effects (1994).

59.4 SAMPLING AND ANALYSIS CONSIDERATIONS

Determination of DDE 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 DDE, 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; DDE is then detected with an electron capture detector or halogen specific detector (Methods 608 and 8080) or a mass spectrometer (Methods 625 and 8250).

Other method which have been developed to determine DDE and other trace level pesticides involve column preconcentration where the aqueous sample is passed through an adsorbent bed to trap the compound of interest (3122, 3176). DDE is then eluted with an organic solvent and analyzed by GC.

The EPA procedures recommended for DDE 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 using either soxhlet extraction or sonication methods. Neat and diluted organic liquids may be analyzed by direct injection.

Typical DDE 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
0.004 µg/L (Method 608)	2.7 µg/kg (Method 8080)
5.6 µg/L (Method 625)	3.7 µg/g (Method 8250)
56 µg/L (Method 8250)	
0.04 µg/L (Method 8080)	

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Note: The nonsequential numbers of the references reflect the order of references as they appear in the master bibliography.

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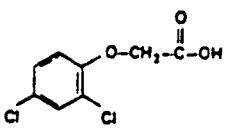
COMMON SYNONYMS:	CAS REG.NO.: 94-75-7 FORMULA: $C_8H_6Cl_2O_3$ NIOSH NO: AG6825000 STRUCTURE: 	AIR W/V CONVERSION FACTOR at 25°C 9.03 mg/m³ ≈ 1 ppm; 0.1107 ppm ≈ 1 mg/m³. MOLECULAR WEIGHT: 221.04
2,4-Dichlorophenoxy acetic acid Agrotect® Dicotox® P[illegible]ox®		

REACTIVITY	For general compatibility classification purposes, 2,4-D is considered to be both an organic acid and a halogenated organic compound. Reactions of organic acids with amines, caustics or nitriles typically evolve heat, while those with oxidizing mineral acids, azo or diazo compounds, hydrazines, or isocyanates evolve heat and usually innocuous gases. Reactions with nitrides, strong reducing agents, and certain elemental metals may evolve flammable gases and possible heat, while those with alkali or alkaline earth elemental metals may also cause a fire. Reactions with inorganic fluorides or sulfides, or strong oxidizing agents may evolve toxic gases and possible heat. Reactions with cyanides or dithiocarbamates may produce both toxic and flammable gases, with the later classification also producing heat. Reactions with alcohols, glycols, aldehydes, epoxides, or polymerizable compounds may initiate a violent exothermic polymerization reaction. Explosive materials may explode. Reactions of halogenated organic materials 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 and 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. (511)

PHYSICO-CHEMICAL DATA	• Physical State: Solid, powder (at 20°C)	(54)
	• Color: White to yellow	(2,54)
	• Odor: none to slight phenolic odor	(2,54)
	• Odor Threshold: no data	
	• Density: 1.5650 g/mL (at 30°C)	(59)
	• Freeze/Melt Point: 138.0 to 141.0°C	(2,51)

PHYSICO-CHEMICAL DATA	• Boiling Point: 160.00°C under 0.4 mm Hg pressure	(2)
	• Flash Point: Combustibility of various formulations varies over wide range.	(1734)
	• Flammable Limits: No data	
	• Autoignition Temp.: No data	
	• Vapor Pressure: <1.00E-05 mm Hg, (minimum is <.0001) (at 25°C)	(507)
	• Satd. Conc. in Air: 1.2000E-01 mg/m^3 (at 20°C)	(1219)
	• Solubility in Water: 6.20E+02 mg/L (at 25°C)	(1118)
	• Viscosity: Not pertinent	
	• Surface Tension: Not pertinent	
	• Log (Octanol-Water Partition Coeff.): 2.81	(2150)
	• Soil Adsorp. Coeff.: 6.00E+01	(1210)
	• Henry's Law Const.: 1.90E-10 $atm \cdot m^3/mol$ (at 20°C)	(1210)
	• Bioconc. Factor: 3.10E+01 (estim)	(659)

PERSISTENCE IN THE SOIL-WATER SYSTEM	2,4-D is expected to be relatively mobile but non-persistent in natural soils due to limited sorption and relatively rapid degradation. Risk of groundwater contamination is low except under conditions of heavy application, high soil pH and heavy rainfall shortly after application.

PATHWAYS OF EXPOSURE	The primary pathway of concern from the soil/ground-water system is the migration of 2,4-D to groundwater drinking water supplies. Degradation in the environment will minimize exposure by this pathway, however. Other exposure pathways are unlikely to be significant.

HEALTH HAZARD DATA	Signs and Symptoms of Short-term Human Exposure: (38) Massive exposure to 2,4-D may cause weakness, stupor, muscle twitching and convulsions. Contact may cause skin rash. Acute Toxicity Studies: ORAL: LD_{50} 370 mg/kg — Rat LD_{50} 347 mg/kg — Mouse LD_{50} 500 mg/kg — Hamster LD_{50} 100 mg/kg — Dog LD_{Lo} 80 mg/kg — Human LD_{Lo} 93 mg/kg — Human SKIN: LD_{50} 1500 mg/kg — Rat LD_{50} 1400 mg/kg — Rabbit Long-Term Effects: Weakness, myotonia Pregnancy/Neonate Data: Embryo- and fetotoxic Genotoxicity Data: Conflicting data Carcinogenicity Classification: IARC- None assigned (inadequate evidence in animals) NTP - None assigned EPA - Group D (not classifiable as to human carcinogenicity)
HANDLING PRECAUTIONS	Handle chemical only with adequate ventilation • Concentrations of 10-100 mg/m³: Any chemical cartridge respirator with an organic vapor cartridge and dust filter, including pesticide respirators which meet the requirements of this class or any supplied-air respirator or any self-contained breathing apparatus • 100-500 mg/m³: A gas mask with a chinstyle or a front or- back-mounted organic vapor canister and dust and mist filter, including pesticide respirators which meet the requirements of this class or any supplied-air respirator with a full facepiece, helmet or hood or any self-contained breathing apparatus with a full facepiece or a type C supplied-air respirator operated in pressure-demand or other positive pressure or continuous-flow mode • >500 mg/m³: Self- contained breathing apparatus with a full facepiece operated in pressure-demand or other positive pressure mode • Chemical goggles if there is a probability of eye contact • Protective clothing to prevent repeated or prolonged skin contact.

ENVIRONMENTAL AND OCCUPATIONAL STANDARDS AND CRITERIA

AIR EXPOSURE LIMITS:

Standards
- OSHA PEL (8-hr TWA): 10 mg/m³
- AFOSH PEL (8-hr TWA): 10 mg/m³; STEL (15 min): 20 mg/m³

Criteria
- NIOSH IDLH (30-min): 500 mg/m³
- NIOSH REL: no data
- ACGIH TLV® (8-hr TWA): 10 mg/m³
- ACGIH STEL (15-min TWA): deleted

WATER EXPOSURE LIMITS:

Drinking Water Standards (991)
MCLG: 70 µg/L (proposed)
MCL : 70 µg/L (proposed)
MCL : 100 µg/L (Interim)

EPA Health Advisories and Cancer Risk Levels (397?)
The EPA has developed the following Health Advisories which provide specific advice on the levels of contaminants in drinking water at which adverse health effects would not be anticipated.

- 1-day (child): 1000 µg/L
- 10-day (child): 300 µg/L
- longer-term (child): 100 µg/L
- longer-term (adult): 400 µg/L
- lifetime (adult): 70 µg/L

WHO Drinking Water Guideline (666)
A health-based guideline for drinking water of 100 µg/L is recommended for 2,4-D. A daily per capita consumption of two liters of water was assumed. Some individuals may be able to detect 2,4-D by taste and odor at levels >50 µg/L.

EPA Ambient Water Quality Criteria
- Human Health (355)
  - No criterion established; 2,4-D is not a priority pollutant.
- Aquatic Life (355)
  - No criterion established; 2,4-D is not a priority pollutant.

REFERENCE DOSES:
- ORAL: 10 µg/kg/day (3744)

REGULATORY STATUS (as of 01-MAR-89)

Promulgated Regulations

- Federal Programs

Clean Water Act (CWA)

2,4-D is designated a hazardous substance. It has a reportable quantity (RQ) limit of 45.4 kg (347,3764). 2,4-D is listed as an organic pesticide chemical. Effluent limitations in the pesticide chemicals manufacturing point source category are set at 0.010 kg/1000 kg of organic pesticide chemicals maximum for any one day (891).

Safe Drinking Water Act (SDWA)

2,4-D is on the list of 83 contaminants required to be regulated under the SDWA of 1974 as amended in 1986 (3781). Under the National Interim Primary Drinking Water Regulations, the maximum contaminant level (MCL) for 2,4-D is 0.1 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 (3801). In states with an approved Underground Injection Control program, a permit is required for the injection of 2,4-D-containing wastes designated as hazardous under RCRA (295).

Resource Conservation and Recovery Act (RCRA)

2,4-D is identified as a hazardous waste (U240) and listed as a hazardous waste constituent (3783, 3784). Solid wastes which contain a TCLP extract concentration equal to or greater than 10 mg/L 2,4-D are listed as hazardous in that they exhibit the characteristics defined as EP toxicity (988). 2,4-D is included on EPA's ground-water monitoring list. EPA requires that all hazardous waste treatment, storage, and disposal facilities monitor their ground-water for chemicals on this list when suspected contamination is first detected and annually thereafter (3775). For ground-water protection, the maximum concentration of 2,4-D-containing hazardous waste in ground-water is 0.1 mg/L (989). Effective July 8, 1987, the land disposal of untreated hazardous wastes which contain halogenated organic compounds in total concentrations greater than or equal to 1000 mg/kg is prohibited. Effective August 8, 1988, the underground injection into deep wells of these wastes is prohibited. Certain variances exist until May, 1990 for land and injection well disposal of some wastewaters and nonwastewaters for which Best Demonstrated Available Technology (BDAT) treatment standards have not been promulgated by EPA (3786). EPA requires 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 40 CFR 264.343 or 265.343 (3782).

Toxic Substances Control Act (TSCA)

Under TSCA Section 4, EPA requires that manufacturers and processors of 2,4-D perform human health effects studies and chemical fate testing in support of the RCRA program (3792).

Comprehensive Environmental Response Compensation and Liability Act (CERCLA)
2,4-D 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 2,4-D but these depend upon the concentrations of the chemicals in the waste stream (3766). Under SARA Title III Section 313, manufacturers, processors, importers, and users of 2,4-D must report annually to EPA and state officials their releases of this chemical to the environment (3787).

Federal Insecticide, Fungicide and Rodenticide Act (FIFRA)
Tolerances have been established for residues of 2,4-D acids, salts and esters in or on raw agricultural commodities. Levels range from 0.05 to 1000 ppm (979). Pesticide registration standards for 2,4-D have been issued by EPA (3798).

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 2,4-D shall not exceed an 8-hour time-weighted average (TWA) of 10 mg/m^3 (3539).

Hazardous Materials Transportation Act (HMTA)
The Department of Transportation has designated 2,4-D as a hazardous material with a reportable quantity of 45.4 kg, subject to requirements for packaging, labeling and transportation (3180).

Food, Drug and Cosmetic Act (FDCA)
The following tolerances have been established for residues of 2,4-D:

- 5 ppm in sugarcane molasses resulting from application of 2,4-D to sugarcane fields;
- 2 ppm in the milled fractions (except flour) derived from barley, oats, rye and wheat to be ingested as, or converted to food;
- 0.1 ppm (negligible residue) in potable water.

Such residues are permitted only for certain applications under the control of Federal Agencies as itemized in 21 CFR Section 193.100 (887). The level for 2,4-D in bottled drinking water is 0.1 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

  All states have adopted EPA Ambient Water Quality Criteria and NPDWRs (see Water Exposure Limits section) as their promulgated state regulations, either by narrative reference or by relisting the specific numeric criteria. These states have promulgated additional or more stringent criteria:

  ILLINOIS

  Illinois sets an MCL of 0.01 mg/L for finished water for public water supplies (3322).

  NEW YORK

  New York has an ambient water quality standard of 4.4 μg/L for Class GA ground-waters and 100 μg/L for Class A, A-S, AA and AA-S surface waters (3500).

  VERMONT

  Vermont has a preventive action limit of 35 μg/L and an enforcement standard of 70 μg/L for 2,4-D in ground-water (3682).

  WISCONSIN

  Wisconsin has a preventive action limit of 20 μg/L and an enforcement standard of 100 μg/L for 2,4-D in ground-water (3840).

Proposed Regulations

- Federal Programs

  Safe Drinking Water Act (SDWA)

  EPA has proposed a maximum contaminant level goal (MCLG) of 70 μg/L for 2,4-D as part of the National Primary Drinking Water Regulations (3772). EPA plans to repropose this MCLG and propose a new MCL of 70 μg/L in May, 1989, with final action scheduled for 1991 (3759).

  Resource Conservation and Recovery Act (RCRA)

  EPA has proposed that solid wastes be listed as hazardous because they exhibit the characteristic defined as EP toxicity when the TCLP extract concentration is equal to or greater than 1.4 mg/L 2,4-D. Final promulgation of this Toxicity Characteristic Rule is expected in June, 1989 (1565).

- State Water Programs

  MOST STATES

  Most states are in the process of revising their water programs and proposing changes in their regulations which will follow EPA's changes when they become final. Contact with the state officer is advised. Changes are projected for 1989-90 (3683).

MINNESOTA
Minnesota has proposed a Recommended Allowable Limit (RAL) of 70 µg/L for 2,4-D in drinking water (3451).

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 2,4-D is 0.1 mg/L. The total maximum allowable concentration for pesticides and related products is 0.5 mg/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)
2,4-D 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 Classification, Packaging and Labeling of Pesticides (786)
2,4-D 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)
2,4-D 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 organohalogen compounds at sea be prohibited.

60.1 MAJOR USES

Dichlorophenoxyacetic acid (2,4-D) is a systemic herbicide widely used for control of broad leaf weeds in cereal crops and sugarcane and on turf, pastures and non-cropland. It is also used to control the ripening of bananas and citrus fruits, to delay preharvest dropping of some fruits and in some countries as a fungicide for the control of Alternaria rots when lemons are to be held for storage (1607).

Technical-grade 2,4-D is available in the U.S. as the free acid but is rarely used due to its solubility; the more soluble forms such as alkali salts, amine salts or esters are generally used in commercial formulations of 2,4-D (2051). Technical 2,4-D may range in purity from less than 90% to 99% and can be contaminated with low levels of chlorinated dibenzo-p-dioxins (<60 ppb). 2,3,7,8-TCDD is not normally found in 2,4-D products (2050, 2051). The amine formulations can also contain trace impurities of N-nitrosamines that form from nitrite which is added as a corrosion inhibitor (2050, 2051).

60.2 ENVIRONMENTAL FATE AND EXPOSURE PATHWAYS

60.2.1 Transport in Soil/Ground-water Systems

60.2.1.1 Overview

2,4-D is expected to be relatively mobile in the soil/ground-water system when present at low dissolved concentrations. Bulk quantities of the solution (e.g., from a spill, heavy spray application, or improper disposal of excess formulations) could be transported even more rapidly through the unsaturated zone. However, as discussed later in this section, 2,4-D has been shown to be highly susceptible to degradation in the soil/ground-water system and is not expected to be persistent.

2,4-D herbicides have been used extensively on agricultural and forest lands. In herbicide formulations, 2,4-D is usually a relatively minor component with the esters and/or amines comprising the bulk of the active ingredients. For example, in Agent Orange, the phenoxyacetic acids (2,4-D and 2,4,5-T) represent only about 1% while the n-butyl esters of 2,4-D and 2,4,5-T represent 49.5% and 48.8%, respectively (1850). Agent Purple, which was used prior to 1964, is a 50:30:20 mixture of the n-butyl esters of 2,4-D and the n-butyl and isobutyl esters of 2,4,5-T (1650). Hydrolysis of the isopropyl, butyl, and isooctyl esters of 2,4-D in the environment is rapid, with reported half-lives on the order of 100 hours in neutral soil water; hydrolysis was almost instantaneous in the presence of a base or in a suspension of soils at pH 7.0-7.5 (1851). Biological hydrolysis of these materials has also been reported to be very rapid (1852). Since 2,4-D, as the predominant breakdown product of the 2,4-D esters and amines, is more stable than the original materials, its fate in the

environment is of prime concern. Therefore, this chapter will focus on a discussion of the transport and transformation of the acid, 2,4-D.

2,4-D is a moderately strong organic acid with reported pKa values ranging from 2.8 to 3.3 (1866, 2050) and thus is almost completely dissociated to the anionic form at typical environmental pH levels. For example, the extent of 2,4-D dissociation in pure water at pH 3, 4, 5, 6, and 7 is approximately 50%, 90%, 99%, 99.9%, and 99.99%, respectively. In general, the dissociated form (i.e., the 2,4-D anion) is expected to be more soluble in water, less strongly sorbed to soils, and less likely to be bioaccumulated than the undissociated form. Thus, the importance of the soil/ground-water pH levels in determining the mobility of 2,4-D is difficult to overstate.

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 soil concentrations of 2,4-D among soil particles, soil-water, and soil air. Portions of 2,4-D associated with the water and air phases of the soil generally have higher mobility than the adsorbed portion. Partitioning estimates are given for the total chemical (dissociated as well as undissociated 2,4-D) at various pHs and for the undissociated form of the chemical, the latter being valid only for very low pHs (i.e., less than the pKa of 2.6 to 3.3). Estimates for the unsaturated topsoil model indicate that while most of the undissociated 2,4-D in the modeled system is expected to be associated with the stationary phase, most of the 2,4-D present in the soil at common environmental pHs (>5) will be in the mobile soil-water phase and thus easily leached. An insignificant portion of 2,4-D 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), a higher percentage of the undissociated 2,4-D (80%) and almost all of the 2,4-D present at environmental pH levels is predicted to be present in the soil-water phase (Table 60-1) and available for transport with flowing ground-water. Ground-water underlying 2,4-D-contaminated soils with low organic content appears to be vulnerable to contamination. However, data discussed later in this section demonstrate that rapid biodegradation of 2,4-D (which is not addressed in this partitioning model) largely prevents 2,4-D from being a serious threat to ground-water.

Due to the extensive use of 2,4-D herbicides, several groups have studied its persistence in soils. In general, 2,4-D has a low K_{oc} value, low Henry's law constant, and high rate of degradation. Volatilization is not expected to be important. The chemical is not expected to persist in the soil/ground-water system due to rapid degradation, and leaching of residual amounts may be rapid (1350, 2050, 1210). The organic content and microbial activity of the soil, the pH of the soil, and extremes in the rate of 2,4-D application have been reported to affect the persistence of 2,4-D in soil. Extensive degradation of 2,4-D in neutral soil within one month has been reported by Moreale et al. (1854); lower rates of degradation were reported in acid

TABLE 60-1
EQUILIBRIUM PARTITIONING CALCULATIONS
FOR 2,4-D 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]			
• Undissociated 2,4-D	92	8	<1E-06
• Total 2,4-D[e]			
pH 3	46	54	<1E-06
pH 4	9.2	90.8	<1E-07
pH 5	0.9	99.1	<1E-09
pH 6	0.09	99.91	<1E-09
pH 7	0.009	99.99	<1E-10
Saturated deep soil[d]			
• Undissociated 2,4-D	20	80	
• Total 2,4-D[e]			
pH 3	10	90	
pH 4	2	98	
pH 5	0.2	99.8	
pH 6	0.02	99.98	
pH 7	0.002	99.998	

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 top soil 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} = 60 (1210).
c) Henry's law constant taken as 1.9E-10 atm · m^3/mol at 25° (1210).
d) Used sorption coefficient $K_p = 0.001 \times K_{oc}$
e) The distribution for total 2,4-D assumes that all of the dissociated fraction partitions to the soil-water compartment and that the approximate percentage of dissociation is as follows: 50% at pH 3, 90% at pH 4, 99% at pH 5, 99.9% at pH 6, and 99.99% at pH 7.

soils. Reported half-lives for 2,4-D in soils range from four days (1855) to 1-2 weeks (1850, 808, 2050, 1856). The time reported for 90% disappearance of 2,4-D applied to soil is on the order of 2 months; after 10-55 weeks, less than 1% could be identified (1854, 1857, 1858). A somewhat higher persistence has been noted in forestry soils than in agricultural soils; the higher rate of application and lower pH has been cited in explaining this observation (1859).

Under normal herbicide application rates, no evidence of 2,4-D persistence from one season to the next has been detected (1862). Only where 2,4-D herbicides were applied at massive doses (~1000 lb/A) were there significant residues after 10 years (1850). Initial 2,4-D soil concentrations of 100-500 ppm were reported to decrease 45% to 98% at two Air Force test sites monitored over a 12-month period (1860). A decrease in pesticide degradation, possibly due to a reduction in the number of active organisms, and rapid leaching were offered as explanations for the increased persistence at high concentrations. At a simulated work disposal site, high concentrations of 2,4-D migrated in a manner similar to unadsorbed chemicals (1861).

Although 2,4-D is expected to be relatively non-persistent in the soil/ground-water environment, trace levels have been observed in surface and ground-waters. In a Canadian surface water quality monitoring program, 59% of the stations monitored exhibited detectable levels of 2,4-D (1852); in another study, 66 of 949 stream waters showed 2,4-D residues (1862). Frank et al. (1863) reported 2,4-D contamination of well water in an agricultural area; serious contamination occurred after a spill near the well. All three of these reports indicate that transport to surface and well waters occurred as a direct result of spray activity in the vicinity of streams (aerial drift) or transport with storm runoff near the time of 2,4-D application. Although substantial quantities of 2,4-D have been detected in run off following the first rainfall event after application (due to high solubility and weak sorption), 2,4-D runoff concentrations decline rapidly and generally account for less than 1-5% of the application (1864, 1865) with most of the loss associated with the water phase.

60.2.1.2 Sorption on Soils

2,4-D is weakly adsorbed to most soils and rapid migration has been reported in field and laboratory studies (1866, 1852, 1864, 2050, 1867, 1854, 1868). Adsorption is a function of the organic content and the pH of the soil system. The acid dissociation constant (pKa) of 2,4-D has been reported to range from 2.64-3.31 (1866, 2050). Rippen et al. (1869) report that 2,4-D is 90% dissociated at pH 4 and 99.99% dissociated at pH 7. Since the pH of most soils is greater than 4.5 and that of most natural waters is greater than 6 (1864), 2,4-D is expected to exist in the environment primarily in the anionic form. The dissociated ion is poorly adsorbed due to high water solubility and the possible repulsion of the anion by the surface negative charge of soil organic matter and clay (1866). In soils with pH 7 and 7.9, Rippen et al. (1869) reported no observed adsorption; some adsorption was observed at pH 5.8. Strong sorption onto clays in acidic environments has been reported (1870, 1871).

Table 60-2 presents Freundlich adsorption data for 2,4-D sorbed to soils. The data indicate that, in general, 2,4-D is weakly sorbed to environmental soils and that adsorption is a function of organic content of the soil. In addition, the observed variation in K_{oc} values with pH supports the expected decrease in sorption with increasing pH. It has been reported (1865, 1866) that a small portion of adsorbed 2,4-D is resistant to desorption after prolonged field exposure. The desorption-resistant fraction is dependent upon initial concentration and may be more significant in deep soils where biodegradation is expected to be slower. In soils ranging from 0.1% to 2.5% organic carbon with pH less than 5, the percent of irreversibly adsorbed 2,4-D ranged from 13% to 29% (1866).

In view of the high solubility of 2,4-D at environmental pH levels, rapid leaching may be expected and has been reported in several studies. Wheeler et al. (1870) reported that the shape of the 2,4-D flux curve in drainage waters from a treated citrus grove was determined by the shape of the water flow curve; soil pH was the predominant factor in 2,4-D mobility and facilitated its movement as the ionized species. In laboratory experiments (1854) with surface soil (1.8% organic content), 200 mm of percolating water leached less than 15% of applied 2,4-D below 25 cm; in the same experiment with subsurface soil (0.1% organic carbon) 90% was leached below the 25 cm depth. Other studies (1864) also reported that most (~90%) of the surface applied 2,4-D residues remained in the top 15-30 cm of soil, with only low levels detected at greater depths. One study (1872) reported no detectable residues below 5 cm depth one year after normal application to chaparral vegetation and soil.

At high levels of 2,4-D application, the percent adsorption has been reported to decrease with increasing initial concentration (1858). Majka et al. (1868) reported very little 2,4-D retardation when applied to either acidic or basic soils at massive rates (560-2800 kg/ha). For 2,4-D applied at normal application rates, resulting in a soil solution range of 0.01 to 10 ppm, adsorption appears to be independent of solution concentration (1854).

60.2.1.3 Volatilization from Soils

Due to its low vapor pressure and relatively high water solubility, evaporation of 2,4-D from aqueous solution is expected to be negligible as indicated by the extremely low values reported for Henry's law constant, 1.3 - 1.9E-10 atm · m^3/mol (1210, 808). The rate of volatilization from soil is generally significantly lower than that from water. Therefore, volatilization of 2,4-D from surface soils or in soil air will not be an important transport process, particularly in the presence of any soil moisture.

TABLE 60-2
FREUNDLICH ADSORPTION CONSTANTS FOR 2,4-D ON SOILS

Soil Type	K_F[a]	1/n[a]	K_{oc}[b]	Ref.
Surface soils:				
Soignes silt/loam, 8.52% o.c., pH 3.40	16.2	0.76	190	1854
Spa City clay loam, 6.70% o.c., pH 3.25	23.9	0.86	357	1854
Meerdael silt loam, 6.19% o.c., pH 4.00	7.0	0.88	114	1854
Fleron silty clay loam, 5.59% o.c., pH 3.75	2.0	0.94	36	1854
Bullingen silt loam, 5.45% o.c., pH 3.55	1.8	0.91	34	1854
Strodam AB-horizen, 5.11% o.c., pH 3.88	2.4	0.97	50	1866
Stavelot silt loam, 4.37% o.c., pH 3.90	7.6	0.92	174	1854
Bernard-Fagne silt loam, 4.17% o.c., pH 3.60	13.2	0.88	316	1854
Zolder sand, 3.20% o.c., pH 3.84	10.4	0.86	471	1854
Gribskov B-horizon, 2.58% o.c., pH 3.59	6.3	0.91	240	1866
Heverlee III sandy loam, 2.50% o.c., pH 5.84	0.8	0.92	34	1854
Lubbeek I silt loam, 1.98% o.c., pH 6.62	0.8	0.92	39	1854
Stookrooie II loamy sand, 1.85% o.c., pH 5.64	1.8	0.93	98	1854
Gribskov C-horizon, 1.82% o.c., pH 4.07	2.8	0.85	160	1866
Roskilde agricultural soil, 1.64% o.c., pH 5.40	2.5	0.93	150	1866
Gribskov A-horizon, 1.41% o.c., pH 3.23	2.8	0.91	200	1866
Nodebais silt loam, 1.25% o.c., pH 6.20	0.4	0.89	31	1854
Lubbeek III silt loam, 1.12% o.c., pH 6.91	0.4	0.91	38	1854
Lubbeek II sandy loam, 0.91% o.c., pH 6.71	0.3	0.91	34	1854
Zolder sand, 0.32% o.c., pH 4.23	1.0	0.88	297	1854
Tisvilde C-horizon, 0.15% o.c., pH 4.21	0.1	0.65	90	1866
Strodam C-horizon, 0.09% o.c., pH 4.95	0.2	0.93	180	1866
Subsoils:				
Bjodstrup clayey till, 0.13% o.c., pH 7.64	0.1	0.84	100	1866
Zolder sand, 0.12% o.c., pH 4.73	0.4	0.93	350	1854
Lubbeek II sand, 0.12% o.c., pH 6.46	0.1	0.88	73	1854
Esrum sandy till, 0.06% o.c., pH 4.71	0.2	1.03	380	1866
Tirstrup meltwater sand, 0.05% o.c., pH 6.14	0.3	0.91	540	1866
Lubbeek II sand, 0.04% o.c., pH 6.43	0.05	0.88	125	1854

a) K_F = Freundlich adsorption coefficient, and 1/n = Exponential factor on concentration in Freundlich adsorption equation.
b) K_{oc} = soil adsorption constant per unit weight organic carbon ($K_{oc} = K_F$/o.c.). Calculation of K_{oc} assumes Freundlich constant n = 1.

The vapor pressures of the alkyl esters of 2,4-D are reported to be several orders of magnitude higher than that of the 2,4-D acid (2050), and significant airborne losses of the esters from commercial herbicide formulations have been

reported (1874, 1875). Volatilization is related to soil moisture and vapor losses from dry soil have been reported to be minimal (1874). Ambient air monitoring performed during Herbicide Orange disposal operations indicated very minor evaporative emissions of 2,4-D during handling of concentrated herbicide solutions (1873).

60.2.2 Transformation Processes in Soil/Ground-water Systems

2,4-D is an acidic compound (pKa = 2.6-3.3) and has a strong tendency to hydrolyze in the presence of water. At pH levels above 5.0, 2,4-D is expected to be greater than 99% dissociated. Degradation reactions (oxidation, reduction, hydrolysis, substitution) have been reported to occur in water when activated by sunlight (1850, 1864). Half-lives for 2,4-D in clear shallow water exposed to 12 hours per day unobstructed sunlight was estimated at 20 days. In another experiment, 30-70% of a dried film of 2,4-D on glass was degraded after seven days of irradiation (1876); other authors have reported that 2,4-D is stable under dry conditions (1864).

Numerous studies have shown that 2,4-D is readily biodegraded by micro-organisms which are prevalent in the natural environment (1865, 1877, 1878, 846, 1885) and that microbial metabolism is the predominant (or even sole) factor affecting decay in soils (1879). Most half-lives reported for the biodegradation of 2,4-D in soils range from a few days to two weeks, with more than 90% degradation within a few months.

Degradation experiments have established that both aromatic and side chain carbons of 2,4-D can be rapidly converted to CO_2 (1880, 846). Degradation products that have been identified in culture media are 2,4-dichlorophenol, 2,4-dichloroanisole, 4-catechol, chloromuconic acids, and chlorohydroxyphenoxyacetic acids (3445, 1877, 1885). None of these degradation products persist in the environment.

Breakdown of 2,4-D has been reported to follow a well established degradation pattern of two first-order reactions: a slow initial reaction (lag phase) during which microbial enrichment occurred, followed by a rapid first-order decline in concentration (1879, 1885, 1881). In the literature, the duration of the lag phase has been reported to range from a few days to four weeks, and the time for 50% disappearance has been reported to range from four days to seven weeks; the time for total disappearance has been reported to be seven days to 14 weeks (1879).

In general, degradation of 2,4-D in soil is not correlated specifically with soil properties but has been shown to depend primarily on microbial population and numbers of 2,4-D degraders available (1885, 1882). The effect of 2,4-D sorption on degradation is not clear. Young (1889) reported no degradation of 2,4-D sorbed on charcoal in spite of the presence of degrading organisms; and other data generated in a vigorously controlled environment using a single strain of bacteria indicated that sorbed 2,4-D is completely protected from biodegradation (1890). Another study, on the other hand, reported extensive degradation of 2,4-D adsorbed onto aerobic lake sediments (1888).

The breakdown of 2,4-D has been shown to be dependent on the availability of soil moisture; little or no degradation was observed in dry soils (1882, 1884, 1874, 1886, 1887). The importance of the presence of oxygen has also been demonstrated in that degradation slows significantly under flooded (anaerobic) conditions; e.g., over six weeks, 53% 2,4-D loss was observed in a moist field compared to 16% loss under flooded conditions (1884). In other studies, the rate of 2,4-D degradation has been reported to be 6 to 40 times slower under anaerobic conditions than under aerobic conditions (846, 1888), suggesting that aerobic microorganisms were responsible for the rapid degradation observed in aerobic soils.

Most data indicate no adverse impact on soil biota due to normal application of 2,4-D (0.3-5 kg/ha); however, several studies have reported significant reduction in the soil bacterial population following repeated applications of high doses (1891, 1892). Biodegradation of 2,4-D was observed to be slow at soil concentrations above 1000-5000 ppm (1891, 1892, 1893, 1894). Parker and Doxtader (1881) reported a significant increase in lag time as herbicide concentration increased.

The observed decrease in 2,4-D biodegradation at high herbicide concentration may be due to either the toxicity of 2,4-D to microorganisms or the decrease in soil pH affected by the high 2,4-D application rate. Moreale et al. (1854) reported low rates of degradation at pH < 6.0 due to the increased 2,4-D adsorption as well as decreased microbial populations in acid soils; after one month at pH > 6.0, 80-95% of 2,4-D was degraded compared to < 10% after one month at pH < 6.0. The degradation rate for high levels of formulated 2,4-D was higher than for the technical-grade material; this may be due to the fact that the technical-grade material was observed to lower the soil pH significantly while the 2,4-D formulation had little effect on soil pH (1892). The other formulation chemicals may also serve as a carbon source and thereby reduce the toxic effect of 2,4-D.

In summary, 2,4-D has the potential to be rapidly degraded in the soil environment. The rate of biodegradation is related to the availability of degrading microbial populations; massive doses of 2,4-D may be degraded much more slowly. There is evidence that the form in which 2,4-D is released to the environment (i.e., technical-grade vs. herbicide formulation) may impact the extent to which high concentrations decrease the rate of biodegradation. Since the concentration of soil microorganisms capable of biodegradation is fairly low and drops off significantly with depth, biodegradation in the soil/ground-water system may be limited. Thus, 2,4-D transported vertically into the subsoil may represent a potential threat of ground-water contamination. In ground-waters, 2,4-D degradation is expected to be slow ($t_{1/2}$ = 200 days) principally due to the limited microbial populations (1883).

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

The above discussion of fate pathways suggests that 2,4-D is nonvolatile, weakly sorbed to soil and has a low potential for bioaccumulation. These fate characteristics suggest several potential exposure pathways.

Volatilization of 2,4-D from a disposal site is expected to result in negligible exposure to workers or residents in the area because 2,4-D in either dissociated or undissociated form is nonvolatile. The potential for ground-water contamination exists due to the weak sorption of the undissociated acid on soil, and the even weaker retention of the dissociated acid, which is expected to be the predominant form under virtually all pH levels of environmental concern. The susceptibility of 2,4-D to degradation, however, should reduce its occurrence in drinking water supplies. 2,4-D has been detected in many ground-waters (992), but as described below it has rarely been detected in national surveys of drinking-water systems, including those served by ground-water supplies.

The movement of 2,4-D in ground-water or its movement with soil particles may result in discharge to surface water. As a result, ingestion exposures may occur from the use of surface waters as drinking water supplies, and dermal exposures may result from the recreational use of surface waters. Ingestion exposure may also occur from the consumption of aquatic organisms or domestic animals that have contact with contaminated water. However, due to the low bioconcentration factor for 2,4-D, this is unlikely to be an important exposure pathway from soil/ground-water systems.

60.2.4 Other Sources of Human Exposure

Nearly sixty percent of the 2,4-D sold in the United States is used on agricultural crop sites; the remainder is applied to range and pasture land, lawns, forests, industrial and commercial sites, or used for aquatic weed control (992). Thus, it is distributed widely in the environment.

Exposure to 2,4-D in drinking water does not appear to be common, although it has been detected in drinking water in four states (992). The highest value reported in the literature is 50 $\mu g/L$, but in one national study, only 1 of 117 water systems sampled contained concentrations of 2,4-D above 0.5 $\mu g/L$ and none of 92 rural water systems sampled in another study contained above 0.01 $\mu g/L$ of 2,4-D (2050).

Contaminated surface waters may be another source of human exposure. The National Surface Water Monitoring Program, between 1976 and 1981, detected 2,4-D in 1.6% of the samples (detection limit not specified) with a maximum concentration of 1.91 ppb; the occurrence in sediment samples was less common (0.2%) with a maximum concentration of 14.9 ppb (1242). In surface waters of the western prairies of Canada, 2,4-D was detected much more frequently, possibly because of a lower detection limit. At 59% of 186 sites sampled between 1971 and 1977, 2,4-D was detected at above 0.004 $\mu g/L$, with a maximum concentration of 4.33 $\mu g/L$ (1852). The source of 2,4-D contamination of Canadian well waters was reported to include herbicide drift from spraying operations, spillage or runoff, rather than ground-water contamination (1863, 1917).

Air exposures to 2,4-D are not expected to be significant based on available data. In a monitoring study of 16 cities, the maximum concentration detected was 4 ng/m^3 (1916).

Diet appears to be a minor exposure pathway for 2,4-D. There have been no findings of 2,4-D in FDA adult market basket surveys since 1973 (2050). Between 1976 and 1979, no 2,4-D was detected in annual market basket surveys for infants (6 months old) and only in 1976 was any found in the diet of toddlers (2 years old) (1244). The estimated daily intake in that case was 0.006 μg/kg of body weight. 2,4-D has been found in individual food samples, however. In 1982, compliance reports of the FDA revealed that 1 of 10 food samples tested positive for 2,4-D (992).

Several studies have reported that 2,4-D is secreted in milk. Following oral administration, traces of 2,4-D were found in milk of lactating rats for 6 months (3211). 2,4-D was also eliminated in the milk of cows grazing in pastures treated with 2,4-D or its butyl or isooctyl ester (3090, 3365).

60.3 HUMAN HEALTH CONSIDERATIONS

60.3.1 Animal Studies

60.3.1.1 Carcinogenicity

Osborne-Mendel rats ingested 0, 5, 25, 125, 625 or 1250 ppm 2,4-D (96.7% pure) in the diet for 104 weeks. A dose-related increased incidence of malignant neoplasms was reported in male rats for all doses. Sarcomas consisted mainly of lymphosarcomas while carcinomas were seen in the endocrine system. Thirty-one percent of all treated females developed lymphosarcomas. Neoplasms of the mammary gland were also increased in 2,4-D-treated rats (53/111 in animals treated with 5 to 1250 ppm). It was concluded that 2,4-D was carcinogenic to male and female rats in this study resulting in an increased incidence of lymphosarcomas in both male and female rats and neoplasms of the mammary gland in females (2123). This study was considered inadequate by IARC (1607) due to the small number of animals (i.e., 25 of each sex per group) tested per treatment group.

No increased incidence of neoplasms was reported in mice treated with 0 or 46.4 mg/kg 2,4-D (90% pure) in 0.5% gelatin daily by stomach tube for 21 days followed by 149 ppm 2,4-D in the diet for 18 months (2136).

Innes et al. (2136) injected mice subcutaneously with a single dose of 215 mg/kg 2,4-D (90% pure) suspended in dimethylsulfoxide on day 28 of age. Animals were observed for 18 months. No significant increase in tumors was noted.

A skin painting study in mice was conducted by Archipov and Kozlova (2125). Cross strains of CBA x C57/BL mice received one drop of a 0.5% solution of 3-methylcholanthrene in benzene on the skin for 3 weeks. Mice were then painted with either a 10% solution of the amine salt of 2,4-D in acetone or a 10% solution of commercial 2,4-D and observed for 20 months. Papillomas developed on the skin of 17.7% of the mice treated with 3-methylcholanthrene followed by 2,4-D, but not in

mice receiving 3-methylcholanthrene alone or 2,4-D alone. 2,4-D was concluded to be a promoter of neoplasms of the skin in mice.

IARC (13, 57) considered the available animal studies inadequate to evaluate the carcinogenicity of 2,4-D. Recent reports, however, have generated concern about potential carcinogenic effects of 2,4-D and suggest further investigation is needed. Rare brain tumors were reported in 10% of male rats treated with 40 mg/kg 2,4-D; final results of this study are expected in June, 1987 (2105). Also, a recent epidemiological study involving Kansas farmers using phenoxyherbicides including 2,4-D revealed an increased incidence of non-Hodgkin's lymphoma (2118, 2119) (see Section 60.3.2.2 for further discussion).

60.3.1.2 Genotoxicity

2,4-D does not appear to be genotoxic in a number of tests including bacteria (2126, 2127, 3470), a dominant lethal study in mice (998) and recessive lethal tests in Drosophila (2128, 3863). Conflicting results are reported on the effects of 2,4-D on blood lymphocytes in culture vs. in vivo (2108, 3476).

2,4-D was not mutagenic in strain WP2 of Escherichia coli (2126) or in strains TA1535, TA1536, TA1537 or TA1538 of Salmonella typhimurium (2127, 3470).

The rate of gene conversion was shown to increase in Saccharomyces cerevisiae D4 at 2,4-D concentrations above 400 μg/mL (2127). Mitogenic recombination in S. cerevisiae D5 was also increased by 30 μg/mL of 2,4-D (2127).

No effect was reported in recessive lethal tests in Drosophila melanogaster (2128), either by injection or feeding (3863). 2,4-D also did not increase dominant lethal mutations in mice given either an intraperitoneal injection of 125 mg/kg or 15 mg/kg/day orally for 5 days (998).

Death occurred 2 to 5 hours following intraperitoneal administration of 5 μg/kg 2,4-D to Wistar rats while a dose-related clastogenic effect was noted in rats administered 1.25 or 2.5 μg/kg of 2,4-D (2106). In another report, male Wistar rats injected intraperitoneally with 35 or 70 mg/kg (1/20 and 1/10 LD_{50}) 2,4-D at zero and 24 hours and sacrificed 6 hours after the second injection showed a significant increase in chromosome aberrations in their bone marrow cells (3006).

When Chinese hamster ovary (CHO) cells were treated in culture with 2,4-D, an increase in sister chromatid exchanges was observed, but only without exogenous metabolic activation; an increase in chromosomal aberrations was observed only with metabolic activation (3235). In contrast to the positive effects in culture, Linnainmaa (2108) found no increase in sister chromatid exchanges in peripheral lymphocytes of rats or in the bone marrow cells of Chinese hamsters treated intragastrically with 100 mg/kg.

Mustonen et al. (3476) examined the lymphocytes of forest workers who worked with commercial preparations of 2,4-D. No chromosomal aberrations were observed in these cells even though urinalysis indicated that these workers had absorbed 2,4-D. Linnainmaa (2109) also found no significant differences in sister chromatid exchange frequencies in peripheral lymphocytes of 35 forestry workers whose blood was examined before, during or after spraying foliage with 2,4-D.

Mustonen et al. also treated human blood in culture with pure and with commercial 2,4-D. No chromosomal aberrations were observed in lymphocytes treated with the pure preparation, but a significant increase in chromosome aberrations, particularly chromatid exchanges, was observed with 0.5, 1.0 and 1.25 mM of the commercial 2,4-D. The authors suggest that the commercial 2,4-D may contain chlorophenol contaminants.

Korte and Jalal (2107) reported a statistically significant increase in chromosome gaps and deletions in human lymphocyte cultures treated with 50 or 60 μg/mL of 2,4-D. Sister chromatid exchanges were also significantly increased in these cells with concentrations of 10 to 60 μg/mL. Turkula and Jalal (2110) also reported a significant increase in sister chromatid exchanges in human lymphocytes treated in culture with 50 μg/mL of 2,4-D but not with 100 or 250 μg/mL; they attribute the negative effects to the possibility that a high proportion of cells "either do not enter the division phase or fail to survive."

60.3.1.3 Teratogenicity, Embryotoxicity and Reproductive Effects

Oral administration of 2,4-D was associated with mild embryo- and fetotoxicity when given to pregnant Sprague-Dawley rats (2057). Animals received 0, 12.5, 25, 50, 75 or 87.5 mg/kg/day on gestational days 6 through 15. No dose-related teratogenic effects were reported; however, an embryotoxic response was observed. Fetuses treated with high doses (>50 mg/kg) of 2,4-D displayed subcutaneous edema, delayed ossification or split centers of ossification in the sternebrae, missing sternebrae, delayed ossification of the skull bones and wavy ribs. No difference was noted in the development or survival of pups for 21 days following birth in the control and treated groups. No effect on fertility, gestation, viability or lactation were observed.

CD-1 mice were exposed by gavage to 87.5 mg/kg/day of 2,4-D on gestational days 8 through 12 in a study conducted by Kavlock et al. (3350). The treatment resulted in 7% maternal death. The litter size was similar to that of the controls; however, the day 1 average pup weight was reduced in a statistically significant manner (1.53 g vs 1.65 g for controls). Pup viability and body weight on day 3 were not affected by the treatment.

No deleterious effects on fertility or average litter size were reported in a 3-generation, 6-litter reproduction study in Osborne-Mendel rats fed 0, 100, 500 or 1500 ppm 2,4-D in the diet (2115). However, the percent of pups born which

survived to weaning and the weights of weanlings in the 1500 ppm treatment group were sharply reduced.

The teratogenic effect of the 2,4-D isooctyl ester and the 2,4-D propylene glycol butyl ether ester were studied in CD rats (2053). Pregnant rats received molar equivalent doses of 0, 6.25, 12.5, 25 or 87.5 mg/kg 2,4-D of each ester. Treatment was administered orally on gestational days 6 through 15. Fetal examination on gestational day 20 revealed the presence of external hematomas in all treatment groups. An increased incidence of 14th lumbar rib buds was also seen in both groups given the 87.5 mg/kg molar-equivalent doses, an indication of embryotoxicity. Neither the 2,4-D isoocytyl ester nor the 2,4-D propylene glycol butyl ether ester produced adverse effects on maternal welfare or pup viability.

60.3.1.4 Other Toxicologic Effects

60.3.1.4.1 Short-term Toxicity

Acute toxicity of 2,4-D is characterized by sudden stiffness in the extremities, incoordination, lethargy, stupor and coma. Myotonia (tonic spasms of muscle) may develop, particularly in the lower extremities. Ventricular fibrillation is the apparent cause of death (2). Autopsy findings usually include mild liver and kidney injury (38). The oral LD_{50} value in the rat is 370 mg/kg while the dermal LD_{50} value is 1500 mg/kg (51).

Dogs died several hours to 3 days following oral or intraperitoneal administration (doses not specified) of sodium or ammonium salts of 2,4-D (2130). Progressive symptoms included muscular incoordination, lethargy, paralysis of the hind quarters, stupor, coma and death. Skeletal muscle changes resembled those seen in congenital myotonia. Centrilobular degeneration and parenchymal damage in the liver was observed in dogs given massive doses of 2,4-D.

Dogs given 100 to 400 mg/kg 2,4-D orally suffered myotonia, gastrointestinal mucosal irritation, moderate hepatic necrosis and mild renal tubular degeneration (2131).

Desi et al. (2056) described the toxic effects of 2,4-D on the nervous system. Rats were intraperitoneally injected with 200 mg/kg 2,4-D daily until death. A progressive decrease in conditioned reflex response was observed over the 6-day treatment period. Histological examination revealed demyelinization in the dorsal portion of the spinal tract. An EEG revealed the appearance of large slow waves. The authors speculated that the neurological effects produced by 2,4-D were due to the action of the compound on the reticular formation followed by cerebral tissue effects. The demyelinization observed in the spinal cord may be responsible for the hind-limb paralysis noted by other investigators (2130, 2131) after poisoning with 2,4-D.

Effects of 2,4-D on normal and regenerating peripheral nerves were then studied in Fischer rats (2112). 2,4-D at a dose of 100 mg/kg, was injected intraperitoneally 6 days/week for 3 weeks. None of the animals developed signs of polyneuropathy and nerve conduction velocity remained normal after the three weeks of treatment.

The effect of 2,4-D on denervated muscle was studied by Eberstein and Goodgold (2111). The right limb of male Wistar rats was surgically denervated by excision. Rats were injected intraperitoneally with 225 mg/kg 2,4-D either one hour prior to administration of anesthesia or 30 to 45 minutes after anesthesia. Contraction activity was then recorded. Results indicate a 2,4-D-induced prolonged relaxation time in muscles denervated for more than 10 days. The increase in relaxation time is similar to that observed in intact muscles treated with 2,4-D and is characteristic of myotonia.

The effect of 2,4-D on hypersensitivity was studied in BALB/c mice (2113). The 2,4-D-protein conjugate did elicit specific IgE production in mice following secondary sensitization and was concluded to produce antibody-mediated rather than cell-mediated hypersensitivity.

60.3.1.4.2 Subchronic and Chronic Toxicity

Subchronic toxicity of 2,4-D was studied in rats by Chen et al. (2114). CDF Fischer 344 rats were fed 0, 15, 60, 100 or 150 mg/kg/day technical-grade 2,4-D in the diet for 13 weeks. The high-dose group experienced growth retardation, decreased food intake and a significant increase in serum glutamic pyruvic transaminase activity. Histopathologic alterations included swelling of hepatocytes in animals given 100 or 150 mg/kg 2,4-D. The 60, 100 and 150 mg/kg treatment groups showed dose-related microscopic changes in the convoluted tubules of the kidneys. The only change noted in the 15 mg/kg treatment group was a significant increase in relative kidney weight.

Hansen et al. (2115) found no significant effect on growth rate, survival rate, organ weight or hematologic values in Osborne-Mendel rats fed 0, 50, 25, 125, 625 or 1250 ppm 2,4-D daily in the diet for 2 years or in beagle dogs fed 0, 10, 50, 100 or 500 ppm 2,4-D daily in the diet for 2 years.

60.3.2 Human and Epidemiologic Studies

60.3.2.1 Short-term Toxicologic Effects

Signs and symptoms of 2,4-D poisoning in man include vomiting, abdominal cramps, diarrhea, anorexia, muscle weakness, myotonia and excessive salivation (49).

A case of severe iritis following exposure to a herbicide containing 2,4-D as the active ingredient was reported by McMillin and Samples (2054). The incident occurred after a previously healthy male rubbed his eyes with unwashed hands while moving containers of Weedone LV4. Within 3 hours, visual acuity had decreased.

Other symptoms included ocular irritation, headache, photophobia and generalized weakness. Examination of the eye nine days later showed ciliary flush and marked vasodilation of the large vessels of the iris. The man's condition resolved over the next three weeks. This case is thought to be the first reported occurrence of ocular toxicity from 2,4-D.

Sare (2117) reported a case of headaches and double vision in a weed sprayer for an industrial spraying firm. Questioning of the subject revealed the symptoms to occur at the end of the work day and only after 2,4-D use.

A case of acute inhalation of 2,4-D occurred while spraying the herbicide along a railway right-of-way (2055). The engineer and conductor on the train received an intense exposure to the herbicide. After the second day of exposure, both men noted itching and burning of the oral and nasal mucosa and the conjunctiva. Small ulcerations appeared on areas of the skin which came in contact with the herbicide. The following day, significant chest discomfort and a cough producing a mucoid sputum were reported. Mild headache, muscle twitching and throat soreness ensued. Chest X-rays and pulmonary function tests revealed no abnormalities of air flow, lung volumes or diffusing capacity despite non-specific complaints from both patients.

The majority of 2,4-D exposure cases are due to inhalation or dermal contact with a spraying mixture. A rare case of 2,4-D poisoning following accidental ingestion was reported by Berwick (2122). A farmer inadvertently swallowed a mouthful (~30 mL) of a concentrated weed killer containing 2,4-D. The victim's tongue and throat felt badly burned and nausea and retching followed. Gastric lavage was performed approximately one hour after ingestion. The victim appeared normal but was sweating profusely and complained of a burning sensation in the mouth, chest and abdomen. He continued to vomit and complained of gastritis for approximately 18 hours. At this time he complained of chest pain and tender muscles. Body temperature rose to 39.4°C (103°F) and cyanosis developed. A complete loss of respiratory movements of the intercostal muscles ensued and oxygen therapy was initiated. Muscles of the upper extremities exhibited spontaneous fibrillary twitching. As the victim began to recover, he still complained of muscle soreness and urine turned dark brown. Urinalysis revealed oxymyoglobin. Myoglobinuria has not previously been reported in 2,4-D poisoning. Generalized skeletal muscle damage was evident as shown by elevated serum glutamic oxaloacetic transaminase, serum glutamic pyruvic transaminase, lactic dehydrogenase, aldolase and creatine phosphokinase levels. The man was discharged 2 weeks after admission. Loss of sexual potency was reported for 4 months. A 36-month follow-up revealed no signs or symptoms of peripheral neuropathy.

60.3.2.2 Chronic Toxicologic Effects

Chronic toxicity of 2,4-D has rarely been reported. Possible chronic symptoms may include dermatitis, weakness and myotonia (2050).

A recent herbicide epidemiology study conducted in Kansas by NCI found an association between the use of herbicides and non-Hodgkin's lymphoma (2344). The study covered a total of 424 cancer cases in white males -- 133 soft-tissue sarcomas, 121 Hodgkin's disease and 170 non-Hodgkin's lymphoma. A control group of 948 men from the general white population was also included. The study found that farmers who used phenoxy herbicides (particularly 2,4-D) had a 60% higher incidence of non-Hodgkin's lymphoma than non-farmers in the state, and farmers exposed to phenoxy herbicides for more than 20 days each year had six times the risk of developing non-Hodgkin's lymphoma as non-farmers. Furthermore, farmers that mixed and applied the herbicides themselves had eight times the risk and farmers who began using the herbicide before 1946 had a 70% greater incidence of non-Hodgkin's lymphoma compared to farmers who began using the chemical in the 1950's and 1960's. It is unclear, however, that 2,4-D causes cancer since the farmers were exposed to a variety of products.

Woods et al. (3848) also found elevated risks of developing non-Hodgkin's lymphoma among farmers, forestry herbicide applicators, and individuals potentially exposed to phenoxy herbicides in any occupation for 15 years or more. An association between increased cancer risk and a specific phenoxy herbicide could not be shown.

An increased incidence of soft tissue sarcomas was reported in individuals exposed to phenoxyacid herbicides. Eriksson et al. (2025) reported a 6-fold increase in the incidence of soft tissue sarcoma following exposure to dioxin- and furan-free herbicides. The increased risk was related to 2,4,5-T, silvex, chlorophenol, 2,4-D and other phenoxy herbicide exposure.

In the above and additional epidemiology studies relating an increased risk of several types of cancers to exposure to phenoxyacid herbicides, it was impossible to separate the effects of exposure to contaminants and other chemicals present in the herbicide formulations from the effects of exposure to 2,4-D alone (3268, 3267, 3046, 3412, 3686). Other studies showed no relationship between exposure to phenoxyacid herbicides and an increased risk of cancer (3594, 3838, 3558, 3346).

Casey and Collie (2116) reported a case of developmental delay and unusual phenotypic abnormalities in a child whose parents had prolonged exposure before and during pregnancy to 2,4-D. Both parents participated in forestry spraying of a herbicide consisting of 2,4-D and 2,4-D amine. Spraying occurred 7 hours a day, 6 days a week from 6 months prior to conception until pregnancy was confirmed.

A case-control epidemiologic study on the relationship between 2,4-D exposure and spontaneous abortion was conducted by Carmelli and Morgan (2121). Telephone interviews were conducted on 134 women reporting miscarriages and 311 controls (most recent live births) from the agricultural industry. No association between spontaneous abortions and husband or wife 2,4-D exposure were reported in the agricultural workers; however, an increased risk was noted in the forestry group.

Long-term occupational exposure to 2,4-D reportedly resulted in gastric colic, anorexia, somnolence, a sweet taste in the mouth, increased hearing sensitivity, a sensation of drunkenness and heaviness of the legs (2132).

Examination of 292 workers engaged in 2,4-D amine and butyl ester manufacturing revealed rapid fatigue, weakness, headache and vertigo in 63% of the workers (2133). Approximately 20% of these workers experienced hypotension, bradycardia, dyspepsia and gastritis.

Wallis et al. (2134) reported neurological changes in a worker exposed to 2,4-D over a one-year period. The worker developed painful paresthesias in the hands and feet followed by painful muscular stiffness in all four limbs. Over the next two years his condition deteriorated. Examination revealed fasciculation of facial, trunk and extremity muscles. A biopsy of the right sural nerve (i.e., calf of the leg) showed degenerative changes.

60.3.3 Levels of Concern

IARC (13, 57) lists 2,4-D as having inadequate evidence of carcinogenicity in animals.

A maximum contaminant level of 0.10 mg/L has been set for 2,4-D in drinking water (296). For noncarcinogenic risks, the USEPA (3977) has issued Health Advisories of 1.0 mg/L (1 day) and 0.3 mg/L (10 days) and 0.1 mg/L (longer term) for children, and 0.4 mg/L (longer term) and 0.07 mg/L (lifetime) for adults. The WHO (666) recommends a level of 100 μg/L for 2,4-D in drinking water.

OSHA (3539) currently permits a time-weighted average of 10 mg/m^3 for 2,4-D. The ACGIH (3005) also has set 10 mg/m^3 as a TWA for 2,4-D.

60.3.4 Hazard Assessment

The carcinogenicity of 2,4-D and its derivatives such as the amine salts and esters has not been adequately tested. One feeding study (2123) conducted with rats suggests an increased incidence of lymphosarcomas, but IARC (1607) considers this study inadequate for evaluation due to the small number of animals in the test population.

Available genotoxicity studies do not suggest that 2,4-D is a potent mutagen. Conflicting reports exist regarding the effects of 2,4-D on blood lymphocytes; positive effects were noted in culture with concentrations of 10 μg/mL or greater (2107, 2110) while in vivo studies were negative (2108, 2109, 3476). Bacterial tests and a dominant lethal test in mice were also negative (2127, 998, 3470, 998).

Mild embryo- and fetotoxicity were noted in rats and mice exposed to 50-87.5 mg/kg/day of 2,4-D during gestation. No teratogenic effects were recorded in either study (2057, 3350). A three generation study indicated no adverse effects on fertility

or litter size in rats fed 100-1500 ppm 2,4-D in the diet during gestation but post-natal survival of the pups exposed to 1500 ppm was sharply reduced (2113).

Acute toxic effects of 2,4-D exposure are characterized by sudden stiffness of the extremities, incoordination, lethargy, stupor and myotonia (2, 2130). The oral LD_{50} value in the rat is 370 mg/kg (51). Death has been ascribed to ventricular fibrillation. The no-effect level for long-term exposure is not firmly established. One 13-week feeding study in rats indicated dose-related alterations in liver and kidney pathology at dosages of 60 mg/kg/day and above (2114). Another investigator noted no effects in rats fed up to 1250 ppm or dogs fed up to 500 ppm in the diet for two years (2115).

In humans, poisoning with 2,4-D results in vomiting, abdominal cramps, diarrhea, anorexia, muscle weakness, myotonia and excessive salivation (49); chronic toxicity other than occupational has rarely been reported. Long-term occupational exposure can result in gastric colic, anorexia, fatigue, a sensation of drunkenness and heaviness of the legs (2132, 2133).

Instances of peripheral neuropathy with incomplete recovery have been reported following exposure to 2,4-D (2134, 2132). Several recent epidemiology studies have shown that groups exposed to phenoxy herbicides have a higher incidence of several types of cancers (2344, 3848, 2025). It is unclear, however, in these and other epidemiology studies, that 2,4-D causes cancer since workers were exposed to a variety of products.

60.4 SAMPLING AND ANALYSIS CONSIDERATIONS

Determination of 2,4-D 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 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 2,4-D in aqueous samples include EPA Methods 8150 (63), 8250 (63), and 509B (1422). Prior to analysis, a measured volume of sample, approximately 1 liter, is acidified and subsequently extracted with ethyl ether using a separatory funnel. The sample extract is hydrolyzed with potassium hydroxide and any extraneous organic material removed by a solvent wash. Because chlorinated phenoxy herbicides may occur in water in various forms (e.g., acid, salt, ester), this hydrolysis step is included to convert all forms of the herbicide to the acid form for analysis. 2,4-D in the acid form is then extracted and converted to the methyl ester of 2,4-D using diazomethane (Method 8150) or boron trifluoride-methanol (Method 509B) as the derivatizing agent. Additional cleanup procedures are specified if interferences are present in the sample matrix. Excess reagent is removed and an aliquot of the concentrated sample is injected onto a gas

chromatographic (GC) column. The GC column is programmed to separate the semi-volatile organics; 2,4-D methyl ester is then detected with an electron capture detector (Methods 8150 and 509B) or with a mass spectrometer (Method 8250). Indentifications for unknown samples should be confirmed by analysis on a second chromatographic column (if using retention time as the identifier).

The EPA procedures recommended for 2,4-D analysis in soil and waste samples, Methods 8150 and 8250 (63) differ from the aqueous procedures primarily in the preparation of the sample extract. Solid samples are initially extracted with acetone/ethyl ether using a wrist-action shaker. The solvent extract is washed, concentrated and then derivatized.

In addition to the methods described above, solid-phase extraction with C18 columns has been recently used to isolate and concentrate phenoxy-acid herbicides in aqueous samples (3832, 3640, 3294). Separations for analytical determinations are then made by thin-layer chromatography (3640) or high performance liquid chromatography (3832, 3249). These methods are direct and rapid. They should improve the accuracy of the analysis over the derivatization methods described above. Other GC columns than those specified by the EPA procedures have also been examined and found to improve separations (3825, 3824). An isotope dilution GC/MS method (3403) and enzymatic immunoassays (3216) have been used to determine 2,4-D in water.

Typical 2,4-D detection limits that can be obtained in wastewaters and non-aqueous samples (wastes, soils, etc.) are shown below. A detection limit for 2,4-D was not indicated in Method 8250 but would be in the range of 1-10 μg/L for aqueous samples and 1 μg/g for nonaqueous samples. The actual detection limit achieved in a given analysis will vary with instrument sensitivity and matrix effects.

Aqueous Detection Limit	Nonaqueous Detection Limit
12 μg/L (Method 8150) 0.01-0.05 μg/L (Method 509B)	0.8 μg/kg (Method 8150)

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Note: The nonsequential numbers of the references reflect the order of references as they appear in the master bibliography.

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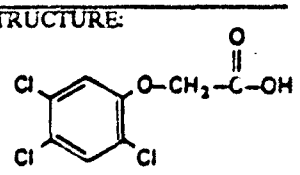
COMMON SYNONYMS:	CAS REG.NO.: 93-76-5 FORMULA: $C_8H_5Cl_3O_3$ NIOSH NO: AJ8400000 STRUCTURE: 	AIR W/V CONVERSION FACTOR at 25°C 10.44 mg/m³ ≈ 1 ppm; 0.096 ppm ≈ 1 mg/m³ MOLECULAR WEIGHT: 255.49
2,4,5-Trichlorophenoxy acetic acid Forron®		

REACTIVITY	For general compatibility classification purposes, 2,4,5-T is considered to be both an organic acid and a halogenated organic compound. Reactions of organic acids with amines, caustics, or nitriles typically evolve heat, while those with oxidizing mineral acids, azo or diazo compounds, hydrazines or isocyanates evolve heat and usually innocuous gases. Reactions with nitrides, strong reducing agents, and certain elemental metals may evolve flammable gases and possibly heat, while those with alkali or alkaline earth elemental metals may also cause a fire. Reactions with inorganic fluorides or sulfides, or strong oxidizing agents may evolve toxic gases and possibly heat. Reactions with cyanides or dithiocarbamates may produce both toxic and flammable gases, with the latter classification also producing heat. Reactions with alcohols, glycols, aldehydes, epoxides or polymerizable compounds may initiate a violent exothermic polymerization reaction. Explosive materials may explode. 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 (511).

PHYSICO-CHEMICAL DATA	• Physical State: Solid (at 20°C)	(23)
	• Color: Light Tan	(23)
	• Odor: Odorless	(54)
	• Odor Threshold: No data	
	• Density: 1.6620 g/mL (at 30°C)	(59)
	• Freeze/Melt Point: 151.00 to 158.00°C	(23,38)
	• Boiling Point: Decomposes above melting point.	(38)
	• Flash Point: No data	

PHYSICO-CHEMICAL DATA (Cont.)	• Flammable Limits: No data	
	• Autoignition Temp.: No data	
	• Vapor Pressure: Essentially zero	(38)
	• Satd. Conc. in Air: Not pertinent	
	• Solubility in Water: 3.00E+02 mg/L, (max) (at 20°C)	(38)
	• Viscosity: No data	
	• Surface Tension: No data	
	• Log (Octanol-Water Partition Coeff.): 3.13	(1219)
	• Soil Adsorp. Coeff.: 6.50E+02	(611)
	• Henry's Law Const.: 1.21E-09 atm · m³/mol (at 25°C)	(1219)
	• Bioconc. Factor: 6.50E+01 (estim)	(659)

PERSISTENCE IN THE SOIL-WATER SYSTEM	2,4,5-T is expected to be highly dissociated, relatively mobile, and non-persistent in natural soils due to limited sorption and relatively rapid degradation. Risk of groundwater contamination is low except under conditions of heavy application, high soil pH and heavy rainfall shortly after application.

PATHWAYS OF EXPOSURE	The primary pathway of concern from the soil/groundwater system is the migration of 2,4,5-T to groundwater drinking water supplies. Degradation in the environment will minimize exposure by this pathway, however, and other exposure pathways are unlikely to be significant.

HEALTH HAZARD DATA	Signs and Symptoms of Short-term Human Exposure: (38) Exposure to 2,4,5-T may cause abdominal pain, nausea, vomiting, diarrhea, and blood in the stool. Skin irritation may also occur. Acute Toxicity Studies: (3504) ORAL: LD_{50} 300 mg/kg — Rat LD_{50} 381 mg/kg — Guinea Pig LD_{50} 242 mg/kg — Mouse LD_{50} 310 mg/kg — Chicken LD_{50} 425 mg/kg — Hamster LD_{50} 100 mg/kg — Dog SKIN: LD_{50} 1535 mg/kg — Rat Long-Term Effects: Reduced body weight gain; liver and kidney alterations (animal data) Pregnancy/Neonate Data: Possible teratogen in mice Genotoxicity Data: Negative Carcinogenicity Classification: IARC - Group 3 (evidence for carcinogenicity to animals and humans inadequate) NTP - None assigned EPA - Group D (not classifiable as to human carcinogenicity)

HANDLING PRECAUTIONS (38)	Handle chemical only with adequate ventilation. Concentrations of 10-50 mg/m³: Any dust and mist respirator, except single-use • 50-100 mg/m³: Any dust and mist respirator, except single-use or quarter-mask respirator or any fume respirator or high efficiency particulate filter respirator or any supplied-air respirator or any self-contained breathing apparatus • 100-500 mg/m³: A high efficiency particulate filter respirator with full facepiece or any supplied-air respirator with a full facepiece, helmet or hood or any self-contained breathing apparatus with full facepiece • 500-5000 mg/m³: A power 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 clothing to prevent repeated or prolonged skin contact.

ENVIRONMENTAL AND OCCUPATIONAL STANDARDS AND CRITERIA

AIR EXPOSURE LIMITS:

Standards
- OSHA TWA (8-hr): 10 mg/m³
- AFOSH PEL (8-hr TWA): 10 mg/m³; STEL (15-min): 30 mg/m³

Criteria
- NIOSH IDLH (30-min): 5000 mg/m³
- ACGIH TLV(R) (8-hr TWA): 10 mg/m³

ENVIRONMENTAL AND OCCUPATIONAL STANDARDS AND CRITERIA (Cont.)

WATER EXPOSURE LIMITS:

Drinking Water Standards
None established

EPA Health Advisories and Cancer Risk Levels
The EPA has developed the following Health Advisories which provide specific advice on the levels of contaminants in drinking water at which adverse health effects would not be anticipated.

- 1-day (child): 800 µg/L
- 10-day (child): 800 µg/L
- longer-term (child): 800 µg/L
- longer-term (adult): 1000 µg/L
- lifetime (adult): 70 µg/L

WHO Drinking Water Guideline
No information available.

EPA Ambient Water Quality Criteria
- Human Health (355)
  - No criterion established; 2,4,5-T is not a priority pollutant.
- Aquatic Life (355)
  - No criterion established; 2,4,5-T is not a priority pollutant.

REFERENCE DOSES:
ORAL: 1.000E+01 µg/kg/day (3744)

REGULATORY STATUS (as of 01-MAR-89)

Promulgated Regulations

- Federal Programs

Clean Water Act (CWA)
2,4,5-T is designated a hazardous substance. It has a reportable quantity (RQ) limit of 454 kg (347, 3764).

Safe Drinking Water Act (SDWA)
2,4,5-T is on the first priority list of drinking water contaminants for which National Primary Drinking Water Regulations will be developed (3781). In states with an approved Underground Injection Control program, a permit is required for the injection of 2,4,5-T-containing wastes designated as hazardous under RCRA (295).

Resource Conservation and Recovery Act (RCRA)
2,4,5-T is identified as a hazardous waste (U232) and listed as a hazardous waste constituent (3783, 3784). Non-specific sources of 2,4,5-T-containing waste are wastes from production or manufacturing use of tri-, tetra-, or pentachloro- phenols and their pesticide derivatives, discarded unused formulations containing these compounds, and residues resulting from incineration or thermal treatment of soil contaminated with these formulations (325). 2,4,5-T is on EPA's ground-water monitoring list. EPA requires that all hazardous waste treatment, storage, and disposal facilities monitor their ground-water for chemicals on this list when suspected contamination is first detected and annually thereafter (3775). Effective July 8, 1987, the land disposal of untreated hazardous wastes containing halogenated organic compounds in total concentrations greater than or equal to 1000 mg/kg is prohibited. Effective August 8, 1988, underground injection into deep wells of these wastes is prohibited. Certain variances exist until May, 1990 for some wastewaters and nonwastewaters for which Best Demonstrated Available Technology (BDAT) treatment standards have not been promulgated by EPA (3786). EPA requires 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 (3782).

Comprehensive Environmental Response Compensation and Liability Act (CERCLA)
2,4,5-T 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 2,4,5-T but these depend upon the concentrations of the chemicals in the waste stream (3766).

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 2,4,5-T shall not exceed an 8-hour time-weighted average (TWA) of 10 mg/m^3 (3539).

Hazardous Materials Transportation Act (HMTA)
The Department of Transportation has designated 2,4,5-T as a hazardous material with a reportable quantity of 454 kg, subject to requirements for packaging, labeling and transportation (3180).

- State Water Programs

ALL STATES
All states have adopted EPA Ambient Water Quality Criteria and NPDWRs (see Water Exposures Limits section) as their promulgated state regulations, either by narrative reference or by relisting the specific numeric criteria. These states have promulgated additional or more stringent criteria:

KANSAS
Kansas has an action level of 21 µg/L for ground-water (3213).

NEW YORK
New York has an MCL of 50 µg/L for drinking water and a water quality standard of 35 µg/L for ground-water classed for drinking water supply (Class GA) (3501).

VERMONT
Vermont has a preventive action limit of 10.5 µg/L and an enforcement standard of 21 µg/L for ground-water (3682).

Proposed Regulations

- Federal Programs

No proposed regulations are pending.

- State Water Programs

MOST STATES
Most states are in the process of revising their water programs and proposing changes in their regulations which will follow EPA's changes when they become final. Contact with the state officer is advised. Changes are projected for 1989-90 (3683).

MINNESOTA
Minnesota has proposed a Recommended Allowable Limit (RAL) of 21 µg/L for 2,4,5-T in drinking water (3451).

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 2,4,5-T is 0.1 mg/L. The total maximum allowable concentration for pesticides and related products is 0.5 mg/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)
2,4,5-T 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 Classification, Packaging and Labeling of Pesticides (786)
2,4,5-T 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)
2,4,5-T 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 organohalogen compounds at sea be prohibited.

61.1 MAJOR USES

2, 4, 5-Trichlorophenoxy acetic acid (2,4,5-T) is an organic acid that possesses the property of regulating plant growth at low concentrations and killing plants at high concentrations. It has been used to induce coloration in fruit, as a fruit set and antidrop agent, for brush control and to control aquatic and herbaceous land plants (2143). In 1979, EPA ordered an emergency ban on 2,4,5-T production based on a report of an increase in spontaneous abortions in women of a forestry community. That ban has never been lifted and all uses have been canceled. This effect may have been caused, at least in part, by the contaminant 2,3,7,8-tetrachlorodibenzo-p-dioxin (2,3,7,8-TCDD).

61.2 ENVIRONMENTAL FATE AND EXPOSURE PATHWAYS

61.2.1 Transport in Soil/Ground-water Systems

61.2.1.1 Overview

2,4,5-T is expected to be relatively mobile in the soil/ground-water system when present at low dissolved concentrations. Bulk quantities of the solution (e.g., from a spill, heavy spray application, or improper disposal of excess formulations) could be transported rapidly through the unsaturated zone. However, as discussed later in this section, 2,4,5-T has been shown to be highly susceptible to degradation in the soil/ground-water system and is not expected to be persistent.

2,4,5-T herbicides have been used extensively on agricultural and forest lands. In herbicide formulations, 2,4,5-T is usually a relatively minor component with the esters and/or amines comprising the bulk of the active ingredients. For example, in Agent Orange, the phenoxyacetic acids (2,4-D and 2,4,5-T) represent only about 1% while the n-butyl esters of 2,4-D and 2,4,5-T represent 49.5% and 48.8%, respectively (1850). Agent Purple, which was used prior to 1964, is a 50:30:20 mixture of the n-butyl esters of 2, 4-D and the n-butyl and isobutyl esters of 2,4,5-T (1650). Under most environmental conditions, except very low pH levels, the alkyl esters of 2,4,5-T will be hydrolyzed in a matter of days. In a laboratory hydrolysis study, 58% of the 2,4,5-T applied to water at 1 ppm was detected after 4 hours, 33% after 8 hours, and 12% after 16 hours (1895). Biological hydrolysis of these materials has also been reported to be very rapid (1852). Since 2,4,5-T, as the predominant breakdown product of the 2,4,5-T esters and amines, is more stable than the original materials, its fate in the environment is of prime concern. Therefore, this chapter will focus on a discussion of the transport and transformation of the acid, 2,4,5-T.

2,4,5-T is a moderately strong organic acid with reported pKa values ranging from 2.84 to 2.88 (1864, 1897) and thus is almost completely dissociated to the anionic form at typical environmental pH levels. For example, the extent of 2,4,5-T

dissociation in pure water at pH 3, 4, 5, 6, and 7 is approximately 50%, 90%, 99%, 99.9%,and 99.99%, respectively. In general, the dissociated form (i.e.,the 2,4,5-T anion) is expected to be more soluble in water, less strongly sorbed to soils, and less likely to be bioaccumulated than the undissociated form. Thus, the soil/ground-water pH level is very important in determining the mobility of 2,4,5-T.

In general, transport pathways can be assessed by using an equilibrium partitioning model, as shown in Table 61-1. These calculations predict the partitioning of low soil concentrations of 2,4,5-T among soil particles, soil-water, and soil air. Portions of 2,4,5-T associated with the water and air phases of the soil generally have higher mobility than the adsorbed portion. Partitioning estimates are given for the total chemical (dissociated as well as undissociated 2,4,5-T) at various pHs and for the undissociated form of the chemical, the latter being valid only for very low pHs (i.e., less than the pKa of 2.8). Estimates for the unsaturated topsoil model indicate that while most of the undissociated 2,4,5-T in the modeled system is expected to be associated with the stationary phase, most of the 2,4,5-T present in the soil at common environmental pHs (>5) will be in the mobile soil-water phase and thus easily leached. An insignificant portion of 2,4,5-T 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), a higher percentage of the undissociated 2,4,5-T (27%) and almost all of the 2,4,5-T present at environmental pH levels is predicted to be present in the soil-water phase (Table 61-1) and available for transport with flowing ground-water. Ground-water underlying 2,4,5-T-contaminated soils with low organic content appears to be vulnerable to contamination. However, data discussed later in this section demonstrate that biodegradation of 2,4,5-T (which is not addressed in this partitioning model) largely prevents 2,4,5-T from being a serious threat to ground-water.

Due to the extensive use of 2,4,5-T herbicides, several groups have studied its persistence in soils. In general, 2,4,5-T has a low K_{oc} value, low Henry's law constant, and high rate of degradation. Volatilization is not expected to be important, the chemical is not expected to persist in the soil/ground-water system due to rapid degradation, and leaching of residual amounts may be rapid (1850, 1864, 1985). The organic content and microbial activity of the soil, the pH of the soil, and extremes in the rate of 2,4,5-T application have been reported to affect the persistence of 2,4,5-T in soil. Extensive degradation of 2,4,5-T in neutral soil within one month has been reported (1864, 1857, 1872, 1895); lower rates of degradation were reported in acid soils. Reported half-lives for 2,4,5-T in soils range from 14 to 45 days (1859, 1850). The time reported for 90% disappearance of 2,4,5-T applied to soil is on the order of 1-6 months (1857, 1864, 1895); after 55 weeks, less than 1% could be identified (1857). A somewhat higher persistence has been noted in forestry soils than in agricultural soils; the higher rate of application and lower pH has been cited in explaining this observation (1859).

TABLE 61-1
EQUILIBRIUM PARTITIONING CALCULATIONS
FOR 2,4,5-T 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]			
• Undissociated 2,4,5-T	99.2	0.8	<1E-07
• Total 2,4,5-T[e]			
pH 3	49.6	50.4	<1E-07
pH 4	9.9	90.1	<1E-08
pH 5	1	99	<1E-09
pH 6	0.1	99.9	<1E-10
pH 7	0.01	99.99	<1E-11
Saturated deep soil[d]			
• Undissociated 2,4,5-T	73	27	
• Total 2,4,5-T[e]			
pH 3	37	63	
pH 4	7	93	
pH 5	0.7	99.3	
pH 6	0.07	99.93	
pH 7	0.01	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 soil sorption coefficient estimated according to Means et al. (611): K_{oc} = 650.
c) Henry's law constant taken as 1.21E-09 atm · m³/mol at 25°C (Arthur D. Little, Inc. estimate).
d) Used sorption coefficient $K_p = 0.001 \times K_{oc}$.
e) The distribution for total 2,4,5-T assumes that all of the dissociated fraction partitions to the soil-water compartment and that the approximate percentage of dissociation is as follows: 50% at pH 3, 90% at pH 4, 99% at pH 5, 99.9% at pH 6, and 99.99% at pH 7.

Under normal herbicide application rates, 2,4,5-T is not expected to persist from one season to the next (1862). Only where 2,4,5-T herbicides were applied at massive doses (~1000 lb/A) were there significant residues after 10 years (1850). Initial 2,4,5-T soil concentrations of 200-3700 ppm were reported to decrease 18% to 98% at two Air Force test sites monitored over a 12-month period (1860). A decrease in pesticide degradation, possibly due to a reduction in the number of active organisms, and rapid leaching were offered as explanations for the increased persistence at high concentrations.

Although 2,4,5-T is expected to be relatively non-persistent in the soil/ground-water environment, trace levels have been observed in surface and ground-waters. In a Canadian surface water quality monitoring program, 36% of the stations monitored exhibited detectable levels of 2,4,5-T (1852); in another study, 21 of 949 stream waters showed 2,4,5-T residues (1862). Frank et al. (1863) reported 2,4,5-T contamination of well water in an agricultural area; serious contamination occurred after a spill near the well. All three of these reports indicate that transport to surface and well waters occurred as a direct result of spray activity in the vicinity of streams (aerial drift) or transport with storm runoff near the time of 2,4,5-T application. Although substantial quantities of 2,4,5-T have been detected in runoff following the first rainfall event after application(due to high solubility and weak sorption), 2,4,5-T run off concentrations decline rapidly and generally account for less than 1-5% of the application (1864, 1865, 1895) with most of the loss associated with the water phase.

61.2.1.2 Sorption on Soils

2,4,5-T is weakly adsorbed to most soils and rapid migration has been reported in field and laboratory studies (1852, 1864. 1867, 1868, 1899). The acid dissociation constant (pKa) of 2,4,5-T has been reported to range from 2.34-2.88 (1864, 1897). Since the pH of most soils is greater than 4.5 and that of most natural waters is greater than 6.0, environmental 2,4,5-T is expected to exist primarily in the anionic form which is poorly adsorbed due to its high water solubility and possible repulsion by the surface negative charge of soil organic matter and clay (1864). Strong sorption onto clays in acidic environments has been reported (1871, 1889). In general, it is expected that 2,4,5-T, like 2,4-D, will be weakly sorbed to environmental soils and that adsorption is a function of organic content and the pH of the soil. The observed variation in 2,4-D K_{oc} values supports the expected decrease in sorption with increasing pH; a similar trend is expected for 2,4,5-T.

In view of the high solubility of 2,4,5-T at environmental pH levels, rapid leaching may be expected. Vertical transport to 90 cm has been reported (1864, 1899, 1868); migration of 2,4,5-T in acid soils (e.g., forest soils at pH 3-4) is expected to be much slower (1899). Majka et al. (1868) reported very little retardation of 2,4,5-T applied to either acidic or basic soils at massive rates (560-2800 kg/ha). The persistence of unadsorbed 2,4,5-T in the soil environment is expected to be minimal. Several studies (1864, 1868, 1872) have reported that most (~90%) of the undegraded, 2,4,5-T remained in the top 2.5-10 cm of soil, with only low levels

depths. One study (1872) reported no detectable residues below 5 cm depth one year after normal application to chaparral vegetation and soil.

61.2.1.3 Volatilization from Soils

Due to its low vapor pressure and relatively high water solubility, evaporation of 2,4,5-T from aqueous solution is expected to be negligible (1864). The extremely low value calculated for the Henry's law constant, 1.21E-09 atm · m^3/mol (1210, 808) confirms that volatilization will be minimal. The rate of volatilization from soil is generally significantly lower than that from water. Therefore, volatilization of 2,4,5-T from surface soils or in soil air will not be an important transport process, particularly in the presence of any soil moisture.

The vapor pressures of the alkyl esters of 2,4-D and 2,4,5-T are reported to be several orders of magnitude higher than those of the acids (2050), and significant airborne losses of the 2,4-D esters from commercial herbicide formulations have been reported (1874, 1875). Volatilization is related to soil moisture and vapor losses from dry soil have been reported to be minimal (1874). Ambient air monitoring performed during Herbicide Orange disposal operations indicated very minor evaporative emissions of 2,4,5-T during handling of concentrated herbicide solutions (1873).

61.2.2 Transformation Processes in Soil/Ground-water Systems

2,4,5-T is an acidic compound (pKa = 2.84 - 2.88) and has a strong tendency to hydrolyze in the presence of water. At pH levels above 5.0, 2,4,5-T is expected to be greater than 99% dissociated. Degradation reactions (oxidation, reduction, hydrolysis, substitution) have been reported to occur in water when activated by sunlight (1850, 1864, 1895, 1896, 1897). A half-life for 2,4,5-T in clear shallow water exposed to 12 hours per day unobstructed sunlight was estimated at about 40 days, twice that of 2,4-D. In another experiment, 57-97% of a dried film of 2,4,5-T on glass was degraded after seven days of irradiation (1876); other authors have reported that 2,4,5-T is stable under dry conditions (1864). Skurlatov et al. (1897) have reported rapid photolysis of 2,4,5-T in natural waters, enhanced by the presence of humic substances; the half-life reported for direct photolysis of anionic 2,4,5-T is 15 days. The major product of photodecomposition is 2, 4, 5-trichlorophenol.

Numerous studies have shown that 2,4,5-T is readily biodegraded by micro-organisms and that microbial metabolism is the predominant (or even sole) factor affecting decay in soils (1866, 1878, 1885, 1887, 1900, 1903, 1904, 1905). Most half-lives reported for the biodegradation of 2,4,5-T in soils range from 10 to 45 days (1901, 1887, 1856). Degradation of 2,4,5-T in ground-water was reported to be very low (10%) (1906).

Degradation experiments have established that both aromatic and side chain carbons of 2,4-D can be rapidly converted to CO_2 (1905, 1885, 1894). Principal degradation products include 2,4,5-trichlorophenol and 2,4,5-trichloroanisole which are not expected to accumulate in the environment (1895, 1903, 1904, 1905).

Breakdown of 2,4,5-T, like 2,4-D, has been reported to follow a well established degradation pattern of two first-order reactions: a slow initial reaction (lag phase) during which microbial enrichment occurred, followed by a rapid first-order decline in concentration. Rosenberg and Alexander (1905) report a lag period of 2.5 months followed by rapid cometabolism with 2,4-D. Several authors report no increase in 2,4,5-T breakdown rate with adaptation (1856, 1901); an increase has been reported after addition of growth supplement (1878).

In general, degradation of 2,4,5-T in soil is not correlated specifically with soil properties but has been shown to depend primarily on microbial population and numbers of 2,4,5-T degraders available (1885). Data on the effect of sorption on 2,4,5-T degradation are limited; behavior of 2,4,5-T is expected to be similar to that of 2,4-D. Young (1889) reported no degradation of 2,4-D sorbed on charcoal in spite of the presence of degrading organisms. Most data for 2,4-D indicate no adverse impact on soil biota due to normal application; however, several studies have reported significant reduction in the soil bacterial population and the rate of biodegradation following repeated applications of high doses (1881,1891,1892,1893, 1894). Biodegradation of 2,4,5-T may also be slower at high concentrations.

The breakdown of 2,4,5-T has been shown to be dependent on the availability of soil moisture; little or no degradation was observed in dry soils (1884, 1887, 1902). Low soil temperatures have also been shown to minimize decomposition (1899). Half-lives for 2,4,5-T degradation ranged from 4 days at 35 °C and 34% soil moisture to 60 days at 10°C and 20% soil moisture (1902). The importance of the presence of oxygen has also been demonstrated in that degradation slows significantly under flooded (anaerobic) conditions; e.g., over six weeks, 53% 2,4,5-T loss was observed in a moist field compared to 16% loss under flooded conditions (1884). However, anaerobes have been shown to degrade 2,4,5-T by dechlorination to 2,5-D which can then be further degraded (1907).

In summary, 2,4,5-T has the potential to be rapidly degraded in the soil environment. The rate of biodegradation is related to the availability of degrading microbial populations, and massive doses may be degraded more slowly. Since the concentration of soil microorganisms capable of biodegradation is fairly low and drops off significantly with depth, biodegradation in the soil/ground-water system may be minimal. Thus, 2,4,5-T transported vertically into the subsoil may represent a potential threat of ground-water contamination. In ground-waters, 2,4,5-T degradation is expected to be slow, possibly due to limited microbial populations.

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

The above discussion of fate pathways suggests that undissociated 2,4,5-T is nonvolatile, moderately sorbed to soil, and has a moderate potential for bioaccumulation. These fate characteristics suggest several potential exposure pathways.

Volatilization of 2,4,5-T from a disposal site is expected to result in negligible exposure to workers or residents in the area because 2,4,5-T in either dissociated or undissociated form is non-volatile. The potential for ground-water contamination exists due to the moderate sorption of the undissociated acid on soil, and the weaker retention of the dissociated acid, which is expected to be the predominant form under virtually all pH levels of environmental concern. The susceptibility of 2,4,5-T to degradation, however, should reduce its occurrence in drinking water supplies. No literature was found indicating that ground-water used as drinking water has been contaminated with 2,4,5-T.

The movement of 2,4,5-T in ground-water or its movement with soil particles may result in discharge to surface water. As a result, ingestion exposures may occur from the use of surface waters as drinking water supplies and dermal exposures may result from the recreational use of surface waters. In some cases, the potential for uptake of 2,4,5-T by aquatic organisms or domestic animals may be important. However, due to its lack of persistence and moderate bioconcentration factor, only in unusual circumstances (e.g., a large spill) are the exposure pathways from soil/ground-water systems expected to be significant.

61.2.4 Other Sources of Human Exposure

Peak production of 2,4,5-T in the United States occurred between 1960 and 1968; in 1979 after an EPA ban on most of its permitted uses, production in the U.S. ceased (1918). Therefore, 2,4,5-T is not expected to be widespread in the environment given the absence of its current use and its lack of persistence. The year in which studies of human exposure to the chemical in the environment were conducted should always be noted.

According to a 1979 report, 2,4,5-T had never been detected in drinking water at detection limits in the parts per trillion range (1895). The same report notes that between August 1967 and September of 1968, 2,4,5-T was detected at concentrations ranging from 0.01 to 0.07 ppb in a study of 11 waterways in agricultural areas of the western U.S. In a Canadian study of 11 agricultural watersheds conducted between 1975 and 1977 in which 2,4,5-T had been applied to non-agricultural land, concentrations ranging from 0.1 $\mu g/L$ (the detection limit) to 1.1 $\mu g/L$ were measured in 21 of 949 water samples (1919). Losses of the herbicide were correlated to drift from spraying operations and storm runoff into streams, especially when precipitation occurred shortly after application. Wells in Canada have also been found to be contaminated by 2,4,5-T from the same sources and from spillage; in none of 25 cases was ground-water identified as the source of contamination (1863). Recent accounts of the presence of 2,4,5-T in surface water or ground-water were not found in the literature.

Data on human exposure to 2,4,5-T in air are limited. In 1972, the most recent year for which data were found, 2,4,5-T (not including esters) was detected in three states in a monitoring program of predominantly agricultural areas of 28 states (1895). Concentrations ranged from 0.8-1.7 ng/m^3 (1895).

Exposure to 2,4,5-T in food can be expected to be negligible. Market basket surveys of chemicals in the diets of adults (1245) and infants and toddlers (1244) conducted in 1978 and 1979 reported no 2,4,5-T in the diets. None was detected in surveys consisting of 155 total diet samples (detection limit 0.02 ppm) taken between 1969 and 1974 either (1895). Even in samples taken between 1964 and 1969 during the period of peak 2,4,5-T usage, contamination was minimal -- 3 of 1600 food composites (1895). The Advisory Committee to the EPA on 2,4,5-T concluded in 1971 that the risk of human exposure from food, air or water was negligible (213).

61.3 HUMAN HEALTH CONSIDERATIONS

The industrial production of 2,4,5-T always results in low level 2, 3, 7, 8-tetrachlorodibenzo-p-dioxin (2,3,7,8-TCDD) contamination. The presence of this unwanted side-product of synthesis may result in toxicological effects unrelated to the 2,4,5-T itself and must be considered in any health-related analysis of 2,4,5-T (the toxic effects of 2,3,7,8-TCDD are discussed in Chapter 63 of this guide).

61.3.1 Animal Studies

61.3.1.1 Carcinogenicity

2,4,5-T does not appear to be carcinogenic in the majority of rodent species tested; however, uncertainty still exists due to limitations in available studies.

Two hybrid strains of C57BL/6 mice were orally treated with 21.5 mg/kg 2,4,5-T in 0.5% gelatin (TCDD content not reported) for 3 weeks followed by 60 ppm 2,4,5-T in the diet for 18 months (2136). No increased incidence of tumors were reported. No increased incidence of tumors was reported in mice given a single subcutaneous injection of 215 mg/kg 2,4,5-T and observed for 18 months (1607).

The carcinogenic effects of commercial-grade 2,4,5-T (TCDD level not reported) were studied by Leuschner et al. (2142) in Sprague-Dawley rats. Rats were obtained from the F_1 generation of a reproductive study in which the dams were fed 0, 3, 10, or 30 mg/kg 2,4,5-T daily in the diet. F_1 rats were placed on the same diet for 130 weeks. No significant increase in neoplastic lesions was found. However, a dose-related trend of interstitial cell tumors of the testes was observed in the high-dose group.

Muranyi-Kovacs et al. (2019) reported an increased incidence of rare tumors in XVII/G and C3HF mice given 100 mg/L of 2,4,5-T (contaminated with <0.05 ppm TCDD) in the drinking water for 2 months followed by 80 ppm 2,4,5-T mixed in the diet until death. A significant increase in the incidence of neoplastic lesions was reported in the C3HF mice along with cutaneous tumors, sebaceous squamous cell carcinomas, osteogenic tumors and leukemia. These tumors are extremely rare in C3HF mice. Also, hyperplastic lesions and papilloma were observed in the bladders

of 2,4,5-T-treated mice. (The investigators noted that bladder papilloma have never before been observed in this mouse colony.)

Kociba et al. (2022) fed Sprague-Dawley rats 0, 3, 10 or 30 mg/kg/day of 2,4,5-T (<0.33 ppb TCDD) in the diet for 2 years. Very high mortality occurred in all groups early in the study resulting in a reduced number of animals at risk for late developing tumors. Despite the high mortality rate, a statistically significant increase in squamous cell carcinomas of the tongue were found in male rats fed 30 mg/kg of 2,4,5-T. Examination of tongues of rats in the Leuschner et al. study (2142) did not reveal any neoplastic lesions. However, based on the rarity of the tongue tumors, it was concluded that the data are highly suggestive of carcinogenicity.

Phenoxyacetic acid herbicides, as a group, are considered Group 2B compounds, but IARC (1250) classifies 2,4,5-T and its esters as Group 3 compounds. The USEPA classifies 2,4,5-T in Cancer Group D (3742).

61.3.1.2 Genotoxicity

The majority of reports indicate that 2,4,5-T is not mutagenic. No effects were reported in strains TA1535, TA100, TA1537 and TA98 of Salmonella typhimurium (2058) even when tested at concentrations up to 1 mg/plate with or without metabolic activation (3470); the WP2 strain of Escherichia coli (1607), the a21 strain of Serratia marcescens (3092) or the D4 strain of Saccharomyces cerevisiae (2006).

Adult Drosophila melanogaster receiving a 250 mg/kg diet of 2,4,5-T for 5-6 days exhibited disturbances in somatic pairing between homologous chromosomes and also, some chromosome abnormalities (2007). Concentrations of 0, 250 or 1000 mg/kg 2,4,5-T fed to 2-day-old male Drosophila for 15 days resulted in a significant increase in sex-linked recessive lethal mutations (2008). These data are contradicted by Zimmering et al. (3863) who fed or injected adult males with 10,000 ppm of 2,4,5-T and observed no increase in sex-linked recessive lethals compared with controls. Negative results were reported for non-disjunction and sex chromosome loss or exchange in D. melanogaster (1250).

No effects on preimplantation loss, fertilization quota, or the rate of dead implants were reported in a dominant lethal test in female rats fed 2,4,5-T for 8 weeks (2058). Analysis of the spermatogonia of male Chinese hamsters did not reveal any chromosome-damaging effects (2058), but Davring and Hultgren (3157) observed significant increases in chromosomal aberrations in the bone marrow cells of male mice injected intraperitoneally either acutely or subchronically with commercial preparations of 2,4,5-T.

Small increases in chromosomal aberration frequencies have been reported in individuals occupationally exposed to 2,4,5-T. However, because exposure included a mixture of compounds, these effects could not be attributed specifically to 2,4,5-T exposure (2009). No evidence of chromosome damage was found in a large group of workers exposed to 2,4,5-T during its production (2010).

61.3.1.3 Teratogenicity, Embryotoxicity and Reproductive Effects

The true teratogenic effects of 2,4,5-T are rather ambiguous due to the potential (and probable) contamination with the known teratogen, 2,3,7,8-TCDD. No clear cut teratogenic effects have been reported in rats, rabbits or monkeys (1607); cleft palate has been reported in mice treated with 2,4,5-T (2021). Some studies do indicate an adverse effect on behavior of animals exposed prenatally to 2,4,5-T.

2,4,5-T produced no congenital malformations or increases in the frequency of developmental variations in New Zealand white rabbits orally given 10, 20 or 40 mg/kg 2,4,5-T (containing 0.5 ppm TCDD) daily on gestation days 6-18. No adverse effects on maternal or fetal weight gain were noted (1607).

No teratogenic effects were reported in rhesus monkeys when 0.05, 1 or 10 mg/kg of 2,4,5-T (containing less than 0.05 mg/kg TCDD) was administered to pregnant females in gelatin capsules by stomach tube daily on gestational days 22 to 38 (1607). Also, no adverse effects were reported in fetuses of rhesus monkeys treated with 5, 10, 20 or 40 mg/kg 2,4,5-T (containing 0.5 mg/kg TCDD) three times a week for 4 weeks between gestational days 20-48. Fetuses were removed by hysterectomy after 100 days of gestation (1607).

Crampton and Rogers (2059) orally administered 0, 6, 12, 25 or 100 mg/kg of 2,4,5-T (containing 0.03 ppm TCDD) to Long-Evans rats on day 8 of gestation. No significant effects on litter size, sex ratio, gestation time, pup weight or gross morphology were found. Male offspring from the 25 or 100 mg/kg 2,4,5-T groups were behaviorally tested at 5 months of age while rats treated with 6 or 12 mg/kg 2,4,5-T were tested at day 65. Abnormalities in exploratory behavior were detected after exposure to a single dose of 2,4,5-T as low as 6 mg/kg on gestational day 8.

Behavioral effects in chickens exposed in 2,4,5-T prior to hatching were reported by Sanderson and Rogers (2060). A single dose of 7-53 mg/kg of 2,4,5-T (containing 0.03 ppm TCDD) was injected into chick eggs on either day 8 or day 15 of incubation. An additional group received an intraperitoneal injection of 75-225 mg/kg of 2,4,5-T two days after hatching. Hatchability of chicks given 2,4,5-T on day 15 of incubation was 70%. Between 5 and 10% of the hatched chicks showed abnormal leg development and either dragged one leg or held it off the ground. Approximately 5% of the treated chicks showed depigmentation of feathers and down. Behavioral testing of chicks without deformities two weeks after hatching revealed alterations in general activity, jumping and visual learning rate.

Both Crampton (2059) and Sanderson (2060) concluded that the developing nervous system appears to be susceptible to very low doses of 2,4,5-T, which may be of great concern to humans. Species variation, based on the rate of metabolism and excretion of 2,4,5-T, indicate that chicks and rats are similar in sensitivity whereas humans have at least a 3-fold greater sensitivity.

Davies et al. (3154) reported abortions and stillbirths in cattle at 6 to 9 months gestation, 2 to 3 weeks after exposure to 2,4,5-T, aerially sprayed as a defoliant in an adjacent paddock. Some calves were born alive but weak, and died within a few days. Total calf losses were 48 out of 77 (63%). Exposure concentrations were not measured.

2,4,5-T was at first reported to be teratogenic in rats and mice, producing an increased incidence of cleft palate (C57BL/6 and AKR strains of mice) and cystic kidneys (C57BL/6 mice and Holtzman rats) (2020). However, it was later discovered that the 2,4,5-T sample used contained 30 ppm of 2,3,7,8-TCDD. In a follow-up study, Courtney and Moore (2021) investigated the teratogenic potential of 2,4,5-T and 2,3,7,8-TCDD alone or in combination in order to determine the teratogenic agent responsible for the deformities. Both technical (0.5 ppm TCDD) and analytical (<0.05 ppm TCDD) grade 2,4,5-T and 2,3,7,8-TCDD were tested in CD-1, C57B1/6J, and DBA/2J mice and CD rats. Compounds were administered subcutaneously on gestational days 6 through 15 as a solution in 100% dimethyl sulfoxide in a volume of 100 uL/animal/injection. Both samples of 2,4,5-T (100 mg/kg) and TCDD (3μg/kg) produced cleft palate in all three strains of mice. Technical grade 2,4,5-T produced kidney malformations in CD-1 mice. All animals treated with 3μg/kg TCDD also developed kidney abnormalities. Administration of 100 mg/kg 2,4,5-T with 1μg/kg TCDD produced no potentiation effect in CD-1 mice. 2,4,5-T was neither teratogenic nor fetotoxic in CD rats.

Developmental anomalies were reported in Wistar rats orally administered 2,4,5-T (TCDD was not present within a detection limit of 0.5 mg/kg) at a daily dose level of 0, 25, 50, 100 or 150 mg/kg from gestational day 6 through 15 (2062). Administration of 100 or 150 mg/kg of 2,4,5-T significantly reduced the number of live fetuses and fetal weights. The proportion of skeletal anomalies was also significantly increased. Anomalies included unilateral or bilateral wavy ribs, additional ribs, retarded ossification of frontal and parietal bones and a wide variety of sternal defects. Other effects included fused ribs, small-sized distorted scapula, laterally convex or distorted humerus shaft, and bent radius or ulna. These anomalies are minor deviations, not life-threatening to the animal and reflect retarded development rather than malformations. No changes in behavior or subsequent reproductive performance were detected.

The effects of 2,4,5-T on the estrus cycle, pregnancy and fetal development of Swiss-Webster mice were studied by Greer (2061). Animals were injected (route not specified) with 16 mg/100 g bw pure 2,4,5-T (less than 0.004 ppm TCDD) or with 8 mg/100 g bw commercial 2,4,5-T (containing 2.7 ppm TCDD). Interruption of the estrus cycle occurred in 12.5% of the animals given pure 2,4,5-T and in 42.9% of the animals given commercial 2,4,5-T. Permanency of this effect was tested by allowing animals to mate after 14 days of treatment. Pure 2,4,5-T delayed impregnation for a longer time period than commercial 2,4,5-T (20.7 days for the pure 2,4,5-T group vs. 11.1 days for the commercial 2,4,5-T group vs. 9.3 days for control animals). Pregnancy did eventually occur, so the effect was considered transitory. Animals exposed to commercial 2,4,5-T had a greater number of resorption sites (3.8 vs. 2.2 in

the pure 2,4,5-T vs. 1.2 in control animals) indicating that 2,4,5-T and TCDD may act synergistically to increase fetotoxicity. No fetal abnormalities were observed in any of the animals studied.

Results of a three-generation reproductive study with rats were reported by Smith et al. (2063). Purified 2,4,5-T (TCDD not present at a detection limit of 0.03 ppb) in acetone was mixed in the diet at dosage levels of 0, 3, 10 or 30 mg/kg 2,4,5-T/day. Sprague-Dawley rats were fed the diet for 90 days then allowed to mate. F_1 rats were fed the test diet from weaning until day 130 of age when they were allowed to mate. F_2 rats also followed this treatment schedule. All females were fed the test diet throughout gestation and lactation. Fertility was decreased in the matings for the F_3 litters at the 10 mg/kg/day dose level. Postnatal survival was also significantly decreased in the F_2 litters of the 10 mg/kg and the F_1, F_2 and F_3 litters of the 30 mg/kg/day treatment groups. A significant decrease in relative thymus weight was also seen in the F_3 rats given the high dose of 2,4,5-T. Smith et al. concluded that the only apparent adverse reproductive effect of long term 2,4,5-T treatment in rats was a tendency toward a reduction in postnatal survival at the 30 mg/kg/day dose level. No effect was seen in rats given 3 mg/kg/day 2,4,5-T (2063).

Several recent studies have utilized the CD-1 mouse in teratology screens that used growth, viability, and behavioral endpoints (3350, 3635). When dams were gavaged on days 8-12 with 200 mg/kg/day of 2,4,5-T, 7% maternal mortality resulted. The number of live pups on days 1 and 3, and body weight of pups on day 1, showed a statistically significant decrease. Other mice gavaged with 130 mg/kg of 2, 3, 5-T during the same gestational period produced smaller litters (7.1 vs 10.8), but no reduction in birth weights, growth, or in figure-eight maze activity on days 22, 58, or 200 were observed. In another screen with the same administration and dose period but with dose stated as "one which causes up to 10% maternal death or other overt clinical signs of toxicity", 2,4,5-T was listed as a teratogen. A decrease in live pups/litter, an increase in dead pups litter, and a decrease in average birth weight were observed in this screen.

61.3.1.4 Other Toxicologic Effects

61.3.1.4.1 Short-term Toxicity

2,4,5-T itself appears to be of low toxicity. Contamination of commercial preparations of 2,4,5-T with 2,3,7,8-TCDD and 2, 3, 6, 7-TCDD result in toxic effects. These two TCDD compounds are potent animal teratogens, acnegenic agents and are highly hepatotoxic. The oral LD_{50} of 2,4,5-T ranges from 381 to 820 mg/kg in the rat (3933, 51) while the acute percutaneous LD_{50} for the rat ranges from 1535 to greater than 5000 mg/kg (3933, 1118).

Signs of 2,4,5-T exposure in animals include ataxia, skin irritation, acne-like rash and blood in stools. A single oral dose of 100 mg/kg bw 2,4,5-T fed to pigs caused anorexia, vomiting, diarrhea, and ataxia. Autopsy revealed hemorrhagic enteritis and congestion of the liver and kidneys (2069).

The low toxicity of 2,4,5-T is thought to be due to its rapid excretion via the kidneys. The renal function of rats given 100 mg/kg 2,4,5-T was evaluated by Koschier and Hong (2070). Male Sprague-Dawley rats were infused with 2,4,5-T at the rate of 0.193 mL/min for 150 minutes. 2,4,5-T had no effect on urinary flow rate, glomerular filtration rate, renal plasma flow, mean arterial blood pressure or the fractional resorption of sodium, chloride, potassium and water.

Analytical-grade 2,4,5-T (containing no detectable TCDD at a sensitivity of 0.05 mg/kg) was fed to Long-Evans rats in the diet at a dosage level of 10 mg/animal/day for 1 to 11 days (2013). Liver enlargement was the only effect induced by 2,4,5-T. The increase in relative liver weight was dose dependent and was associated with substantial increases in total RNA and total protein. Enlargement was reversible and subsided following removal of 2,4,5-T from the diet.

61.3.1.4.2 Subchronic and Chronic Toxicity

The long-term toxicity of 2,4,5-T was reported by Kociba et al. (2022). Sprague-Dawley rats consumed a diet containing 0, 3, 10 or 30 mg/kg of 2,4,5-T daily for 2 years (TCDD content <0.33 ppb). A decrease in body weight gain, increase in total urine volume, urinary coproporphyrin and uroporphyrin, an increase in relative kidney weight and morphological alterations in the kidney, liver and lung were signs of toxicity in the rats fed 30 mg/kg/day 2,4,5-T. Minimal toxic effects were noted in the group fed 10 mg/kg/day and primarily involved the presence of mineral deposits in the renal pelvis. No treatment related effects were observed in the 3 mg/kg/day group.

A subchronic animal study involved rats fed 0, 3, 10, 30 or 100 mg/kg 2,4,5-T (containing less than 1 mg/kg TCDD) daily for 90 days (1607). No effects were noted in the animals fed 3, 10 or 30 mg/kg 2,4,5-T; however, animals fed 100 mg/kg showed a depression in body weight gain, a slight decrease in food intake and elevated serum alkaline phosphatase levels. A slight decrease in red cell counts and hemoglobin were reported in male rats. Hepatocellular swelling was observed in livers, however, this finding was inconsistent. No other effects were noted.

61.3.2 Human and Epidemiologic Studies

61.3.2.1 Short-term Toxicologic Effects

Very little information was found on the short-term toxic effects of 2,4,5-T in humans.

Nausea and severe abdominal pain were reported in three children who ate blackberries contaminated with 2,4,5-T (17).

Severe erythema and edema of the skin and mucous membranes developed in 2 children exposed to 2,4,5-T spray and to poison oak (2144). Speculation as to whether the lesions may have been due to the 2,3,7,8-TCDD contaminant was presented, however, no conclusion was made.

61.3.2.2 Chronic Toxicologic Effects

The majority of data available in the literature deals with human exposure to 2,4,5-T and its TCDD contaminant during the manufacturing process.

Suskind (2064) evaluated the long-term health effects of Monsanto workers involved in the production of 2,4,5-T between 1948 and 1969. The study consisted of 418 current and former employees including those involved in a 1949 accident. Health data from the exposed employees were compared with a control group of workers from other areas of the plant. No evidence was found between 2,4,5-T exposure and adverse long-term effects on the cardiovascular system, including hypertension and coronary artery disease. Reproductive evaluation among families in which the male parent was exposed resulted in no excess risk of miscarriage, stillbirth or birth defects. Incidents of cancer were also within normal values. The only adverse effect reported by Suskind was evidence of chloracne in workers exposed to TCDD. Skin elasticity in afflicted areas was also lost (2064).

A follow-up study performed by Suskind and Hertzberg (2065) involved 367 subjects with 204 individuals involved in 2,4,5-T production and maintenance from 1948 to 1969 and 163 control workers in the same plant, but not associated at any time with 2,4,5-T production. Approximately 86% of the exposed group developed chloracne versus none in the control group. Physical examination revealed 52.7% of the exposed workers still had chloracne and 74.8% of the subjects with persistent chloracne also had actinic elastosis. Actinic elastosis is usually a problem found in persons of light coloration exposed to years of sunlight. It is characterized by swelling and fragmentation of the elastic tissue elements of the dermis. The condition also occurred significantly, but to a lesser extent in persons with a previous history of chloracne (47.1%). A history of upper GI tract ulcers was reported four times more frequently in the exposed group. There was no association between the history of upper GI tract ulceration and chloracne status. Complaints of loss of libido or impotence were also reported more frequently in the exposed group.

Kramer (2014) described the health of employees exposed to 2,4,5-T at Dow Chemical in comparison to a large control group. The control population of 4600 non-exposed Dow employees did not significantly vary from the general population. No differences were found between the study and control groups when tested for central nervous system disorders, mucous membrane irritation, pulmonary disease, cardiovascular disease, gastrointestinal and hepatic disorders, renal disease, asthenia and psychiatric disorders.

The mortality experience of 204 employees of a 2,4,5-T manufacturing plant was investigated by Ott et al. (2024). Personnel involved for at least one full year in

2,4,5-T production from 1950 to 1971 were included in the study. Also, workers involved in selective high exposure positions for at least one month were included. Personnel were potentially exposed to other substances,including styrene-butadiene latex, silvex and 2-methyl-4-chlorophenoxyacetic acid, during their employment. Analysis of the plant atmosphere in 1969 revealed a range of 2,4,5-T concentrations from <0.1 to 6.2 mg/m^3 Dust levels were high enough to be noticeably irritating and resulted in nasal irritation, sneezing and a bitter taste. Distribution of employees revealed more than 75% of the men had worked with 2,4,5-T for less than 12 months and none of the men were exposed to 2,4,5-T over a working lifetime. No cases of chloracne were found in medical records of all subjects indicating no evidence of 2,3,7,8-TCDD exposure. No adverse mortality effects were observed in association with the work environment.

Reports of four 2,4,5-T-exposed cohorts by epidemiologists from Dow Chemical Corporation and the Monsanto Company were reviewed by Honchar and Halperin (2011). A pooling of all data showed a total of 105 deaths, 3 (2.9%) of which were due to soft tissue sarcoma. In comparison, only 0.07% of the deaths in U.S. males, 20-84 years of age, were reported to be due to soft tissue sarcoma in 1975. The workers from the 4 studies were exposed to either 2,4,5-T or to 2, 4, 5-trichlorophenol (TCP). Both of these compounds are known to be contaminated with 2,3,7,8-TCDD. Each individual study revealed no excess risk for soft tissue sarcoma; however, combining the results revealed three cases (one malignant fibrous histiocytoma of soft tissue origin, one fibrosarcoma, and one generalized liposarcoma) suggesting a common pattern.

Workers using 2,4,5-T, trichlorophenol or pentachlorophenol in Sweden's lumber industry from 1950 to 1970 were reported to have a 6-fold higher incidence of soft tissue sarcoma (2041). Hardell and Sandstrom believe that 2,3,7,8-TCDD contamination of the herbicides may be responsible for the increased risk. These results are considered questionable since identification of herbicide users was done with a questionnaire and any error in recall by 2 of the subjects would remove the increased risk factor.

Eriksson et al. (2025) confirmed the Swedish findings (2041) and reported a 6-fold increase in the risk of soft tissue sarcoma in dioxin- and furan-free herbicides. The increased risk was related to 2,4,5-T, silvex, chlorophenols, 2,4-D and other phenoxy acids.

A study performed by Dow Chemical found no association between exposure to 2,4,5-T and its TCDD contaminants with pregnancy outcome (2066). The survey included 370 employees exposed to 2,4,5-T and their wives along with a control group of 345 wives and employees in the same division, but never exposed to the test compound. No statistically significant differences were found between the two groups in the occurrences of miscarriage, stillbirth, infant death or congenital malformation. It was noted that the number of pregnancies was considerably different for the two groups. Those not exposed to the herbicide had 2031 conceptions while those exposed had 737 (36.3%).

The possible association between the incidence of congenital malformations and the occupation of the father was also investigated by Balarajan and McDowall (2068). Malformation ratios were calculated based on the number of malformations for a certain occupational group and the occupation of the father as stated on the malformation form. Malformations for facial clefts were consistently high in groups suspected of being exposed to 2,4,5-T. Gardeners and groundsmen showed an increased ratio for spina bifida, anencephaly, and facial clefts. Agricultural workers also showed high incidence of spina bifida and facial clefts. Individual analysis of exposure was not performed and exposure to agents in addition to phenoxyacids was likely. The limited information does indicate a consistent excess ratio for cleft palates that should be investigated further.

The highest exposure to 2,4,5-T occurs in workers involved in manufacturing and spraying the compound. In New Zealand, herbicide sprayers work mainly with backpacks or conduct boom spraying from vehicles. Most of subjects were involved with spraying for 4 to 6 months each year. Protective clothing was usually disregarded and the sprayer became drenched in the chemical daily. Smith et al. (2067) investigated the reproductive outcome among these New Zealand herbicide sprayers and their wives. The study group consisted of 989 respondents and each pregnancy outcome occurring between 1969 and 1980 was classified according to whether or not the father sprayed 2,4,5-T during the year of the pregnancy outcome, or the previous year. The relative risk estimates of miscarriage, stillbirth and congenital defects among the 2,4,5-T sprayers were not statistically significant.

A high incidence of spontaneous abortion was reported in a group of women living in Alsea, Oregon. These women were thought to have been exposed to aerial spraying of 2,4,5-T. The USEPA initiated a study (referred to as the Alsea II study) based on the Spontaneous Abortion Rate Index and seasonal patterns of 2,4,5-T spray application (2226). The Spontaneous Abortion Rate Index is defined as "the ratio of the number of hospitalized spontaneous abortions to the number of births corresponding to the spontaneous abortions, based on the residence zip code of the women contributing to each event." EPA concluded that the 1972-1977 Spontaneous Abortion Rate Index for the study area was significantly higher than in rural or urban control areas. There was also a statistically significant seasonal cycling in the Abortion Index for the study area with an outstanding peak in June. The correlation between the Spontaneous Abortion Rate Index and spraying patterns in the study area was statistically significant when a lag time of 2 to 3 months was included.

Milby et al. (2227) found the statistical method and basic design of the Alsea II study sufficiently flawed to make the study of no use in human risk assessments.

However, based on the Alsea II study, EPA issued an emergency suspension order in 1979 for all 2,4,5-T and its esters used for weed and brush control in forests, right of ways, pastures, irrigation canals and other water ways, turfs and homes (992). The suspension was lifted and all registrations for herbicides containing 2,4,5-T or its esters are now canceled.

61.3.3 Levels of Concern

The NAS-NRC (213) recommended a concentration of 700 μg/L of 2,4,5-T in drinking water, based on an acceptable daily intake (ADI) of 10 μg/day and consumption of two liters of contaminated water daily, assuming 20% of the total ADI comes from drinking water. The ADI was based on the no-adverse-effect level of 10 mg/kg/day for dogs and mice and up to 30 mg/kg/day in rats. The USEPA has issued Health Advisories of 800 μg/L for both short-term and long-term exposures for children and long-term and lifetime exposures of 1000 and 70 μg/L for adults (3742). The Oral Reference Dose is 10 μg/kg/day.

Both OSHA (3539) and the ACGIH (3005) have established time-weighted-averages of 10 mg/m^3 for this herbicide.

61.3.4 Hazard Assessment

2,4,5-T is a member of the chlorophenoxy family of herbicides. Commercial formulations of 2,4,5-T are contaminated with varying levels of 2,3,7,8-TCDD. The presence of this highly toxic contaminant may be responsible for some of the observed toxic effects and confounds interpretation of the available data with regard to the toxicity of 2,4,5-T alone.

The carcinogenicity of 2,4,5-T has been examined in mice by oral (2136, 2019) and subcutaneous (1607) administration and in rats via the diet (2022) but inadequate numbers of animals were used. Although an increased incidence of tumors was noted in C3HF mice given 2,4,5-T orally (2019), the limitations of the study do not allow adequate assessment of the carcinogenicity of 2,4,5-T based on these data. Negative findings were noted in another rat feeding study (2142). Based on available data, IARC (1250) classifies 2,4,5-T and its esters as Group 3 (inadequate data) compounds. The USEPA likewise classifies 2, 4 ,5-T as lacking sufficient human data (Group D) for classification as a carcinogen (3742).

A range of mutagenicity assays indicate 2,4,5-T is not mutagenic (1607, 2058, 2006, 2010, 3470, 3863). A three-generation reproductive study with rats fed purified 2,4,5-T suggested no adverse reproductive effects in rats given 3 mg/kg/day; post-natal survival and fertility were decreased in animals exposed to 10 mg/kg/day (2063). No clear-cut teratogenic effects of 2,4,5-T have been observed in rats, rabbits and monkeys (1607). An increase in cleft palate was reported for mice subcutaneously injected with 2,4,5-T (100 mg/kg) during gestation (2021). The contribution of the 2,3,7,8-TCDD contaminant to this response is unclear but similar responses occur with TCDD exposure (2021).

Acute exposure to 2,4,5-T induces ataxia, skin irritation, acne-like rash and blood in the stools; the oral LD_{50} of 2,4,5-T is listed as 820 mg/kg for the rat (51). Few chronic studies are available for 2,4,5-T. Depression of body weight gain was the primary effect noted in rats at levels of 10 mg/kg/day and above (2022,1607).

Data on human exposure to 2,4,5-T are derived primarily from exposure during the manufacturing process. Exposures are often poorly characterized and due to multiple agents in addition to 2,4,5-T itself. These studies indicate an excess risk for the development of soft tissue sarcomas among exposed workers (2011, 2041, 2025). The presence of dioxin contaminants preclude clear delineation of the causative agent.

Exposure to 2,4,5-T has also been linked to an increased risk of miscarriage, stillbirth and congenital defects but statistically significant data are lacking (2066-2068).

61.4 SAMPLING AND ANALYSIS CONSIDERATIONS

Determination of 2,4,5-T 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 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 2,4,5-T in aqueous samples include EPA Methods 8150 and 8250 (63) and 509B (1422). Prior to analysis, a measured volume of sample, approximately 1 liter, is acidified and subsequently extracted with ethyl ether using a separatory funnel. The sample extract is hydrolyzed with potassium hydroxide and any extraneous organic material removed by a solvent wash. Because chlorinated phenoxy acid herbicides may occur in water in various forms (e.g., acid, salt, ester), this hydrolysis step is included to convert all forms of the herbicide to the acid form for analysis. 2,4,5-T in the acid form is then extracted and converted to the methyl ester of 2,4,5-T using diazomethane (Method 8150) or boron trifluoride-methanol (Method 509B) as the derivatizing agent. Additional cleanup procedures are specified if interferences are present in the sample matrix. Butyl ester derivatives of this compound have also been reported (3168). Excess reagent is removed and an aliquot of the concentrated sample is injected onto a gas chromatographic (GC) column. The GC column is programmed to separate the semi-volatile organics; 2,4,5-T methyl ester is then detected with an electron capture detector, microcoulometric detector or electrolytic conductivity detector (Methods 8150, and 509B) or with a mass spectrometer (Method 8250). Identifications for unknown samples should be confirmed by analysis on a second chromatographic column (if using retention time as the identifier) or by gas chromatography/mass spectrometry.

The EPA procedures recommended for 2,4,5-T analysis in soil and waste samples, Methods 8150 and 8250 (63) differ from the squeous procedures primarily in the preparation of the sample extract. Solid samples are initially extracted with

acetone/ethyl ether using a wrist-action shaker. The solvent extract is washed, concentrated and then derivatized.

In addition to the methods described above, solid-phase extraction has been used to concentrate phenoxy-acid herbicides in aqueous samples (3640, 3294, 3261). Separations for analytical determinations are then made by thin-layer chromatography (3640) or high performance liquid chromatography (3294, 3261). These methods are direct, accurate, and also offer higher analytical precision than the derivatization procedures described above.

Typical 2,4,5-T detection limits that can be obtained in wastewaters and non-aqueous samples (wastes, soils, etc.) are shown below. A detection limit for 2,4,5-T was not indicated in Method 8250 but would be in the range of 1-10 µg/L for aqueous samples and 1 µg/g for non-aqueous samples. The actual detection limit achieved in a given analysis will vary with instrument sensitivity and matrix effects.

Aqueous Detection Limit	Non-Aqueous Detection Limit
2.0 µg/L (Method 8150) 0.002-0.01 µg/L (Method 509B)	1.3 µg/g (Method 8150)

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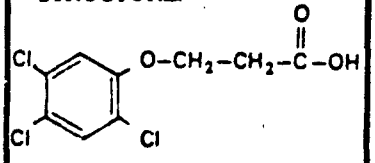
COMMON SYNONYMS:	CAS REG.NO: 93-72-1 FORMULA: $C_9H_7Cl_3O_3$ NIOSH NO: UF8225000 STRUCTURE: 	AIR W/V CONVERSION FACTOR at 25°C 11.02 mg/m³ ≈ 1 ppm 0.0907 ppm ≈ 1 mg/m³ MOLECULAR WEIGHT: 269.51
(2,4,5-trichloro-phenoxy) propanoic acid 2,4,5-TP 2-(2,4,5-Trichloro-phenoxy)-propanoic acid Fenoprop Silvex		

REACTIVITY	For general compatibility classification purposes, 2,4,5-TP is considered to be both an organic acid and a halogenated organic compound. Reactions of organic acids with amines, caustics, or nitriles typically evolve heat, while those with oxidizing mineral acids, azo or diazo compounds, hydrazines, or isocyanates evolve heat and usually innocuous gases. Reactions with nitrides, strong reducing agents, and certain elemental metals may evolve flammable gases and possibly heat, while those with alkali or alkaline earth metals may also cause a fire. Reaction with inorganic fluorides or sulfides, or strong oxidizing agents may evolve toxic gases and possibly heat. Reaction with cyanides or dithiocarbamates may produce both toxic and flammable gases, with the latter classification also producing heat. Reactions with alcohols, glycols, aldehydes, epoxides, or polymerizable compounds may initiate a violent exothermic polymerization reaction. Explosive materials may explode. Reactions of halogenated organic materials 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. 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 (511).

PHYSICO-CHEMICAL DATA	• Physical State: Solid (at 20°C)	(59,2015)
	• Color: Colorless to white	(54,2015)
	• Odor: Low odor	(59)
	• Odor Threshold: No data	
	• Density: 1.2085 g/mL (at 20°C)	(59)
	• Freeze/Melt Point: 180.40 to 181.60°C	(23)
	• Boiling Point: Not pertinent	
	• Flash Point: Nonflammable	(60)

PHYSICO-CHEMICAL DATA (Cont.)	• Flammable Limits: No data • Autoignition Temp.: No data • Vapor Pressure: 6.46E-06 mm Hg (at 25°C)	(2015)
	• Satd. Conc. in Air: 9.5000E-02 mg/m³ (at 20°C)	(1219)
	• Solubility in Water: 1.40E+02 mg/L (at 25°C)	(1118)
	• Viscosity: No data • Surface Tension: No data • Log (Octanol-Water Partition Coeff.): No data	
	• Soil Adsorp. Coeff.: 2.50E+03	(29)
	• Henry's Law Const.: 1.00E-09 atm · m³/mol (at 20°C)	(1219)
	• Bioconc. Factor: 1.70E+02 (estim)	(659)

PERSISTENCE IN THE SOIL-WATER SYSTEM	2,4,5-TP is expected to be highly dissociated and relatively mobile in natural soils due to limited sorption. The persistence of 2,4,5-TP in soils is not well documented; available data indicate that biodegradation may be important. Contamination of groundwater may occur under conditions of heavy application, high soil pH and heavy rainfall shortly after application.

PATHWAYS OF EXPOSURE	The primary pathway of concern from the soil/groundwater system is the migration of 2,4,5-TP to groundwater drinking water supplies. Degradation in the environment will minimize exposures by this pathway, however, and other exposure pathways are unlikely to be significant.

HEALTH HAZARD DATA	Signs and Symptoms of Short-term Human Exposure: (59) No adverse effects were reported in human volunteers ingesting a single 1 mg/kg dose of 2,4,5-TP. No other acute human exposure studies were found.

HEALTH HAZARD DATA	Acute Toxicity Studies: ORAL: LD_{50} 650 mg/kg — Rat (59) LD_{50} 276 mg/kg — Mouse (3504) SKIN: LD_{50} 3200 mg/kg acid equivalent (as tris (2-hydroxyethyl)ammonium salt/kg); value is >3200 — Rabbit (1118) Long-Term Effects: Possible liver and kidney damage Pregnancy/Neonate Data: Teratogenic, embryotoxic, and fetotoxic in animals Genotoxicity Data: Limited evidence is negative. Carcinogenicity Classification: IARC - None assigned NTP - No data EPA - No data
HANDLING PRECAUTIONS (38)	Handle chemical only with adequate ventilation • Concentrations of 10-50 mg/m³: any dust and mist respirator, except single-use • 50-100 mg/m³: any dust and mist respirator, except single-use or quarter-mask respirator or any fume respirator or high efficiency particulate filter respirator or any supplied-air respirator or any self-contained breathing apparatus • 100-500 mg/m³: a high efficiency particulate filter respirator with full facepiece or any supplied-air respirator with a full facepiece, helmet or hood or any self-contained breathing apparatus with full facepiece • 500-5000 mg/m³: a power 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 clothing to prevent repeated or prolonged skin contact.

ENVIRONMENTAL AND OCCUPATIONAL STANDARDS AND CRITERIA

AIR EXPOSURE LIMITS:

Standards
- OSHA TWA (8-hr): 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 (296,991)
MCLG: 50 µg/L (proposed)
MCL : 50 µg/L (proposed)
MCL : 10 µg/L (interim)

EPA Health Advisories and Cancer Risk Levels (3977)
The EPA has developed the following Health Advisories which provide specific advice on the levels of contaminants in drinking water at which adverse health effects would not be anticipated.

- 1-day (child): 200 µg/L
- 10-day (child): 200 µg/L
- longer-term (child): 70 µg/L
- longer-term (adult): 300 µg/L
- lifetime (adult): 50 µg/L.

WHO Drinking Water Guideline
No information available.

EPA Ambient Water Quality Criteria
- Human Health (355)
  - No criterion established; 2,4,5-TP is not a priority pollutant.
- Aquatic Life (355)
  - No criterion established; 2,4,5-TP is not a priority pollutant.

REFERENCE DOSES:

ORAL: 7.500E+00 µg/kg/day (3744)

REGULATORY STATUS (as of 01-MAR-89)

Promulgated Regulations

- Federal Programs

Clean Water Act (CWA)

2,4,5-TP is designated a hazardous substance. It has a reportable quantity (RQ) limit of 45.4 kg (347, 3764). Effluent limitations, set at 0.010 kg/1000 kg of organic pesticide chemicals, are applicable to discharges resulting from the manufacture of 2,4,5-TP (891).

Safe Drinking Water Act (SDWA)

2,4,5-TP is on the list of 83 contaminants required to be regulated under the SDWA of 1974 as amended in 1986 (3781). Under the National Primary Drinking Water Regulations (296), the maximum contaminant level (MCL) for 2,4,5-TP is 0.01 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 (3801). In states with an approved Underground Injection Control program, a permit is required for the injection of 2,4,5-TP-containing wastes designated as hazardous under RCRA (295).

Resource Conservation and Recovery Act (RCRA)

2,4,5-TP is identified as a hazardous waste (U233) and listed as a hazardous waste constituent (3783, 3784). Non-specific sources of 2,4,5-TP-containing waste are wastes from production or manufacturing use of tri-, tetra-, or pentachlorophenols and their pesticide derivatives, discarded unused formulations containing these compounds, and residues resulting from incineration or thermal treatment of soil contaminated with these formulations (325). Solid wastes which contain a TCLP extract concentration equal to or greater than 1 mg/L of 2,4,5-TP are listed as hazardous in that they exhibit the characteristics defined as EP toxicity (988). 2,4,5-TP is on EPA's ground-water monitoring list. EPA requires that all hazardous waste treatment, storage, and disposal facilities monitor their ground-water for chemicals on this list when suspected contamination is first detected and annually thereafter (3775). For ground-water protection, the maximum concentration of 2,4,5-TP-containing hazardous waste in ground-water is 0.01 mg/L (989). Effective July 8, 1987, the land disposal of untreated hazardous wastes which contain halogenated organic compounds in total concentrations greater than or equal to 1000 mg/kg is prohibited. Effective August 8, 1988, the underground injection into deep wells of these wastes is prohibited. Certain variances exist until May, 1990 for some wastewaters and nonwastewaters for which Best Demonstrated Available Technology (BDAT) treatment standards have not been promulgated by EPA (3786). EPA requires 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 40 CFR 264.343 or 265.343 (3782).

Comprehensive Environmental Response Compensation and Liability Act (CERCLA)
2,4,5-TP 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 2,4,5-TP but these depend upon the concentrations of the chemicals in the waste stream (3766).

Federal Insecticide, Fungicide and Rodenticide Act (FIFRA)
A tolerance of 0.05 ppm has been established for residues of 2,4,5-TP in or on raw agricultural commodity pears resulting from post-harvest application of the triethanolamine salt to pear trees (980). An interim tolerance of 0.1 ppm has been established for apples, plums, rice and sugarcane (2307).

Marine Protection Research and Sanctuaries Act (MPRSA)
Ocean 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 2,4,5-TP as a hazardous material with a reportable quantity of 45.4 kg, subject to requirements for packaging, labeling and transportation (3180).

Food, Drug and Cosmetic Act (FDCA)
The level for 2,4,5-TP in bottled drinking water is 0.01 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
All states have adopted EPA Ambient Water Quality Criteria and NPDWRs (see Water Exposure Limits section) as their promulgated state regulations, either by narrative reference or by relisting the specific numeric criteria. These states have promulgated additional or more stringent criteria:

NEW YORK
New York also has a water quality standard of 0.26 µg/L for ground-water classed for drinking water supply, and an ambient water quality standard of 10 µg/L for surface waters classed for drinking water supply (3501).

VERMONT
Vermont also has a preventive action limit of 5 µg/L and an enforcement standard of 10 µg/L for 2,4,5-TP in ground-water (3682).

WISCONSIN
Wisconsin also sets a preventive action limit of 2 µg/L and an enforcement standard of 10 µg/L for 2,4,5-TP in ground-water (3840).

Proposed Regulations

- Federal Programs

  Safe Drinking Water Act (SDWA)
  EPA has proposed a maximum contaminant level goal (MCLG) of 52 µg/L for 2,4,5-TP as part of the National Primary Drinking Water Regulations (3751). EPA will repropose an MCLG of 50 µg/L and propose an MCL of 50 µg/L in May, 1989, with final action scheduled for December, 1990 (3759).

  Resource Conservation and Recovery Act (RCRA)
  EPA has proposed that solid wastes be listed as hazardous because they exhibit the characteristic defined as EP toxicity when the TCLP extract concentration is equal to or greater than 0.14 mg/L 2,4,5-TP Final promulgation of this Toxicity Characteristic Rule is expected in June, 1989 (1565).

- State Water Programs
  No proposed regulations are pending.

  MOST STATES
  Most states are in the process of revising their water programs and proposing changes in their regulations which will follow EPA's changes when they become final. Contact with the state officer is advised. Changes are projected for 1989-90 (3683).

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 2,4,5-TP is 0.1 mg/L. The total maximum allowable concentration for pesticides and related products is 0.5 mg/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)
2,4,5-TP 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)
2,4,5-TP 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 organohalogen compounds at sea be prohibited.

62.1 MAJOR USES

2-(2,4,5-Trichlorophenoxy)propionic acid (2,4,5-TP) is a broad spectrum herbicide which is usually contaminated with 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD), a toxic by-product formed during the manufacturing process (see Chapter 63) (507). 2,4,5-TP acts as a hormone-type weed killer and is readily absorbed by leaves and stems. It is effective in controlling brush and woody plants, aquatic weeds, and broad leaved weeds in maize and sugar cane (1118). Amine salts of 2,4,5-TP are used 7 to 14 days before harvest to reduce pre-harvest drop of apples (1118). Due to a close similarity to other chlorophenoxy herbicides such as 2,4,5-T (see Chapter 61), use of 2,4,5-TP has been restricted in the U.S. (23, 54).

62.2 ENVIRONMENTAL FATE AND EXPOSURE PATHWAYS

62.2.1 Transport in Soil/Ground-water Systems

62.2.1.1 Overview

There is very little information in the literature that specifically addresses the environmental fate and transport of 2,4,5-TP. However, since 2,4,5-TP is structurally very similar to 2,4,5-T (2,4,5-trichlorophenoxyacetic acid), its behavior in the soil/ground-water system is also expected to be similar. The discussion of environmental fate presented in this section is largely based on 2,4,5-T data (see Chapter 61) and the limited observations reported for 2,4,5-TP.

2,4,5-TP is expected to be relatively mobile in the soil/ground-water system when present at low dissolved concentrations. Bulk quantities of the solution (e.g., from a spill, heavy spray application, or improper disposal of excess formulations) could be transported rapidly through the unsaturated zone. However, as discussed later in this section, 2,4,5-TP may be susceptible to degradation in the soil/ground-water system and is not expected to be persistent.

2,4,5-TP is expected to be highly dissociated to the anionic form at typical environmental pHs; pK_a values are expected to be in the same range as those reported for 2,4,5-T (~3). The dissociated form is expected to be more soluble in water, less strongly sorbed to soils, and less likely to be bioaccumulated than the undissociated form. Thus, the soil/ground-water pH level is very important in determining the mobility of 2,4,5-TP.

In general, transport pathways can be assessed by using an equilibrium partitioning model, as shown in Table 62-1. These calculations predict the partitioning of low soil concentrations of 2,4,5-TP among soil particles, soil water, and soil air. Portions of 2,4,5-TP associated with the water and air phases of the soil

TABLE 62-1
EQUILIBRIUM PARTITIONING CALCULATIONS FOR 2,4,5-TP
IN MODEL ENVIRONMENTS[a,b,c,d]

Soil Environment	Estimated Percent of Total Mass of Chemical in Each Compartment		
	Soil	Soil-Water	Soil-Air
Unsaturated topsoil at 25°C			
• Undissociated 2,4,5-TP	99.8	0.2	1E-08
• Total 2,4,5-TP[e]			
pH3	49.9	50.1	<1E-0[illegible]
pH4	10	90	<1E-09
pH5	1	99	<1E-10
pH6	0.1	99.9	<1E-11
pH7	0.01	99.99	<1E-12
Saturated deep soil			
• Undissociated 2,4,5-TP	91	9	
• Total 2,4,5-TP[e]			
pH3	45	55	
PH4	9	91	
pH5	0.9	99.1	
pH6	0.09	99.91	
pH7	0.01	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 partition coefficient reported for organic component of soil (29): K_{oc} = 2500.
c) Henry's law constant taken as approximately 1E-09 atm · m³/mol at 25°C (Arthur D. Little, Inc. estimate).
d) Used sorption coefficient $K_p = 0.001 \times K_{oc}$
e) The distribution for total 2,4,5-TP assumes that all of the dissociated fraction partitions to the soil-water compartment and that the approximate percentage of dissociation is as follows: 50% at pH 3, 90% at pH 4, 99% at pH 5, 99.9% at pH 6, and 99.99% at pH 7.

generally have higher mobility than the adsorbed portion. Partitioning estimates are given for the total chemical (dissociated as well as undissociated 2,4,5-TP) at various pHs and for the undissociated form of the chemical, the latter being valid only for very low pHs (i.e., less than the pK_a of ~3). Estimates for the unsaturated topsoil model indicate that while most of the undissociated 2,4,5-TP in the modeled system is expected to be associated with the stationary phase, most of the 2,4,5-TP present in the soil at common environmental pHs (>5) will be dissociated and partition to the mobile soil-water phase. An insignificant portion of 2,4,5-TP 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), a higher percentage of the undissociated 2,4,5-TP (9%) and almost all of the 2,4,5-TP present at environmental pH levels is predicted to be present in the soil-water phase (Table 62-1) and available for transport with flowing ground water. Ground water underlying 2,4,5-TP-contaminated soils with low organic content may be vulnerable to contamination. However, data available for 2,4,5-TP and 2,4,5-T indicate that biodegradation (which is not addressed in this partitioning model) may reduce the threat of ground water contamination.

Under normal herbicide application rates, 2,4,5-TP is not expected to persist from one season to the next; only where other phenoxy herbicides (2,4-D and 2,4,5-T) were applied at massive doses were there significant residues after 10 years (1862). At common application rates, 2,4,5-TP soil concentrations were reported to be reduced to one-half the initial concentration after 35 days (1908). Although the phenoxy herbicides are expected to be relatively non-persistent in the soil/ground-water environment, trace levels have been observed in surface and ground waters (1852, 1862, 1863). Most reports indicate that transport to surface and well waters occurred as a direct result of spray activity in the vicinity of streams (aerial drift) or transport with storm runoff near the time of application. Runoff concentrations decline rapidly and generally account for less than 1-5% of the application, with most of the loss associated with the water phase (1864, 1865, 1866).

62.2.1.2 Sorption on Soils

The acid dissociation constant (pK_a) of 2,4,5-TP is expected to be approximately 3.0. Since the pH of most soils is greater than 4.5 and that of most natural waters is greater than 6.0, environmental 2,4,5-TP is expected to exist primarily in the anionic form which is poorly adsorbed due to its high water solubility and possible repulsion by the surface negative charge of soil organic matter and clay (1864). Strong sorption of 2,4,5-TP (undissociated) onto clays in acidic environments has been reported (1871). In general, it is expected that 2,4,5-TP, like 2,4,5-T and 2,4-D, will be weakly sorbed to environmental soils and that adsorption is a direct function of organic content and varies with the pH of the soil. The observed variation in K_{oc} values for 2,4-D (see Chapter 60) supports the expected decrease in sorption with increasing pH; a similar trend is expected for 2,4,5-TP. Some leaching and vertical transport of 2,4,5-TP may occur.

62.2.1.3 Volatilization from Soils

Due to the low vapor pressure and relatively high water solubility expected for the dissociated 2,4,5-TP, evaporation from aqueous solution is expected to be negligible. Since the rate of volatilization from soil is generally significantly lower than that from water, 2,4,5-TP volatilization from surface soils or in soil-air will not be an important transport process, particularly in the presence of any soil moisture.

62.2.2 Transformation Processes in Soil/Ground-water Systems

2,4,5-TP is an acidic compound (pK_a = ~3) and, like other phenoxy herbicides, has a strong tendency to hydrolyze in the presence of water. At pH levels above 5, 2,4,5-TP is expected to be greater than 99% dissociated. Degradation reactions (oxidation, reduction, hydrolysis, substitution) have been reported to occur with other phenoxy herbicides (2,4-D and 2,4,5-T) in water when activated by sunlight (1850, 1864, 1895, 1896, 1897).

Reports on the microbial degradation of 2,4,5-TP are few and, in fact, contradictory. Several authors have reported the resistance of 2,4,5-TP to biodegradation (1910, 1911), largely attributed to the number of chlorines on the aromatic ring and to the presence of a chlorine in the meta position. On the other hand, Ou and Sikka (1909) have reported extensive 2,4,5-TP biodegradation, including destruction of the aromatic ring, by the synergistic action of two species of aquatic microorganisms; no degradation was observed with pure cultures. The mixed culture was unable to use 2,4,5-TP as its sole source of carbon but cometabolized rapidly in the presence of an external carbon source. No metabolites, except traces of 2,4,5-trichlorophenol and 3,5-dichlorocatechol, were observed. Houston (1878) also demonstrated ready biodegradation of 2,4,5-TP in the presence of a supplemental carbon source (soluble, readily-available organic matter). The rate of biodegradation of 2,4,5-TP was similar to that of 2,4,5-T and slower than that of 2,4-D.

In general, the extent of 2,4,5-TP biodegradation in soils can be estimated based on data for 2,4,5-T. Biodegradation is expected to be dependent on microbial populations, soil moisture, and soil temperature; increased sorption is expected to decrease biodegradation; and the presence of oxygen is expected to enhance biodegradation. Half-lives in soil are expected to be approximately 5-6 weeks based on data for 2,4,5-T as well as 2,4,5-TP. Since the availability of soil microorganisms capable of biodegradation is probably low and is expected to drop significantly with depth, biodegradation of 2,4,5-T in deep soils may be minimal. Therefore, 2,4,5-TP that is transported downward to the subsoil may represent a potential threat to ground water.

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

The above discussion of fate pathways suggests that undissociated 2,4,5-TP is nonvolatile, moderately to strongly sorbed to soil, and has a moderate potential for bioaccumulation. These fate characteristics suggest several potential exposure pathways.

Volatilization of 2,4,5-TP from a disposal site is expected to result in negligible exposure to workers or residents in the area since 2,4,5-TP in either dissociated or undissociated form is nonvolatile. The potential for ground-water contamination exists despite the sorption of the undissociated acid to soil. The dissociated form of the acid, which is expected to be the predominant form under virtually all pH levels of environmental concern, would be only weakly retained. The susceptibility of 2,4,5-TP to degradation, however, should lessen its occurrence in drinking water supplies. Mitre (83) reported that 2,4,5-TP has been detected in 2 of 546 National Priority List sites; in both cases it was found only in ground water, not in surface water or air. In Florida, 2,4,5-TP has been found in ground-water supplies at concentrations ranging from 0.04 to 0.30 μg/L as well as in finished drinking water (992).

The movement of 2,4,5-TP in ground water or its movement with soil particles may result in discharge to surface water. As a result, ingestion exposures may occur from the use of surface waters as drinking water supplies, and dermal exposures may result from the recreational use of surface waters. In some cases, the potential for uptake of 2,4,5-TP by aquatic organisms or domestic animals may be important. However, the susceptibility of 2,4,5-TP to degradation and its moderate potential for bioaccumulation suggest that these exposures from soil/ground-water systems will be insignificant except in unusual circumstances (e.g. a large spill).

62.2.4 Other Sources of Human Exposure

The EPA issued an emergency suspension order covering certain uses of 2,4,5-TP in 1979; all registrations for herbicides containing 2,4,5-TP are now cancelled (992). Due to its lack of persistence and the absence of current use, concentrations of 2,4,5-TP in the environment are expected to be negligible at present.

2,4,5-TP has been found in the drinking water of three states (992). One large surface water system (of eighty sampled) was found to contain 0.02 μg/L in 1975, but in a study conducted between 1977 and 1981, it was detected in none of 105 surface water systems nor was it detected in excess of the detection limit (0.1 μg/L) in a 1978 study of 21 rural surface water systems (992). Between 1965 and 1968, however, 2,4,5-TP was detected in surface waters of 15 Western states at concentrations ranging from 0.01 to 0.21 ppb (213).

No data on the concentration of 2,4,5-TP in air were found for this study, and data on concentrations in food are also sparse. Market basket surveys have not reported the presence of 2,4,5-TP in the diet of infants, toddlers, or adults (1244, 1245). A 1975 study found residues on unwashed apples of 97 μg/kg initially, decreasing to 36 μg/kg after 4 months of storage (992). The little data available suggest that 2,4,5-TP exposure in food is likely to be negligible, as is exposure from air.

62.3 HUMAN HEALTH CONSIDERATIONS

Commercial formulations of 2,4,5-TP are contaminated with low levels of 2,3,7,8-TCDD; early samples of 2,4,5-TP may have contained high concentrations of 2,3,7,8-TCDD. Some of the toxic effects associated with exposure to 2,4,5-TP are generally considered to be caused, at least in part, by this contaminant. However, the toxic effects of pure 2,4,5-TP have not been studied well.

62.3.1 Animal Studies

62.3.1.1 Carcinogenicity

2,4,5-TP does not elicit an increased tumor incidence in rodents administered the compound either orally or subcutaneously.

No increased incidence of tumors was reported in male and female Wistar rats orally administered the potassium salt of 2,4,5-TP at doses of up to 7.9 mg/kg (acid equivalent) daily for 2 years (2017).

B6C3F_1 or B6AKF_1 mice were orally administered 46.6 mg/kg bw/day of 2,4,5-TP in 0.5% gelatin for 3 weeks followed by administration of 121 ppm 2,4,5-TP daily in the diet for 18 months (2136). No significant increase in the incidence of neoplasms was observed.

Innes et al. (2136) subcutaneously injected B6C3F_1 or B6AKF_1 mice with a single dose of 215 mg/kg 2,4,5-TP suspended in dimethyl sulfoxide on day 28 of age. Animals were observed for 18 months. Again no significant increase in neoplasms was observed.

NCI considers both the oral and subcutaneous mouse studies by Innes et al. (2136) relatively insensitive for detecting a possible oncogenic effect. IARC has not reviewed 2,4,5-TP specifically, although it has reviewed other phenoxy herbicides (1607).

62.3.1.2 Genotoxicity

Andersen et al. (2016) reported no genotoxic activity for 2,4,5-TP when tested in the Ames assay using 8 strains (not specified) of Salmonella typhimurium. A spot test was used without metabolic activation, a method that would be considered inadequate today. No other studies were found in the literature concerning the genotoxicity of 2,4,5-TP.

62.3.1.3 Teratogenicity, Embryotoxicity and Reproductive Effects

Results of an unpublished Dow Chemical Company study on the teratogenic effects of 2,4,5-TP (containing <0.05 ppm TCDD) was reported by the USEPA (2018). Pregnant Sprague-Dawley rats were exposed to 25-100 mg/kg/day of 2,4,5-TP by gavage on days 6-15 of gestation. Fetal examination revealed skeletal anomalies including cleft palate, retarded ossification and extra cervical ribs. Microphthalmia (abnormal smallness of the eyeball) and cardiovascular abnormalities were also seen in exposed fetuses.

A dose of 1.5 mM/kg/day or approximately 398 mg/kg/day of 2,4,5-TP (<0.1 ppm TCDD) was administered to CD-1 mice either orally in corn oil:acetone or subcutaneously in dimethyl sulfoxide (DMSO) on gestational days 12 through 15 (2137). A significant increase in maternal weight gain was reported in both test groups and was thought to be due to increased liver weight. Animals injected with the 2,4,5-TP:DMSO showed an average fetal mortality of 25%. Both routes of exposure were associated with a significant ($P < 0.01$) decrease in fetal weight and a slight but statistically insignificant increased incidence of cleft palate.

Although contamination of 2,4,5-TP by 2,3,7,8-TCDD may have contributed to the teratogenic effects of this compound, the extent of this interaction is unclear.

62.3.1.4 Other Toxicologic Effects

Commercial 2,4,5-TP is contaminated to a varying extent with 2,3,7,8-TCDD which renders any toxicological assessment difficult. It is not clear whether the reported effects are due to 2,4,5-TP alone, the 2,3,7,8-TCDD contaminant or a combination of both.

62.3.1.4.1 Short-term Toxicity

Signs of acute toxicity generally include depression, posterior quarter muscle weakness, irritation of the stomach and minor liver and kidney damage (2015). The oral LD_{50} values for the rat and mouse were found to be 650 mg/kg (2138, 59) and 276 mg/kg (3933), respectively.

62.3.1.4.2 Subchronic and Chronic Toxicity

Little data other than reports of unpublished Dow Chemical Co. data exist on the chronic effects of 2,4,5-TP in experimental animals.

Rats fed 300 or 600 mg/kg Kuron® (a herbicide containing polypropylene glycol butyl ether esters of 2,4,5-TP which is 45% 2,4,5-TP equivalent) daily in the diet for 90 days showed a statistically significant reduction in growth rate when compared to control animals. Histopathologic examination revealed signs of malnutrition in the 600 mg/kg treatment group (2275).

Two female beagle dogs fed 0.1% Kurosal® SL (a formulation containing the potassium salt of 2,4,5-TP, equivalent to 53% 2,4,5-TP) in the diet for 89 days showed growth depression, moderate pathological changes in the liver of one dog, and an increased alkaline phosphatase value and decreased hemoglobin and hematocrit in the second dog. Dogs fed diets containing 0.01 or 0.03% Kurosal® SL for 89 days showed no evidence of adverse effects (2275).

Mullison (2275) fed male and female rats the sodium salt of 2,4,5-TP for 90 days at 100, 300, 1000 or 3000 ppm. Growth was decreased at 300 ppm (277 ppm acid equivalent) and above. Liver weight was increased at 100 ppm (92 ppm acid equivalent) for females and at 300 ppm for males. Histopathologic examination showed liver and kidney damage in both sexes at all dietary concentrations except for kidneys of females at the 100 ppm treatment level.

Six Delaine-Merino sheep were given daily oral doses of 2,4,5-TP for 21 consecutive days without any apparent ill effects. The dose of 2,4,5-TP was subsequently increased to 150 mg/kg for an additional 10 days. Signs of poisoning (anorexia, muscular spasms, severe depression and prostration) were observed in 2 sheep only. One died after 29 doses, the other following 31 doses. Necropsy revealed inflamed and swollen lymphatics, enteritis, enlarged and congested spleen and rumen stasis (2302).

Gehring and Betso (2017) conducted a 2-year feeding trial with the potassium salt of 2,4,5-TP. Wistar rats were given 0, 0.26, 0.8, 2.6 or 7.9 mg acid equivalents/kg bw/day while beagle dogs were fed 0, 0.9, 2.6, 8.2 or 9.9 mg acid equivalents/kg bw/day for 2 years. A significant increase in the relative kidney:body weight ratio was reported in rats at all dose levels. Since no other kidney alterations were noted, Gehring and Betso concluded that the increased kidney weight was due to physiological adaptation rather than toxicity. Mild degeneration and necrosis of hepatocytes with a slight fibroblastic proliferation was reported in male dogs fed the 2.6 mg/kg dose of 2,4,5-TP. These same effects were seen in both male and female dogs fed the 8.2 or 9.9 mg/kg dose level of 2,4,5-TP in addition to elevated SGPT and SGOT levels (values not specified) in female dogs. Since the purity of the 2,4,5-TP sample in relation to dioxin contamination was not evaluated in this study,

the observed liver changes in dogs could not, with any certainty, be attributed solely to the effects of 2,4,5-TP.

Administration of 50 mg/kg/day 2,4,5-TP to cattle for 90 days resulted in erosion of the rumen mucosa and chronic enteritis (17). Necropsy revealed enlarged, friable livers and congestion of the lower respiratory passages.

62.3.2 Human and Epidemiologic Studies

62.3.2.1 Short-term Toxicologic Effects

Little data were found in the literature pertaining to the acute health effects of 2,4,5-TP exposure in humans.

Seven men and one woman orally given 1 mg/kg 2,4,5-TP exhibited no adverse effects (59). The average amount of 2,4,5-TP and its conjugates excreted and recovered was 80.3%.

Human dermal absorption of 2,4,5-TP is estimated to range from <0.001 mg/kg/hour to a maximum of 0.095 mg/kg/hour when exposed skin is wet with spray (2139).

62.3.2.2 Subchronic and Chronic Toxicologic Effects

Available data for long-term human exposure deal with occupational exposure to mixed phenoxy herbicides including 2,4,5-TP, chlorophenols, 2,3,7,8-TCDD and other industrial chemicals during manufacture and use. There are no data to assess the toxic effects of 2,4,5-TP alone in humans.

Reduced nerve conduction velocity was reported in workers occupationally exposed to 2,4,5-TP along with other phenoxy herbicides (2140).

Case-controlled epidemiological studies of populations in Scandinavian countries suggest a six-fold increase in the risk of soft tissue sarcoma among individuals exposed to dioxin- and furan-free phenoxy herbicides, including 2,4,5-TP (2025). Cases of soft tissue sarcomas have also been reported in U.S. workers exposed to phenoxy herbicides (2242, 2306). A review of these studies can be found in references 2015, 1607 and 2135. The complexity of exposure of workers to a mixture of chlorophenoxy herbicides and their contaminants preclude any conclusion regarding the causative agent(s) and attribution of the increased incidence of soft tissue sarcomas to any specific herbicide remains uncertain.

62.3.3 Levels of Concern

Under the National Interim Primary Drinking Water Regulations, the maximum contaminant level for 2,4,5-TP allowed in drinking water is 0.01 mg/L.

The USEPA (3742) has issued Health Advisories for noncarcinogenic risks for both children and adults. For a 10-kg child, the one-day, ten-day, and longer-term advisories are 0.2, 0.2, and 0.07 mg/L, respectively. It is assumed that the average child consumes one liter of drinking water daily. For a 70-kg adult, the longer-term advisory is 0.3 mg/L, assuming an intake of two liters of water daily. The lifetime advisory is 0.05 mg/L. The RfD, an estimate of a daily exposure to the human population that is likely to be without appreciable risk of deleterious effects over a lifetime, is 0.0075 mg/kg/day.

The NAS-NRC (213) recommended a concentration of 5.25 μg/L of 2,4,5-TP in drinking water, based on an acceptable daily intake (ADI) of 52.5 μg/day and consumption of two liters of contaminated water daily, assuming 20% of the total ADI comes from drinking water. The ADI was based on the no-observed-adverse-effect level of 750 μg/kg/day for dogs in a two year feeding study (2017).

Neither OSHA (3539) nor the ACGIH (3005) have established criteria for this herbicide.

62.3.4 Hazard Assessment

2,4,5-TP is a member of the chlorophenoxy family of herbicides. Commercial formulations of 2,4,5-TP are contaminated with varying levels of 2,3,7,8-TCDD. The presence of this highly toxic contaminant may be responsible for some of the observed toxic effects and confounds interpretation of the available data with regard to the toxicity of 2,4,5-TP alone.

No significant increase in tumor incidence was observed in either rats or mice fed 2,4,5-TP in the diet (2017, 2136). A single genotoxicity assay for histidine reversion in Salmonella typhimurium yielded negative results.

A teratogenic effect, primarily an increase in cleft palate, was reported for both rats (25-100 mg/kg) and mice (~398 mg/kg) orally exposed to 2,4,5-TP during gestation (2013, 2137). The contribution of the 2,3,7,8-TCDD contaminant to this response is unclear. Therefore, conclusive evidence of the teratogenicity of 2,4,5-TP cannot be established at this time.

The liver and kidney appear to be the target organs for 2,4,5-TP (2017, 2275). Acute exposure to 2,4,5-TP induces muscular weakness, depression and changes in liver enzymes (2015). The oral LD_{50} is 650 mg/kg for the rat (2138). Few long-term exposure studies are available for 2,4,5-TP, and those that are available are primarily

reports of unpublished studies. Exposure of rats to 100 ppm of 2,4,5-TP (sodium salt) for 90 days produced histological changes in the liver and kidneys (2275) while adverse effects were noted in the liver of dogs exposed to 2.6 mg (acid equivalent)/kg bw/day for two years (2017).

Available human data for 2,4,5-TP are limited to studies which have assessed the effects of mixed occupational exposures to chlorophenoxy herbicides, including 2,4,5-TP, chlorophenols and dioxin contaminants. These studies indicate an excess risk for the development of soft tissue sarcomas among exposed workers (2025, 2242, 2306). The presence of dioxin contaminants and the lack of definitive data for 2,4,5-TP exposure alone, preclude any conclusion regarding the contribution, if any, of 2,4,5-TP to the observed response.

62.4 SAMPLING AND ANALYSIS CONSIDERATIONS

Determination of 2,4,5-TP 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 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 2,4,5-TP in aqueous samples include EPA Methods 8150 and 8250 (63) and 509B (1422). Prior to analysis, a measured volume of sample, approximately 1 liter is acidified and subsequently extracted with ethyl ether using a separatory funnel. The sample extract is hydrolyzed with potassium hydroxide and any extraneous organic material removed by a solvent wash. Because chlorinated phenoxy acid herbicides may occur in water in various forms (e.g., acid, salt, ester), this hydrolysis step is included to convert all forms of the herbicide to the acid form for analysis. 2,4,5-TP in the acid form is then extracted and converted to the methyl ester of 2,4,5-TP using diazomethane (Method 8150) or boron trifluoride-methanol (Method 509B) as the derivatizing agent. Additional cleanup procedures are specified if interferences are present in the sample matrix. Excess reagent is removed and an aliquot of the concentrated sample is injected onto a gas chromatographic (GC) column. The GC column is programmed to separate the semi-volatile organics; 2,4,5-TP methyl ester is then detected with an electron capture detector, microcoulometric detector or electroanalytic conductivity detector (Methods 8150 and 509B) or with a mass spectrometer (Method 8250). Identifications for unknown samples should be confirmed by analysis on a second chromatographic column (if using retention time as the identifier) or by GC/mass spectrometry.

The EPA procedures recommended for 2,4,5-TP analysis in soil and waste samples, Methods 8150 and 8250 (63) differ from the aqueous procedures primarily in the preparation of the sample extract. Solid samples are initially extracted with

acetone/ethyl ether using a wrist-action shaker. The solvent extract is washed, concentrated, and then derivatized.

In addition to the methods described above, solid-phase extraction with C18 columns has been recently used to isolate and concentrate phenoxy-acid herbicides in aqueous samples (3640, 3294). Separations are performed by thin-layer chromatography (3640) or high performance liquid chromatography (3294). These methods are direct and rapid. The analytical precision should also be greater than that obtained using derivatization methods described above.

Typical 2,4,5-TP detection limits that can be obtained in wastewaters and non-aqueous samples (wastes, soils, etc.) are shown below. A detection limit for 3,4,5-TP was not indicated in Method 8250 but would be in the range of 1-10 μg/L for aqueous samples and 1 μg/g for non-aqueous samples. The actual detection limit achieved in a given analysis will vary with instrument sensitivity and matrix effects.

Aqueous Detection Limit	Non-Aqueous Detection Limit
1.7 μg/L (Method 8150) 0.002-0.01 μg/L (Method 509B)	1.1 μg/g (Method 8150)

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Note: The nonsequential numbers of the references reflect the order of references as they appear in the master bibliography.

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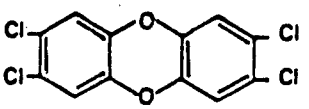
2,3,7,8-TETRACHLORODIBENZO-P-DIOXIN

COMMON SYNONYMS:	CAS REG.NO: 1746-01-6 FORMULA: $C_{12}H_4Cl_4O_2$ NIOSH NO: HP3500000 STRUCTURE:	AIR W/V CONVERSION FACTOR at 25°C 13.16 mg/m³ ≈ 1 ppm; 0.076 ppm ≈ 1 mg/m³ MOLECULAR WEIGHT: 321.96
2,3,7,8-TCDD 2,3,7,8-Tetrachlorodibenzo (B,E)(1,4)Dioxin 2,3,7,8-Tetrachlorodibenzo-p-dioxin Dioxin TCDD		

REACTIVITY	This substance is a trace contaminant in 2,4,5-T. The reactivity and flammability hazards of dioxin are therefore considered similar and subordinate to those of 2,4,5-T. (See Chapter 61.)

PHYSICO-CHEMICAL DATA	• Physical State: Solid, crystalline (at 20°C)	(2141)
	• Color: Colorless to white	(2141)
	• Odor: No Data	
	• Odor Threshold: No data	
	• Density: No data	
	• Freeze/Melt Point: 302.00 to 305.00°C	(2141)
	• Boiling Point: Decomposes	(2)
	• Flash Point: Not pertinent	
	• Flammable Limits: Not pertinent	
	• Autoignition Temp.: Not pertinent	
	• Vapor Pressure: 1.40E-09 mm Hg (at 25°C)(2340)	(2340)
	• Satd. Conc. in Air: 3.0000E-02 mg/m³ (at 20°C)	(1219)
	• Solubility in Water: 1.90E-05 mg/L (at 20°C)	(2343)
	• Viscosity: No data	
	• Surface Tension: No data	
	• Log (Octanol-Water Partition Coeff.): 6.15 to 7.28	(2183,2184,2185)
	• Soil Adsorp. Coeff.: 2.30E+06	(2168)
	• Henry's Law Const.: 1.60E-05 atm · m³/mol (at 25°C)	(2169)
	• Bioconc. Factor: 2.30E+05	(659)

PERSISTENCE IN THE SOIL-WATER SYSTEM	2,3,7,8-TCDD is expected to be relatively immobile in the soil/ground-water system due to strong sorption properties; surface-applied contamination is expected to be confined to the uppermost 6-12 inches and contamination of underlying groundwater is not expected. Vapor-phase diffusion and subsequent volatilization from surface soils may be significant in the absence of other transport processes; translocation of sorbed 2,3,7,8-TCDD with soil particles may also be important. Photodegradation is expected to be the predominant transformation process. Although some biodegradation of 2,3,7,8-TCDD has been reported, it is not expected to be rapid in environmental soils.
PATHWAYS OF EXPOSURE	The primary pathway of concern from the soil/ground-water system is the migration of 2,3,7,8-TCDD to groundwater drinking water supplies, although this is not likely to occur in most situations. Bioaccumulation by aquatic organisms or domestic animals may be an important exposure pathway in some instances, but uptake by crops from soils is unlikely to be significant.
HEALTH HAZARD DATA	Signs and Symptoms of Short-term Human Exposure: (54) Acute effects of 2,3,7,8-TCDD exposure include chloro-acne, hepatotoxicity, psychological alterations, weight loss, thymic atrophy, thrombocytopenia, suppression of cellular immunity, and death. The liver appears to be the target organ following acute exposure.

HEALTH HAZARD DATA (Cont.)	Acute Toxicity Studies: (3744) ORAL: LD_{50} 114 µg/kg — Mouse LD_{50} 20 µg/kg — Rat LD_{50} 2 µg/kg — Monkey LD_{50} 1157 µg/kg — Hamster LD_{50} 0.5 µg/kg — Guinea Pig LD_{50} 115 µg/kg — Rabbit LD_{50} 1 µg/kg — Dog SKIN: LD_{50} 275 µg/kg — Rabbit TD_{Lo} 107 µg/kg — Human LD_{Lo} 80 µg/kg — Mouse Long-Term Effects: Chloracne, gastric ulcers, impaired liver function, peripheral neuropathy, and psychiatric disturbances Pregnancy/Neonate Data: Teratogenic in animals at doses below those producing maternal toxicity Fetotoxic, gonadotoxic; adverse reproductive effects Genotoxicity Data: Primarily negative Carcinogenicity Classification: IARC - Group 2B (possibly carcinogenic to humans) NTP - None assigned EPA - Group B2 (probable human carcinogen; sufficient evidence in animals and inadequate evidence in humans)

HANDLING PRECAUTIONS (2345)	All contact with 2,3,7,8-TCDD should be avoided. If exposure cannot be avoided, use a self-contained breathing apparatus with full facepiece operated in pressure-demand or other positive pressure mode or a combination type C supplied-air respirator, with full facepiece, operated in pressure-demand mode and equipped with auxiliary positive pressure self-contained air supply. To prevent contact with TCDD, a disposable bilayer protective clothing ensemble should be used. The outer layer should consist of a zippered coverall with attached hood, elastic sleeves, gloves and closure boots made of non-woven fabric (Tyvek®) if dust exposure is probable; or disposable laminates or synthetic elastomers (Saranax®, coated Tyvek®, butyl, nitrile or neoprene rubber) if exposure to liquid is expected. The inner disposable layer should consist of a cotton coverall, undergarments and gloves.

ENVIRONMENTAL AND OCCUPATIONAL STANDARDS AND CRITERIA

AIR EXPOSURE LIMITS:

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

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

WATER EXPOSURE LIMITS:

Drinking Water Standards (3742)
MCLG (tentative): 0

ENVIRONMENTAL AND OCCUPATIONAL STANDARDS AND CRITERIA (Cont.)

EPA Health Advisories and Cancer Risk Levels

In the absence of formal drinking water standards, the EPA has developed the following Health Advisories which provide specific advice on the levels of contaminants in drinking water at which adverse health effects would not be anticipated.

- 1-day (child): 1E-03 µg/L
- 10-day (child): 1E-04 µg/L
- longer-term (child): 1E-05 µg/L
- longer-term (adult): 4E-05 µg/L
- 1E-04 cancer risk level: 2E-05 µg/L

WHO Drinking Water Guideline

No information available.

EPA Ambient Water Quality Criteria

- Human Health (2141)
  - Based on ingestion of contaminated water and aquatic organisms, the ambient water concentrations should be zero. Since zero may not be an attainable level at this time, the levels that may result in an increased cancer risk of 1E-05, 1E-06 and 1E-07 over the lifetime are estimated to be 1.3E-07, 1.3E-03 and 1.3E-09 µg/L, respectively.
  - Based on ingestion of contaminated aquatic organisms only, the levels corresponding to 1E-05, 1E-06, 1E-07 cancer risk are 1.4E-07, 1.4E-08, 1.4E-09 mg/L, respectively.

- Aquatic Life (2141)
  - Not enough data are available to allow derivation of criteria. The acute values for some fresh water species are > 1.0 µg/L. Some chronic values are <0.01 µg/L.

REFERENCE DOSES:

ORAL: 1.000E-06 µg/kg/day (3744)

REGULATORY STATUS (as of 01-MAR-89)

Promulgated Regulations

- Federal Programs

Clean Water Act (CWA)

2,3,7,8-TCDD is listed as a toxic pollutant, subject to general pretreatment regulations for new and existing sources, and effluent standards and guidelines (351, 3763). Effluent limitations specific to this chemical have been set in the following point source categories: electroplating (3767), steam electric power generating (3802), and metal finishing (3768). Limitations vary depending on the type of industry and plant.

Safe Drinking Water Act (SDWA)

2,3,7,8,-TCDD is on the list of 83 contaminants required to be regulated under the SDWA of 1974 as amended in 1986 (3781). In states with an approved Underground Injection Control program, a permit is required for the injection of 2,3,7,8-TCDD-containing wastes designated as hazardous under RCRA (295).

Resource Conservation and Recovery Act (RCRA)

2,3,7,8-TCDD is identified as a hazardous waste constituent (3783). Non-specific sources of 2,3,7,8-TCDD-containing waste are wastes from production or manufacturing use of tri-, tetra-, or pentachlorophenols and their pesticide derivatives, discarded unused formulations containing these compounds, and residues resulting from incineration or thermal treatment of soil contaminated with these formulations (325). 2,3,7,8-TCDD is included on EPA's ground-water monitoring list. EPA requires that all hazardous waste treatment, storage, and disposal facilities monitor their ground-water for chemicals on this list when suspected contamination is first detected and annually thereafter (3775). Effective November 8, 1988, the land disposal of untreated dioxin-containing wastes is prohibited. Effective August 8, 1988, the underground injection into deep wells of these wastes is prohibited. If the waste contains TCDD in a concentration greater than 1 ppb, it must be treated in accordance with the criteria established for incineration and thermal treatment. Certain variances exist until May, 1990 for some contaminated soils and wastewaters for which Best Demonstrated Available Technology (BDAT) treatment standards have not been promulgated by EPA (1755, 3786).

Comprehensive Environmental Response Compensation and Liability Act (CERCLA)

2,3,7,8-TCDD 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 2,3,7,8-TCDD but these depend upon the concentrations of the chemicals in the waste stream (3766).

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 2,3,7,8-TCDD a hazardous material with a reportable quantity of 0.454 kg, subject to requirements for packaging, labeling and transportation (3180).

- State Water Programs

ALL STATES
All states have adopted EPA Ambient Water Quality Criteria and NPDWRs (see Water Exposure Limits section) as their promulgated state regulations, either by narrative reference or by relisting the specific numeric criteria. These states have promulgated additional or more stringent criteria:

KANSAS
Kansas has an action level of 2 pg/L for 2,3,7,8-TCDD in ground-water (3213).

MISSOURI
Missouri has a surface water quality criterion of 0.014 pg/L for protection of aquatic life and 0.130 pg/L for drinking water supply waters (3457).

NEW YORK
New York has an MCL of 5 μg/L for 2,3,7,8-TCDD in drinking water, a water quality standard of 35 pg/L for ground-water classed for drinking water supply, and an ambient water quality standard for aquatic life of 1 pg/L for all fresh water classes of surface water (3501, 3500).

SOUTH DAKOTA
South Dakota requires 2,3,7,8-TCDD to be nondetectable, using designated test methods, in ground-water (3671).

VERMONT
Vermont has a preventive action limit of .022 pg/L and an enforcement standard of .22 pg/L for 2,3,7,8-TCDD in ground-water (3682).

Proposed Regulations

- Federal Programs

  Safe Drinking Water Act (SDWA)

  EPA will propose an MCL and MCLG for 2,3,7,8-TCDD in March, 1990, with final action scheduled for March, 1991 (3759).

- State Water Programs

  MOST STATES

  Most states are in the process of revising their water programs and proposing changes to their regulations which will follow EPA's regulations when they become final. Contact with the state officer is advised. Changes are projected for 1989-90 (3683).

  MINNESOTA

  Minnesota has proposed a Recommended Allowable Limit (RAL) of 20 pg/L for drinking water (3451). Minnesota has also proposed chronic criteria of 2 pg/L for designated ground-waters and .002 pg/L for designated surface waters, for the protection of human health (3452).

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 betaken 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 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 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 Major Accident Hazards of Certain Industrial Activities (1794)
2,3,7,8-TCDD manufacturers are required to notify competent authorities if it is stored or processed in quantities in excess of 1 kg. 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.

63.1 MAJOR USES

No use exists for 2,3,7,8-TCDD except as a chemical for research purposes. It is a contaminant primarily formed during the production of 2,4,5-trichlorophenol from 1,2,4,5-tetrachlorobenzene. It is known to contaminate several herbicides including 2,4,5-T and 2,4,5-TP. 2,3,7,8-TCDD may also be formed during the pyrolysis of chlorinated phenols, chlorinated benzenes, and polychlorinated diphenyl ethers which makes emission from municipal incinerators probable (2141).

63.2 ENVIRONMENTAL FATE AND EXPOSURE PATHWAYS

63.2.1 Transport in Soil/Ground-water Systems

63.2.1.1 Overview

2,3,7,8-TCDD is expected to be immobile in the soil/ground-water system when present at low concentrations. Quantities of 2,3,7,8-TCDD dissolved in organic solvents (e.g., from herbicide spray applications, or improper disposal of contaminated wastes) could be transported more rapidly through the unsaturated zone.

In general, transport pathways can be assessed by using an equilibrium partitioning model, as shown in Table 63-1. These calculations predict the partitioning of low soil concentrations of 2,3,7,8-TCDD among soil particles, soil water, and soil air. Portions of 2,3,7,8-TCDD associated with the water and air phases of the soil generally have higher mobility than the adsorbed portion. Estimates for the unsaturated topsoil model and the saturated deep soil model indicate that most of the 2,3,7,8-TCDD in the modeled systems is expected to be associated with the stationary phase and that ground water underlying contaminated soils would not be vulnerable to contamination. These models predict that an insignificant portion of 2,3,7,8-TCDD is expected in the gaseous phase of the soil, implying that diffusion of vapors through the soil-air pores up to the ground surface is not important.

A non-equilibrium steady-state model has been reported to provide a more realistic environmental distribution pattern for 2,3,7,8-TCDD (2175). While the results indicate that there is still strong partitioning to the solid phases (69.5% soil, 29.5% sediment), removal to the air represents 86% of the 2,3,7,3-TCDD loss.

Several studies summarized by Young et al. (1850) document the limited mobility of 2,3,7,8-TCDD in the soil system; migration was thought to occur primarily through erosion of contaminated soil particles. In spite of the strong sorption properties, evidence of 2,3,7,8-TCDD contamination of ground water, as well as soil, near a chemical waste disposal site, has been reported (2179). Since TCDD is more soluble

TABLE 63-1
EQUILIBRIUM PARTITIONING CALCULATIONS
FOR 2,3,7,8-TCDD 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]	100	1E-04	1E-07
Saturated deep soil[d]	99.99	0.01	-

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} = 2.3E+06 (2168).
c) Henry's law constant taken as 1.6E-05 atm · m^3/mol at 25°C (2169).
d) Used sorption coefficient K_p = 0.001 x K_{oc}.

in organic solvents than in water, the presence of residual organic solvents could result in enhanced mobility of TCDD in the soil/ground-water system.

Vertical distribution of 2,3,7,8-TCDD through the uppermost soil layers and horizontal distribution beyond the boundaries of the initial contamination have also been documented. Increased vertical movement in soil may occur as a result of saturation of sorption sites, migration with organic solvents, and human activity. Data from Air Force test sites (2170, 2171) indicate some vertical migration, with most 2,3,7,8-TCDD remaining in the upper 6 inches of soil. Several groups have examined the distribution of 2,3,7,8-TCDD in environmental soils in the vicinity of the Seveso industrial accident. Soil concentrations of 2,3,7,8-TCDD have been reported to drop sharply in the top 8 cm of soil and remain relatively constant from 8-cm to 24-cm depth (2172, 2174). Concentrations measured at depths below 8 cm were approximately one order of magnitude less than the levels down to 8 cm, and the highest levels were generally found at depths from 0.5 cm to 1.5 cm. Other authors (2173) report penetration to 20 cm in soils near Seveso.

For many compounds with low water solubility, migration and loss in the vapor phase can be significant, particularly in areas of low particle movement (2177). Soil column experiments have shown that 2,3,7,8-TCDD movement in soil can be modeled by vapor transport processes (2177, 2178). The rate of dispersion was very slow (10

cm in 12 years); the rate of downward movement was approximately equal to the rate of upward movement; there was a measurable change in diffusion as the temperature was changed from 25°C to 40°C; and the loss of moisture after 30 days resulted in a much lower migration rate. The initial depth of the contamination also affected the observed fate. Over 12 years, very little loss through volatilization and/or erosion was observed in an experiment where 2,3,7,8-TCDD had been applied 10 cm below the surface of the soil (2178).

In general, persistence studies indicate that 2,3,7,8-TCDD levels in soil diminished sharply within the first 6-15 months, followed by negligible changes; the initial decrease was attributed to photodecomposition and heat-promoted volatilization at the surface (2172, 2173, 2174). Half-lives of greater than one year have been reported for 2,3,7,8-TCDD in soils of 0.9-2.5% organic content (2176). However, most other studies state that no accurate estimate of persistence was possible.

63.2.1.2 Sorption on Soils

2,3,7,8-TCDD is expected to be strongly sorbed onto soil particles. Reported values of log K_{oc} range from 6.15 to 7.28 (2183, 2184, 2185, 2141, 2175); values of K_{oc} range from 4.6E+05 to 8.9E+06 (2168, 2186, 2187). Sorption is expected to be rapid while subsequent soil/water equilibrium and desorption are expected to be slow (2187, 2188). 2,3,7,8-TCDD is more tightly bound to soils of higher organic content and becomes increasingly bound to soil as a function of time (2176, 2180, 2182).

The medium in which 2,3,7,8-TCDD is dispersed at the time of soil application or environmental release has also been shown to affect its sorption on soil. Since the solubility of TCDD in organic solvents is generally greater than in water, its partitioning to soils is likely to be less and the amount available to be carried with the mobile liquid phase will be greater. Increased leaching of 2,3,7,8-TCDD with several organic solvents has been reported (2177, 2182, 2190). Slow aqueous leaching of 2,3,7,8-TCDD in soil/ground-water systems has been reported (2190, 1864, 1908, 2172); however, in the absence of co-solvents that solubilize 2,3,7,8-TCDD, the extent of leaching is expected to be minimal and substantial ground-water contamination is unlikely.

Since 2,3,7,8-TCDD is strongly adsorbed to soil particles and aqueous leaching is expected to be minimal, translocation of sorbed 2,3,7,8-TCDD is expected to be a major fate process (1864, 2174, 2191, 2192). Transport of TCDD-contaminated soil into surface waters by erosion has been described by several authors (2193, 2170, 2195). The 2,3,7,8-TCDD is expected to remain strongly adsorbed and persist in the suspended sediment or bottom sediment of the surface waters. Isensee and Jones (2196) concluded that dioxin adsorbed to soil would result in significant concentrations of 2,3,7,8-TCDD dissolved in water only if the soil particles were washed into a small body of water.

63.2.1.3 Volatilization from Soils

Due to its low vapor pressure, extensive volatilization of 2,3,7,8-TCDD is not expected. However, several authors (1908, 2169, 2178, 2197, 2177, 2193) have demonstrated the volatility of TCDD from soil in both laboratory and field experiments. Although volatilization losses are expected to be slow, they will be environmentally significant in the absence of other transport/transformation processes. Freeman and Schroy (2198) predicted that 90% of the TCDD at Times Beach had been lost through volatilization over the course of 10 years (with subsequent photolysis); 57% loss was estimated to have occurred in the first summer.

The two important parameters governing volatilization losses of TCDD are the initial depth profile and vapor-phase diffusion within the soil (2177). There is a lack of direct experimental data on the latter, but diffusion is expected to be affected by the temperature and moisture content of the soil. The surface temperature of soils is highly variable and is expected to significantly affect the rate of diffusion/volatilization; the fluctuation of sub-surface temperatures is much less dramatic. Diffusion/volatilization of other chemicals of low water solubility and low volatility, such as pesticides, has been reported to decrease dramatically under dry soil conditions (2199). The soil moisture content below which a dramatic drop in volatilization is observed roughly corresponds to a monomolecular layer of water covering the soil surface (1513); the volatilization rate was not greatly affected by minor increases above that level.

The depth of the initial chemical application will also affect the apparent half-life of the compound in soil, since volatilization is largely a surface phenomenon. Podoll et al. (2169) reported rapid volatilization of 2,3,7,8-TCDD at the soil/air interface, with a significant amount of tightly sorbed residue. In the same study, very low TCDD volatilization was reported when the contamination was buried to a depth of a few mm in dry soil.

63.2.2 Transformation Processes in Soil/Ground-water Systems

2,3,7,8-TCDD is susceptible to photodecomposition but is generally resistant to other chemical degradation in the environment. In laboratory experiments, 2,3,7,8-TCDD was readily degraded by photolytic dechlorination in the presence of a hydrogen donor (alcohols, ether, esters, hydrocarbons) and ultraviolet light (1864, 1850, 2191, 2203, 2204, 2205). Degradation of polychlorinated dibenzodioxins occurred by preferential dechlorination at the 2,3,7,8-positions (2206, 2207, 2205); continued irradiation resulted in some decomposition of the dibenzo-p-dioxin structure (1864). Photolytic half-lives of 56.8 minutes for 2,3,7,8-TCDD in n-hexadecane (2205) and 41 minutes in isooctane/octanol (2170) have been reported. In the absence of a hydrogen donor or after evaporation of hydrogen-donating solvents, negligible photolysis was observed (1864, 2204, 2203). In an aqueous suspension, no appreciable photolysis of 2,3,7,8-TCDD was detected; however, addition of a surfactant resulted in significant photolysis (2201, 2202, 1864).

The environmental significance of 2,3,7,8-TCDD photolysis is not well documented. However, several studies have reported that photolysis is the major route of TCDD disappearance and that under some conditions no other degradation would occur (1853, 2174). Crosby and Wong (2208) reported rapid photolysis of TCDD in Herbicide Orange (60-100% in six hours); Young et al. (1850) reported that herbicide formulations containing known concentrations of TCDD lost most or all of the TCDD in a single day when exposed to sunlight on leaves, soil, or grass. Typical half-lives for phototransformation of TCDD in aqueous environmental systems range from 1.77 days in summer to 5.42 days in winter (2181). Soil is expected to exert a protective effect against photolytic degradation; Nash and Beall (1908) estimate the time required for a 50% reduction of an initial soil concentration of 1-100 ppm to be 435-650 days.

Dioxins have exhibited relatively strong resistance to microbial degradation in soils (2198, 2176, 2180, 2201, 1864). Of 100 strains of microorganisms that had previously been shown to degrade persistent pesticides, only five strains exhibited some ability to degrade 2,3,7,8-TCDD (2180). Although an Air Force study (1850) attributed loss of 2,3,7,8-TCDD in soil to biodegradation, subsequent data (2198) demonstrated that all of the initial 2,3,7,8-TCDD was still contained in the test plots, and attributed the apparent biodegradation to vapor diffusion, variations in initial loadings, and analytical problems.

Recently, several authors (2194, 2189, 2200) have demonstrated that although TCDD is relatively stable, some biodegradation does occur. Matsumura et al. (2194) established that TCDD is biodegraded in aquatic sediments and in soils; after 4 months, approximately 66% was reported to remain in soil. The addition of nutrients significantly increased the rate of degradation. Degradation in cultures was substantially greater than in soils due to the number of microorganisms available and to the fact that TCDD in soil systems is strongly sorbed and not immediately available to the microorganisms. The authors speculated that due to the relatively low lipid solubility of TCDD, penetration of the microbial cell membrane may be a limiting factor. A strong stimulatory effect on TCDD biodegradation was observed when ethyl acetate was used as a carrier; use of a different carrier (such as corn oil) completely abolished TCDD-metabolizing activity.

Quensen and Matsumura (2200) reported that 5 ppb of 2,3,7,8-TCDD was metabolized by pure cultures of two microorganisms isolated from soil; again, the degree of metabolism was strongly dependent on the carrier solvent used, with ethyl acetate giving the best results; metabolism was also reported to increase when alternative carbon sources were reduced. Only a slight indication of TCDD metabolism in unaltered soil was reported due to strong sorption and limited microbial uptake. Degradation may be fastest during the first few days, before TCDD becomes strongly bound to soil.

Bumpus et al. (2189) also reported 2,3,7,8-TCDD degradation by microbial cultures under nitrogen-deficient conditions. The authors note that in some cases

microorganisms may possess the ability to degrade an environmental pollutant but the pollutant may not be present in sufficiently high concentrations to induce the enzymes required for degradation. In the reported study, degradation of relatively low 2,3,7,8-TCDD concentrations (9 ng/10 mL culture) was observed because the degradation process was initiated by nitrogen starvation rather than the presence of sufficient quantities of the contaminant.

In summary, some photodegradation of 2,3,7,8-TCDD may occur at the surface of environmental soils. However, in most soil/ground-water systems, biodegradation is expected to be of minimal importance since the natural concentration of microorganisms capable of degrading 2,3,7,8-TCDD is expected to be low, and to drop off sharply with increasing depth.

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

The above discussion of fate pathways suggests that 2,3,7,8-TCDD is moderately volatile, very strongly sorbed to soil and has a high potential for bioaccumulation. These fate characteristics suggest several potential exposure pathways.

Volatilization of 2,3,7,8-TCDD from a disposal site could result in inhalation exposure to workers or residents in the area. The potential for ground-water contamination is limited by its strong adsorptive characteristics. However, the persistence of this chemical has allowed its transport to drinking water supplies. Mitre (83) reported that dioxin (isomer not specified) was detected at 8 of 546 National Priority List sites. It was detected in ground water at 3 sites, in surface water at 6 sites, and in air at 4 sites. 2,3,7,8-TCDD has not been found in finished drinking water, and data showing its presence in ground waters used as drinking water supplies are not available (992).

The movement of 2,3,7,8-TCDD at low concentrations in ground water or its movement with soil particles may result in discharge to surface water. As a result, ingestion exposures may occur from the use of surface waters as drinking water supplies, and dermal exposures may result from the recreational use of surface waters. More important, however, is the potential for uptake of 2,3,7,8-TCDD by aquatic organisms or domestic animals. The high bioconcentration factor and the persistence of 2,3,7,8-TCDD suggests that these can be important exposure pathways from soil/ground-water systems.

63.2.4 Other Sources of Human Exposure

The presence of 2,3,7,8-TCDD in the environment is largely associated with the use of the herbicides 2,4,5-T, 2,4,5-TP, and their related esters. Since most of the uses of these products were restricted in 1979 (1918), they now represent a minor source of 2,3,7,8-TCDD to the environment. The persistent nature of 2,3,7,8-TCDD suggests that residues may remain from past use of these herbicides and, as described

below, combustion sources may represent an exposure source to newly formed 2,3,7,8-TCDD.

2,3,7,8-TCDD does not appear to be a common contaminant of surface waters. It was detected in 1 of 491 ambient water samples reported in the STORET data base (1417). The same database reports its presence in 2 of 157 sediment samples.

Data on the levels of 2,3,7,8-TCDD in air are few. Tetrachloro-dibenzo-p-dioxins have been detected in air particulate matter from Washington, D.C. and St. Louis at concentrations of several ppb (mass of chemical/mass of particulate matter) (1919). The amount of the 2,3,7,8-isomer was not specified, thus this value can be taken only as an upper limit of the 2,3,7,8-TCDD concentration. Some measurements of 2,3,7,8-TCDD concentrations in air have been made under special circumstances. Average concentrations of 1.1 ppb were detected near a disposal site in Jacksonville, Arkansas, and concentrations up to 0.09 ng/m^3 have been reported following the agriculturai application of silvex (992).

2,3,7,8-TCDD has been detected in the stack emissions of a facility that burned raw municipal waste; its average concentration in the stack effluent was 0.41 ng/dry standard cubic meter (ground-level concentrations were not specified) (1920). The same study found no 2,3,7,8-TCDD in the emissions of a facility that burned refuse-derived fuel and coal.

Food appears to be an insignificant exposure source to 2,3,7,8-TCDD. It has been detected in the fat of cattle, which had grazed on land treated with 2,4,5-T, at concentrations of 4-70 parts per trillion, and levels between 1 and 700 parts per trillion have been reported in fish and shellfish (992). The estimated maximum daily intake for people who regularly consume fish from the Great Lakes region has been estimated at 0.39-8.4 ng/day. Studies of human milk (1921) and chicken and pork samples (1922) have failed to detect 2,3,7,8-TCDD. Because 2,3,7,8-TCDD is not taken up significantly by plants and because vegetables are typically washed before eating, exposure to 2,3,7,8-TCDD translocated into vegetables or present in dust on their surface is expected to be minimal (1921).

In general, human exposure to 2,3,7,8-TCDD is low. A mean daily adult dose of 0.1-0.2 ng has been estimated based on concentrations detected in abdominal fat (1922). Some of the largest exposures to humans have occurred from accidental releases, as in the case of a chemical reactor explosion in Italy, or by contact with locally contaminated soil as occurred in Missouri (1919). The formation of 2,3,7,8-TCDD during an electrical fire involving a transformer that contained PCBs and tetrachlorobenzenes has suggested another potential exposure pathway (1923).

63.3 HUMAN HEALTH CONSIDERATIONS

63.3.1 Animal Studies

63.3.1.1 Carcinogenicity

2,3,7,8-TCDD is carcinogenic in rodents resulting in an increased incidence of carcinomas of the liver and respiratory tract.

Sprague-Dawley rats were fed diets containing 0, 0.001, 0.01, or 0.1 μg/kg/day 2,3,7,8-TCDD for up to 2 years. High early mortality was observed in all groups in this study but was only statistically significant in the high-dose group. This early mortality is particularly significant since it reduced the number of animals at risk during the time of expected tumor manifestation, thereby reducing the sensitivity of the study. 2,3,7,8-TCDD induced a highly statistically significant increase of both hepatocellular carcinomas and hepatocellular neoplastic nodules in female rats at doses of 0.01 and 0.1 μg/kg/day. The high-dose level of 2,3,7,8-TCDD also included a statistically significant increase in stratified squamous cell carcinomas of the hard palate and/or nasal turbinates in both males and females, squamous cell carcinoma of the tongue in males, and highly significant keratinizing squamous cell carcinomas of the lung in females. Results indicate 2,3,7,8-TCDD is highly carcinogenic when fed to rats for up to 2 years (2046).

A second rat feeding study was conducted in Osborne-Mendel rats by NCI (2102). Animals were orally administered 0, 0.01, 0.05, or 0.5 μg/kg/week of 2,3,7,8-TCDD suspended in a vehicle of 9:1 corn oil-acetone for 104 weeks. All surviving animals were examined 1-3 weeks after the treatment period ended. Male rats showed a statistically significant dose-related increase in the incidence of follicular-cell adenomas or carcinomas of the thyroid. Male rats in the high-dose group also had a significantly increased incidence in subcutaneous tissue fibromas. The incidence of hepatocellular carcinoma and neoplastic nodules, subcutaneous tissue fibrosarcoma, and adrenal cortical adenomas were all significantly increased in high-dose treated female rats. Carcinogenic effects reported in this study confirm earlier findings (2046) that oral administration of 2,3,7,8-TCDD is carcinogenic in rats.

Male B6C3F, mice were orally administered 0, 0.01, 0.05, or 0.5 μg/kg/week of 2,3,7,8-TCDD while female mice received 0, 0.04, 0.2, or 2 μg/kg/week of 2,3,7,8-TCDD suspended in a vehicle of 9:1 corn oil-acetone for 104 weeks (2102). 2,3,7,8-TCDD induced a statistically significant increase in the incidence of hepatocellular carcinomas and neoplastic nodules in high-dose male mice. High-dose females had a significantly increased incidence of hepatocellular adenomas or carcinomas, fibrosarcoma, lymphoma, and thyroid follicular-cell adenoma. Results indicate 2,3,7,8-TCDD mainly affects the liver, producing hepatocellular carcinomas in mice orally administered 2,3,7,8-TCDD.

Carcinogenicity was also evaluated in mice following dermal applications of TCDD (2103). 2,3,7,8-TCDD suspended in acetone was applied to the clipped backs of Swiss-Webster mice 3 days/week for 99 or 104 weeks. Female mice received 0.005 μg TCDD per application and male mice received 0.001 μg TCDD. Controls were treated with acetone while another group of mice went untreated. The incidence of fibrosarcoma in the integumentary system in TCDD-treated female mice was significantly higher than in corresponding controls (8/27 vs. 2/41 in the acetone controls). 2,3,7,8-TCDD applied to the skin was not carcinogenic for male Swiss-Webster mice; however, dermal application of 0.005 μg TCDD 3 days/week for 104 weeks was carcinogenic for female Swiss-Webster mice causing fibrosarcomas in the integumentary system. The study did note that only one dose/sex was used and that the maximal tolerated dose was not determined, especially in male mice and that the number of mice tested was marginal. Despite these criticisms, the study was considered valid (2103).

IARC (1250) has classified 2,3,7,8-TCDD as a group 2B compound. Both oral and dermal exposure to 2,3,7,8-TCDD produced tumors in mice and rats. Evidence is considered inadequate to determine the carcinogenic effects of TCDD in man. The USEPA classifies 2,3,7,8-TCDD as a B2 compound and assigns an 1E-04 Cancer Risk of 2×10^{-5} μg/L (3742).

63.3.1.2 Genotoxicity

The genotoxicity of 2,3,7,8-TCDD is confounded by its extreme toxicity. 2,3,7,8-TCDD showed no genotoxic activity in strains TA98, TA100, TA1530, TA1535, TA1537, TA1538, TA1532, hisG46, TA1950, TA1975, or TA1978 of Salmonella typhimurium (2086, 2087, 3470, 3238) with or without metabolic activation. However, Seiler et al. (2088) and Hussain et al. (2089) reported a positive response in S. typhimurium TA1532, a strain no longer used in short-term testing. This positive finding has not been reproduced. 2,3,7,8-TCDD induced an increase in the reverse mutation rate of Escherichia coli Sd-4 and a weak induction of prophage in E. coli K-39 cells (2089).

Positive results for reversion and gene conversion were reported in vitro in a host-mediated assay in yeast D7 (2090).

2,3,7,8-TCDD was negative in a sex-linked recessive lethal test in Drosophila (2079). Zimmering et al. (3863) found this compound almost insoluble, but injected Drosophila males with 50, 100, or 150 ppm. The two higher doses resulted in almost no progeny, but at 50 ppm, the frequency of sex-linked recessive lethals was at control levels.

No increase in sister chromatid exchange or chromosome aberrations in Chinese hamster ovary cells were reported following treatment with 2,3,7,8-TCDD (2079). Galloway et al. (3235) also did not observe any increase in sister chromatid exchanges

or in chromosomal aberrations in cultured Chinese hamster cells treated with 2,3,7,8-TCDD dissolved in ethanol.

Althaus et al. (3018) examined nuclei of cultured rat hepatocytes from Holtzman males treated with 2,3,7,8-TCDD up to the toxic dose and measured unscheduled DNA synthesis; results with TCDD were similar to the negative controls.

No dominant lethal mutations were induced in male Wistar rats orally administered 4, 8, or 12 mg/kg/day 2,3,7,8-TCDD for 7 days (2091). Conversely, Giavini et al. (3244) treated female rats by gavage daily for 2 consecutive weeks at 0, 0.125, 0.5, and 2 μg/kg, caged them with untreated males after treatment, and killed them on day 21 of gestation; at the lowest dose no adverse effects were seen, but at the highest dose there was a significant increase in pre-and post-implantation loss and in the incidence of malformed fetuses.

Luster et al (3411) observed that bone marrow progenitor cells were suppressed following acute exposure of mice to 2,3,7,8-TCDD at doses as low as 1.0 μg/kg body weight and that this compound was bound to the DNA of bone marrow cells possessing a specific receptor for TCDD. Meyne et al. (3447) injected two strains of mice (C57B1/6J, a high-affinity TCDD receptor strain, and DBA/2J, a low-affinity TCDD receptor strain) intraperitoneally with doses as high as 150 μg/kg, a dose that is hepatotoxic, and examined bone marrow cells for chromosomal aberrations, sister chromatid exchanges, and the presence of micronuclei. For all endpoints, cells from treated mice had no increase over those of control mice. In a similar study, Brooks et al. (3084) injected male C57B1/6J (high TCDD receptor strain) mice, performed partial hepatectomies to stimulate liver cell proliferation, and checked the regenerating hepatocytes for chromosomal aberrations; there was no increase in chromosomal aberrations but many signs of hepatotoxicity.

Lim et al. (3397) examined the lymphocytes of Rhesus monkeys fed 25 ppt in their diet for four years. Even though they observed a significant variation between animals within each group, the average sister chromatid exchange level in the treated group did not differ significantly from the controls. The same observation held true with respect to the level of chromosome aberrations.

Reggiani (3586) examined lymphocytes of 22 people exposed to 2,3,7,8-TCDD during the Seveso incident and concluded that the chromosome aberrations found were within the normal range. Tenchini et al. (3705) examined maternal and fetal tissue from women who had been exposed during the same incident. The authors concluded that "...the increased frequencies of aberrant cells in fetal specimens from exposed pregnancies are artifacts due to factors inherent in the growth in culture of the tissue fragments."

63.3.1.3 Teratogenicity, Embryotoxicity and Reproductive Effects

2,3,7,8-TCDD is a potent teratogen producing cleft palate and cystic kidney in laboratory animals. 2,3,7,8-TCDD has also been shown to induce abortion in monkeys.

Schantz et al. (2209) fed Rhesus monkeys a diet containing 50 parts per trillion 2,3,7,8-TCDD for 20 months. During month 7 of the study, females were mated to control males. Fetal development was seriously affected during 2,3,7,8-TCDD ingestion resulting in 4 abortions and 1 stillbirth. Two monkeys did not conceive despite repeated matings and only two animals carried their young to term. This study has generated concern since effects resulted from a daily dose of 0.0015 μg/kg.

The most prominent embryotoxic effect of TCDD in mice is the induction of cleft palate. Nau and Bass (2028) measured TCDD levels in relationship to the occurrence of cleft palate in NMRI mice. [^{14}C]-TCDD was injected intraperitoneally at a dose of 25 μg/kg on gestational day 7 or 10, or 5 μg/kg/day on gestational days 7 through 11. TCDD levels were determined on gestational day 13 while examination for cleft palate was performed on gestational day 18. Embryonic TCDD levels were not expected to differ among the 3 treatment groups owing to a half-life of TCDD in mice of approximately 4 weeks. However, TCDD levels in the group treated with a single 25 μg/kg injection on gestational day 7 were significantly lower than the other two treatment groups. The animals dosed with TCDD on gestational day 7 showed a 16% incidence of cleft palate versus 84% and 65% incidences in the groups treated on day 10 and on days 7-11, respectively. Fetal weight was also significantly decreased in these two treatment groups. It appears that 2,3,7,8-TCDD exerts a direct effect on the mid-gestational embryo to produce cleft palate (2027).

The above findings were corroborated by Galloway et al. (2029) in a study that found the inducible cytochrome P-450 enzyme system to be expressed in mouse embryos at day 7.5 to 8.5 of gestation. These results indicate that both the Ah receptor and cytochrome P-450 are functional at an early embryonic age and that the Ah locus is most likely responsible for benzo(a)pyrene- and TCDD- associated embryo toxicity and teratogenesis in mice soon after gestational day 7.

2,3,7,8-TCDD orally administered to pregnant Sprague-Dawley rats at doses of 0, 0.125, 0.5, or 2 μg/kg/day on gestational days 1 to 3 did not increase the incidence of pre- and post-implantation losses (2098). The only noticeable adverse effect was a significant reduction in the fetal weight in the 0.5 and 2 μg/kg/day dose groups.

To study the etiology of TCDD-produced kidney abnormalities in mice, Abbott et al. (3002) gavaged C57B1/6N dams with 12 μg/kg TCDD on day 10 of gestation. Fetal urinary systems were examined daily on days 14-17. On day 15 the lumina of the ureters were occluded by epithelial cells. Hydronephrosis became pronounced by day 17.

Since no effects of 2,3,7,8-TCDD toxicity appeared to manifest from treatment during early pregnancy, Giavini et al. (2099) examined effects of TCDD when introduced to the fetus over a longer time period of gestation. Pregnant New Zealand white rabbits were treated by gavage with 0, 0.1, 0.25, 0.5, or 1 μg/kg 2,3,7,8-TCDD [in corn oil:acetone (9:1) solution] from gestational days 6-15. Signs of toxicity were evident in dams treated with 0.25 μg/kg TCDD or higher resulting in death of 2 animals in the 0.5 μg/kg group and 4 animals in the 1 μg/kg group. The post-implantation loss rate was significantly increased in the groups treated with 0.25 μg/kg and higher. A significant increase in extra ribs was the principal skeletal anomaly found in all treated groups. This anomaly was considered an index of fetal toxicity rather than a sign of teratogenicity. Hydronephrotic kidney was also seen in all treated groups and one fetus in the 0.1 μg/kg group showed a double kidney with double ureter.

The effect of 2,3,7,8-TCDD on animals prior to mating was studied by Giavini et al. (2097). Female CRCD rats were administered 0, 0.125, 0.5, or 2 μg/kg 2,3,7,8-TCDD (99% purity in 9:1 corn oil:acetone solution) for 2 consecutive weeks by gavage prior to mating. Signs of maternal toxicity included a decrease in activity in the 2 μg/kg group and a significant decrease in weight gain in the 0.5 and 2 μg/kg groups. A significant increase in the post-implantation loss was recorded at 0.5 and 2 μg/kg dose levels (10.2 and 30.3%, respectively, vs. 2.9% in controls). This loss was attributed to impaired ovulation and an increased mortality rate of embryos before and after implantation. Fetuses in the high-dose TCDD group developed a significant number of severe morphological alterations including cystic kidney, subcutaneous edema, and gastrointestinal hemorrhage.

Murray et al. (2101) conducted a three-generation reproduction study in Sprague-Dawley rats administered 0, 0.001, 0.01, or 0.1 μg/kg 2,3,7,8-TCDD daily in the diet. Due to its high toxicity, the 0.1 μg/kg treatment was discontinued. Breeding performance was significantly disrupted in the F_1 and F_2 animals fed 0.01 μg/kg 2,3,7,8-TCDD. Fertility, litter size at birth, prenatal survival, and postnatal body weights and survival were significantly decreased in these generations. A significant increase in the average length of time from cohabitation to parturition in the F_1 and F_2 rats fed 0.01 μg/kg TCDD indicated an interference with the estrous cycle. In fact, morphological alterations were reported in the ovaries and uterus of rats orally given 1 μg TCDD/kg/day for 90 days (2100). These results indicate that TCDD may seriously affect reproduction at extremely low doses.

Exposure to 2,3,7,8-TCDD has been associated with altered metabolism of thyroid hormones and changes in plasma concentrations of thyroxine. Lamb et al. (2026) investigated the effect of TCDD and exogenously administered thyroxine on the induction of cleft palate in CS706/6N mice. Pregnant mice were dosed by gavage with 3 μg/kg/day 2,3,7,8-TCDD on gestational days 10 through 13. Both T_3 (3,5,3'-triiodo-L-thyronine) and T_4 (L-thyroxine) administration increased the incidence

of cleft palate in TCDD-treated animals in a dose-related manner. The increase was thought to be related to an interaction of TCDD with T_3 or T_4.

McKinney et al. (2210) have shown that T_3 or T_4 will bind to the Ah receptor with a 5- to 10-fold preference for T_3. These data seem to be consistent with data provided by Lamb et al (2026) in that the potency of T_3 is five times greater than T_4 in increasing the induction of cleft palate by TCDD.

Other studies have indicated synergistic increases in teratogenicity when mice are exposed to TCDD and hydrocortisone (3068), polychlorinated biphenyls (3069), 2,3,7,8-tetrachlorodibenzofuran (3831), or other dioxins and furans (3382). The widespread environmental occurrence of such combinations suggests a need for further evaluation of these interactions.

63.3.1.4 Other Toxicologic Effects

63.3.1.4.1 Short-term Toxicity

2,3,7,8-TCDD has an extremely high acute toxicity in animals with single oral LD_{50} values ranging from 0.5 μg/kg bw in the guinea pig to 1157 μg/kg bw in the hamster (3933). Death following a lethal dose of 2,3,7,8-TCDD is often delayed for several weeks. Acute TCDD exposure produces a variety of toxic effects including hepatic necrosis, thymic atrophy, depletion of lymphoid organs, immunosuppression, lesions of the myocardium, and hemorrhage and atrophy of the adrenal glands. The main target organs appear to be the liver and thymus; however, toxic effects vary among species (1607).

The dermal toxicity of TCDD was evaluated in rabbits at a dose of 0, 31.6, 63, 126, 252, or 500 μg/kg bw 2,3,7,8-TCDD applied to the shaved abdomen as a 0.01% solution in acetone (2047). The test area was covered to prevent ingestion. Animals were observed for 3 weeks. Marked individual differences were observed in the susceptibility, with the time of death ranging from 12-22 days post-treatment. The dermal LD_{50} in the rabbit was estimated to be 0.275 mg/kg.

Schwetz et al. (2047) studied the effects of 2,3,7,8-TCDD in the rabbit eye. Approximately 2 mg 2,3,7,8-TCDD (vehicle not stated) was instilled into the conjunctival sac of one eye. The contralateral eye served as the control. A delayed conjunctival chemosis occurred 13-22 days after treatment. By day 27, the chemosis had subsided but the rim of the eyelid was thickened and encrusted. No sign of corneal injury or iritis was observed in any of the treated animals.

The toxic effects of a single oral dose of 2,3,7,8-TCDD were investigated in the Rhesus monkey by McConnell et al. (2048). Animals were given a single dose of 0, 70, or 350 μg/kg 2,3,7,8-TCDD in corn oil by oral gavage. The earliest sign of toxicity was a decrease in body weight observed on day 3. Weight loss continued throughout the study and by death, animals had lost 13-38% of their body mass.

Puffiness of the eyelids progressing to a narrowing of the eye opening, purulent exudate and occasional pustules, edema, loss of facial hair, and loss of toe and finger nails were also observed by the 5th week of the experiment. Necropsy revealed a thick paste-like substance in the eyelids and ear canal. Body fat was completely absent and a depletion of lymph tissue, particularly the thymus, was noted. Gastric ulcers were observed in all treated animals. A specific cause of death could not be determined.

2,3,7,8-TCDD exposure in rats (route and dose not specified) resulted in extensive hemorrhages of the heart, liver, brain, adrenal glands, and GI tract along with ulcers and necrosis of the glandular stomach and atrophy of the uterus in females (2080). Death in mice was frequently attributed to terminal hemorrhages.

Fowler et al. (2081) treated rats with a single dose of 0, 5, or 25 μg/kg 2,3,7,8-TCDD (carrier vehicle not stated) by gavage. Livers were examined on day 1, 3, 6, 9, 16, and 28 post-treatment. The major ultrastructural change observed was a dose-related increase in the smooth and rough endoplasmic reticulum in cells near the bile canaliculi. The initial increase appeared by day 3 with a maximal response by day 9. Cells returned to normal by day 28. Necrosis and proliferative changes in the rat liver were the predominant lesions. Results indicate an induction of protein and RNA synthesis by 2,3,7,8-TCDD in the liver of rats.

Following administration of a lethal dose of 2,3,7,8-TCDD, all animals experience a prolonged wasting syndrome prior to death (2027). This syndrome is characterized by a loss of adipose tissue, involution of lymphoid organs, and degeneration of the seminiferous tubules of the testicles.

Investigations by Christian et al. (2049) showed TCDD treatment to profoundly affect intermediary metabolism in the mature rat during an early stage of toxicity when body weight loss was minimal. Changes in carbohydrate, protein, and lipid metabolism were not the result of a reduction in caloric intake, but reflected alterations in hepatic metabolism.

Rozman et al. (2052) investigated the effects of changes in intermediary metabolism relating to thermogenesis and the development of TCDD-induced wasting syndrome. Male Sprague-Dawley rats were given a single intraperitoneal injection of 0 or 150 μg/kg 2,3,7,8-TCDD in corn oil/4% anisole solution and sacrificed 1, 3, 7, or 14 days after treatment. TCDD-treated animals gained weight until the end of the experiment. Liver damage involved fatty infiltration followed by extensive degenerative changes. Examination of brown adipose tissue revealed a decrease in the number of fat droplets and hypertrophy of brown adipocytes one day after dosing. Brown adipose tissue is a major site of nonshivering and diet-induced thermogenesis which plays a major role in the overall energy balance of animals. Rozman suggests that the wasting syndrome results from a wasteful utilization of energy due to impaired aerobic metabolism in brown adipose tissue.

An alternate theory on the wasting syndrome was proposed by Seefeld and Peterson (2072). These investigators suggest that TCDD-induced weight loss in the rat occurs secondary to a reduction in the animals' set point for regulated body weight, and not as a result of reduced food intake or impaired metabolism. A group of male rats was fed ground food ad libitum until a body weight of 300 grams was reached. A second group of rats was placed on a restrictive diet to reduce body weight to 210 grams. Both groups of animals were orally administered a single dose of 25 μg/kg 2,3,7,8-TCDD (vehicle carrier not identified) and allowed food ad libitum. The animals weighing 300 grams developed hypophagia and lost weight until leveling off at 260 grams. The animals in the reduced weight group became hyperphagic and gained 50 grams during the 12 day observation period immediately following 2,3,7,8-TCDD treatment. Interestingly, both groups converged at the same weight level of 260 grams and consumed comparable amounts of food thereafter. These data indicate a reduction in the body weight set point which is directly related to the dose of TCDD administered.

The actual mechanism of 2,3,7,8-TCDD immunotoxicity is unknown; however, several theories exist. Faith and Luster (2083) reported that lymphocytes from the spleen, thymus, bone marrow, and lymph nodes of Fischer rats exposed to 2,3,7,8-TCDD showed abnormal homing patterns within the body. 2,3,7,8-TCDD exposure apparently altered the cell surface markers so that spleen lymphocytes from exposed rats were taken up by the thymus of unexposed recipient rats. 2,3,7,8-TCDD was suggested to either change cellular metabolism which results in an altered cell membrane, or to alter the cell membrane by insertion of TCDD directly into the proteolipid structure.

Kurl et al. (2084) reported that 2,3,7,8-TCDD caused changes in thymic transcription and RNA synthesis that may lead to cell surface changes. These cell surface changes could presumably result in altered antigen recognition and cell-to-cell recognition causing immunosuppression and thymic atrophy.

Pratts theory (2027) was further supported when Clark et al. (2085) reported that a 10- to 100-fold greater dose of 2,3,7,8-TCDD was required to suppress cytotoxic T-cells in DBA/2 mice than in C57B1 mice. These results indicate that susceptibility to 2,3,7,8-TCDD immunotoxicity segregates with the Ah locus. This receptor-mediated mechanism was further supported by the susceptibility of the C57B1/6 x DBA/2J hybrid mouse to 2,3,7,8-TCDD suppression of the cytotoxic T-cell.

63.3.1.4.2 Subchronic and Chronic Toxicity

DeCaprio et al. (2032) investigated the subchronic effects of TCDD following oral administration. Hartley guinea pigs were fed diets containing 0, 2, 10, 76, or 430 parts per trillion 2,3,7,8-TCDD for 90 days. Additional guinea pigs were fed 430 parts per trillion 2,3,7,8-TCDD in the feed for 11, 21, or 35 days and allowed to recover for 79, 69, or 55 additional days, respectively. Results indicate a no-observed-effect level (NOEL) of 0.61 (males) and 0.68 (females)ng

2,3,7,8-TCDD/kg/day for the 90-day feeding exposure. Animals in the 430 parts per trillion treatment group had a 60% mortality rate after consumption of approximately 1.6 μg/kg 2,3,7,8-TCDD. These animals also exhibited body weight loss, thymic atrophy, and liver enlargement. In general, toxic effects were similar to those observed after acute 2,3,7,8-TCDD administration. In the animals allowed to recover following TCDD administration, the treatment-related mortality in each group was 0, 10, and 70%, respectively. These results indicate a cumulative toxic effect with a lower LD_{50} value of 0.8 μg/kg than values obtained following acute exposure (2.5-19 μg/kg).

In addition to the increased incidence of hepatocellular carcinomas and squamous cell carcinomas of the lung, hard palate and tongue discussed in Section 63.3.1, low levels of TCDD produced a variety of toxic effects (2046). Sprague-Dawley rats were fed 0, 0.001, 0.01, or 0.1 μg/kg TCDD per day for two years. The liver was the organ most consistently affected and exhibited multiple hepatocellular degeneration, inflammation, and necrosis. Females treated at the 0.1 μg/kg/day dose level developed isolated incidences of thymic and/or splenic atrophy. Other effects related to treatment at this level included an increased incidence of hemorrhage in the brain and spinal cord and an increase in myocardial degenerative changes. Mesenteric and thoracic periarteritis accompanied by thrombosis and hepatoma were also increased in treated animals. Throughout the study, female rats were more sensitive to the toxic effects of TCDD than male rats. However, females treated with the high dose of 2,3,7,8-TCDD had a significantly decreased incidence of pituitary, uterine, and mammary changes than control animals.

King and Roesler (2092) observed liver toxicity in Sprague-Dawley rats orally administered 0, 0.1, or 1 μg/kg/week 2,3,7,8-TCDD in a 9:1 corn oil-acetone solution for 28 weeks. In addition to decreased body weight gain, histological changes in the liver were noted. Fatty changes in the liver were considered the most important observation. Male rats appeared to be more susceptible to the liver changes than female rats. Fatty changes decreased in severity during the recovery period but were still present 12 weeks after cessation of exposure. Other changes in the liver included mild necrosis, subtle distortion of liver architecture and slight hyperchromatic nuclei.

Subcutaneous edema, involution of the thymus, a decreased number of thymocytes, and focal necrosis and pigment accumulation in the liver were reported in rats orally treated with 0.1 or 1 μg/kg 2,3,7,8-TCDD, 5 days/week for 13 weeks (2093). Histological examination showed the liver and thymus to be the primary points of 2,3,7,8-TCDD attack; however, there were signs of aortic thrombosis and adrenal hemorrhage in one animal and signs of severe anemia in another, suggesting possible involvement of the hematopoietic system prior to death.

Hematopoietic involvement was further indicated in the monkey by Allen et al. (2094). Female Rhesus monkeys maintained on a diet containing 500 parts per trillion 2,3,7,8-TCDD for 9 months developed alopecia, swollen eyelids, and

periorbital edema after 3 months of treatment. All blood parameters except for blood proteins decreased. In animals that survived the 9-month treatment period, toxic symptoms continued to develop during the 4-month observation period. Hematological changes observed during the treatment period were consistent with microscopic findings of bone marrow degeneration at autopsy. Allen suggested that decreased platelet levels resulted in poor clotting and the widespread hemorrhage observed in many organs, particularly the stomach. The decreased RBC-count resulted in a loss of oxygen carrying capacity and an increase in cardiac workload and hypertrophy of the heart. Cellular hypertrophy, hyperplasia, and metaplasia of the epithelium of the salivary gland, bile duct, lung, and stomach were also observed. The ultimate cause of death was attributed to severe pancytopenia (deficiency of all cell elements of the blood).

Subchronic administration of 2,3,7,8-TCDD also induces porphyria (2095). Female Sprague-Dawley rats were given 0, 0.01, 0.1, or 1 μg/kg 2,3,7,8-TCDD by gavage weekly for 16 weeks. Liver porphyrins were elevated approximately 1000-fold in animals treated with 1 μg/kg/week. After a 6-month recovery period the porphyrin levels in animals exposed to 1 μg/kg/week were still 100-fold higher than control values. The rate-limiting enzyme in heme synthesis, delta-aminolevulinic acid synthetase, was also elevated at both the end of the treatment period and the end of the 6-month recovery period. The AHH, cytochrome P-450 and glucuronyl transferase enzyme systems all returned to normal levels by 6 months. Results indicate that a 6-month recovery period is not sufficient to reverse 2,3,7,8-TCDD induced porphyria.

Long-term low-level exposure to TCDD under field conditions had minimal effect on the health and reproduction of the beach mouse (2033). Mice occupied a 3 km^2 military test area that was sprayed with 73,000 kg 2,4,5-T from 1962-1970. No 2,4,5-T residue was found in the area; however, 10 to 1500 parts per trillion 2,3,7,8-TCDD residues were still present in 1978. Liver tissue of the beach mice inhabiting the test site contained 300 to 2900 parts per trillion 2,3,7,8-TCDD. Histological examination revealed no abnormalities, but animals collected in 1978 were estimated to be 50 generations removed from the population examined in 1973 and even further removed from the actual exposed population.

63.3.2 Human and Epidemiologic Studies

63.3.2.1 Short-term Toxicologic Effects

Acute exposure to 2,3,7,8-TCDD results in nausea and vomiting, headache, and eye, skin, and respiratory tract irritation. Other symptoms may include drenching and sweating with extensive dehydration and weight loss, increase in body temperature, severe respiratory distress, fatty degeneration of the liver, cyanosis, elevated blood urea nitrogen followed by fast deterioration of general condition, and death from acute congestive heart failure (2079). The initial skin reaction resembles a chemical burn and is followed by chloracne several days or weeks later. Chloracne is a

cutaneous eruption of comedones, cysts and pustules which usually occur on the face and shoulders as a result of squamous metaplasia of the dermal glands (2035). It is characterized by hyperplasia and hyperkeratosis of the interfollicular epidermis, hyperkeratosis, and squamous metaplasia of the sebaceous glands (2038).

No 2,3,7,8-TCDD was detected during biochemical analysis of the chloracne lesions in exposed children; however, it was revealed that cholesterol was the primary component of the lipid fraction of the lesions (2036). No difference was reported in the composition of cysts analyzed at different times following TCDD exposure. Passi (2036) concluded that the squamous metaplasia affects mainly the cells of the sebaceous gland duct and the cutaneous pathology induced by exposure to TCDD was related to a hyperproliferative reaction of the entire cutaneous epithelium. The temporary condition of squamous metaplasia was also considered to be due to the direct toxic effect of 2,3,7,8-TCDD. Long-term investigations were recommended to confirm this finding.

A case of acute exposure occurred in three scientists attempting to prepare a pure 2,3,7,8-TCDD standard (2095). Within several weeks of exposure, all scientists reported chloracne, gastrointestinal pain, headache, and fatigue. Delayed symptoms consisting of personality changes, loss of energy and drive, impaired taste, gastrointestinal symptoms, hirsutism (abnormal hairiness), and hypercholesterolemia all occurred 2-3 years after exposure. One scientist reported loss of mental and muscular coordination and blurred vision. Most symptoms were reported to subside with time.

A 6-year-old girl became severely ill after playing in a horse arena that had been sprayed with 2,3,7,8-TCDD contaminated waste oil to control dust (2210). Symptoms included headache, nosebleeds, diarrhea, lethargy, hemorrhagic cystitis, and focal pyelonephritis (inflammation of the kidney due to bacterial infection). Three other children developed chloracne 1.5 months after playing in the arena. Adults in contact with the soil developed headache, skin lesions, and joint pain. Re-examination of the severely affected girl 5.3 years following exposure revealed no residual signs of toxicity (2211).

The majority of acute human exposure studies reported in the literature result from explosions or accidental release of 2,3,7,8-TCDD in trichlorophenol manufacturing plants.

The first cases of chloracne associated with TCDD exposure occurred after a 1949 explosion in a chemical factory producing 2,4,5-T in Nitro, West Virginia. A total of 228 workers were exposed. Symptoms included acute respiratory symptoms, skin and eye irritation, headache, dizziness, and nausea. These symptoms disappeared within two weeks of exposure and were followed by an acneform eruption, severe muscle pain affecting the extremities, thorax and shoulders, fatigue, nervousness and irritability, dyspnea, complaint of decreased libido, and intolerance to cold. Physical examination revealed severe generalized chloracne, hepatic enlargement and

tenderness, peripheral neuritis, delayed prothrombin time, and an increase in total serum lipids. Nerve biopsy of one of the patients revealed myelin degeneration. Liver and nervous system symptoms subsided four years after the initial TCDD exposure. Chloracne, though much improved, still remained (2043).

Mortality analysis of 122 workers 30 years after the original West Virginia accident was inconclusive due to the small size of the cohort and the few reported deaths. The limited data did not suggest any difference in the expected death rates and cancer rates in the general population versus the test group (2043).

A second accidental release of 2,3,7,8-TCDD was reported in 1953 at a 2,4,5-T plant in West Germany (2034). As the cloud dispersed through the building, a white residue was left on all surfaces. Chloracne rapidly appeared in all exposed workers. Five years after the accident, a mechanic was acutely exposed to 2,3,7,8-TCDD while welding an autoclave. Despite protective clothing, the man inhaled some vaporized lubricant containing 2,3,7,8-TCDD after lifting his mask to wipe his forehead. Four days later, acute dermatological and neurological symptoms developed. The victim was hospitalized six months after the incident for pancreatitis and liver enlargement. A large mass of tissue was discovered in the upper left abdominal region which resulted in death 3 months later. Autopsy revealed pancreatic necrosis, perforation of the stomach, liver abscesses, and chloracne of the trunk.

Long-term mortality of the German employees exposed to acute doses of 2,3,7,8-TCDD following the 1953 accident was reported by Thiess et al. (2034). Twenty-seven years after the accident, 74 employees were located to participate in the study. Seven 2,3,7,8-TCDD-exposed workers developed malignant neoplasms (compared with an expected value of 4.1). The observed incidence of carcinomas of the stomach in the TCDD cohort was also significantly higher ($p < 0.05$) when compared to the expected value in three reference populations.

The most recent acute TCDD exposure episode occurred in Seveso, Italy in July 1976. A runaway reaction occurred in the ICMESA plant in Meda, Italy during the production of 2,4,5-trichlorophenol. A cloud containing several hundred grams of 2,3,7,8-TCDD was released into the atmosphere and travelled through Seveso, Italy before dissipating. The exact nature of the cloud was not known and people in Seveso were not evacuated until 2 weeks after the incident. By April, 1977 a total of 164 children under 15 years of age developed chloracne. Comparison of children with chloracne and children never exposed to 2,3,7,8-TCDD revealed significant differences (2037). Effects on the gastro-intestinal tract consisting of lack of appetite, nausea, vomiting, abdominal pain, and gastritis were significantly ($p < 1.6 \times 10^{-4}$) increased in the children with chloracne. Urinary tract effects and inflamed joints were also significantly increased in the exposed children ($p < 0.06$).

A study was conducted by Mocarelli et al. (2038) on 1500 children age 6 to 10 years old at the time of the Seveso accident. This cohort was followed yearly for 5 years. Children exposed to the highest concentration of TCDD showed alterations in

serum gamma-glutamyltransferase and alanine amino transferase activities when compared to the control group. The observed abnormalities were slight and disappeared with time. It was concluded that the acute phase of the TCDD intoxication passed with no appreciable consequences. However, long-term effects may still manifest themselves. A cancer registry has been established in the area in order to monitor the exposed population for many years (2038).

Lymphocytes and fibroblasts obtained from the blood of Seveso residents were cultured and analyzed for chromosome damage by DeCarli (2040). A higher frequency of mitotic samples with at least one aberrant cell was found in the TCDD-exposed individuals when compared to the control population samples. The significance of this finding is not known; however, based on plant and animal data, chromosomal damage may prove to be a long-term effect of 2,3,7,8-TCDD exposure in humans.

63.3.2.2 Chronic Toxicologic Effects

Chronic effects of TCDD include chloracne, impaired liver function, altered blood chemistry, hyperpigmentation and hyperkeratosis, lipid abnormalities, peripheral neuropathy, and psychiatric disturbances (2079). Other toxic effects are presently unknown but may be linked to the enzyme-inducing action of TCDD. Three potential long-term health risks associated with TCDD exposure are chromosome damage, heart attacks and cancer (2039). Studies designed to investigate these potential adverse effects are a problem due to the small size of the group exposed.

A clinical study of 436 employees in a 2,4,5-T manufacturing plant was conducted in order to determine the long-term health effects of chemicals associated with the production of 2,4,5-T, particularly the 2,3,7,8-TCDD contaminant (2043). The test group included workers involved in the normal processes of 2,4,5-T production from 1948 to 1969 as well as workers involved in an accident occurring in 1949. The test group consisted of 204 exposed, 103 control, and 51 questionable exposure subjects. Approximately 53% of the exposed group developed chloracne with an association between the persistence of chloracne and the presence of elastic tissue degeneration of the skin. The occurrence of ulcers in the upper part of the gastrointestinal tract was four times higher in the exposed group compared to the control group. A significant decrease in pulmonary function was shown only in present smokers exposed to 2,3,7,8-TCDD.

The long-term health effects of chronic 2,3,7,8-TCDD intoxication were also studied in 55 trichlorophenol production workers exhibiting symptoms between 1965 to 1968 (2044). The first symptoms of intoxication included gradual chloracne formation, malaise, fatigue, weakness in the lower extremities, and pain under the right rib cage. The majority of subjects developed chloracne. Other effects included pathological changes in glucose tolerance, mild liver lesions, peripheral neuron lesions of the lower extremities, and various psychological disorders. Interestingly, the severity of illness was not related to the duration of exposure, job status or age. In

some patients, symptoms became most severe 3 to 4 years following the TCDD exposure. Pathological deviations in lipid metabolism were still present up to 10 years after the exposure in the majority of patients. The patient most severely affected by 2,3,7,8-TCDD died 2 years after exposure from an unusual type of severe arteriosclerosis of the cerebri, liver, pancreas, and kidneys. Two additional deaths due to bronchogenic lung carcinoma were reported 2 and 3 years after exposure. No conclusion on the carcinogenicity of 2,3,7,8-TCDD were made based on the small size of the test group. One other death due to liver cirrhosis was also reported. No reproductive or developmental abnormalities were reported in exposed patients or offspring of exposed patients.

The effect of paternal exposure to 2,3,7,8-TCDD on pregnancy outcome was investigated by Townsend et al. (2078). Wives of 370 Dow Chemical employees potentially exposed to TCDD during chlorphenol production were interviewed along with 345 wives of a control group of employees never exposed to TCDD. Results indicated no statistically significant difference in adverse pregnancy outcomes in either group, nor were there any trends in adverse effects with increased duration of exposure.

Lipid abnormalities have been reported in TCDD-exposed workers (2042). Forty-one subjects exposed to 2,3,7,8-TCDD and diagnosed with chloracne were compared with 54 subjects working in the same area and exposed to varying levels of TCDD but who never developed chloracne. The control group consisted of 120 engineers never exposed to organic chemicals. Mean cholesterol and triglyceride levels were significantly higher in the two groups exposed to TCDD than in the control group ($p < 0.001$). Martin hypothesized that enzyme induction by 2,3,7,8-TCDD was responsible for the abnormal lipid concentrations. Elevated serum cholesterol levels are considered to be one of the major risk factors for ischemic heart disease. No data were found in the literature on the incidence of heart disease among 2,3,7,8-TCDD-exposed workers.

The porphyrias are a group of diseases associated with inherited or acquired disturbances in heme biosynthesis. Porphyria cutaneous tarda (PCT) is a chemically induced porphyria which consists of a disturbance in normal porphyrin metabolism due to a decrease in activity in the hepatic enzyme, uroporphyrinogen decarboxylase. This enzyme is involved in the decarboxylation of uroporphyrinogen to yield co-proporphyrinogen. Hepatic disease and photosensitivity resulting in the formation of a vesicular or bullous skin rash and skin fragility is noted with PCT. Certain investigators have linked TCDD exposure with PCT. However, the majority of studies including those involving the Seveso population, have never shown any association. Jones and Chelsky (2045) re-evaluated the studies associating 2,3,7,8-TCDD with PCT and found hexachlorobenzene present in the environment of all workers with PCT. Hexachlorobenzene is a known inducer of PCT and was considered the responsible factor in these patients. Based on this re-evaluation, PCT is not likely to be a sign of TCDD toxicity as previously believed.

In early 1971, waste by-products from a hexachlorophene and 2,4,5-T production facility in South West Missouri were mixed with waste oils and sprayed on roads and horseback riding arenas to control dust. It was later revealed that this mixture contained 2,3,7,8-TCDD. The long-term health effect of this population has been closely followed by many investigators (2238, 2239, 2240).

Stehr et al. (2075) investigated 104 individuals exposed to 2,3,7,8-TCDD in Missouri for different durations. The high-risk group contained 68 subjects exposed to 2,3,7,8-TCDD between 1971 and 1983 while the low-risk group contained 36 subjects. No firm indication of increased disease prevalence related to TCDD exposure was found in this study group. Stehr stressed that although results appear largely negative, no definitive conclusions can be reached since the latency period of long-term TCDD toxicity is believed to be approximately 30 years. Further attention should be focused on potential health effects in the urinary tract, liver, neurological, and immune systems.

Hoffman et al. (2074) also performed a comprehensive examination on 154 exposed and 155 unexposed individuals living in the Quail Run Mobile Home Park in Missouri. Roads sprayed in this area are believed to be contaminated with the highest concentrations of 2,3,7,8-TCDD. TCDD levels ranged from 39 to 1100 ppb. No significant detrimental health effects were reported in the exposed group. The exposed population, however, showed a 12% increase in the incidence of anergy (the lack of response to skin tests for sensitivity to antigens indicating a depression in immune system operation) in comparison to 1% of the control population. The exposed group also had an elevated frequency of abnormal T-cells and abnormal T-cell function. Hoffman concluded that long term exposure to 2,3,7,8-TCDD is associated with depressed cell-mediated immunity.

Remmer of the American Council on Science and Health (2077) disagrees with the Quail Run findings and feels statistics reported in the study do not show a clear connection between liver and immune system deficiencies and TCDD exposure. Also, differences in socioeconomic levels and in alcohol consumption between the exposed and unexposed groups were not adequately controlled in the Quail Run Study.

63.3.3 Levels of Concern

Based on sufficient evidence to conclude that 2,3,7,8-TCDD is a carcinogen in experimental animals, the USEPA has specified an ambient water quality criterion for this compound of zero. In that attainment of a zero concentration level may not be feasible in some cases, the concentrations of 2,3,7,8-TCDD in water calculated to result in incremental lifetime cancer risks of 1E-05, 1E-06, and 1E-07 from ingestion of both water and contaminated aquatic organisms were estimated to be 1.3E-07, 1.3E-08 and 1.3E-09 $\mu g/L$, respectively (2141). 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 1E-05 implies that a lifetime daily consumption of two liters of drinking

water and 6.5 g of fish at the criterion level of 1.3×10^{-7} µg/L of 2,3,7,8-TCDD 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.

Based on carcinogenic findings in mice, the USEPA (667) calculated an upper limit incremental unit cancer risk of 1.56E+05 $(mg/kg/day)^{-1}$ for 2,3,7,8-TCDD. The 10^{-4} cancer risk level in drinking water is 2E-05 µg/L (3742).

IARC (1250) classifies 2,3,7,8-TCDD as a group 2B carcinogen (sufficient evidence in animals). The USEPA classifies 2,3,7,8-TCDD in the B2 cancer group (3742).

For noncarcinogenic risks, the USEPA (3742) has issued Health Advisories for exposures to 2,3,7,8-TCDD in drinking water. For short-term exposures, they are 1E-03 µg/L (1 day) and 1E-04 µg/L (10 days) for a 10-kg child; for longer-term exposures, they are 1E-05 µg/L for a 10-kg child and 4E-05 µg/L for a 70-kg adult.

Neither OSHA (3539) nor the ACGIH (3005) have established exposure criteria for 2,3,7,8-TCDD.

63.3.4 Hazard Assessment

2,3,7,8-TCDD is classified by IARC (1250) as a group 2B compound based on its ability to induce tumors in rodents. Oral administration resulted in hepatocellular carcinomas in rats (2046, 2102) and mice (2102). Squamous cell carcinomas of the hard palate, tongue and lung, and fibrosarcomas have also been reported in rats (2046,2102) while lymphomas, fibrosarcomas, and thyroid follicular cell adenomas were observed in mice (2102). Dermal application of 2,3,7,8-TCDD resulted in a significant increase in fibrosarcomas in the integumentary system of female Swiss-Webster mice, but no carcinogenic response was seen in males (2103).

Human exposure data are inadequate to evaluate carcinogenic effects due to small study group size and few deaths (2044, 2043) but an increased incidence in carcinomas of the stomach has been reported (2034).

2,3,7,8-TCDD has proved to be nongenotoxic in most of the short-term tests in which it has been studied. Conflicting mutagenicity data have been reported for Salmonella typhimurium (2086, 2087, 2088, 2089, 3470) and a weak response was seen in E. coli (2089). Recessive lethal testing in Drosophila (2079, 3863) and dominant letnal testing in rats (2091) were negative. No sister chromatid exchange or chromosome aberrations were reported in Chinese hamster ovary cells (2079, 3235) or in rats (2031) treated with 2,3,7,8-TCDD, or in the lymphocytes of Rhesus monkeys fed 25 ppt for four years (3397). Chronic 2,3,7,8-TCDD treatment in rats for 13 weeks produced chromosome breaks in bone marrow cells (2031), but acute treatment

did not induce chromosomal aberrations (3447, 3084), sister chromatid exchanges, or micronuclei in the bone marrow cells of mice treated with a single hepatotoxic dose (3447). A slight increase in chromosomal aberrations was observed in abortuses from women who had been exposed to 2,3,7,8-TCDD in Seveso, but the authors feel that this result is an artifact (3705).

2,3,7,8-TCDD is a potent teratogen, producing cleft palate and cystic kidney in mice (2028, 2026) and rats (2097). Spontaneous abortions have been reported in monkeys (2209) while fetotoxic effects were seen in rabbits (2099). A 3-generation study in rats revealed a disruption of breeding performance and interference with the estrous cycle at doses as low as 0.01 mg/kg TCDD (2101). Morphological alterations in the female reproductive tract of the rat have also been reported following oral TCDD treatment (2100).

Toxic effects of 2,3,7,8-TCDD vary among species with oral LD_{50} values ranging from 0.5 μg/kg in the guinea pig to 1157 μg/kg in the hamster (3933). Death is often delayed for several weeks (1607). Monkeys are extremely sensitive to the toxic effects of TCDD with a wasting syndrome, alopecia, edema, and gastric ulcer predominating (2048). Gastric ulceration has also been reported in rats (2080) but the liver and thymus are usually considered the target organs in rodents (2081, 2083, 2084).

Chronic effects of TCDD include thymus and liver alterations in rats (2046, 2092, 2093, 2095) and guinea pigs (2032). Hematopoietic involvement has been suggested in rats (2093) and monkeys (2094).

Chloracne is the characteristic lesion which manifests in individuals exposed to 2,3,7,8-TCDD. Other acute signs of exposure include headaches, fatigue, altered blood chemistry, gastrointestinal symptoms, and kidney changes (2096, 2210, 2043, 2037, 2211). Effects are usually considered reversible with time. Mortality analysis of acutely exposed factory workers was inconclusive (2043); however, one death has been reported following inhalation of 2,3,7,8-TCDD vapor (2034).

Chronic effects of TCDD exposure are similar to those observed following acute exposure (2043, 2044). A four-fold increase in the incidence of gastric ulcers has also been reported (2043). The small size of study groups and the inability to ascertain exposure to the pure compound have limited the usefulness of most studies (2044, 2039, 2078, 2042, 2238, 2239, 2240, 2075, 2074, 2077). Although the majority of results appear negative, the latency period for the development of adverse effects is believed to be approximately 30 years for 2,3,7,8-TCDD (2075).

63.4 SAMPLING AND ANALYSIS CONSIDERATIONS

Determination of 2,3,7,8-TCDD 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 2,3,7,8-TCDD in aqueous samples include EPA Methods 613 (65) and 8280 (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 capillary gas chromatographic (GC) column using a solvent flush technique. The GC column is programmed to separate the semi-volatile organics; 2,3,7,8-TCDD is then detected with a mass spectrometer. Optimized gas chromatographic conditions have been reported (3231). Both EPA methods provide for selected column chromatographic cleanup procedures to aid in the elimination of interferences.

The EPA procedure recommended for 2,3,7,8-TCDD analysis in soil and waste samples, Method 8280 (63), differs from the aqueous procedures primarily in the preparation of the sample extract. Solid samples are extracted with methanol/ petroleum ether using a wrist-action shaker for two hours. Neat and diluted organic liquid may be analyzed by direct injection. The selected column chromatographic cleanup procedure is also applicable to these sample extracts.

Typical 2,3,7,8-TCDD detection limits that can be obtained in aqueous samples are 2 ng/L (Method 613) or 0.4 ng/L (Method 8280). Detection limits in non-aqueous samples are about 0.2 ng/g (Method 8280). The actual detection limit achieved in a given analysis will vary with instrument sensitivity and matrix effects.

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Note: The nonsequential numbers of the references reflect the order of references as they appear in the master bibliography.

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3933. National Institute of Occupational Safety and Health (NIOSH). 1988. Registry of Toxic Effects of Chemical Substances Database National Library of Medicine's MEDLARS system.

COMPLEX MIXTURES

This chapter deals with a complex mixture and/or class of compounds. The format used for this less well-defined group of compounds was modified as necessary but follows the outline of earlier chapters as closely as possible. It should be noted, however, that the composition of these materials can vary according to the route of synthesis, the formulating ingredients added, the interactions of the active ingredients, or the storage conditions These factors can influence the nature of the material that is ultimately utilized and probably are reflected in many of the experimental findings reported in the following chapters.

The typical components and approximate composition of the mixtures are provided if that information was available. Physical/chemical properties often were not available or varied depending on formulation. Many of these mixtures are blended to modify their physical properties according to the intended use. Furthermore, the formulations vary with season as well as with geographic locations of product use. In some cases, therefore, the range for the class of compounds was given.

In addition to the data for the mixture itself, the chapter that follows also contains sections on the principal components and major additives of the mixture, their fate in the environment and a brief overview of their toxicity.

CHEMICAL COMPOSITION:

Approximate Composition:

Alkanes	61.0%
Cycloalkanes	29.0%
Alkylbenzenes	8.0%
Indans/tetralins	1.1%
Naphthalenes	0.0% <1%

REACTIVITY	Various sources typically report that hydrocarbon mixtures are incompatible with strong acids, alkalis, and strong oxidizers such as liquid chlorine and oxygen. The NFPA reports vigorous reactions, ignition, or explosions involving chlorine, fluorine, or magnesium perchlorate. Jet fuels are considered to be miscellaneous combustible or flammable materials for compatibility classification purposes. Such substances typically evolve heat, fire, and toxic or flammable gases in reactions with oxidizing mineral acids, organic peroxides or hydroperoxides, or strong oxidizing agents.(505,507,511).

PHYSICO-CHEMICAL DATA	• Physical State: Liquid (at 20°C)	(60)
	• Color: Colorless to light brown	(60)
	• Odor: Fuel-oil	(60)
	• Odor Threshold: 1 ppm	(60)
	• Density: 0.7500 g/mL (at 20°C)	(1934)
	• Freeze/Melt Point: -72.00°C	(1933)
	• Boiling Point: 60.00 to 270.00°C	(1933)
	• Flash Point: -23.00 to -1.00°C closed cup; -29°C	(23,51,60,1934)
	• Flammable Limits: 1.30 to 8.00% by volume	(60,506)
	• Autoignition Temp.: 240.0 to 242.0°C	(23,51,60,506)
	• Vapor Pressure: 9.10E+01 mm Hg (at 20°)	(1934)

PHYSICO-CHEMICAL DATA (Cont.)	• Satd. Conc. in Air: 6.6000E+05 mg/m³ (at 20°C)	(ADL estim)
	• Solubility in Water: 300 mg/L (at 20°C)	(2251)
	• Viscosity: 0.829 cp (at 21°C)	(60)
	• Surface Tension: 2.5000E+01 dyne/cm (estim) (at 20°C)	(60)
	• Log (Octanol-Water Partition Coeff.): 3.00 to 7.00. Range for typical components	(See Table 64-4)
	• Soil Adsorp. Coeff.: 2.40E+02 to 5.00E+06 (range for typical components)	(See Table 64-4)
	• Henry's Law Const.: 1.00E-04 to 1.00E+01 atm · m³/mol. Range for typical components	(See Table 64-4).
	• Bioconc. Factor: 5.00E+01 to 5.00E+05 (range for typical components)	(ADL estim)

PERSISTENCE IN THE SOIL-WATER SYSTEM	JP-4 hydrocarbons are expected to be relatively mobile and non-persistent in most soil systems. Persistence in deep soils and groundwater may be higher. Volatilization, photooxidation and biodegradation are important fate processes. Surface spills are expected to be weathered by evaporation and photooxidation. Downward migration of weathered JP-4 surface spills and sub-surface discharges represent a potential threat to underlying groundwater. Biodegradation of JP-4 hydrocarbons is expected to be significant under environmental conditions favorable to microbial oxidation; naturally-occcurring, hydrocarbon-degrading microorganisms have been isolated from polluted soils and, to a lesser extent, non-polluted soils.

PATHWAYS OF EXPOSURE	The primary pathway of concern from the soil/groundwater system is the contamination of groundwater drinking water supplies by JP-4 from leaking storage tanks or large spills. Vapors from leaked or spilled fuel may diffuse through soils and migrate into structures, resulting in inhalation exposures. Inhalation exposure may also occur from the direct volatilization of spills, and in some instances, aircraft fuel jettisoning may result in the contamination of surface water and agricultural land, leading to ingestion with water or food.

HEALTH HAZARD DATA	Signs and Symptoms of Short-term Human Exposure: (60, 1932) Short-term exposure to high vapor levels can cause irritation of the respiratory tract, headaches, nausea, and mental confusion. In extreme cases, loss of consciousness can occur. Ingestion is irritating to the stomach. Aspiration of the liquid into the lungs can give rise to chemical pneumonitis. The liquid may cause defatting, drying and irritation of the skin. Both the vapor and the liquid are irritating to the eyes. Acute Toxicity Studies: ORAL: No Data SKIN: No data INHALATION: No data Long-Term Effects: Liver and kidney damage (animal), neurological damage (human) Pregnancy/Neonate Data: No data Genotoxicity Data: Limited data are negative Carcinogenicity Classification: IARC - No data NTP - No data EPA - No data

HANDLING PRECAUTIONS (1967)	No specific respirator guidelines were found for JP-4. The following guidelines are for kerosene with a boiling range of 175-325°C • Less than or equal to 1000 mg/m^3: chemical cartridge respirator with half-mask facepiece and organic vapor cartridge or supplied-air respirator with half-mask facepiece operated in demand mode • 1000-5000 mg/m^3: gas mask with full facepiece and organic canister; supplied- air respirator with full facepiece or self-contained breathing apparatus with full facepiece operated in demand mode • Appropriate protective clothing including gloves, aprons and boots • Chemical goggles if there is probability of eye contact.

ENVIRONMENTAL AND OCCUPATIONAL STANDARDS AND CRITERIA

AIR EXPOSURE LIMITS:

Standards

- OSHA TWA (8-hr): petroleum distillates (naphtha) 400 ppm
- AFOSH PEL (8-hr TWA): petroleum distillates (naphtha) 400 ppm; STEL (15-min): 500 ppm

Criteria

- NIOSH IDLH (30-min): petroleum distillates (naphtha) - 10,000 ppm; gasoline - none established
- ACGIH TLV® (8-hr TWA): petroleum distillates (naphtha) - none established; gasoline - 300 ppm
- ACGIH STEL (15-min): petroleum distillates (naphtha) - none established; gasoline - 500 ppm

ENVIRONMENTAL AND OCCUPATIONAL STANDARDS AND CRITERIA (Cont.)

WATER EXPOSURE LIMITS:

Drinking Water Standards
None established

EPA Health Advisories and Cancer Risk Levels
None established

WHO Drinking Water Guideline
No information available.

EPA Ambient Water Quality Criteria
- Human Health (355)
  - None established; JP-4 is not a priority pollutant.
- Aquatic Life (355)
  - None established; JP-4 is not a priority pollutant.

Oil and Grease (2012)
For domestic water supply: Virtually free from oil and grease, particularly from the tastes and odors that emanate from petroleum products.

For aquatic life:

- To protect several important freshwater and marine species, each having a demonstrated high susceptibility to oils and petrochemicals, the lowest continuous flow 96-hour LC_{50} should be reduced a hundred-fold.
- levels of oils or petrochemicals in the sediment which cause deleterious effects to the biota should not be allowed;
- surface waters shall be virtually free from floating non-petroleum oils of vegetable and animal origin as well as petroleum-derived oil.

REFERENCE DOSES:
No reference dose available.

REGULATORY STATUS (as of 01-MAR-89)

Promulgated Regulations

- Federal Programs

  Clean Water Act (CWA)
  Oil and grease are designated conventional pollutants under the CWA (351). Effluent limitations for oil and grease exist in almost all point source categories under the general pretreatment regulations for new and existing sources, and effluent limitations and guidelines. Limitations vary depending on the industry (3763).

  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 petroleum distillates (naphtha) shall not exceed an 8-hour time-weighted average (TWA) of 400 ppm (3539).

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

- State Water Programs

  ALL STATES
  All states have adopted EPA Ambient Water Quality Criteria and NPDWRs (see Water Exposure Limits section) as their promulgated state regulations, either by narrative reference or by relisting the specific numeric criteria. These states have promulgated additional or more stringent criteria:

  ALASKA
  Alaska has an aquatic life criterion of 15 µg/L for total hydrocarbons and 10 µg/L for total aromatic hydrocarbons in fresh and marine surface waters (3016).

  ARKANSAS
  Arkansas requires that oil and grease shall not exceed 10 mg/L average or 15 mg/L maximum when discharging to surface waters (3587).

FLORIDA
Florida requires that oil and grease not exceed 10 mg/L in Class V waters (navigation, industrial use) and 5 mg/L for all other surface waters (3220).

MASSACHUSETTS
Massachusetts requires that the maximum discharge concentration of oil and grease of petroleum origin not exceed 15 mg/L in surface waters (3432).

NEBRASKA
Nebraska requires that petroleum oils not exceed 10 mg/L in surface waters (3719).

NEW YORK
New York has set a maximum contaminant level of 50 µg/L for kerosene in drinking water (3501).

SOUTH DAKOTA
South Dakota has a water quality standard of 10 mg/L for all petroleum products in surface waters (3672).

VIRGINIA
Virginia has a water quality standard of 1 mg/L for petroleum hydrocarbons in ground-water (3135).

WYOMING
Wyoming has a water quality standard of 10 mg/L for surface waters and Class II and III ground-waters. In addition, Class I domestic ground-water is required to be virtually free of oil and grease (3853, 3852).

Proposed Regulations

- Federal Programs
  No federal regulations are pending.

- State Water Programs
  No state regulations are pending.

MOST STATES
Most states are in the process of revising their water programs and proposing changes to their regulations which will follow EPA's regulations when they become final. Contact with the state officer is advised. Changes are projected for 1989-90 (3683).

EEC Directives

Directive on Fishing Water Quality (536)
Petroleum products must not be present in salmonid and cyprinid waters in such quantities that they: (1) form a visible film on the surface of the water or form coatings on the beds of water-courses and lakes, (2) impart a detectable "hydrocarbon" taste to fish and, (3) produce harmful effects in fish.

Directive on the Quality Required of Shellfish Waters (537)
The mandatory specifications for petroleum hydrocarbons specify that they may not be present in shellfish water in such quantities as to produce a visible film on the surface of the water and/or a deposit on the shellfish which has harmful effects on the shellfish.

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 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 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.

64.1 MAJOR USES AND COMPOSITION

64.1.1 Major Uses

Jet Fuel 4 (JP-4) is a turbine engine fuel used exclusively by the U.S. Air Force; it constitutes 85% of the turbine fuels used by the Department of Defense (1933).

64.1.2 Composition

Jet fuel petroleum products are made by blending various proportions of distillate stocks, such as naphtha, gasoline and kerosene to meet military and commercial specifications. Most of the available characterization data (e.g., military specifications) address gross performance properties. There is considerable variability in the concentration of major components, as well as in the performance characteristics, of JP-4 fuel derived from different crude oil supplies (1843, 2246, 2247, 2251). In general, the reported distillation range for JP-4 fuel is approximately 140°C to 270 °C (1844); most of the hydrocarbons fall in the range of C_4 to C_{14}. A typical JP-4 composition expressed as percent volume by compound category has been reported (1845) to be: paraffins (61%), monocycloparaffins (24%), dicycloparaffins (5%), alkylbenzenes (8%), indans and tetralins (1%) and naphthalenes (<1%). JP-4 fuel may contain olefinic hydrocarbons up to 5% (volume) and total sulfur up to 0.4% (weight) (1844).

The individual major components of JP-4 representing at least 0.1% by weight have been characterized by several authors (1822, 1845) and account for approximately 70-75% by weight of the fuel. The approximate distribution of the major components by compound category is: n-alkanes, 32%; branched alkanes, 31%; cycloalkanes, 16%; benzenes and alkylbenzenes, 18%; and naphthalenes, 3% (1846). Table 64-1 presents detailed data on the specific hydrocarbon composition of one JP-4 fuel.

Although they are generally considered minor components, there are many non-hydrocarbons present in petroleum-derived distillates. In general, these become major concerns in the heavy distillates and residues (almost 70% of total composition in heavy oils) and are much less important components in middle distillates, such as JP-4. Sulfur compounds represent the largest class of non-hydrocarbons found in petroleum; this group might include aliphatic and aromatic compounds, such as thiols, sulfides, disulfides, and thiophenes, as well as elemental sulfur, hydrogen sulfide, and carbon sulfide. The majority of crude oils have low oxygen content. Most of the oxygen is in the form of fatty acids and acids with aromatic functional groups; smaller contributions come from alcohols, ketones, esters, fluorenones, furans, dibenzofurans, and benzonaphthofurans. The level of nitrogen compounds is generally less than 0.1%, but may be higher (0.5-15%) in heavy distillates and residues. Nitrogen

TABLE 64-1
MAJOR COMPONENTS OF ONE JP-4 SAMPLE

Fuel Component	Percent by Weight
n-Butane	0.12
Isobutane	0.66
n-Pentane	1.06
2,2-Dimethylbutane	0.10
2-Methylpentane	1.28
3-Methylpentane	0.89
n-Hexane	2.21
Methylcyclopentane	1.16
2,2-Dimethylpentane	0.25
Benzene	0.50
Cyclohexane	1.24
2-Methylhexane	2.35
3-Methylhexane	1.97
trans-2,3-Dimethylcyclopentane	0.36
cis-1,3-Dimethylcyclopentane	0.34
cis-1,2-Dimethylcyclopentane	0.51
n-Heptane	3.67
Methylcyclohexane	2.27
2,2,3,3-Tetramethylbutane	0.24
Ethylcyclopentane	0.26
2,5-Dimethylhexane	0.37
2,4-Dimethylhexane	0.58
1,2,4-Trimethylcyclopentane	0.25
3,3-Dimethylhexane	0.26
1,2,3-Trimethylcyclopentane	0.25
Toluene	1.33
2,2,-Dimethylhexane	0.71
2-Methylheptane	2.70
4-Methylheptane	0.92
cis-1,3-Dimethylcyclohexane	0.42
3-Methylheptane	3.04
1-Methyl-3-ethylcyclohexane	0.17
1-Methyl-2-ethylcyclohexane	0.39
Dimethylcyclohexane	0.43
n-Octane	3.80
1,3,5-Trimethylcyclohexane	0.99
1,1,3-Trimethylcyclohexane	0.48

Source: 1845

TABLE 64-1 (Cont.)

Fuel Component	Percent by Weight
2,5-Dimethylheptane	0.52
Ethylbenzene	0.37
m-Xylene	0.96
p-Xylene	0.35
3,4-Dimethylheptane	0.43
4-Ethylheptane	0.18
4-Methyloctane	0.86
2-Methyloctane	0.88
3-Methyloctane	0.79
o-Xylene	1.01
1-Methyl-4-ethylcyclohexane	0.48
n-Nonane	2.25
Isopropylbenzene	0.30
n-Propylbenzene	0.71
1-Methyl-3-ethylbenzene	0.49
1-Methyl-4-ethylbenzene	0.43
1,3,5-Trimethylbenzene	0.42
1-Methyl-2-ethylbenzene	0.23
1,2,4-Trimethyibenzene	1.01
n-Decane	2.16
n-Butylcyclohexane	0.70
1,3-Diethylbenzene	0.46
1-Methyl-4-propylbenzene	0.40
1,3-Dimethyl-5-ethylbenzene	0.61
1-Methyl-2-isopropylbenzene	0.29
1,4-Dimethyl-2-ethylbenzene	0.70
1,2-Dimethyl-4-ethylbenzene	0.77
n-Undecane	2.32
1,2,3,4-Tetramethylbenzene	0.75
Naphthalene	0.50
2-Methylundecane	0.64
n-Dodecane	2.00
2,6-Dimethylundecane	0.71
2-Methylnaphthalene	0.56
1-Methylnaphthalene	0.78
n-Tridecane	1.52
2,6-Dimethylnaphthalene	0.25
n-Tetradecane	0.73

Source: 1845

compounds that may be present in petroleum fuels, particularly in heavier distillates than JP-4, include pyridines, quinolines, acridines, amines, pyrroles, indoles and carbazoles (1848).

In addition to the aliphatic/aromatic hydrocarbon content and trace N-containing, O-containing and S-containing species, JP-4 distillate fuel may also contain trace inorganic elements. All metals through atomic number 42, except rubidium and niobium, have been found in petroleum. Generally, the concentrations are quite low; the most prevalent metals are nickel and vanadium (1848). Table 64-2 presents the results of an analysis of the trace elements in one JP-4 fuel sample. The JP-4 concentration of these elements is expected to vary from one crude oil source to another.

Actual stocks of JP-4 fuel may also contain a number of additives used as anti-oxidants, metal deactivators, corrosion or icing inhibitors, or electrical conductivity agents. A list of some of the chemicals that may be used for these purposes is provided in Table 64-3. The composition of JP-4, particularly older stocks, may also vary due to contaminants from the storage container. In addition, microbes can be anticipated to grow well on these hydrocarbons; bacterial and/or fungal contamination may also affect the composition of JP-4 stocks.

64.2 ENVIRONMENTAL FATE AND EXPOSURE PATHWAYS

For the purposes of this chapter, the discussions of the environmental behavior of JP-4 will be limited to a discussion of the major components; the environmental behavior of the trace elements and the many diverse additives will not specifically be addressed.

Transport and transformation of individual JP-4 constituents will vary depending on the physicochemical (and biological) properties of the constituents. Some constituents will dissolve more quickly (in percolating ground-waters), be sorbed less strongly on soils (thus being transported more rapidly), and may be more or less susceptible to degradation by chemical or biological action. Thus, the relative concentrations of the constituents of the fuel will vary with time and distance from the site of initial contamination. This effect is called "weathering." (This term is also used to describe the changes to oil following spills into surface waters where film spreading and breakup, and differential volatilization, dissolution and degradation all are involved.)

TABLE 64-2
CONTENT OF TRACE ELEMENTS IN ONE SAMPLE OF
PETROLEUM-DERIVED JP-4

Trace Element	Parts per Million By Weight
Al	NA[a]
Sb	<0.5
As	0.5
Be	NA
Cd	<0.03
Ca	NA
Cl	NA
Cr	<0.05
Co	NA
Cu	<0.05
Fe	<0.05
Pb	0.09
Mg	NA
Mn	NA
Hg	<1
Mo	NA
Ni	<0.05
Se	<0.3
Si	NA
Ag	NA
Na	NA
Sr	NA
Th	NA
Sn	NA
Ti	NA
V	<0.05
Zn	<0.05

Source: 1843

a) NA indicates data not available

TABLE 64-3
ADDITIVE COMPOUNDS APPROVED FOR USE IN MILITARY JP-4 FUEL

Antioxidants (≤24 mg/L)[a]

2-6-di-t-butylphenol
2-6-di-t-butyl-4-methylphenol
6-t-butyl-2,4-dimethylphenol
Other alkyl phenols (mono,di,tri; methyl, ethyl, isopropyl, t-butyl)
N,N′-di-sec-butyl-p-phenylenediamine[c]

Metal Deactivators (≤5.8 mg/L)[a]

N,N′-disalicylidene-1,2-propanediamine
N,N′-disalicylidene-1,2-cyclohexanediamine
N,N′-disalicylidene-1,2-ethanediamine[a]

Corrosion Inhibitors

MIL-I-25017/QPL-25017[a]
Amine carboxylates (5-20 ppm)[b]: $(RCOO^-)\ NH_3R'^+$), R = C_{16}-C_{18}
Ethylene diamine dinonyl naphthalene sulfonates[c]

Icing Inhibitors

MIL-I-27686[a]
Carboxylates (40-150 ppm)[b]: $RCOO^-$, R = C_{16}-C_{18}
C_1-C_3 alcohols[c]
Dimethylformamide[c]
Ammonium dinonylnaphthalene[c]

Electrical Conductivity Additive[a]

ASA-3 (Shell Chemical Co., Houston, TX)

a) Reference 1844
b) Reference 1847
c) Reference 1824

TABLE 64-4
EQUILIBRIUM PARTITIONING OF SELECT JP-4 HYDROCARBONS IN MODEL ENVIRONMENTS[a]

Compound	log K_{ow}	K_{oc}[b]	H[c]	Unsaturated Topsoil (%)			Saturated Deep Soil[d] (%)	
				Soil	Water	Air	Soil	Water
Hexane	3.90[e]	3,830	1.68	77.5	0.1	22.4	94.1	5.9
Octane	5.18[e]	73,000	2.96	97.4	0.01	2.6	99.7	0.3
Dodecane	7.06[f]	5.5E+06	7.4	99.9	0.0001	0.09		
Isopentane	3.37[f]	900	1.36	50.3	0.3	49.4	79.1	20.9
Trimethylpentane	4.87[f]	36,000	1.9-3.3	94.7	0.01	5.3	99.3	0.7
Methylcyclopentane	3.47[f]	1,400	0.36	85.4	0.3	14.3	85.5	14.5
Cyclohexane	3.44[e]	1,330	0.18	91.6	0.4	8.0	84.8	15.2
Methylcyclohexane	4.10[f]	6,070	0.39	95.9	0.08	4.0	96.2	3.8
Toluene	2.69[g]	240	6.6E-03	96.5	1.9	1.6	52.1	47.9
Xylenes	3.16[e]	700	7E-03	98.8	0.7	0.5	74.4	25.6
Trimethylbenzenes	3.65[h]	2,150	5E-03	99.6	0.2	0.2	90.0	10.0.
Methylnaphthalenes	3.87[e]	3,570	4.4E-04	99.8	0.1	0.01	93.7	6.3

[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]Reference 652.

[c]Taken from Reference 74 unless otherwise specified. Units equal atm-m^3/mol.

[d]Used sorption coefficient $K_p = 0.001 \times K_{oc}$.

[e]Reference 29.

[f]Arthur D. Little, Inc., estimate according to equations provided in Reference 31.

64.2.1 Transport in Soil/Ground-water Systems

64.2.1.1 Equilibrium Partitioning Model

In general, soil/ground-water transport pathways for low concentrations of pollutants in soil can be assessed by using an equilibrium partitioning model. For the purposes of assessing the environmental transport of JP-4 fuel, a group of specific hydrocarbons was selected from the dominant JP-4 hydrocarbon classes, i.e., alkanes, cycloalkanes, and alkylbenzenes. These specific compounds were chosen on the basis of their relatively high concentrations in JP-4 and span the boiling point range of the JP-4 hydrocarbons. Table 64-4 lists the hydrocarbons that were selected and presents the predicted partitioning of low soil concentrations of those hydrocarbons among soil particles, soil water, and soil air. The portions associated with the water and air phases of the soil are expected to have higher mobility than the adsorbed portion.

Estimates for the unsaturated topsoil indicate that sorption is expected to be an important process for all the dominant hydrocarbon categories. Partitioning to the soil-vapor phase is also expected to be important for the lower molecular weight aliphatic hydrocarbons (C_4 - C_8), which are characterized by high vapor pressures and low water solubility. The alkyl benzenes have higher water solubilities and transport with infiltrating water may be important for these compounds; volatilization, on the other hand, may be less important. In saturated, deep soils (containing no soil air and negligible soil organic carbon), a significant percent of both aliphatic (particularly less than C_7) and aromatic hydrocarbons is predicted to be present in the soil-water phase and available for transport with flowing ground-water.

In interpreting these results, it must be remembered that this model is valid only for low soil concentrations (below aqueous solubility) of the components. Large releases of JP-4 (spills, leaking underground storage tanks) may exceed the sorptive capacity of the soil, thereby filling the pore spaces of the soil with the fuel. In this situation, the hydrocarbon mixture would move as a bulk fluid and the equilibrium partitioning model would not be applicable.

Overall, ground-water underlying soil contaminated with JP-4 hydrocarbons is expected to be vulnerable to contamination by at least some of these components. The type of spill (surface vs. sub-surface) is of particular importance, since volatilization from the surface is expected to be a significant removal process for low molecular weight aliphatics. At this point, it should be mentioned that environmental fate/exposure/toxicology chapters for several of the components in Table 64-4 were included in other sections of the IRP Toxicology Guide. The JP-4 components addressed in other sections include: benzene, toluene, xylenes, ethyl benzene, and naphthalene.

64.2.1.2 Transport Studies

Due to the extensive use of JP-4 and other aviation fuels and their potential for environmental release during use, storage or transport, several groups have addressed its fate. The fate of JP-4 in the soil environment is basically a function of the solubility, volatility, sorption, and degradation of its major components. The relative importance of each of these processes is influenced by the type of contamination (e.g., surface spill vs. underground release, major vs. minor quantity), soil type (e.g., organic content, previous history of soil contamination), and environmental conditions (e.g., pH, temperature, oxygen content).

Transport processes have been shown to be more significant than transformation processes in determining the initial fate of petroleum hydrocarbons released to soil/ground-water systems (1845, 1848, 1846). For JP-4 released to surface soils or waters, transport to the atmosphere through volatilization has been shown to be the primary fate pathway for most of the JP-4 hydrocarbons; subsequent atmospheric photolysis is expected to be rapid (1845). Using a model fuel mixture containing approximately fifteen compounds representative of major JP-4 hydrocarbons, Spain et al. (1846) demonstrated that compounds having up to nine carbons are weathered almost exclusively by evaporation; larger compounds were weathered primarily by evaporation and biodegradation; dimethylnaphthalene and highly substituted aromatics ($>C_{14}$) were shown to be persistent in these tests. Reduced temperatures tend to increase JP-4 persistence by retarding the rates of volatilization and biodegradation (1846, 1822).

Compared with the marine environment, infiltration into porous soils slows the evaporative loss of volatile hydrocarbons. McGill et al. (2267) concluded that up to 20-40% of crude oils may volatilize from soils. Elevated temperatures, lateral spreading and adsorption onto surface vegetation may facilitate evaporation at such levels. Volatilization of JP-4 components is expected to be more extensive than volatilization of crude oils. Purging of the water soluble fraction of JP-4 fuel with nitrogen and air demonstrated a rapid loss of JP-4 hydrocarbons (80% loss in 2 minutes) (2250).

Under conditions of limited volatilization (low temperatures, subsurface release or concentrated spill), downward migration into the soil and to the ground-water may be important. Several authors (1811, 2243, 2252) have reported that oil substances released in significant quantities to soils result in a separate organic phase that moves downward through the unsaturated zone to the less permeable layer, the soil/ground-water boundary, where they tend to accumulate and s[illegible] horizontally. The organic layer floats on the ground-water and is carried in the ge[illegible]l direction of ground-water flow. At the oil-water interface, some hydrocarbons are leached according to their aqueous solubility. The pattern of migration of the hydrocarbon phase may be very different from that of the ground-water. Due to fluctuations in ground-water elevation, over time the organic layer on top of the aquifer may be transported into several zones where the components occur in the gaseous phase (able to diffuse in all

directions, including upward), liquid phase (adsorbed onto rock particles or sealed under water) or dissolved/emulsified in water (1811).

Migration through soils may be retarded to some extent by sorption. In general, sorption of aviation kerosene on soils has been reported to be weak. Migration is expected to be fastest through previously contaminated soils where the sorptive sites may be unavailable; on the other hand, soil-water content increases sorption and slows migration of JP-4 hydrocarbons. Sorption may also alter the availability of hydrocarbons for biodegradation and other weathering processes (1846, 1811, 2248).

The migration of JP-4 hydrocarbons in fissured rock is much less uniform than in porous soils. Preferential spreading through crevices may occur, sometimes changing the direction of flow. Determination of the potential ground-water contamination in fissured rock is thus very difficult (1811).

Sediment-water sorption studies (2248) were performed on jet fuel dissolved in water; 3 sediments and 3 clays were utilized. The observed adsorption constants were small compared to those of other non-polar organics. For the individual JP-4 components the magnitude of the adsorption constant is dependent on the size and complexity of the hydrocarbon, and bears an inverse relationship to its aqueous solubility. The nature of adsorbent was important (non-swelling clays were reported to be poor adsorbents compared to sediments), but the organic carbon content exhibited only a casual relationship to adsorbent ability. Temperature and pH did not have an important effect over naturally occurring ranges: increasing salinity produced a small increase in hydrocarbon adsorption. Reversible adsorption was observed in experiments with benzenes and naphthalenes; strong sorbent-sorbate bonding (chemisorption) does not occur with light hydrocarbons found in JP-4 fuel.

In the vicinity of Prague airport (1811), release of aviation kerosene (similar to JP-4) resulted in extensive soil/ground-water contamination. The petroleum hydrocarbons spread as a separate organic phase as well as dissolved contaminants in the aquifer. In porous formations, pollution caused by the oil phase extended tens of hundreds of meters, while the contamination from dissolved hydrocarbons extended hundreds to thousands of meters. Within five months, a 1-m thick layer of oil extended 700 m by 200 m on the surface of the ground-water aquifer: an area of 15 km^2 was polluted by the dissolved hydrocarbons.

The transport of JP-4 contamination to ground-water aquifers and subsequent dissolution of JP-4 hydrocarbons in ground-water have been discussed in several papers (1811, 1845, 2245, 2241, 1849). Crude oil and petroleum products have been shown to produce qualitatively similar water-soluble fractions (1849, 2241, 2248, 2250). The water-soluble portion of JP-4 distillate fractions were shown to be almost entirely aromatic (87-99%) even though the distillate fuels themselves were higly aliphatic in nature. The aliphatic hydrocarbons either volatilized ($<C_{12}$) or were essentially not water soluble ($>C_{12}$). In deep, saturated soils with no soil-air, some low molecular weight aliphatics may be transported and dissolved in ground-water. Table 64-5 presents fuel-water partition coefficients for some JP-4 hydrocarbons; the

data support the observation that the light aromatics represent the greatest threat to contamination of ground-water supplies. In general, a decreasing degree of petroleum contamination has been observed over time in the absence of further aquifer pollution; some removal due to sorption onto rock particles and degradation by microorganisms is suspected (2244, 2243, 2255).

In summary, the physical distribution of JP-4 contamination affects its impact on, and removal from, the soil environment. Lateral spreading along the surface increases the contaminated area while facilitating evaporative removal of the low molecular weight hydrocarbons. Subsurface release or vertical penetration mediated by gravitation and capillary forces decreases evaporation, reduces the importance of transformation pathways (see below), and may lead to ground-water contamination.

64.2.2 Transformation Processes in Soil/Ground-water Systems

64.2.2.1 Chemical Transformation

Photooxidation has been reported to play a significant role in the chemical degradation of petroleum hydrocarbons in the environment (1845, 1848, 2252, 2259). Alkanes, benzenes, and mono-substituted benzenes have been shown to be relatively resistant to photolysis in aqueous systems; xylenes photolyzed slowly while trisubstituted benzenes and naphthalenes photolyzed at rates competitive with volatilization (1845). Penetration of oil below the soil surface limits exposure to solar radiation while extensive lateral spreading of oil over impermeable or rocky surfaces may promote substantial photooxidative degradation.

The oxygenated products of photooxidation are generally more water-soluble than the parent hydrocarbons and are thus more likely to be leached from soil; enhanced toxicity of the oxygenated hydrocarbons has also been observed (2248, 2252). Larson et al. (2260) have reported that in marine environments weathering of crude oils resulted in decreased growth of algae.

64.2.2.2 Biological Degradation

Natural ecosystems have considerable exposure to petroleum hydrocarbons from natural emissions, accidental contamination through oil spills and storage tank leaks, and deliberate application to land in land-farming waste disposal activities; therefore, their biodegradation is of environmental importance. Numerous authors have observed the biodegradation of petroleum hydrocarbons, and several extensive reviews and reports are available (1846, 2252, 2255, 2249, 2253). Hydrocarbon degrading bacteria and fungi are widely distributed in marine, freshwater, and soil environments. As reported in the review by Atlas (2255), an extensive and diverse group of bacteria and fungi have been shown to have the ability to degrade petroleum hydrocarbons.

TABLE 64-5
JP-4 FUEL-WATER PARTITION COEFFICIENTS (K_{fw})
FOR SELECTED HYDROCARBONS[a]

Compound	Log K_{fw}[b]
Methylcyclopentane	4.97
Benzene	3.39
Cyclohexane	4.69
2-Methylhexane	5.57
3-Methylhexane	5.56
n-Heptane	5.50
Methylcyclohexane	4.87
Toluene	3.44
n-Octane	5.98
Ethylbenzene	3.68
m-Xylene	3.57
p-Xylene	3.88
o-Xylene	3.85
1,2,4-Trimethylbenzene	3.95
Isopropylbenzene	4.25
Naphthalene	3.88
2-Methylnaphthalene	4.35
1-Methylnaphthalene	4.67

a) Reference 1845
b) K_{fw} = (concentration of chemical in fuel) ÷ (concentration of chemical in water) at equilibrium, T = 20°C. Fuel-water ratio = 1:1000.

The qualitative hydrocarbon content of petroleum mixtures largely determines their degradability. In general, microorganisms exhibit decreasing ability to degrade aliphatic hydrocarbons with increasing chain length; however, Haines and Alexander (2254) showed that n-alkanes up to C_{44} were metabolized. n-Alkanes are considered more easily biodegraded than branched or cyclic alkanes; aromatics are generally more rapidly biodegraded than alkanes.

The relative biodegradation susceptibility of petroleum hydrocarbons has been summarized in a review by Bossert and Bartha (2252): n-alkanes, n-alkylaromatics, and aromatics of the C_{10} - C_{22} range are the most readily biodegradable; n-alkanes, alkylaromatics, and aromatics in the C_5 - C_9 range are biodegradable at low concentrations by some microorganisms but are removed by volatilization and unavailable for biodegradation in most environments; n-alkanes in the C_1 - C_4 range are biodegradable by only a narrow range of specialized hydrocarbon degraders; and

n-alkanes, alkylaromatics, and aromatics above C_{12} are generally not available to degrading microorganisms. Hydrocarbons with condensed ring structures, such as polycyclic aromatic hydrocarbons, have been shown to be relatively resistant to biodegradation. The biodegradability of some hydrocarbons may be enhanced when present in petroleum mixtures.

Fatty acids and long chain n-alkanes not originally present in weathered petroleum samples have been observed after biodegradation; generation of tar balls, which are quite resistant to microbial degradation, has also been reported (2252, 2255, 2257, 2258). Therefore, enhanced solubilization or sorption of some metabolic intermediates (some of which may be more toxic than the original hydrocarbons) may be significant in the soil environment (2249).

Although the microbiota of most non-contaminated soils include many naturally occurring hydrocarbon-degrading populations, the addition of petroleum selectively enriches that sector able to adapt and utilize the new substrate. The available review articles (citing laboratory studies and field studies) confirm that the distribution of hydrocarbon-utilizing microorganisms reflects the historical exposure of the environment to hydrocarbons (2252, 2255, 2257, 2249). In unpolluted ecosystems, hydrocarbon utilizers generally constitute less than 0.1% of the microbial community; in oil-polluted ecosystems, they can constitute up to 100% of the viable microorganisms (2255). Walker et al. (2257) reported that all classes of petroleum hydrocarbons were degraded by microorganisms in an oil-exposed sediment but not in a similar unexposed sediment.

Biodegradability has been shown to be related to JP-4 hydrocarbon concentrations. When concentrations are too low, biodegradation may cease. However, at high concentrations the components or their metabolic intermediates may be toxic and inhibit degradation (2249). Biodegradation of petroleum hydrocarbons has also been shown to be dependent on other environmental factors including: temperature, oxygen and moisture, nutrients, salinity, and pH (2252, 2249, 2255, 1846). Petroleum biodegradation has been reported to occur over a wide range of temperatures: Huddleston and Cresswell (2261) reported biodegradation at -1.1°C; Dibble and Bartha (2262) reported that the highest rates occurred between 30°C and 40°C with no increase observed above 37°C; and Atlas and Bartha (2263) reported that the degradation rate roughly doubles with each 5°C increase in the 5° to 20°C range; degradation in arctic environments has been reported to be dramatically reduced (2255, 2266).

Oxygen has been reported to be necessary for the initial steps of hydrocarbon degradation; reports of anaerobic degradation have been sporadic and controversial (2252, 2255, 2249). Oxygen depletion has been shown to lead to sharply reduced hydrocarbon utilization in soils (2261). Tilling of soil has been shown to have a positive effect on petroleum degradation (1811, 2256).

In the presence of large quantities of hydrocarbon substrates, the availability of nutrients, particularly nitrogen and phosphorus, becomes increasingly important and

the addition of fertilizers has a notable positive effect on biodegradation (2249, 2252, 2255); in subsoil treated with 1-10% oil, the addition of fertilizer had little effect (2256).

There are limited data available on the effects of pH and salinity on biodegradation of petroleum. In general, degradation was reported to decrease with increasing salinity (2249), although the effect of different microbial populations in the experiment was not determined. Hydrocarbon degradation was reported to be low in naturally acidic soils and increased up to pH 7.8 (2262).

The fate of petroleum hydrocarbons from various actual environental incidents has been summarized by Atlas (2255). Following a release in Searsport, ME, microbial degradation of JP-4 residues in cold anoxic marine sediments was essentially zero; however microbial degradation did apparently occur during transport from the spill location to the marine sediment (2266). Microbial degradation of petroleum hydrocarbons in ground-water, river water and soils has also been reported (2255).

In summary, biodegradation of the petroleum hydrocarbons comprising JP-4 fuel is expected to be rapid under conditions favorable for microbial activity and when fuel components are freely available to the microorganisms. Degradation may be limited and/or slow in environments with few degrading organisms, low pH, low temperatures, and high salinity (e.g., arctic environments). It should be mentioned that Walker et al. (2257) state that even under optimum conditions, total and complete biodegradation is not expected to occur except possibly over an extremely long time period.

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

The above discussion of fate pathways suggests that the major components of JP-4 fuel are highly volatile but vary in their potential for bioaccumulation and tendency to sorb to soil. They range from moderately to strongly sorbed to soil, and their bioaccumulation potential ranges from low to high. The variability in the properties of the components suggests that they may have somewhat different potential exposure pathways.

Spills of JP-4 would result in the evaporative loss of the more highly volatile components leaving those of lesser volatility in the soil. The fraction remaining in the soil is expected to be relatively mobile and will be carried by gravity to the saturated zone of the soil. In this zone, the more soluble components (aromatic and lower molecular weight aliphatic compounds) will dissolve into the ground-water or form emulsions with ground-water, while the insoluble fraction will float as a separate phase on top of the water table.

The movement of dissolved hydrocarbons in ground-water is much greater than the separate liquid phase, reaching distances of hundred to thousands of meters compared to tens of meters for the movement of the separate phase. In the presence of cracks and fissures; however, the flow of the separate hydrocarbon phase

is greatly enhanced. The movement of JP-4 fuel in ground-water may contaminate drinking water supplies, resulting in ingestion exposures. Ground-water discharges to surface water or the movement of contaminated soil particles to surface water drinking water supplies may also result in ingestion exposures and in dermal exposures from the recreational use of these waters. The potential also exists for uptake by fish and domestic animals, which may also result in human exposures due to the bioconcentration of various fuel components.

Volatilization of JP-4 hydrocarbons in soil is another potential source of human exposure. Exposures may be more intensive when the soil is contaminated directly from leaking underground storage tanks and pipes, rather than from spills. In such cases, the more volatile components do not have an opportunity to evaporate before penetrating the soil. Once in the soil, the hydrocarbons evaporate, saturating the air in the soil pores, and the vapors diffuse in all directions including upward to the surface. The vapors may diffuse into the basements of homes or other structures in the area, resulting in inhalation exposures to the buildings' occupants.

64.2.4 Other Sources of Human Exposure

The volatile nature of JP-4 fuel suggests that inhalation exposures to residents in the vicinity of air fields may occur during large spills. Volatilization also occurs during routine fuel handling operations and from fuel losses during the cooling of jet engines (1811), but these sources are expected to result in negligible exposures to residents in the area. However, workers in the immediate area could receive much greater exposures.

Human exposure to JP-4 fuel may result from fuel-jettisoning by aircraft. The effect of the evaporated fuel vapors is considered negligible (1912), but several exposure pathways exist for the fraction reaching the ground. The composition and fraction of the jettisoned JP-4 fuel that reaches the ground depends upon the altitude of its release and the temperature at ground level. For example, at a ground temperature of -20°C, over 20% of the JP-4 released below 400 meters may reach the ground but at a ground temperature of 20°C, less that 1% of the JP-4 fraction will reach the ground regardless of the altitude of release. At altitudes above 3000 meters, release height has almost no effect on the JP-4 fraction reaching the ground; however the surface area of fuel distribution will be affected (1913).

Because the volume of fuel released in a jettison may range from a few thousand to over 50,000 liters (1912), the amount reaching the ground may lead to significant human exposure if released at a low altitude. Contamination of surface water, crops and pasture land may result in human ingestion. However, significant human exposure is expected to be rare since Air Force directives specify that, whenever possible, release be made over unpopulated areas and at altitudes above 1500 meters (6000 meters in some aircrafts) (1912).

64.3 HUMAN HEALTH CONSIDERATIONS

64.3.1 Animal Studies

64.3.1.1 Carcinogenicity

The carcinogenicity of petroleum-derived and shale-derived JP-4 was evaluated in Fischer 344 rats and C57BL/6 mice. The animals were exposed to vapor concentrations of 500 or 1000 mg/m^3 in whole-body inhalation chambers. Exposure was for 6 hours daily, 5 days per week for 1 year. The animals were held for an additional year. The only effects observed during the exposure phase were decreased body weight and decreased kidney and liver weights in high- and low-dosed male rats and decreased spleen and kidney weights in low-dosed female rats. Histopathologic evaluation of the tissues have been in progress by the USAF since 1985; however, results are not available at this time (1936).

No other studies dealing with the carcinogenicity of JP-4 were located.

64.3.1.2 Genotoxicity

Brusick and Matheson evaluated the genotoxicity of JP-4 (1813) and JP-8 (3087) jet fuels in a number of in vitro and in vivo assays. Test results have been negative in almost all cases. An observed increase in unscheduled DNA synthesis may be artifactual because scintillation counting rather than autoradiography was the method used to measure UDS.

Negative results were obtained in the five standard strains of Salmonella typhimurium with and without microsomal activation. Test concentrations ranged from 0.001 to 5.1 μL per plate. Concentrations above 1 μL per plate were toxic to most of the bacterial strains. Negative results were also seen in strain D4 of Saccharomyces cerevisiae and in the TK mouse lymphoma cell assay (1813, 3087).

Benz and Beltz (3061) exposed beagles via inhalation to jet fuels JP-4, JP-5 or JP-10 and observed no increase in sister chromatid exchanges or micronuclei in peripheral lymphocytes. These investigators also exposed beagle lymphocytes in vitro to these jet fuels and observed similar results.

In the dominant lethal assay, negative results were obtained from male mice given doses of 0.01, 0.03 or 0.09 mL/kg/day for 5 days for JP-4 (1813) and 0.13, 0.4, and 1.3 mL/kg/day for 5 days for JP-8 (3087). Results were negative overall for JP-4 in rats but significant preimplantation loss was observed after the fourth mating. In this study, rats received doses of 0.09, 0.3 or 0.9 mL/kg/day of JP-4 by intraperitoneal injection for 5 days (1813). No evidence for dominant lethality was seen in the JP-8 experiments with doses of 0.1, 0.3 and 1.0 mL/kg/day for 5 days (3087).

64.3.1.3 Teratogenicity, Embryotoxicity and Reproductive Effects

No information is currently available concerning the teratogenic, embryotoxic, or reproductive effects of JP-4.

64.3.1.4 Other Toxicologic Effects

64.3.1.4.1 Short-term Toxicity

No information was found regarding the acute toxic effects of JP-4 in animals. Due to the nature of its components, CNS effects would be expected. Vapors would be irritating to the eyes and mucous membranes and the liquid would cause irritation and defatting of the skin (200).

In tests conducted in New Zealand white rabbits, both petroleum- and shale-derived JP-4 produced no signs of irritation when 0.1 mL of undiluted material was applied to eyes. Both fuel types were also tested for primary skin irritation on intact and abraded rabbit skin. Undiluted material (0.5 mL) was applied and covered for 24 hours. Neither fuel type caused any irritation after 24 hours. By 72 hours, moderate erythema was seen in both instances. Shale-derived JP-4 caused mild edema compared to none in the petroleum-derived JP-4 group. After one week, mild edema and erythema were seen in the shale-derived JP-4 group, in the petroleum-derived group there was mild exfoliation and erythema but no edema. In skin sensitization tests conducted in guinea pigs, petroleum-derived JP-4 exhibited no sensitization response. In contrast, shale-derived JP-4 demonstrated responses indicative of a mild to moderate sensitizer (1930).

Somewhat conflicting results concerning the severity of skin irritation resulting from exposure to 0.5 mL of shale-derived JP-4 have been presented by Hansen et al. (1981, 3265). The JP-4 was applied to abraded and intact skin of New Zealand white rabbits for 24 hours. Test animals were observed and scored by the Draize technique for signs of erythema and edema at 24 hours, 72 hours, and on days 4 through 21. At 72 hours, four of the six test rabbits had severe erythema and slight edema at all test sites. The edema subsided by day 8; however, the erythema remained severe until day 12, at which time it began to subside until it was completely gone by day 21. In this study, shale-derived JP-4 was rated as severely irritating with a primary irritation score of 5.50.

No LD_{50} data were found for JP-4. An oral LD_{50} of 20 g/kg has been reported for kerosene in guinea pigs (47).

64.3.1.4.2 Chronic Toxicity

Chronic inhalation studies have been conducted with JP-4 in various species.

Beagle dogs, Fischer 344 rats and C57BL/6 mice were subjected to whole body vapor exposures of petroleum-derived JP-4 for 90 days. The animals were exposed to

500 or 1000 mg/m³ continuously. Animals were sacrificed immediately following the exposure period. Histopathology revealed significant exposure-related lesions in both rodent species. In female mice, the incidence of centrilobular hepatocellular fatty change was 88% in the low-dose group and 89% in the high-dose group. These lesions were absent in the control group and were thought to be the result of mild reversible toxic insult. In male rats, 100% of the kidneys in both groups exhibited hyaline droplet formation in the proximal tubular epithelium. In 96% and 100% of the low- and high-dose male rats, respectively, the renal tubules near the corticomedullary junction were dilated and plugged with necrotic cell debris. All lesions found in exposed and control dogs were changes consistent with aging and not due to JP-4 exposure (1930).

In a 90-day study on shale-derived JP-4, Fischer 344 rats and C57BL/6 mice were given whole body vapor exposures to 400 or 1000 mg/m³ continuously. Groups of animals were sacrificed immediately after exposure and at 2 weeks, 2 months and 9 months post-exposure. Blood values at all post-exposure periods were all within normal limits. In the male rats, there was a significant difference in kidney and liver weights in the animals sacrificed immediately after exposure. This difference was no longer present 9 months post-exposure (1936).

Intermittent whole body vapor exposures at higher levels for 8 months failed to show any treatment-related histopathologic effects in dogs, rats, mice or monkeys; vapor level exposures were 2500 or 5000 mg/m³, 6 hours per day, 5 days per week. The only abnormalities observed in high-dose animals were increases in weight and in the organ to body weight ratios for the male rat kidney, liver, lung and spleen. There was also a 27% incidence of rat murine bronchitis (1933).

64.3.2 Human and Epidemiologic Studies

64.3.2.1 Short-term Toxicologic Effects

Acute exposure to petroleum distillates is known to cause CNS depression in man. For fuels with high vapor pressures such as JP-4, there is the possibility of significant vapor exposures, particularly in poorly ventilated or closed handling areas. Short-term exposure to high concentrations can lead to headache, nausea, mental confusion, and irritation of the respiratory system. In extreme cases, loss of consciousness can occur (1932). One case of jet fuel intoxication by the inhalation route was reported by Davies (1931). In this instance, a pilot was exposed to vapor levels of 3000-7000 ppm in the cockpit of his aircraft for approximately 7 minutes. He complained of feeling sleepy and groggy and his speech was slurred but he managed to land the aircraft safely. Neurological examination revealed a staggering gait, a positive Romberg test (indicates peripheral ataxia) and generalized muscular weakness and possibly decreased sensation to painful stimuli over the dorsal surface of the right forearm. The pilot did not feel "normal" for 36 hours. He was observed during the next few days and appeared in good condition. He was examined 5 months after the incident at which time he felt fine.

Petroleum fuels generally have a low oral toxicity. Ingestion is likely to occur only through accidents and the taste and smell will usually limit the amount swallowed. Aspiration of the liquid into the lungs can cause pneumonitis (1932).

The lower boiling point hydrocarbons that are present in most liquid fuels defat the skin and cause dryness and irritation. Prolonged or repeated skin contact may result in oil acne or oil folliculitis (1832).

Eye irritation can be caused by exposure to high vapor concentrations or if the liquid is splashed into the eyes (1932).

64.3.2.2 Chronic Toxicologic Effects

It has been clearly demonstrated that hydrocarbon fuels induce nephrotoxicity and renal carcinogenicity in male rats. However, these agents have failed to produce significant toxic or neoplastic changes in other major organs or in female rats. The mechanism responsible for the renal lesions in unknown at the present time; however, research is currently underway to assess the role of the male rat-specific protein, alpha-2u-globulin, in the initial formation of hyaline droplets and tubular degeneration (3418). Because the etiology of this species- and sex-specific nephrotoxicity is unknown, the question remains as to whether exposure to hydrocarbon fuel vapors would produce similar effects in humans. All epidemiological information to date is negative; however, the studies have either been limited in scope and/or the observed chronic effects could be attributed to individual components in the fuels. Consequently, no definitive studies are available at this time to determine the potential for human nephrotoxicity or renal carcinogenicity from exposure to hydrocarbon fuels (3746).

Long-term exposure to jet fuel causes neurological effects. Knave et al. (1929) conducted a cross-sectional epidemiologic study in 30 Swedish aircraft factory workers exposed to jet fuel with the following composition: aromatic hydrocarbons 12 vol %; olefin hydrocarbons 0.5 vol %; saturated hydrocarbons 87.5 vol%. Duration of exposure ranged from 2 to 32 years with a mean of 17.1 years. Exposure levels ranged from 128-432 mg/m^3. Controls were age-matched and were employed for a similar time period but had no exposure. Twenty-one of the 30 exposed workers experienced recurrent acute symptoms, such as dizziness, headache, nausea, pain upon inhalation, feelings of suffocation, slight cough and palpitations. Thirteen subjects also reported fatigue during and after work. No significant differences were seen at different exposure levels. Among chronic neurasthenic symptoms, the most obvious differences between control and exposed workers were fatigue, depressed mood, lack of initiative, dizziness, palpitations, thoracic oppression, sleep disturbances and headaches. In psychological tests, the exposed subjects had a greater irregularity of performance on a test of complex reaction time; a greater performance decrement over time in a simple reaction time task and poorer performance in a task of perceptual speed when compared to the non-exposed subjects. There was also a significant difference between the groups when EEG's were ranked as to configuration of alpha activity. Symptoms indicative of polyneuropathy (e.g., restless

legs, muscle cramps, diffuse pain in the extremities, paresthesia, numbness) occurred with a higher prevalence in exposed workers. Measurements of peripheral nerve functions indicated differences in exposed workers vs. non-exposed groups. The same group of investigators conducted similar studies in other jet fuel workers and obtained similar results (1926-1928).

In a study on the effects of jet fuel on liver function, Dossing et al. (1925) found no changes in the biochemical indices of liver injury in 91 fuel-filling attendants employed on Danish air force bases for periods up to 31 years (median = 7.6 years). The median jet fuel concentration was 31 mg/m^3 with a range of 1 to 1020 mg/m^3

64.3.3 Toxicology of JP-4 Components

A brief overview of the toxicology of the major hydrocarbon components of JP-4 (see Table 64-4) are summarized below. The acute toxicity values for these components are presented in Table 64-6.

n-Hexane

Hexane may be the most highly toxic member of the alkanes. When ingested, it causes nausea, vertigo, bronchial and general intestinal irritation and CNS effects. It also presents an acute aspiration hazard. Acute exposure occurs primarily through inhalation. Non-specific symptoms such as vertigo, headache, nausea and vomiting are the first to be manifested. At high concentrations, a narcosis-like state appears as a result of CNS depression. Pre-narcotic symptoms occur at vapor concentrations ranging from 1500-2500 ppm. n-Hexane irritates the eyes and mucous membranes. These effects can be seen after an exposure of 880 ppm for 15 minutes. Skin contact primarily causes fat removal and cutaneous irritation. Chronic exposure to n-hexane vapors causes peripheral neuropathy. The first clinical sign of neural damage is a feeling of numbness in the toes and fingers. Progression leads to further symmetrical sensory impairment in the distal portions of the extremities and to loss of muscular stretching reflexes. Ultimately, symmetrical muscular weakness develops, chiefly in the distal portion of the extremities. Paralysis develops with varying degrees of impaired grasping and walking. This may include muscular atrophy (sensorimotor polyneuropathy). The development of electrophysiological changes parallels the severity of the clinical picture. In the most severe cases, nerve conductivity is neutralized. In some cases, cranial nerve involvement is also observed. After exposure ceases, recovery begins within 6 to 10 months in mild to moderate cases, but may take up to 3 years in serious cases. The threshold level at which neuropathy occurs has not been firmly established but symptoms have been observed in people exposed to concentrations ranging from 10 to 200 ppm for 9-12 months.

In animals, signs of narcosis are seen after mice are exposed to vapor levels of 16,000 ppm for 5 minutes. Death generally occurred at concentrations between 43,800 and 52,000 ppm after 9-119 minutes. The oral LD_{50} is cited as 24 mL/kg for 14-day-old rats and 49 mL/kg for young adult rats.

TABLE 64-6
ACUTE TOXICITY OF COMPONENTS OF JP-4

Component*	Oral LD_{50}	Dermal LD_{50}	LC_{50}
n-hexane	24-49 mL/kg [rat] (1935) 28,710 mg/kg [rat] (1937)	no data	33,000 ppm ·4 hr [rat] (1935)
octane	no data	no data	no data
dodecane	no data	no data	no data
isopentane	no data	no data	1000 mg/L [mouse] (12)
isooctane	no data	no data	no data
methylcyclo-pentane	no data	no data	no data
methycyclo-hexane	2250 mg/kg [rat] (47)	no data	no data
cyclohexane	29,820 mg/kg [rat] (1935)	no data	no data
benzene	3800 mg/kg [rat] (59) 4700 mg/kg [mouse] (47)	no data	10,000 ppm ·7 hr [rat] (47)
toluene	5000 mg/kg [rat] (47)	12,124 mg/kg [rabbit] (47)	5320 ppm ·8 hr [mouse] (47)
xylenes	4300 mg/kg [rat] (47)	no data	5000 ppm ·4 hr [rat] (47)
ethyl benzene	3500 mg/kg [rat] (47)	5000 mg/kg [rabbit] (59)	no data

TABLE 64-6 (Cont.)

Component*	Oral LD_{50}	Dermal LD_{50}	LC_{50}
trimethylbenzenes	no data	no data	18 mg/m³ ·4 hr [rat] (47)
1-methylnaphthalene	1840 mg/kg [rat] (47)	no data	no data
2-methylnaphthalene	1630 mg/kg [rat] (47)	no data	no data

*See Table 64-1 for component concentrations in sample JP-4 fuel.

Long term inhalation experiments in rats suggest that the first signs of neurotoxicity appear after they are exposed to levels of 200 ppm for 24 weeks. This higher threshold to induce neurotoxicity in animals may be due to differences in metabolism. Specifically, 2-hexanol is the chief metabolite in animals, while 2,5-hexanedione, which is neurotoxic, predominates in man. Chronic topical application of a solvent containing 35.2% n-hexane caused axonal swelling and myelin degeneration in chicks. No clinical signs were seen. Dosage was 1 g/kg/day for 64 days. In rabbits, topical application of 0.5 mL/day for up to 10 days caused redness, irritation and scab formation. N-hexane is neither carcinogenic or teratogenic. One in vivo study in rats that inhaled 150 ppm for 5 days found an increased number of chromosome aberrations in the bone marrow cells. No studies on mutagenicity, reproductive toxicity or carcinogenicity in man were found (12, 1930, 1935).

Octane

By the oral route, octane may be more toxic than its lower homologues. If it is aspirated into the lungs, it may cause rapid death due to cardiac arrest, respiratory paralysis and asphyxia. The narcotic potency of octane is approximately that of heptane but it does not exhibit the CNS effects seen with hexane or heptane.

In humans, the only reported effects are blistering and burning due to prolonged skin contact.

In animals, octane is a mucous membrane irritant. At high concentrations, it causes narcosis. It is expected that severe exposure in humans will produce the same effects. Mice exposed to vapor levels of 32,000 ppm suffered respiratory arrest after 4 minutes of exposure. Exposure to 12,840 ppm for 185 minutes caused a decreased respiratory rate, followed by death within 24 hours. No narcosis was seen after 48 minutes of exposure to 5350 ppm (12, 46, 1938).

Dodecane

Dodecane is not highly toxic. The lowest toxic dose for mice is 11 g/kg when administered percutaneously for 22 weeks. Dodecane is a potentiator of skin tumorigenesis by benzo(a)pyrene. It decreased the effective threshold dose by a factor of 10. Dodecane and phenyldodecane applied topically to the progeny of rats treated with benzo(a)pyrene, chrysene or benzo(b)triphenylene on the seventeenth day of gestation produced tumors in offspring. No additional information is available (12, 1937).

Isopentane

Isopentane is a CNS depressant. Effects may include exhilaration, dizziness, headache, loss of appetite, nausea, confusion, inability to do fine work, a persistent taste of gasoline and in extreme cases, loss of consciousness. Inhalation of up to 500 ppm appears to have no effect on humans. "Very high" vapor concentrations are irritating to the skin and eyes. Repeated or prolonged skin contact will dry and defat skin resulting in irritation and dermatitis. The LC_{50} in the mouse is estimated to be 1000 mg/L (12).

Iso-octane (2, 2, 4-trimethylpentane)

The iso-octanes are moderately toxic by the oral route. If aspirated into the lungs of rats, they will cause pulmonary lesions. When injected intramuscularly into rabbits, iso-octane produced hemorrhage, edema, interstitial pneumonitis, abscess formation, thrombosis and fibrosis. Inhalation of 16,000 ppm caused respiratory arrest in mice and 5 minutes exposure to 1000 ppm was highly irritating (1937).

Methylcyclopentane

Methylcyclopentane resembles cyclopentane in its toxicity. Cyclopentane is a CNS depressant. Humans can tolerate 10-15 ppm. In mice, 38 ppm causes loss of reflexes, narcosis and death demonstrating that no safety margin exists. Methylcyclopentane also exhibits no safety margin between the onset of narcosis and death. When applied to guinea pig skin, cyclopentane produced dryness and slight erythema. Methylcyclopentane would be expected to have the same effect (12).

Methylcyclohexane

No systemic poisonings by methylcyclohexane have been reported in man. At high vapor concentrations it causes narcosis in animals and it is expected that it would produce the same effect in humans. The no-effect level is about 300 ppm in primates and 1200 ppm in rabbits. Rabbits did not survive 70 minutes of exposure to 15,227 ppm. Death was preceded by conjunctival congestion, dyspnea, severe convulsions and rapid narcosis. There were no signs of intoxication in rabbits exposed to 2880 ppm for a total of 90 hours, but slight cellular injury was observed in the liver and kidneys. In primates, lethal concentrations caused mucous secretion, lacrimation, salivation, labored breathing and diarrhea.

In chronic inhalation studies, exposure to 2000 ppm, 6 hours per day, 5 days per week for 2 years produced no tumors in rats, mice, hamsters or dogs. The only significant toxic effect found was renal changes in male rats. These included renal tubular dilation, papillary hyperplasia and medullary mineralization.

Dermal application of the liquid produced local irritation, thickening and ulceration (12, 46, 54, 17, 1936).

Cyclohexane

Cyclohexane is a CNS depressant of low toxicity. Symptoms of acute exposure are excitement, loss of equilibrium, stupor and coma. Rarely, death results due to respiratory failure. The anesthesia that is induced is weak and of brief duration but more potent than that caused by hexane. The oral LDLo in rabbits ranges from 5.5 to 6.0 g/kg. Within 1.5 hours the animals exhibited severe diarrhea, widespread vascular damage and collapse. Degenerative lesions were seen in the heart, lung, liver, kidney and brain. A one-hour vapor exposure to 26,752 ppm caused rapid narcosis and tremor and was lethal to all exposed rabbits. In mice, concentrations causing narcosis vary from 14,600 to 122,000 ppm.

Cyclohexane is nominally absorbed through the skin although massive applications (>180.2 g/kg) to rabbit skin resulted in microscopic changes in the liver and kidneys and caused the death of all animals.

The danger of chronic poisoning is relatively slight because this compound is almost completely eliminated from the body. No toxic changes were seen in rabbits exposed to vapor levels of 434 ppm, 6 hours daily for 50 exposures, but some microscopic changes were seen in the liver and kidneys when the exposure was to 786 ppm for the same period.

In man, no systemic poisonings by cyclohexane have been reported. A vapor level of 300 ppm is somewhat irritating to the eyes and mucous membranes. It has been reported that cyclohexane may potentiate the toxic effects of TOCP but no additional details of this interaction are available (12, 17, 46, 54, 1937).

Benzene

The primary effects of benzene inhalation and ingestion are on the central nervous system (54). Benzene is carcinogenic in both animals and man. Several reports have established a relationship between benzene exposure and leukemia. For more information, refer to the chapter on benzene in the Installation Restoration Program Toxicology Guide.

Toluene

Toluene is a CNS depressant with a low toxicity. For more information, refer to the chapter on toluene in the Installation Restoration Program Toxicology Guide.

Xylenes

Acute exposure to high concentrations of xylene vapors may cause CNS depression. Both the liquid and the vapor are irritating to the eyes, mucous membranes and skin (46). The National Toxicology Program recently reported that there was no evidence of carcinogenicity of mixed xylenes in either mice or rats given daily doses ranging from 250 to 1000 mg/kg by gavage for 2 years (1939).

For more information, refer to the chapter on xylenes in the Installation Restoration Program Toxicology Guide.

Ethyl Benzene

Ethyl benzene is primarily an irritant to the skin, eyes and upper respiratory tract. Systemic absorption causes CNS depression (46). For more information, refer to the chapter on ethyl benzene in the Installation Restoration Program Toxicology Guide.

Trimethylbenzenes

The trimethylbenzenes occur in 3 isomeric forms. The 1,3,5-isomer (mesitylene) and the 1,2,4-isomer (pseudocumene) are toxicologically similar. High vapor concentrations (5000-9000 ppm) cause CNS depression in animals. Loss of reflexes was seen in mice exposed to 8130-9140 ppm of the 1,2,4-isomer or 8130 ppm of the 1,3,5-isomer. Rats exposed to 1700 ppm of an isomeric mixture for 10-21 days had no adverse effects or fatalities.

The fatal intraperitoneal dose of the 1,2,4-isomer for the guinea pig is 1.788 g/kg, while the fatal dose of the 1, 3, 5-isomer by the same route is 1.5-2 g/kg for the rat. For the 1,2,3-isomer, an oral LDLo of 5000 mg/kg has been reported in the rat. Trimethylbenzene liquid is a primary skin irritant. Deposition into the lungs causes pneumonitis at the site of contact.

The only report of human exposure described symptoms of nervousness, tension, anxiety, asthmatic bronchitis, hypochromic anemia and changes in the coagulability of the blood. Vapor concentrations ranged from 10-60 ppm. Exposure was to a mixture containing 30% of the 1, 3, 5-isomer and 50% of the 1, 2, 4-isomer (2,12).

Methylnaphthalene

The only adverse effects of methylnaphthalene reported in man are skin irritation and photosensitization (17). Oral LD_{50} values of 1840 mg/kg and 1630 mg/kg have been reported for 1-methylnaphthalene and 2-methylnaphthalene, respectively, in the rat (47).

JP-4 Additives

Additives used in JP-4 are listed in Table 64-3. Little toxicological data were found regarding these compounds. The information that was available is outlined below:

6-t-butyl-2,4-dimethylphenol

An oral LD_{50} of 530 mg/kg in the rat was reported (47).

N,N'-di-sec-butyl-p-phenylenediamine

A percutaneous LD_{50} of 5000 mg/kg was reported in guinea pigs. The lowest lethal oral dose reported in rats is 200 mg/kg. The LDLo in rats is 600 mg/m. for 6 hours (1937).

N,N-dimethylformamide

An oral LD_{50} of 2800 mg/kg in the rat and 3750 mg/kg in the mouse have been reported.

In humans, N,N-dimethylformamide is irritating to the eyes, skin and mucous membranes. Case reports have indicated that the liver is the main target organ following acute and chronic exposure to dimethyl-formamide. One of the earliest manifestations of excessive exposure is ethanol intolerance followed at higher exposure levels by symptoms of nausea, vomiting and abdominal pain (1937, 2316).

64.3.4 Levels of Concern

No criteria or standards specific for JP-4 were located. EPA (2012) does list a criterion for oil and grease that requires domestic water supplies to be virtually free from oil and grease, particularly with regard to taste and odor.

OSHA (3539) has set a 8-hr TWA exposure limit of 400 ppm for petroleum distillates (naphtha). The ACGIH (3005) recommends a threshold limit value of 300 ppm for gasoline, with a short-term exposure limit of 500 ppm.

64.3.5 Hazard Assessment

Toxicological data available for JP-4 are limited. No data are currently available regarding the carcinogenicity of JP-4 but a study is in progress (1936). Shale- and petroleum-derived JP-4 have been tested in F344 rats and C57BL/6 mice at vapor concentrations of 500 or 1000 mg/m³. Histopathology is now in progress.

Genotoxicity tests in bacterial and mammalian test systems are negative as are dominant-lethal tests for both rats and mice (1813). No data on teratogenicity, fetotoxicity, or reproductive toxicity are available.

Acute eye irritation studies with undiluted shale- or petroleum-derived JP-4 have produced negative responses in rabbits (1930). Skin irritation studies with the same test samples indicated no effect at 24 hours; by 72 hours, mild erythema was induced with both samples and mild edema with the shale-derived sample (1930). Hansen et al. (1981, 3265) obtained a primary irritation score of 5.50, severely irritating, for shale-derived JP-4 in a primary dermal irritation study with New Zealand white rabbits. Skin sensitization studies in guinea pigs were negative for the petroleum-derived sample but suggested mild to moderate sensitization with the shale-derived JP-4 sample (1930).

Continuous inhalation exposure to petroleum-derived JP-4 at levels of 500 and 1000 mg/m³ for 90 days produced fatty changes in the liver of mice and rats and kidney damage in rats; no significant effects were noted in dogs (1930). Intermittent exposure to higher concentrations (5000 mg/m³) produced increases in organ weights of the kidney, liver, lung and spleen of rats but no histopathologic changes (1933).

Human exposure to petroleum distillates is known to cause headache, nausea, mental confusion, CNS depression and respiratory tract irritation. Aspiration can produce chemical pneumonitis (1932).

Neurological effects have been linked to chronic exposure to jet fuels in aircraft factory workers. Average exposure concentrations ranged from 128 to 432 mg/m³ for 2 to 32 years. Performance decrement and polyneuropathy correlated with exposure. Other symptoms included depression, irritability, lassitude, disturbed sleep rhythm and changes in conduction velocities in peripheral motor nerves (1929).

64.4 SAMPLING AND ANALYSIS CONSIDERATIONS

Determination of the presence of JP-4 fuel in soil and water requires collection of a representative field sample and laboratory analysis for the specific major components attributed to JP-4; however, the relative concentrations of the constituents, and even the constituents themselves, will vary with time and distance from the site of initial contamination due to weathering. The major component categories in JP-4 fuel have been identified as the following:

n-alkanes
branched alkanes
cycloalkanes
benzenes and alkylbenzenes
naphthalenes

Since many of the components may be highly volatile, care is also required to prevent losses during sample collection and storage. EPA protocols for analysis of constituents within these classes dictate that the samples should be collected in airtight containers with no headspace. Analyses should also be completed within 14 days of sampling.

A combination of capillary column gas chromatography (GC) and gas chromatography/mass spectrometry (GC/MS) techniques has been used to identify the principal components in JP-4 fuel (ESL-TR-81-54, SRI). Fuel samples, and probably any samples collected in the field that are primarily organic in nature, require the separation (prior to GC or GC/MS analysis) of the aliphatic, monoaromatic and polycyclic aromatic hydrocarbon fractions using liquid solid column chromatography. The various column eluates, with or without dilution in carbon disulfide, are then analyzed by GC or GC/MS techniques. Aqueous samples need to be liquid-liquid extracted with an appropriate solvent (i.e., trichlorotrifluoroethane) prior to analysis; solid samples would be extracted with trichlorotrifluoroethane using soxhlet extraction or sonication methods (Standard Methods). An aliquot of the sample extract, with or without concentration, is then analyzed by GC or GC/MS. (Sampling and Analysis Considerations for some specific components in JP-4, i.e., benzene, toluene, xylenes, ethyl benzene and naphthalene, have been addressed in Volume 1.)

Alternatively, the "oil and grease" content can be measured. This determination would not be the measurement of an absolute quantity of a specific component, but rather the quantitative determination of groups of components with similar physical characteristics (i.e., common solubility in trichlorotrifluoroethane). The "oil and grease" content is defined as any material recovered from extraction with trichlorotrifluoroethane and measured gravimetrically; extraction methods are those described above for aqueous and soil samples.

The total hydrocarbon content of JP-4 in water can also be determined by infrared (IR) spectrophotometry (3599). Since various fuels have distinctive gas

chromatographic profiles it may also be possible to distinguish JP-4 from other fuels present in environmental samples by examining selected peak areas or peak ratios for certain hydrocarbons (3599).

A detection limit for JP-4 was not determined; the detection limit for specific components is expected to be in the range of 37 μg/L for aqueous samples and μg/g for non-aqueous samples.

64.5 REFERENCES

Note: The nonsequential numbers of the references reflect the order of references as they appear in the master bibliography.

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COMPLEX MIXTURES

This chapter deals with a complex mixture and/or class of compounds. The format used for this less well-defined group of compounds was modified as necessary but follows the outline of earlier chapters as closely as possible. It should be noted, however, that the composition of these materials can vary according to the route of synthesis, the formulating ingredients added, the interactions of the active ingredients, or the storage conditions. These factors can influence the nature of the material that is ultimately utilized and probably are reflected in many of the experimental findings reported in the following chapters.

The typical components and approximate composition of the mixtures are provided if that information was available. Physical/chemical properties often were not available or varied depending on formulation. Many of these mixtures are blended to modify their physical properties according to the intended use. Furthermore, the formulations vary with season as well as with geographic locations of product use. In some cases, therefore, the range for the class of compounds was given.

In addition to the data for the mixture itself, the chapter that follows also contains sections on the principal components and major additives of the mixture, their fate in the environment and a brief overview of their toxicity.

COMMON SYNONYMS:	CAS REG NO: NIOSH NO.:	CHEMICAL COMPOSITION:
Automotive gasoline Benzin Motor spirits Petrol	8006-61-9 LX3300000 MOLECULAR WEIGHT: Not applicable Air W/V Conversion: (25°C) 4.5 mg/m^3 = 1 ppm; 0.222 ppm = 1 mg/m^3	Approximate Composition N-alkanes 15.0% - 17.0% Cycloalkanes 3.0% - 5.0% Benzenes and Alkylbenzenes 20.0% - 49.0% Branched alkanes 28.0% - 36.0% Olefins 1.0% - 11.0% Naphthalenes 0.0% - ≤1.0%

REACTIVITY	Several sources indicate that strong oxidizers are incompatible with gasoline and that vigorous reactions, ignition, and/or explosion may be expected. The NFPA specifically notes such events when chlorine, fluorine, or magnesium perchlorate are mixed with hydrocarbons. Gasoline is considered a miscellaneous combustible or flammable material for compatibility classification purposes. Such substances typically evolve heat, fire, and toxic or flammable gases in reactions with oxidizing mineral acids, alkali or alkaline earth elemental metals, nitrides, organic peroxides or hydroperoxides, or strong oxidizing agents. Reactions with explosive materials may result in an explosion, while those with strong reducing agents may evolve heat and flammable gases. Non-oxidizing mineral acids generally evolve heat and innocuous gases. High fire hazard and moderate explosion hazard when exposed to heat, flame, sparks, etc (51, 505, 507, 511).

PHYSICO-CHEMICAL DATA	• Physical State: Liquid (at 20°C)	(60)
	• Color: Colorless to pale brown or pink	(60)
	• Odor: Characteristic	(54,60)
	• Odor Threshold: 0.250 ppm	(60)
	• Density: 0.7321 g/mL (at 20°C)	(60)
	• Freeze/Melt Point: No data	(60)
	• Boiling Point: 38.00 to 204.00°C	(39,60)
	• Flash Point: -46.00 to 38.00°C closed cup, depending on grade	(60,506,507)

PHYSICO-CHEMICAL DATA	• Flammable Limits: 1.2-1.50 to 7.1-7.60% by volume, depending on grade	(60,504, 506,507)
	• Autoignition Temp.: 257.0 to 471.0°C (varies with grade)	(51,60 510,513,507)
	• Vapor Pressure: 2.63E+02 to 6.75E+02 mm Hg (at 38°C)	(1932)
	• Satd. Conc. in Air: No data	
	• Solubility in Water: Insoluble	(60)
	• Viscosity: 0.451 cp (at 20°C)	(60)
	• Surface Tension: 1.9000E+01 to 2.3000E+01 dyne/cm (at 20°C)	(60)
	• Log (Octanol-Water Partition Coeff.): 2.13 to 4.87	(See Table 65-3)
	• Soil Adsorp. Coeff.: 6.50E+01 to 3.60E+04	(See Table 65-3)
	• Henry's Law Const.: 4.80E-04 to 3.30E+00 atm · m^3/mol (at 20°C)	(See Table 65-3)
	• Bioconc. Factor: No data	

PERSISTENCE IN THE SOIL-WATER SYSTEM	Gasoline hydrocarbons are expected to be relatively mobile and moderately persistent in most soil systems. Persistence in deep soils and groundwater may be higher. Volatilization, photooxidation and biodegradation are important fate processes. Surface spills are expected to be weathered by evaporation and photooxidation. Downward migration of weathered surface spills and sub-surface discharges represent a potential threat to underlying groundwater. Biodegradation of gasoline hydrocarbons is expected to be significant under environmental conditions favorable to microbial oxidation; naturally-occurring, hydrocarbon-degrading microorganisms have been isolated from polluted soils and, to a lesser extent, non-polluted soils.

PATHWAYS OF EXPOSURE	The primary pathway of concern from the soil/ground-water system is the migration of gasoline to ground water drinking water supplies from leaking underground storage tanks or large spills. The use of this water may cause inhalation exposures as well as ingestion and dermal exposures. Vapors from leaked or spilled gasoline may diffuse through soil and migrate into structures, resulting in inhalation exposures.

HEALTH HAZARD DATA	Signs and Symptoms of Short-term Human Exposure: (54) Gasoline vapor is a CNS depressant. Low vapor levels (500-1000 ppm) may produce flushing, staggering gait, slurred speech and mental confusion. High vapor levels (>5000 ppm) may cause coma and death from respiratory failure. Ingestion and aspiration may cause chemical pneumonitis, pulmonary edema and hemorrhage, and kidney damage. Gasoline is irritating to the skin, conjunctiva and mucous membranes. Prolonged contact may defat skin and cause dermatitis. Certain individuals may develop hypersensitivity. Acute Toxicity Studies: INHALATION: LC_{Lo} 135,000 mg/m³ · 5 min — Mammal (51) TC_{Lo} 2,250-4,500 mg/m³ · 30-60 min (Neurotoxicity) — Human (3504) LC_{Lo} 22,500 mg/m³ (5000 ppm) — Human (3504) LC_{50} 300,000 mg/m³ · 5 min — Mouse (3504) LC_{50} 300,000 mg/m³ · 5 min — Guinea pig (3504) LC_{50} 300,000 mg/m³ · 5 min — Rat (3504) TC_{Lo} 900 ppm · 1 hr (eye irritation) — Human (3504) ORAL: LD_{50} 13,600 mg/kg — Rat (1924) Long-Term Effects: Chronic inhalation produces pulmonary changes and kidney damage, lead toxicity with leaded gas. Pregnancy/Neonate Data: Negative Genotoxicity Data: Limited data are conflicting Carcinogenicity Classification: IARC - None assigned NTP - None assigned EPA - Group B2 (probable human carcinogen; sufficient evidence in animals and inadequate evidence in humans)

HANDLING PRECAUTIONS (45,52)	Handle only with adequate ventilation. There are no specific respirator guidelines for gasolines. • Chemical goggles if there is probability of eye contact • Nitrile, PVA or other protective clothing to prevent prolonged or repeated skin contact with the liquid.

ENVIRONMENTAL AND OCCUPATIONAL STANDARDS AND CRITERIA

AIR EXPOSURE LIMITS:

Standards
- OSHA TWA (8-hr): 300 ppm; STEL (15-min): 500 ppm
- AFOSH (8-hr TWA): 300 ppm; STEL (15-min): 500 ppm

Criteria
- NIOSH IDLH (30-min): None established
- NIOSH REL: None established
- ACGIH TLV® (8-hr TWA): 300 ppm
- ACGIH STEL (15-min): 500 ppm

WATER EXPOSURE LIMITS:

Drinking Water Standards
None established.

EPA Health Advisories and Cancer Risk Levels
None established.

WHO Drinking Water Guideline
No information available.

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

ENVIRONMENTAL AND OCCUPATIONAL STANDARDS AND CRITERIA (Cont.)

- Aquatic Life (355)
  - No criterion established; automotive gasoline is not a priority pollutant.

Oil and Grease (2012)
For domestic water supply: Virtually free from oil and grease, particularly from the tastes and odors that emanate from petroleum products.

For aquatic life:

- To protect several important freshwater and marine species, each having a demonstrated high susceptibility to oils and petrochemicals, the lowest continued flow 96-hour LC_{50} should be reduced a hundred-fold.
- Levels of oils or petrochemicals in the sediment which cause deleterious effects to the biota should not be allowed.
- Surface waters shall be virtually free from floating non-petroleum oils of vegetable and animal origin as well as petroleum-derived oil.

REFERENCE DOSES:
No reference dose available.

REGULATORY STATUS (as of 01-MAR-89)

Promulgated Regulations

- Federal Programs

  Clean Water Act (CWA)
  Oil and grease are designated conventional pollutants under the CWA (351). Effluent limitations for oil and grease exist in almost all point source categories under the general pretreatment regulations for new and existing sources, and effluent standards and guidelines. Limitations vary depending on the type of industry (3763).

  Toxic Substances Control Act (TSCA)
  Manufacturers and processors of the C9 aromatic hydrocarbon fraction must test it for neurotoxicity, mutagenicity, developmental toxicity, reproductive effects and oncogenicity. The C9 fraction is obtained from the reforming of crude petroleum. It consists of ethyltoluenes and trimethylbenzenes (1988). Testing will be conducted by the American Petroleum Institute. Interim reports must be submitted at 6-month intervals (1987).

Occupational Safety and Health Act (OSHA)
Employee exposure to gasoline shall not exceed an 8-hour time-weighted average (TWA) of 300 ppm, or a 15-minute short-term exposure limit (STEL) of 500 ppm in any 8-hour work day (3539).

Hazardous Materials Transportation Act (HMTA)
The Department of Transportation has designated gasoline as a hazardous material which is subject to requirements for packaging, labeling and transportation (305).

- State Water Programs

ALL STATES
All states have adopted EPA Ambient Water Quality Criteria and NPDWRs (see Water Exposure Limits section) as their promulgated state regulations, either by narrative reference or by relisting the specific numeric criteria. These states have promulgated additional or more stringent criteria:

ALASKA
Alaska has an aquatic life criterion of 15 μg/L for total hydrocarbons and 10 μg/L for total aromatic hydrocarbons in fresh and marine surface waters (3016).

ARKANSAS
Arkansas requires that oil and grease shall not exceed 10 mg/L average or 15 mg/L maximum when discharging to surface waters (3587).

FLORIDA
Florida requires that oil and grease not exceed 10 mg/L in Class V waters (navigation, industrial use) and 5 mg/L for all other surface waters (3220).

MASSACHUSETTS
Massachusetts requires that the maximum discharge concentration of oil and grease of petroleum origin not exceed 15 mg/L in surface waters (3432).

NEBRASKA
Nebraska requires that petroleum oils not exceed 10 mg/L in surface waters (3719).

NEW YORK
New York has set a maximum contaminant level of 50 μg/L for kerosene in drinking water (3501).

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 nonbioaccumulative in the marine environment or are rapidly rendered harmless by physical, chemical or biological processes in the sea (309).

SOUTH DAKOTA
South Dakota has a water quality standard of 10 mg/L for all petroleum products in surface waters (3672).

VIRGINIA
Virginia has a water quality standard of 1 mg/L for petroleum hydrocarbons in ground-water (3135).

WYOMING
Wyoming has a water quality standard of 10 mg/L for surface waters and Class II and III ground-waters. In addition, Class I domestic ground-water is required to be virtually free of oil and grease (3853, 3852).

Proposed Regulations

- Federal Programs
  No proposed regulations are pending.

- State Water Programs
  No proposed regulations are pending.

MOST STATES
Most states are in the process of revising their water programs and proposing changes to their regulations which will follow EPA's when they become final. Contact with the state officer is advised. Changes are projected for 1989-90 (3683).

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 vis 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 Fishing Water Quality (536)
Petroleum products must not be present in salmonid and cyprinid waters in such quantities that they: (1) form a visible film on the surface of the water or form coatings on the beds of water-courses and lakes, (2) impart a detectable "hydrocarbon" taste to fish and, (3) produce harmful effects in fish.

Directive on the Quality Required of Shellfish Waters (537)
The mandatory specifications for petroleum hydrocarbons specify that they may not be present in shellfish water in such quantities as to produce a visible film on the surface of the water and/or a deposit on the shellfish which has harmful effects on 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 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)
Petroleum and coal tar distillates with flash points below 21 degree C are classified as flammable substances and are subject to packaging and labeling regulations. Because of the variable composition of other petroleum and coal tar distillates (excluding those used as motor fuels) they are considered preparations and their labeling shall be done in accordance with the procedures outlined in the Directive relating to the Classification Packaging and Labeling of Dangerous Preparations (solvents).

EEC Directives - Proposed
Proposal for a Council Directive on the Dumping of Waste at Sea (1793)
EEC has proposed that the dumping of crude oil, petroleum hydrocarbons, lubricants and hydraulic fluids at sea be prohibited.

65.1 MAJOR USES AND COMPOSITION

65.1.1 Major Uses

Gasoline is a volatile mixture of flammable liquid hydrocarbons derived chiefly from crude petroleum and used principally as a fuel for internal combustion engines. Consumption of gasoline by motor vehicles in this country was approximately 103 billion gallons in 1983, down from a peak consumption of 116 billion gallons in 1978 (1409).

65.1.2 Composition

Automotive gasoline is composed of several hundred hydrocarbons in the range of C_4 to C_{11} and with boiling points from approximately 30 °C to 210 °C. General composition expressed as percent weight by compound category has been reported to be: 49% to 62% aliphatic hydrocarbons (28-36% branched alkanes, 15-17% n-alkanes, and 3-5% cycloalkanes), 1% to 11% olefinic hydrocarbons, 20% to 49% benzenes and alkylbenzenes and up to 1% naphthalenes (2320, 1843, 1849).

The concentrations of specific hydrocarbons in different gasoline samples are highly variable and are expected to become even more variable as the availability of leaded gasoline is reduced. For example, as reforming severity was adjusted to achieve the required increase in octane levels of unleaded gasoline pools, average aromatic content increased from 22% in 1970 to 27% in 1980 and 1984; as leaded gasoline is phased out, the aromatic content will increase further to 35%. Olefin content also increased from 8% in 1980 to 11% in 1984 (2319).

The individual components of gasoline have been characterized by several authors (2320, 2311, 1843). Table 65-1 summarizes the available hydrocarbon composition data for various gasolines. Petroleum-derived distillates may also contain many non-hydrocarbon components. These may become major concerns in heavy distillates and residues but are much less important in light distillates such as automotive gasoline where only trace quantities of sulfur-, nitrogen-, and oxygen-containing compounds have been detected. Large variations in trace element concentrations were reported but no quantitative data were available (1843).

Automotive gasoline also contains a number additives used as octane improvers, antioxidants, metal deactivators, corrosions or icing inhibitors, detergents or demulsifiers. A list of some of the chemical classes and specific chemicals that may be used for these purposes is provided in Table 65-2.

TABLE 65-1
COMPOSITION DATA (% W/W) FOR VARIOUS GASOLINES[a]

Hydrocarbon	Leaded[a]	Unleaded[a]	Super Unleaded[a]
· n-Alkanes			
C_5	2.2	3.0	1.9
C_6	11.0	11.6	12.9
C_7	2.3	1.2	0.2
C_8	0.8	0.7	0.4
C_{10}-C_{13}	0.6	0.8	0.2
· Branched Alkanes			
C_4	1.6	2.2	1.2
C_5	17.3	15.1	8.6
C_6	9.7	8.0	6.2
C_7	2.7	1.9	1.4
C_8	2.0	1.8	8.7
C_9	2.7	2.1	1.2
C_{10}-C_{13}	0.5	1.0	1.1
· Cycloalkanes			
C_6	3.9	3.0	3.0
C_7	1.0	1.4	0.2
C_8	0.6	0.6	0.2
· Olefins			
C_6	1.1	1.8	1.0
· Aromatics			
Benzene	3.9	3.2	4.4
Toluene	4.5	4.8	6.0
Xylenes	5.6	6.6	7.4
Ethylbenzene	1.2	1.4	1.4
C_9-benzenes	3.4	4.2	5.7
C_{10}-benzenes	5.6	7.6	5.8
Others	2.0	2.7	1.6
· Unknowns	7.8	6.6	13.8

a) Reference 2320

TABLE 65-2
GASOLINE ADDITIVES[a]

Anti-Knock Compounds (leaded gasoline)

Tetraethyl lead (TEL)[b]
Tetramethyl lead (TML)
Methylcyclopentadienyl manganese tricarbonyl (MMT)

Lead Scavenging Agents

Ethylene dibromide (EDB)[b]
1,2-Dichloroethane

Octane Enhancers (unleaded gasoline)

Methyl t-butyl ether (MTBE)
t-Butyl alcohol (TBA)
Ethanol
Methanol

Antioxidants

N,N′-Dialkylphenylenediamines
2,6-Dialkyl and 2,4,6-trialkylphenols
Butylated methyl, ethyl and dimethyl phenols
Triethylene tetramine di(monononylphenolate)

Metal Deactivators

N,N′-Disalicylidene-1,2-ethanediamine
N,N′-Disalicylidene-propanediamine
N,N′-Disalicylidene-cyclohexanediamine
Disalicylidene-N-methyl-dipropylene-triamine

Ignition Controllers

Tri-o-cresylphosphate (TOCP)[b]

Icing Inhibitors

Isopropyl alcohol

TABLE 65-2 - (Cont.)
GASOLINE ADDITIVES[a]

Detergents/Dispersants
Alkylamine phosphates
Poly-isobutene amines
Long chain alkyl phenols
Long chain alcohols
Long chain carboxylic acids
Long chain amines
Corrosion Inhibitors
MIL-I-25017/QPL-25017[c]
Carboxylic acids
Phosphoric acids
Sulfonic acids

a) References 1409, 2325, 2326, 2327, 2328, 1847
b) Compounds addressed in other chapters of IRP Toxicology Guide
c) As cited in 2328

65.2 ENVIRONMENTAL FATE AND EXPOSURE PATHWAYS

In this chapter, the discussions of the environmental behavior of gasoline will be limited to a discussion of its major components; the environmental behavior of the trace elements and the many diverse additives will not specifically be addressed. Many of the hydrocarbons characteristics of gasoline have been addressed previously in the more extensive environmental fate section of the JP-4 chapter since these hydrocarbons are common to both petroleum fuels. The general discussions of aliphatic and aromatic hydrocarbons and their behavior in soil/ground-water systems will not be repeated here; the reader is referred to the relevant sections of the JP-4 chapter.

Transport and transfo nation of individual gasoline constituents will depend on the physicochemical (and biological) properties of the constituents. Some constituents will dissolve more quickly (in the percolating ground-waters), be sorbed less strongly on the soils (thus being transported more rapidly), and may be more or less susceptible to degradation by chemical or biological action. The relative concentrations of the constituents of the fuel will vary with time and distance from the site of contamination. This effect is called "weathering." (This term is also used to describe the changes to oil following spills into surface waters where film spreading

and breakup, and differential volatilization, dissolution and degradation are all involved.)

65.2.1 Transport in Soil/Ground-water Systems

65.2.1.1 Equilibrium Partitioning Model

In general, soil/ground-water transport pathways for low concentrations of pollutants in soil can be assessed by using an equilibrium partitioning model. For the purposes of assessing the environmental transport of automotive gasoline, a group of specific hydrocarbons was selected from the dominant hydrocarbon classes, i.e., alkanes, cycloalkanes, and aromatics. These specific compounds were chosen on the basis of their relative concentrations, and were intended to span the boiling point average of the gasoline hydrocarbons. Table 65-3 identifies the selected hydrocarbons and presents the predicted partitioning of low soil concentrations of those hydrocarbons among soil particles, soil water, and soil air. The portions associated with the water and air phases of the soil are expected to have higher mobility than the adsorbed portion.

Estimates for the unsaturated topsoil indicate that sorption is expected to be an important process for all the dominant hydrocarbon categories. Partitioning to the soil-vapor phase is also expected to be important for the lower molecular weight aliphatic hydrocarbons (C_4 - C_8), which are characterized by high vapor pressure and low water solubility. The alkyl benzenes have higher water solubilities and transport with infiltrating water may be important for these compounds; volatilization, on the other hand, may be less important. In saturated, deep soils (containing no soil air and negligible soil organic carbon), a significant percent of both aliphatic (particularly less than C_7) and aromatic hydrocarbons is predicted to be present in the soil-water phase and available for transport with flowing ground-water.

In interpreting these results, it must be remembered that this model is valid only for low soil concentrations (below aqueous solubility) of the components. Large releases of gasoline (spills, leaking underground storage tanks) may exceed the sorptive capacity of the soil, thereby filling the pore spaces of the soil with the fuel. In this situation, the hydrocarbon mixture would move as a bulk fluid and the equilibrium partitioning model would not be applicable.

Overall, ground-water underlying soil contaminated with gasoline hydrocarbons is expected to be vulnerable to contamination by at least some of these components. The type of spill (surface vs. sub-surface) is of particular importance, since volatilization from the surface is expected to be a significant removal process for low molecular weight aliphatics. At this point, it should be mentioned that environmental fate/exposure/toxicology chapters for several of the components in Table 65-3 are

TABLE 65-3
EQUILIBRIUM PARTITIONING OF SELECT
GASOLINE HYDROCARBONS IN MODEL ENVIRONMENTS[a]

				UNSATURATED TOPSOIL %			SATURATED DEEP SOIL[d] %	
COMPOUND	Log K_{aw}	K_{aw}[b]	H[c]	Soil	Water	Air	Soil	Water
Hexane	3.90[f]	3,830	1.68	77.5	0.1	22.4	94.1	5.9
Isopentane	3.37[f]	900	1.36	50.3	0.3	49.4	79.1	20.9
Methylpentane	3.90[f]	3,830	1.69	77.6	0.1	22.3	94.1	5.9
Trimethylpentane	4.87[f]	36,000	1.9-3.3	94.7	0.01	5.3	99.3	0.7
Cyclohexane	3.44[e]	1,330	0.18	91.6	0.4	8.0	84.8	15.2
Benzene	2.13[e]	65	5.43E-03	88.1	7.1	4.8	21.4	78.6
Toluene	2.69[g]	240	6.6E-03	96.5	1.9	1.6	52.1	47.9
Xylenes	3.16[e]	700	7E-03	98.8	0.7	0.5	74.4	25.6
Trimethylbenzenes	3.65[h]	2,150	5E-03	99.6	0.2	0.2	90.2	10.0
Naphthalene	3.30[f]	962	4.82E-04	99.4	0.5	0.03	80.2	19.8

a) Calculations based on Mackay's equilibrium partioning 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) Reference 652
c) Taken from Reference 74 unless otherwise specified. Units equal atm · m^3/mol.
d) Used sorption coefficient $K_p = 0.001 \times K_{aw}$.
e) Reference 29.
f) Arthur D. Little, Inc., estimate according to equations provided in Reference 31.
g) Reference 10.
h) Reference 31.

included in other sections of the IRP Toxicology Guide. The gasoline components addressed include: benzene, toluene, xylenes, ethyl benzene, and naphthalene. Major gasoline additives (TOCP, tetraethyl lead, ethylene dibromide, and ethylene dichloride) are addressed in other sections of the IRP Toxicology Guide.

65.2.1.2 Transport Studies

Hundreds of thousands of underground gasoline storage tanks are currently used at service stations, commercial locations, residences, and petroleum depots; and almost all the gasoline used for transportation purposes in the U.S. is stored underground at least once before its intended use. Since it is possible for one gallon of gasoline containing 1% benzene by volume to contaminate 10 million liters (2.69 million gallons) of water to the drinking standard of 1 ppb, underground gasoline storage tanks are a major environmental concern (2320).

Many authors have documented ground-water contamination as a result of hydrocarbon spills. For example, Osgood (2322) reported over 200 hydrocarbon spills in Pennsylvania in a 2.5-year period; in that time, 14 public water supplies were polluted or threatened, 104 wells seriously damaged, and one spill resulted in the subsurface discharge of over 270,000 gallons of gasoline. Matis (2323) reported over 60 cases of ground-water contamination in Maryland from 1969 to 1970. Drinking water contamination caused by gasoline migration and subsequent penetration of a subsurface water supply line has also been reported (2321); the most serious contaminant was ethylene dibromide (EDB), a gasoline additive. EDB has been reported to be present in leaded gasoline in sufficient quantities to constitute a threat to ground-water following a gasoline discharge to the environment (2320).

Due to the extensive use of gasoline and its potential for environmental release during use, storage or transport, several groups have addressed its fate. The fate of gasoline in the soil environment is basically a function of the solubility, volatility, sorption, and degradation of its major components. The relative importance of each of these processes is influenced by the type of contamination (e.g., surface spill vs. underground release, major vs. minor quantity), soil type (e.g., organic content, previous history of contamination), and environmental conditions (e.g., pH, temperature, oxygen content).

Transport processes have been shown to be more significant than transformation processes in determining the initial fate of petroleum hydrocarbons released to soil/ground-water systems (1845, 1848, 1846). For gasoline released to surface soils or waters, transport to the atmosphere through volatilization is expected to be the primary fate pathway; subsequent atmospheric photolysis is expected to be rapid (1845). Spain et al. (1846) demonstrated that compounds having up to nine carbons are weathered almost exclusively by evaporation; larger compounds were weathered primarily by evaporation and biodegradation. Composition data for gasoline vapor indicate that C_4 - C_6 aliphatic hydrocarbons are rapidly volatilized (2324).

Under conditions of limited volatilization (low temperatures, subsurface release or concentrated spill) downward migration into the soil and to the ground-water may be important. Several authors (1811, 2243, 2252, 2329) have reported that oil substances released in significant quantities to soils result in a separate organic phase that moves downward through the unsaturated zone to the less permeable layer, the soil/ground-water boundary, where they tend to accumulate and spread horizontally.

Some residual gasoline is left behind in the area through which the gasoline has percolated; the residue tends to be more concentrated in fine sand than in the coarser materials (2329). Solubilized gasoline components may leach from residually contaminated soils for long periods of time. Induced soil venting has been demonstrated to be a rapid and efficient method for removal of gasoline trapped in soils following a spill or leak (2320). The importance of subsurface volatilization of gasoline components has also been demonstrated in an article by Yaniga (2330). Volatilization of gasoline components from residual contamination and contamination accumulated at the ground-water interface resulted in detection of gasoline vapors in nearby basements.

The organic layer floating on the ground-water is carried in the general direction of ground-water flow. At the oil-water interface, some hydrocarbons are leached according to their aqueous solubility. The pollution caused by the hydrocarbon phase is much less extensive (10s-100s of meters) than pollution caused by hydrocarbons dissolved in ground-water (100s-1000s of meters) (1811). Furthermore, the pattern of migration of the hydrocarbon phase may be very different from that of the ground-water. Due to fluctuations in ground-water elevation over time, the organic layer on top of the aquifer may be transported into several zones where the components occur in the gaseous phase (able to diffuse in all directions, including upward), liquid phase (adsorbed onto rock particles or sealed under water) or dissolved/emulsified in water (1811, 2329).

Migration through soils may be retarded to a minor extent by sorption. Migration is expected to be fastest through previously contaminated soils where the sorptive sites may be unavailable: on the other hand, soil-water content increases sorption and slows migration of hydrocarbons. In fissured rock, the migration of hydrocarbons is much less uniform than in porous soils. Preferential spreading through crevices, sometimes changing the direction of flow, may occur. Determination of the potential ground-water contamination in fissured rock is thus very difficult (1811).

The water-soluble portion of gasoline was shown to be almost entirely aromatic (87-94%), even though the product itself was almost 50% aliphatic; the aliphatic hydrocarbons either volatilized or were essentially not water-soluble (1849). In deep, saturated soils with no soil air, some low molecular weight aliphatics may be dissolved in and transported with ground-water; however, the light aromatics represent the greatest threat of contamination to ground-water supplies.

In summary, the physical distribution of gasoline contamination affects its impact on, and removal from, the soil environment. Lateral spreading along the surface increases the initial contaminated area while facilitating evaporative removal of the low molecular weight hydrocarbons. Subsurface release or vertical penetration mediated by gravitation and capillary forces decreases evaporation, reduces the importance of some transformation pathways (see below), and may lead to ground-water contamination.

65.2.2 Transformation Processes in Soil/Ground-water Systems

65.2.2.1 Chemical Transformation

No data were available on chemical transformation of gasoline in the environment. However, as discussed in Chapter 64, photooxidation has been reported to play a significant role in the chemical degradation of some petroleum hydrocarbons in the environment (1845, 1848, 2252, 2259). Alkanes, benzenes, and mono-substituted benzenes have been shown to be relatively resistant to photolysis in aqueous systems; xylenes photolyzed slowly while trisubstituted benzenes and naphthalenes photolyzed at rates competitive with volatilization (1845). Penetration of oil below the soil surface limits exposure to solar radiation while extensive lateral spreading of oil over impermeable or rocky surfaces may promote substantial photooxidative degradation. The oxygenated products of photooxidation are generally more water-soluble than the parent hydrocarbons and are thus more likely to be leached from soil; enhanced toxicity of the oxygenated hydrocarbons has also been observed (2248, 2252).

65.2.2.2 Biological Degradation

Natural ecosystems have considerable exposure to petroleum hydrocarbons from natural emissions, accidental contamination through oil spills and storage tank leaks, and deliberate application to land in disposal activities such as land-farming waste; therefore, their biodegradation is of environmental importance. Numerous authors have observed the biodegradation of petroleum hydrocarbons, and several extensive reviews and reports are available (1846, 2252, 2255, 2249, 2253). An extensive and diverse group of petroleum hydrocarbon-degrading bacteria and fungi are widely distributed in the environment. The reader is referred to the chapter on JP-4 for a more detailed summary of the biodegradation of petroleum hydrocarbons.

The qualitative hydrocarbon content of petroleum mixtures largely determines their degradability. In general, microorganisms exhibit decreasing ability to degrade aliphatic hydrocarbons with increasing chain length. n-Alkanes are considered more easily biodegraded than branched or cyclic alkanes; aromatics are generally more rapidly biodegraded than alkanes. The composition of gasoline suggests that most of the aromatic species will be highly biodegradable, and many of the aliphatic species that are not volatilized will be moderately biodegradable. In a study of the biodegradation of individual components of gasoline using microorganisms isolated from ground-water, the aliphatics and aromatics were shown to be sources of carbon

for Nocardia and Pseudomonas cultures, respectively (2331). Very few of the remaining components supported bacterial growth; co-oxidation was suggested as a possible mechanism for removal of non-growth components.

Although the microbiota of most non-contaminated soils include many naturally occurring hydrocarbon-degrading populations, the addition of petroleum selectively enriches that sector able to adapt and utilize the new substrate. Other environmental factors shown to have a major effect on biodegradability are availability of oxygen and moderate temperatures.

In summary, biodegradation of the petroleum hydrocarbons comprising automotive gasolines is expected to be rapid under conditions favorable for microbial activity and when fuel components are freely available to the microorganisms. Degradation may be limited and/or slow in environments with few degrading organisms, low pH, low temperatures, and high salinity (e.g., arctic environments). It should be mentioned that Walker et al. (2257) state that even under optimum conditions, total and complete biodegradation is not expected to occur except possibly over an extremely long time period.

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

The above discussion of fate pathways suggests that the major components of gasoline are highly volatile but vary in their potential for bioaccumulation and tendency to sorb to soil. They range from moderately to strongly sorbed to soil, and their bioaccumulation potential ranges from low to high. The variability in the properties of the components suggests they may have somewhat different potential exposure pathways.

Spills of gasoline would result in the evaporative loss of the more highly volatile components leaving those of lesser volatility in the soil. The fraction remaining in the soil is expected to be relatively mobile and will be carried by gravity to the saturated zone of the soil. There, the more soluble components will dissolve into the ground-water or form emulsions with it. These components are primarily aromatic and lower molecular weight aliphatic compounds; in one study using unleaded gasoline, approximately 95% of the water soluble fraction was benzene and substituted benzenes (2318). The insoluble fraction of gasoline floats as a separate phase on top of the water table.

The movement of gasoline dissolved in ground-water is especially important because of its relative solubility (173-200 mg/L (2287, 2297)). Furthermore, the movement of dissolved hydrocarbons in ground-water is much greater than that of the separate liquid phase, reaching distances of hundreds to thousands of meters compared to tens of meters for the movement of the separate phase. In the presence of cracks and fissures, however, the flow of the separate hydrocarbon phase is greatly enhanced. The movement of gasoline in ground-water may contaminate drinking water supplies, resulting in ingestion exposures. Ground-water discharges to surface water or the movement of contaminated soil particles to surface water

drinking water supplies may also result in ingestion exposure and in dermal exposures from the recreational use of these waters. The potential also exists for the uptake of some gasoline components (e.g., naphthalene and methylnaphthalene) by fish and domestic animals, which may also result in human exposures due to the bioconcentration of these components.

Ground-water contaminated with gasoline can lead to inhalation exposures in homes using this water. In one study of homes in Maine (2313), concentrations of total benzene, toluene and xylene measured in air of the closed bathrooms while hot showers were running were 2.05, 3.15, and 30 ppm in homes with 5, 3, and 20 ppm, respectively, of total hydrocarbons in their water. In the two homes with the highest total concentrations, xylene accounted for roughly 63% of the concentration in air, toluene 29-32% and benzene 5-9%; in the other home 95% was benzene, the rest toluene. The author of this study suggested that odor may be a sensitive indicator of gasoline contamination in water. In the houses with high hydrocarbon contamination, an offensive odor was noticeable, especially during sampling (2313). Even though no benzene, toluene or xylene was detected in the air of three homes with less than 0.5 ppm total hydrocarbons in their water, in two of these homes gasoline odors were present in the bathroom. However, a modelling study (2314) indicates that petroleum-based pollutants (benzene, toluene, xylene) present in water at 5 to 50 ppb -- levels below detectable taste or odor threshholds -- may result in peak air concentrations that cause mucous membrane irritation.

Volatilization of gasoline hydrocarbons in soil is another potential source of human exposure. This exposure pathway is likely to be more significant for gasoline than other petroleum products because of its high volatility. Exposures may be more intensive when the soil is contaminated directly from leaking underground storage tanks and pipes, rather than from surface spills. In such cases, the more volatile components do not have an opportunity to evaporate before penetrating the soil. Once in the soil, the hydrocarbons evaporate saturating the air in the soil pores, and diffusing in all directions including upward to the soil surface. The vapors may diffuse into the basement of homes or other structures in the area resulting in inhalation exposures to the building's occupants.

65.2.4 Other Sources of Human Exposure

Data on ambient concentrations of gasoline in air and water as well as food and drinking water are not readily available in the literature. Exposure information on specific components may be found in other chapters of the IRP Toxicology Guide.

The volatile nature of automotive gasoline suggests that inhalation may represent a significant exposure pathway. The average concentrations of automotive gasoline to which residents of communities near bulk terminals, bulk plants, and service stations (employing no special controls) are exposed have been estimated as 1.41, 0.073, 0.026 ppm, respectively (2311). It should be emphasized that these values are averaged over a lifetime and in all cases the concentrations are estimated from emission rates. Exposure to service station employees and individuals filling their tanks at self-service

operations are much higher. At one high-volume station, the mean concentration to which an individual filling his own tank of gas was exposed (for ten minutes) was 4.2 ppm (2283). In a study of gasoline vapor exposures at a single-island service station in Raleigh, North Carolina, the exposure during refueling was predominantly to volatile C_4 and C_5 hydrocarbons (3074).

65.3 HUMAN HEALTH CONSIDERATIONS

65.3.1 Animal Studies

65.3.1.1 Carcinogenicity

Most of the evidence regarding carcinogenicity of gasoline has been provided in a study conducted by MacFarland et al. (3616) for the American Petroleum Institute (API). Reports of this study appear in several forms throughout the literature. A chronic inhalation study of gasoline vapor was conducted in mice and rats; the gasoline employed was unleaded, with the benzene content adjusted to 2%. Groups of both sexes of $B6C3F_1$ mice and Fischer 344 rats were exposed to gasoline vapor at concentrations of 67, 292 or 2056 ppm for 6 hours per day, 5 days per week for periods ranging from 103 to 113 weeks. After as little as three months of exposure to 2056 ppm, macroscopic lesions were evident in the kidney of male rats. Microscopic observations included an increased incidence of renal disease with tubular degeneration, regeneration or cystic dilatation among males exposed to 292 or 2056 ppm. At 24 months, an increase in the occurrence of primary renal neoplasm was seen in the male rats at all doses, with some evidence of a dose-response relationship. In addition, a compound related increase in liver nodules and masses was seen in female mice exposed to the intermediate and high concentrations. Histopathologic examination revealed primary hepatocellular tumors (adenomas and carcinomas) in these animals.

These unexpected findings of species and sex-specific carcinogenic effects were not evident until late in the study. To better understand the significance to human health, the American Petroleum Institute contracted with Universities Associated for Research and Education in Pathology, Inc. (UAREP) for assistance in interpretation of the findings. The UAREP reviewed the chronic inhalation study, "old rat nephropathy" syndrome, and the basic morphological and functional similarities and differences in the kidneys of the rat, mouse, and man (2299). This review concluded that the significance of the hepatocellular carcinoma in female mice was questionable. The UAREP felt that other studies on different hydrocarbons demonstrated acute toxic effects on the female liver including fatty metamorphosis, whereas these effects were not reported in the API chronic inhalation study.

The finding of renal carcinoma in male rats was clearly significant. The lesions were seen as early as 90 days and were dose-related. The lesions could be clearly distinguished from the old rat nephropathy, which is composed of chronic lesions involving all components of the kidney. However, administration of unleaded gasoline

appeared to accentuate all the lesions characteristic of old rat nephropathy. It was not possible to evaluate the potential role of the superimposed old rat nephropathy on the initiation, development, and progression of renal neoplasia induced by unleaded gasoline. Thus the UAREP review concluded that:

> "The chronic inhalation study demonstrated that unleaded gasoline inhalation produced acute, subchronic and chronic toxicity in the kidneys of male rats. Simultaneously,there was the development of preneoplastic lesions and ultimately the appearance of adenomas and adenocarcinomas in these male rats. The link between acute and chronic toxicity and carcinogenicity is not clear, nor can it (be) determined from the data generated in this bioassay. Although the pattern of acute and chronic non-neoplastic toxic lesions is somewhat unique for gasoline- related hydrocarbons, the morphological appearance of the preneoplastic and neoplastic lesions is similar to that produced by a number of renal carcinogens."

Based on an evaluation of this chronic inhalation bioassay conducted by MacFarland et al. (3616), the USEPA (3471) concluded that there is sufficient evidence to conclude that gasoline vapors are carcinogenic in animals.

65.3.1.2 Genotoxicity

Limited studies of unleaded gasoline have shown conflicting results. Unleaded gasoline failed to induce reversion in the Ames Salmonella plate or suspension assays performed with and without metabolic activation (2300, 3391). In a test for the induction of somatic mutations, Nylander et al. (3528) fed Drosophila larvae 1.0 and 2.5% gasoline (petrol) and found a significant increase in mutations affecting the adult eye.

In cytogenetic studies, no chromosomal abnormalities were seen in the bone marrow of rats treated intraperitoneally with unleaded gasoline (2300, 3391), nor were sister chromatid exchanges increased in human lymphoblasts treated in vitro (2301). When unleaded gasoline was tested in the L5178Y mouse lymphoma assay (3391) and in a similar assay employing a human lymphoblastoid line (2301), no increase in mutation frequency was observed in either system.

A dose-related increase in unscheduled DNA synthesis (UDS) was observed in rat hepatocytes treated in vitro with 0.05 to 0.10% (v/v) gasoline, whereas these doses were toxic in both mouse and human hepatocyte cultures (3408). Weak UDS activity was observed in hepatocytes isolated from male and female mice treated 12 hours previously by gastric intubation with 2 g unleaded gasoline/kg (3408). Because unleaded gasoline induces kidney tumors, Loury et al. (3407) treated rat kidney cells in vitro and rats in vivo and did not observe an increase in unscheduled DNA synthesis in these cells.

Unleaded gasoline did not induce dominant lethal mutations in sperm cells of CD-1 male mice (2300). The mice were exposed to gasoline vapors for 6 hours per

day, five days per week for eight weeks prior to mating with untreated females. Doses of 400 ppm and 1600 ppm did not cause any significant reduction in the fertility of the treated males, nor was any significant increase in pre- or post-implantation loss of embryos noted. It should be noted; however, that deaths occurred among the treated males during the treatment period (the cause and significance are unknown).

65.3.1.3 Teratogenicity, Embryotoxicity and Reproductive Effects

The American Petroleum Institute reported that rats exposed by inhalation to 400 or 1600 ppm of unleaded gasoline on gestational days 6-15 gave negative results in a teratology study (3627).

65.3.1.4 Other Toxicologic Effects

65.3.1.4.1 Short-Term Toxicity

Gasolines generally act as anesthetics. They are also mucous membrane irritants (2). An oral LD_{50} of 13.6 g/kg was reported in the rat for unleaded gasoline. A single dose of 18 g/kg produced 90% mortality. A significant degree of gastrointestinal distress was observed. Necropsy revealed hemorrhagic gastroenteritis, gastrointestinal tympani and pneumonia with abscess formation (1924).

Acute anesthetic and toxic effects of gasoline vapors were studied as early as 1921 in dogs. Central nervous system effects were observed at approximately 10,000 ppm, and death at about 25,000 ppm (2290).

Toxicity of a gasoline component mixture was evaluated in a short-term inhalation study performed by Halder et al. (2292). A blend consisting of 25% (w/w) each of n-butane, n-pentane, isobutane and isopentane was vaporized to more closely approximate ambient exposure (in contrast to complete volatilization). Rats exposed to 44, 432 or 4437 ppm of vapor for 6 hours per day, 5 days per week for 3 weeks showed no clinical signs of distress. No gross or histopathologic lesions were noted, including in the kidneys. All other parameters of body and organ weights, hematology or blood chemistry were within normal range.

Studies on the acute effects of gasoline ingestion by rats revealed nephrotoxicity in male rats. Olson et al. (3535) provided male Fischer 344 rats with 0.04 to 2.0 mL/kg body weight of unleaded gasoline by intragastric intubation once daily for 9 days. The unleaded gasoline caused reversible hyaline droplet formation (protein resorption) in the proximal convoluted tubules of the kidneys. This effect was believed to be due to a hydrocarbon-induced defect in the degradation of renal alpha2u-globulin, a protein synthesized in the liver and excreted in urine, and was obvious after a single administration of 2 mL/kg unleaded gasoline (3535). Shale-derived distillate fuel has also been shown to produce this effect (2294). Over a three day period, hepatic lesions and alterations in serum chemistry and hematology

were noted. By fourteen days, lymphoid depletion in the thymus was observed, as was congestion of multiple organs (2294).

Unleaded motor gasoline was slightly irritating to the shaved skin of New Zealand rabbits after a 24 hour dermal exposure to 0.5 mL. In a subacute dermal study, doses of 2.5 to 8 mL/kg were applied daily for a total of 10 days. No mortality was seen. Severe dermal irritation and weight loss were observed. Necropsy revealed pale and congested livers and kidneys (1924).

Gasoline containing tetraethyl lead caused no more injury than gasoline alone when applied to rabbit eyes. A single drop applied without local anesthetic caused discomfort and blepharospasm lasting several minutes. The conjunctiva became mildly hyperemic but rapidly returned to normal. Ten drops applied during a 5 minute period (after local anesthesia) caused blepharospasm lasting 15 minutes. The conjunctiva became moderately edematous and hyperemic but recovery was prompt and complete (19).

65.3.1.4.2 Chronic Toxicity

To evaluate the long-term effects of gasoline inhalation, rats and monkeys were exposed to either 284 or 1552 ppm unleaded gasoline vapors or 103 and 374 ppm leaded gasoline vapor 6 hours per day, 5 days per week, for 90 days (2290). Although vomiting was noted in certain monkeys after 2 weeks exposure, no remarkable changes in body weight, hematology, or CNS responses were noted in either species. Lead deposition in the liver, kidney, brain and blood were observed in those animals treated with leaded gasoline. Upon histopathologic examination, male rats exposed to 1552 ppm unleaded gasoline displayed regenerative epithelium and dilated tubules in the kidney.

Pulmonary changes in rats exposed to leaded gasoline vapor were reviewed by Cooper (2296). Changes in male rats ranged from minor foci of interstitial fibrosis to widespread sclerosis after 6 weeks exposure to 100 ppm. After eight weeks, tachypnea and prostration were evident. Such observations were confirmed in female rats similarly exposed. Ultrastructural changes emerged sequentially as degeneration, hypertrophy and/or hyperplasia and finally development of interstitial sclerosis and irregular alveolar collapse. A number of these changes are thought related to the fact that gasoline vapor inhalation caused a decrease in pulmonary surfactant. Surfactant, functioning to decrease surface tension and stabilize surface forces, was reduced after only 5 days exposure.

Repeated exposure of albino rabbits eyes to gasoline vapor levels of 3 mg/L air daily for 10 months has been reported to cause histologically recognizable disturbances of the corneal and conjunctival epithelium. Exposure to a vapor level of 616 ppm of a C_9 - C_{10} fraction of a high octane motor fuel induced cataracts in 70% of exposed rats. Exposure was for a total of 2424 hours. The petroleum fraction was composed mainly of alkyl benzenes. It contained no naphthalene, a known inducer of cataracts in animals (19).

Other changes seen in animals after chronic gasoline inhalation include a depression in body weight in rats and mice, a reduction in the incidence of cystic or enlarged uteri of female mice, and mild multifocal, dose-related pulmonary inflammation in rats (2298).

65.3.2 Human and Epidemiologic Studies

Before reviewing the adverse effects of gasoline on humans, it is important to note that human exposure is considerably different from that used in animal studies. Due to the differential volatility of the hydrocarbon compounds present in gasoline, the vapor produced under experimental conditions does not mimic ambient vapor composition. The animals are exposed to completely volatilized gasoline whereas human exposure is to partial volatilization. The larger hydrocarbons, which are less volatile, are present in lower proportion in ambient vapors than in completely volatilized gasoline. Thus, since certain subsets of the higher molecular weight compounds are thought to be responsible for nephrotoxicity, it is likely that the animal studies overestimate the toxic effect in humans.

65.3.2.1 Short-term Toxicologic Effects

The primary mode of exposure to gasoline is by inhalation. The most common symptoms of intoxication are headaches, blurred vision, dizziness and nausea (2). Most of the adverse physical effects in humans have been documented by cases of intentional gasoline inhalation or "sniffing." Absorption of the volatile components across the lungs is generally rapid and quite efficient. Levels as low as 500-1000 ppm for 30 to 60 minutes can result in an euphoric condition consisting of ataxia (decreased muscle coordination), drowsiness and dizziness. Increased levels (1000-3000 ppm) lead to irritation, headache, nausea, and vomiting. Levels in excess of 5000 ppm can cause dizziness or deep anesthesia within minutes, and occasionally coma and death are reported (2277, 2284). In general, the euphoria, lethargy and decreased sensory perception last several hours after exposure (2280). The intoxicating feeling is believed to be due to the neurotoxic effects of n-hexane and the narcotic properties of the C_4 to C_8 saturated hydrocarbons (2277).

Deaths from gasoline sniffing have rarely been reported. In a study of 110 "sudden sniffing deaths" occurring during the 1960's, 3.6% were thought to be associated with gasoline inhalation. Sudden death has been reported in an adolescent who exercised after inhaling gasoline fumes while siphoning gasoline from a car. Death was presumably from a cardiac arrhythmia induced by the fumes (1570).

Symptoms in severe oral intoxication are mild excitation, loss of consciousness, occasional convulsions, cyanosis, congestion and capillary hemorrhaging of the lung and internal organs, followed by death due to circulatory failure. In mild cases, symptoms include inebriation, vomiting, vertigo, dizziness, confusion and fever (12). In adults, ingestion of 20-50 g may produce severe poisoning. One case of accidental ingestion caused immediate severe burning of the pharynx and gastric region. After

immediate gastric lavage, no general symptoms were noted. Liver function tests were slightly elevated, indicating hepatic damage, which was probably due to gasoline's lipid solubility. Another case of accidental ingestion of gasoline presented with nausea, abdominal cramps and red-brown urine. Upon further investigations, acute reversible toxic injury was found to the upper portions of both kidneys (2278). It should be noted that ingestion can be accompanied by aspiration. This can lead to chemical injury, irritation to the lung and mucosal surfaces and generalized chemical pneumonitis. Symptoms are lethargy, moderate respiratory distress with laboratory confirmation of leukocytosis and increased serum levels of liver enzymes. Hypoxemia (low blood oxygen levels) accompanying aspiration pneumonitis accounts for the CNS manifestation, not direct CNS toxicity of the gasoline. Most symptoms are reversible within 48 hours (2279).

Dermal exposure to gasoline vapor and liquid is also possible. Considering the physical/chemical properties of the volatile components, they should be readily absorbed through the skin (2286). Liquid gasoline is irritating to the skin. Prolonged contact causes a chemical burn (2228). Hypersensitivity may develop in certain individuals (54).

Exposure of volunteers to gasoline vapors indicated no ocular irritation at a concentration of 140 ppm. Irritation of the eyes and throat was seen at vapor levels of 270 to 900 ppm. If splashed into the eye, pain and irritation occurs, but there is only slight, transient corneal epithelial disturbance (19).

65.3.2.2 Chronic Toxicologic Effects

The possible long-term effects of chronic inhalation of gasoline have been reported as anorexia, weight loss, weakness and cramps (2284). The neurological and encephalopathic effects seen in severe cases include incoordination and tremors; however, these effects appear reversible with therapy and cessation of exposure (1570). Post-mortem findings of gasoline sniffers frequently show cerebral and pulmonary edema; if death is delayed, necrosis of the liver and kidney is evident. The minor components of gasoline such as benzene, xylene and tetraethyl lead contribute more to these chronic effects than do the aliphatic hydrocarbons (2284, 2277).

Hunter et al. (2282) conducted a study on a community of 500 American Indians with prevalent gasoline abuse. The results showed increased mean blood levels (specific components not reported) in women and fetuses and a high incidence of mental retardation (4% of live births). This study suggested that the retardation was due to prenatal exposure to organic lead present in the gasoline vapors.

It has been clearly demonstrated that hydrocarbon fuels induce nephrotoxicity and renal carcinogenicity in male rats. It has also been shown that unleaded gasoline induces hepatocellular carcinomas in female mice. However, these agents have failed to produce significant toxic or neoplastic changes in other major organs or in female rats. The mechanism responsible for the renal lesions in unknown at the present

time; however, research is currently underway to assess the role of the male rat-specific protein, alpha-2u-globulin, in the initial formation of hyaline droplets and tubular degeneration (3418). Because the etiology of this species- and sex-specific nephrotoxicity is unknown, the question remains as to whether exposure to hydrocarbon fuel vapors would produce similar effects in humans. The USEPA reviewed 55 epidemiologic studies to determine if an association existed between gasoline exposure and human cancer risk (3471). Collectively, the studies provided limited evidence that occupational exposure in the petroleum industry is associated with certain types of cancer; however, it was concluded that the evidence for evaluating the carcinogenic potential of gasoline is inadequate under USEPA guidelines. Consequently, based on sufficient evidence in animal studies and inadequate evidence in epidemiologic studies, the USEPA classified unleaded gasoline as a probable human carcinogen, EPA category B2.

65.3.3 Toxicology of Gasoline Components

A brief overview of the toxicology of the major hydrocarbon components of automotive gasoline (see Table 65-3) are summarized below. The acute toxicity values for these components are presented in Table 65-4.

n-Hexane

Hexane may be the most highly toxic member of the alkanes. When ingested, it causes nausea, vertigo, bronchial and general intestinal irritation and CNS effects. It also presents an acute aspiration hazard. Acute exposure occurs primarily through inhalation. Non-specific symptoms, such as vertigo, headache, nausea and vomiting are the first to be manifested. At high concentrations, a narcosis-like state appears as a result of CNS depression. Pre-narcotic symptoms occur at vapor concentrations ranging from 1500-2500 ppm. n-Hexane irritates the eyes and mucous membranes. These effects can be seen after an exposure of 880 ppm for 15 minutes. Skin contact primarily causes fat removal and cutaneous irritation.

Chronic exposure to n-hexane vapors causes peripheral neuropathy. The first clinical sign of neural damage is a feeling of numbness in the toes and fingers. Progression leads to further symmetrical sensory impairment in the distal portions of the extremities and to loss of muscular stretching reflexes. Ultimately, symmetrical muscular weakness develops, chiefly in the distal portion of the extremities. Paralysis develops with varying degrees of impaired grasping and walking. This may include muscular atrophy (sensorimotor poly-neuropathy). The development of electrophysiological changes parallels the severity of the clinical picture. In the most severe cases, nerve conductivity is neutralized. In some cases, cranial nerve involvement is also observed. After exposure ceases, recovery begins within 6 to 10 months in mild to moderate cases, but may take up to 3 years in serious cases. The threshold level at which neuropathy occurs has not been firmly established but symptoms have been observed in people exposed to concentrations ranging from 10 to 200 ppm for 9 to 12 months.

In animals, signs of narcosis are seen after mice are exposed to vapor levels of 16,000 ppm for 5 minutes. Death generally occurred at concentrations between 43,800 and 52,000 ppm after 9 to 119 minutes. The oral LD_{50} is cited as 24 mL/kg for 14-day-old rats and 49 mL/kg for young adult rats.

Long-term inhalation experiments in rats suggest that the first signs of neurotoxicity appear after they are exposed to levels of 200 ppm for 24 weeks. This higher threshold to induce neurotoxicity in animals may be due to differences in metabolism. Specifically, 2-hexanol is the chief metabolite in animals, while 2,5-hexanedione, which is neurotoxic, predominates in man. Chronic topical application of a solvent containing 35.2% n-hexane caused axonal swelling and myelin degeneration in chicks. No clinical signs were seen. Dosage was 1 g/kg/day for 64 days. In rabbits, topical application of 0.5 mL/day for up to 10 days caused redness, irritation and scab formation. N-hexane is neither carcinogenic or teratogenic. One in vivo study in rats that inhaled 150 ppm for 5 days found an increased number of chromosome aberrations in the bone marrow cells. No studies on mutagenicity, reproductive toxicity or carcinogenicity in man were found (12, 1930, 1935).

Isopentane

Isopentane is a CNS depressant. Effects may include exhilaration, dizziness, headache, loss of appetite, nausea, confusion, inability to do fine work, a persistent taste of gasoline and in extreme cases, loss of consciousness. Inhalation of up to 500 ppm appears to have no effect on humans. "Very high" vapor concentrations are irritating to the skin and eyes. Repeated or prolonged skin contact will dry and defat skin resulting in irritation and dermatitis. The LC_{50} in the mouse is estimated to be 1000 mg/L (12).

2-Methylpentane (isohexane, 3-methylpentane)

No physiological data are available but isohexanes are expected to be mucous membrane irritants and to have a low oral toxicity. Isohexanes are predicted to have narcotic properties and are documented to be cardiac sensitizers but are not expected to have neurotoxic properties (12).

Cyclohexane is a CNS depressant of low toxicity. Symptoms of acute exposure are excitement, loss of equilibrium, stupor and coma. Rarely, death results due to respiratory failure. The anesthesia, which is induced, is weak and of brief duration but more potent than that caused by hexane. The oral LD_{50} in rabbits ranges from 5.5 to 6.0 g/kg. Within 1.5 hours the animals exhibited severe diarrhea, widespread vascular damage and collapse. Degenerative lesions were seen in the heart, lung, liver, kidney and brain. A one-hour vapor exposure to 26, 752 ppm caused rapid narcosis and tremor and was lethal to all exposed rabbits. In mice, concentrations causing narcosis vary from 14,600 to 122,000 ppm.

TABLE 65-4
ACUTE TOXICITY OF COMPONENTS OF AUTOMOTIVE GASOLINE

Component	Oral LD_{50}	Dermal LD_{50}	LC_{50}
n-hexane	24-49 mL/kg [rat] (1935) 28,710 mg/kg [rat] (1937)	no data	33,000 ppm · 4 hr [rat] (1935)
octane	no data	no data	no data
dodecane	no data	no data	no data
isopentane	no data	no data	1000 mg/L [mouse] (12)
isooctane	no data	no data	no data
methylcyclopentane	no data	no data	no data
methycyclohexane	2250 mg/kg [rat] (47)	no data	no data
cyclohexane	29,820 mg/kg [rat] (1935)	no data	no data
benzene	3800 mg/kg [rat] (59) 4700 mg/kg [mouse] (47)	no data	10,000 ppm · 7 hr [rat] (47)
toluene	5000 mg/kg [rat] (47)	12,124 mg/kg [rabbit] (47)	5320 ppm · 8 hr [mouse] (47)
xylenes	4300 mg/kg [rat] (47)	no data	5000 ppm · 4 hr [rat] (47)
ethyl benzene	3500 mg/kg [rat] (47)	5000 mg/kg [rabbit] (59)	no data
trimethylbenzenes	no data	no data	18 mg/m^3 · 4 hr [rat] (47)
1-methyinaphthalene	1840 mg/kg [rat] (47)	no data	no data
2-methylnaphthalene	1630 mg/kg [rat] (47)	no data	no data

Cyclohexane is nominally absorbed through the skin although massive applications (>180.2 g/kg) to rabbit skin resulted in microscopic changes in the liver and kidneys and caused the death of all animals.

The danger of chronic poisoning is relatively slight because this compound is almost completely eliminated from the body. No toxic changes were seen in rabbits exposed to vapor levels of 434 ppm, 6 hours daily for 50 exposures, but some microscopic changes were seen in the liver and kidneys when the exposure was to 786 ppm for the same period.

In man, no systemic poisonings by cyclohexane have been reported. A vapor level of 300 ppm is somewhat irritating to the eyes and mucous membranes. It has been reported that cyclohexane may potentiate the toxic effects of TOCP but no additional details of this interaction are available (12, 17, 46, 54, 1937).

Benzene

The primary effects of benzene inhalation and ingestion are on the central nervous system (54). Benzene is carcinogenic in both animals and man. Several reports have established a relationship between benzene exposure and leukemia. For more information, refer to the chapter on benzene in the Installation Restoration Program Toxicology Guide.

Toluene

Toluene is a CNS depressant with a low toxicity. For more information, refer to the chapter on toluene in the Installation Restoration Program Toxicology Guide.

Xylenes

Acute exposure to high concentrations of xylene vapors may cause CNS depression. Both the liquid and the vapor are irritating to the eyes, mucous membranes and skin (46). The National Toxicology Program recently reported that there was no evidence of carcinogenicity of mixed xylenes in either mice or rats given daily doses ranging from 250 to 1000 mg/kg by gavage for 2 years (1939).

For more information, refer to the chapter on xylenes in the Installation Restoration Program Toxicology Guide.

Trimethylbenzenes

The trimethylbenzenes occur in 3 isomeric forms. The 1, 3, 5-isomer (mesitylene) and the 1, 2, 4-isomer (pseudocumene) are toxicologically similar. High vapor concentrations (5000-9000 ppm) cause CNS depression in animals. Loss of reflexes was seen in mice exposed to 8130-9140 ppm of the 1, 2, 4-isomer or 8130 ppm of the

1, 3, 5-isomer. Rats exposed to 1700 ppm of an isomeric mixture for 10-21 days had no adverse effects or fatalities.

The fatal intraperitoneal dose of the 1, 2, 4-isomer for the guinea pig is 1.788 g/kg, while the fatal dose of the 1, 3, 5-isomer by the same route is 1.5-2 g/kg for the rat. For the 1, 2, 3-isomer, an oral LD_{Lo} of 5000 mg/kg has been reported in the rat. Trimethylbenzene liquid is a primary skin irritant. Deposition into the lungs causes pneumonitis at the site of contact.

The only report of human exposure described symptoms of nervousness, tension, anxiety, asthmatic bronchitis, hypochromic anemia and changes in the coagulability of the blood. Vapor concentrations ranged from 10-60 ppm. Exposure was to a mixture containing 30% of the 1, 3, 5-isomer and 50% of the 1, 2, 4-isomer (2, 12).

Naphthalene

Ingestion or prolonged inhalation of naphthalene produces nausea, vomiting and disorientation. It is irritating to the skin and eyes and prolonged vapor exposure has led to cataract formation in humans (17). Hemolytic anemia is the most severe effect associated with naphthalene exposure, but this effect is seen predominantly in individuals with an enzyme deficiency (54).

Gasoline Additives

Additives used in automotive gasoline are listed in Table 65-2. The toxicological information that was available is outlined below.

Tetraethyl lead (TEL)

Acute exposure to TEL causes symptoms of headache, anxiety, insomnia, fatigue and appetite loss (38). The more severe effects are seizures and acute metabolic encephalopathy, which is characterized by hallucinations, disorientation, violence and paranoia (2277). The contribution of TEL to the short-term effects of gasoline inhalation is not clear. It is not known if the amount inhaled during a single episode of gasoline "sniffing" is sufficient to cause the hallucinations and behavioral changes caused by TEL alone or if TEL potentiates the short-term effects of other volatile hydrocarbons present in gasoline; however, the long-term effects are currently considered to be due to TEL (2277). The oral LD_{50} in the rat is 14 mg/kg (19). More information can be found in the chapter on TEL in the Installation Restoration Program Toxicology Guide.

Tetramethyl lead

Tetramethyl lead affects the nervous system in animals and causes signs of increased irritability. Although not documented, it is expected to produce psychosis, mania and convulsions in humans (46). In the rat, an oral LD_{50} of 109 mg/kg was reported (47). It is likely that intoxication by tetramethyl lead will be similar to that

caused by tetraethyl lead (46). Information on tetraethyle lead can be found in the chapter on that compound in the Installation Restoration Program Toxicology Guide.

Methylcyclopentadienyl manganese tricarbonyl (MMT)

In its concentrated form, MMT is highly toxic by all routes of exposure. The primary site of action in animals is the CNS, where the effects of MMT are similar to those caused by tetraethyl lead. The oral LD_{50} in the rat is 50 mg/kg. Human exposure data are limited. It is expected that when MMT is blended with fuels, it has a low order of toxicity.

Concentrated MMT penetrates the skin readily. When 5-15 mL was spilled on a worker's skin, nausea, headache and giddiness resulted in a 2-5 minute period; however, gasoline solutions are not as readily absorbed as the pure material (2, 1937, 1409).

Ethylene dibromide (EDB)

EDB is irritating to the eyes and mucous membranes. It also causes symptoms of CNS depression. Acute exposures have resulted in lung, liver and kidney damage (1745, 1759, 38, 54). EDB is carcinogenic in rodents by oral, inhalation and dermal routes (142, 1606, 1743, 1744). ACGIH has classified EDB as a suspected human carcinogen with a recommendation that exposure be avoided (3). The oral LD_{50} in the rat is 146 mg/kg (1759). More information can be found in the chapter on EDB in the Installation Restoration Program Toxicology Guide.

1,2-Dichloroethane

Acute ingestion or inhalation of 1,2-dichloroethane results in symptoms of CNS depression, gastrointestinal upset and systemic injury to the liver, kidneys and lungs (12). The oral LD_{50} in the rat is 670 mg/kg (47). More information can be found in the chapter on 1,2-dichloroethane in the Installation Restoration Program Toxicology Guide.

Methyl-t-butyl ether (MTBE)

In rats, an oral LD_{50} of 4 mL/kg was reported (1937). In recently conducted acute and subchronic tests, it was reported that MTBE caused a deepening of barbiturate sleep, a reduction of spontaneous motor activity and reduced performance connected with disturbances of the motor coordination system; however, the severity of these effects does not indicate serious toxic damage to the CNS. The study concluded that MTBE "does not even minimally increase the neurologic effects with respect to gasoline itself." The level of exposure or the species that were tested were not reported (2293).

t-Butyl alcohol

At high concentrations, t-butyl alcohol causes narcosis in animals and it is expected to cause the same effect in humans. Other than slight skin irritation, no effects have been reported from industrial exposure. The oral LD_{50} in the rat is 3500 mg/kg (46).

Ethanol

Ethanol is irritating to the eyes and mucous membranes. It is also a CNS depressant. The acute toxicity of ethanol is low for both animals and man. Overexposure causes ataxia, incoordination and drowsiness (2,46). An oral LD_{50} of 14 g/kg was reported for the rat (47).

Methanol

Methanol causes optic neuropathy and metabolic acidosis. Poisoning has occurred primarily from ingestion of adulterated alcoholic beverages. After ingestion there is a latency period of 18 to 48 hours after which exposed individuals develop symptoms of nausea, abdominal pain, headache and shortness of breath. Visual symptoms range from blurred or double vision to changes in color perception, constricted visual fields and complete blindness. Other symptoms of intoxication include dizziness, behavioral disturbances, neuritis and acidosis. The degree of acidosis has been found to parallel the severity of the poisoning. Evidence suggests that exposure to vapor concentrations of 200-375 ppm causes recurrent headaches and visual disturbances are seen at vapor levels of 1200-8300 ppm (2,46). An oral LD_{50} of 13 g/kg was reported in the rat (47).

Tri-ortho-cresyl phosphate (TOCP)

TOCP affects the spinal cord and peripheral nervous system. Symptoms of acute exposure, including nausea, vomiting, diarrhea and abdominal pain, are followed by a latent period of 3 to 30 days. At this time, there is muscle soreness, numbness of fingers, calf muscles and toes which progresses to foot and wrist drop. These effects are manifested after ingestion, inhalation or dermal absorption (54). An oral LD_{50} of 1160 mg/kg has been reported in the rat (47). More information can be found in the chapter on TOCP in the Installation Restoration Program Toxicology Guide.

Isopropyl alcohol

Isopropyl alcohol has moderate narcotic properties. Ingestion causes CNS depression and it is expected that sustained inhalation of high vapor concentrations will produce the same effect. It is also irritating to the eyes and mucous membranes (2, 46). An oral LD_{50} of 5840 mg/kg was reported for the rat (47).

65.3.4 Levels of Concern

The ACGIH (3005) recommends an occupational exposure limit of 300 ppm for automotive gasoline, with a short-term exposure limit of 500 ppm. The OSHA (3539) has established a 8-hr TWA of 300 ppm and a 15-min STEL of 500 ppm.

No other criteria or standards have been established with regard to human health and safety.

65.3.5 Hazard Assessment

A single study (3616) on the potential carcinogenic effects of gasoline is available. Mice and rats were exposed by inhalation to the vapors of unleaded gasoline (benzene content, 2%), 6 hours per day, 5 days per week for two years. Exposure levels ranged from 67 to 2056 ppm. Dose-related renal carcinomas were observed in gasoline-exposed male rats. The significance of the sex-specific and species-specific findings is unclear. Based on an evaluation of this chronic inhalation bioassay conducted by MacFarland et al. (3616), the USEPA (3471) concluded that there is sufficient evidence to conclude that gasoline vapors are carcinogenic in animals; however, there is inadequate evidence from epidemiologic studies. Therefore, the USEPA has classified unleaded gasoline as in Category B2, probable human carcinogen.

Mutagenicity studies suggest no genotoxic effects for unleaded gasoline (2301, 2300, 3391, 3408). Negative teratogenic findings were also reported (2228), although information is limited.

Animals studies indicate that kidney damage is the predominant toxic effect of acute ingestion and chronic inhalation exposure to unleaded gasoline (2290, 2294). Pulmonary changes (fibrosis and sclerosis) were also evident with inhalation exposure (2296).

Humans exposed via inhalation to 500-1000 ppm gasoline for 30 to 60 minutes develop ataxia, drowsiness and dizziness; levels of 1000-3000 ppm result in irritation, headache, nausea and vomiting; exposure to greater than 5000 ppm can cause deep anesthesia within minutes, and occasionally, coma and death (2277, 2284).

Ingestion of 20 to 50 g of gasoline may produce severe intoxication in adults (12). Symptoms of poisoning are similar to those noted above for inhalation exposures.

65.4 SAMPLING AND ANALYSIS CONSIDERATIONS

Determination of the presence of automotive gasoline in soil and water requires collection of a representative field sample and laboratory analysis for the specific major components attributed to gasoline; however, the relative concentrations of the

constituents, and even the constituents themselves, will vary with time and distance from the site of initial contamination due to weathering. The major component categories in automotive gasoline have been identified as the following:

n-alkanes
branched alkanes
cycloalkanes
benzene and alkylbenzenes
naphthalenes

Since many of the components are highly volatile, care is also required to prevent losses during sample collection and storage. EPA protocols for analysis of constituents within these classes dictate that the samples should be collected in airtight containers with no headspace. Analysis should also be completed within 14 days of sampling.

A combination of capillary column gas chromatography (GC) and gas chromatography/mass spectrometry (GC/MS) techniques may be used to identify the principal components in automotive gasoline. Fuel samples, and probably any samples collected in the field that are primarily organic in nature, may require the separation (prior to GC or GC/MS analysis) of the aliphatic, monoaromatic and polycyclic aromatic hydrocarbon fractions using liquid solid column chromatography. The various column eluates, with or without dilution in carbon disulfide, can then be analyzed by GC or GC/MS techniques. Aqueous samples need to be liquid-liquid extracted with an appropriate solvent (i.e., trichlorotrifluoroethane) prior to analysis; solid samples would be extracted with trichlorotrifluoroethane using soxhlet extraction or sonication methods (1422). An aliquot of the sample extract, with or without concentration, is then analyzed by GC or GC/MS. Sampling and analysis considerations for some specific components in gasoline, i.e., benzene, toluene, xylenes, ethyl benzene and naphthalene have been addressed in Volume 1.

A purge and trap procedure for the determination of the total volatile components of gasoline in water has also been reported (3059). Headspace analysis of contaminated soil using an ion-mobility spectrometer (3193) and monitors based upon laser-induced fluorescence-optical-fiber detection (3127) have been described. Since gasoline also has a distinctive gas chromatographic profile, pattern recognition has been used to determine traces of fuel isolated from water (3689).

Alternatively, the "oil and grease" content can be measured. This determination would not be the measurement of an absolute quantity of a specific component, but rather the quantitative determination of groups of components with similar physical characteristics (i.e., common solubility in trichlorotrifluoroethane). The "oil and grease" content is defined as any material recovered from extraction with trichlorotrifluoroethane and measured gravimetrically; extraction methods are those described above for aqueous and soil samples.

A detection limit for automotive gasoline was not determined; the detection limit for specific components is expected to be in the range of µg/L for aqueous samples and µg/g for non-aqueous samples.

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Note: The nonsequential numbers of the references reflect the order of references as they appear in the master bibliography.

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COMPLEX MIXTURES

This chapter deals with a complex mixture and/or class of compounds. The format used for this less well-defined group of compounds was modified as necessary but follows the outline of earlier chapters as closely as possible. It should be noted, however, that the composition of these materials can vary according to the route of synthesis, the formulating ingredients added, the interactions of the active ingredients, or the storage conditions. These factors can influence the nature of the material that is ultimately utilized and probably are reflected in many of the experimental findings reported in the following chapters.

The typical components and approximate composition of the mixtures are provided if that information was available. Physical/chemical properties often were not available or varied depending on formulation. Many of these mixtures are blended to modify their physical properties according to the intended use. Furthermore, the formulations vary with season as well as with geographic locations of product use. In some cases, therefore, the range for the class of compounds was given.

In addition to the data for the mixture itself, the chapter that follows also contains sections on the principal components and major additives of the mixture, their fate in the environment and a brief overview of their toxicity.

COMMON SYNONYMS:	CAS REG. NO.	NIOSH NO.
Fuel Oil No.: 1*	8008-20-6	OA5500000
Coal oil		
Fuel oil no. 1		
JP-1		
Kerosene		
Range oil		
Fuel Oil No.: 1-D*		
Diesel oil (light)		
Fuel oil 1-D		
Fuel Oil No.: 2*	68476-30-2	HZ1800000
Diesel oil		
Fuel oil no. 2		
Home heating oil		
Fuel Oil No.: 2-D*		
Diesel oil (medium)		
Fuel oil 2-D		
Fuel Oil No.: 4*	68476-31-3	
Fuel oil no. 4		
Residual fuel oil no. 4		
Fuel Oil No.: 5*		
Fuel oil no. 5		
Navy special fuel oil		
Residual fuel oil no. 5		
Fuel Oil No.: 6*	68553-00-4	
Bunker c oil		
Fuel oil no. 6		
Residual fuel oil no. 6		
Fuel Oil No.: UNSP**		LS8950000
Fuel oil		

CHEMICAL COMPOSITION:

*The composition given in the record is for generic "FUEL OIL"

**Olefinic hydrocarbons 1.0% - 2.0%
Aromatic hydrocarbons 35.0%
Aliphatic hydrocarbons 64.0%

PHYSICO-CHEMICAL DATA (Fuel Oil No. 1)	• Physical State: Liquid (at 20°C)	(60)
	• Color: Colorless to brown	(60)
	• Odor: Kerosene-like	(60)
	• Odor Threshold: No data	
	• Density: 0.8100 to 0.9360 g/mL (at 15°C)(range for 1,4,5, and 1D)	(60)
	• Freeze/Melt Point: -48 to 18°C	(60)
	• Boiling Point: 151 to >588°C	
	• Flash Point: 38.00 to 74.00°C for various grades of fuel oil No.1	(12,51,60, 504,506,507)
	• Flammable Limits: 0.6-1.3% to 5.0 to 7.50% for fuel oils 1-5	(51,60,501, 506)
	• Autoignition Temp.: 177.0 to 329.0°C depending on grade for fuel oils 1-5	(51,60,506, 507,513)
	• Vapor Pressure: 2.12-26.4 mm Hg (at 21°C)	(60)
	• Satd. Conc. in Air: No data	
	• Solubility in Water: ~5 mg/L (at 20°C)	(2297)
	• Viscosity: 1.152 to 1.965 cp (at 21°C)	(60)
	• Surface Tension: 21-32 dyne/cm (at 20°C)	(60)
	• Log (Octanol-Water Partition Coeff.): 3.3-7.06	(See Table 66-3)
	• Soil Adsorp. Coeff.: 9.6E+02 to 5.5E+06	(See Table 66-3)
	• Henry's Law Const.: 5.9E-05 to 7.4 atm · m^3/mol (at 20°C)	(See Table 66-3)
	• Bioconc. Factor: No data	

PHYSICO-CHEMICAL DATA (Fuel Oil No. 1-D)	• Physical State: Liquid (at 20°C)	(60)
	• Color: Colorless to brown	(60)
	• Odor: Kerosene-like	(60)
	• Odor Threshold: No data	
	• Density: 0.8100 to 0.9360 g/mL (at 15°C)	(60)
	• Freeze/Melt Point: -48 to 18°C	(60)
	• Boiling Point: 151 to >588°C	(60)
	• Flash Point: Ranges from 38-74°C	(12,51,60,504, 506,507)
	• Flammable Limits: 0.6 to 7.5%	(51,60,506,507)
	• Autoignition Temp.: 177.0 to 329.0°C depending on grade for fuel oil No. 1-5	(51,60,506, 507,513)
	• Vapor Pressure: 2.12 to 26.4 mm Hg (at 21°C)	(60)
	• Satd. Conc. in Air: No data	
	• Solubility in Water: ~5 mg/L (at 20°C)	(2297)
	• Viscosity: 1.152 to 1.965 cp (at 21°C)	(60)
	• Surface Tension: 21 to 32 dyne/cm (at 20°C)	(60)
	• Log (Octanol-Water Partition Coeff.): 3.3 to 7.06	(See Table 66-3)
	• Soil Adsorp. Coeff.: 9.6E+02 to 5.5E+06	(See Table 66-3)
	• Henry's Law Const.: 5.9E-05 to 7.4	(See Table 66-3)
	• Bioconc. Factor: No data	

PHYSICO-CHEMICAL DATA (Fuel Oil No.2)	• Physical State: Liquid (at 20°C)	(60)
	• Color: Colorless to brown	(60)
	• Odor: Kerosene-like	(60)
	• Odor Threshold: No data	(60)
	• Density: 0.8700 to 0.9500 g/mL (at 20°C)	(60)
	• Freeze/Melt Point: -48 to 18°C	(60)
	• Boiling Point: 151 to >588°C	(60)
	• Flash Point: Ranges from 38-74°C for various grades of fuel oil No. 1 to 69-169°C for grades of fuel oil No. 5	(504,506,507)
	• Flammable Limits: 0.60 to 7.50% by volume	(51,60,506,507)
	• Autoignition Temp.: 177.0 to 329.0°C depending on grade for fuel oils 1-5	(51,60,506, 507,514)
	• Vapor Pressure: 2.12 to 26.4 mm Hg (at 21°C)	(60)
	• Satd. Conc. in Air: No data	
	• Solubility in Water: ~5 mg/L (at 20°C)	(2297)
	• Viscosity: 1.152 to 1.955 cp (at 21°C)	(60)
	• Surface Tension: 21-32 dyne/cm (at 20°C)	(60)
	• Log (Octanol-Water Partition Coeff.): 3.3 to 7.06	(See Table 66-3)
	• Soil Adsorp. Coeff.: 9.6E+02 to 5.5E+06	(See Table 66-3)
	• Henry's Law Const.: 5.9E-05 to 7.4	(See Table 66-3)
	• Bioconc. Factor: No data	

PHYSICO-CHEMICAL DATA (Fuel Oil No. 2-D)	• Physical State: Liquid (at 20°C)	(60)
	• Color: Colorless to brown	(60)
	• Odor: Kerosene-like	(60)
	• Odor Threshold: No data	
	• Density: 0.870 to 0.950 g/mL (at 20°C)	(60)
	• Freeze/Melt Point: -48 to 18°C	(60)
	• Boiling Point: 151 to >588°C	(60)
	• Flash Point: Ranges from 38-74°C for various grades of fuel oil No. 1 to 69-169°C for grades of fuel oil No. 5	(12,51,60,504, 506,507)
	• Flammable Limits: 0.6 to 7.5%	(51,60,506,507)
	• Autoignition Temp.: 177.0 to 329.0°C depending on grade for fuel oil No. 1-5	(51,60,506, 507,513)
	• Vapor Pressure: 2.12 to 26.4 mm Hg (at 21°C)	(60)
	• Satd. Conc. in Air: No Data	
	• Solubility in Water: ~5 mg/L (at 20°C)	(2297)
	• Viscosity: 1.152 to 1.965 cp (at 21°C)	(60)
	• Surface Tension: 21 to 32 dyne/cm (at 20°C)	(60)
	• Log (Octanol-Water Partition Coeff.): 3.3 to 7.06	(See Table 66-3)
	• Soil Adsorp. Coeff.: 9.62E+02 to 5.5E+05	(See Table 66-3)
	• Henry's Law Const.: 5.9E-05 to 7.4	(See Table 66-3)
	• Bioconc. Factor: No data	

PHYSICO-CHEMICAL DATA (Fuel Oil No.4)	• Physical State: Liquid (at 20°C)	(60)
	• Color: Colorless to brown	(60)
	• Odor: Kerosene-like	(60)
	• Odor Threshold: No data	(60)
	• Density: 0.810 to 0.9360 g/mL (at 15°C)	(60)
	• Freeze/Melt Point: -43 to 18°C	(60)
	• Boiling Point: 151 to >588°C	(60)
	• Flash Point: Ranges from 38-74°C for various grades of fuel oil No. 1 to 69-169°C for grades of fuel oil No. 5	(12,51,60, 504, 506)
	• Flammable Limits: 0.60-1.3 to 5.0-7.5 % by volume, for fuel oils No. 1-5	(51,60,506, 507)
	• Autoignition Temp.: 177.0 to 329.0°C depending on grade for fuel oil No. 1-5	(51,60, 506 507, 573)
	• Vapor Pressure: 2.12 to 26.4 mm Hg (at 21°C)	(60)
	• Satd. Conc. in Air: No data	
	• Solubility in Water: ~5 mg/L (at 20°C)	(2297)
	• Viscosity: 14.50 to 493.50 cp (at 38°C)	(60)
	• Surface Tension: 21-32 dyne/cm (at 20°C)	(60)
	• Log (Octanol-Water Partition Coeff.): 3.3 to 7.06	(See Table 66-3)
	• Soil Adsorp. Coeff.: 9.62E+02 to 5.5E+06	(See Table 66-3)
	• Henry's Law Const.: 5.9E-05 to 7.4	(See Table 66-3)
	• Bioconc. Factor: No data	

PHYSICO-CHEMICAL DATA (Fuel Oil No. 5)	• Physical State: Liquid (at 20°C)	(60)
	• Color: Colorless to brown	(60)
	• Odor: Kerosene-like	(60)
	• Odor Threshold: No data	
	• Density: 0.8100 to 0.9360 g/mL (at 15°C)	(60)
	• Freeze/Melt Point: -48 to 18°C	(60)
	• Boiling Point: 151 to >588°C	
	• Flash Point: Ranges from 69-169°C for various grades of fuel oil No. 5	(504,506,507)
	• Flammable Limits: 0.6-1.3 to 5.0-7.5% by volume for fuel oils No. 1-5	(51,60,506, 507)
	• Autoignition Temp.: 177.0 to 329.0°C for fuel oil No. 1-5	(51,60.506, 507,513)
	• Vapor Pressure: 2.12 to 26.4 mm Hg (at 21°C)	(60)
	• Satd. Conc. in Air: No data	
	• Solubility in Water: ~5 mg/L (at 20°C)	(2297)
	• Viscosity: 14.50 to 493.5 cp (at 21°C)	(60)
	• Surface Tension: 21-32 dyne/cm (at 20°C)	(See Table 66-3)
	• Log (Octanol-Water Partition Coeff.): 3.3 to 7.06	(See Table 66-3)
	• Soil Adsorp. Coeff.: 9.62E+02 to 5.5E+06	(See Table 66-3)
	• Henry's Law Const.: 5.9E-05 to 7.4	(See Table 66-3)
	• Bioconc. Factor: No data	

PHYSICO-CHEMICAL DATA (Fuel Oil No.6)	• Physical State: Liquid (at 20°C)	(60)
	• Color: Colorless to brown	(60)
	• Odor: Kerosene-like	(60)
	• Odor Threshold: No data	
	• Density: 0.8700 to 0.9500 g/mL (at 20°C)	(60)
	• Freeze/Melt Point: -48 to 18°C	(60)
	• Boiling Point: 151 to >583°C	(60)
	• Flash Point: No data	
	• Flammable Limits: No data	
	• Autoignition Temp.: No data	
	• Vapor Pressure: 2.12 to 26.4 mm Hg (at 21°C)	(60)
	• Satd. Conc. in Air: No data	
	• Solubility in Water: ~5 mg/L (at 20°C)	(2297)
	• Viscosity: 14.50 to 493.50 cp (at 38°C)	(60)
	• Surface Tension: 21-32 dyne/cm (at 20°C)	(60)
	• Log (Octanol-Water Partition Coeff.): 3.3 to 7.06	(See Table 66-3)
	• Soil Adsorp Coeff.: 9.62E-02 to 5.5E+06	(See Table 66-3)
	• Henry's Law Const.: 5.9E-05 to 7.4	(See Table 66-3)
	• Bioconc. Factor: No data	

PHYSICO-CHEMICAL DATA (Fuel Oil UNSP)	• Physical State: Liquid (at 20°C)	(60)
	• Color: Colorless to brown	(60)
	• Odor: Characteristic kerosene-like	(60)
	• Odor Threshold: No data	
	• Density: No data	(60)
	• Freeze/Melt Point: -48.0 to 18.0°C	(60)
	• Boiling Point: 151.00 to >588.00°C	(60)
	• Flash Point: No data	(12,51,60, 504,506,507)
	• Flammable Limits: No data	(51,60,506, 507)
	• Autoignition Temp.: No data	(51,60,506, 50,513)
	• Vapor Pressure: 2.12E+00 to 2.64E+01 mm Hg (at 21°C)	(60)
	• Satd. Conc. in Air: Not available	
	• Solubility in Water: ~5 mg/L (at 20°C)	(2297)
	• Viscosity:	(60)
	• Surface Tension: 2.100E+01 to 3.200E+01 dyne/cm (at 20°C)	(60)
	• Log (Octanol-Water Partition Coeff.): 3.30 to 7.06	(See Table 66-3)
	• Soil Adsorp. Coeff.: 9.62E+02 to 5.50E+06	(See Table 66-3)
	• Henry's Law Const.: 5.90E-05 to 7.40 atm · m^3/mol (at 20°C)	(See Table 66-3)
	• Bioconc. Factor: Not available	

REACTIVITY	Various sources typically report that fuel oils are incompatible with strong oxidizers such as liquid chlorine and oxygen. The NFPA reports vigorous reactions, ignition, or explosions involving chlorine, fluorine, or magnesium perchlorate. Fuel oils are considered to be miscellaneous combustible or flammable materials for compatibility classification purposes. Such substances typically evolve heat, fire, and toxic or flammable gases in reactions with oxidizing mineral acids, organic peroxides or hydroperoxides, or strong oxidizing agents. Reactions with explosive materials may result in an explosion. (505, 507, 511).
PERSISTENCE IN THE SOIL-WATER SYSTEM	Diesel oil hydrocarbons are expected to have moderate mobility and moderate persistence in most surface soils; persistence in deep soils and groundwater may be higher. Volatilization, sorption, photooxidation, and biodegradation are all potential fate processes. Surface spills may be weathered to a limited extent by evaporation; downward migration of weathered surface spills and sub-surface discharges represent a potential threat to underlying groundwater. Biodegradation of fuel oil hydrocarbons is expected to occur under environmental conditions favorable to microbial oxidation; naturally-occurring, hydrocarbon-degrading microorganisms have been isolated from polluted soils and, to a lesser extent, non-polluted soils. The hydrocarbons of residual fuel oils are expected to be less mobile (lower aqueous solubility, higher sorption and lower volatility) and more persistent (slower biodegradation) than the lighter diesel oil hydrocarbons.
PATHWAYS OF EXPOSURE	The primary pathway of concern from the soil/groundwater system is the migration of fuel oils to ground water drinking water supplies from leaking underground storage tanks or large spills. Vapors from leaked or spilled fuels may diffuse through soil and migrate into structures resulting in inhalation exposures.

HEALTH HAZARD DATA	Signs and Symptoms of Short-term Human Exposure: (17, 54) The primary systemic effect is CNS depression. Inhalation of high concentrations mat cause headache, nausea, confusion, drowsiness, convulsions and coma. Ingestion may cause nausea, vomiting and in severe cases, drowsiness progressing to coma. Aspiration may cause extensive pulmonary injury. The liquid may produce primary skin irritation. Dermal absorption may induce nephropathy. Minimal eye injury from direct contact. Acute Toxicity Studies: ORAL: LD_{50} 5 1-20 g/kg Rat (1924) Long-Term Effects: Kidney damage (animals); CNS depression and dermatoses (humans) Pregnancy/Neonate Data: Negative Genotoxicity Data: Limited evidence Carcinogenicity Classification: IARC - None assigned NTP - Equivocal evidence for carcinogenicity of marine diesel fuel in $B6C3F_1$ mice. EPA - No data
HANDLING PRECAUTIONS (1967)	No specific respirator guidelines were found for fuel oils. The following guidelines are for kerosene with a boiling range of 175-325°C • Less than or equal to 1000 mg/m^3: chemical cartridge respirator with half-mask facepiece and organic vapor cartridge or supplied air respirator with half-mask facepiece operated in demand mode • 1000-5000 mg/m^3: gas mask with full facepiece and organic canister, supplied-air respirator with full facepiece or self-contained breathing apparatus with full facepiece operated in demand mode • Appropriate protective clothing including gloves, aprons and boots • Chemical goggles if there is probability of eye contact.

ENVIRONMENTAL AND OCCUPATIONAL STANDARDS AND CRITERIA

AIR EXPOSURE LIMITS:

Standards
- OSHA TWA (8-hr): petroleum distillates (naphtha)-400 ppm
- AFOSH PEL (8-hr TWA): petroleum distillates (naphtha)-400 ppm; STEL (15-min): 500 ppm

Criteria
- NIOSH IDLH (30-min): petroleum distillates (naphtha)-10,000 ppm
- NIOSH REL TWA (10-hr): petroleum distillates (naphtha)-350 mg/m^3
- NIOSH CL (15-min): petrolium distillates (naphtha)-1800 mg/m^3
- ACGIH TLV® (8-hr TWA): petroleum distillates (naphtha)-none established
- ACGIH STEL (15-min TWA): petroleum distillates (naphtha)-none established

WATER EXPOSURE LIMITS:

Drinking Water Standards
None established

EPA Health Advisories and Cancer Risk Levels
None established

WHO Drinking Water Guideline
No information available.

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

REFERENCE DOSES:
No reference dose available.

Oil and Grease (2012)
For domestic water supply: Virtually free from oil and grease, particularly from the tastes and odors that emanate from petroleum products.

ENVIRONMENTAL AND OCCUPATIONAL STANDARDS AND CRITERIA (Cont.)

For aquatic life:

- To protect several important freshwater and marine species, each having a demonstrated high susceptibility to oils and petrochemicals, the lowest continued flow 96-hour LC_{50} should be reduced a hundred-fold.
- levels of oils or petrochemicals in the sediment which cause deleterious effects to the biota should not be allowed;
- surface waters shall be virtually free from floating non-petroleum oils of vegetable and animal origin as well as petroleum-derived oil.

REGULATORY STATUS (as of 01-MAR-89)

Promulgated Regulations

- Federal Programs

Clean Water Act (CWA)
Oil and grease are designated conventional pollutants under the CWA (351). Effluent limitations for oil and grease exist in almost point source categories under the general pretreatment regulations for new and existing sources, and effluent standards and guidelines. Limitations vary depending on the type of industry (3763).

Toxic Substances Control Act (TSCA)
Manufacturers and processors of the C_9 aromatic hydrocarbon fraction must test it for neurotoxicity, mutagenicity, developmental toxicity, reproductive effects and oncogenicity. The C_9 fraction is obtained from the reforming of crude petroleum. It consists of ethyltoluenes and trimethylbenzenes (1988). Testing will be conducted by the American Petroleum Institute. Interim reports must be submitted at 6-month intervals (1987).

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 nonbioaccumulative 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 petroleum distillates (naphtha) shall not exceed an 8-hour time-weighted average (TWA) of 400 ppm (3539).

Hazardous Materials Transportation Act (HMTA)
The Department of Transportation has designated fuel oils as hazardous materials which are subject to requirements for packaging, labeling and transportation (305).

- State Water Programs

ALL STATES
All states have adopted EPA Ambient Water Quality Criteria and NPDWRs (see Water Exposure Limits section) as their promulgated state regulations, either by narrative reference or by relisting the specific numeric criteria. These states have promulgated additional or more stringent criteria:

ALASKA
Alaska has an aquatic life criterion of 15 µg/L for total hydrocarbons and 10 µg/L for total aromatic hydrocarbons in fresh and marine surface waters (3016).

ARKANSAS
Arkansas requires that oil and grease shall not exceed 10 mg/L average or 15 mg/L maximum when discharging to surface waters (3587).

FLORIDA
Florida requires that oil and grease not exceed 10 mg/L in Class V waters (navigation, industrial use) and 5 mg/L for all other surface waters (3220).

MASSACHUSETTS
Massachusetts requires that the maximum discharge concentration of oil and grease of petroleum origin not exceed 15 mg/L in surface waters (3432).

NEBRASKA
Nebraska requires that petroleum oils not exceed 10 mg/L in surface waters (3719).

NEW YORK
New York has set a maximum contaminant level of 50 µg/L for kerosene in drinking water (3501).

SOUTH DAKOTA
South Dakota has a water quality standard of 10 mg/L for all petroleum products in surface waters (3672).

VIRGINIA
Virginia has a water quality standard of 1 mg/L for petroleum hydrocarbons in ground-water (3135).

WYOMING

Wyoming has a water quality standard of 10 mg/L for surface waters and Class II and III ground-waters. In addition, Class I domestic ground-water is required to be virtually free of oil and grease (3853, 3852).

Proposed Regulations

- Federal Programs

  No federal regulations are pending.

- State Water Programs

  No state regulations are pending.

MOST STATES

Most states are in the process of revising their water programs and proposing changes to their regulations which will follow EPA's changes when they become final. Contact with the state officer is advised. Changes are projected for 1989-90 (3683).

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 Fishing Water Quality (536)

Petroleum products must not be present in salmonid and cyprinid waters in such quantities that they: (1) form a visible film on the surface of the water or form coatings on the beds of water-courses and lakes, (2) impart a detectable "hydrocarbon" taste to fish and, (3) produce harmful effects in fish.

Directive on the Quality Required of Shellfish Waters (537)

The mandatory specifications for petroleum hydrocarbons specify that they may not be present in shellfish water in such quantities as to produce a visible film on the surface of the water and/or a deposit on the shellfish which has harmful effects on 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 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)
Petroleum and coal tar distillates with flash points below 21 degree C are classified as flammable substances and are subject to packaging and labeling regulations. Because of the variable composition of other petroleum and coal tar distillates (excluding those used as motor fuels), they are considered preparations and their labeling shall be done in accordance with the procedures outlined in the Directive Relating to the Classification Packaging and Labeling of Dangerous Preparations (solvent).

Directive on Disposal of Waste Oils (1986)
Establishments collecting and/or disposing of waste oils must carry out safe collection and disposal of waste oils so that there will be no avoidable risk of water, air or soil pollution. A permit from the competent authority must be registered and adequately supervised for collecting, disposing or regenerating waste oils. PCBs and PCTs must not be present in amounts greater than 50 ppm in regenerated waste oil.

EEC Directives - Proposed
Proposal for a Council Directive on the Dumping of Waste at Sea (1793)
EEC has proposed that the dumping of crude oil, petroleum hydrocarbons, lubricants and hydraulic fluids at sea be prohibited.

66.1 MAJOR USES

Fuel oils have various uses for which they are specifically formulated. Fuel oil number 1 is used almost exclusively for domestic heating. Fuel oil number 2 is used as a general purpose domestic or commercial fuel in atomizing type burners. Number 4 oil is used in commercial or industrial burner installations not equipped with preheating facilities. Numbers 5 and 6 are used in furnaces and boilers of utility power plants, ships, locomotives, metallurgical operations and industrial power plants (23).

Diesel fuel is available in different grades. Number 1-D is used for engines in service requiring frequent speed and load changes. Number 2-D is used for engines in industrial and heavy mobile service while number 4-D is used in low and medium speed engines (2342).

66.1.2 Composition

The discussion of fuel oil in this section largely focuses on diesel fuel. Limited information on residual fuel oils, which are generally defined as the product remaining after removal of the appreciable quantities of the more volatile components, is included, but environmental fate data are not specifically addressed. Residual fuel oils are expected to be extremely complex in composition, with higher concentrations of the many high molecular weight asphaltic compounds and impurities present in the original crude oils. Available data suggest sulfur values ranging from 0.18 to 4.36% by weight; trace element data indicate that concentrations of many elements vary by one or more orders of magnitude, as shown in Table 66-1 (1843). The environmental transport and transformation of the high molecular weight organics is expected to be minimal and is not addressed in detail.

Diesel fuel is usually that fraction of petroleum that distills after kerosene in the 200°C to 400°C range. Several commercial grades of diesel fuels are obtained by blending various feedstocks to achieve established specifications. Due to differences in feed stocks, refining methods, and blending practices, the composition of diesel fuel samples is expected to be highly variable. Sulfur content has been reported to vary by several orders of magnitude (0-0.57% by weight); similar variations have been documented for a number of trace elements, as shown in Table 66-1 (1843).

Diesel fuel is predominantly a mixture of C_{10} through C_{19} hydrocarbons. Composition by chemical class has been reported to be approximately 64% aliphatic hydrocarbons (straight chain alkanes and cycloalkanes), 1-2% olefinic hydrocarbons and 35% aromatic hydrocarbons, including alkylbenzenes and 2-3 ring aromatics (1847). Other authors have reported a somewhat lower aliphatic content (1849). As discussed in the Chapter on JP-4, petroleum distillates may contain many

TABLE 66-1
TRACE ELEMENT CONTENT IN PETROLEUM-DERIVED FUEL OILS[a]

	Range of Eleven Residual Oils	Range of Six Domestic Diesel Fuels[b]
Arsenic	<0.01 - 2.0	0.012 - 0.13
Beryllium	<0.0023 - 0.22	
Cadmium	<0.01 - 0.83	0.089 - 0.89
Chromium	0.09 - 1.9	0.55 - 2.8
Iron		3.8 - 71.0
Lead		<0.49 - 2.0
Manganese	<0.0095 - 27	0.29 - 6.2
Mercury	0.007 - 0.17	
Molybdenum	<0.01 - 1.1	0.018 - 0.27
Nickel	6.0 - 51	<6.1 - 23.0
Selenium	0.02 - 4.2	
Vanadium	1.0 - 110	<0.06 - 0.16
Zinc		1.3 - 4.8

a) Reference 1843
b) ppm by weight

non-hydrocarbon components in varying concentrations.

Fuel oils also contain a number of additives used as ignition improvers, combustion catalysts, antioxidants, flow improvers, metal deactivators, detergents and demulsifiers. Many compounds added to fuel oils are similar to those added to gasoline. A list of some of the chemical classes and specific chemicals that may be added to diesel fuel is provided in Table 66-2.

66.2 ENVIRONMENTAL FATE AND EXPOSURE PATHWAYS

A discussion of the environmental behavior of fuel oil is limited by the lack of data defining its major components. The environmental behavior of hydrocarbons selected from the major classes will be addressed; however, trace elements and the many diverse additives will not be specifically addressed. Many of the hydrocarbons characteristic of diesel fuel have been addressed previously in the more extensive environmental fate section of the JP-4 chapter since these hydrocarbons are common to both petroleum fuels. The general discussions of aliphatic and aromatic hydrocarbons and their behavior in soil/ground water systems will not be repeated here; the reader is referred to the relevant sections of the chapter on JP-4.

TABLE 66-2
COMMON ADDITIVES IN DIESEL FUELS

Ignition Improvers (Cetane Improvers)

- Alkyl nitrate and nitrites (C_3 -C_8) primarily octyl nitrate
- Nitro and nitroso compounds
- Peroxides

Combustion Catalysts/Deposit Modifiers

- Organometallics of barium, calcium, manganese, and iron
- Mn, MnO
- Mg, MgO, MgO_2
- Al_2O_3

Antioxidants

- N,N′-Dialkylphenylenediamines
- 2,6-Dialkyl and 2,4,6-trialkylphenols

Cold Flow Improvers

- Ethylene vinyl acetate copolymers
- Ethylene vinyl chloride copolymers
- Polyolefins
- Chlorinated hydrocarbons

Metal Deactivators

- N,N′-Disalicylidene-alkyldiamines

Detergents/Dispersants

- Long chain alcohols
- Long chain amines
- Long chain alkyl phenols
- Long chain carboxylic acids
- Sulfonates
- Succinimides

Source: References 2326, 2327, 2335, 2336

66.2.1 Equilibrium Partitioning Model

In general, soil/ground water transport pathways for low concentrations of pollutants in soil can be assessed by using an equilibrium partitioning model. For the purposes of assessing the environmental transport of diesel fuel, a group of specific hydrocarbons was selected from the dominant hydrocarbon classes, i.e., alkanes, cycloalkanes, and aromatics; there were no available data to confirm the presence of the selected compounds in a typical diesel fuel sample. Table 66-3 identifies the selected hydrocarbons and presents the predicted partitioning of low soil concentrations of those hydrocarbons among soil particles, soil water, and soil air. The portions associated with the water and air phases of the soil are expected to have higher mobility than the adsorbed portion.

Estimates for the unsaturated topsoil indicate that sorption is expected to be an important process for all the dominant hydrocarbon categories. Partitioning to the soil-vapor phase is much less important than for other petroleum distillates since many of the lower molecular weight aliphatic hydrocarbons (C_4 - C_9) characterized by high vapor pressure and low water solubility are not expected to be major components of diesel fuel. The aromatics have slightly higher water solubilities and transport with infiltrating water may be more important for these compounds. Volatilization, on the other hand, is not expected to be important. In saturated, deep soils (containing no soil air and negligible soil organic carbon), a significant percent of the aromatic hydrocarbons is predicted to be present in the soil-water phase and available for transport with flowing ground water. Partitioning to the air and water phases is expected to be even less important for the organic components of residual fuel oils compared to components of diesel oil. Sorption to soil particles is expected to be significant.

In interpreting these results, it must be remembered that this model is valid only for low soil concentrations (below aqueous solubility) of the components. Large releases of diesel fuel (spills, leaking underground storage tanks) may exceed the sorptive capacity of the soil, thereby filling the pore spaces of the soil with the fuel. In this situation, the hydrocarbon mixture would move as a bulk fluid and the equilibrium partitioning model would not be applicable.

66.2.2 Transport and Transformation Processes

Transport and transformation of individual fuel oil constituents will depend on the physicochemical (and biological) properties of the constituents. Some constituents will dissolve more quickly in percolating ground water; be sorbed less strongly on the soils and thus transported more rapidly; and may be more or less susceptible to degradation by chemical or biological action. Thus, the relative concentrations of the constituents of the fuel will vary with time and distance from the site of contamination. This effect is called "weathering". (This term is also used to describe the changes to oil following spills into surface waters. The oil film spreads and breaks up, involving differential volatilization, dissolution and degradation.)

TABLE 66.3
EQUILIBRIUM PARTITIONING OF POTENTIAL DIESEL FUEL HYDROCARBONS IN MODEL ENVIRONMENTS[a]

COMPOUND	Log K_{ow}	K'_{ow}	H[c]	UNSATURATED TOPSOIL %			SATURATED DEEP SOIL[d] %	
				Soil	Water	Air	Soil	Water
Octane	5.18[e]	73,000	2.96	97.4	0.01	2.6	99.7	0.3
Dodecane	7.06[f]	5.5E+06	7.4	99.9	0.0001	0.09	99.9	0.004
Trimethylpentane	4.87[f]	36,000	1.9-3.3	94.7	0.01	5.3	99.3	0.7
Trimethylcyclohexane	5.02[h]	50,500	1.6	98.0	0.01	2.0	99.5	0.5
Trimethylbenzenes	3.65[h]	2,150	5E-03	99.6	0.2	0.2	90.0	10.0
Naphthalene	3.30[g]	962	4.82E-04	99.4	0.5	0.03	80.2	19.8
Methylnaphthalenes	3.87[g]	3,570	4.4E-04	99.8	0.1	0.01	93.7	6.3
Anthracene	4.5[g]	13,500	5.9E-05	99.9	0.04	0.0003	98.3	1.7

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) Reference 652
c) Taken from reference 74 unless otherwise specified. Units equal atm · m³/mol.
d) Used sorption coefficient $K_p = 0.001 \times K_{ow}$.
e) Reference 29.
f) Arthur D. Little, Inc., estimate according to equations provided in Reference 31.
g) Reference 10.
h) Reference 31.

Transport processes have been shown to be more significant than transformation processes in determining the initial fate of lower molecular weight petroleum hydrocarbons released to soil/ground water systems. However, due to the lower water solubilities and lower vapor pressures of the higher molecular weight hydrocarbons, environmental transformation processes may be increasingly significant for hydrocarbons in the C_{10} - C_{19} range characteristic of diesel fuel and in the $>C_{19}$ range expected in residual fuel oils. Spain et al. (1846) demonstrated that compounds having up to nine carbons are weathered almost exclusively by evaporation; larger compounds were weathered by evaporation and biodegradation.

Under conditions of limited volatilization (low temperatures, subsurface release, or concentrated spill), other transport processes may be important, including downward migration into the soil, sorption to soils, and transport to ground water. Several authors (1811, 2243, 2252, 2329) have reported that oil substances released in significant quantities to soils result in a separate organic phase, which moves downward through the unsaturated zone to the less permeable layer, the soil/ground water boundary. In this layer, the oils tend to accumulate and spread horizontally.

The organic layer floating on the ground water is carried in the general direction of ground water flow. At the oil-water interface, some hydrocarbons are leached according to their aqueous solubility. As discussed in the chapter on JP-4, the pollution caused by the hydrocarbon phase is much less extensive (10s to 100s of meters) than pollution caused by hydrocarbons dissolved in ground water (100s to 1000s of meters) (1811). Furthermore, the pattern of migration of the two types of pollution may be very different. Due to fluctuations in ground water elevation over time, the organic layer on top of the aquifer may be transported into several zones. The components may occur in the gaseous phase (able to diffuse in all directions, including upward), liquid phase (adsorbed onto rock particles or sealed under water), or dissolved/emulsified in water (1811, 2329).

Migration through soils may be retarded by sorption. Sorption is expected to be significant for high molecular weight aliphatics, particularly $>C_{20}$. Migration is expected to be fastest through previously contaminated soils where the sorptive sites may be unavailable; on the other hand, soil-water content increases sorption and slows migration of hydrocarbons. In fissured rock, the migration of hydrocarbons is much less uniform than in porous soils. Preferential spreading through crevices may occur, sometimes changing the direction of flow. Determination of the potential ground water contamination in fissured rock is thus very difficult (1811).

The water-soluble portion of No. 2 fuel oil (a higher temperature distilling fraction than diesel oil) was shown to be almost entirely aromatic (99%) even though the product itself was 48% aliphatic; the aliphatic fuel oil hydrocarbons have very low water solubility compared with the aromatics (1849, 2238). The largest percentage (40%) of the water-soluble fraction of fuel oil was represented by C_{11}-aromatics (1849). In deep, saturated soils with no soil air, the aromatics represent the greatest threat of contamination to ground water supplies. Solubility in aqueous solutions of

polar, non-hydrocarbon components of some higher boiling petroleum fractions, such as diesel oil and other fuel oils, has also been reported (2238).

In summary, the physical distribution of fuel oil contamination affects its impact on, and removal from, the soil environment. Lateral spreading along the surface increases the initial contaminated area while facilitating evaporative removal or sorption of different hydrocarbons. Subsurface release or vertical penetration mediated by gravitation and capillary forces decreases evaporation, reduces the importance of some transformation pathways (see below), and may lead to ground water contamination.

Photooxidation has been reported to play a significant role in the chemical degradation of petroleum hydrocarbons in the environment (1845, 1848, 2252, 2259, 2337). Alkanes, benzenes, and mono-substituted benzenes have been shown to be relatively resistant to photolysis in aqueous systems; xylenes photolyzed slowly while trisubstituted benzenes and naphthalenes photolyzed at rates competitive with volatilization (1845). Lee et al. report that anthracene and other polycyclic aromatic hydrocarbons (PAH) in the carbon range of diesel fuel are subject to photochemical oxidation. Benzo(a)pyrene is the most susceptible of the PAH compounds, suggesting that the residual fuel oils may be even more affected by photodegradation than diesel oil. Penetration of oil below the soil surface limits exposure to solar radiation while extensive lateral spreading of oil over impermeable or rocky surfaces may promote substantial photooxidative degradation. The oxygenated products of photooxidation are generally more water-soluble than the parent hydrocarbons and are thus more likely to be leached from soil. Enhanced toxicity of the oxygenated hydrocarbons has also been observed (2248, 2252).

Natural ecosystems have considerable exposure to petroleum hydrocarbons from natural emissions, accidental contamination through oil spills and storage tank leaks, and deliberate application to land in waste disposal activities such as land-farming; therefore, their biodegradation is of environmental importance. Numerous authors have observed the biodegradation of petroleum hydrocarbons, and several extensive reviews and reports are available (1846, 2252, 2255, 2249, 2253). An extensive and diverse group of petroleum hydrocarbon-degrading bacteria and fungi are widely distributed in the environment. Although the microbiota of most non-contaminated soils include many naturally occurring hydrocarbon-degrading populations, the addition of petroleum selectively enriches that sector able to adapt and utilize the new substrate. Other environmental factors shown to have a major effect on biodegradability are availability of oxygen and moderate temperatures. The reader is referred to the chapter on JP-4 for a more detailed summary of the biodegradation of petroleum hydrocarbons. The qualitative hydrocarbon content of petroleum mixtures largely determines their degradability. In general, microorganisms exhibit decreasing ability to degrade aliphatic hydrocarbons with increasing chain length; aromatics are generally more rapidly biodegraded than alkanes. The composition of diesel oil suggests that some of the aromatic species will be biodegradable. Biodegradation of the high molecular weight aromatics expected to be present in residual oils will be slower (2339).

In summary, biodegradation of the petroleum hydrocarbons comprising diesel and fuel oils may occur under conditions favorable for microbial activity and when fuel components are freely available to the microorganisms. Degradation may be limited and/or slow in environments with few degrading organisms, low pH, low temperatures, and high salinity (e.g., arctic environments). It should be mentioned that Walker et al. (2257) state that even under optimum conditions, total and complete biodegradation is not expected to occur except possibly over an extremely long time period.

66.2.3 Primary Routes of Exposure from Soil/Ground Water Systems

The above discussion of fate pathways suggests that pure fuel oils have low vapor pressure but that their components vary in their volatility from water. The components are strongly or very strongly sorbed to soil. The polycyclic aromatic hydrocarbons in fuel oils have a moderate or high potential for bioaccumulation, while the longer-chain aliphatic compounds have low potential for bioaccumulation. These fate characteristics suggest that the various components may have somewhat different potential exposure pathways.

Volatilization of fuel oils from a disposal site or spill would not be expected to result in significant inhalation exposures to workers or residents in the area. Gravity would tend to carry bulk quantities of the oil down towards the water table leaving only a relatively small fraction on the soil surface to volatilize. Volatilization of the remaining oil would occur very slowly because of its low vapor pressure, especially for the heavier weight fuel oils, and because of strong sorption to soil.

Ground water contamination may result from large spills that reach the water table. There, the more soluble components will dissolve in the ground water or form emulsions with it. The soluble fraction is mainly aromatic and lower molecular weight aliphatic compounds. In one study using No. 2 fuel oil, 40% of the water soluble fraction was made up of aromatic compounds composed of 11 carbon atoms and 25% each of compounds containing 10 and 12 carbon atoms (2318). The hydrocarbons dissolved in the ground water may move hundreds to thousands of meters. By comparison, the undissolved fraction, which floats on the surface of the water table as a separate phase, would be expected to move only tens of meters, unless cracks or fissures were present.

The movement of fuel oil components in ground water may contaminate drinking water supplies, resulting in ingestion exposures. Ground water discharges to surface water or the movement of contaminated soil particles to surface water drinking water supplies may also result in ingestion exposures and in dermal exposures from the recreational use of these waters. The potential also exists for the uptake of polynuclear aromatic compounds in fuel oil (e.g., naphthalene, methylnaphthalene and higher weight PAH's) by fish and domestic animals, which may also result in human exposures. Exposures to high concentrations of fuel oil components in drinking water and food are expected to be rare because tainting becomes apparent at relatively low concentrations (982).

Volatilization of fuel oil hydrocarbons in soil is another potential source of human exposure. Despite their relatively low vapor pressure, the more volatile components of fuel oil in soil evaporate, saturating the air in the soil pores, and diffusing in all directions including upward to the surface. The vapors may diffuse into basements of homes or other structures in the area, resulting in inhalation exposures to the building's occupants. Exposures may be more intensive when the soil is contaminated from leaking underground storage tanks and pipes, rather than from surface spills, because the more volatile components do not have an opportunity to evaporate before penetrating the soil. Even then, this exposure pathway is expected to be much less important for fuel oils than for more volatile petroleum products like gasoline.

66.2.4 Other Sources of Human Exposure

Data on ambient concentrations of fuel oil in air and water as well as in food and drinking water are not readily available in the literature. Exposure information on specific components may be found in other chapters of this Guide. Several population groups susceptible to exposure to fuel oil may be identified. Personnel involved in fuel handling operations may experience direct dermal contact if protective gloves and clothing are not worn. They may also receive small inhalation exposures from the more volatile components.

66.3 HUMAN HEALTH CONSIDERATIONS

66.3.1 Animal Studies

66.3.1.1 Carcinogenicity

Generally, number 1 and number 2 fuel oils are not carcinogenic even though they contain aromatic hydrocarbons (2219). In contrast, industrial fuels such as number 6 oil are residual oils that often contain highly condensed aromatic products from severe cracking processes. They may be carcinogenic to animals if they contain PAH components that boil above 370°C (2219).

Certain currently available fuel oils may be carcinogenic because they are derived from the blending of fractions boiling below 370°C with those boiling at higher temperatures. Some of these high-boiling fuels that are derived from catalytic cracking processes may contain carcinogens (2219).

Studies have demonstrated a direct relationship between tumor potency and the concentration of high-boiling fractions that are added to form blends. It was determined that when not more than 10 volume % of 700°F-plus catalytic gas oil or clarified oil is present, the tumor potency values of the blends are less than 20 and therefore have borderline significance. The tumor potency value is a representation of the tumor formation rate in response to application to mouse skin. For a value of

20, 500 days would be required for a 50% tumor response (1818) (see Table 66-4). Examination of boiling ranges of blended petroleum products may not provide an accurate assessment of their carcinogenic potential. In the opinion of Bingham et al. (2219), these materials are probably carcinogenic and their potency may be underestimated or overestimated if the diluent contains cocarcinogens or inhibitors.

Frazier and Mahlum (1819) tested the initiation activity of a fuel oil blend (FOB) that contained part of a heavy molecular weight distillate boiling at 288-454°C and 2.9 parts of a distillate boiling between 176 and 288°C. The FOB (25 mg) was applied to the clipped backs of CD-1 mice in a 50 μL volume. Two weeks after initiation, the animals received doses of 5 μg phorbol myristate acetate in 50 μL acetone twice weekly for 24 weeks. Negative controls were treated with acetone. Positive controls were initiated with 50 μg benzo[a]pyrene (BAP) or dimethylbenzanthracene (DMBA). The FOB showed significant initiating activity. Approximately 60 tumors were seen after approximately 170 days. Greater than 200 tumors were observed in the BAP positive controls. Hydrotreated FOB was also tested in the same manner. Hydrotreatment has been suggested as a possible method for reducing biological activity of coal-derived materials. In this group about 17% of the animals developed a total of 12 tumors. Each tumor-bearing mouse had an average of 2.4 tumors. The hydrotreated FOB was also tested for promoting activity. In these studies, mice were initiated with 50 μg DMBA. After 2 weeks, they were promoted twice weekly for 24 weeks with 50 μL of a 1:3 solution of hydrotreated FOB in acetone. The control group was treated with acetone for 2 weeks and similarly promoted with the hydrotreated FOB. The hydrotreated FOB possessed measurable tumor promoting activity. When DMBA was used as the initiator, 41% of the mice had tumors after 6 months. Each mouse had an average of 2.5 tumors. No tumors were reported in mice treated with hydrotreated FOB on noninitiated (acetone-treated) skin.

Biles (3064) conducted skin painting carcinogenesis bioassays on diesel fuel, two types of No. 2 fuel oil (Amoco furnace oil and No. 2 burner fuel). Male C3H/HeN mice (50/group) were exposed to 50 microliters of undiluted material, twice per week for lifetime. All three fuels produced increased incidences of malignant skin tumors; 27% for diesel fuel, 28% for Amoco furnace oil, and 18% for No. 2 burner fuel.

NTP (3483) conducted 2-year dermal studies to determine the carcinogenic potential of petroleum-derived marine diesel fuel and JP-5 navy fuel. Male and female B6C3F$_1$ (50/group) were exposed to doses of 0, 250, or 500 mg/kg of each of the fuels by dermal application to the clipped dorsal interscapular region. Due to excessive irritation and ulceration at the site of application, animals in the high-dose group for both fuels were killed early. Consequently, the length of exposure to marine diesel fuel was 5 days/week for 84 weeks for both sexes of mice in the high-dose group and 5 days/week for 103 weeks for mice in the low-dose groups. The length of exposure to JP-5 was 5 days/week for 90 weeks for female mice in the high dose-group and 5 days/week for 103 weeks for the other groups. Squamous cell papillomas or carcinomas (combined) occurred with a positive trend ($P<0.05$) at the site of application in male mice exposed to marine diesel fuel. No neoplasia were

TABLE 66-4
POTENCIES OF TWO BLENDED FUEL OILS FOR THE SKIN OF C3H MICE

Base Blending Stock	Cracked Residuum Added[a] (%)	Content of BaP[b] (%)	Dosage[b] (mg/mouse)	Number of Mice	Final Effective Number[c]	Number of Mice Developing Tumors		Average Time of Appearance of Papillomas (Weeks)
						Malignant	Benign	
A[d]	0	0.01	20	19	17	1	1	--
			50	20	17	3	7	5.8±1.7[e]
B[d]	0	0.00	20	40	23	0	1	
A	5	0.05	20	30	27	15	8	41.5 ± 3.6
			50	30	27	13	8	28.3 ± 3.3
B	5	0.04	20	40	31	9	11	49.1 ± 5.5
			50	28	27	9	9	36.9 ± 3.3
A	10	0.08	20	30	26	19	7	40.4 ± 3.2
			50	30	25	22	3	32.2 ± 2.5
B	10	0.075	20	40	35	22	13	40.5 ± 1.9
			50	30	30	9	18	26.7 ± 1.6
A	20	0.16	20	25	23	12	9	25.2 ± 2.8
B	20	0.15	20	29	28	11	16	23.4 ± 1.7

a. Residuum (>700°F) from thermal cracking of FCC clarified oil.
b. Applied twice weekly
c. Number alive at time of appearance of median tumor plus number of tumor-bearing mice which died earlier.
d. Base stock A is cracked Bunker fuel; Base stock B is West Texas uncracked residuum.
e. Limits of confidence (P = 0.05). Reference 1820

Source: 1820

observed following exposure to JP-5. Consequently, NTP has determined that under the conditions of this study, marine diesel fuel at doses of 250 and 500 mg/kg results in dose-related increased incidences of squamous cell neoplasms of the skin; thereby, providing equivocal evidence of carcinogenicity in male and female B6C3F$_1$ mice. NTP also concluded that under the conditions of this 2-year dermal study, no evidence of carcinogenicity for male and female B6C3F$_1$ mice was provided for JP-5 at doses of 250 and 500 mg/kg.

Results presented by Schultz et al. (3628) on the skin tumorigenic potential of petroleum- and shale-derived marine diesel fuel and JP 8 indicate that all four fuels are weakly tumorigenic in male and female C3Hf/Bd mice, with the shale-derived fuels being slightly more active. Groups of 10 to 15 mice were dermally exposed to 6 doses of each fuel ranging from 6 to 45 mg, either 3 times/week for 40 weeks for 2 times/week for 60 weeks.

66.3.1.2 Genotoxicity

API has conducted a battery of 3 tests to evaluate the genotoxicity of diesel fuel and number 2 fuel oil (1914).

Number 2 fuel oil (50% catalytically cracked stock) gave positive results in each test. In the Ames assay, it was judged to be equivocal rather than negative because the relatively high mutant frequencies in S. typhimurium strain TA98 were observed at 4 concentrations. In a mouse lymphoma assay, it was genotoxic under activation and non-activation conditions. At a test concentration of 1200 µg/mL, the mutation frequency was 17 times the solvent control without metabolic activation. In a rat bone marrow cytogenetic study, Sprague-Dawley rats were administered number 2 fuel oil dissolved in corn oil by gavage at dosages ranging from 0.125 to 1.25 g/kg/day for 5 days. The percentage of aberrant cells ranged from 7.5 to 12.5%. A high percentage of cells with chromatid breaks was seen at all treatment levels. In both cases, the increases were statistically significant only at the low and high dose levels.

Ellenton and Hallett (3197) tested fraction 4 of Number 2 fuel oil in Salmonella typhimurium TA100 and found it to be genotoxic with S9. All the aromatic fractions of this oil caused significant increases in sister chromatid exchanges in the presence of metabolic activation but not in chromosome aberrations in Chinese hamster ovary cells treated in culture.

Diesel fuel gave negative results in both the Ames and mouse lymphoma assay. Positive results were obtained in the rat bone marrow cytogenetic assay. The diesel fuel was administered undiluted by intraperitoneal injection. Dose was 0.6, 2.0 or 6.0 mL/kg/day for 1 or 5 days. Single injections at the mid- or high-dose, as well as the high-dose in the 5 day protocol caused statistically significant increases in chromosome abnormalities (1914). Henderson et al. (3285) separated diesel fuel into aliphatic and aromatic fractions by extraction with dimethyl sulfoxide. These fractions were devoid of genotoxic activity in the Ames test and exhibited low cytotoxicity to Chinese hamster ovary cells treated in culture.

Lebowitz et al. (3391) did not observe any evidence of clastogenic activity in bone marrow cells of rats treated with kerosene intraperitoneally. Zeiger et al. (3859) tested Navy fuel JP-5 (a specially refined kerosene) with and without metabolic activation and found it negative in 4 of the 5 standard Salmonella test strains. In this same publication, diesel fuel-marine was also found to be negative under the same experimental conditions.

66.3.1.3 Teratogenicity, Embryotoxicity and Reproductive Effects

A teratology study of Fuel Oil #2 was sponsored by the American Petroleum Institute and conducted at Litton Bionetics. From days 6 through 15 of gestation, pregnant CRL:COBS CD(SD)BR rats were exposed to airborne concentrations of 0, 86.9 or 408.4 ppm of Fuel Oil # 2 for 6 hours daily. No maternal toxicity was observed at either dose level. Also, there was no evidence of teratogenicity, embryotoxicity or inhibition of fetal growth and development (3056).

The API also sponsored a teratology study with rats exposed by inhalation to diesel fuel at concentrations of 100 or 400 ppm for 6 hour/day on days 6-15 of gestation (3627). Although a decrease in maternal food consumption was observed at the 400 ppm exposure level, all embryotoxic and teratogenic results were negative.

66.3.1.4 Other Toxicologic Effects

66.3.1.4.1 Short-term Toxicity

The following fuel oils were evaluated for acute toxicity in six tests:

Number 2 fuel oil
- low-catalytic cracked (10%)
- medium-catalytic cracked (30%)
- high-catalytic cracked (50%)

Number 6 fuel oil
- API gravity 11.7/2.7% Sulfur content
- API gravity 17.1/0.8% Sulfur content
- API gravity 23.1/0.2% Sulfur content
- API gravity 5.2/1.2% Sulfur content

Diesel Fuel (marketplace sample)

Kerosene
- Hydrodesulfurized (API #81-07)
- Deodorized

Kerosene-type jet fuels
- Jet Fuel A (purity unknown)
- JP-5
- JP-8

The 6 tests that were conducted were:

- Acute oral toxicity in rats
- Acute dermal and subacute dermal toxicity in rabbits
- Primary eye and dermal irritation in rabbits
- Dermal sensitization in guinea pigs

Results of these tests are discussed below.

The acute oral toxicity was evaluated in Sprague-Dawley rats. The number 2 oils caused 70 to 100% mortality with doses of 16.5 to 21 g/kg. LD_{50} values ranged from 12.0 to 17.5 g/kg. Toxic signs included alopecia, lethargy, diarrhea, dermal irritation and open sores around the genital area. The number 6 fuel oil with an API specific gravity of 5.2 and 1.2% sulfur content was the most toxic material tested. The LD_{50} was 5.1 g/kg. A dose of 25 g/kg caused 100% mortality. None of the other number 6 fuel oils caused mortality at 22-24 g/kg. A significant degree of gastrointestinal distress was observed at doses greater than 15-20 g/kg until the material cleared the gastrointestinal tract. This was thought to be due to volume overload. Mortality generally occurred 2-3 days after dosing. Necropsy revealed evidence of hemorrhagic gastroenteritis and pneumonia with abscess formation (1929).

A marketplace sample of diesel fuel had an LD_{50} of 7.5 g/kg in rats and caused 90% mortality at a dose of 16.6 g/kg. Toxic signs were the same as those seen with the number 2 oils (1924).

An oral LD_{50} of 20 g/kg in rats has been reported for kerosene. In acute oral studies with kerosene-type jet fuels, ingestion of 25 mL/kg of Jet Fuel A resulted in slightly congested livers and kidneys in rats (3195) Parker et al. (3549) report an oral LD_{50} in rats of >60 mL/kg for JP-5. Smith et al. (3664) report an oral LD_{50} in mice of >16 mL/kg for JP-8.

In acute dermal studies conducted with rabbits, number 6 heavy fuel oil (API gravity 5.2/1.2% sulfur) induced significant signs of toxicity at 5 g/kg. It caused severe dermal irritation, weight loss, anorexia, ataxia and lethargy. Mortality was 37.5%. Necropsy revealed acute toxic hepatitis, gastrointestinal irritation and congested lungs. Other grades of number 6 and number 2 oils as well as diesel oil produced mild to moderate dermal irritation but no systemic signs of toxicity (1924). However, Elars Bioresearch Lab (3194) found that at postmorten 4 of 8 rabbits had congested kidneys following the dermal application of 5 mL/kg of diesel fuel for 24 hours.

In the subacute dermal study, doses ranging from 1 to 10 mL/kg were applied to rabbits clipped free of hair. The area remained bandaged for 24 hours at which time the patches were removed and a new dose applied. This continued for 5 consecutive days followed by a 2 day rest period and a repeat application for 5 consecutive days.

In this test, the number 6 fuel oil (API gravity 5.1/1.2% sulfur) produced the greatest degree of toxicity at the lowest dose (75% mortality at 2.5 mL/kg). Clinical signs included severe weight loss, anorexia and signs of dermal irritation. Gross necropsy revealed hemorrhagic gastroenteritis, and congested, mottled livers with multifocal necrosis and centrilobular vacuolar degeneration. In all cases, the number 6 oils caused inflammation, dermal congestion and edema, dermal necrosis, acanthosis and parakeratosis. Liver necrosis and degeneration were also seen but the severity was not as great as that with 5.1/1.2% sulfur. All 3 number 2 oils caused weight loss, anorexia and various degrees of dermal irritation. At a dose of 10 mL/kg, mortality ranged from 75 to 100%. Gross necropsy lesions at all dosage levels included renal and hepatic congestion. At the 10 mL/kg level, multifocal hepatic necrosis was observed (1924). With the same test protocol, Elars Bioresearch Lab (3194) observed 67% mortality in rabbits at a dose of 8 mL/kg of diesel fuel (marketplace) and histopathology revealed evidence of hepatic toxicity at this level.

In subacute dermal studies with hydrodesulfurized kerosene following the same protocol as described in the preceding paragraph, Hazleton Raltech (3281) observed acute dermal corrosion at doses of 2.5, 4, and 10 mL/kg. Evidence of hepatic toxicity and 100% mortality were observed at the 10 mL/kg dose-level. A dose of 8 mL/kg of Jet Fuel A resulted in 75% mortality in rabbits. Clinical signs included acute dermal corrosion, necrosis with alopecia at the test site, and depressed behavior. Histopathology confirmed hepatic toxicity and hyperplastic changes in the transitional epithelium of the urinary bladder (3195).

In 14-day dermal studies conducted by NTP (3483) with petroleum-derived marine diesel fuel and JP-5, all B6C3F$_1$ mice died at doses of 20,000 and 40,000 mg/kg of marine diesel fuel, all male mice died at the 40,000 mg/kg dose of JP-5, and all female mice died at doses of 30,000 and 40,000 mg/kg of JP-5. The skin lesions observed at doses of marine diesel fuel ranging from 2000 to 40,000 mg/kg and doses of JP-5 ranging from 5000 to 40,000 mg/kg included diffuse hyperplasia of the epidermis, hyperkeratosis, and acute inflammation.

In primary dermal irritation tests, the number 2 oils were moderately irritating while the number 6 oils were minimally to slightly irritating. Diesel fuel was extremely irritating. Signs included severe erythema and edema with blistering and open sores. The test was conducted by applying 0.5 mL of undiluted material to abraded rabbit skin. The test area was then covered for 24 hours at which point the bandage was removed and the animals scored according to the Draize technique (1924).

Hydrodesulfurized kerosene was moderately irritating when 0.5 mL was applied to rabbit skin (3281). Jet Fuel A was mildly irritating (3195) and JP-8 was mildly to moderately irritating (3416); whereas, JP-5 was non-irritating to rabbit skin in the patch test (3144).

The number 6 oils were minimally to moderately irritating when 0.1 mL was applied to rabbit eyes. These materials produced conjunctival redness, swelling and discharge. Few corneal opacities were produced but eyes returned to normal within

72 hours. Diesel fuel was non-irritating and number 2 oils ranged from practically non-irritating to mildly irritating (1924).

Hydrodesulfurized kerosene was practically non-irritating when 0.1 mL was applied to rabbit eyes (3281). Jet Fuel A was mildly irritating (3195); whereas, JP-5 (3144) and JP-8 (3416) were non-irritating to rabbit eyes.

In dermal sensitization studies, 0.5 mL of the following fuel oils were non-sensitizing in guinea pigs: number 2 fuel oil (3196), diesel fuel (marketplace) (3194) and Jet Fuel A (3195). However, 0.1 mL of JP-5 in peanut oil resulted in mild sensitization (3144); JP-8 evoked a delayed-type sensitization in guinea pigs (3416); and deodorized kerosene caused sensitization by the maximization test (3495).

Short-term inhalation studies have been conducted with diesel fuel and deodorized kerosene. Kainz and White (1984, 2334) subjected male CD-1 mice to nose only exposure of 0.065, 0.135 or 0.204 mg/L uncombusted diesel fuel vapor for 8 hours per day on 5 consecutive days. The mice developed vasodilation, ataxia, poor grooming habits, and in some cases, tremors. All signs varied with the dose and duration of exposure. Dose-related effects in neurological testing indicate that the uncombusted diesel vapors may also act as a neurodepressant. Dalbey et al. (3148) exposed rats to diesel fuel aerosol concentrations of 1.3, 2.0, 4.0, or 6.0 mg/L for exposure periods of 2 or 6 hours, at either one exposure a week for 9 weeks or 3 exposures a week for 3 weeks and observed neuromuscular disturbances, decreased pulmonary function and accumulation of alveolar macrophages in the lungs at concentration · time values of 8 and 12 mg · hr/L. Carpenter et al. (3101) reported slight loss of coordination of the extremities in rats exposed to 7.5 mg/L of deodorized kerosene 6 hours/day for 4 days. Noa and Illnait (3507) exposed male guinea pigs to kerosene aerosols for 15 minutes daily for 21 days. The concentration during the first 10 minutes of exposure was 20.4 mg/L and was raised to 34 mg/L during the last 5 minutes of exposure. Within 15 days, changes in the aorta that were typical of early atherosclerotic lesions were observed.

66.3.1.4.2 Subchronic and Chronic Toxicity

Subchronic (90-day) inhalation toxicity studies have been conducted with fuel oils of military interest, including marine diesel fuel and the kerosene-derived jet fuels, JP-5, and JP-8. Several investigators have observed a dose-related nephropathy in male rats exposed continuously to either 0.05 or 0.3 mg/L of petroleum- or shale-derived marine diesel fuel for 90 days (3144, 3086; 3415); however, these effects were not observed in female rats, female mice, or beagle dogs. Renal lesions consisted of increased cytoplasmic hyaline droplets in the proximal tubular epithelium, necrosis of proximal tubular cells, and intratubular plugs of necrotic cell debris at the corti-comedullary junction. The effects were more severe at the higher concentration (0.3 mg/L). MacEwen and Vernot also observed depressed body weight gain in male rats at both exposure levels.

MacNaughton and Uddin (3418) found similar results in male rats exposed continuously by inhalation to either 150 or 750 mg/m³ of petroleum- and shale-derived JP-5 for 90 days. Male rats exhibited decreased growth rate and histopathological changes in the kidneys including dilated tubules near the corticomedullary junction that were plugged with granular, necrotic debris and increased hyaline droplets in the proximal tubular cells. Mild, reversible, dose-related fatty changes in hepatocytes were also observed in mice at both concentrations. Bruner (3086) observed the same postexposure pattern of tubular degeneration in male rats exposed to petroleum and shale-derived marine diesel fuel for 90 days. Bruner (3086) also observed reversible hepatocellular fatty changes in mice exposed to 0.05 and 0.3 mg/L of petroleum derived marine diesel fuel for 90 days.

At 19 months postexposure to petroleum- and shale-derived JP-5 and marine diesel fuel, MacNaughton and Uddin (3418) and Bruner (3086), respectively, found that the tubular degeneration in the exposed male rats was more severe than in control rats and was accompanied by marked mineralization and pelvic urothelial hyperplasia and; therefore was distinguishable from the old rat nephropathy observed in the control rats.

Renal effects were not as pronounced in male rats exposed continuously by inhalation to 0.5 or 1.0 mg/L of JP-8 for 90 days (3416). Kidney function was slightly impaired in both exposure groups at two weeks post-exposure. However, increased mortality (50% greater than controls in males and 20% greater than controls in females) was observed in mice at both concentrations one-year post exposure. Death was attributed to sequelae of chronic dermatitis.

In chronic dermal studies with petroleum- and shale-derived marine diesel fuel and JP-8, Schultz et al. (3628) reported similar effects as observed in the inhalation studies with jet fuels. Groups of 10 to 15 C3Hf/Bd mice were dermally exposed to 6 doses of each fuel ranging from 6 to 45 mg in 50 microliters of cyclohexane, either 3 times/week for 40 weeks or 2 times/week for 60 weeks. The primary systemic effects were a significant reduction in body weight, a significant increase in spleen weights, and dose-related renal lesions, including atrophic and degenerative nephrons and papillary necrosis.

Thirteen-week dermal studies with petroleum-derived marine diesel fuel and JP-5 were conducted by NTP (3403) as range-finding studies to establish the doses to be tested in 2-year toxicology and carcinogenesis studies. Male and female B6C3F$_1$ mice (10/group) were exposed to doses of 0, 250, 500, 1000, 2000, and 4000 mg/kg of marine diesel fuel by dermal application to the clipped dorsal interscapular region. Doses of JP-5 used in the 13-week study were 0, 500, 1000, 2000, 4000, and 8000 mg/kg. Decreased body weights were observed in male mice at doses of marine diesel fuel greater than or equal to 500 mg/kg and an increased severity of mild chronic active dermatitis was observed for both sexes at the highest dose, 4000 mg/kg. Fifty percent mortality was observed in male mice following exposure to the highest dose of JP-5, 8000 mg/kg. Other observed effects in male and female mice exposed to doses of JP-5 greater than or equal to 1000 mg/kg included increased severity of

dermatosis, slight to moderate splenic extramedullary hematopoiesis, and slight hepatic karyomegaly. Based on the results of these 13-week studies, the doses selected for the 2-year studies were 250 and 500 mg/kg for both fuels.

In the 2-year NTP studies (3483), body weight gain was decreased by week 30 in all dose-groups of mice receiving marine diesel fuel and in the high-dose group (500 mg/kg) of mice receiving JP-5. Animals in the high-dose group for both fuels were killed early due to excessive irritation and ulceration at the site of application (both sexes for marine diesel fuel at 84-weeks exposure and females for JP-5 at 90-weeks exposure). For both fuels, the survival of both dosed groups of female mice was significantly lower than that of the controls. Chronic dermatitis, consisting of hyperplasia of the epithelium with accumulation of keratin on the surface and acute to chronic inflammation of the dermis, was observed at increased incidences in all mice exposed to both fuels. There was a 2- to 3-fold dose-related increase in the severity of the lesions compared with the controls.

66.3.2 Human and Epidemiologic Studies

66.3.2.1 Short-term Toxicologic Effects

The chief systemic reaction to petroleum hydrocarbons, such as fuel oils, is central nervous system depression (17). Toxicological effects are expected to resemble those of kerosene; i.e., a low oral, moderate dermal and high aspiration hazard (12). Provided that aspiration does not occur, the mean oral lethal dose of kerosene for an adult is estimated to be 4 to 6 ounces. However, twice this amount has been tolerated and less than one-half of an ounce has caused death (17). This estimate may be low since oral LD_{50} values in rats, rabbits and guinea pigs exceed 20 mL/kg. Following the accidental ingestion of petroleum distillates (diesel fuel, kerosene, etc.), the primary symptoms include pulmonary complications, cough, pneumonia, fever, vomiting, abdominal pain, diarrhea, drowsiness, lethargy, convulsions, and dramatic reduction in blood lipid levels (3421, 3054). In fatal poisonings, death may occur within 2 to 24 hours after ingestion. The difference between cases of uncomplicated ingestion and the lethal dose where aspiration occurs may be as great as a pint and a teaspoonful. The characteristic lesion resulting from aspiration is an acute and often fatal bronchopneumonia. Kerosene and related hydrocarbons are also irritating to the skin and mucous membranes. Percutaneous absorption may be significant (17).

Dermal exposure to diesel oil has caused nephrotoxicity. A man who cleaned his hands and arms with diesel oil over several weeks experienced symptoms of epigastric and loin pain, thirst, nocturia, nausea, anorexia, scrotal swelling, severe exhaustion and pitting ankle edema. Renal biopsy revealed acute tubular necrosis with patchy degeneration and necrosis of the proximal and distal tubular epithelium (1814). Another case was described by Barrientos et al. (1815) who reported acute oliguric failure in a patient who had washed his hair with diesel oil. A renal biopsy performed the next day showed tubular dilation and a proliferation of cells in the

glomeruli. Similar nephrotoxic effects were reported as a result of inhalation of diesel oil vapors in a truck cab over a 10 day period (1816).

Liquid petroleum hydrocarbons cause little or no injury on direct eye contact. Kerosene and petroleum oil on rabbit and human corneas are essentially innocuous (19).

66.3.2.2 Chronic Toxicologic Effects

Limited information is available concerning the effects of long-term exposure to fuel oils. Numerous epidemiology studies evaluating the effects of petroleum exposure have been conducted. While most have shown overall standardized mortality ratios to be lower than those of the general population, elevated numbers of deaths have been observed for cancers at several sites. However, these elevations are not found consistently in all of the studies and may be the result of confounding exposures to individual components in the fuel oils. Cancers have been observed in the lung, nasal cavity and sinuses, digestive system, brain, skin, pancreas and kidney. Leukemias and lymphomas have also been reported (1817).

It has been clearly demonstrated that hydrocarbon fuel vapors induce nephrotoxicity and renal carcinogenicity in male rats. However, these agents have failed to produce significant toxic or neoplastic changes in other major organs or in female rats. The mechanism responsible for the renal lesions is unknown at the present time; however, research is currently underway to assess the role of the male rat-specific protein, alpha-2u-globulin, in the initial formation of hyaline droplets and tubular degeneration (3418). Because the etiology of this species- and sex-specific nephrotoxicity is unknown, the question remains as to whether exposure to hydrocarbon fuel vapors would produce similar effects in humans. All epidemiological information to date is negative; however, the studies have either been limited in scope and/or the observed chronic effects could be attributed to individual components in the fuels. Consequently, no definitive studies are available at this time to determine the potential for human nephrotoxicity or renal carcinogenicity from exposure to hydrocarbon fuels (3746).

Knave et al. (3376) conducted studies with aircraft factory workers occupationally exposed to jet fuels at concentrations ranging from 500 to 3000 ppm. The acute symptoms included dizziness, respiratory tract symptoms, palpitations, pressure on the chest, nausea, and headache (3376). In a second study (3366), workers had been exposed to concentrations of jet fuel ranging from 85 to 924 mg/m^3, with values up to 3214 mg/m^3, for up to 20 years. The exposed and control groups were matched regarding age, employment duration, and education. Significant findings were a greater incidence of neurasthenia, anxiety, and mental depression, and slight impairment in reaction time and perceptual speed in the exposed group.

Jee et al. (3338) reported a prevalence of dermatoses among ball-bearing factory workers in Taiwan with major exposure to kerosene. The reference group were zipper-manufacturing workers with a similar age distribution, educational background

and income, and major exposure to textiles and plastics (no exposure to kerosene). In the kerosene-exposed group, 65% had erythema with or without desquamation over the interdigital spaces, 15% had eczematous lesions, 4% had defatting dermatitis, and 16% were asymptomatic. In the reference group, the only observed dermatoses was <1% with hand eczema.

66.3.3 Toxicology of Fuel Oil Components

A brief overview of the toxicology of the major hydrocarbon components of fuel oils are summarized below (see Table 66-5).

n-Hexane

Hexane may be the most highly toxic member of the alkanes. When ingested, it causes nausea vertigo, bronchial and general intestinal irritation and CNS effects. It also presents an acute aspiration hazard. Acute exposure occurs primarily through inhalation. Non-specific symptoms such as vertigo, headache, nausea and vomiting are the first to be manifested. At high concentrations, a narcosis-like state appears as a result of CNS depression. Pre-narcotic symptoms occur at vapor concentrations ranging from 1500-2500 ppm. n-Hexane irritates the eyes and mucous membranes. These effects can be seen after an exposure of 880 ppm for 15 minutes. Skin contact primarily causes fat removal and cutaneous irritation.

Chronic exposure to n-hexane vapors causes peripheral neuropathy. The first clinical sign of neural damage is a feeling of numbness in the toes and fingers. Progression leads to further symmetrical sensory impairment in the distal portions of the extremities and to loss of muscular stretching reflexes. Ultimately, symmetrical muscular weakness develops, chiefly in the distal portion of the extremities. Paralysis develops with varying degrees of impaired grasping and walking. This may include muscular atrophy (sensorimotor polyneuropathy). The development of electrophysiological changes parallels the severity of the clinical picture. In the most severe cases, nerve conductivity is neutralized. In some cases, cranial nerve involvement is also observed. After exposure ceases, recovery begins within 6 to 10 months in mild to moderate cases, but may take up to 3 years in serious cases. The threshold level at which neuropathy occurs has not been firmly established but symptoms have been observed in people exposed to concentrations ranging from 10 to 200 ppm for 9-12 months.

In animals, signs of narcosis are seen after mice are exposed to vapor levels of 16,000 ppm for 5 minutes. Death generally occurred at concentrations between 43,800 and 52,000 ppm after 9-119 minutes. The oral LD_{50} is cited as 24 mL/kg for 14-day-old rats and 49 mL/kg for young adult rats.

Long-term inhalation experiments in rats suggest that the first signs of neurotoxicity appear after they are exposed to levels of 200 ppm for 24 weeks. This higher threshold to induce neurotoxicity in animals may be due to differences in metabolism. Specifically, 2-hexanol is the chief metabolite in animals, while 2,5-hexanedione

TABLE 66-5
ACUTE TOXICITY OF COMPONENTS OF FUEL OILS

Component	Oral LD_{50}	Dermal LD_{50}	LC_{50}
n-hexane	24-49 mL/kg [rat] (1935) 28,710 mg/kg [rat] (1937)	no data	33,000 ppm ·4 hr [rat] (1935)
octane	<----------	no data	---------->
dodecane	<----------	no data	---------->
isopentane	no data	no data	1000 mg/L [mouse] (12)
isooctane	<----------	no data	---------->
methylcyclopentane	<----------	no data	---------->
methycyclohexane	2250 mg/kg [rat] (47)	no data	no data
cyclohexane	29,820 mg/kg [rat] (1935)	no data	no data
benzene	3800 mg/kg [rat] (59) 4700 mg/kg [mouse] (47)	no data	10,000 ppm ·7 hr [rat] (47)
toluene	5000 mg/kg [rat] (47)	12,124 mg/kg [rabbit] (47)	5320 ppm ·8 hr [mouse] (47)
xylenes	4300 mg/kg [rat] (47)	no data	5000 ppm ·4 hr [rat] (47)
ethyl benzene	3500 mg/kg [rat] (47)	5000 mg/kg [rabbit] (59)	no data
trimethylbenzenes	no data	no data	18 mg/m(3) ·4 hr [rat] (47)
1-methylnaphthalene	1840 mg/kg [rat] (47)	no data	no data
2-methylnaphthalene	1630 mg/kg [rat] (47)	no data	no data

which is neurotoxic, predominates in man. Chronic topical application of a solvent containing 35.2% n-hexane caused axonal swelling and myelin degeneration in chicks. No clinical signs were seen. Dosage was 1 g/kg/day for 64 days. In rabbits, topical application of 0.5 mL/day for up to 10 days caused redness, irritation and scab formation. N-hexane is neither carcinogenic or teratogenic. One in vivo study in rats that inhaled 150 ppm for 5 days found an increased number of chromosome aberrations in the bone marrow cells. No studies on mutagenicity, reproductive toxicity or carcinogenicity in man were found (12, 1930, 1935).

Octane

By the oral route, octane may be more toxic than its lower homologues. If it is aspirated into the lungs, it may cause rapid death due to cardiac arrest, respiratory paralysis and asphyxia. The narcotic potency of octane is approximately that of heptane but it does not exhibit the CNS effects seen with hexane or heptane.

In humans, the only reported effects are blistering and burning due to prolonged skin contact.

In animals, octane is a mucous membrane irritant. At high concentrations, it causes narcosis. It is expected that severe exposure in humans will produce the same effects. Mice exposed to vapor levels of 32,000 ppm suffered respiratory arrest after 4 minutes of exposure. Exposure to 12,840 ppm for 185 minutes caused a decreased respiratory rate, followed by death within 24 hours. No narcosis was seen after 48 minutes of exposure to 5350 ppm (12,46,1938).

Dodecane

Dodecane is not highly toxic. The lowest toxic dose for mice is 11 g/kg when administered percutaneously for 22 weeks. Dodecane is a potentiator of skin tumorigenesis by benzo(a)pyrene. It decreased the effective threshold dose by a factor of 10. Dodecane and phenyldodecane applied topically to the progeny of rats treated with benzo(a)pyrene, chrysene or benzo(b)triphenylene on the seventeenth day of gestation produced tumors in offspring. No additional information is available (12, 1937).

Isopentane

Isopentane is a CNS depressant. Effects may include exhilaration, dizziness, headache, loss of appetite, nausea, confusion, inability to do fine work, a persistent taste of gasoline and in extreme cases, loss of consciousness. Inhalation of up to 500 ppm appears to have no effect on humans. "Very high" vapor concentrations are irritating to the skin and eyes. Repeated or prolonged skin contact will dry and defat skin resulting in irritation and dermatitis. The LC_{50} in the mouse is estimated to be 1000 mg/L (12).

Iso-octane (2,2,4-trimethylpentane)

The iso-octanes are moderately toxic by the oral route. If aspirated into the lungs of rats, they will cause pulmonary lesions. When injected intramuscularly into rabbits, iso-octane produced hemorrhage, edema, interstitial pneumonitis, abscess formation, thrombosis and fibrosis. Inhalation of 16,000 ppm caused respiratory arrest in mice and 5 minutes exposure to 1000 ppm was highly irritating (1937).

Methylcyclopentane

Methylcyclopentane resembles cyclopentane in its toxicity. Cyclopentane is a CNS depressant. Humans can tolerate 10-15 ppm. In mice, 38 ppm causes loss of reflexes, narcosis and death demonstrating that no safety margin exists. Methylcyclopentane also exhibits no safety margin between the onset of narcosis and death. When applied to guinea pig skin, cyclopentane produced dryness and slight erythema. Methylcyclopentane would be expected to have the same effect (12).

Methylcyclohexane

No systemic poisonings by methylcyclohexane have been reported in man. At high vapor concentrations it causes narcosis in animals and it is expected that it would produce the same effect in humans. The no-effect level is about 300 ppm in primates and 1200 ppm in rabbits. Rabbits did not survive 70 minutes of exposure to 15,227 ppm. Death was preceded by conjunctival congestion, dyspnea, severe convulsions and rapid narcosis. There were no signs of intoxication in rabbits exposed to 2880 ppm for a total of 90 hours, but slight cellular injury was observed in the liver and kidneys. In primates, lethal concentrations caused mucous secretion, lacrimation, salivation, labored breathing and diarrhea.

In chronic inhalation studies, exposure to 2000 ppm, 6 hours per day, 5 days per week for 2 years produced no tumors in rats, mice, hamsters or dogs. The only significant toxic effect found was renal changes in male rats. These included renal tubular dilation, papillary hyperplasia and medullary mineralization.

Dermal application of the liquid produced local irritation, thickening and ulceration (12, 46, 54, 17, 1936).

Cyclohexane

Cyclohexane is a CNS depressant of low toxicity. Symptoms of acute exposure are excitement, loss of equilibrium, stupor and coma. Rarely, death results due to respiratory failure. The anesthesia which is induced is weak and of brief duration but more potent than that caused by hexane. The oral LDLo in rabbits ranges from 5.5 to 6.0 g/kg. Within 1.5 hours the animals exhibited severe diarrhea, widespread vascular damage and collapse. Degenerative lesions were seen in the heart, lung, liver, kidney and brain. A one-hour vapor exposure to 26,752 ppm caused rapid

narcosis and tremor and was lethal to all exposed rabbits. In mice, concentrations causing narcosis vary from 14,600 to 122,000 ppm.

Cyclohexane is nominally absorbed through the skin although massive applications (>180.2 g/kg) to rabbit skin resulted in microscopic changes in the liver and kidneys and caused the death of all animals.

The danger of chronic poisoning is relatively slight because this compound is almost completely eliminated from the body. No toxic changes were seen in rabbits exposed to vapor levels of 434 ppm, 6 hours daily for 50 exposures, but some microscopic changes were seen in the liver and kidneys when the exposure was to 786 ppm for the same period.

In man, no systemic poisonings by cyclohexane have been reported. A vapor level of 300 ppm is somewhat irritating to the eyes and mucous membranes. It has been reported that cyclohexane may potentiate the toxic effects of TOCP but no additional details of this interaction are available (12, 17, 46, 54, 1937).

Benzene

The primary effects of benzene inhalation and ingestion are on the central nervous system (54). Benzene is carcinogenic in both animals and man. Several reports have established a relationship between benzene exposure and leukemia. For more information, refer to the chapter on benzene in the Installation Restoration Program Toxicology Guide.

Toluene

Toluene is a CNS depressant with a low toxicity. For more information, refer to the chapter on toluene in the Installation Restoration Program Toxicology Guide.

Xylenes

Acute exposure to high concentrations of xylene vapors may cause CNS depression. Both the liquid and the vapor are irritating to the eyes, mucous membranes and skin (46). The National Toxicology Program recently reported that there was no evidence of carcinogenicity of mixed xylenes in either mice or rats given daily doses ranging from 250 to 1000 mg/kg by gavage for 2 years (1939). For more information, refer to the chapter on xylenes in the Installation Restoration Program Toxicology Guide.

Ethyl Benzene

Ethyl benzene is primarily an irritant to the skin, eyes and upper respiratory tract. Systemic absorption causes CNS depression (46). For more information, refer to the chapter on ethyl benzene in the Installation Restoration Program Toxicology Guide.

Trimethylbenzenes

The trimethylbenzenes occur in 3 isomeric forms. The 1,3,5-isomer (mesitylene) and the 1,2,4-isomer (pseudocumene) are toxicologically similar. High vapor concentrations (5000-9000 ppm) cause CNS depression in animals. Loss of reflexes was seen in mice exposed to 8130-9140 ppm of the 1,2,4-isomer or 8130 ppm of the 1,3,5-isomer. Rats exposed to 1700 ppm of an isomeric mixture for 10-21 days had no adverse effects or fatalities.

The fatal intraperitoneal dose of the 1,2,4-isomer for the guinea pig is 1.788 g/kg, while the fatal dose of the 1,3,5-isomer by the same route is 1.5-2 g/kg for the rat. For the 1,2,3-isomer, an oral LDLo of 5000 mg/kg has been reported in the rat. Trimethylbenzene liquid is a primary skin irritant. Deposition into the lungs causes pneumonitis at the site of contact.

The only report of human exposure described symptoms of nervousness, tension, anxiety, asthmatic bronchitis, hypochromic anemia and changes in the coagulability of the blood. Vapor concentrations ranged from 10-60 ppm. Exposure was to a mixture containing 30% of the 1,3,5-isomer and 50% of the 1,2,4-isomer (2,12).

Methylnaphthalene

The only adverse effects of methylnaphthalene reported in man are skin irritation and photosensitization (17). Oral LD_{50} values of 1840 mg/kg and 1630 mg/kg have been reported for 1-methylnaphthalene and 2-methylnaphthalene, respectively, in the rat (47).

Naphthalene

Ingestion or prolonged inhalation of naphthalene produces nausea, vomiting and disorientation. It is irritating to the skin and eyes and prolonged vapor exposure has led to cataract formation in humans (17). Hemolytic anemia is the most severe effect associated with naphthalene exposure, but this effect is seen predominantly in individuals with an enzyme deficiency (54).

For more information, refer to the chapter on naphthalene in the Installation Restoration Toxicology Guide.

Anthracene

Anthracene asserts phototoxic and photoallergic action on the human skin. It is carcinogenically inactive (12). Various mutagenicity studies have produced negative responses (2315). The lowest toxic oral dose in the rat is 20 g/kg (47).

66.3.4 Toxicology of Fuel Oil Additives

The toxicity of selected fuel oil additives is outlined below.

Manganese Compounds

Manganese affects the CNS. Intoxication occurs mostly in the chronic form known as manganism which is similar to Parkinsonism. Usually manganism occurs after 1-2 years exposure to manganese oxides although it may develop after only a few months. Initial symptoms include headache, asthenia (loss of strength and energy), restless sleep and personality change. This is followed by an intermediate phase with visual hallucinations, double vision, impaired hearing, uncontrollable impulses, mental confusion and euphoria. In advanced stages, the patient experiences excessive salivation, muscle weakness, muscle rigidity, tremor of the upper extremities and head, and impaired gait. In manganism with neurologic symptoms, the course is frequently progressive although some cases are stationary and others recover (2,46).

Inhalation of high concentrations of manganese oxide causes metal fume fever - a 24-48 hour illness characterized by chills, fever, aching muscles, dry mouth and throat, and headache (46).

Magnesium Oxide

Magnesium oxide fumes are irritating to the eyes and nose. It also causes metal fume fever which is a 24-48 hour influenza-type illness (46).

Aluminum Oxide

Aluminum oxide is a nuisance dust which has little adverse effect on the lungs at low exposure levels. Excessive concentrations may cause deposits in the eyes, ears and nasal passages or may cause mild injury to the skin and mucous membranes (46).

Peroxides

In general, peroxides are strong oxidizing agents capable of skin irritation, burns or eye damage (200).

Alkyl Nitrate and Nitrites/Nitro and Nitroso Compounds

Methemoglobinemia (a loss of the oxygen carrying capacity of the blood), is the main toxic effect of nitrite and nitrate ingestion.

Early symptoms include headache, fatigue, nausea, vomiting, chest pain and cyanosis. With increasing methemoglobin concentrations, there may be weakness, dizziness, incoordination, joint pain and muscular tremors (200, 480).

Various N nitroso derivatives have caused malignant tumors in various organ systems in laboratory animals. Generally, as the molecule increases in size, carcinogenic activity decreases (12). Exposure to these compounds should be avoided. Specific information on 2 nitroso compounds - N-nitrosodimethylamine and N-nitrosodiphenylamine - may be found in other sections of the Guide.

66.3.5 Levels of Concern

There are no criteria or standards for fuel oils. OSHA (3539) has set an 8-hour time- weighted-average exposure limit for petroleum distillates (naphtha) at 400 ppm.

66.3.6 Hazard Assessment

Fuel oils contain several polycyclic aromatic hydrocarbons which are carcinogens and/or cocarcinogens (2219). A fuel oil blend was highly active in both cellular assays and skin painting studies (1819). NTP (P44) has determined that marine diesel fuel at doses of 250 and 500 mg/kg results in increased incidences of squamous cell neoplasms of the skin, thus providing equivocal evidence for carcinogenicity in male and female B6C3F$_1$ mice. Other investigators have observed increased incidences of skin tumors in mice exposed to diesel fuel, No. 2 fuel oils, and jet fuel JP-8 (P45, P47). Positive mutagenic findings were observed in an Ames test, a mouse lymphoma assay and a rat bone marrow study for fuel oil number 2 (1914). Diesel fuel gave negative results in both the Ames and mouse lymphoma assay but positive results in the rat bone marrow assay (1914). A reproductive study with rats exposed by inhalation at levels up to 408 ppm suggested no adverse effects (1915).

Acute toxic effects of ingested fuel oils included alopecia, dermal irritation and open sores in the genital area of exposed rats. The oral LD_{50} values ranged from 5.1 to >20 g/kg for rats (1924).

Dermal studies in rabbits indicated severe dermal irritation, weight loss, anorexia, ataxia, lethargy, hemorrhagic gastroenteritis, and necrosis and degeneration of the liver following doses of fuel oils ranging from 2.5 to 10 mL/kg (1924, 3194, 3195, 3281). Fuel oils are also minimally to moderately irritating to rabbit eyes (1924).

Short-term inhalation exposure to diesel fuel and kerosene resulted in neurodepression and decreased pulmonary function in rats and mice (2334, 3148, 3101). Subchronic inhalation exposure (90 days) to marine diesel fuel (at concentrations of 0.05 and 0.3 mg/L) and kerosene-derived jet fuels (JP-5 at concentrations of 150 and 750 mg/m^3 and JP-8 at concentrations of 0.5 and 1.0 mg/L) has resulted in dose-related nephropathy in male rats (3086, 3418, 3416). Chronic dermal exposure to marine diesel fuel and JP-5 produced chronic dermatitis in B6C3F$_1$ mice exposed to 250 or 500 mg/kg for 2 years (3483).

In humans, CNS depression is the chief systemic reaction to fuel oils following either short-term (17) or long-term exposure (3376, 3366). Ingestion of less than 1/2 ounce has been fatal (17). Accidental ingestion of petroleum distillates can produce

chemical pneumonitis upon aspiration, neurodepression, and gastrointestinal distress (3421). Dermal and inhalation exposuresto diesel fuel have induced nephropathy in humans (1814,1815,1816). Chronic dermal exposure may also result in dermatitis, erythema, and eczematous lesions (3338).

66.4 SAMPLING AND ANALYSIS CONSIDERATIONS

Determination of the presence of fuel oils in soil and water requires collection of a representative field sample and laboratory analysis for the specific major components attributed to fuel oil; however, the relative concentrations of the constituents, and even the constituents themselves, will vary with time and distance from the site of initial contamination due to weathering. The major component categories in fuel oil have been identified as the following:

n-alkanes
branched alkanes
benzene and alkylbenzenes
naphthalenes
polynuclear aromatic hydrocarbons

A combination of capillary column gas chromatography (GC) and gas chromatography/mass spectrometry (GC/MS) techniques may be used to identify the principal components in the field that are primarily organic in nature. These may require the separation (prior to GC or GC/MS analysis) of the aliphatic, monoaromatic and polycyclic aromatic hydrocarbon fractions using liquid solid column chromatography. The various column eluates, with or without dilution in carbon disulfide, can then be analyzed by GC or GC/MS techniques. Aqueous samples need to be liquid-liquid extracted with an appropriate solvent (i.e., trichlorotrifluorethane) prior to analysis; solid samples would be extracted with trichlorotrifluoroethane using soxhlet extraction or sonication methods (1422). An aliquot of the sample extract, with or without concentration, is then analyzed by GC or GC/MS. Sampling and analysis considerations for some specific components in fuel oil, i.e., benzene, toluene, xylenes, ethyl benzene and naphthalene, have been addressed in Volume 1.

A dynamic purge and trap procedure for the determination of fuel oil in water has also been reported (3058). Water samples spiked with low concentrations of the fuel showed good recoveries. Other methods that have been used to analyze fuel oil in water include infrared spectrophotometry (IR) (3560) and fourier transform IR (3449). In the latter case a 0.5 ppb detection limit was reported for a 1 L sample extract. Solid phase extraction cartridges for preliminary separation of hydrocarbons in petroleum containing samples have also been described (3712).

Alternatively, the "oil and grease" content can be measured. This determination would not be the measurement of an absolute quantity of a specific component, but rather the quantitative determination of groups of components with similar physical characteristics (i.e., common solubility in trichlorotrifluoroethane). The "oil and

grease" content is defined as any material recovered from extraction with trichlorotrifluoroethane and measured gravimetrically; extraction methods are those described above for aqueous and soil samples.

A detection limit for fuel oils was not determined; the detection limit for specific components is expected to be in the range of μg/L for aqueous samples and μg/g for non-aqueous samples.

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Note: The nonsequential numbers of the references reflect the order of references as they appear in the master bibliography.

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COMPLEX MIXTURES

This chapter deals with a complex mixture and/or class of compounds. The format used for this less well-defined group of compounds was modified as necessary but follows the outline of earlier chapters as closely as possible. It should be noted, however, that the composition of these materials can vary according to the route of synthesis, the formulating ingredients added, the interactions of the active ingredients, or the storage conditions. These factors can influence the nature of the material that is ultimately utilized and probably are reflected in many of the experimental findings reported in the following chapters.

The typical components and approximate composition of the mixtures are provided if that information was available. Physical/chemical properties often were not available or varied depending on formulation. Many of these mixtures are blended to modify their physical properties according to the intended use. Furthermore, the formulations vary with season as well as with geographic locations of product use. In some cases, therefore, the range for the class of compounds was given.

In addition to the data for the mixture itself, the chapter that follows also contains sections on the principal components and major additives of the mixture, their fate in the environment and a brief overview of their toxicity.

COMMON SYNONYMS:	CHEMICAL COMPOSITION:	CAS REG NO: NIOSH NO.:
Dry cleaning safety solvent Mineral spirits PD-680 Solvent naphtha Stoddard solvent White spirits	Approximate Composition Linear and branched alkanes 30.0% - 50.0% Cycloalkanes 30.0% - 40.0% Aromatics 10.0% - 20.0% Benzene trace Olefins trace	8052-41-3 WJ8925000 AIR W/V CONVERSION FACTOR at 25°C 5.77 mg/m^3 = 1 ppm; 0.173 ppm = 1 mg/m^3 MOLECULAR WEIGHT: 135.00-145 (average)

REACTIVITY	Stoddard solvent is considered to be a miscellaneous combustible material for compatibility classification purposes. Those with oxidizing mineral acids or organic peroxides or hydroperoxides may produce heat, fire, and toxic gases, while those with strong oxidizing agents may produce heat, fire, and innocuous gases. Reactions with explosive materials may result in an explosion (38, 507, 511).

PHYSICO-CHEMICAL DATA	• Physical State: Liquid (at 20°C)	(2)
	• Color: Colorless	(2)
	• Odor: Mild petroleum	(507)
	• Odor Threshold: 0.900 ppm	(1970)
	• Density: 0.7700 g/mL (at 20°C)	(507)
	• Freeze/Melt Point: No data	
	• Boiling Point: 154.00 to 202.00°C	(2)
	• Flash Point: 37.80 to 60.00°C (variable)	(23,38, 51,507)
	• Flammable Limits: 0.80 to 6.00% by volume	(38,51,506)
	• Autoignition Temp.: 227.0 to 260.0°C (variable)	(23,38,51, 506)
	• Vapor Pressure: 3.00 mm Hg (at 20°C)	(507)
	• Satd. Conc. in Air: 2.20E+04 to 2.40E+04 mg/m^3 (at 20°C)	(1219)
	• Solubility in Water: Insoluble	(507)
	• Viscosity: 0.910 to 0.950 cp (at 20°C)	(5)

PHYSICO-CHEMICAL DATA	• Surface Tension: No data • Log (Octanol-Water Partition Coeff.): 3.16 to 7.06 (See Table 67-2) • Soil Adsorp. Coeff.: 7.00E+02 to 5.50E+06 (See Table 67-2) • Henry's Law Const.: 4.40E-04 to 7.40 atm · m³/mol (at 20°C) (See Table 67-2) • Bioconc. Factor: No data
PERSISTENCE IN THE SOIL-WATER SYSTEM	Stoddard solvent hydrocarbons are expected to be relatively mobile and moderately persistent in most soil systems. Persistence in deep soils and groundwater may be higher. Volatilization, photooxidation and biodegradation are potentially important fate processes. Surface spills are expected to be weathered by evaporation and photooxidation. Downward migration of weathered surface spills and sub-surface discharges represent a potential threat to underlying groundwater. Biodegradation of C7-C12 hydrocarbons is expected to be significant under environmental conditions favorable to microbial oxidation; naturally-occurring, hydrocarbon-degrading microorganisms have been isolated from polluted soils and, to a lesser extent, non-polluted soils.
PATHWAYS OF EXPOSURE	The primary pathway of concern from the soil/groundwater systems is the contamination of ground water drinking water supplies resulting from large spills of Stoddard solvent or leaking underground storage tanks. Vapors from leaked or spilled solvent may diffuse through soils and migrate into structures resulting in inhalation exposures. Inhalation exposures may also occur from the direct volatilization of surface spills. Ingestion with food is not expected to be significant.

HEALTH HAZARD DATA	Signs and Symptoms of Short-term Human Exposure: (38) Overexposure to Stoddard solvent causes irritation of the eyes, nose and throat and may cause dizziness. Prolonged overexposure to the liquid may cause skin irritation. Acute Toxicity Studies: INHALATION: LC_{Lo} 10,000 mg/m³ · 2.5 hr Cat (47) Long-Term Effects: kidney damage Pregnancy/Neonate Data: Fetotoxic at maternally toxic doses Genotoxicity Data: Negative Carcinogenicity Classification: IARC - No data NTP - No data EPA - No data
HANDLING PRECAUTIONS (38,507)	Handle only with adequate ventilation • Vapor levels of 500 to 1000 ppm: chemical cartridge respirator with a full facepiece and organic vapor cartridges • 1000 to 5000 ppm: any supplied-air respirator or self-contained breathing apparatus with full facepiece; gas mask with organic vapor canister • Chemical goggles if there is probability of eye contact • The use of impermeable gloves is advised to prevent skin irritation.

ENVIRONMENTAL AND OCCUPATIONAL STANDARDS AND CRITERIA

AIR EXPOSURE LIMITS:

Standards
- OSHA TWA (8-hr): 100 ppm
- AFOSH PEL (8-hr TWA): 100 ppm; STEL (15-min): 150 ppm

Criteria
- NIOSH IDLH (30-min): 5000 ppm
- NIOSH REL (10-hr TWA): 350 mg/m^3
- NIOSH CL (15-min): 1800 mg/m^3
- ACGIH TLV® (8-hr TWA): 100 ppm
- ACGIH STEL (15-min): STEL deleted

WATER EXPOSURE LIMITS:

Drinking Water Standards
None established.

EPA Health Advisories and Cancer Risk Levels
None established.

WHO Drinking Water Guideline
No information available.

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

REGULATORY STATUS (as of 01-MAR-89)

Promulgated Regulations

- Federal Programs

  Marine Protection Research and Sanctuaries Act (MPRSA)
  Ocean 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 Stoddard solvent shall not exceed an 8-hour time-weighted average of 100 ppm (3539).

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

- State Water Programs

  ALL STATES
  All states have adopted EPA Ambient Water Quality Criteria and NPDWRs (see Water Exposure Limits section) as their promulgated state regulations, either by narrative reference or by relisting the specific numeric criteria:

  ALASKA
  Alaska has a water quality criterion for the protection of aquatic life of 15 µg/L for total hydrocarbons and 10 µg/L for total aromatic hydrocarbons in fresh and marine surface waters (3016).

  ARKANSAS
  Arkansas requires that oil and grease shall not exceed 10 mg/L average or 15 mg/L maximum when discharging to surface waters (3587).

  FLORIDA
  Florida requires that oil and grease not exceed 10 mg/L in Class V waters (navigation, industrial use) and 5 mg/L for all other surface waters (3220).

  MASSACHUSETTS
  Massachusetts requires that the maximum discharge concentration of oil and grease of petroleum origin not exceed 15 mg/L in surface waters (3432).

  NEBRASKA
  Nebraska requires that petroleum oils not exceed 10 mg/L in surface

NEW YORK
New York has set a maximum contaminant level of 50 μg/L for kerosene in drinking water (3501).

SOUTH DAKOTA
South Dakota has a water quality standard of 10 mg/L for all petroleum products in surface waters (3672).

VIRGINIA
Virginia has a water quality standard of 1 mg/L for petroleum hydrocarbons in ground-water (3135).

WYOMING
Wyoming has a water quality standard of 10 mg/L for surface waters and Class II and III ground-waters. In addition, Class I domestic ground-water is required to be virtually free of oil and grease (3853, 3852).

OTHER STATES
Other states follow EPA Ambient Water Quality Criteria for oil and grease.

Proposed Regulations

- Federal Programs
  No federal regulations are pending.

- State Water Programs
  No state regulations are pending.

MOST STATES
Most states are in the process of revising their water programs and proposing changes to their regulations which will follow EPA's changes when they become final. Contact with the state officer is advised. Changes are projected for 1989-90 (3683).

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 Fishing Water Quality (536)
Petroleum products must not be present in salmonid and cyprinid waters in such quantities that they: (1) form a visible film on the surface of the water or form coatings on the beds of water-courses and lakes, (2) impart a detectable "hydrocarbon" taste to fish and, (3) produce harmful effects in fish.

Directive on the Quality Required of Shellfish Waters (537)
The mandatory specifications for petroleum hydrocarbons specify that they may not be present in shellfish water in such quantities as to produce a visible film on the surface of the water and/or a deposit on the shellfish which has harmful effects on the shellfish.

Directive on the Discharge of Dangerous Substances (535)
Organohalogens, organopnosphates, 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 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)
Petroleum and coal tar distillates with flash points below 21°C are classified as flammable substances and are subject to packaging and labeling regulations. Because of the variable composition of her petroleum and coal tar distillates (excluding those used as motor fuels), they are considered preparations and their labeling shall be done in accordance with the procedures outlined in the Directive Relating to the Classification, Packaging and Labeling of Dangerous Preparations (solvents).

EEC Directives - Proposed
Proposal for a Council Directive on the Dumping of Waste at Sea (1793)
EEC has proposed that the dumping of crude oil, petroleum hydrocarbons, lubricants and hydraulic fluids at sea be prohibited.

67.1 MAJOR USES AND COMPOSITION

67.1.1 Major Uses

Stoddard solvent is produced from a straight-run distillate of paraffinic or mixed base crude oil. It is used as a diluent in paints, coatings and waxes; as a dry cleaning agent; as a degreaser and cleaner; and as a herbicide (2).

67.1.2 Composition

Stoddard solvent is a mixture of C_7 through C_{12} hydrocarbons, predominantly C_9 through C_{11}, with a boiling range between 160°C to 210°C. Flash point dry-point test and odor data are used to classify Stoddard solvent into the following four types: regular Stoddard solvent, 140 flash solvent, odorless solvent, and low end point solvent. Chemically, Stoddard solvent is a mixture of 30-50% straight and branched alkanes, 30-40% cycloalkanes, and 10-20% aromatics. Benzene and olefins are present in trace quantities only (2228). The 140 flash aliphatic solvent is composed of organic compounds with carbon chain lengths ranging from C_9 to C_{12}. Its boiling range is 185-207°C and it is composed of 60.8% paraffins, 24.5% monocycloparaffins, 11.2% dicycloparaffins, 3.03% alkyl benzenes, 0.3% indans and tetralins, and 0.07% benzenes (1967). Both types will be discussed in some sections of the chapter which follows.

A characterization of the individual hydrocarbon components of Stoddard solvent was not available. Table 67-1 presents the available characterization by chemical classes.

67.2 ENVIRONMENTAL FATE AND EXPOSURE PATHWAYS

A discussion of the environmental behavior of Stoddard solvent is limited by the lack of analytical data defining its specific components. Many of the hydrocarbons expected to be components of Stoddard solvent were addressed previously in the more extensive environmental fate section of Chapter 64 (Jet Fuel 4). The general discussions of aliphatic and aromatic hydrocarbons and their behavior in soil/ground-water systems will not be repeated here; the reader is referred to the relevant sections of Chapter 64.

67.2.1 Equilibrium Partitioning Model

In general, soil/ground-water transport pathways for low concentrations of pollutants in soil can be assessed by using an equilibrium partitioning model. For the purposes of assessing the environmental transport of Stoddard solvent, a group of specific

TABLE 67-1
COMPOSITION DATA FOR STODDARD SOLVENT

Carbon Range	C_7-C_{12}
Straight/Branched Alkanes	48%
Cycloalkanes	38%
Aromatics:	
Benzenes	0.1%
Alkylbenzenes	14%
Indans/Tetralins	< 1%

(Reference 1967)

hydrocarbons within the C_7-C_{12} range was selected from the dominant hydrocarbon classes, i.e., alkanes, cycloalkanes, and aromatics; there are no available data to confirm the presence of the selected hydrocarbons in typical Stoddard solvent sample. Table 67-2 identifies the selected hydrocarbons and presents the predicted partitioning of low soil concentrations of those hydrocarbons among soil particles, soil water, and soil air. The portions associated with the water and air phases of the soil are expected to have higher mobility than the adsorbed portion.

Estimates for the unsaturated topsoil indicate that sorption is expected to be an important process for all the dominant hydrocarbon categories. Partitioning to the soil-vapor phase in this model is not very important for the C_7-C_{12} hydrocarbons. The alkyl benzenes have higher water solubilities and transport with infiltrating water may be important for these compounds; volatilization is still expected to be low. In saturated, deep soils (containing no soil air and negligible soil organic carbon), a significant percentage of the aromatic hydrocarbons is predicted to be present in the soil-water phase and available for transport with flowing ground water.

In interpreting these results, it must be remembered that this model is valid only for low soil concentrations (below aqueous solubility) of the components. Large releases of solvent (spills, leaking underground storage tanks) may exceed the sorptive capacity of the soil, thereby filling the pore spaces of the soil. In this situation, the hydrocarbon mixture would move as a bulk fluid and the equilibrium partitioning model would not be applicable.

TABLE 67-2

EQUILIBRIUM PARTIONING OF POTENTIAL
STODDARD SOLVENT HYDROCARBONS IN MODEL ENVIRONMENTS[a]

COMPOUND	Log K_{ow}	K_{oc}[b]	H[c]	UNSATURATED TOPSOIL (%)			SATURATED DEEP SOIL[d] (%)	
				Soil	Water	Air	Soil	Water
Octane	5.18 (e)	73,000	2.96	97.4	0.01	2.6	97.7	0.3
Dodecane	7.06 (f)	5.5×10^6	7.4	99.9	0.0001	0.09	99.9	0.004
Trimethylpentane	4.87 (f)	36,000	1.9-3.3	94.7	0.01	5.3	99.3	0.7
Methylcyclohexane	4.10 (f)	6,070	0.39	95.9	0.08	4.0	96.2	3.8
Trimethylcyclohexane	5.02 (h)	50,500	1.6	98.0	0.01	2.0	99.5	0.5
Xylenes	3.16 (e)	700	7×10^{-3}	98.8	0.7	0.5	74.4	25.6
Trimethylbenzenes	3.65 (h)	2,150	5×10^{-3}	99.6	0.2	0.2	90.0	10.0
Naphthalene	3.30 (e)	962	4.82×10^{-4}	99.4	0.5	0.03	80.2	19.8
Methylnaphthalenes	3.87 (e)	3,570	4.4×10^{-4}	99.8	0.1	0.01	93.7	6.3

[a]Calculations based on Mackay's equilibrium partioning 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]Reference 652.

[c]Taken from Reference 74 unless otherwise specified. Units equal $atm \cdot m^3/mol$.

[d]Used sorption coefficient $K_p = 0.001 \times K_{oc}$.

[e]Reference 29.

[f]Arthur D. Little, Inc., estimate according to equations provided in Reference 31.

[g]Reference 10.

[h]Reference 31.

67.2.2 Transport and Transformation Processes

Transport and transformation of Stoddard solvent constituents will depend on the physicochemical (and biological) properties of the constituents. Some constituents will dissolve more quickly in the percolating ground waters and be sorbed less strongly on the soils, thus being transported more rapidly, and may or may not be susceptible to degradation by chemical or biological action. The relative concentrations of the constituents of the solvent will vary with time and distance from the site of contamination. This effect is called "weathering." (This term is also used to describe the changes to petroleum materials following spills into surface waters where film spreading and breakup, and differential volatilization, dissolution and degradation are all involved.)

There are no available data specific to the transport and transformation of Stoddard solvent in soil/ground water systems. In general, the low water solubility and moderate vapor pressure of Stoddard solvent suggest that volatilization with subsequent photo-oxidation in the atmosphere may be important. Even though the most volatile hydrocarbons (i.e., < C_7) are not expected to be major components of Stoddard solvent, volatilization from surface soils is expected to be a major fate process for the alkanes which have very low water solubility. The aromatic hydrocarbons likely to be present in Stoddard solvent are moderately soluble in water and may be available to be dissolved in and transported with infiltrating water. Sorption to organic materials may limit the actual rates of leaching and volatilization from soils.

As discussed in detail in Chapter 64, large surface spills or subsurface discharges of petroleum distillates may result in a separate organic phase on the surface of the ground water. Migration of the organic phase may be very different from that of the ground water itself and the solvent hydrocarbons dissolved in the ground water.

Biodegradation may be an important transformation process for Stoddard solvent in soil/ground water systems; some photo-oxidation of surface spills may also occur. Data presented in Chapter 64 suggest that microorganisms capable of degrading C_7 to C_{12} aliphatic and aromatic hydrocarbons are not uncommon in the environment, and under conditions favorable to microbial activity, biodegradation maybe rapid. It should be mentioned that Walker et al. (2257) state that even under optimum conditions, total and complete biodegradation of petroleum hydrocarbons is not expected to occur except possibly over an extremely long time period.

Overall, ground water underlying soil contaminated with Stoddard solvent hydrocarbons may be vulnerable to contamination by at least some of these components. The type of spill (surface vs. sub-surface) is of importance since volatilization from the surface may be a significant removal process particularly for the lower molecular weight aliphatics. At this point, it should be mentioned that

environmental fate/exposure/toxicology chapters for xylene and naphthalene listed in Table 67-2 were included in other chapters of the IRP Toxicology Guide.

67.2.3 Primary Routes of Exposure from Soil/Ground Water Systems

The above discussion of fate pathways suggests that the major components of Stoddard solvent are volatile but vary in their potential for bioaccumulation and sorption to soil. They range from moderately to strongly sorbed to soil, and their potential for bioaccumulation ranges from low to high. The variability in the properties of the components suggests they have somewhat different exposure pathways.

Spills of Stoddard solvent would result in the evaporative loss of the more highly volatile components, leaving those of lesser volatility in the soil. The fraction remaining in the soil is expected to be relatively mobile assuming the spill is large enough to exceed the sorptive capacity of the soil. Gravity will carry the bulk fluid to the saturated zone of the soil. There, the more soluble components (aromatic and lower molecular weight aliphatic compounds) will dissolve into the ground water or form emulsions with it, while the insoluble fraction will float as a separate phase on top of the water table.

The movement of dissolved hydrocarbons in ground water is much greater than for the separate liquid phase, reaching distances of hundreds to thousands of meters compared to tens of meters for the separate liquid phase. In the presence of cracks and fissures, however, the flow of the separate phase is greatly enhanced. The movement of Stoddard solvent in ground water may contaminate drinking water supplies, resulting in ingestion exposures. Ground water discharges to surface water or the movements of contaminated soil particles to surface water drinking water supplies may also result in ingestion exposures, as well as in dermal exposures from the recreational use of these waters. The uptake of Stoddard solvent by fish and domestic animals is not expected to be a significant exposure pathway for humans because the hydrocarbons with the greatest potential for bioaccumulation, polycyclic aromatic compounds, account for such a small fraction of the mixture.

Volatilization of Stoddard solvent in soil is another potential source of human exposure. Once in the soil, the hydrocarbons evaporate, saturating the air in the soil pores, and diffusing in all directions including upward to the surface. The vapors may diffuse into the basements of homes or other structures in the area, resulting in inhalation exposures to the buildings' occupants. Exposures may be more intensive when the soil is contaminated directly from leaking underground storage tanks and pipes rather than from surface spills. In such cases the more volatile components do not have an opportunity to evaporate before penetrating the soil. Obviously, such an exposure scenario requires a substantial release of Stoddard solvent into the soil, and is more likely to occur if the solvent is being handled in bulk rather than in drums.

67.2.4 Other Sources of Human Exposure

Data on the ambient concentrations of Stoddard solvent in air and water as well as in food and drinking water are not readily available in the literature. Exposure information on some specific components may be found in other chapters of this guide. Groups expected to receive the largest exposure to Stoddard solvent include those who use it as a solvent cleaner. Inhalation exposures are likely, as are dermal exposures if protective gloves and clothing are not worn. The same is also true for those using paints or paint thinners that contain Stoddard solvent. Dry cleaners using Stoddard solvent can also expect to experience inhalation and dermal exposures. Although traces of the solvent may remain on clothes after dry cleaning, inhalation and dermal exposures that result from wearing dry-cleaned clothes are not expected to be significant.

67.3 HUMAN HEALTH CONSIDERATIONS

67.3.1 Animal Studies

67.3.1.1 Carcinogenicity

There are no carcinogenicity data available for Stoddard solvent. However, a life-time skin painting study with male C3H/HeJ mice was conducted using a commercial product consisting of a mixture of Stoddard solvent (90.9% by volume) and two additional components (6.6% of a calcium soap of oxidized wax acids with minor amount of calcium petroleum sulfonate and 2.5% ethylene glycol monobutyl ether). By the end of the test period (864 days), 6 of the 50 mice painted with the mixture had developed squamous cell carcinomas in the treated area. Mice in the negative control group (white mineral oil, U.S.P.) had no tumors (3205). However, it is difficult to evaluate the results of this study considering the potential influence of the two other components.

67.3.1.2 Mutagenicity

Stoddard solvent is not mutagenic in either in vitro or in vivo systems. The American Petroleum Institute evaluated Stoddard solvent in three tests (1914). In the Ames assay, there was no significant increase in the numbers of revertant colonies of Salmonella typhimurium strains TA98, 100, 1535, 1537, and 1538 both with and without microsomal activation. Negative results were also reported in the L5178Y mouse lymphoma assay and in a dominant lethal assay in which CD rats were administered ip doses of 0.087, 0.289 or 0.863 mL/kg/day for 5 days. Gochet et al. (1968) reported negative results in the micronucleus test with mouse bone marrow cells and in the in vitro induction of sister chromatid exchange in human lymphocytes.

67.3.1.3 Teratogenicity, Embryotoxicity and Reproductive Effects

There were no treatment-related effects on implantation, fetal resorption or number of viable fetuses after mated female CD rats were exposed to vapor levels of 100 or 300 ppm for 6 hours daily on days 6-15 of gestation. In the high exposure group there was a statistically significant increase in the total incidence of fetuses with ossification variation but the types and relative incidences were comparable to historical controls (1969). A study conducted by API also reported negative results in rats that were exposed by inhalation to 100 or 400 ppm of the agent for 6 hours daily on day 6-15 of gestation (3627). The lowest dose selected was the Threshold Limit Value previously established in toxicity studies.

Wistar rats were exposed to air containing the agent for 6 hours/day on days 6-15 of gestation (237, 482, or 953 ppm) or on days 3-20 of gestation (950 ppm). In the two groups exposed to 950 or 953 ppm, mildly decreased maternal weight gain and increased eye irritation were observed (3334). Neither the reproductive data nor the incidences of skeletal or visceral malformation were observed for any group. However, the group exposed on days 3-20 displayed lower fetal body weights, delayed ossification, and an increase of fetuses with extra ribs. This fetotoxicity occurred only at dose levels which also resulted in maternal toxicity.

67.3.1.4 Other Toxicologic Effects

67.3.1.4.1 Short-term Toxicity

Stoddard solvent vapor is a mild narcotic and a mucous membrane irritant (46). A comprehensive series of studies have been conducted by Carpenter and associates (1970) to evaluate the toxicity of both Stoddard solvent and 140 flash aliphatic solvent. The Stoddard solvent used had a flash point of 109 deg F (43°C) and a boiling range of 307-382°F (153-194°C). Rats had no ill effects after 8 hours at 420 ppm while the no-effect level for dogs was 510 ppm in the same time period.

Eight hours at 1400 ppm was not lethal to rats but toxic symptoms included eye irritation, bloody exudate around the nostrils, and slight loss of coordination. Similar symptoms were seen after exposure to 800 ppm for 8 hours, but there was no loss of coordination (1970). A female beagle exposed to 1400 ppm had eye irritation, salivation, tremors and convulsions within a 5-hour period while a second was asymptomatic during and after the 8-hour inhalation period. Both animals survived. All cats inhaling 1700 ppm died within an 8-hour exposure period (1970). The 140 flash aliphatic solvent had a boiling range of 363-402°F (183-206°C). Exposure to vapor levels of 33 or 43 ppm for 8 hours had no effect on either dogs or rats, respectively. Cats exposed to vapor levels of 43 ppm for 6 hours also had no adverse effects (1971).

Rector et al. (1972) exposed rats, guinea pigs, rabbits, dogs and monkeys to mineral spirits which met Stoddard solvent specifications. The animals were exposed

6 hours daily, 5 days per week for a total of 30 exposures to vapor levels of 290 ppm. The only effects seen were minor congestion and emphysema of guinea pig lungs.

Grant reported that Stoddard solvent caused little injury on direct contact with the rabbit eye (19).

67.3.1.4.2 Chronic Toxicity

There is evidence that long-term exposure to Stoddard solvent causes toxic effects on the kidneys of male rats. These changes are limited to the proximal portion of the tubule and are characterized by an increase in the incidence of regenerative tubular epithelia and hyalin droplet nephropathy (2309). Some rat strains appear to be more susceptible than others. The predisposition of male rats to the occurrence of hyalin droplets is thought to be related to the large amount of protein excreted by the male kidney (2309).

When Sprague-Dawley and Fischer 344 rats of both sexes were exposed to Stoddard solvent vapor at concentrations of 100 or 800 ppm, 6 hours daily, 5 days per week for 8 weeks, kidney changes were seen in males only. The Fischer 344 rats appeared to be slightly more responsive than the Sprague-Dawley rats. The primary structural change was an increased incidence of regenerative tubular epithelia in the cortex. At the corticomedullary junction there were dilated tubules filled with proteinaceous material. Changes in urine parameters were observed after 4 to 8 weeks of exposure. In male rats, these included a reduction in urine concentrating ability, an increase in total urine protein and glucose, and an increase in the excretion of epithelial cells in the urine. None of these changes were observed in female rats (2309).

Phillips and Egan (1974) exposed Sprague-Dawley rats of both sexes to dearomatized white spirit (flash point 104°F/40°C) at vapor levels of 300 or 900 ppm for 6 hours daily, 5 days per week for up to 12 weeks. They observed nephrotoxicity in male rats only from both exposure groups. The effects began four weeks after the onset of exposure and were indicative of mild tubular toxicity. The incidence and severity increased with increasing concentrations and exposure duration. There were no other significant toxic effects.

In a similar study, Carpenter et al. (1970) exposed male rats to 330 ppm for 65 days on the same dosing schedule and observed marked tubular regeneration which they attributed in part to the inherent murine nephrosis of the Harlan-Wistar rats employed. Phillips and Egan (1974) upon re-evaluation of Carpenter's data, found the kidney changes to be identical to those observed in their study. They concluded that the hydrocarbons eliciting the most pronounced renal tubular changes have a boiling range of 120-200°C and a carbon length of C_9-C_{11}.

In a 12-month study, male Sprague-Dawley rats exposed to vapor levels of 6500 mg/m^3 white spirit, 8 hours daily, 5 days per week, had a decreased urinary

concentrating ability, a decreased net acid excretion following a mild ammonium chloride load, and an increased urinary lactate dehydrogenase (LDH) activity, all of which indicate an alteration in the distal tubule of the kidney (1973).

No toxic effects were reported in male Harlan-Wistar rats exposed to 140 flash aliphatic solvent at vapor levels of up to 37 ppm, 6 hours daily, 5 days per week for 72 days or in dogs exposed for 73 days (1971).

In a 28-day dermal toxicity study, Stoddard solvent was classified as a moderate irritant in male and female animals (species was not reported) at a dose of 200 mg/kg. At a dose of 1000 mg/kg, it was a moderate irritant to females and a severe irritant to males. It was a severe irritant to both sexes at 2000 mg/kg (2310).

67.3.2 Human and Epidemiologic Studies

67.3.2.1 Short-term Toxicologic Effects

Stoddard solvent is an eye, nose, and throat irritant in humans. Acute exposure to high vapor concentrations can cause headaches and produce narcotic effects (38). Pedersen and Cohr (1975) found that 6-hour exposures to vapor levels of 50-200 ppm white spirit produced dryness of the mucous membranes, anorexia, nausea, vomiting, diarrhea and fatigue. In another study, one of six volunteers exposed to a vapor level of 150 ppm for 15 minutes experienced eye irritation while all six reported irritation after 15 minutes at 470 ppm. Two subjects at this level also reported slight dizziness (1970).

Inhalation of 17-49 ppm 140 flash aliphatic solvent for 15 minutes per day for 2 days caused slight temporary dryness of the eyes (1971).

Acute exposure to Stoddard solvent was also found to prolong reaction time and impair short-term memory for visual stimuli. The subjects were exposed to vapor levels of 4000 mg/m^3 for 35-40 minutes (1976).

Dermal exposures to the liquid have caused dermatitis and jaundice (38).

67.3.2.2 Chronic Toxicologic Effects

NIOSH (1967) has reported numerous cases of long-term dermal and inhalation exposure. Industrial exposures to unknown but fairly high concentrations over long periods have resulted in headaches, eye, nose and throat irritation, fatigue, bone marrow hypoplasia, and in extreme cases, death (38).

Scott et al. (2332) reported four cases of aplastic anemia in individuals known to have been exposed to Stoddard solvent. Three of these cases were fatal. In the first fatality, Stoddard solvent and carbon tetrachloride exposures occurred 2 or 3 times a month for a 2-year period. The patient experienced excessive uterine bleeding, purpura, and moderate bone marrow hypoplasia. At autopsy, focal hyperplasia was

found. In the second case, dermal exposure to Stoddard solvent occurred 4 or 5 times a week during a 6-month period. This individual had also been taking diphenhydramine and tripelennamine hydrochloride for several years to control seasonal allergies. Two months after exposure ended, symptoms of anemia were seen. Autopsy revealed moderate bone marrow hypoplasia (2332).

In the third fatal case, dermal exposure occurred over a 2-year period. Symptoms included purpura, pallor, fatigue, and slightly hypoplastic bone marrow. Autopsy findings revealed marked hypoplasia. The patient had denied using other potentially toxic solvents (2332).

The fourth case was an individual who had used a Stoddard-type solvent in a large open tub, once a year for 20 years, usually indoors. A slight reduction in all formed blood elements was seen. The patient survived after a splenectomy was performed. The authors concluded that these cases implicated Stoddard-type solvents as possible myelotoxic agents but since no information was given on solvent composition, it is not possible to rule out other myelotoxic compounds such as benzene (2332).

Dermal exposure to undiluted Stoddard solvent for 10 weeks resulted in follicular dermatitis and jaundice. One year after exposure, tests revealed latent jaundice and possibly permanent liver damage (2333).

67.3.3 Levels of Concern

OSHA (3539) currently permits exposure to 100 ppm as an 8-hour time-weighted-average. The ACGIH (3005) has set a time-weighted-average of 100 ppm, with a short-term exposure limit of 200 ppm.

67.3.4 Hazard Assessment

No carcinogenicity tests have been conducted for Stoddard solvent. A life-time skin painting study with mice using a commercial product containing Stoddard solvent and two additional components (a calcium soap of oxidized wax acids and ethylene glycol monobutyl ether) produced a low incidence of squamous cell carcinomas. However, the results are difficult to interpret because of the presence of other components. Mutagenicity data are negative for bacteria and mammalian cells in culture; negative results were also obtained in a rat dominant lethal study and mouse micronucleus test (1914, 1968).

Exposure of pregnant rats to vapor levels of 300 ppm, 6 hours daily during gestation was without effect (1969). Stoddard solvent was fetotoxic in rats only at maternally toxic doses (950 ppm) (3334).

Animal studies indicate mild narcotic effects and irritation of mucous membranes with acute exposure (46). Long-term exposures result in kidney damage (2309).

particularly in male rats. The incidence and severity of renal toxicity appeared to increase with concentration and exposure duration (1974, 2309, 1970).

In humans, acute exposure produces eye, nose and throat irritation, nausea, vomiting, diarrhea and fatigue (38,1975). High vapor concentrations can produce headaches and narcotic effects (38). Prolonged industrial exposures to very high concentrations of Stoddard solvent have been linked to fatigue, bone marrow hypoplasia, and aplastic anemia (38, 1967, 2332); it is unclear, however, if other myelotoxic solvents were also involved.

67.4 SAMPLING AND ANALYSIS CONSIDERATIONS

Determination of the presence of Stoddard solvent in soil and water requires collection of a representative field sample and laboratory analysis for the specific major components attributed to Stoddard solvent; however, the relative concentrations of the constituents, and even the constituents themselves, will vary with time and distance from the site of initial contamination due to weathering. The major component categories in Stoddard solvent have been identified as the following:

n-alkanes
branched alkanes
cycloalkanes
benzene and alkylbenzenes

A combination of capillary column gas chromatography (GC) and gas chromatography/mass spectrometry (GC/MS) techniques may be used to identify the principal components in Stoddard solvent. Samples, and probably any samples collected in the field which are primarily organic in nature, may require the separation (prior to GC or GC/MS analysis) of the aliphatic and aromatic hydrocarbon fractions using liquid solid column chromatography; the various column eluates, with or without dilution in carbon disulfide, can then be analyzed by GC or GC/MS techniques. Aqueous samples need to be liquid-liquid extracted with an appropriate solvent (i.e., trichlorotrifluoroethane) prior to analysis; solid samples would be extracted with trichlorotrifluoroethane using soxhlet extraction or sonication methods (1422). An aliquot of the sample extract, with or without concentration, is then analyzed by GC or GC/MS. Sampling and Analysis Considerations for some specific components in Stoddard solvent, i.e., benzene, toluene, xylenes and ethyl benzene, have been addressed in Volume 1. Purge and trap procedures can be used to determine these volatile constituents. It should be noted, however, that recent studies (3430) show large losses of volatiles from soil handling. At the present, the best procedure is to collect the needed sample in an EPA VOA vial, seal with a foil-lined septum cap, and analyze the entire contents in the vial using a modified purge and trap apparatus.

Alternatively, the "oil and grease" content can be measured. This determination would not be the measurement of an absolute quantity of a specific component, but rather the quantitative determination of groups of components with similar physical characteristics (i.e., common solubility in trichlorotrifluoroethane). The "oil and grease" content is defined as any material recovered from extraction with trichlorotrifluoroethane and measured gravimetrically; extraction methods are those described above for aqueous and soil samples.

A detection limit for Stoddard solvent was not determined; the detection limit for specific components is expected to be in the range of 10 μg/L for aqueous samples and 1 μg/kg for nonaqueous samples.

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COMPLEX MIXTURES

This chapter deals with a complex mixture and/or class of compounds. The format used for this less well-defined group of compounds was modified as necessary but follows the outline of earlier chapters as closely as possible. It should be noted, however, that the composition of these materials can vary according to the route of synthesis, the formulating ingredients added, the interactions of the active ingredients, or the storage conditions. These factors can influence the nature of the material that is ultimately utilized and probably are reflected in many of the experimental findings reported in the following chapters.

The typical components and approximate composition of the mixtures are provided if that information was available. Physical/chemical properties often were not available or varied depending on formulation. Many of these mixtures are blended to modify their physical properties according to the intended use. Furthermore, the formulations vary with season as well as with geographic locations of product use. In some cases, therefore, the range for the class of compounds was given.

In addition to the data for the mixture itself, the chapter that follows also contains sections on the principal components and major additives of the mixture, their fate in the environment and a brief overview of their toxicity.

CHEMICAL COMPOSITION	Mineral Base: Water in oil emulsions Linear and branched chained aliphatics Oil in water emulsions Synthetic: Polyglycols Phosphate esters Silicate esters Silicones Organic esters Olefin oligomers Alkylated aromatics Polybutenes Cycloaliphatics Polyphenyl ethers

REACTIVITY	Many hydraulic fluids primarily consist of a blend of various hydrocarbons. Hydrocarbons are typically incompatible with strong oxidizers, and may be considered miscellaneous combustible or flammable materials for compatibility classification purposes. Such substances typically evolve heat, fire, and toxic or flammable gases in reactions with oxidizing mineral acids, organic peroxides or hydroperoxides, or strong oxidizing agents. Reactions with explosive materials may result in an explosion, while those with strong reducing agents may evolve heat and flammable gases. Other types of hydraulic fluids may include or be comprised of various types of glycols, glycol ethers, esters, and various additives. Reactivity hazards for these must be determined on a case-by-case basis (23, 505, 507, 511).

PHYSICO-CHEMICAL DATA	• Physical State: Liquid (at 20°c)	(23)
	• Color: Yellow brown; varies with use	(60)
	• Odor: Odorless to slight ammonia	(2233)
	• Odor Threshold: No data	
	• Density: 0.9020 g/mL (at 20°C)	(60)
	• Freeze/Melt Point: Not pertinent	(60)
	• Boiling Point: 190.50 to 287.80°C	(23)
	• Flash Point: Varies with particular blend and product	
	• Flammable Limits: No data	
	• Autoignition Temp.: No data	
	• Vapor Pressure: No data	
	• Satd. Conc. in Air: Not pertinent	

PHYSICO-CHEMICAL DATA (Cont.)	• Solubility in Water: No data • Viscosity: 56.000 to 150.000 cp (at 40°C) (21) • Surface Tension: 36.00 to 37.50 dyne/cm (at 20°C) (60) • Log (Octanol-Water Partition Coeff.): No data • Soil Adsorp. Coeff.: No data • Henry's Law Const.: Not available • Bioconc. Factor: No data
PERSISTENCE IN THE SOIL-WATER SYSTEM	Hydrocarbon-based fluids are expected to be highly immobile and persistent in the soil/ground-water system. Major loss mechanisms are volatilization and aerobic biodegradation. Other ester, ether and glycol-based oils may be moderately mobile and much less persistent due to hydrolysis and biodegradation.
PATHWAYS OF EXPOSURE	The primary pathway of concern from the soil/ground-water system is the contamination of ground water drinking water supplies with hydraulic fluids, especially those based on organic and phosphate esters and polyglycols. Runoff to surface water drinking water supplies may be an important exposure pathway for mineral-oil based fluids. Inhalation exposures and ingestion with food are not expected to be significant.
HEALTH HAZARD DATA	Signs and Symptoms of Short-term Human Exposure: (60) Minimal gastrointestinal tract irritation is expected from ingestion of hydraulic fluids. Diarrhea may occur. Pulmonary irritation may result from aspiration. Skin or eye contact may produce irritation. Long-Term Effects: Possible neuropathy due to triarylphosphate contaminants. Pregnancy/Neonate Data: No data Genotoxicity Data: No data Carcinogenicity Classification: IARC - No data NTP - No data EPA - No data
HANDLING PRECAUTIONS (60)	Wear protective gloves; goggles or faceshield.

ENVIRONMENTAL AND OCCUPATIONAL STANDARDS AND CRITERIA

AIR EXPOSURE LIMITS:

Standards
- OSHA TWA (8-hr TWA): petroleum distillates (naphtha)-400 ppm
- AFOSH TWA) (8-hr): petroleum distillates (naphtha)-400 ppm; STEL (15-min) -500 ppm

Criteria
- NIOSH IDLH (30-min): petroleum distillates (naphtha)-10,000 ppm
- NIOSH REL: petroleum distillates (naphtha)-350 mg/m^3
- NIOSH CL (15-min): petroleum distillates (naphtha)-1800 mg/m^3
- ACGIH TLV®: petroleum distillates (naphtha) - none established

WATER EXPOSURE LIMITS:

Drinking Water Standards
None established

EPA Health Advisories and Cancer Risk Levels
None established

WHO Drinking Water Guideline
No information available.

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

Oil and Grease (2012)
For domestic water supply: Virtually free from oil and grease, particularly from the tastes and odors that emanate from petroleum products.

For aquatic life:

- To protect several important freshwater and marine species, each having a demonstrated high susceptibility to oils and petrochemicals, the lowest continued flow 96-hour LC_{50} should be reduced a hundred-fold.
- levels of oils or petrochemicals in the sediment which cause deleterious effects to the biota should not be allowed;
- surface waters shall be virtually free from floating non-petroleum oils of vegetable and animal origin as well as petroleum-derived oil.

REFERENCE DOSES:

No reference dose available.

REGULATORY STATUS (as of 01-MAR-89)

Promulgated Regulations

- Federal Programs

Clean Water Act (CWA)
Oil and grease are designated conventional pollutants under the CWA (351). Effluent limitations for oil and grease exist in almost point source categories under the general pretreatment regulations for new and existing sources, and effluent standards and guidelines. Limitations vary depending on the type of industry (3763).

Toxic Substances Control Act (TSCA)
Manufacturers and processors of the C_9 aromatic hydrocarbon fraction must test it for neurotoxicity, mutagenicity, developmental toxicity, reproductive effects, and oncogenicity. The C_9 fraction is obtained from the reforming of crude petroleum. It consists of ethyltoluenes and trimethylbenzenes (1988). Testing will be conducted by the American Petroleum Institute. Interim reports must be submitted at 6-month intervals (1987).

Marine Protection Research and Sanctuaries Act (MPRSA)
Ocean 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 petroleum distillates (naphtha) shall not exceed an 8-hour time-weighted average (TWA) of 400 ppm (3539).

Hazardous Materials Transportation Act (HMTA)
The Department of Transportation has designated petroleum distillates as hazardous materials which are subject to requirements for packaging, labeling and transportation (305).

- State Water Programs

ALL STATES
All states have adopted EPA Ambient Water Quality Criteria and NPDWRs (see Water Exposure Limits section) as their promulgated state regulations, either by narrative reference or by relisting the specific numeric criteria:

ALASKA
Alaska has a water quality criterion for the protection of aquatic life of 15 µg/L for total hydrocarbons and 10 µg/L for total aromatic hydrocarbons in fresh and marine surface waters (3016).

ARKANSAS
Arkansas requires that oil and grease shall not exceed 10 mg/L average or 15 mg/L maximum when discharging to surface waters (3587).

FLORIDA
Florida requires that oil and grease not exceed 10 mg/L in Class V waters (navigation, industrial use) and 5 mg/L for all other surface waters (3220).

MASSACHUSETTS
Massachusetts requires that the maximum discharge concentration of oil and grease of petroleum origin not exceed 15 mg/L in surface waters (3432).

NEBRASKA
Nebraska requires that petroleum oils not exceed 10 mg/L in surface waters (3719).

NEW YORK
New York has set a maximum contaminant level of 50 μg/L for kerosene in drinking water (3501).

SOUTH DAKOTA
South Dakota has a water quality standard of 10 mg/L for all petroleum products in surface waters (3672).

VIRGINIA
Virginia has a water quality standard of 1 mg/L for petroleum hydrocarbons in ground-water (3135).

WYOMING
Wyoming has a water quality standard of 10 mg/L for surface waters and Class II and III ground-waters. In addition, Class I domestic ground-water is required to be virtually free of oil and grease (3853, 3852).

Proposed Regulations

- Federal Programs
  No federal regulations are pending.

- State Water Programs
  No state regulations are pending.

MOST STATES
Most states are in the process of revising their water programs and proposing changes to their regulations which will follow EPA's changes when they become final. Contact with the state officer is advised. Changes are projected for 1989-90 (3683).

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 Fishing Water Quality (536)
Petroleum products must not be present in salmonid and cyprinid waters in such quantities that they: (1) form a visible film on the surface of the water or form coatings on the beds of water-courses and lakes, (2) impart a detectable "hydrocarbon" taste to fish and, (3) produce harmful effects in fish.

Directive on the Quality Required of Shellfish Waters (537)
The mandatory specifications for petroleum hydrocarbons specify that they may not be present in shellfish water in such quantities as to produce a visible film on the surface of the water and/or a deposit on the shellfish which has harmful effects on the shellfish.

Directive on the Discharge of Dangerous Substances (535)
Organoha ogens, 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 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)
Petroleum and coal tar distillates with flash points below 21°C are classified as flammable substances and are subject to packaging and labeling regulations. Because of the variable composition of other petroleum and coal tar distillates (excluding those used as motor fuels) they are considered preparations and their labeling shall be done in accordance with the procedures outlined in the Directive Relating to the Classification, Packaging and Labeling of Dangerous Preparation (solvents).

Directive on Disposal of Waste Oils (1986)
Establishments collecting and/or disposing of waste oils must carry out these operations so that there will be no avoidable risk of water, air or soil pollution. A permit from the competent authority must be registered and adequately supervised for collecting, disposal and regenerating waste oils. PCBs and PCTs must not be present in amounts greater than 50 ppm in regenerated waste oil.

EEC Directives - Proposed
Proposal for a Council Directive on the Dumping of Waste at Sea (1793)
EEC has proposed that the dumping of crude oil, petroleum hydrocarbons, lubricants and hydraulic fluids at sea be prohibited.

68.1 MAJOR USES AND COMPOSITION

68.1.1 Major Uses

Hydraulic fluids are used in all kinds of applications but especially in machinery that moves or lifts objects. Aircraft, automobiles, trucks, forklifts, compressors, garden tractors and many others all use hydraulic fluids in their hydraulic components to magnify a relatively small force to do useful work. Automobiles need hydraulic fluids as transmission and brake fluids, while supersonic jet and commercial aircraft use them in landing gear and other equipment (21).

68.1.2 Composition

Traditionally, most hydraulic fluids have been mineral base oils, specifically those high in paraffins. Their advantages include stability to oxidation and good resistance to foaming and wear. Another major advantage of mineral base fluids over synthetics is their lower cost (1823, 1824).

The development of synthetic hydraulic fluids arose from the need for fluids with a greater range of operating temperatures. Synthetic hydraulic fluids such as the phosphate esters provide excellent fire resistance, increasing the maximum operating temperature by perhaps 150°C over mineral oils. In most aircraft, hydraulic lines pass close to high temperature parts while high altitudes and speeds can produce temperatures well below 0°C. Commonly, temperatures can range from -53°C to 260°C (1824). It is this range of operating temperatures that dictates the type of fluid and additives used. Under these conditions, synthetic fluids of high autoignition temperatures and superior temperature-viscosity characteristics are used especially if there is the possibility of fluid leakage or spray on or near hot surfaces. Table 68-1 provides a list of typical hydraulic fluids including mineral base and synthetic base fluids.

Mineral base and synthetic base hydraulic fluids are fortified with approximately 0-20 volume percent additives (1825), which in most cases are identical to those used in the crankcase oils (see Chapter 69, Table 69-2). The most common additives in hydraulic fluids are used to modify physical/chemical characteristics; they include viscosity improvers, inhibitors of rust and corrosion, and inhibitors of wear, foaming and oxidation. Generally, detergent use is minimal (21, 1823, 1824). Tables 68-2 and 68-3 list reported hydraulic oil/lubricating oil base stocks and their additives.

TABLE 68-1
HYDRAULIC OILS

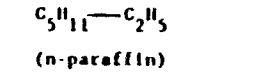
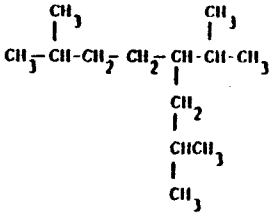
Base Stock	Structure/Composition	Properties/Characteristics
Mineral Base Oils:		
1. Straight paraffinic stock (linear and branched chained aliphatics)[a]	Examples of typical components include:  (n-paraffin)  (isoparaffin) less typical components include: cycloparaffins, aromatic hydrocarbons, mixed aliphatic and aromatic hydrocarbons	Boiling point range approximately 300-600°C. MW approximately 150-1000. Carbon numbers approximately C_{15} - C_{50}. Densities approximately 0.8-1.0 g/mL at 15°C.

TABLE 68-1
(Cont.)

Base Stock	Structure/Composition	Properties/Characteristics
2. Oil in water emulsions. (oil is mineral base paraffinic stock)[b]	Up to 20% oil used but commonly only 1-4%. Greater than 80% water.	Used as a fire resistant hydraulic fluid. Temperature range limited to approximately 0° - 71°C.
3. Water in oil emulsions[b]	Approximately 60% oil. Approximately 40-45% water.	Used as a fire resistant hydraulic fluid.
Synthetic Base Oils:		
4. Polyoxyalkylene glycols[b] (polyglycols)	$R^1O\left[CH_2-CH(R^3)-O\right]_n R^2$	Can be formulated to be water soluble or water insoluble; the more polyethylene in character, the better the water solubility MW typically 400-3000.
	R^1 / R^3 / R^2	Densities approximately 0.95 - 1.7 g/ml.
	1. H / H / H	
	2. H / CH_3 / H	
	3. C_4H_9 / CH_3 / H	Vapor pressures of some polyglycols are reported to be less than 0.01 mm Hg at 20°C.
	4. C_4H_9 / CH_3 / C_2H_5	
	1. polyethylene glycol 2. polypropylene glycol 3. a monoether 4. a diether (examples of some possible R groups)	

TABLE 68-1
(Cont.)

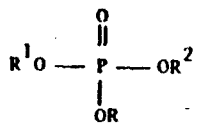
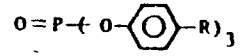
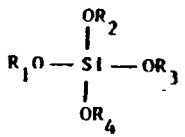
Base Stock	Structure/Composition	Properties/Characteristics
5. Phosphate esters[c]		Excellent fire resistance properties. MW typically 200-600. Densities approximately 0.9-1.5 g/mL. Boiling points for trialkylphosphates approximately 190-300°C. Used in extreme temperature applications.
	R can be H or organic groups. At least 1 R must be an organic group. Three classes: trialkylphosphates, triaryl phosphates, alkyl-aryl phosphates; i.e.,:	
		
	(a triaryl phosphate)	
	Oxygen(s) may be replaced by sulfur to give thiophosphates.	
6. Silicate esters[c]	Two classes:	MW typically 300-800. Densities approximately 0.8-1.1 g/mL at 20°C. Vapor pressures 0.1-5.0 mm Hg at 205°C. Boiling points approximately 93°-482°C. Used in extreme temperature applications.
		
	(Orthosilicates)	

TABLE 68-1
(Cont.)

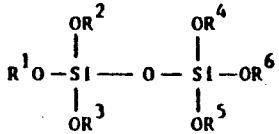
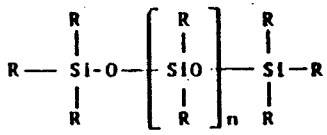
Base Stock	Structure/Composition	Properties/Characteristics
		
	(disiloxanes) (dimer silicates)	
	R's can be alkyl or aryl	
7. Silicones[c]		MW typically 1000-150,000. Densities approximately 0.75-1.1 g/mL, can be as high as 1.4 g/mL. Vapor pressures approximately 5 mm Hg at 149°C.
	R can be alkyl or aryl. Commonly R-CH_3 giving rise to the methyl and dimethyl silicone polymers	

TABLE 68-1
(Cont.)

Base Stock	Structure/Composition	Properties/Characteristics
8. Organic esters[c]	Includes: Monoesters (monobasic acid esters or polyolesters) diesters triester polyesters $RO-C-(CH_2)_n-C-OR$ (a diester-most common, based on a dibasic acid) (n is commonly 8-10) Diesters are derived from C_6 - C_{10} acids (i.e., adipic, azelaic, sebacic) and C_6 - C_9 alcohols (i.e., 2-ethylhexyl, 3,5,5-trimethylhexyl, isodecyl,[b] and tridecyl alcohols).	MW typically 200-600; can be approximately 1000 for complex esters. Vapor pressures approximately 0.3 - 4.0 mm Hg at 205°C. Their uses include automotive engine oils (occasionally blended 50/50 with mineral oils), and jet and aircraft engines. Organic esters are the most common synthetic lubricants used. Used widely by the military in aircraft applications.

TABLE 68-1
(Cont.)

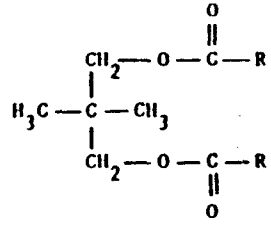
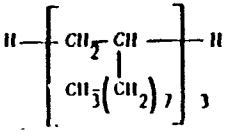
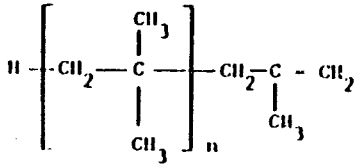
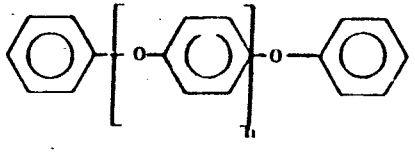
Base Stock	Structure/Composition	Properties/Characteristics
	 (a neopentyl polyol ester based on neopentyl glycol)	
9. Synthetic hydrocarbons:[a,b] Olefin oligomers (poly-alpha-olefins)	 (oligomer of 1-decene)	Resembles paraffinic mineral oils. Uses include synthetic hydrocarbon fluid in SAE 5W-20 motor oil and military aircraft fluids.
Alkylated aromatics	Typically reaction products of C_{10}-C_{14} alkyl groups and benzene/toluene/xylenes/ethylbenzenes, (i.e., dialkylated benzenes).[a]	Used in synthetic automotive engine oils.

TABLE 68-1
(Cont.)

Base Stock	Structure/Composition	Properties/Characteristics
Polybutenes (polyisobutylenes)	 (polyisobutylene) (typically C_{20} - C_{100})	Decomposition temperatures around 290°C. The lower MW polymers (C_{20}-C_{100}) are used as lubricants while the higher MW are used as additive viscosity index improvers. Used in many high temperature applications.
Cycloaliphatics		Used commonly as hydraulic fluids.
10. Polyphenyl ethers[c]	 Connections can be para, meta, or ortho; can be alkyl or halogen substituted (i.e., bis(p-phenoxyphenyl)ether)[b]	MW typically 150-700. Densities approximately 0.8 - 12 g/mL at 20°C.

[a] Reference 1821
[b] Reference 21
[c] Reference 1822

TABLE 68-2
SOME REPORTED MINERAL OIL AND SYNTHETIC OIL BASES FOR HYDRAULIC OIL/LUBRICATING OIL[a]

MINERAL BASE OILS[b]
straight paraffinic stock
water/oil mixtures (emulsions)
mineral oil/trialkyl thiophosphate ester blends
e.g., $(OP(OC_2H_4SC_8H_{17})_3)$/mineral oil
mineral oil/silicate ester/polyglycol blends

SYNTHETIC BASE OILS
Organic Esters[c] (monobasic and dibasic acid esters, triesters, and polyesters)
isooctyl adipate
isodecyl adipate
2-ethylhexyl sebacate
pentaerythritol
2-ethyl-2-hydroxymethyl-1,3-propanediol
trimethylolpropane
dioctyl sebacate
di(3-methylbutyl)adipate
di(2-ethylbutyl)azelate
trimethylolethane
dibasic acid ester/silicate ester blend (~15% diester)
dibasic acid ester/polyglycol blend
dibasic acid ester/synthetic hydrocarbon blend (~33% diester)

Polyoxyalkylene Glycols (polyglycols)[d]
polypropylene glycol
polyethylene glycol
polybutylene glycol
polyglycol/water blend
polyglycol/mineral oil/silicate ester blend
polyglycol/dibasic acid ester blend

Phosphate Esters[e]
tert-butyl-triphenylphosphate
triphenylphosphate
phenyl-m-tolyl-p-chlorophenylphosphate
tricresylphosphate
tri(2-ethylhexyl)phosphate
diorganodithiophosphate
triethylphosphate
phenyl-m-trifluoromethylphenyl-1-naphthylphosphate

TABLE 68-2 (Cont.)

trixylylphosphate
trialkyl thiophosphate esters ($OP(OC_2H_4SC_8H_{17})_3$)/mineral oil blend
phosphate ester/polyglycol blends (tributoxyethyl/tributoxyethoxyethyl phosphates)
phosphate esters/dimethyl silicone polymer blend

Silicate Esters[d]
tetraethyl silicate
tetra(2-ethylhexyl) silicate
tetra(2-ethylbutyl) silicate
hexa(2-ethylbutoxy)) disiloxane
di-(2-ethylhexyl)silicate
cresyltriisopropyl silicate
silicate ester/dibasic acid ester blends
silicate ester blends with chlorofluorocarbons, mineral oils, silicones, polyglycols; e.g., bis(2-ethylhexyl)propylene glycol and butylmethyl propylene glycol/tetra alkyl orthosilicates or hexalkoxy disiloxanes

Silicones[f]
methyl, dimethyl polysiloxane
phenylmethyl polysiloxane
chlorophenyl polysiloxane
trifluoropropylmethyl polysiloxane

Synthetic Hydrocarbons[g]
alpha olefins (olefin oligomers)
2,3-dicyclohexyl-2,3-dimethyl butane
dialkylated benzene
polyisobutylene
synthetic hydrocarbon/dibasic acid ester blend (~33% diester)

Others[h]
polychlorotrifluoroethylene
perfluoroheptane
trifluorotrichloroethane
bis(p-phenoxyphenyl)ether

a) This table contains specific base chemicals or chemical classes used in hydraulic oils and/or lubricating oils. These chemicals may or may not be typical but all were reported in the literature as possible fluid bases.
b) References 21,1822
c) References 21,1826,1834
d) References 21,1822
e) References 1822,1829
f) References 1822,1826
g) References 21,183
h) Reference 1822

TABLE 68-3
SOME CHEMICAL ADDITIVES USED IN MINERAL AND SYNTHETIC BASE HYDRAULIC OIL/LUBRICATING OIL[a]

Chemical/Class Name	Typical Range Used
Oxidation Inhibitors	0-2.0% wt.[b]
2,6-di-tert-butyl-p-cresol	
phenothiazine	
2,5-di-n-butylaminobenzoquinone	
2,5-di-piperidylbenzoquinone	
2,5-di-tert-butyl-p-benzoquinone	
pyridine	
quinoline	
hydroquinone	
R_3Sb or R_3SbS R=butyl or phenyl groups	
phenyl-alpha-naphthylamine	
triethanolamine	
2-naphthol	
zinc dithiophosphate	
Antiwear and Extreme Pressure Additives	0-6% wt.[c]
tricresylphosphate	
zinc diorganodithiophosphate	
zinc diisodecyldithiophosphate	
zinc di-n-butyldithiophosphate	
n-tosyltetrapropenyl succinimide	
hexadecyldiethyldithiocarbanate	
benzyl disulfide	
tungsten sulfide	
Rust and Corrosion Inhibitors	0-2.0% wt.[d]
barium dinonylnaphthylene	
n-tosyltetrapropenyl succinimide	
zinc dithiophosphate	
dicyclohexamine	
diisobutyl ketone	
Viscosity Index (VI) Improvers	0-20% wt.[e]
polyisobutylenes	
polymethacrylates	
polyalkylstyrenes	
ethylene-propylene copolymers	
styrene-butadiene copolymers	
hydroxy cellulose ether	
silicone polymers (methyl and dimethyl polysiloxanes)	

TABLE 68-3 (Cont.)

Detergents/Dispersants	0-20% wt.[f]
polyisobutenyl succinic anhydrides	
borated alkenyl succinimides	
oxazoline	
phosphonates and thiophosphates	
alkyl phenols and alkyl phenol sulfides	
alkyl methacrylate-dimethylaminoethyl methacrylate copolymers	
alkyl methacrylate-n-vinylpyrrolidone copolymers	
vinyl acetate-dialkyl fumarate-maleic anhydride copolymers	

a) This table contains specific chemical additives used in hydraulic oils and/or lubricating oil. These chemicals may or may not be the typical additives but all were reported in the literature as possible chemical additives.
b) References 21, 1823, 1831, 1832, 1834, 1835, 1836
c) References 21, 1821, 1825, 1826, 1827, 1833
d) References 21, 1821, 1822, 1823, 1825
e) References 21, 1824, 1825, 1832, 1835, 1836
f) References 21, 1822, 1827

68.2 ENVIRONMENTAL FATE AND EXPOSURE PATHWAYS

68.2.1 Transport in Soil/Ground-water Systems

Most hydraulic fluids (except the more water soluble esters and glycols and oil-water emulsions) are expected to be quite immobile in the soil/ground-water environment. Bulk quantities of the oil (from a spill or improper disposal) might be carried slowly through the unsaturated zone to the top of the water table, but the high viscosity and low water solubility would mitigate this response. Most likely, at least with moderate to small spills, the oil would remain entrained in the pores of the soil near the surface. This would be more likely for low porosity and high organic carbon content soils, and less likely for sandy, porous soils.

Transport and subsequent fate of dissolved constituents of these oils will vary depending on the physicochemical (and biological) properties of the constituents. Some constituents will dissolve more quickly in the percolating ground-waters, be sorbed less strongly on the soils (thus being transported more rapidly), and may be more, or less, susceptible to degradation by chemical or biological action. The relative concentrations of the constituents of the oil will vary with time and distance from the site of initial contamination. This effect is called "weathering". (This term is also used to describe changes to oil following spills into surface waters where film spreading and breakup, and differential volatilization, dissolution and degradation all are involved.)

As noted in Tables 68-1, 68-2, and 68-3, there are a wide variety of base materials and additives that may be present in hydraulic fluids. More focused

discussions of the soil/ground-water mobility and persistence of hydrocarbon-based oils are presented in Chapter 69 (Mineral Base Crank Case Oil) of this Guide. Chapter 70 (Synthetic Crankcase Oil) generally covers some of the same esters and glycols which are used in hydraulic fluids. Some data on phosphate esters are provided in Chapter 49 of this Guide.

No equilibrium partitioning model calculations (as have been given for most other chemicals in this Guide) are given for these fluids. This is due to the wide variety of materials (chemical classes) covered by the category of hydraulic fluids, to the lack of any real data on their physicochemical properties of environmental importance, and to the wide range of partitioning behaviors that could be shown from the highly immobile aliphatic and aromatic hydrocarbons to the mobile organic esters, polyglycols and phosphate ester fluids. To provide model outputs in this case would involve excessive speculation (on the needed physicochemical properties) and allow easy misuse of model results.

The aqueous phase mobility of oil constituents could be significantly enhanced if the oil was in the form of a very fine emulsion, or if the percolating ground-water contained a significant amount of dissolved organic carbon (e.g., humic and fulvic acids, fatty acids, or chlorinated solvents) from other natural sources or other discharged materials. The dissolved organic carbon, much of it possibly in the form of colloidal particles, could absorb the oil constituents and assist in their transport through the soil/ground-water system.

Volatilization of constituents from the hydraulic fluids would be slow because of the low vapor pressures involved (presumably <1 mm Hg at 25°C for individual constituents, with many below 1E-06 mm Hg). However, given that spilled oils may remain near the soil surface, making volatilization easier, that the material is resistant to leaching and degradation; and that the Henry's law constant may be moderately high, at least for the hydrocarbons, it is thus presumed that volatilization will be a major loss mechanism for spilled hydraulic fluid over time periods of weeks to years. Because the lower molecular weight (more liquid) constituents would tend to volatilize first, the remaining material would generally have lower volatilities and lower water solubilities.

68.2.2 Transformation Processes in Soil/Ground-water Systems

An assessment of environmental persistence for hydraulic fluids is difficult given the variety of materials involved and the lack of pertinent data. Thus, most of the statements given below are both general and speculative in nature. Only the phosphate esters have been the subject of several environmental studies (see Chapter 49 of this Guide and references 1490 and 1496).

Hydraulic fluid oils are expected to be moderately persistent in the soil/ground-water environment because of their resistance to hydrolysis, oxidation and biodegradation. The general resistance to hydrolysis (for saturated and unsaturated

hydrocarbons) is described by Harris (529). However, the organic esters, phosphate esters and polyglycols would be somewhat more susceptible to hydrolysis, especially under basic conditions.

The assessment of the resistance to biodegradation is more complex. Most of the molecules are so large that passage through cell walls (where metabolism or degradation is relatively easy) is hindered and much of the biodegradation must be carried out by extracellular enzymes secreted by the microbes. Such difficulties aside, many studies on petroleum hydrocarbon materials (oils as well as light distillates) have shown moderate to high eventual susceptibility to biodegradation for the bulk of the material (1842). A period of microbial adaptation may be required. The organic esters, phosphate esters and polyglycols would be expected to be more readily biodegraded.

Different constituents of the oil will differ significantly in their biodegradability for reasons related to molecular size, structure and toxicity. For example, highly branched alkanes are much less biodegradable than linear alkanes, and polycyclic aromatic hydrocarbons with three or more rings are very resistant to biodegradation (515). For all hydrocarbons, aerobic biodegradation would be expected to be much more important than anaerobic biodegradation (1841). Because of this, and because of the decrease in microbiological activity with increasing soil depth, oil constitutents reaching deep anaerobic soils could persist for very long time periods.

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

The above discussion of fate pathways suggests that the components of hydraulic fluids will vary widely in their volatility, tendency to sorb to soil, and potential for bioaccumulation. However, the base stock of hydraulic fluids manufactured with mineral oils are expected to be very strongly sorbed to soil because of their high molecular weight and low water solubility. These compounds have extremely low volatility in pure form, but when present in water may have relatively high volatility due to their low solubility. They are not expected to be readily bioaccumulated because their large size makes their passage through cell walls difficult.

Polyglycol-based hydraulic fluids and fractions composed of phosphate esters and organic esters are expected to have low volatility (because of their high water solubility and low vapo. pressure) and be weakly sorbed to soil. They would also be expected to have a low potential for bioaccumulation because of their high solubility and susceptibility to biodegradation. Despite the variability in the properties of the components of hydraulic fluids, several potential exposure pathways can be inferred.

Volatilization of hydraulic fluids that are spilled or improperly disposed of is not expected to result in significant exposure of workers or residents in the area, regardless of the type of fluid. Oil-based fluids would be rapidly sorbed to the soil, and only a very small fraction of the oil would volatilize. Fluids based on polyglycols, organic esters and phosphate esters would not readily volatilize.

Ground-water contamination may be a significant exposure pathway for water soluble hydraulic fluids, including oil-water emulsions, polyglycols, organic esters and phosphate esters. Exposure may occur through the direct use of ground-water drinking water supplies or indirectly through ground-water discharge to surface waters. Surface waters may also be contaminated by the discharge of soil particles to which hydraulic fluids (especially mineral oil base fluids) have been sorbed. Where surface waters have been contaminated, ingestion exposures may occur from their use as drinking water supplies and dermal exposures may result from their recreational use. The uptake of hydraulic fluids by aquatic organisms or domestic animals is not expected to result in significant exposure.

68.2.4 Other Sources of Human Exposure

Data on ambient concentrations of hydraulic fluids in air and water, as well as food and drinking water, are not available in the literature. This should not be surprising since they are complex mixtures, are not distributed widely in the environment, and (except for the mineral base fluids) consist mainly of non-persistent compounds.

Aside from those involved in their manufacture, the personnel likely to receive the greatest exposure to hydraulic fluids are those employed in servicing and maintaining equipment. Although inhalation exposures are not expected to be large, these personnel may experience large dermal exposures if protective gloves and clothing are not worn during maintenance operations. Operators of hydraulic equipment would be expected to experience only small exposures because the very nature of hydraulic systems is to keep the fluid contained, and volatilization from reservoirs is likely to be minimal.

68.3 HUMAN HEALTH CONSIDERATIONS

Hydraulic fluids do not appear to be toxic to animals (2228); however, the composition and level of additives vary greatly. Major components usually include ethylene glycol, polyethylene glycol and tri-ortho cresyl phosphate (TOCP). A review of the toxicity of TOCP and ethylene glycol may be found in Chapter 49 and Chapter 43, respectively, of the IRP Toxicology Guide.

68.3.1 Animal Studies

68.3.1.1 Carcinogenicity

No specific data on the carcinogenicity of hydraulic fluids were found.

68.3.1.2 Mutagenicity

No specific studies on the mutagenicity of hydraulic fluids were found in the literature.

68.3.1.3 Teratogenicity, Embryotoxicity and Reproductive Effects

No specific studies were located in the literature.

68.3.1.4 Other Toxicologic Effects

68.3.1.4.1 Short-term Toxicity

MLO 82-233 is a synthetic hydrogenated polyalpha olefin with a nominal $C_{30}H_{62}$ formula while MLO 82-585 is a naphthionic type petroleum oil. Both compounds contain tricresyl phosphate with unspecified amounts of TOCP. Neither hydraulic fluid was toxic following ingestion of 5 mL/kg in Sprague-Dawley rats, dermal application of 2 mg/kg in New Zealand rabbits, or a 6-hour whole body inhalation study with 1148 mg/m^3 in Sprague-Dawley rats. No ocular irritation occurred when 0.1 mL of either fluid was instilled in the eye of albino rabbits. The synthetic hydraulic fluid also did not produce irritation when applied undiluted to the intact or abraded skin of albino rabbits; however, the petroleum hydraulic fluid produced a moderate, reversible primary skin reaction. Neither hydraulic fluid was considered a skin sensitizer or a delayed neurotoxin (2231).

Similarly, no oral or dermal toxicity was reported. There was no indication of eye or skin irritation or skin sensitization following exposure of Fischer 344 rats and New Zealand white rabbits to a cyclotriphosphazene-based hydraulic fluid, containing 0.1% tolytriazole as a copper corrosion inhibitor (1936).

The Navy hydraulic fluid, Plurasafe® MC200, produced a slight skin sensitizing reaction in guinea pigs (1936). One animal responded to the challenge dose of 0.1 mL hydraulic fluid with a mild erythematous reaction at 24 hours which increased in severity by 48 hours. One week later, animals were challenged a second time which resulted in two additional cases of sensitization.

Triaryl phosphate hydraulic fluids administered orally to white Vantress hens daily for 5 days resulted in signs of toxicity identical to TOCP poisoning. After a latent period of 8 to 14 days, treated birds tired easily and squatted in a characteristic pose. Leg weakness, loss of balance, and clumsiness soon followed. Maximum paralysis occurred 15 to 16 days after treatment along with excessive salivation, lacrimation, and severe diarrhea. Death was attributed to a combination of toxicity, starvation, and dehydration (2230).

In an inhalation study involving six synthetic hydraulic fluids (2233), exposure of Sprague-Dawley rats to 6.43 mg/L (duration not stated) of one of the fluids (N501 - Supplied by Gulf R&D Company) resulted in the death of all animals within 24 hours of exposure. Signs of toxicity included rough coat, labored respiration, and lethargy. The LC_{50} value was found to be 2 mg/L for a 4-hour exposure. No mortality or toxic effects were reported in rats exposed to the remaining five compounds. The investigators attributed the toxic effects of N501 to one or more of the additives.

68.3.1.4.2 Chronic Toxicity

A long-term continuous inhalation study was performed with a triaryl phosphate hydraulic fluid used by the U.S. Navy (2230). The fluid contained a mixture of tricresyl phosphates, trixylenyl phosphates, and other trialkyphenyl phosphates. The TOCP content was reported to be less than 1.5%. Animals were exposed in a chamber to 1.8 to 110 mg/m^3 hydraulic fluid mist 24 hours/day for 36 to 163 days. No neurotoxic signs were reported in dogs, monkeys or rats. Rabbits exposed to high doses of hydraulic fluids (101 or 103 mg/m^3) developed lacrimation and generalized hind leg paralysis. An extensor type paralysis, lacrimation and thick, mucous salivation were reported in chickens exposed to the hydraulic fluid mist. These signs of cholinergic stimulation were indistinguishable from those induced by TOCP (see Chapter 49 of this Guide).

A 90-day aerosol exposure to a phosphate ester base hydraulic fluid, Durad MP280, resulted in toxicity 3 days after exposure to 100 mg/m^3 was initiated (2233). Rabbits became anorexic and lethargic, and cachexia and head droop were noted prior to death. All animals died by the 49th exposure day. Kyphosis (hunch back) was noted in rats exposed to 100 mg/m^3 of Durad MP280 along with a rough hair coat and unkempt appearance. A decrease in weight gain was also reported (2233).

68.3.2 Human and Epidemiologic Studies

68.3.2.1 Short-term Toxicologic Effects

No acute human data were found on hydraulic fluids.

68.3.2.2 Chronic Toxicologic Effects

Jarvholm et al. (3337) describe polyneuropathy experienced by a 48-year-old mechanic who was heavily exposed to hydraulic fluids containing 0.5% isopropylated triphenylphosphate for two years. While testing hydraulic systems in ships, the mechanic was frequently exposed to hydraulic fluid by extensive dermal contact as well as to oil mists by inhalation. The symptoms included weakness in his arms and forearms. Slight muscular weakness persisted for a follow-up period of more than three years. The investigators suggest a possible association between heavy occupational exposure to hydraulic fluids containing triarylphosphates and polyneuropathy.

Employees of a coal company using Solcenic-3A hydraulic fluid or working near its area of use reported eye, skin, or respiratory irritation. Solcenic-2 fluid produced no symptoms (3141). Chemical analysis showed that Solcenic-3A contained dipropylene glycol isomers and ethanolamine, compounds which may lower the Solcenic-3A odor threshold. The symptoms were attributed to a reaction to its strong vapor.

68.3.3 Toxicology of Hydraulic Fluid Components

The composition of hydraulic fluid varies greatly and usually depends upon the specific conditions of use. Since the exact composition of the oils is constantly changing and difficult to define, the toxicology of component classes are briefly discussed below. See Table 68-4 for the acute toxicity data of specific compounds.

Organic esters

Organic esters generally found in lubricating oils and hydraulic fluids include adipates (hexane dioic acid ester), sebacates (1,8-octane dicarboxylic acid ester), and dibasic acid esters. Dibasic acid esters are primarily non-toxic via ingestion or skin absorption. The only effect noted from dermal contact may be a drying of the skin (1822). Di(2-hexoxyethyl)succinate is a sebacate which is relatively non-toxic to animals. In humans it is expected to have a low toxicity. Large doses may produce CNS depression, nausea, vomiting, and transient liver and kidney injury (12). Not all neopentyl esters have been tested for toxicity, but studies with trimethylopropane ester showed a toxic level comparable to that of mineral oil (1822).

Polyglycols

Ingestion of polyglycols is unlikely, but small amounts produce no toxic effect. No cases of skin irritation or skin sensitization have been reported; mild irritation to the eyelid has been reported but effects were only transitory. Usually no inhalation hazard exists but at high temperatures, where vapors are likely to form, adequate ventilation should be provided (1822).

Ucon® fluids are a mixture of polyalkylene glycols and diesters. 50-HB-260, 50-HB-5100, 25-H-2005 and 75-H-1400 exhibit a low single-dose oral toxicity with LD_{50} values for the male rat ranging from 5.95 to >64 mL/kg bw; oral LD_{50} values for the rabbit range from 1.77 to 35.4 mL/kg bw. The lower molecular weight compounds are more toxic. A dose-related granular degeneration of the cytoplasm of the smooth muscle in the intestinal wall was noted in dogs fed 25-H-2005 for two years. The significance of this finding is unknown. No other adverse effects were shown. The only adverse effect observed in rats fed up to 0.5 g/kg/day of 25-H-2005 for two years was a slight growth depression in females (12).

TABLE 68-4
ACUTE TOXICITY OF SELECTED COMPONENTS OF HYDRAULIC FLUID

Compound	Oral (mg/kg)	Dermal (mg/kg)	Inhalation (ppm)
2-ethylhexylsebacate	LD_{50} [rat]: 1280	-	-
pentaerythritol	LD_{50} [mouse]: 25,500	-	-
polypropylene glycol	LD_{50} [rat]: 419	-	-
polyethylene glycol	LD_{50} [rat]: 33,750	-	-
triphenylphosphate	LD_{Lo} [rat]: 3000	-	-
tricresylphosphate	LD_{Lo} [rat]: 4680	-	-
tri-ortho-cresyl-phosphate	LD_{50} [rat]: 3000 LD_{Lo} [human]: 1000	- -	- -
tri(2-ethylhexyl) phosphate	LD_{50} [rat]: 37,000	LD_{Lo} [rabbit]: 20,000	
triethylphosphate	LD_{Lo} [rat]: 1600	-	-
tetraethyl silicate	LD_{Lo} [rat]: 1000	-	LC_{Lo} [rat]: 1000 · 4 hr
tetra(2-ethylbutyl) silicate	LD_{50} [rat]: 20,000	-	-
trifluorotrichloroethane	LD_{50} [rat]: 43,000	-	TC_{Lo} [rat]: 87,000 · 6 hr

Source: 47

No carcinogenic effects were observed in rats orally administered Ucon(rtm) fluids in the diet or in mice dermally exposed to these compounds (13).

Polyethylene glycol applied to the open wounds of rabbits resulted in metabolic acidosis and changes in blood chemistry consistent with nephrotoxicity (2225). Effects were attributed to the metabolism of polyethylene glycol to toxic compounds (such as hydroxyglycolic and diglycolic acid homologues) which are efficient chelators of calcium. The mechanism of damage was similar to that associated with ethylene glycol-mediated renal failure. See discussion of the toxic effects of ethylene glycol in Chapter 43 of the Installation Restoration Program Toxicology Guide, Volume 2.

No adverse changes in clinical, biochemical, or hematological parameters developed in rats fed 2 mL/kg/day polyethylene glycol 400 (duration not specified) (2224). Examination of monkeys administered the same treatment revealed a deposition of oxalate crystals in the cortical tubules of the kidney (2224).

Phosphate esters

Organic phosphates possess excellent thermal stability and chemical solvency properties which makes them valuable hydraulic fluid components (1822).

Organic phosphates are readily absorbed through the skin and can be inhaled. Ingestion is rare. Signs of toxicity following excessive exposure reflect stimulation of the autonomic and central nervous systems, resulting from inhibition of acetylcholinesterase and the consequent accumulation of acetylcholine. The initial effect is on smooth muscle, cardiac muscle, and exocrine glands. Early signs of toxicity include intestinal cramps, tightness in the chest, blurred vision, headaches, diarrhea, decreased blood pressure, and salivation. The second stage of intoxication results from stimulation of the peripheral motor system and of all autonomic ganglia. Toxic signs include stimulation and/or paralysis of the somatic, autonomic and central nervous systems.

Chronic administration of low doses of organic phosphates produce a measurable decrease in cholinesterase activity. Toxic effects are nonexistent to slight and may result in diarrhea and tremors. Delayed paralysis in man and animals due to a degeneration of the axons in the spinal cord and peripheral nerves has also been associated with organic phosphates, particularly tri-o-cresyl phosphate (TOCP) (13). See Chapter 49 of the Installation Restoration Program Toxicology Guide for a complete discussion on TOCP.

Silicate esters

The toxicity of the orthosilicates and disiloxanes vary widely and range from almost completely innocuous to rather poisonous (1822). Injection of ethyl silicate compounds into the skin of rabbits produced transient erythema, edema, and slight necrosis at the injection site. When instilled into the rabbit eye, it produced transient irritation. Inhalation of 400 ppm by rats for 7 hours/day for 30 days caused mortality

and lung, liver, and kidney pathological effects. Inhalation of 88 ppm caused no effects (12).

Silicones

Generally, silicones are not irritating to the skin and cause no corneal damage when splashed into the eye. Slight temporary irritation to the eye has been reported in some individuals with effects disappearing within 24 hours. Toxic materials may also be emitted during decomposition of fluorinated silicone polymers at temperatures above 570°F (1822).

In chronic feeding experiments, rats treated with hexamethyl disiloxane (HMS) showed widespread systemic irritation. Rabbits injected intradermally with HMS developed edema and necrosis at the injection sites. Siloxanes injected into the rabbit eye resulted in transient irritation with complete clearing after 48 hours. When inhaled at 4400 ppm for 19 to 26 days, HMS caused slight depression in the rat and guinea pig, with a very slight increase in rat liver and kidney weights (12,13).

Silicone resins had no influence on health when fed for 94 days to rats, and did not result in irritation to rabbit skin or eyes. No toxic effects were reported when injected into rats intraperitoneally (12).

Rats fed a dietary level of 0.3% Antifoam A® for two years showed no significant toxic effect. Long-term feeding studies in mice reported similar results; however, a single subcutaneous injection of 0.2 mL antifoam showed a greater incidence of cysts at the site of injection (13).

Polydimethyl siloxane caused no evident changes when tested for reproductive and teratologic effects in rats and rabbits, or testicular effects in rabbits. Dimethylphenylmethyl polysiloxane, tris(trimethylsiloxy)phenylsilane, and trifluoropropylmethyl polysiloxane were also negative in male reproductive studies (13).

Other

Other components of hydraulic fluids include polyphenyl ethers. Studies with phenyl ether show no toxicological effects following inhalation of vapors or contact with skin. Bis(p-phenoxyphenyl)ether, bis(m-phenoxyphenyl)ether, and m-bis(m-phenoxyphenoxy)benzene cause no irritation in skin tests with rabbits and only mild transient irritation in acute eye tests. These compounds were practically non-toxic in acute oral and intraperitoneal tests with rats. Phenolic degradation products formed during use of these materials under severe conditions are expected to increase toxicity (1822).

Hydraulic Fluid Additives

Information available on additives used in hydraulic fluid is limited. Selected compounds are briefly discussed below. Refer to Table 68-5 for the acute toxicity data of specific additives.

2,6-di-tert-butyl-p-cresol

2,6-Di-tert-butyl-p-cresol, more commonly known as butylated hydroxytoluene or BHT, is used as an oxidation inhibitor in synthetic crankcase oil and hydraulic fluids.

BHT inhibits tumorigenesis when multiple doses are administered before a carcinogen while the incidence of hepatomas induced by 2-acetylaminofluorene and the number of pulmonary adenomas induced by urethane were augmented by post-treatment with BHT (17). The NCI bioassay for carcinogenic effects of BHT in rats and mice was negative (17).

A reported teratogenic effect of anophthalmia in rats has never been duplicated (17).

Various morphological and biochemical changes have been observed in experimental animals fed extremely high doses of BHT. Adverse effects included a dose-dependent reduction in growth rate and alveolar epithelial damage in mice which progressed to fibrosis when pure oxygen followed the BHT exposure.
Dose-dependent fatalities occurred from massive hemorrhages into the pleural and peritoneal cavities while survivors suffered hemorrhages of the epididymis, testis, nasal cavity, and pancreas. Liver changes in rats, mice and monkeys included enlargement, induction of microsomal enzymes, and an increased synthesis of hepatic smooth endoplasmic reticulum (17).

BHT is mildly irritating to human skin and severely irritating to rabbit eyes (17).

Phenothiazine

At one time, phenothiazine was used in human medicine as an anthelmintic and urinary antiseptic. Currently, it is an important antipsychotic drug used to diminish motor activity and alter psychotic behavior (17,16).

Side effects of phenothiazine include toxic hepatitis and jaundice, leukocytosis, leukopenia, eosinophilia, and hemolytic anemia. Dermatitis, hypersensitivity, and photosensitivity have also been reported in phenothiazine treated individuals (17,16)

TABLE 68-5
ACUTE TOXICITY OF SELECTED ADDITIVES OF HYDRAULIC FLUID

Compound	Oral (mg/kg)	Dermal (mg/kg)	Inhalation (ppm)
2,6-di-tert-butyl-p-cresol	LD_{50} [rat]: 890	-	-
phenothiazine	LD_{50} [rat]: 5000 LD_{Lo} [child]: 425	- -	- -
pyridine	LD_{50} [rat]: 891	LD_{Lo} [rabbit]: 1121	LC_{50} [rat]: 4000 · 4 hr
quinoline	LD_{50} [rat]: 331	LD_{50} [rabbit]: 540	
hydroquinone	LD_{50} [rat]: 320 LD_{Lo} [human]: 29	- -	- -
phenyl-alpha-naphthylamine	LD_{50} [rat]: 1625	-	-
triethanolamine	LD_{50} [rat]: 8680	-	-
2-naphthol	LD_{50} [rat]: 2420	-	-
zinc dithiophosphate	LD_{Lo} [rabbit]: 2130	-	-
tricresyl phosphate	LD_{Lo} [rat]: 4680	-	-
tri-ortho-cresyl phosphate	LD_{50} [rat]: 3000 LD_{Lo} [human]: 1000		
diisobutylketone	LD_{50} [rat]: 5750	LD_{50} [rabbit]: 20,000	LC_{Lo} [rat]: 2000 · 4 hr LC_{Lo} [human]: 50

Reference: 47

Tri-ortho-cresyl phosphate (TOCP)

TOCP is known to cause peripheral nervous system damage leading to neuromuscular problems (2216). For a complete discussion of the toxicological effects of TOCP, see Chapter 49 of this Guide.

Zinc dithiophosphate

Zinc dialkyldithiophosphate (ZDDP) has a low acute systemic toxicity with an oral LD_{50} value of greater than 2 g/kg bw and a dermal LD_{50} value in excess of 3 g/kg (2317).

Undiluted ZDDP is a severe eye irritant; however, the diluted product, used as the additive in hydraulic fluids and synthetic crankcase oils, is regarded as non-irritating. Prolonged contact with undiluted ZDDP is irritating to the skin and produces moderate to severe erythema and edema. Repeated contact results in fissuring and exfoliation (2317).

In subchronic toxicity studies, ZDDP primarily affected the reproductive organs of male rabbits. Dermal application of 5 to 25% ZDDP five days a week for three consecutive weeks resulted in decreased sperm counts and some testicular atrophy (2216). Some studies suggest that the male reproductive effects may be physiological and related to body weight loss and reduced food consumption rather than to the toxic effects of ZDDP (1217).

Pyridine

Pyridine is absorbed from the respiratory and gastrointestinal tracts. Skin absorption is not significant although contact may result in dermatitis. Short-term toxic effects in animals are linked to central nervous depression. Prolonged daily administration of pyridine to rats produced hepatorenal damage (17).

Acute toxicity resulting from the ingestion of several ounces of pyridine produced severe vomiting, diarrhea, hyperpyrexia, and delirium. Death occurred 43 hours post-ingestion. Autopsy revealed pulmonary edema and membranous tracheobronchitis which was thought to result from aspiration of pyridine into the lung. A small oral dose of 2 to 3 mL pyridine in man produced mild anorexia, nausea, fatigue and mental depression (17).

Hydroquinone

Hydroquinone is irritating to the skin but not corrosive. Skin lesions in man are generally described as depigmentation. Fatal human doses range from 5 to 12 grams. Systemic effects include tremors and convulsions plus occasional, severe hemolytic

anemia. No effect was reported following human ingestion of 300 to 500 mg hydroquinone daily for three to five months (17).

68.3.4 Levels of Concern

No criteria or standards specific for hydraulic fluid were located. EPA (2012) does list a criterion for oil and grease which requires domestic water supplies to be virtually free from oil and grease, particularly with regard to taste and odor.

68.3.5 Hazard Assessment

Toxicological data located for hydraulic fluids are scant. No data are currently available regarding the carcinogenicity, mutagenicity, or reproductive effects of these materials. Limited animal studies suggest low toxicity by oral and dermal routes in rats and rabbits (2231, 1936) but also indicate the potential for increased toxicity due to additives used in various formulations (2233). In general, hydraulic fluids do not appear to be eye or skin irritants although specific formulations have produced sensitization (1936).

Long-term inhalation exposure to a mist of phosphate-based hydraulic fluid at concentrations up to 110 mg/m^3 continuously for up to 163 days produced no significant pathology in dogs, monkeys, or rats; limb paralysis was noted in rabbits and chickens which were indistinguishable from effects induced by TOCP (2230). Another inhalation study resulted in the death of treated rabbits exposed to 100 mg/m^3 of a phosphate-based hydraulic fluid for up to 49 exposures (2233). Similarly exposed rats exhibited a rough coat, poor grooming and a decrease in body weight gain (2233).

68.4 SAMPLING AND ANALYSIS CONSIDERATIONS

Determination of the presence of hydraulic fluids in soil and water requires the collection of a representative field sample and laboratory analysis for the specific major components generally attributed to hydraulic fluids; however, the relative concentrations of the constituents, and even the constituents themselves, will vary with time and distance from the site of initial contamination due to weathering. The major component categories in hydraulic fluids have been identified as the following:

Straight and branched chain aliphatic hydrocarbons (paraffins)
Cycloparaffins
Aromatic hydrocarbons
Organic esters
Polyglycols
Phosphate esters
Silicones and silicate esters

A combination of capillary column gas chromatography (GC) and gas chromatography/mass spectrometry (GC/MS) techniques may be used to identify the principal components in hydraulic fluids. Oil samples, and any samples collected in the field which are primarily organic in nature, may require separation (prior to GC or GC/MS analysis) using liquid solid column chromatography; the various column eluates, with or without dilution in carbon disulfide, can then be analyzed by GC or GC/MS techniques. Aqueous samples need to be liquid-liquid extracted with an appropriate solvent (e.g., trichlorotrifluoroethane) prior to analysis; solid samples would be extracted with trichlorotrifluoroethane using soxhlet or sonication methods. An aliquot of the sample extract, with or without concentration, could then be analyzed by GC or GC/MS for the specific components of interest. (Sampling and analysis considerations for some specific components possibly present in hydraulic fluids, i.e., benzene, toluene, xylenes, ethyl benzene, naphthalene, TOCP and ethylene glycol, have been addressed in previous chapters.)

Alternatively, the "oil and grease" content can be measured. This determination would not be the measurement of an absolute quantity of a specific component but rather the quantitative determination of groups of components with similar physical characteristics (i.e., common solubility in trichlorofluoroethane). The oil and grease content is defined as any material recovered from extraction with trichlorotrifluoroethane and measured gravimetrically; the extraction methods are those described above for aqueous and soil samples.

A detection limit for hydraulic fluids cannot be determined; the detection limit for specific components is expected to be in the range of $\mu g/L$ for aqueous samples and $\mu g/g$ for non-aqueous samples.

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COMPLEX MIXTURES

This chapter deals with a complex mixture and/or class of compounds. The format used for this less well-defined group of compounds was modified as necessary but follows the outline of earlier chapters as closely as possible. It should be noted, however, that the composition of these materials can vary according to the route of synthesis, the formulating ingredients added, the interactions of the active ingredients, or the storage conditions. These factors can influence the nature of the material that is ultimately utilized and probably are reflected in many of the experimental findings reported in the following chapters.

The typical components and approximate composition of the mixtures are provided if that information was available. Physical/chemical properties often were not available or varied depending on formulation. Many of these mixtures are blended to modify their physical properties according to the intended use. Furthermore, the formulations vary with season as well as with geographic locations of product use. In some cases, therefore, the range for the class of compounds was given.

In addition to the data for the mixture itself, the chapter that follows also contains sections on the principal components and major additives of the mixture, their fate in the environment and a brief overview of their toxicity.

CHEMICAL COMPOSITION	Branched alkanes Cycloalkanes Benzenes and alkylbenzenes Naphthalenes Polynuclear aromatic hydrocarbons (C_{15} - C_{50}) Linear alkanes
REACTIVITY	Hydrocarbon blends are typically incompatible with strong oxidizers. These oils and fuels are usually classified as miscellaneous combustible or flammable materials for compatibility classification purposes. Such substances typically evolve heat, fire, and toxic or flammable gases in reactions with oxidizing mineral acids, organic peroxides or hydroperoxides, or strong oxidizing agents. Reactions with explosive materials may result in an explosion (505, 507, 511).
PHYSICO-CHEMICAL DATA	• Physical State: Liquid, oily (at 20°C) (60) • Color: Yellow brown; depends on use (60) • Odor: Lube oil odor (60) • Odor Threshold: No data • Density: 0.84 to 0.95 g/mL (at 15°C) (60) • Freeze/Melt Point: -34.4°C (60) • Boiling Point: 360.0°C (39) • Flash Point: Usually 135°C or greater (60) • Flammable Limits: No data • Autoignition Temp.: Usually 163°C or greater (60) • Vapor Pressure: No data • Satd. Conc. in Air: Not pertinent • Solubility in Water: Insoluble (60) • Viscosity: 275.00 cp (at 38°C) (60) • Surface Tension: 3.600E+01 to 3.750E+01 dyne/cm (at 20°C) (60) • Log (Octanol-Water Partition Coeff.): No data • Soil Adsorp. Coeff.: No data • Henry's Law Const.: Not available • Bioconc. Factor: No data
PERSISTENCE IN THE SOIL-WATER SYSTEM	Most constituents are expected to be highly immobile in the soil/ground-water system due to very low water solubilities and high soil sorption. Major loss mechanisms are volatilization and aerobic biodegradation. However, loss rates are slow and oils should be considered persistent. "Weathering" effects seen.

PATHWAYS OF EXPOSURE	The primary pathway of concern from the soil/ground-water system is the migration of mineral base crankcase oil to ground water drinking water supplies. The strong sorption of the oil components militates against this, but increases the possibility of surface water contamination from runoff carrying soil particles to which the oil has been sorbed. Inhalation exposures and ingestion with food are not expected to be significant.

HEALTH HAZARD DATA	Signs and Symptoms of Short-term Human Exposure: (60) Ingestion of crankcase oil results in minimal gastrointestinal tract irritation with an increased frequency of bowel passage. Inhalation may cause pulmonary irritation which may increase in severity several hours after exposure. Skin contact may cause dermatitis. Acute Toxicity Studies: ORAL: LD_{50} >21.5 g/kg — Rat (1924) SKIN: LD_{50} >15 g/kg — Rodent (13) Long-Term Effects: Dermatitis, respiratory tract irritation Pregnancy/Neonate Data: No data Genotoxicity Data: Used motor oil positive in Salmonella Carcinogenicity Classification: IARC - Group 3 (not classifiable as to its carcinogenicity to humans) NTP - None assigned EPA - No data

HANDLING PRECAUTIONS (60)	Protective equipment includes protective gloves and goggles or face shield.

ENVIRONMENTAL AND OCCUPATIONAL STANDARDS AND CRITERIA

AIR EXPOSURE LIMITS:

Standards
- OSHA TWA (8-hr): petroleum distillates (naphtha)-400 ppm
- AFOSH TWA (8-hr): petroleum distillates (naphtha)-400 ppm; STEL (15-min): 500 ppm

Criteria
- NIOSH IDLH (30-min): petroleum distillates (naphtha)-10,000 ppm
- NIOSH REL (10-hr TWA): petroleum distillates (naphtha)-350 mg/m^3
- NIOSH CL (15-min): petroleum distillates (naphtha)-1800 mg/m^3
- ACGIH TLV® (8-hr TWA): petroleum distillates (naphtha)-none established
- ACGIH STEL (15-min): None established

WATER EXPOSURE LIMITS:

Drinking Water Standards
None established

EPA Health Advisories and Cancer Risk Levels
None established

WHO Drinking Water Guideline
No information available.

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

Oil and Grease (2012)
For domestic water supply: Virtually free from oil and grease, particularly from the tastes and odors that emanate from petroleum products.

For aquatic life:

- To protect several important freshwater and marine species, each having a demonstrated high susceptibility to oils and petrochemicals, the lowest continuous flow 96-hour LC_{50} should be reduced a hundred-fold.
- levels of oils or petrochemicals in the sediment which cause deleterious effects to the biota should not be allowed;
- surface waters shall be virtually free from floating non-petroleum oils of vegetable and animal origin as well as petroleum-derived oil.

REFERENCE DOSES:
No reference dose available.

REGULATORY STATUS (as of 01-MAR-89)

Promulgated Regulations

- Federal Programs

Clean Water Act (CWA)
Oil and grease are designated conventional pollutants under the CWA (351). Effluent limitations for oil and grease exist in almost all point source categories under the general pretreatment regulations for new and existing sources, and effluent standards and guidelines. Limitations vary depending on the type of industry (3763).

Toxic Substances Control Act (TSCA)
Manufacturers and processors of the C_9 aromatic hydrocarbon fraction must test it for neurotoxicity, mutagenicity, developmental toxicity, reproductive effects and oncogenicity. The C_9 fraction is obtained from the reforming of crude petroleum. It consists of ethyltoluenes and trimethylbenzenes (1988). Testing will be conducted by the American Petroleum Institute. Interium reports must be submitted at 6-month intervals (1987).

Marine Protection Research and Sanctuaries Act (MPRSA)
Ocean 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 petroleum distillates (naphtha) shall not exceed an 8-hour time-weighted average (TWA) of 400 ppm (3539).

Hazardous Materials Transportation Act (HMTA)
The Department of Transportation has designated petroleum distillates as hazardous materials which are subject to requirements for packaging, labeling and transportation (305).

- State Water Programs

ALL STATES
All states have adopted EPA Ambient Water Quality Criteria and NPDWRs (see Water Exposure Limits section) as their promulgated state regulations, either by narrative reference or by relisting the specific numeric criteria. These states have promulgated additional or more stringent criteria:

ALASKA
Alaska has a water quality life criterion for the protection of aquatic life of 15 µg/L for total hydrocarbons and 10 µg/L for total aromatic hydrocarbons in fresh and marine surface waters (3016).

ARKANSAS
Arkansas requires that oil and grease shall not exceed 10 mg/L average or 15 mg/L maximum when discharging to surface waters (3587).

FLORIDA
Florida requires that oil and grease not exceed 10 mg/L in Class V waters (navigation, industrial use) and 5 mg/L for all other surface waters (3220).

MASSACHUSETTS
Massachusetts requires that the maximum discharge concentration of oil and grease of petroleum origin not exceed 15 mg/L in surface waters (3432).

NEBRASKA
Nebraska requires that petroleum oils not exceed 10 mg/L in surface waters (3719).

NEW YORK
New York has set a maximum contaminant level of 50 µg/L for kerosene in drinking water (3501).

SOUTH DAKOTA
South Dakota has a water quality standard of 10 mg/L for all petroleum products in surface waters (3672).

VIRGINIA
Virginia has a water quality standard of 1 mg/L for petroleum hydrocarbons in ground-water (3135).

WYOMING
Wyoming has a water quality standard of 10 mg/L for surface waters and Class II and III ground-waters. In addition, Class I domestic ground-water is required to be virtually free of oil and grease (3853, 3852).

Proposed Regulations

- Federal Programs
  No federal regulations are pending.

- State Water Programs
  No state regulations are pending.

MOST STATES
Most states are in the process of revising their water programs and proposing changes to their regulations which will follow EPA's changes when they become final. Contact with the state officer is advised. Changes are projected for 1989-90 (3683).

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 Fishing Water Quality (536)
Petroleum products must not be present in salmonid and cyprinid waters in such quantities that they: (1) form a visible film on the surface of the water or form coatings on the beds of water-courses and lakes, (2) impart a detectable "hydrocarbon" taste to fish and, (3) produce harmful effects in fish.

Directive on the Quality Required of Shellfish Waters (537)
The mandatory specifications for petroleum hydrocarbons specify that they may not be present in shellfish water in such quantities as to produce a visible film on the surface of the water and/or a deposit on the shellfish which has harmful effects on 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 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)
Petroleum and coal tar distillates with flash points below 21°C are classified as flammable substances and are subject to packaging and labeling regulations. Because of the variable composition of the petroleum and coal tar distillates (excluding those used as motor fuels) they are considered preparations and their labeling shall be done in accordance with the procedures outlined in the Directive Relating to the Classification Packaging and Labeling of Dangerous Preparations (solvents).

Directive on Disposal of Waste Oils (1986)
Establishments collecting and/or disposing of waste oils must carry out these operations so that there will be no avoidable risk of water, air or soil pollution. A permit from the competent authority must be registered and adequately supervised for collecting, disposing, or regenerating waste oils. PCBs and PCTs must not be present in amounts greater than 50 ppm in regenerated waste oil.

EEC Directives - Proposed
Proposal for a Council Directive on the Dumping of Waste at Sea (1793)
EEC has proposed that the dumping of crude oil, petroleum hydrocarbons, lubricants and hydraulic fluids at sea be prohibited.

69.1 MAJOR USES AND COMPOSITION

69.1.1 Major Uses

Mineral based crankcase oils are used widely in various engines to lubricate moving parts. Some examples of their uses are in automotive engines, railroad and truck diesel engines, marine equipment (ships and naval equipment), jet and other aircraft engines, as well as most small 2- and 4-stroke engines.

The major determining factor in choosing a specific oil is the severity of operating conditions. For instance, jet engine oils, by far, are subject to a wider range of operating temperatures and shear levels than automotive engine oils, and there are different mineral oil base stocks that are better suited to accommodate these conditions. In applications of severe conditions such as marine engines or outdoor equipment where moisture is a problem or higher temperatures are encountered (e.g., in supersonic jet engines), the chosen base stock can be formulated with additives to improve performance. Although mineral base oils can be improved by additives to meet some of these severe conditions they cannot compete well against the newer, more versatile synthetic oils. As a result their major uses are in slower and cooler running diesel and automotive engines (21, 1821).

69.1.2 Composition

Mineral base crankcase oils are primarily mixtures of straight and branched chain hydrocarbons (paraffins), cyclo paraffins, naphthenic, aromatic and polynuclear aromatic compounds with carbon numbers of approximately C_{15}-C_{50}, molecular weights of approximately 150-1000, and a boiling point range of approximately 300-600°C. Their densities generally lie between 0.80-1.0 kg/L at 15°C (1821). The structures of typical compounds in these mixtures are given in Figure 69-1.

The base oils may also contain trace levels (typically <1 ppm) of several polynuclear aromatic hydrocarbons (PAH) (Table 69-1). Used oils may contain higher PAH concentrations as well as a variety of other impurities from engine operation (e.g., some heavy metals and breakdown products). The base mineral oils contain hundreds to thousands of different hydrocarbons, and may contain a substantial fraction of nitrogen- and sulfur-containing compounds. Some additional information on the specific chemicals in these oils can be gleaned from analyses of the heavy end crude oil distillates from which they are made. Figure 69-2 summarizes the results of one series of studies based on five crude oils. Each heavy end distillate [which had a boiling point range (370-535°C) similar to that for mineral based crankcase oils (300-600°C)] was separated into seven (or eight) fractions, and the four concentrates with the most material were further characterized. The original work (1837), and references cited therein, contain extensive lists of identified chemicals

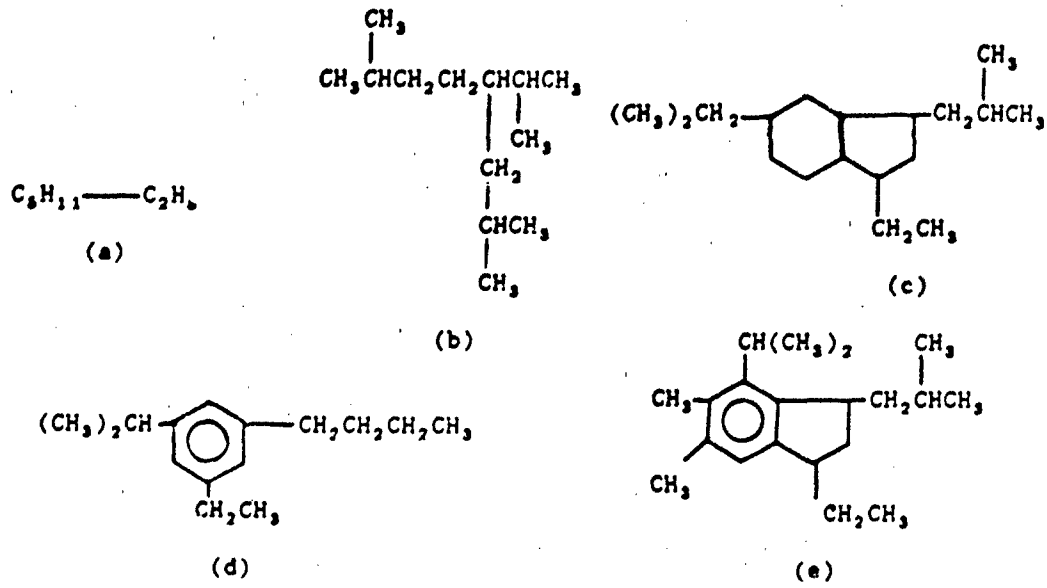


FIGURE 69-1

Typical structures in mineral base lubricating oil. (a) n-paraffin, (b) isoparaffin, (c) cycloparaffin, (d) aromatic hydrocarbon, (e) mixed aliphatic and aromatic ring. Source: Reference 21

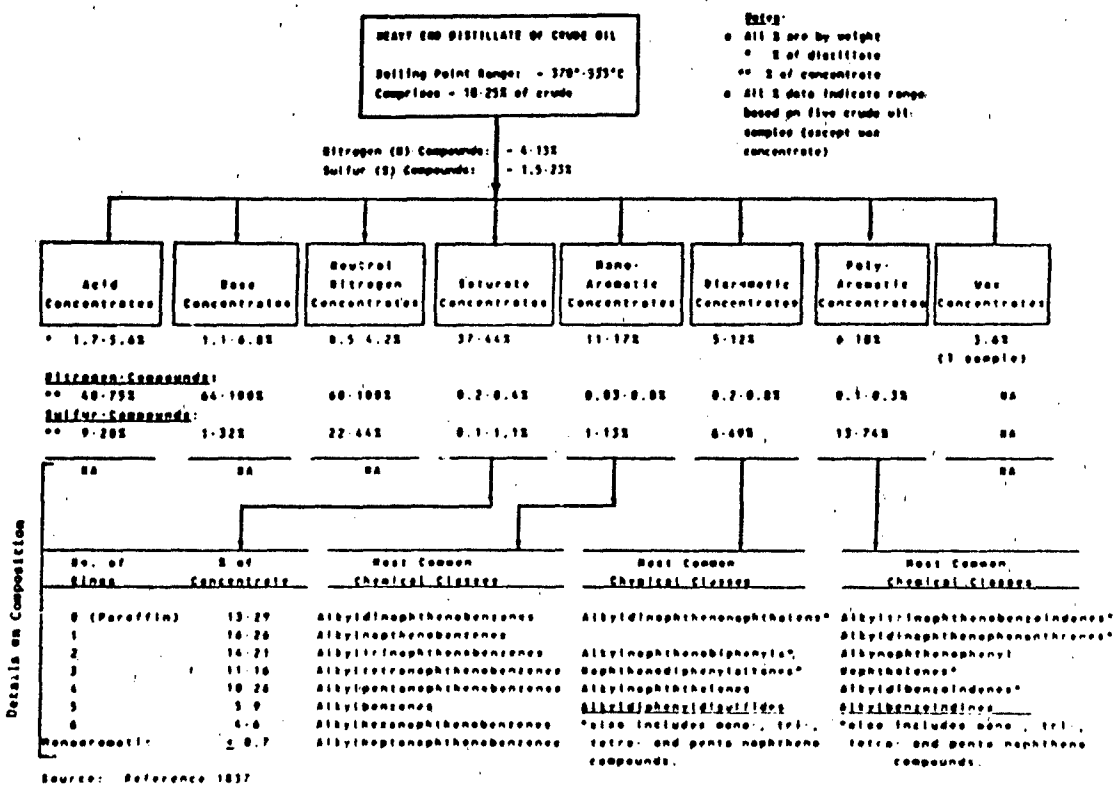
TABLE 69-1
RANGES AND MOST FREQUENT CONCENTRATIONS
OF POLYNUCLEAR AROMATIC COMPOUNDS IN VARIOUS MOTOR OILS
(FRESH AND USED) (MG/KG)

	Fresh motor oil (22 samples)	Used Motor Oils (54 samples)	
Polynuclear aromatic compound	Range	Most frequent	Range
Fluoranthene	0.008 - 2.75	0.070	0.2 - 109
Pyrene	0.039 - 6.53	0.300	0.3 - 326
Benzo[b]naphtho[2,1-d]thiophene	0.097 - 9.43	0.700	0.7 - 6.2
Chrysene + triphenylene	0.182 - 11.9	0.700	1.6 - 74
Benzofluoranthenes [b+j+k]	0.013 - 0.234	0.080	0.3 - 44
Benzo[e]pyrene	0.030 - 0.402	0.200	0.2 - 49
Benzo[a]pyrene	0.008 - 0.266	0.060	0.1 - 35
Perylene	0.007 - 0.224	0.060	0.1 - 10
Indeno[1,2,3-cd]pyrene	0.001 - 0.020	0.001	0.1 - 12
Benzo[ghi]perylene	0.010 - 0.139	0.020	0.2 - 85
Anthanthrene	0.002 - 0.030	0.010	0.02 - 11
Coronene	0.001 - 0.016	0.020	0.00 - 29

Source: Reference 1821

FIGURE 69-2
COMPOSITION OF HEAVY END DISTILLATES OF CRUDE OIL

(Note that composition of a mineral crankcase oil may differ from heavy end distillates because of the production processes used) would remain entrained in the pores of the soil near the surface. This would be more likely for low porosity and high organic carbon content soils, and less likely for sandy, porous soils.



Source: Reference 1817

TABLE 69-2
COMPOSITIONAL INFORMATION FOR VARIOUS BLENDED MINERAL BASE OILS

Product Type	Mineral oil Base Stock (Vol %)	Additives (Vol. %)					
		Detergent/ Dispersant Package	VI Improvers	Rust Inhibitors	Oxidation Inhibitors	Antiwear Additives	Antifoaming Agents
<u>Non-diesel engine oil</u>							
API service classification of a typical SAE 30 automotive motor oil SA-SE[a]	93.2-99.995	0-6.8		0-.005	0-1.0		
Monograde automotive engine oil SAE 10-SAE 50	93.2	6.8					
Multigrade automotive engine oil: 10W/30	87.7	6.8	5.5				
10W/40	85.7	6.8	7.5				
Marine engine oil: SAE 30	85.0	15.0					
Base engine oils:							
SAE 30 (Two cycle)	98.945			0.05		1.0	0.005
SAE 40 (Four cycle)	97.0	3.0					
SAE 40 (Dual Fuel-oil)	96.5	3.5					
<u>Diesel Engine Oils</u>							
Monograde diesel oils							
SAE30 CC[a]	94.0	6.0					
CD	92.0	8.0					
Railway diesel oil							
SAE 40 Class II[b]	89.5	10.5					
Marine diesel oil							
SAE 30 (low speed)	98.5	0.5				1.0	
SAE 30 (med. speed)	92.3	7.7					

TABLE 69-2 (Cont.)

Product Type	Mineral oil Base Stock (Vol %)	Additives (Vol. %)					
		Detergent/ Dispersant Package	VI Improvers	Rust Inhibitors	Oxidation Inhibitors	Antiwear Additives	Antifoaming Agents
Universal Engine Oil[c]							
Monograde engine oil							
SAE 30 SE/CD	88.0	12.0					
Multigrade engine oil							
15W/40 SE/CD	79.5	12.0	8.5				

a) Each Classification SA-SE and CA-CD is formulated to meet the needs of newer more powerful engines
b) Classes I-IV represent improvements in additive package
c) Universal oil is formulated to meet the specifications for automotive and diesel engine oils

Source: Reference 1823

and/or chemical classes. The information in Figure 69-2 (and the original reference) should be used with caution since the material analyzed was not a refined lubricating oil. To make such oils, the heavy end distillates are typically further treated by such processes as solvent extraction, dewaxing, acid treatment, and hydrofinishing. These processes alter the chemical composition. A less aromatic character is a common goal of such treatments.

Crankcase oils are often formulated to meet specific requirements or operating conditions and in many cases, additives are incorporated to accomplish this. These additives in concentrations of most commonly 0-20% vol. (1821), and occasionally as much as 30% serve a variety of functions that are intended to either protect surfaces, improve oil and machine performance or preserve the lubricant (21). Table 69-2 lists typical compositions of some mineral base engine oils. Formulations are dependent upon intended use. Specific chemical additives are given in Table 69-3.

69.2 ENVIRONMENTAL FATE AND EXPOSURE PATHWAYS

69.2.1 Transport in Soil/Ground-water Systems

Mineral base crankcase oils are expected to be highly immobile in the soil/ground-water environment. Bulk quantities of the oil from a spill or improper disposal might be carried slowly through the unsaturated zone to the top of the water table, but the high viscosity and low water solubility would mitigate this. Most likely, at least with moderate to small spills, the oil would remain entrained in the pores of the soil near the surface. This would be more likely for low porosity and high organic carbon content soils, and less likely for sandy, porous oils.

Transport and subsequent fate of dissolved constituents of these oils will vary depending on the physicochemical (and biological) properties of the constituents. Some constituents will dissolve more quickly in the percolating ground-waters, be sorbed less strongly on the soils (thus being transported more rapidly), and may be more or less susceptible to degradation by chemical or biological action. The relative concentrations of the constituents of the oil will vary with time and distance from the site of initial contamination. This effect is called "weathering". (This term is also used to describe changes to oil following spills into surface waters where film spreading and breakup, and differential volatilization, dissolution, and degradation all are involved.)

Almost all of the hydrocarbon constituents in these oils would fall into a highly immobile class for consideration of movement of dissolved constituents through the soil/ground-water system. While no data are available, it is roughly estimated that all such constituents would have solubilities in pure water of less than 1 mg/L [e.g., ethyl naphthalene, $C_{12}H_{12}$ is 0.8 mg/L (1839)] and most might be orders of magnitude less

TABLE 69-3
CHEMICAL ADDITIVES

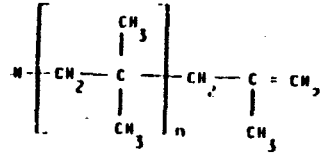
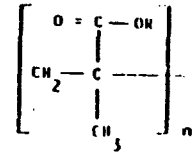
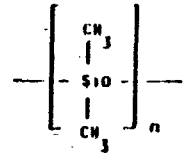
Type of Additive	Chemical Name/Class	Structure	Properties/Characteristics
Viscosity index (VI) improvers	1. Polyisobutylenes		MW of 10,000-20,000 are common but can be as high as 1,700,000.[a]
	2. Polymethacrylates		Decomposition temperature for polyisobutylenes approximately 290°C.[b] Common in multigrade engine oils from 4.5% - 12% vol.[c]
	3. Polyalkylstyrenes		
	4. Ethylene propylene co-polymers	(polyisobutylene)	
	5. Styrene-butadiene copolymers		
		(polymethacrylate)	
Pour point depressors	1. Polymethacrylates		Higher MW than for VI improvers.
	2. Alkyl-aryl polymers		< 1.0% vol. used. Usually as little as 0.2% vol.
Antifoam additives	1. Methyl silicone polymers		Approximately .001 - .005% vol. used. MW of approximately 1,000-150,000 are common.[a,b]
		(dimethyl silicone polymer)	Adequate service up to 205°C.[a]

TABLE 69-3 (Cont.)

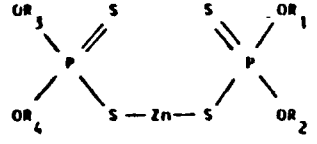
Type of Additive	Chemical Name/Class	Structure	Properties/Characteristics
Friction modifiers	1. Organic acids, amines, natural fats, oils, waxes		These compounds are very similar to antiwear compounds in composition and amounts used.
	2. Organic phosphorus compounds (i.e., *tricresylphosphate*)		
	3. Colloidal graphite: molybdenum disulfide		
Emulsifiers	1. Cationic, anionic, and nonionic materials based on long chain aliphatic acids, amines, alcohols, and esters and ethers.		
Oxidation inhibitors	1. Aromatic amines (i.e., N-phenyl-1-naphthylamine, *phenothiazine*)	 (zinc dithiophosphate) R = alkyl, aryl or combination	Most commonly added from 0-2% vol.[b]
	2. Phenols (i.e., 2-naphthol, di-tert-butyl-p-cresol) (BPC)		
	3. Zinc, calcium, barium, magnesium, dithiophosphates		

TABLE 69-3 (Cont.)

Type of Additive	Chemical Name/Class	Structure	Property/Characteristics
	4. Salicylates		
	5. Phenates and sulfonates		
Rust and Corrosion Inhibitors	1. Zinc dithiophosphate		0 2.0% vol. is typical.[a]
	2. Derivatives of di-basic organic acids (alkylsuccinic acids) and organic amines (i.e., dicyclohexyamine)		
	3. Organic sulfonate and phosphate salts, polyhydric alcohols		
Antiwear and Extreme Pressure Additives	1. Oxygen-containing fatty acids, esters, ketones		0 1.5% vol. is typical.[b]
	2. Oxygen/sulfur-containing compounds (sulfurized fats)		
	3. Aliphatic chlorine compounds (chlorinated wax)		

TABLE 69-3 (CONT.)

Type of Additive	Chemical Name/Class	Structure	Properties/Characteristics
	6. Organic phosphorus compounds (i.e., tricresyl phosphate), thiophosphates, phosphites, (i.e., zinc dioctylmedithiophosphate)		
Detergents/Dispersants	1. Calcium and barium salts of organic sulfonates	$R-SO_3-Me-SO_3-R$ or $R-SO_3-Me-OH$ (Me = Ca or Ba) (organic sulfonates)	Most detergents added from 2-20% vol.[a,b]
	2. Phosphonates and thiophosphates	$R-P(=X)(Me)_2$ (X = O or S) (Me = Ca or Ba) (phosphonates thiophosphates)	MW 500-2000.[b]
	3. Barium or calcium salts of alkyl phenols or alkyl phenol sulfides		
	4. Calcium and barium alkyl substituted salicylates		
	5. Aliphatic amines, amides, ethers		
	6. Reaction products of polybutenes and P_2S_5 and ethylene oxide		

TABLE 69-3 (Cont.)

Type of Additive	Chemical Name/Class	Structure	Properties/Characteristics
7.	Alkyl methacrylate dimethyl aminoethyl methacrylate copolymers		
8.	Alkyl methacrylate n vinylpyrrolidone copolymers		
9.	Vinyl acetate dialkyl fumarate maleic anhydride copolymers		
10.	Polyisobutenyl succinimides	(Re : Co or Ba) (alkyl phenolates)	

X : S or O

(reaction products of polybutenes and P_2S_5 and ethylene oxide)

TABLE 69-3 (Cont.)

Type of Additive	Chemical Name/Class	Structure	Properties/Characteristics
Biocides	1. Boron compounds		
	2. Phenols and chlorophenol derivatives		
	3. Triazines		

a) Reference 1822
b) Reference 21
c) Reference 1824

than this [e.g., eicosane, $C_{20}H_{42}$, is estimated to have a solubility of at 1E-07 mg/L (1840)]. The corresponding soil sorption constants (K_{oc}) estimated from such solubilities would all be over 10,000 and most would be over 1,000,000 indicating very strong sorption to soils containing organic matter. Constituents with low molecular weight, high aromatic character, and/or nitrogen and sulfur hetero atoms will tend to be the most mobile.

No equilibrium partitioning model calculations (as have been given for most other chemicals in this Guide) are given for these oils. All such calculations (for all major constituents of the oil) would show that essentially all of the oil was sorbed to the soil and that negligible amounts were present in the soil-air or soil-water compartments.

A small fraction of the constituents of the oils may be significantly more water soluble and mobile than the rest. These might include, for example, low molecular weight nitrogen- and sulfur-containing molecules naturally present in the oil, as well certain additives such as are shown in Table 69-3.

The aqueous-phase mobility of oil constituents could be significantly enhanced if the oil was in the form of a very fine emulsion, or if the percolating ground-water contained a significant amount of dissolved organic carbon (e.g., humic and fulvic acids, fatty acids, or chlorinated solvents) from other natural sources, or other discharged materials. The dissolved organic carbon, much of it possibly in the form of colloidal particles, could absorb the oil constituents and assist in their transport through the soil/ground-water system.

Volatilization of constituents from the crankcase oil would be very slow because of the very low vapor pressures involved (presumably < 1E-03 mm Hg at 25°C for individual constituents, with many below 1E-06 mm Hg). However, given that spilled oils may remain near the soil surface (making volatilization easier), that the material is resistant to leaching and degradation, and that the Henry's law constant may be moderately high, it is thus presumed that volatilization will be a major loss mechanism for spilled crankcase oil over time periods of weeks to years. Because the lower molecular weight (more liquid) constituents would tend to volatilize first, the remaining material would generally have lower volatilities and lower water solubilities.

69.2.2 Transformation Processes in Soil/Ground-water Systems

Mineral base crankcase oils are expected to be persistent in the soil/ground-water environment because of their resistance to hydrolysis, oxidation, and biodegradation. The general resistance to hydrolysis (for saturated and unsaturated hydrocarbons) is described by Harris (529). The resistance to oxidation is a major component of their utility as long-lasting lubricants; as noted in Table 69-3, anti-oxidants are sometimes present in the oils.

The assessment of the resistance to biodegradation is more complex. Most of the oil molecules are so large that passage through cell walls (where metabolism or degradation is relatively easy) is hindered and much of the biodegradation must be carried out by extracellular enzymes secreted by the microbes. Such difficulties aside, many studies on petroleum hydrocarbon materials (oils as well as light distillates) have showed moderate to high eventual susceptibility to biodegradation for the bulk of the material (1842). A period of microbial adaptation may be required.

Different constituents of the oil will differ significantly in their biodegradability for reasons related to molecular size, structure, and toxicity. For example, highly branched alkanes are much less biodegradable than linear alkanes, and polycyclic aromatic hydrocarbons with three or more rings are very resistant to biodegradation (515). For all hydrocarbons, aerobic biodegradation would be expected to be much more important than anaerobic biodegradation (1841). Because of this, and because of the decrease in microbiological activity with increasing soil depth, oil constituents reaching deep anaerobic soils could persist for very long time periods.

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

The above discussion of fate pathways suggests that pure mineral based crankcase oil has low volatility, but that individual components may vary in their volatility from water. These components are strongly or very strongly sorbed to soil but are expected to have a low potential for bioaccumulation. These fate characteristics suggest several potential exposure pathways.

Volatilization of mineral based crankcase oils from a disposal site would not be expected to result in significant inhalation exposures to workers or residents in the area. Gravity would tend to carry bulk quantities of the oil down toward the water table, leaving only a relatively small fraction on the soil surface to volatilize. Volatilization of this remaining oil would occur very slowly because of its low vapor pressure and strong sorption to soil.

Ground-water contamination may result from large spills that reach the water table. Ingestion exposures may occur directly through the use of contaminated waters as drinking water supplies, or indirectly through ground-water discharge to surface waters used for drinking water. These surface waters may also result in dermal exposures if they are used for recreation. Because waters containing petroleum-derived products have objectionable tastes and odors at concentrations well below any tolerable health concentrations (982), significant ingestion exposures from drinking water are expected to be rare.

69.2.4 Other Sources of Human Exposure

A potentially major source of human exposure of mineral base crankcase oil is surface water contamination resulting from the run off from roads and runways. Roughly two billion liters of used lubricating oils are estimated to be released

annually into the environment of the U.S., of which three quarters of a billion liters were used as road oil or incorporated in asphalt (1821). The more soluble fraction of the oil applied to roads intentionally or leaked from crankcases will be carried from the roadway with rainfall, either into sewage or drainage systems (if any) or as run off to surface waters. Less soluble components may be transported in much the same way if they are sorbed to soil particles that are carried by the water.

Data on ambient concentrations of mineral base crankcase oils in air and ambient water, as well as food and drinking water are not generally available in the literature. The gross parameter "oil and grease" is often used to characterize water, soil and sediment samples. However, this measure does not directly correspond to the concentration of mineral base crankcase oil.

The ingestion of crankcase oil that has been taken up by aquatic species is a potential exposure pathway, although two factors militate against this. Relatively low concentrations of oil can lead to tainting, thereby rendering the food unpalatable. Oysters, for example, have been found to exhibit tainting when exposed to crude oil concentrations as low as 1-10 μg/L (982). The large aliphatic hydrocarbons that make up the bulk of crankcase oil are not expected to bioaccumulate thus minimizing the concentrations in aquatic species. The polycyclic aromatic compounds in oil (especially used oil) would be expected to bioaccumulate, however, and thus are a potentially greater source of exposure.

The personnel likely to receive the greatest exposure to mineral base crankcase oils are those involved in servicing and maintaining equipment in which they are used. Although inhalation exposures are not expected to be large because of the low volatility of these oils, significant dermal exposures may occur. Unless gloves and protective clothing are worn, hands and forearms are likely to come in contact with the oils.

69.3 HUMAN HEALTH CONSIDERATIONS

69.3.1 Animal Studies

69.3.1.1 Carcinogenicity

Male C3H/HeJ mice (50/group) were treated with 50 mg of used or unused samples of composite motor oil (15 brands of SAE 10W-40 mineral base oil) applied twice a week to the shaved interscapular skin for 104 weeks (2212). The control group received no treatment. Histological lesions in animals treated with the new motor oil included 1 papilloma, 2 squamous cell carcinomas and 1 fibrosarcoma. One animal in this group had a lymphomatous infiltrate in the skin which was part of a systemic lymphoma. The tumor incidence in animals treated with used motor oil was much higher, with histological lesions consisting of 4 papillomas, 8 keratoacanthomas, 16 squamous cell carcinomas and 1 hemangiosarcoma. No tumors were reported in

the control group. It was concluded that unused composite motor oil was relatively nontoxic and only slightly carcinogenic to male C3H/H3J mice. Used composite motor oil, on the other hand, was considered slightly to moderately carcinogenic.

Albino mice receiving skin applications of an engine lubricating oil additive containing lead naphthenate developed a 17% incidence of skin papillomas and a 51% incidence of skin carcinomas (2234). Further investigation of the components of the additive revealed an 82.7% incidence of skin papillomas and carcinomas from the base oil component while the additive concentrate produced only one papilloma (2235).

A commercial motor oil [Permalube®] was applied twice a week (dose not specified) to the skin of female mice (strain not specified) for 66 weeks (2220). No increased incidence of tumors was reported. A second group of mice were given a single application of the carcinogen 7,12-dimethyl-benz(a)anthracene [1% in Supra® 34 mineral oil] and treated with motor oil twice a week for 66 weeks. Again, no tumors were found.

Graf and Winter (2221) found a level of 26 µg/L of the carcinogen benz(a)pyrene (BaP) in new motor oil. After heavy use, the BaP level rose to 5800 µg/L, indicating a carcinogenic potential in used motor oil which should be considered when disposing or recycling the product.

IARC (1821) considers the data available on the carcinogenicity of crankcase oil inadequate to evaluate (i.e., category 3) and states that any carcinogenic activity of individual products is dependent upon the processing of the base oils and the nature and concentration of additives. One sample of used gasoline engine oil was shown to produce a statistically significant dose-related increase in the incidence of skin papillomas and carcinomas (2237) and was considered by IARC to be sufficient evidence of carcinogenicity in experimental animals.

69.3.1.2 Mutagenicity

Motor oil showed no mutagenic activity when tested in strains TA1535, TA1537, TA1538, TA98 and TA100 of Salmonella typhimurium both with and without metabolic activation (2217).

Pasquini and Monarca (2218) also showed that unused motor oil was nonmutagenic in the Salmonella/microsome test and contained only trace amounts of polycyclic aromatic hydrocarbons (PAH). Used motor oil was highly mutagenic and contained high quantities of carcinogenic PAH.

Dutcher et al. (3337) compared the mutagenic activity of used crankcase oil (UCO) from diesel and spark-ignition (gasoline) passenger cars in Salmonella typhimurium. Direct assays with UCO did not detect mutagenic activity in S. typhimurium strain TA98. However, extracts prepared from samples of both diesel

and gasoline-powered vehicles (to concentrate mutagens from UCO) showed a dose-dependent mutagenicity in the presence and absence of metabolic activation. The mutagenic potency of diesel-UCO extracts appeared to be similar to gasoline-UCO extracts. Unused crankcase oil extracts had a lower mutagenic activity and generally required metabolic activation.

A study by Manabe et al. (3141) investigated the potential mutagenicity of wastewater collected from oil-water separating tanks of gasoline stations. Wastewater samples were fractionated into neutral, acidic, and basic fractions and tested for mutagenic activity in Salmonella typhimurium strains TA98 and TA100 in the presence and absence of metabolic activation. The neutral fractions displayed a high mutagenic activity, attributed to water from car washing and contamination by used crankcase oil. 1-Nitropyrene (1-NP) accounted for up to 58.5% of the mutagenic activity of the neutral fraction. An additional experiment measured the mutagenic activity of fractionated crankcase oil used in a gasoline and in a diesel engine using S. typhimurium strains TA98, TA100, TA98NR, and TA98/1,8-DNP(6) in the presence or absence of metabolic activation. The results were similar to those with wastewater. The neutral fraction showed the highest mutagenic activity; the mutagenicity in strain TA98 was higher in the absence than in the presence of metabolic activation and was higher than in strain TA100. Decreasing mutagenic activity was found in strains TA98NR and TA/1,8-DNP(6), suggesting that used crankcase oil contains 1-NP (the two strains do not respond to 1-NP). However, the presence of 1-NP in the neutral fraction of crankcase oil accounted for a smaller portion of the total mutagenic activity than that in waste water.

Abdelnasser et al. (3190) studied the formation of mutagens in crankcase oils. New crankcase oils were exposed to elevated temperatures to determine if pyrolysis or oxidation could degrade this complex mixture to a mutagenic species. Heating to 100°C for 100 hr did not produce mutagenic activity in Salmonella typhimurium strain TA98 with or without microsomal activation. Crankcase oil was also exposed to nitrogen dioxide, sulfur dioxide, ammonia, hydrogen sulfide, or nitrous oxide under various experimental conditions. Nitrogen dioxide was the only chemical capable of producing mutagenic substances in crankcase oil. Without metabolic activation, the product of this experiment was highly mutagenic in tester strain TA98.

Motor oil did not demonstrate the potential to induce forward mutations in L5178Y mouse lymphoma cells either with or without metabolic activation (2217). The compound was, however, considered extremely toxic in the test system. Motor oil orally administered to rats for five consecutive days at concentrations as high as 1250 mg/kg/day did not result in any significant increase in chromosomal mutations of bone marrow cells (2217).

69.3.1.3 Teratogenicity, Embryotoxicity and Reproductive Effects

An avian study by Hoffman et al. (3293) investigated the embryotoxic and biochemical effects of clean (CCO) and waste crank case oil (WCO) on birds' eggs.

At 48 hours of development, mallard duck eggs were exposed externally to 2, 5, or 15 μL/egg of WCO or 15 μL/egg of CCO, while bobwhite quail eggs received 0.5, 1, or 3 μL/egg of WCO or 3 μL/egg of CCO in a similar manner. WCO was highly embryotoxic to both species compared to CCO and resulted in dose-dependent mortality, reduced growth, and abnormal survivors. Abnormal survivors included embryos with edema, incomplete ossification, and eye and brain defects. Biochemical effects, growth retardation, and mortality at lower dose levels were more pronounced in mallards than in bobwhites. In mallards, the LD_{50} value was 23.5 μL/egg for virgin crankcase oil and 5.3 μL/egg for waste crankcase oil (3292).

No data on the potential teratogenicity or adverse reproductive effects of mineral base crankcase oil in mammalian species were located in the literature.

69.3.1.4 Other Toxicologic Effects

69.3.1.4.1 Short-term Toxicity

Doll (3177) described the clinical signs observed in a cow after ingestion of used motor oil (tractor crankcase oil). Six hours after exposure the animal displayed the following symptoms: total loss of appetite, severe muscle tremors, discoloration of mucous membranes, increased heart beat, slightly increased breathing, fecal discoloration, and increased frequency of fecal excretion. Hematologic analysis showed moderate leukopenia resulting from absolute lymphopenia. Treatment consisting of rumentomy and removal of ingesta resulted in complete recovery.

The short-term pulmonary irritation of unused and used mineral base motor oil (Mobil Special Motor Oil SAE 10W-30) was studied by Costa and Amdur (2213). Guinea pigs were exposed (head only) to 0, 10, 40 or 100 mg/m^3 motor oil mist for one hour. No irritation or other effects were seen in the 10 and 40 mg/m^3 treatment groups. Animals exposed to 100 mg/m^3 of either used and unused motor oil mist developed a slight, but statistically significant increase in respiratory frequency. It was concluded that these changes in respiration were related to the overall stress of the exposure situation rather that to any specific irritant action of the oil mist.

The acute oral toxicity of crankcase oil in Sprague-Dawley rats was studied by the American Petroleum Institute (API) (2214). Dosing with 15 mL/kg or 25 mL/kg crankcase oil by gavage caused diarrhea lasting 3 days. Some rats seemed lethargic but recovered completely by day 7. The oral LD_{50} was considered to be greater than 25 mL/kg.

A dose of 0.1 mL mineral base crankcase oil instilled into the eye of New Zealand white rabbits was mildly irritating. Two animals showed opacities which dissipated by day 7. The conjunctiva of one rabbit was slightly irritated. One animal eye treated with 0.1 mL crankcase oil for 30 seconds and then flushed for one minute with distilled warm water showed slight conjunctival irritation (2214).

Mineral base motor oil was found to be slightly irritating when applied to the shaved backs of New Zealand white rabbits for 24 hours (2214). By 72 hours, edema disappeared but some erythema was present. Examination 6 days after treatment revealed no signs of irritation; however, skin at the test site was dry and flaky. Application of 5 mL/kg crankcase oil for 4 hours to New Zealand white rabbits also revealed skin irritation but no obvious treatment-related signs of systemic toxicity (2214). Gross post-mortem examinations revealed no abnormalities.

Doses of 0, 4, or 8 mL/kg crankcase oil were applied to the shaved skin of New Zealand white rabbits for 5 consecutive days followed by a two-day rest period and a second 5-day treatment period. The most significant effect was a dose-related progressive dermal deterioration. The skin at the test site was thick, cracked, bloody, and edematous. In addition to these signs, the animals treated with 8 mL/kg had a decrease in general activity, alopecia and became emaciated, with an average body weight loss of 0.28 kg. The test material produced acanthosis (i.e., diffuse hyperplasia and thickening of the epidermis), acute inflammation, chronic inflammation, crusting, dermal congestion, dermal edema, hyperkeratosis, and parakeratosis in both the 4 and 8 mL/kg treatment groups. It caused acute dermal corrosion in the 8 mL/kg treatment group (2214).

The potential of crankcase oil to cause dermal sensitization in guinea pigs was studied by API (2214). A dose of 0.5 mL crankcase oil was placed on a gauze patch and applied to the depilated backs of male albino guinea pigs for 6 hours, 3 times a week for 3 weeks. After a two-week rest period, animals were challenged with 0.5 mL crankcase oil. No sensitizing effect was noted.

69.3.1.4.2 Chronic Toxicity

Early studies (2215) have shown that administration of 132 mg/m^3 motor oil vapor continuously for alternating 30-minute periods for 100-343 days produced little lung damage in rats, rabbits or mice. Exposed monkeys showed an increased incidence of infectious pneumonia and developed severe gastric ulcers. Death was attributed to hyperplastic gastritis, presumably caused by the swallowing of oil that was deposited in the nasal passages.

69.3.2 Human and Epidemiologic Studies

69.3.2.1 Short-term Toxicologic Effects

Accidental ingestion of crankcase oil may produce irritation of the mucous membranes of the digestive system and result in nausea, vomiting, and diarrhea (2216). Vomiting should not be induced after ingestion because of the low viscosity of crankcase oil which makes its aspiration into the lungs probable. Once this occurs, chemical pneumonitis is likely to follow.

No adverse health effects are expected during normal short-term skin exposure to crankcase oil. Repeated dermal exposure to crankcase oil may result in irritation due to the defatting of the skin. A diffuse erythema with some edema combined with broken hairs and occasional pustules are the main characteristics of dermatitis produced by crankcase oil (2216). Repeated exposure of the eyes may also result in irritation (2216).

Health hazards from vapors of crankcase oil are unlikely but when significant vapor concentrations are repeatedly inhaled, irritation of the mucous membranes of the upper respiratory tract is expected. Systemic effects may include headache, nausea, dizziness, and general malaise (2216).

69.3.2.2 Chronic Toxicologic Effects

Repeated long-term dermal exposure to crankcase oil may produce skin rash and oil acne. Oil acne is characterized by blackheads, pimples, and pustules. Some poorly refined base oils cause warty swelling or sores (2216).

Prolonged and repeated exposure to significant atmospheric concentrations of mineral oils may lead to a benign form of lung fibrosis, possibly preceded by symptoms of bronchopulmonary disease. Inhalation of oils with high polycyclic aromatic hydrocarbon content may result in cancer of the respiratory tract and possibly cancer of the upper gastrointestinal tract (2216).

69.3.3 Toxicology of Mineral Base Crankcase Oil Components

A brief overview of the toxicology of some typical components of mineral base crankcase oil are summarized below. The acute toxicity values for these compounds are presented in Table 69-4.

n-Hexane

Hexane may be the most highly toxic member of the alkanes. When ingested, it causes nausea, vertigo, bronchial and general intestinal irritation and CNS effects. It also presents an acute aspiration hazard. Chronic exposure to n-hexane vapors causes peripheral neuropathy. The first clinical sign of neural damage is a feeling of numbness in the toes and fingers. Progression leads to further symmetrical sensory impairment in the distal portions of the extremities and to loss of muscular stretching reflexes. Ultimately, symmetrical muscular weakness develops, chiefly in the distal portion of the extremities. Paralysis develops with varying degrees of impaired grasping and walking. This may include muscular atrophy (sensorimotor polyneuropathy). The development of electrophysical changes parallels the severity of the clinical picture. In the most severe cases, nerve conductivity is neutralized. In some cases, cranial nerve involvement is also observed. After exposure ceases, recovery begins within 6 to 10 months in mild to moderate cases. but may take up to 3 years in serious cases. The threshold level at which neuropathy occurs has not

TABLE 69-4
ACUTE TOXICITY OF COMPONENTS OF MINERAL BASE CRANKCASE OIL

Component	Oral LD_{50}	Dermal LD_{50}	LC_{50}
n-hexane	24-49 mL/kg [rat] (1935) 28,710 mg/kg [rat] (1937)	no data	33,000 ppm •4 hr [rat] (1935)
octane	<— no data —>		
dodecane	<— no data —>		
isopentane	no data	no data	1000 mg/L [mouse] (12)
methylcyclopentane	<— no data —>		
methycyclohexane	2250 mg/kg [rat] (47)	no data	no data
cyclohexane	29,820 mg/kg [rat] (1935)	no data	no data
benzene	3800 mg/kg [rat] (59) 4700 mg/kg [mouse] (47)	no data	10,000 ppm •7 hr [rat] (47)
toluene	5000 mg/kg [rat] (47)	12,124 mg/kg [rabbit] (47)	5320 ppm •8 hr [mouse] (47)
xylenes	4300 mg/kg [rat] (47)	no data	5000 ppm •4 hr [rat] (47)
ethyl benzene	3500 mg/kg [rat] (47)	5000 mg/kg [rabbit] (59)	no data
1-methylnaphthalene	1840 mg/kg [rat] (47)	no data	no data
2-methylnaphthalene	1630 mg/kg [rat] (47)	no data	no data
fluoranthene	2000 mg/kg [rat] (47)	3180 mg/kg [rabbit] (47)	no data

been firmly established but symptoms have been observed in people exposed to concentrations ranging from 10 to 200 ppm for 9-12 months.

In animals, signs of narcosis are seen after mice are exposed to vapor levels of 16,000 ppm for 5 minutes. Death generally occurred at concentrations between 43,800 and 52,000 ppm after 9-119 minutes. The oral LD_{50} is cited as 24 mL/kg for 14-day-old rats and 49 mL/kg for young adult rats.

Long-term inhalation experiments in rats suggest that the first signs of neurotoxicity appear after they are exposed to levels of 200 ppm for 24 weeks. This higher threshold to induce neurotoxicity in animals may be due to differences in metabolism. Specifically, 2-hexanol is the chief metabolite in animals, while 2,5-hexanedione which is neurotoxic, predominates in man. Chronic topical application of a solvent containing 35.2% n-hexane caused axonal swelling and myelin degeneration in chicks. No clinical signs were seen. Dosage was 1 g/kg/day for 64 days. In rabbits, topical application of 0.5 mL/day for up to 10 days caused redness, irritation, and scab formation. N-hexane is neither carcinogenic nor teratogenic. One in vivo study in rats that inhaled 150 ppm for 5 days found an increased number of chromosome aberrations in the bone marrow cells. No studies on mutagenicity, reproductive toxicity, or carcinogenicity in man were found (12, 1930, 1935).

Octane

By the oral route, octane may be more toxic than its lower homologues. If it is aspirated into the lungs, it may cause rapid death due to cardiac arrest, respiratory paralysis, and asphyxia. The narcotic potency of octane is approximately that of heptane but it does not exhibit the CNS effects seen with hexane or heptane.

In humans, the only reported effects are blistering and burning due to prolonged skin contact.

In animals, octane is a mucous membrane irritant. At high concentrations, it causes narcosis. It is expected that severe exposure in humans will produce the same effects. Mice exposed to vapor levels of 32,000 ppm suffered respiratory arrest after 4 minutes of exposure. Exposure to 12,840 ppm for 185 minutes caused a decreased respiratory rate, followed by death within 24 hours. No narcosis was seen after 48 minutes of exposure to 5350 ppm (12, 46, 1538).

Dodecane

Dodecane is not highly toxic. The lowest toxic dose for mice is 11 g/kg when administered percutaneously for 22 weeks. Dodecane is a potentiator of skin tumorigenesis by benzo(a)pyrene. It decreased the effective threshold dose by a factor of 10. Dodecane and phenyldodecane applied topically to the progeny of rats treated with benzo(a)pyrene, chrysene, or benzo(b)triphenylene on the seventeenth

day of gestation produced tumors in offspring. No additional information is available (12, 1937).

Isopentane

Isopentane is a CNS depressant. Effects may include exhilaration, dizziness, headache, loss of appetite, nausea, confusion, inability to do fine work, a persistent taste of gasoline and, in extreme cases, loss of consciousness. Inhalation of up to 500 ppm appears to have no effect on humans. "Very high" vapor concentrations are irritating to the skin and eyes. Repeated or prolonged skin contact will dry and defat skin resulting in irritation and dermatitis. The LC_{50} in the mouse is estimated to be 1000 mg/L (12).

Methylcyclopentane

Methylcyclopentane resembles cyclopentane in its toxicity. Cyclopentane is a CNS depressant. Humans can tolerate 10-15 ppm. In mice, 38 ppm causes loss of reflexes, narcosis and death demonstrating that no safety margin exists. Methylcyclopentane also exhibits no safety margin between the onset of narcosis and death. When applied to guinea pig skin, cyclopentane produced dryness and slight erythema. Methylcyclopentane would be expected to have the same effect (12).

Methylcyclohexane

No systemic poisonings by methylcyclohexane have been reported in man. At high vapor concentrations it causes narcosis in animals and it is expected that it would produce the same effect in humans. The no-effect level is about 300 ppm in primates and 1200 ppm in rabbits. Rabbits did not survive 70 minutes of exposure to 15,227 ppm. Death was preceded by conjunctival congestion, dyspnea, severe convulsions and rapid narcosis. There were no signs of intoxication in rabbits exposed to 2880 ppm for a total of 90 hours, but slight cellular injury was observed in the liver and kidneys. In primates, lethal concentrations caused mucous secretion, lacrimation, salivation, labored breathing, and diarrhea.

In chronic inhalation studies, exposure to 2000 ppm, 6 hours per day, 5 days per week for 2 years produced no tumors in rats, mice, hamsters, or dogs. The only significant toxic effect found was renal changes in male rats. These included renal tubular dilation, papillary hyperplasia, and medullary mineralization.

Dermal application of the liquid produced local irritation, thickening and ulceration (12, 46, 54, 17, 1936).

Cyclohexane

Cyclohexane is a CNS depressant of low toxicity. Symptoms of acute exposure are excitement, loss of equilibrium, stupor and coma. Rarely, death results due to

respiratory failure. The anesthesia which is induced is weak and of brief duration but more potent than that caused by hexane. The oral LD_{Lo} in rabbits ranges from 5.5 to 6.0 g/kg. Within 1.5 hours the animals exhibited severe diarrhea, widespread vascular damage, and collapse. Degenerative lesions were seen in the heart, lung, liver, kidney and brain. A one-hour vapor exposure to 26,732 ppm caused rapid narcosis and tremor and was lethal to all exposed rabbits. In mice, concentrations causing narcosis vary from 14,600 to 122,000 ppm.

Cyclohexane is nominally absorbed through the skin although massive applications (> 180.2 g/kg) to rabbit skin resulted in microscopic changes in the liver and kidneys and caused the death of all animals.

The danger of chronic poisoning is relatively slight because this compound is almost completely eliminated from the body. No toxic changes were seen in rabbits exposed to vapor levels of 434 ppm, 6 hours daily for 50 exposures, but some microscopic changes were seen in the liver and kidneys when the rabbits were exposed to levels of 786 ppm for the same period.

In man, no systemic poisonings by cyclohexane have been reported. A vapor level of 300 ppm is somewhat irritating to the eyes and mucous membranes. It has been reported that cyclohexane may potentiate the toxic effects of TOCP but no additional details of this interaction are available (12, 17, 46, 54, 1937).

Benzene

The primary effects of benzene inhalation and ingestion are on the central nervous system (54). Benzene is carcinogenic in both animals and man. Several reports have established a relationship between benzene exposure and leukemia. For more information, refer to Chapter 18 of the Installation Restoration Program Toxicology Guide.

Toluene

Toluene is a CNS depressant with a low toxicity. For more information, refer to Chapter 19 of the Installation Restoration Program Toxicology Guide.

Xylenes

Acute exposure to high concentrations of xylene vapors may cause CNS depression. Both the liquid and the vapor are irritating to the eyes, mucous membranes, and skin (46). The National Toxicology Program recently reported that there was no evidence of carcinogenicity of mixed xylenes in either mice or rats given daily doses ranging from 250 to 1000 mg/kg by gavage for 2 years (1939).

For more information, refer to Chapter 21 of the Installation Restoration Program Toxicology Guide.

Ethyl Benzene

Ethyl benzene is primarily an irritant to the skin, eyes and upper respiratory tract. Systemic absorption causes CNS depression (46).

For more information, refer to Chapter 20 of the Installation Restoration Program Toxicology Guide.

Methylnaphthalene

The only adverse effects of methylnaphthalene reported in man are skin irritation and photosensitization (17). Oral LD_{50} values of 1840 mg/kg and 1630 mg/kg in the rat have been reported for 1-methylnaphthalene and 2-methylnaphthalene, respectively (47).

Polynuclear Aromatic Hydrocarbons (PAH)

A number of PAH are present in unused mineral base crankcase oil. The concentration of these components increases significantly in used crankcase oil. The focus of toxicological studies with PAH has been their potential to induce carcinogenic effects. Relevant findings are summarized below.

Fluoranthene

Fluoranthene was not carcinogenic when administered orally and was inactive both as a complete carcinogen or a tumor initiator in several skin painting studies in mice. Repeated application of fluoranthene to mouse skin along with low doses of a complete carcinogen such as benzo[a]pyrene produced a considerable enhancement of carcinogenicity, indicating a strong co-carcinogenic effect (2315).

Mutagenicity studies for fluoranthene are mixed. Fluoranthene induced a significantly greater number of mutations in Salmonella typhimurium TM677 than an equimolar concentration of the positive control, benzo[a]pyrene. Negative results were reported in four other strains of Salmonella as well as in a mouse embryo cell assay (2315).

Based on a no-effect level for mortality in a chronic mouse skin painting study, an assumption of 100% absorption of the applied dose, and an uncertainty factor of 1000, an acceptable human daily intake of 0.4 mg fluoranthene was calculated, which corresponds to an ambient water quality criterion of 42 µg/L (2315).

Pyrene

Pyrene was not carcinogenic in oral studies, but was reported to be a co-carcinogen in skin painting studies with benzo[a]pyrene. Pyrene has also been shown to be a weak tumor initiator in the mouse skin carcinogenesis model (2315).

Pyrene produced negative results in Salmonella typhimurium and in vitro mammalian cells. No induction of DNA repair and no unscheduled DNA synthesis, sister chromatid exchange, or chromosome aberrations were reported (2315).

Few data were found on the toxic effects associated with pyrene exposure. A dermal LD_{L_o} value in the mouse was reported to be 10 g/kg when applied for a 3-week period (47).

Chrysene

Chrysene is regarded as a complete carcinogen for mouse skin as well as an initiator of skin carcinogenesis in the mouse. Local sarcomas have been reported at the site of subcutaneous or intramuscular injections of chrysene (2229).

Mutagenic studies with chrysene have been negative or, at best, only weakly positive. A weak sister chromatid exchange was reported in hamsters, and a slight increase in aberrations was reported in mouse oocytes. No induction of chromosome aberrations were reported in hamster bone marrow cells and negative findings were noted in tests with Salmonella typhimurium and a host mediated assay (2229).

RTECS (47) reports the dermal TD_{L_o} value for the mouse as 3600 µg/kg.

Benzo[b]fluoranthene

Benzo[b]fluoranthene is considered an initiator of skin carcinogenesis as well as a complete carcinogen for mouse skin. Local sarcomas have been reported at the site of subcutaneous or intramuscular injections (2229).

Limited data on the mutagenicity of benzo[b]fluoranthene were found. An in vivo study reported a weak induction of sister chromatid exchange, but no significant induction of chromosomal aberrations in hamster marrow cells (2229).

A dermal TD_{L_o} of 72 mg/kg has been reported in mice treated with benzo[b]fluoranthene for 60 weeks (47).

Benzo[k]fluoranthene

No carcinogenic response was noted in a skin painting study with benzo[k]fluoranthene in NMRI mice treated twice a week with up to 9.2 picograms/mouse/application for their lifetime (2229).

A dermal LD_{L_o} value of 2820 mg/kg was reported in mice treated with benzo[k]fluoranthene for 47 weeks (47).

Benzo[e]pyrene

Benzo[e]pyrene (BeP) is inactive as a procarcinogen because no chemically stable BeP epoxide has been isolated. A 9,10-dihydrobenzo(e)pyrene derivative has been observed to be very weakly active with an average of 0.5 papillomas per mouse (12).

The oral TD_{L_o} in the mouse is 360 mg/kg when administered for 43 weeks while the dermal TD_{L_o} is 240 mg/kg when applied for 30 weeks (47).

Benzo[a]pyrene

Benzo[a]pyrene (BaP) has been the most extensively studied of all PAH. BaP has been shown to be both a local and systemic carcinogen by oral, dermal, and intratracheal routes. It is also a transplacental carcinogen and an initiator of skin carcinogenesis in mice. Forestomach tumors have been induced in mice orally given BaP; the significance of this finding for humans is questionable (2229). BaP is an active mutagen, exhibiting positive mutagenic responses in all of the test systems including induction of in vivo sister chromatid exchange in hamster cells and chromosomal aberrations in both spermatogonia and bone marrow cells of hamster in vivo (2229).

Pregnant rats exposed to 1 mg BaP/g diet during gestation showed an increase in resorptions and dead fetuses, but only one malformed fetus in seven litters. Other studies reported no effect on the developing embryo (2229).

Studies on the toxicity of BaP revealed that a single carcinogenic dose produced a prolonged depression of the immune response to sheep red blood cells. Damage to the hematopoietic and lymphoid systems have also been reported in experimental animals (2229).

The oral TD_{L_o} in the rat is listed as 4095 mg/kg when administered for 52 weeks while an 11-week study in mice revealed a dermal TD_{L_o} of 2310 mg/kg. The TC_{L_o} in humans is listed as 70 ng/m^3 (47).

Indeno[1,2,3-c,d]pyrene

Indeno[1,2,3-c,d]pyrene is considered an initiator and complete carcinogen for mouse skin. Local tumors have also been reported at the site of subcutaneous or intramuscular injections (2229).

Benzo[g,h,i]perylene

A pronounced cocarcinogenic effect was observed in a single experiment conducted with 2000 μg benzo[g,h,i]perylene plus 5 μg BaP applied to the skin of ICR/Ha Swiss mice 3 times a week for 52 weeks (2229). Limited mutagenicity data revealed that benzo[g,h,i]perylene produced mixed results in Salmonella typhimurium (2229).

No toxicity data on benzo[g,h,i]perylene were located.

Anthanthrene

The only toxicity information found on anthanthrene was a dermal TD_{Lo} value of 263 mg/kg in the mouse when applied for 30 weeks (47).

Coronene

A dermal TD_{Lo} of 20 mg/kg has been reported in the mouse when coronene was applied for one week (47).

Additives Used in Mineral Base Crankcase Oil

Little information was found on additives in mineral base crankcase oil. A brief discussion of selected compounds is provided. The available acute toxicity data for some additives can be found in Table 69-5.

2,6-Di-tert-butyl-p-cresol

2,6-Di-tert-butyl-p-cresol, more commonly known as butylated hydroxytoluene or BHT, is used as an oxidation inhibitor in synthetic crankcase oil and hydraulic fluids.

BHT inhibits tumorigenesis when multiple doses are administered before a carcinogen, while the incidence of hepatomas induced by 2-acetylaminofluorene and the number of pulmonary adenomas induced by urethane were augmented by post-treatment with BHT (17). The NCI bioassay for carcinogenic effects of BHT in rats and mice was negative (17).

A reported teratogenic effect of anophthalmia in rats has never been duplicated (17). Various morphological and biochemical changes have been observed in experimental animals fed extremely high doses of BHT. Adverse effects included a dose-dependent reduction in growth rate and alveolar epithelial damage in mice which progressed to fibrosis when pure oxygen followed the BHT exposure. Dose-dependent fatalities occurred from massive hemorrhages into the pleural and peritoneal cavities while survivors suffered hemorrhages of the epididymis, testis, nasal

TABLE 69-5
ACUTE TOXICITY OF SELECTED ADDITIVES
OF MINERAL BASE CRANKCASE OIL

Additive	Oral (mg/kg)	Dermal (mg/kg)	Inhalation (ppm)
Oxidation Inhibitors:			
2,6-Di tert-butyl-p-cresol	LD_{50} [rat]: 890	-	-
Phenothiazine	LD_{50} [rat]: 5000	-	-
	LD_{Lo} [child]: 425	-	-
2-Naphthol	LD_{50} [rat]: 2420	-	-
Zinc dithiophosphate	LD_{Lo} [rabbit]: 2130	-	-
Friction Modifiers:			
Tricresyl phosphate	LD_{50} [rat]: 4680	-	-
Tri-ortho-cresyl phosphate	LD_{50} [rat]: 3000	-	-
	LD_{Lo} [human]: 1000	-	-

Source: 47

cavity, and pancreas. Liver changes in rats, mice, and monkeys included enlargement, induction of microsomal enzymes, and an increased synthesis of hepatic smooth endoplasmic reticulum (17).

BHT is mildly irritating to human skin and severely irritating to rabbit eyes (17).

Phenothiazine

At one time, phenothiazine was used in human medicine as an anthelmintic and urinary antiseptic. Currently, it is an important antipsychotic drug used to diminish motor activity and alter psychotic behavior (17, 16).

Side effects of phenothiazine include toxic hepatitis and jaundice, leukocytosis, leukopenia, eosinophilia, and hemolytic anemia. Dermatitis, hypersensitivity, and photosensitivity have also been reported in phenothiazine-treated individuals (17, 16)

Zinc dithiophosphate

Zinc dialkyldithiophosphate (ZDDP) has a low acute systemic toxicity with an oral LD_{50} value of greater than 2 g/kg bw and a dermal LD_{50} value in excess of 3 g/kg (2317).

Undiluted ZDDP is a severe eye irritant; however, the diluted product, used as the additive in hydraulic fluids and synthetic crankcase oils, is regarded as non-irritating. Prolonged contact with undiluted ZDDP is irritating to the skin and produces moderate to severe erythema and edema. Repeated contact results in fissuring and exfoliation (2317).

In subchronic toxicity studies, ZDDP primarily affects the reproductive organs of male rabbits. Dermal application of 5 to 25% ZDDP five days a week for three consecutive weeks resulted in decreased sperm counts and some testicular atrophy (2216). Some studies suggest that the male reproductive effects may be physiological and related to body weight loss and reduced food consumption rather than to the toxic effects of ZDDP (1217).

Tri-ortho-cresyl phosphate (TOCP)

TOCP is known to cause peripheral nervous system damage leading to neuromuscular problems (2216). For a complete discussion of the toxicological effects of TOCP, see Chapter 49 of this Guide.

Phenates

Phenates are widely used as detergent and inhibitor additives. Calcium phenate affects the male reproductive system. Male New Zealand white rabbits dermally exposed to 25 or 100% calcium phenate at 2 mL/kg/day, 5 days per week for 4 weeks developed a high incidence of aspermatogenesis and hypoplasia. Testes weight was reduced 70%. Examination of treated animals after a 30-day recovery period revealed testes weight loss of less than 10% and a greatly reduced incidence of aspermatogenesis and hypoplasia in the 25% calcium phenate group. The incidence of aspermatogenesis was slightly reduced in the 100% calcium phenate group; however, the incidence of hypoplasia remained at 100%. A 28-day exposure to 2.5% calcium phenate showed no aspermatogenesis or hypoplasia. Testes weight in this group was marginally increased. Exposure to 10% calcium phenate for 28 days showed some testes weight loss but no aspermatogenesis or hypoplasia (2317).

Bacteria and Biocides

Water-based lubricants and mineral oil lubricants contaminated with water can support the growth of bacteria, yeasts, and fungi. Growth does not normally occur in products which do not contain water. Exposure to bacteria in coolants may lead to

increased skin and respiratory infections; however, no evidence of such problems exists (2216). Microbial infection of coolants is usually controlled by the use of either biocides which kill the microorganisms or by biostats which restrict microbial growth. Biocides are moderately to highly toxic to humans by ingestion and may be skin and eye irritants (2216).

69.3.4 Levels of Concern

No criteria or standards specific for mineral base crankcase oil were located. EPA (2012) does list a criterion for oil and grease which requires domestic water supplies to be virtually free from oil and grease, particularly with regard to taste and odor.

69.3.5 Hazard Assessment

Carcinogenicity tests for various mineral base crankcase oils are inadequate to establish the carcinogenicity of specific product formulations which can vary with respect to the base oil and composition of additives. IARC (1821) has classified crankcase oils as Group 3 (inadequate data). Tests conducted with various formulations do suggest enhanced tumorigenic activity with used oils (2212, 2221).

Mutagenic activity of unused motor oil was negative in bacteria, mammalian cells in culture and rat bone marrow cells (2217, 2218). Used motor oil was highly mutagenic in the Ames assay (2218), presumably due to the increased concentration of polycyclic aromatic hydrocarbons in used motor oil. There are no data on the reproductive effects of these materials.

Human ingestion of crankcase oil can produce irritation of mucous membranes, nausea, vomiting and diarrhea (2216). Repeated dermal contact can result in dermatitis and oil acne (2216).

The oral LD_{50} value for mineral base crankcase oil has been estimated to be greater than 25 mL/kg for the rat (2214). Mineral base crankcase oil is mildly irritating to the eyes and skin of rabbits (2214). Repeated dermal application produced inflammation, dermal edema, and hyperkeratosis in rabbits (2214). Inhalation exposure to either used or unused mineral base motor oil mist at concentrations up to 100 mg/m^3 for one hour appeared to present no significant adverse effects in guinea pigs (2213).

69.4 SAMPLING AND ANALYSIS CONSIDERATIONS

Determination of the presence of mineral-based crankcase oils in soil and water requires the collection of a representative field sample and laboratory analysis for the specific major components generally attributed to mineral-based crankcase oils; however, the relative concentrations of the constituents, and even the constituents

themselves, will vary with time and distance form the site of initial contamination due to weathering. The major component categories in mineral-based crankcase oils have been identified as the following:

n-alkanes
branched alkanes
cycloalkanes
benzenes and alkylbenzenes
naphthalenes
polynuclear aromatic hydrocarbons (C_{15}-C_{50})

A combination of capillary column gas chromatography (GC) and gas chromatography/mass spectrometry (GC/MS) techniques may be used to identify the principal components in mineral-based crankcase oils. Oil samples, and probably any samples collected in the field which are primarily organic in nature, require the separation (prior to GC or GC/MS analysis) of the aliphatic, monoaromatic and polycyclic aromatic hydrocarbons fractions using liquid solid chromatography; the various column eluates, with or without dilution in carbon disulfide, can then be analyzed by GC or GC/MS techniques. Aqueous samples need to be liquid-liquid extracted with an appropriate solvent (e.g., trichlorotrifluoroethane) prior to analysis; solid samples would be extracted with trichlorotrifluoroethane using soxhlet extraction or sonication methods (1422). An aliquot of the sample extract, with or without concentration, could then be analyzed by GC or GC/MS for the specific components. Sampling and analysis considerations for some specific components in mineral-based crankcase oils, i.e., benzene, toluene, xylenes, ethyl benzene, and naphthalene have been addressed in Volume 1. Infrared spectrophotometry has also been used to detect crankcase oil in water (3560).

Alternatively, the 'oil and grease' content can be measured. This determination would not be the measurement of an absolute quantity of a specific component, but rather the quantitative determination of groups of components with similar physical characteristics (i.e., common solubility in trichlorofluoroethane). The "oil and grease" content is defined as any material recovered from extraction with trichlorotrifluoroethane and measured gravimetrically; extraction methods are those described above for aqueous and soil samples.

A detection limit for mineral-based crankcase oil cannot be determined; the detection limit for specific components is expected to be in the range of $\mu g/L$ for aqueous samples and $\mu g/g$ for non-aqueous samples.

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Note: The nonsequential numbers of the references reflect the order of references as they appear in the master bibliography.

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COMPLEX MIXTURES

This chapter deals with a complex mixture and/or class of compounds. The format used for this less well-defined group of compounds was modified as necessary but follows the outline of earlier chapters as closely as possible. It should be noted, however, that the composition of these materials can vary according to the route of synthesis, the formulating ingredients added, the interactions of the active ingredients, or the storage conditions. These factors can influence the nature of the material that is ultimately utilized and probably are reflected in many of the experimental findings reported in the following chapters.

The typical components and approximate composition of the mixtures are provided if that information was available. Physical/chemical properties often were not available or varied depending on formulation. Many of these mixtures are blended to modify their physical properties according to the intended use. Furthermore, the formulations vary with season as well as with geographic locations of product use. In some cases, therefore, the range for the class of compounds was given.

In addition to the data for the mixture itself, the chapter that follows also contains sections on the principal components and major additives of the mixture, their fate in the environment and a brief overview of their toxicity.

CHEMICAL COMPOSITION	Organic esters Aromatic hydrocarbons Aliphatic hydrocarbons Polyglycols Phosphate esters
REACTIVITY	Synthetic crankcase oils primarily consist of blends of selected hydrocarbon substances. Hydrocarbons are typically incompatible with strong oxidizers, and may be considered miscellaneous combustible or flammable materials for compatibility classification purposes. Such substances typically evolve heat, fire, and toxic or flammable gases in reactions with oxidizing mineral acids, organic peroxides or hydroperoxides, or strong oxidizing agents. Reaction with explosive materials may result in an explosion (505, 507, 511).
PHYSICO-CHEMICAL DATA	• Physical State: Liquid, oily (at 20°C) (1822) • Color: Depends on use • Odor: Depends on use • Odor Threshold: no data • Density: 0.88 g/mL (at 25°C) (1822) • Freeze/Melt Point: No data (1822) • Boiling Point: Not pertinent • Flash Point: 53.0 to 332.0°C (varies with particular blend) (1822) • Flammable Limits: No data • Autoignition Temp.: 315.0 to 593.0°C (1822) • Vapor Pressure: 3.0 to 4.7 mm Hg (at 204°C) (1822) • Satd. Conc. in Air: Not pertinent • Solubility in Water: No data • Viscosity: 2.0 to 528.0 cp (at 38°C) (1822) • Surface Tension: 23.0 dyne/cm (at 25°C) (1822) • Log (Octanol-Water Partition Coeff.): No data • Soil Adsorp. Coeff.: No data • Henry's Law Const.: No data • Bioconc. Factor: No data

PERSISTENCE IN THE SOIL-WATER SYSTEM	Hydrocarbon-based oils are expected to be highly immobile and persistent in the soil/ground-water system. Major loss mechanisms are volatilization and aerobic biodegradation. Other oils (esters and glycols) may be moderately mobile and much less persistent due to hydrolysis and biodegradation.
PATHWAYS OF EXPOSURE	The primary pathway of concern from the soil/ground-water system is the contamination of groundwater drinking water supplies with synthetic crankcase oils, especially those based on organic and phosphate esters and polyglycols. Runoff to surface water drinking water supplies may be an important exposure pathway for hydrocarbon-based oils. Inhalation exposures and ingestion with food are not expected to be significant.
HEALTH HAZARD DATA	Signs and Symptoms of Short-term Human Exposure: (2236) Headache, dizziness, nausea, vomiting, incoordination, profuse perspiration, lethargy and unequal pupil size were observed in an individual who inhaled vaporized synthetic lubricating oil. Long-Term Effects: No data Pregnancy/Neonate Data: No data Genotoxicity Data: Single report notes findings in bacterium Carcinogenicity Classification: IARC - No data NTP - No data EPA - No data
HANDLING PRECAUTIONS	Protective gloves • Goggles or face shield if possibility of eye contact exists.

ENVIRONMENTAL AND OCCUPATIONAL STANDARDS AND CRITERIA

AIR EXPOSURE LIMITS:

Standards
- OSHA TWA (8-hr TWA): Petroleum distillates (naphtha)-400 ppm
- AFOSH PEL (8-hr TWA): Petroleum distillates (naphtha)-400 ppm; STEL (15-min)-500 ppm

Criteria
- NIOSH IDLH (30-min): Petroleum distillates (naphtha)-10,000 ppm
- NIOSH REL (10-hr TWA): Petroleum distillates (naphths)-350 mg/m^3
- NIOSH CL (15-min): Petroleum distillates (naphtha)-1800 mg/m^3
- ACGIH TLV® (8-hr TWA): Petroleum distillates (naphtha)-None established
- ACGIH STEL (15-min): None established

WATER EXPOSURE LIMITS:

Drinking Water Standards
None established

EPA Health Advisories and Cancer Risk Levels
None established

WHO Drinking Water Guideline
No information available.

EPA Ambient Water Quality Criteria

- Human Health (355)
  - No criterion established; synthetic crankcase oil is not a priority pollutant.
- Aquatic Life (355)
  - No criterion established; synthetic crankcase oil is not a priority pollutant.

Oil and Grease (2012)
For domestic water supply: Virtually free from oil and grease, particularly from the tastes and odors that emanate from petroleum products.

ENVIRONMENTAL AND OCCUPATIONAL STANDARDS AND CRITERIA

For aquatic life:

- To protect several important freshwater and marine species, each having a demonstrated high susceptibility to oils and petrochemicals, the lowest continuous flow 96-hour LC_{50} should be reduced a hundred-fold.
- levels of oils or petrochemicals in the sediment which cause deleterious effects to the biota should not be allowed;
- surface waters shall be virtually free from floating non-petroleum oils of vegetable and animal origin as well as petroleum-derived oil.

REFERENCE DOSES:
No reference dose available.

REGULATORY STATUS (as of 01-MAR-89)

Promulgated Regulations

- Federal Programs

  Clean Water Act (CWA)
  Oil and grease are designated conventional pollutants under the CWA (351). Effluent limitations for oil and grease exist in almost all the point source categories under the general pretreatment regulations for new and existing sources, and effluent standards and guidelines. Limitations vary depending on the type of industry (3763).

  Toxic Substances Control Act (TSCA)
  Manufacturers and processors of the C_9 aromatic hydrocarbon fraction must test it for neurotoxicity, mutagenicity developmental toxicity, reproductive effects and oncogenicity. The C_9 fraction is obtained from the reforming of crude petroleum. It consists of ethyltoluenes and trimethylbenzenes (1988). Testing will be conducted by the American Petroleum Institute. Interim reports must be submitted at 6-month intervals (1987).

Marine Protection Research and Sanctuaries Act (MPRSA)
Ocean 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 petroleum distillates (naphtha) shall not exceed an 8-hour time-weighted average (TWA) of 400 ppm (3539).

Hazardous Materials Transportation Act (HMTA)
The Department of Transportation has designated petroleum distillates as hazardous materials which are subject to requirements for packaging, labeling and transportation (305).

- State Water Programs

ALL STATES
All states have adopted EPA Ambient Water Quality Criteria and NPDWRs (see Water Exposures Limits section) as their promulgated state regulations, either by narrative reference or by relisting the specific numeric criteria. These states have promulgated additional or more stringent criteria:

ALASKA
Alaska has a water quality criterion for the protection of aquatic life of 15 µg/L for total hydrocarbons and 10 µg/L for total aromatic hydrocarbons in fresh and marine surface waters (3016).

ARKANSAS
Arkansas requires that oil and grease shall not exceed 10 mg/L average or 15 mg/L maximum when discharging to surface waters (3587).

FLORIDA
Florida requires that oil and grease not exceed 10 mg/L in Class V waters (navigation, industrial use) and 5 mg/L for all other surface waters (3220).

MASSACHUSETTS
Massachusetts requires that the maximum discharge concentration of oil and grease of petroleum origin not exceed 15 mg/L in surface waters (3432).

NEBRASKA
Nebraska requires that petroleum oils not exceed 10 mg/L in surface waters (3719).

NEW YORK
New York has set a maximum contaminant level of 50 µg/L for kerosene in drinking water (3501).

SOUTH DAKOTA
South Dakota has a water quality standard of 10 mg/L for all petroleum products in surface waters (3672).

VIRGINIA
Virginia has a water quality standard of 1 mg/L for petroleum hydrocarbons in ground-water (3135).

WYOMING
Wyoming has a water quality standard of 10 mg/L for surface waters and Class II and III ground-waters. In addition, Class I domestic ground-water is required to be virtually free of oil and grease (3853, 3852).

Proposed Regulations

- Federal Programs
  No federal regulations are pending.

- State Water Programs
  No state regulations are pending.

MOST STATES
Most states are in the process of revising their water programs and proposing changes to their regulations which will follow EPA's changes when they become final. Contact with the state officer is advised. Changes are projected for 1989-90 (3683).

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 Fishing Water Quality (536)
Petroleum products must not be present in salmonid and cyprinid waters in such quantities that they: (1) form a visible film on the surface of the water or form coatings on the beds of water-courses and lakes, (2) impart a detectable "hydrocarbon" taste to fish and, (3) produce harmful effects in fish.

Directive on the Quality Required of Shellfish Waters (537)
The mandatory specifications for petroleum hydrocarbons specify that they may not be present in shellfish water in such quantities as to produce a visible film on the surface of the water and/or a deposit on the shellfish which has harmful effects on 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 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)
Petroleum and coal tar distillates with flash points below 21°C are classified as flammable substances and are subject to packaging and labeling regulations. Because of the variable composition of other petroleum and coal tar distillates (excluding those used as motor fuels) they are considered preparations and their labeling shall be done in accordance with the procedures outlined in the Directive Relating to the Classification Packaging and Labeling of Dangerous Preparations (solvents).

Directive on Disposal of Waste Oils (1986)
Establishments collecting and/or disposing of waste oils must carry out safe collection and disposal of waste oils so that there will be no avoidable risk of water, air or soil pollution. A permit from the competent authority must be registered and adequately supervised for collecting, disposing or regenerating waste oils. PCBs and PCTs must not be present in amounts greater than 50 ppm in regenerated waste oil.

EEC Directives - Proposed
Proposal for a Council Directive on the Dumping of Waste at Sea (1793)
EEC has proposed that the dumping of crude oil, petroleum hydrocarbons, lubricants and hydraulic fluids at sea be prohibited.

70.1 MAJOR USES AND COMPOSITION

70.1.1 Major Uses

Synthetic crankcase oils are used to a much lesser degree than mineral base crankcase oils, primarily because they are more expensive, and mineral oils can be formulated to meet the same requirements in most applications. Synthetics are used in equipment that creates severe conditions for which a mineral oil cannot offer adequate service. Synthetic base oils offer a dramatically increased range of operating temperatures that makes them almost a necessity in any equipment that is exposed to or produces heat extremes. Such uses include jet and commercial aircraft engines, aircraft hydraulics and instruments, uses in nuclear reaction facilities, and in synthetic base automotive engine oils. Some synthetic base oils also provide excellent fire resistance which makes them attractive choices in applications where there is a possibility of contacting open flames or extremely hot surfaces (21).

70.1.2 Composition

Synthetic oils are composed of greater than 50% synthetic fluids. They can be formulated with additives to improve performance just as mineral base oils are (see Chapter 69, Table 69-3). Occasionally a mineral oil itself serves as the additive (up to 50%) in synthetic blends (1821). Tables 70-1 and 70-2 provide a list of possible synthetic base crankcase oils and compositional information.

In general, the same additives used in mineral base oils (see Chapter 69, Table 69-3) can be used with synthetic oils and will have similar effects. However, there are undoubtedly additives with which solvent characteristics of base oil and solubility will be important determining factors limiting their use. A listing of some of the additives used in synthetic crankcase oil is provided in Table 70-3.

70.2 ENVIRONMENTAL FATE AND EXPOSURE PATHWAYS

70.2.1 Transport in Soil/Ground-water Systems

Most synthetic crankcase oils (except those like the water soluble polyoxyalkylene glycols and phosphate esters) are expected to be highly immobile in the soil/ground-water environment. Bulk quantities of the oil (from a spill or improper disposal) might be carried slowly through the unsaturated zone to the top of the water table, but the high viscosity and low water solubility would mitigate this effect. Most likely, at least with moderate to small spills, the oil would remain entrained in

TABLE 70-1
COMPOSITIONAL AND STRUCTURAL INFORMATION AND CHARACTERISTICS OF COMMON SYNTHETIC CRANKCASE OILS

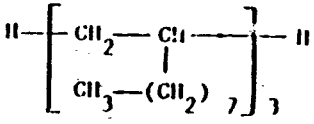
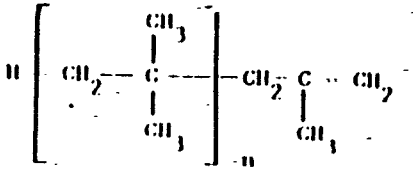
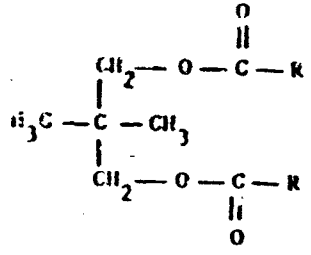
Chemical Name/Class	Structure/Composition	Properties/Characteristics
1. Synthetic Hydrocarbons:[a,b]		
Olefin oligomers (poly-alpha-olefins)	 (oligomer of 1-decene)	Resembles paraffinic mineral oils. Uses include synthetic hydrocarbon fluid in SAE 5W-20 motor oil, and military aircraft fluids.
Alkylated aromatics	Typically reaction products of C_{10}-C_{14} alkyl groups and benzene/toluene/xylenes/ethylbenzenes, (i.e., dialkylated benzenes).[a]	Used in synthetic automotive engine oils.
Polybutenes (polyisobutylenes)	 (polyisobutylene) (typically C_{20} - C_{100})	Decomposition temperatures around 288°C. The lower MW polymers (C_{20}-C_{100}) are used as lubricants while the higher MW materials are used as additive viscosity index improvers. Used in many high temperature applications.

TABLE 70-1 (Cont.)

Chemical Name/Class	Structure/Composition	Properties/Characteristics
Synthetic Hydrocarbons:[a,b] - continued		
Cycloaliphatics		Used commonly as hydraulic fluids.
2. Organic Esters:[c]	Includes: monoesters (monobasic acid esters or polyolesters) diesters triester polyesters $RO-\overset{O}{\overset{\|}{C}}-(CH_2)_n-\overset{O}{\overset{\|}{C}}-OR$ (a diester is most common, based on a dibasic acid) (n is commonly 8-10)	MW typically 200-600; can be approximately 1000 for complex esters. Vapor pressure approximately 0.3 - 4.0 mm Hg at 205°C. Uses include automotive engine oils (occasionally blended 50/50 with mineral oils), and jet and aircraft engines. Organic esters are the most common synthetic lubricants used.

TABLE 70-1 (Cont.)

Chemical Name/Class	Structure/Composition	Properties/Characteristics
Organic Esters[c] - continued	Diesters are derived from C_6 - C_{10} acids (i.e., adipic, azelaic, sebacic) and C_6 - C_9 alcohols (i.e., 2-ethylhexyl, 3,5,5-trimethylhexyl, isodecyl, and tridecyl alcohols);[b]	Used widely by the military in aircraft applications.



(a neopentyl polyol ester based on neopentyl glycol)

TABLE 70-1 (Cont.)

Chemical Name/Class	Structure/Composition	Properties/Characteristics
1. Polyoxyalkylene Glycols[c] (polyglycols)	$RO-\left[CH_2-\underset{R'}{CH}-O\right]_n-R''$	Can be formulated to be water soluble or water insoluble; the more polyethylene in character, the better the water solubility. MW typically 400-3000.
	Examples of some possible R groups:	Densities approximately 0.95 - 1.2 g/mL
	R R' R''	
	1. H H H	
	2. H CH_3 H	Vapor pressures of some polyglycols are reported to be less than 0.01 mm Hg at 20°C. Most common uses include hydraulic brake fluids[b] and aircraft engine oils.
	3. C_4H_9 CH H	
	4. C_4H_9 CH_3 C_2H_5	
	1. polyethylene glycol 2. polypropylene glycol 3. a monoether 4. a diether	

TABLE 70-1 (Cont.)

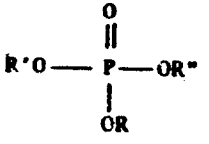
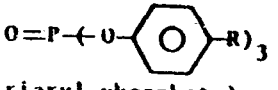
Chemical Name/Class	Structure/Composition	Properties/Characteristics
4. Phosphate esters[c]		Excellent fire resistance. MW typically 200-600. Densities approximately 0.9-1.5 g/mL. Boiling points for trialkylphosphates approximately 190-300°C. Used in extreme temperature applications.
	R can be H or organic groups. At least 1 R must be an organic group. 3 classes: trialkylphosphates, triaryl phosphates, alkyl-aryl phosphates. i.e.:	Used widely in military aircraft as hydraulic fluids and engine lubricants.[6]
	 (a triaryl phosphate)	
	Oxygen(s) may be replaced by sulfur to give thiophosphates.	

TABLE 70-1 (Cont.)

Chemical Name/Class	Structure/Composition	Properties/Characteristics
5. Others		
Silicones Silicate esters Polyphenylethers Chlorofluorocarbons		These are not generally used as crankcase oil, although they may be occasionally used as additives. They have very specialized uses. More commonly used as hydraulic fluids.

[a] Reference 1821
[b] Reference 21
[c] Reference 1822

TABLE 70-2
SOME SYNTHETIC OIL BASES[a]

Organic Esters[b] (monobasic and dibasic acid esters, triesters, and polyesters)
isooctyl adipate
isodecyl adipate
2-ethylhexyl sebacate
pentaerythritol
2-ethyl-2-hydroxymethyl-1,3-propanediol
trimethylolpropane
dioctyl sebacate
di(3-methylbutyl)adipate
di(2-ethylbutyl)azelate
trimethylolethane
dibasic acid ester/silicate ester blend (~15% diester)
dibasic acid ester/polyglycol blend
dibasic acid ester/synthetic hydrocarbon blend (~33% diester)

Polyoxyalkylene Glycols (polyglycols)[c]
polypropylene glycol
polyethylene glycol
polybutylene glycol
polyglycol/water blend
polyglycol/mineral oil/silicate ester blend
polyglycol/dibasic acid ester blend

Phosphate Esters[d]
tert-butyl-triphenylphosphate
triphenylphosphate
phenyl-m-tolyl-p-chlorophenylphosphate
tricresylphosphate
tri(2-ethylhexyl)phosphate
diorganodithiophosphate
triethylphosphate
phenyl m-trifluoromethylphenyl-1-naphthylphosphate
trixylylphosphate
trialkyl thiophosphate esters ($OP(OC_2H_4SC_8H_{17})_3$)/mineral oil blend
phosphate ester/polyglycol blends (tributoxyethyl/tributoxyethoxyethyl phosphates)
phosphate esters/dimethyl silicone polymer blend

TABLE 70-2 - (Cont.)

Silicate Esters.
tetraethyl silicate
tetra(2-ethylhexyl) silicate
tetra(2-ethylbutyl) silicate
hexa(2-ethylbutoxy)) disiloxane
di-(2-ethylhexyl)silicate
cresyltriisopropyl silicate
silicate ester/dibasic acid ester blends
silicate ester blends with chlorofluorocarbons, mineral oils, silicones, polyglycols; e.g., bis(2-ethylhexyl)propylene glycol and butylmethyl
propylene glycol/tetra alkyl orthosilicates or hexalkoxy disiloxanes

Silicones[e]
methyl, dimethyl polysiloxane
phenylmethyl polysiloxane
chlorophenyl polysiloxane
trifluoropropylmethyl polysiloxane

Synthetic Hydrocarbons[f]
alpha olefins (olefin oligomers)
2,3-dicyclohexyl-2,3-dimethyl butane
dialkylated benzene
polyisobutylene
synthetic hydrocarbon/dibasic acid ester blend (~33% diester)

Others[g]
polychlorotrifluoroethylene
perfluoroheptane
trifluorotrichloroethane
bis(p-phenoxyphenyl)ether

a) This table contains specific base chemicals or chemical classes used in synthethic lubricants. These chemicals may or may not be typical but all were reported in the literature as possible fluid bases.
b) References 21, 1826, 1834
c) References 21, 1822
d) References 1822, 1829
e) References 1822, 1826
f) References 21, 1834
g) Reference 1822

TABLE 70-3
SOME CHEMICAL ADDITIVES USED IN SYNTHETIC CRANKCASE OIL[a]

Chemical/Class Name	Typical Range Used
Oxidation Inhibitors	0-2.0% wt.[b]
2,6-di-tert-butyl-p-cresol	
phenothiazine	
2,5-di-n-butylaminobenzoquinone	
2,5-di-piperidylbenzoquinone	
2,5-di-tert-butyl-p-benzoquinone	
pyridine	
quinoline	
hydroquinone	
R_2Sb or R_2SbS R=butyl or phenyl groups	
phenyl-alpha-naphthylamine	
triethanolamine	
2-naphthol	
zinc dithiophosphate	
Antiwear and Extreme Pressure Additives	0-6% wt.[c]
tricresylphosphate	
zinc diorganodithiophosphate	
zinc diisodecyldithiophosphate	
zinc di-n-butyldithiophosphate	
n-tosyltetrapropenyl succinimide	
hexadecyldiethyldithiocarbamate	
benzyl disulfide	
tungsten sulfide	
Rust and Corrosion Inhibitors	0-2.0% wt.[d]
barium dinonylnaphthylene	
n-tosyltetrapropenyl succinimide	
zinc dithiophosphate	
dicyclohexamine	
diisobutyl ketone	
Viscosity Index (VI) Improvers	0-20% wt.[e]
polyisobutylenes	
polymethacrylates	
polyalkylstyrenes	
ethylene-propylene copolymers	
styrene-butadiene copolymers	
hydroxy cellulose ether	
silicone polymers (methyl and dimethyl polysiloxanes)	

TABLE 70-3 (Cont.)

Chemical/Class Name	Typical Range Used
Detergents/Dispersants	0-20% wt.[f]
polyisobutenyl succinic anhydrides	
borated alkenyl succinimides	
oxazoline	
phosphonates and thiophosphates	
alkyl phenols and alkyl phenol sulfides	
alkyl methacrylate-dimethylaminoethyl methacrylate copolymers	
alkyl methacrylate-n-vinylpyrrolidone copolymers	
vinyl acetate-dialkyl fumarate-maleic anhydride copolymers	

a) This table contains specific chemical additives used in crankcase oil. These chemicals may or may not be the typical additives but all were reported in the literature as possible chemical additives
b) References 21, 1823, 1831, 1832, 1834, 1835, 1836
c) References 21, 1821, 1825, 1826, 1827, 1833
d) References 21, 1821, 1822, 1823, 1825
e) References 21, 1824, 1825, 1832, 1835, 1836
f) References 21, 1822, 1827

the pores of the soil near the surface. This would be more likely for low porosity and high organic carbon content soils, and less likely for sandy, porous soils.

Transport and subsequent fate of dissolved constituents of these soils will vary depending on the physicochemical (and biological) properties of the constituents. Some constituents will dissolve more quickly in the percolating ground waters, be sorbed less strongly on the soils (thus being transported more rapidly), and may be more, or less, susceptible to degradation by chemical or biological action. The relative concentrations of the constituents of the oil will vary with time and distance from the site of initial contamination. This effect is called "weathering". (This term is also used to describe changes to oil following spills into surface waters where film spreading and breakup, and differential volatilization, dissolution, and degradation all are involved.)

Almost all of the pure hydrocarbon constituents in these oils (e.g., Class 1 materials listed in Table 70-1) would fall into a highly immobile class for consideration of movement of dissolved constituents through the soil/ground-water system. While no data are available, it is estimated that all such constituents would have solubilities in pure water of less than 1 mg/L. For example, ethylnaphthalene, $C_{12}H_{12}$ has a solubility of 0.8 mg/L (1839), although the solubility of most constituents

might be orders of magnitude less than this [e.g., eicosane, $C_{20}H_{42}$, is estimated to have a solubility of 10^{-7} $\mu g/L$ (1840)]. The corresponding soil sorption constant, (K_{oc}) estimated from such solubilities would all be over 10,000 and most would be over 1,000,000 indicating very strong sorption to soils containing organic matter. Constituents with low molecular weight, high aromatic character, and/or nitrogen and sulfur heteroatoms will tend to be the most mobile.

By contrast, other synthetic oils (e.g., from Classes 2-4 listed in Table 70-1) could have appreciable water solubilities, moderate to low soil sorption constants, and a moderate mobility in the soil/ ground-water system. Few data were found that might show the range of mobilities to be expected. Some data on the phosphate esters are provided in Chapter 49 of this Guide and in references 1490 and 1496.

No equilibrium partitioning model calculations (as have been given for most other chemicals in this Guide) are given for these oils. This is due to the wide variety of materials (chemical classes) covered by the category of synthetic lubricating oils, to the lack of any real data on their physicochemical properties of environmental importance, and to the wide range of partitioning behaviors that could be shown from the highly immobile (Class 1, Table 70-1) to the mobile (Classes 2-4, Table 70-1) oils. To provide model outputs in this case would involve excessive speculation (on the needed physicochemical properties) and allow easy misuse of model results. It should be clear, however, that all such calculations for pure hydrocarbon materials would show that essentially all of the oil was sorbed to the soil and that negligible amounts were present in the soil-air or soil-water compartments.

The aqueous phase mobility of oil constituents could be significantly enhanced if the oil was in the form of a very fine emulsion, or if the percolating ground-water contained a significant amount of dissolved organic carbon (e.g., humic and fulvic acids, fatty acids, or chlorinated solvents) from other natural sources or other discharged materials. The dissolved organic carbon, much of it possibly in the form of colloidal particles, could absorb the oil constituents and assist in their transport through the soil/ground-water system.

Volatilization of constituents from the crankcase oil would be slow because of the low vapor pressures involved (presumably <1 mm Hg at 25°C for individual constituents, with many below 1E-06 mm Hg). However, given that spilled oils may remain near the soil surface, making volatilization easier, that the material is resistant to leaching and degradation, and that the Henry's law constant may be moderately high, at least for the hydrocarbons, it is thus presumed that volatilization will be a major loss mechanism for spilled crankcase oil over time periods of weeks to years. Because the lower molecular weight (more liquid) constituents would tend to volatilize first, the remaining material would generally have lower volatilities and lower water solubilities.

70.2.2 Transformation Processes in Soil/Ground-water Systems

An assessment of environmental persistence for synthetic crankcase oils is difficult, given the variety of materials involved and the lack of pertinent data. Thus, most of the statements given below are both general and speculative in nature. Only the phosphate esters have been the subject of several environmental studies (see Chapter 49 of this Guide and references 1490 and 1496).

Synthetic base crankcase oils are expected to be moderately persistent in the soil/ground-water environment because of their resistance to hydrolysis, oxidation, and biodegradation. The general resistance to hydrolysis (for saturated and unsaturated hydrocarbons) is described by Harris (529). However, the organic esters, phosphate esters, and polyglycols would be somewhat more susceptible to hydrolysis, especially under basic conditions.

The assessment of the resistance to biodegradation is more complex. Most of the hydrocarbon molecules (Class 1, Table 70-1) are so large that passage through cell walls (where metabolism or degradation is relatively easy) is hindered and much of the biodegradation must be carried out by extracellular enzymes secreted by the microbes. Such difficulties aside, many studies on petroleum hydrocarbon materials (oils as well as light distillates) have shown moderate to high eventual susceptibility to biodegradation for the bulk of the material (1842). A period of microbial adaptation may be required. The organic esters, phosphate esters and polyglycols would be expected to be more readily biodegraded.

Different constituents of the oil will differ significantly in their biodegradability for reasons related to molecular size, structure, and toxicity. For example, highly branched alkanes are much less biodegradable than linear alkanes, and polycyclic aromatic hydrocarbons with three or more rings are very resistant to biodegradation (515). For all hydrocarbons, aerobic biodegradation would be expected to be much more important than anaerobic biodegradation (1841). Because of this, and because of the decrease in microbiological activity with increasing soil depth, oil constituents reaching deep anaerobic soils could persist for very long time periods.

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

The above discussion of fate pathways suggests that the pure hydrocarbon constituents of synthetic crankcase oils (e.g., the substances listed in Class 1 in Table 70-1) will have low volatility in pure form, but may be relatively more volatile in water because of their low solubility. They will tend to be strongly or very strongly sorbed to soil. Their bioconcentration factors are expected to be low because, as described above, they are not readily taken up by biota. Organic esters, phosphate esters, and polyglycols (Classes 2-4 in Table 70-1) used as synthetic crankcase oils would be expected to be weakly sorbed to soil, have low volatility and low potential for bioaccumulation. These fate characteristics suggest differences for the two types of synthetic oils.

Volatilization of synthetic crankcase oils that have spilled or are improperly disposed of is not expected to result in significant exposure of workers or residents in the area regardless of the type of fluid. Although the pure hydrocarbon fraction of the fluid will volatilize to some extent, it does so slowly, giving little opportunity for loss from spills to occur before they pass into the soil. The ester and glycol based synthetic oils are not expected to result in significant inhalation exposures because of their low volatility.

Ground-water contamination may be a significant exposure pathway for the water soluble synthetic oils (organic esters, phosphate esters and polyglycols) because they are highly soluble, and would be readily transported in the ground-water. Exposure may occur through the direct use of ground-waters as drinking water supplies or indirectly through the discharge to surface waters. Surface waters may also be contaminated by the discharge of soil particles to which synthetic oils (especially the pure hydrocarbon oils) have been sorbed. Where surface waters have been contaminated, ingestion exposures may occur from their use as drinking water supplies, and dermal exposures may result from their recreational use. The uptake of synthetic crankcase oils by aquatic organisms or domestic animals is not expected to result in significant ingestion exposure because of their low potential for bioconcentration.

70.2.4 Other Sources of Human Exposure

Data on the ambient concentration of synthetic crankcase oils in air and ambient water, as well as food and drinking water, are not available in the literature. Several exposure pathways other than through ground-water contamination may be identified, although the extent of these exposures has not been quantified. Leaking gaskets and seals may result in oil being deposited on roadways or runways, where it is washed into surface waters or (in the case of the soluble fraction) transported through the soil into the ground-water.

Personnel involved in the maintenance of aircraft and other machinery are expected to receive the greatest exposure to synthetic crankcase oils. While inhalation exposures are not expected to be large, direct dermal exposures are likely if protective gloves and clothing are not worn during maintenance operations.

70.3 HUMAN HEALTH CONSIDERATIONS

The majority of data available in the literature describe health effects associated with mineral base crankcase oil exposure. Synthetic lubricants generally do not present any significant additional hazards (2216) and are considered similar in toxicity to mineral base lubricants (see Chapter 69).

70.3.1 Animal Studies

70.3.1.1 Carcinogenicity

No specific data were found.

70.3.1.2 Mutagenicity

Synthetic crankcase oil [Mobil®-1] was mutagenic when tested in strain TA98 of Salmonella typhimurium (2222). No other studies were found.

70.3.1.3 Teratogenicity, Embryotoxicity and Reproductive Effects

No specific data on the teratogenic or reproductive effects of synthetic crankcase oil were found.

70.3.1.4 Other Toxicologic Effects

70.3.1.4.1 Short-term Toxicity

Sprague-Dawley rats and chickens were exposed (head-only) to 47.2-48.5 g (total weight over time) synthetic lubricating oil [Exxon® 2380 turbine engine oil] for 7 hours. No adverse effects were noted up to 40 days post-exposure and no abnormalities were revealed during necropsy (2232).

70.3.1.4.2 Chronic Toxicity

No specific studies dealing with the long-term toxicity of synthetic oils were located in the literature.

70.3.2 Human and Epidemiologic Studies

70.3.2.1 Short-term Toxicologic Effects

An acute case of intoxication following inhalation of vaporized synthetic lubricating oil was reported by Montgomery et al. (2236). A navigator in a military C-130A aircraft gradually developed headache, dizziness, nausea, vomiting, incoordination, and profuse perspiration. Approximately 80 minutes after the onset of symptoms, he was lethargic, had depressed deep tendon reflexes and had unequal pupil size. Clinical status returned to normal within 24 hours. Slight unequal pupil size was the only effect reported during long-term follow-up.

No other studies were found on the acute toxic effects of synthetic crankcase oil.

70.3.2.2 Chronic Toxicologic Effects

No studies were found in the literature dealing with the effects of long-term exposure to synthetic crankcase oil in humans.

70.3.3 Toxicology of Synthetic Crankcase Oil Components

The composition of synthetic crankcase oil varies greatly and usually depends upon the specific conditions of use. Since the exact composition of the oils is constantly changing and difficult to define, the toxicology of component classes are briefly discussed below. See Table 70-4 for the acute toxicity data of specific compounds.

Organic esters

Organic esters generally found in lubricating oils and hydraulic fluids include adipates, sebacates and dibasic acid esters. Dibasic acid esters are generally non-toxic via ingestion or skin absorption. The only effect noted from dermal contact may be a drying of the skin (1822). Di(2-hexoxyethyl)succinate is a sebacate which is relatively non-toxic to animals. In humans it is expected to have a low toxicity. Large doses may produce CNS depression, nausea, vomiting and transient liver and kidney injury (12). Not all neopentyl esters have been tested for toxicity, but studies with trimethylopropane ester showed a toxic level comparable to that of mineral oil (1822).

Polyglycols

Ingestion of polyglycols is unlikely, but small amounts produce no toxic effect. No cases of skin irritation or skin sensitization have been reported; mild irritation to the eyelid has been reported but effects were only transitory. Usually no inhalation hazard exists but at high temperatures, where vapors are likely to form, adequate ventilation should be provided (1822).

Ucon® fluids are a mixture of polyalkylene glycols and diesters. 50-HB-260, 50-HB-5100, 25-H-2005, and 75-H-1400 are low in single-dose oral toxicity with LD_{50} values for the male rat ranging from 5.95 to >64 mL/kg bw; oral LD_{50} values for the rabbit range from 1.77 to 35.4 mL/kg bw. The lower molecular weight compounds are more toxic. A dose-related granular degeneration of the cytoplasm of the smooth muscle in the intestinal wall was noted in dogs fed 25-H-2005 for two years. The significance of this finding is unknown. No other adverse effects were shown. The only adverse effect observed in rats fed up to 0.5 g/kg/day of 25-H-2005 for two years was a slight growth depression in females (12).

No carcinogenic effects were observed in rats orally administered Ucon® fluids in the diet or in mice dermally exposed to these compounds (13).

TABLE 70-4
ACUTE TOXICITY OF SELECTED COMPONENTS OF SYNTHETIC CRANKCASE OIL

Compound	Oral (mg/kg)	Dermal (mg/kg)	Inhalation (ppm)
2-ethylhexylsebacate	LD_{50} [rat]: 1280	-	-
pentaerythritol	LD_{50} [mouse]: 25,500	-	-
polypropylene glycol	LD_{50} [rat]: 419	-	-
polyethylene glycol	LD_{50} [rat]: 33,750	-	-
triphenylphosphate	LD_{Lo} [rat]: 3000	-	-
tricresylphosphate	LD_{Lo} [rat]: 4680	-	-
tri-ortho-cresylphosphate	LD_{50} [rat]: 3000 LD_{Lo} [human]: 1000	- -	- -
tri(2-ethylhexyl) phosphate	LD_{50} [rat]: 37,000	LD_{Lo} [rabbit]: 20,000	
triethylphosphate	LD_{1} [rat]: 1600	-	-
tetraethyl silicate	LD_{Lo} [rat]: 1000	-	LC_{Lo} [rat]: 1000 · 4 hr
tetra(2-ethylbutyl) silicate	LD_{50} [rat]: 20,000	-	-
trifluorotri-chloroethane	LD_{50} [rat]: 43,000	-	TC_{Lo} [rat]: 87,000 · 6 hr

Source: 47

Polyethylene glycol applied to the open wounds of rabbits resulted in metabolic acidosis and changes in blood chemistry consistent with nephrotoxicity (2225). Effects were attributed to the metabolism of polyethylene glycol to toxic compounds (such as hydroxyglycolic and diglycolic acid homologues) which are efficient chelators of calcium. The mechanism of damage was similar to that associated with ethylene glycol-mediated renal failure. See discussion of the toxic effects of ethylene glycol in Chapter 43 of the Installation Restoration Program Toxicology Guide.

No adverse changes in clinical, biochemical or hematological parameters developed in rats fed 2 mL/kg/day polyethylene glycol 400 (duration not specified) (2224). Examination of monkeys administered the same treatment revealed a deposition of oxalate crystals in the cortical tubules of the kidney (2224).

Phosphate esters

Organic phosphates possess excellent thermal stability and chemical solvency properties which makes them valuable synthetic lubricant and hydraulic fluid components (1822).

Organic phosphates are readily absorbed through the skin and can be inhaled. Ingestion is rare. Signs of toxicity following excessive exposure reflect stimulation of the autonomic and central nervous systems, resulting from inhibition of acetylcholinesterase and the consequent accumulation of acetylcholine. The initial effect is on smooth muscle, cardiac muscle, and exocrine glands. Early signs of toxicity include intestinal cramps, tightness in the chest, blurred vision, headaches, diarrhea, decreased blood pressure, and salivation. The second stage of intoxication results from stimulation of the peripheral motor system and of all autonomic ganglia. Toxic signs include stimulation and/or paralysis of the somatic, autonomic, and central nervous systems.

Chronic administration of low doses of organic phosphates produce a measurable decrease in cholinesterase activity. Toxic effects are nonexistent to slight and may result in diarrhea and tremors. Delayed paralysis in man and animals due to a degeneration of the axons in the spinal cord and peripheral nerves has also been associated with organic phosphates, particularly tri-o-cresyl phosphate (TOCP) (13). See Chapter 49 of the Installation Restoration Program Toxicology Guide for a complete discussion on TOCP.

Silicate esters

The toxicity of the orthosilicates and disiloxanes vary widely and range from almost completely innocuous to rather poisonous (1822). Injection of ethyl silicate compounds into the skin of rabbits produced transient erythema, edema, and slight necrosis at the injection site. When instilled into the rabbit eye, it produced transient irritation. Inhalation of 400 ppm by rats for 7 hours/day for 30 days caused mortality and lung, liver, and kidney damage. Inhalation of 68 ppm produced no adverse effects (12).

Silicones

Generally, silicones are not irritating to the skin and cause no corneal damage when splashed into the eye. Slight temporary irritation to the eye has been reported in some individuals with effects disappearing within 24 hours. Toxic materials may also be emitted during decomposition of fluorinated silicone polymers at temperatures above 570°F (1822).

In chronic feeding experiments, rats treated with hexamethyl disiloxane (HMS) showed widespread systemic irritation. Rabbits injected intradermally with HMS

developed edema and necrosis at the injection sites. Siloxanes injected into the rabbit eye resulted in transient irritation with complete clearing after 48 hours. When inhaled at 4400 ppm for 19 to 26 days, HMS caused slight depression in the rat and guinea pig, with a very slight increase in rat liver and kidney weights (12, 13).

Silicone resins had no influence on health when fed for 94 days to rats, and did not result in irritation to rabbit skin or eyes. No toxic effects were reported when injected into rats intraperitoneally (12).

Rats fed a dietary level of 0.3% Antifoam A@ for two years showed no significant toxic effect. Long-term feeding studies in mice reported similar results; however, a single subcutaneous injection of 0.2 mL antifoam showed a greater incidence of cysts at the site of injection (13).

Polydimethyl siloxane caused no evident changes when tested for reproductive and teratologic effects in rats and rabbits, or testicular effects in rabbits. Dimethylphenylmethylpolysiloxane, tris(trimethylsiloxy)phenylsilane, and trifluoropropylmethylpolysiloxane were also negative in male reproductive studies (13).

Other

Other components of synthetic lubricating oil and hydraulic fluids include polyphenyl ethers. Studies with phenyl ether showed no toxicological effects following inhalation of vapors or contact with skin. Bis(p-phenoxyphenyl)ether, bis(m-phenoxyphenyl)ether, and m-bis(m-phenoxyphenoxy)benzene caused no irritation in skin tests with rabbits and only mild transient irritation in acute eye tests. These compounds were practically non-toxic in acute oral and intraperitoneal tests with rats. Phenolic degradation products formed during use of these materials under severe conditions are expected to increase toxicity (1822).

Synthetic Crankcase Oil Additives

Information available on additives used in synthetic crankcase oil is limited. Selected compounds are briefly discussed below. Refer to Table 70-5 for the acute toxicity data of specific additives.

2,6-Ditert-butyl-p-cresol

2,6-Di-tert-butyl-p-cresol, more commonly known as butylated hydroxytoluene or BHT, is used as an oxidation inhibitor in synthetic crankcase oil and hydraulic fluids.

BHT inhibits tumorigenesis when multiple doses are administered before a carcinogen while the incidence of hepatomas induced by 2-acetylaminofluorene and the number of pulmonary adenomas induced by urethane were augmented by

TABLE 70-5
ACUTE TOXICITY OF SELECTED ADDITIVES OF SYNTHETIC CRANKCASE OIL

Compound	Oral (mg/kg)	Dermal (mg/kg)	Inhalation (ppm)
2,6-di-tert-butyl-p-cresol	LD_{50} [rat]: 890	-	-
phenothiazine	LD_{50} [rat]: 5000	-	-
	LD_{Lo} [child]: 425	-	-
pyridine	LD_{50} [rat]: 891	LD_{Lo} [rabbit]: 1121	LC_{50} [rat]: 4000 · 4 hr
quinoline	LD_{50} [rat]: 331	LD_{50} [rabbit]: 540	-
hydroquinone	LD_{50} [rat]: 320	-	-
	LD_{Lo} [human]: 29	-	-
phenyl-alpha-naphthylamine	LD_{50} [rat]: 1625	-	-
triethanolamine	LD_{50} [rat]: 8680	-	-
2-naphthol	LD_{50} [rat]: 2420	-	-
zinc dithiophosphate	LD_{Lo} [rabbit]: 2130	-	-
tricresyl phosphate	LD_{Lo} [rat]: 4680	-	-
tri-ortho-cresyl phosphate	LD_{50} [rat]:3000	-	-
	LD_{Lo} [human]: 1000	-	-
diisobutylketone	LD_{50} [rat]: 5750	LD_{50} [rabbit]: 20,000	LC_{Lo} [rat]: 2000 · 4 hr LC_{Lo} [human]: 50

Source: 47

post-treatment with BHT (17). The NCI bioassay for carcinogenic effects of BHT in rats and mice was negative (17).

A reported teratogenic effect of anophthalmia in rats has never been duplicated (17).

Various morphological and biochemical changes have been observed in experimental animals fed extremely high doses of BHT. Adverse effects included a dose-dependent reduction in growth rate and alveolar epithelial damage in mice which progressed to fibrosis when pure oxygen followed the BHT exposure. Dose-dependent fatalities occurred from massive hemorrhages into the pleural and peritoneal cavities while survivors suffered hemorrhages of the epididymis, testis, nasal cavity, and pancreas. Liver changes in rats, mice and monkeys included enlargement, induction of microsomal enzymes and an increased synthesis of hepatic smooth endoplasmic reticulum (17).

BHT is mildly irritating to human skin and severely irritating to rabbit eyes (17).

Phenothiazine

At one time, phenothiazine was used in human medicine as an anthelmintic and urinary antiseptic. Currently, it is an important antipsychotic drug used to diminish motor activity and alter psychotic behavior (17, 16).

Side effects of phenothiazine include toxic hepatitis and jaundice, leukocytosis, leukopenia, eosinophilia, and hemolytic anemia. Dermatitis, hypersensitivity, and photosensitivity have also been reported in phenothiazine-treated individuals (17,16).

Tri-ortho-cresyl phosphate (TOCP)

TOCP is known to cause peripheral nervous system damage leading to neuromuscular problems (2216). For a complete discussion of the toxicological effects of TOCP, see Chapter 49 of this Guide.

Zinc dithiophosphate

Zinc dialkyldithiophosphate (ZDDP) has a low acute systemic toxicity with an oral LD_{50} value of greater than 2 g/kg bw and a dermal LD_{50} value in excess of 3 g/kg bw (2317).

Undiluted ZDDP is a severe eye irritant; however, the diluted product, used as the additive in hydraulic fluids and synthetic crankcase oils, is regarded as non-irritating. Prolonged contact with undiluted ZDDP is irritating to the skin and produces moderate to severe erythema and edema. Repeated contact results in fissuring and exfoliation (2317).

In subchronic toxicity studies, ZDDP primarily affects the reproductive organs of male rabbits. Dermal application of 5 to 25% ZDDP five days a week for three consecutive weeks resulted in decreased sperm counts and some testicular atrophy (2216). Some studies suggest that the male reproductive effects may be physiological and related to body weight loss and reduced food consumption rather than to the toxic effects of ZDDP (1217).

Pyridine

Pyridine is absorbed from the respiratory and gastrointestinal tracts. Skin absorption is not significant although contact may result in dermatitis. Short-term toxic effects in animals are linked to central nervous depression. Prolonged daily administration of pyridine to rats produced hepatorenal damage (17).

Acute toxicity resulting from the ingestion of several ounces of pyridine produced severe vomiting, diarrhea, hyperpyrexia, and delirium. Death occurred 43 hours post-ingestion. Autopsy revealed pulmonary edema and membranous tracheobronchitis which was thought to result from aspiration of pyridine into the lung. A small oral dose of 2 to 3 mL pyridine in man produced mild anorexia, nausea, fatigue, and mental depression (17).

Hydroquinone

Hydroquinone is irritating to the skin but not corrosive. Skin lesions in man are generally described as depigmentation. Fatal human doses range from 5 to 12 grams. Systemic effects include tremors and convulsions plus occasional, severe hemolytic anemia. No effect was reported following human ingestion of 300 to 500 mg hydroquinone daily for three to five months (17).

70.3.4 Levels of Concern

No criteria or standards specific for synthetic crankcase oil were located. EPA (2012) does list a criterion for oil and grease which requires domestic water supplies to be virtually free from oil and grease, particularly with regard to taste and odor.

70.3.5 Hazard Assessment

Toxicological data located for synthetic crankcase oil are sparse. No data are currently available regarding the carcinogenicity, reproductive, or long-term exposure effects of these materials. A single report indicates a positive response in an Ames mutagenicity assay (2222). Another study noted that rats and chickens exposed to synthetic lubricating oil for 7 hours exhibited no adverse effects (2232).

Intoxication of vaporized synthetic lubricating oil by an aircraft navigator produced headache, dizziness, nausea, vomiting, incoordination, profuse sweating,

lethargy, depressed deep tendon reflexes, and unequal pupil size. Clinical status returned to normal within 24 hours (2236). No other human data were located.

70.4 SAMPLING AND ANALYSIS CONSIDERATIONS

Determination of the presence of synthetic crankcase oils in soil and water requires the collection of a representative field sample and laboratory analysis for the specific major components generally attributed to oils of this type; however, the relative concentrations of the constituents, and even the constituents themselves, will vary with time and distance form the site of initial contamination due to weathering. The major component categories in synthetic crankcase have been identified as the following:

Aliphatic and aromatic hydrocarbons
Organic esters
Polyglycols
Phosphate esters

A combination of capillary column gas chromatography (GC) and gas chromatography/mass spectrometry (GC/MS) techniques may be used to identify the principal components in synthetic crankcase oils. Oil samples, and any samples collected in the field which are primarily organic in nature, may require separation (prior to GC or GC/MS analysis using liquid solid column chromatography; the various column eluates, with or without dilution in carbon disulfide, can then be analyzed by GC or GC/MS techniques. Aqueous samples need to be liquid-liquid extracted with an appropriate solvent (e.g., trichlorotrifluoroethane) prior to analysis; solid samples would be extracted with trichlorotrifluoroethane using soxhlet or sonication methods. An aliquot of the sample extract, with or without concentration, could then be analyzed by GC or GC/MS for the specific components of interest. Sampling and analysis considerations for some specific components possibly present in synthetic crankcase oils, i.e., benzene, toluene, xylenes, ethyl benzene, naphthalene, TOCP and ethylene glycol, have been audressed in previous chapters. Infrared spectrophotometry has also been used to detect crankcase oil in water (3560).

Alternatively, the "oil and grease" content can be measured. This determination would not be the measurement of an absolute quantity of a specific component but rather the quantitative determination of groups of components with similar physical characteristics (i.e., common solubility in trichlorofluoroethane). The oil and grease content is defined as any material recovered from extraction with trichlorotrifluoroethane and measured gravi- metrically; the extraction methods are those described above for aqueous and soil samples.

A detection limit for synthetic crankcase oil cannot be determined; the detection limit for specific components is expected to be in the range of $\mu g/L$ for aqueous samples and $\mu g/g$ for non-aqueous samples.

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APPENDIX 1

USEFUL HANDBOOKS, DATABOOKS, RESPONSE GUIDES AND AIR FORCE DOCUMENTS

A listing of useful handbooks, databooks and response guides, all relating to the release of hazardous or toxic chemicals to the environment, the properties and hazards of the chemicals, initial responses to spills of such chemicals, or subsequent remedial action follow. The contents of each publication is briefly described. The following listing is not intended to be inclusive of all publications of this kind. However, it is felt that the acquisition and central location of these reports (at key Air Force offices) would provide a valuable resource.

- A Method for Determining the Compatibility of Hazardous Wastes

  Authors: H. K. Hatayama et al. (April 1980)

  Available from: U.S. Environmental Protection Agency
  Municipal Environmental Research Laboratory
  Cincinnati, OH
  (EPA Report No. EPA-600/2-80-076)
  (NTIS Report No. PB80-221005)

  Contents: Provides method and chart for defining compatibility of various families of hazardous materials and wastes.

- Accident Management Orientation Guide

  Authors: D. K. Shaver et al. (October 1983)

  Available from: Air Force Rocket Propulsion Laboratory
  Air Force Systems Command
  Edwards Air Force Base
  California 93523
  (Report No. AFRPL-TR-82-075)

  Contents: This document identifies guidelines for mitigating hazards associated with an in-service railroad derailment or a railroad yard accident involving hazardous materials of interest to the Air Force.

- Carbon Adsorption Isotherms for Toxic Organics

  Authors: R. A. Dobbs and J. M. Cohen (April 198( )

  Available from: U.S. Environmental Protection Agency
  Office of Research and Development
  Cincinnati, OH
  (EPA Report No. EPA-600/8-80-023)

  Contents: Provides detailed data on the effectiveness of carbon for removal of organic substances from water.

- Chemical Hazards of the Workplace

  Authors: N. H. Proctor and J. P. Hughes (1978)

  Available from: J. B. Lippincott Company
  Philadelphia, PA

  Contents: Provides data on the toxicological effects of chemicals and suggests medical treatment protocols in more detail than given elsewhere.

- CHRIS Hazardous Chemical Data

  Author: U.S. Coast Guard (1985)

  Available from: Superintendent of Documents
  U.S. Government Printing Office
  Washington, D.C. 20402
  (Stock No. 050-012-00147-2)

  Contents: Provides a wide variety of data on more than 1000 hazardous materials when ordered with various addendums. A separate volume (Stock No. 050-012-00158-8) provides graphs of temperature dependent physical properties.

- Dangerous Properties of Industrial Materials, 7th edition

  Author: N. I. Sax, ed. (1989)

  Available from: Van Nostrand Reinhold
  New York, NY

  Contents: A well-known handbook that provides a brief summary of the toxicology and properties of numerous hazardous substances.

- Dangerous Properties of Industrial Materials Report

  Author: N. I. Sax, ed. (bimonthly publication)

  Available from: Van Nostrand Reinhold Company
  New York, NY

  Contents: Each bimonthly report provides detailed data on the hazards and environmental effects of several chemicals. Much of the data is from the EPA's Oil and Hazardous Materials-Technical Assistance Data System (OHM-TADS) and similar sources.

- Emergency Action Guides

  Authors: P. C. Conlon and A. M. Mason, eds. (1984).

  Available from: Bureau of Explosives
  Association of American Railroads
  1920 L Street N.W.
  Washington, D.C. 20036

  Contents: Provides detailed data and spill response information on each of the 134 materials that comprise over 98 percent of the hazardous commodities transported by rail in the United States.

- Emergency Handling of Hazardous Materials in Surface Transportation

  Author: P. J. Student, ed. (1981)

  Available from: Bureau of Explosives
  Association of American Railroads
  1920 L Street N.W.
  Washington, D.C. 20036

  Contents: Provides brief spill response recommendations for each hazardous material regulated by the U.S. Department of Transportation.

- Emergency Response Guidebook

  Author: Materials Transportation Bureau (1987)

  Available from: U.S. Department of Transportation
  Materials Transportation Bureau
  Attention: DMT-11
  Washington, DC 20590
  (Publication DOT P5800.?)

  Contents: A guide for initial actions to be taken by emergency service personnel during hazardous material incidents.

- Fire Protection Guide on Hazardous Materials

  Author: National Fire Protection Association (1986)

  Available from: National Fire Protection Association
  Batterymarch Park
  Quincy, MA 02269

  Contents: Flash Point Index of Trade Name Liquids Fire Hazard Properties of Flammable Liquids, Gases, and Volatile Solids (NFPA 325M) Hazardous Chemicals Data (NFPA 49) Manual of Hazardous Chemical Reactions (NFPA491M)

- Groundwater Contamination Response Guide, Volume I: Methodology, Volume II: Desk Reference

  Authors: J. H. Guswa and W. J. Lyman (1983)

  Available from: National Technical Information Service
  Springfield, VA
  (as U.S. Air Force Report ESL-TR-82-39)
  or
  Noyes Publications
  Park Ridge, NJ
  (under the title "Groundwater Contamination and Emergency Response Guide" (1984))*

  Contents: Provides an overview of ground-water hydrology and a current technology review of equipment, methods, and techniques used to investigate incidents of ground water contamination by chemicals.

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*Noyes Publications also contain a reproduction of the report by A. S. Donnigian, Jr. et al.: Rapid Assessment of Potential Ground-Water Contamination Under Emergency Response Conditions, a 1983 report to the U.S. Environmental Protection Agency.

- Ground-Water Hydrology Workbook

  Authors: E.W. Artiglia and G.R. New (1984)

  Available from: USAF Occupational and Environmental Health Laboratory
  Brooks AFB, TX 78235
  (Report No. 84-168EQ111DGB)

  Contents: Summarizes introductory articles in ground-water hydrology of importance to base bioenvironmental engineers involved with the IRP program.

- Guidelines Establishing Test Procedures For The Analysis of Pollutants Under the Clean Water Act, Appendix A

  Author: U.S. Environmental Protection Agency (1984)

  Available from: Federal Register
  Volume 49(209):43234
  October 26, 1984

  Contents: Methods for analysis of environmental samples.

- Guidelines for the Selection of Chemical Protective Clothing

  Authors: A.D. Schwope et al. (1987)

  Available from: U.S. Environmental Protection Agency
  Washington, D.C.

  Contents: Denotes compatibility of rubber and plastic clothing materials with various chemicals; provides guidelines for clothing selection and use.

- Guidelines for the Use of Chemicals in Removing Hazardous Substances Discharges

  Authors: C. K. Akers, R. J. Pilie and J. G. Michalovic (1981)

  Available from: U.S. Environmental Protection Agency
  Office of Research and Development
  Cincinnati, OH
  (EPA Report No. EPA-600/2-81-205)

  Contents: Report provides guidelines on the use of various chemical and biological agents to mitigate discharges of hazardous substances.

- Handbook for Evaluating Remedial Action Technology Plans

  Authors: J. Ehrenfeld and J. Bass (1983)

  Available from: U.S. Environmental Protection Agency
  Office of Research and Development
  Cincinnati, OH
  (EPA Report No. EPA-600/1-83-076)

  Contents: Provides information on over 50 remedial action technologies for cleanup of chemically-contaminated sites.

- Handbook of Chemical Property Estimation Methods
  (subtitle: Environmental Behavior of Organic Compounds)

  Authors: W. J. Lyman, W. F. Rechl, D. H. Rosenblatt, eds. (1982)

  Available from: McGraw-Hill Book Co.
  New York, NY

  Contents: Provides estimation methods for (and discussion of) 26 environmentally-important properties of organic chemicals.

- Handbook of Environmental Data on Organic Chemicals, 2nd edition

  Author: K. Verschueren (1983)

  Available from: Van Nostrand Reinhold
  New York, NY

  Contents: Provides detailed property and environmental data on numerous organic substances.

- Handbook of Toxic and Hazardous Chemicals

  Author: M. Sittig (1985)

  Available from: Noyes Publications
  Park Ridge, NJ

  Contents: Discusses a wide range of topics for numerous chemicals, with special emphasis on toxicology and protective measures.

- Hazardous Chemicals Data Book, 2nd edition

  Author: G. Weiss, ed. (1986)

  Available from: Noyes Data Corporation
  Park Ridge, NJ

  Contents: Reproduction of data (physicochemical properties, hazards, toxicity, etc.) related to chemical spill response from (1) CHRIS Hazardous Chemical Data (1978) and (2) Material Safety Data Sheets prepared by Oak Ridge National Laboratory.

- Herbicide Handbook, 5th edition

  Author: Weed Science Society of America (1983)

  Available from: Weed Science Society of America
  309 West Clark Street
  Champaign, IL 61820

  Contents: Provides basic information on physiocochemical properties, uses, environmental fate, physiological and biochemical behavior, and toxicological properties for most herbicides in use. (Previous editions may cover out-of-use herbicides.)

- Manual for the Control of Hazardous Material Spills - Vol. 1: Spill Assessment and Water Treatment Techniques

  Authors: K. R. Huibregtse et al. (November 1977)

  Available from: U.S. Environmental Protection Agency
  Office of Research and Development
  Cincinnati, OH
  (EPA Report No. EPA-600/2-77-227)

  Contents: Provides both general and specific information on responding to spills of hazardous materials, particularly those into water.

- Methods to Treat, Control and Monitor Spilled Hazardous Materials

  Authors: R. J. Pilie et al. (1975)

  Available from: U.S. Environmental Protection Agency
  Industrial Waste Treatment Research Laboratory
  Edison, NJ
  (EPA Report No. EPA-670/2-75-042)

  Contents: Special studies of selected chemical spill response measures plus matrix of possible spill response measures for 250 hazardous liquids.

- NIOSH Manual of Analytical Methods, 3rd edition

  Author: Peter M. Eller, ed. (1984)

  Available from: Superintendent of Documents
  U.S. Government Printing Office
  Washington, D.C. 20402

  Contents: Contains sampling and analytical methods for use in industrial hygiene environmental monitoring.

- NIOSH/OSHA Occupational Health Guidelines for Chemical Hazards

  Authors: F. W. Mackison et al., eds. (January 1981)

  Available from: Superintendent of Documents
  U.S. Government Printing Office
  Washington, D.C. 20402
  (DHHS (NIOSH) Publication No. 81-123)

  Contents: Provides information on toxicology, chemical properties, first aid, and personal protective clothing and equipment for many OSHA-regulated commodities.

- Patty's Industrial Hygiene and Toxicology - Vol. 2A,B,C: Toxicology

  Authors: G.D. Clayton and F.E. Clayton, eds. (1981-1982)

  Available from: John Wiley & Sons
  New York, NY

  Contents: Provides extensive discussion of the properties and toxicology of numerous chemicals.

- Perry's Chemical Engineers Handbook

  Authors: R. H. Perry and D. Green, eds. (1984)

  Available from: McGraw-Hill Book Company
  New York, NY

  Contents: Contains extensive data on the properties of chemicals and on their compatibility with various materials of construction (plus numerous other topics).

- Pesticide Manual, 7th edition

  Author: C. R. Worthing, ed. (1983)

  Available from: British Crop Protection Council Publications
  Worcestershire WR13 15LP
  ENGLAND

  Contents: Provides a brief review of analysis, uses and toxicity of chemical and microbial agents used as active components of pest-control products.

- Post Accident Procedures for Chemicals and Propellants

  - Interim Report for the Period 8/11/80 to 3/31/81 (September 1982) (Report No. AFRPL-TR-82-031)

  - Interim Report for the Period 4/81 to 1/82 (September 1982) (Report No. AFRPL-TR-82-032)

  - Guidelines Manual (January 1983) (Report No. AFRPL-TR-82-077)

  Authors: D. K. Shaver et al.

  Available from: Air Force Rocket Propulsion Laboratory
  Air Force Systems Command
  Edwards Air Force Base
  California 93523

  Contents: This is a series of manuals providing information and data required to respond to spills of chemicals and propellants of special interest to the Air Force.

- Quality Criteria for Water

  Author: U.S. Environmental Protection Agency (July 1976)

  Available from: Superintendent of Documents
  U.S. Government Printing Office
  Washington, D.C. 20402
  (Stock No. 055-001-01049-4)

  Contents: This is EPA's well-known guide to water quality criteria commonly referred to as the "redbook."

- Registry of Toxic Effects of Chemical Substances

  Authors: R. L. Tatken and R. J. Lewis, Sr., eds. (June 1983)

  Available from: Superintendent of Documents
  U.S. Government Printing Office
  Washington, D.C. 20402
  (DHHS [NIOSH] Publication 83-107)

  Contents: Summarizes results of primarily short-term toxicological experiments for thousands of chemicals.

- Standard Methods for the Examination of Water and Wastewater, 15th edition

  Authors: Arnold Greenberg et al., eds. (1985)

  Available from:: American Public Health Association
  1015 18th Street
  Washington, D.C.

  Contents: Methods for analysis of environmental samples.

- Supplement to Development Document, Hazardous Substances Regulations, FWPCA as Amended 1972

  Author: U.S. Environmental Protection Agency (November 1975)

  Available from: U.S. Environmental Protection Agency
  Office of Water Planning and Standards
  Washington, D.C. 20460

  Contents: Discusses the environmental effects of numerous water pollutants.

- Test Methods for Evaluating Solid Waste-Physical Chemical Methods, 3rd edition

  Author: U.S. Environmental Protection Agency (1987)

  Available from: Superintendent of Documents
  U.S. Government Printing Office
  Washington, D.C. 20460
  (Report No. SW-846)

  Contents: Methods for analysis of environmental samples.

- TLVs-Threshold Limit Values for Chemical Substances and Physical Agents in the Work Environment and Biological Exposure Indices with Intended Changes for 1987-1988

  Author: American Conference of Governmental Industrial Hygienists (1987)

  Available from: American Conference of Governmental Industrial Hygienists
  6500 Glenway Ave., Bldg. D-5
  Cincinnati, OH 45211

  Contents: This booklet (or the latest version of it) presents recommended exposure limits for airborne concentrations of toxic materials in the working environment.

- Toxicology of the Eye

  Author: W. M. Grant (1986)

  Available from: Charles C. Thomas - Publisher
  Springfield, IL

  Contents: An excellent source of information on the effects of numerous chemicals and other substances on the eyes.

- USAF OEHL Recommended Sampling Procedures

  Author: USAF Occupational and Environmental Health Laboratory (January 1982)

  Available from: USAF Occupational and Environmental Health Laboratory
  Brooks AFB, TX 78235
  (Limited Distribution)

  Contents: Outlines standardized sampling procedures with appropriate collection and preservation techniques for submission of samples to USAF OEHL for analysis.

- Water-Related Environmental Fate of 129 Priority Pollutants (2 volumes)

  Authors: M. A. Callahan et al. (December 1979)

  Available from: U.S. Environmental Protection Agency
  Washington, D.C.
  (EPA Report No. EPA-440/4-79-029a and -029b)
  (NTIS No. PB80-204373 and PB80-204381)

  Contents: Individual chapters address the fate of priority pollutants in the environment.

PERTINENT AIR FORCE PUBLICATIONS FOR THE USAF INSTALLATION RESTORATION PROGRAM

PUBLICATION	COMMENT
AFR 161-8	Establishes USAF permissible exposure limits for chemical substances.
AFR 161-17	Establishes USAF OEHL consultant services in Environmental Engineering, Industrial Hygiene, Occupational Health, Radiation Protection, and Analytical Chemistry.
AFR 161-44	Establishes USAF drinking water standards for common contaminants. For the most part, these are the same as the National Primary and Secondary Drinking Water Standards.
AFR 19-1	Establishes the USAF Environmental Protection Program.
AFR 19-7	Establishes responsibilities for environmental monitoring for Air Force installations. This regulation defines the roles of the Civil Engineer, the Bioenvironmental Engineer, and others with respect to environmental pollution monitoring.
DEQPPM 80-8	DoD implementation of RCRA.
DEQPPM 80-9	DoD guidance on the proper handling, storage, and disposal of PCB and PCB items.
DEQPPM 81-5	DoD guidance on the Installation Restoration Program to identify and evaluate past DoD hazardous material disposal sites on DoD installations and control migration from such sites.
EO 12088	Requires federal compliance with applicable federal, state, and local pollution control standards (procedural and substantiative) the same as any other industry or private person.
GWMR	Quarterly publication on ground-water monitoring remedial actions. Presents technical articles on contaminant transport, analytical methods, sampling methodology, and data interpretation.
IRPMC	Establishes the management concept for the IRP Phase II program.
LEEV LTR	Policy letters formulated by USAF HQ/LEEV.

NCP	Establishes procedures for response to potential for confirmed contamination of our nation.

APPENDIX 2

U.S. AIR FORCE POINTS OF CONTACT FOR THE INSTALLATION RESTORATION PROGRAM

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  Maj. Patrick T. Fink
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  Office of the Assistant Secretary of the Air Force
  Deputy for Environment and Safety

  Responsible for overall Air Force IRP guidance.

IRP GROUP

- Maj. Scott L. Smith, Branch Chief
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  Responsible for IRP engineering policy formulation.

- Maj. Roy K. Soloman
  AV 297-0275
  Responsible for Environmental Compliance Assessment and Management Program (ECAMP), Environmental Protection Committee, and IRP implementation.

- Col. Raymond A. Malinovsky
  Chief, Environmental Quality Division
  Director of Engineering and Services
  HQ USAF/LEEV
  Bolling Air Force Base
  Washington, DC 20332-5000

- Capt. Gerald L. Hromowyk
  AV 297-0275
  Responsible for spill policy and management information systems.

- Capt. Charles M. Groover
  AV 297-0275
  Responsible for underground storage tanks and training.

- Mr. Earl E. Kneeling
  AV 297-4174
  Responsible for Defense Environmental Restoration Program policy.

- Mr. Jeffery J. Short
  AV 297-0275
  Responsible for Third Party Sites.

- Col. Thayer J. Lewis, Chief
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- Lt. Col. Edward W. Artiglia
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  Responsible for IPR medical service policy formulation.

- Col. Frank P. Gallagher
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  USAF Engineering and Services Center
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  Environics Division

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- Mr. Emile Y. Baladi
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  USAF Occupational and Environmental Health Laboratory Technical Services Division

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- Dr. Jeffrey W. Fisher
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  Harry G. Armstrong Aerospace Medical Research Laboratory Toxic Hazards Division

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  AV 240-2063
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  USAF Occupational and Environmental Health Laboratory Consultant Services Division
  Environmental Health Branch

  Responsible for Toxicology Consultant Service.

- Major Air Command Bioenvironmental Engineers
  See latest edition of the "Worldwide Listing of Bioenvironmental Engineering and Environmental Health Personnel."

  Responsible for implementing IRP policy and management decisions and coordinating with state/local regulatory agencies.

APPENDIX 3

MATH, CONVERSIONS AND EQUIVALENTS

- Calculation of Air W/V Conversion Factors

One liter of air at 25 °C (298.16 °K) contains:

$$\frac{(1 \text{ atm})(1 \text{ liter})}{(.0821 \text{ liter atm/mole})(298.16 \text{ °K})} = 0.040874 \text{ moles of gas.}$$

Hence, one liter of air contains:

MW x 10^4 x 0.040874 grams of a contaminant at 1 ppm.

This is the same as saying 1 m^3 of air contains:

MW x 0.040874 mg of a contaminant at 1 ppm.

For example, chloroform has a MW of 119.39. Thus,

1 ppm = 119.39 x 0.040874 ≈ 4.88 mg/m^3 at 25°C.

- Conversion for Solutes in Water

1 mg/L ≈ 1 ppm (by weight).

- Conversion of Percent in Food, Water or Air to Parts Per Million

X% = X parts per 100 parts

$$\frac{X}{100} (10^6) = \text{ppm.}$$

- Conversion of Parts Per Million in Food or Water to mg/kg bw/day

Since both food intake and body weight vary with age (and some times, with treatment), there is no single factor that precisely converts parts per million (ppm) in food or water to mg/kg body weight/day. However, by assuming 100% absorption and adopting a set of standard values for each species for daily food, water and air intake

and average body weight, one can convert a ppm dosage level, within reasonable limits, to mg/kg bw/day for the sake of comparisons.

The following standard body weights and intake values were used to convert dietary or respiratory intakes to estimated daily dose rate:

Species	Body Weight (kg)	Food Consumption (g/day)	Approximate Water Intake (mL/day)	Minute Volume (m^3/min)
Human	70	700	2000	7.4×10^{-3}
Mouse	0.025	3	4.5	2.3×10^{-5}
Rat	0.3	15	20	1.0×10^{-4}
Monkey	5	250	500	8.6×10^{-4}
Rabbit	2	60	330	1.1×10^{-3}
Dog	10	250	500	5.2×10^{-3}
Guinea pig	0.5	30	85	1.6×10^{-4}

For example, at a dietary concentration of 1 ppm of Chemical X, an average adult mouse would consume 3 g of food per day or 0.12 mg of Chemical X/kg bw/day. This value was calculated as follows:

Intake (mg/kg bw/day) = food consumption (g/day) x dietary concentration (ppm) x $1 g/10^6$ g diet x 1000 mg/g x 1/bw (kg).

- Calculation of Respiratory Uptake

Uptake (mg) = Concentration (mg/m^3) x minute volume (m^3/min) x retention factor (assume 1.0 unless value is known) x time (minutes).

- Temperature Conversions

The formulas given below were used to convert temperatures from one scale to another.

To convert temperatures given in Celsius to Fahrenheit:

$$°F = 9/5\ (°C) + 32$$

To convert temperatures given in Fahrenheit to Celsius:

$$°C = 5/9\ (°F - 32)$$

APPENDIX 4

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INDEX 1

CUMULATIVE 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.

Acetone
See Chapter 40.

Acetylene tetrachloride
See 1,1,2,2-Tetrachloroethane, Chapter 11.

Acetylene trichloride
See Trichloroethylene, Chapter 16.

Agrotect
See 2,4-D, Chapter 60.

Aroclor®
See Chapter 52.

Automotive gasoline
See Chapter 65.

BBP
See Butyl benzyl phthalate, Chapter 46.

Benzene
See Chapter 18.

Benzene chloride
See Chlorobenzene, Chapter 24.

1,2-Benzenedicarboxylic acid, bis (2-ethylhexyl) ester
See Di(2-ethylhexyl)phthalate, Chapter 31.

1,2-Benzenedicarboxylic acid, butyl phenylmethyl ester
See Butyl benzyl phthalate, Chapter 46.

1,2-Benzenedicarboxylic acid, dibutyl ester
See Di-n-butyl phthalate, Chapter 30.

o-Benzenedicarboxylic acid, diethyl ester
See Diethyl phthalate, Chapter 29.

1,2-Benzenedicarboxylic acid, diethyl ester
See Diethyl phthalate, Chapter 29.

Benzenol
See Phenol, Chapter 36.

Benzin
See Automotive gasoline, Chapter 65.

Benzol
See Benzene, Chapter 18.

Benzole
See Benzene, Chapter 18.

Benzyl butyl phthalate
See Butyl benzyl phthalate, Chapter 46.

Bis(2-chloroethyl)ether
See Chapter 33.

Bis(2-ethylhexyl)phthalate
See Di(2-ethylhexyl)phthalate, Chapter 31.

Bromochloromethane
See Chapter 44.

Bunker C oil
See Fuel oils, Chapter 66.

Butanedioic acid,[(dimethoxyphosphinothioyl)-thio]-, diethyl ester
See Malathion, Chapter 50.

2-Butanone
See Methyl ethyl ketone, Chapter 41.

Butyl benzyl phthalate
See Chapter 46.

Butyl phthalate
See Di-n-butyl phthalate, Chapter 30.

Carbolic acid
See Phenol, Chapter 36.

Carbon chloride
See Carbon tetrachloride, Chapter 6.

Carbon dichloride
See Tetrachlorocthylene, Chapter 17.

Carbon oil
See Benzene, Chapter 18.

Carbon tetrachloride
See Chapter 6.

Carbophos
See Malathion, Chapter 50.

CBM
See Bromochloromethane, Chapter 44.

CDBM
See dibromochloromethane, Chapter 3.

Chlordane
See Chapter 48.

Chlorinated hydrochloric ether
See 1,1-Dichloroethane, Chapter 8.

Chlorobenzene
See Chapter 24.

Chlorobenzol
See Chlorobenzene, Chapter 24.

Chlorobromomethane
See Bromochloromethane, Chapter 44.

Chlorodibromomethane
See Dibromochloromethane, Chapter 3.

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.

Chloroethane
See Chapter 7.

Chloroethene
See Vinyl chloride, Chapter 13.

Chloroethylene
See Vinyl chloride, Chapter 13.

2-Chloroethyl ether
See Bis(2-chloroethyl)ether, Chapter 33.

Chloroform
See Chapter 4

2-Chloro-1-hydroxybenzene
See o-Chlorophenol, Chapter 37.

Chloromethyl bromide
See Bromochloromethane, Chapter 44.

Chlorophen
See Pentachlorophenol, Chapter 39.

o-Chlorophenol
See Chapter 37.

2-Chlorophenol
See o-Chlorophenol, Chapter 37.

p-Chlorophenyl chloride
See 1,4-Dichlorobenzene, Chapter 27.

Chlorothene
See 1,1,1-Trichloroethane, Chapter 10.

Chromate of soda
See Sodium chromate, Chapter 53.

Chromic acid, disodium salt
See Sodium chromate, Chapter 53.

Clophen A60
See Aroclor® 1260, Chapter 52.

Coal naphtha
See Benzene, Chapter 18.

Coal oil
See Fuel oils, Chapter 66.

CP-27
See Chlorobenzene, Chapter 24.

Cyanide
See Chapter 56.

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.

2,4-D
See Chapter 60.

DBP
See Di-n-butyl phthalate, Chapter 30.

DCB
See 1,2-Dichlorobenzene, Chapter 25.

1,1-DCE
See 1,1-Dichloroethylene, Chapter 14.

DCEE
See Bis(2-chloroethyl)ether, Chapter 33.

DCM
See Methylene chloride, Chapter 1.

DDD
See Chapter 58.

DDE
See Chapter 59.

DDT
See Chapter 57.

DEHP
See Di(2-ethylhexyl)phthalate, Chapter 31.

DEP
See Diethyl phthalate, Chapter 29.

Diamide
See Hydrazine, Chapter 55.

Diamine
See Hydrazine, Chapter 55.

Diazide
See Chapter 51.

Diazinon®
See Chapter 51.

Dibromochloromethane
See Chapter 3.

1,2-Dibromoethane
See Ethylene dibromide, Chapter 45.

Dibromomethane
See Chapter 2.

Dibromomonochloromethane
See Dibromochloromethane, Chapter 3.

Dibutyl-1,2-benzene dicarboxylate
See Di-n-butyl phthalate, Chapter 30.

Dibutyl phthalate
See Di-n-butyl phthalate, Chapter 30.

m-Dichlorobenzene
See 1,3-Dichlorobenzene, Chapter 26.

o-Dichlorobenzene
See 1,2-Dichlorobenzene, Chapter 25.

p-Dichlorobenzene
See 1,4-Dichlorobenzene, Chapter 27.

1,2-Dichlorobenzene
See Chapter 25.

1,3-Dichlorobenzene
See Chapter 26.

1,4-Dichlorobenzene
See Chapter 27.

m-Dichlorobenzol
See 1,3-Dichlorobenzene, Chapter 26.

o-Dichlorobenzol
See 1,2-Dichlorobenzene, Chapter 25.

p-Dichlorobenzol
See 1,4-Dichlorobenzene, Chapter 27.

Dichlorochlordene
See Chlordane, Chapter 48.

Dichloro-2,2-dichloroethane
See 1,1,2,2-Tetrachloroethane, Chapter 11.

Dichlorodiphenyldichloroethane
See DDD, Chapter 58.

Dichlorodiphenyldichloroethylene
See DDE, Chapter 59.

1,1-Dichloroethane
See Chapter 8.

1,2-Dichloroethane
See Chapter 9.

cis-1,2-Dichloroethene
See cis-1,2-Dichloroethylene, Chapter 15.

trans-1,2-Dichloroethene
See trans-1,2-Dichloroethylene, Chapter 15.

1,2-Dichloro-(E)-ethene
See trans-1,2-Dichloroethylene, Chapter 15.

1,1-Dichloroethene
See 1,1-Dichloroethylene, Chapter 14.

1,1'-(Dichloroethenylidene)bis(4-chlorobenzene)
See DDE, Chapter 59.

Dichloroether
See Bis(2-chloroethyl)ether, Chapter 33.

1,1-Dichloroethylene
See Chapter 14.

cis-1,2-Dichloroethylene
See Chapter 15.

trans-1,2-Dichloroethylene
See Chapter 15.

Dichloroethyl ether
See Bis(2-chloroethyl)ether, Chapter 33.

sym-Dichloroethyl ether
See Bis(2-chloroethyl)ether, Chapter 33.

1,1'-(2,2-Dichloroethylidene)bis(4-chlorobenzene)
See DDD, Chapter 58.

Dichloromethane
See Methylene chloride, Chapter 1.

Dichloromethylmethane
See 1,1-Dichloroethane, Chapter 8.

2,6-Dichlorophenol
See Chapter 38.

2,4-Dichlorophenoxyacetic acid
See 2,4-D, Chapter 60.

alpha, beta-Dichloropropane
See 1,2 Dichloropropane, Chapter 12.

1,2-Dichloropropane
See Chapter 12.

1,2-Dichloro-(Z)-ethene
See cis-1,2-Dichloroethylene, Chapter 15.

Dicotox
See 2,4-D, Chapter 60.

Diesel oil
See Fuel oils, Chapter 66.

Diesel oil (light)
See Fuel oils, Chapter 66.

Diesel oil (medium)
See Fuel oils, Chapter 66.

Diethyl phthalate
See Chapter 29.

Diethyl-o-phthalate
See Diethyl phthalate, Chapter 29.

Dimethylbenzene
See Xylene, Chapter 21.

Dimethyl ketone
See Acetone, Chapter 40.

Dimethylnitrosamine
See N-Nitrosodimethylamine, Chapter 34.

2,4-Dimethylphenol
See Chapter 22.

4,6-Dimethylphenol
See 2,4-Dimethylphenol, Chapter 22.

Dimpylate
See Diazinon®, Chapter 51.

Di-n-butyl phthalate
See Chapter 30.

2,6-Dinitrotoluene
See Chapter 23.

Dioxin
See 2,3,7,8-Tetrachlorodibenzo-p-dioxin, Chapter 63.

Diphenylnitrosamine
See N-Nitrosodiphenylamine, Chapater 35.

Diphenyl N-nitrosoamine
See N-Nitrosodiphenylamine, Chapter 35.

Di-sec-octyl phthalate
See Di(2-ethylhexyl)phthalate, Chapter 31.

Disodium chromate
See Sodium chromate, Chapter 53.

DMN
See N-Nitrosodimethylamine, Chapter 34.

DMNA
See N-Nitrosodimethylamine, Chapter 34.

2,6-DNT
See 2,6-Dinitrotoluene, Chapter 23.

Dry cleaning safety solvent
See Stoddard solvent, Chapter 67.

EB
See Ethyl benzene, Chapter 20.

EDB
See Ethylene Dibromide, Chapter 45.

EDC
See 1,2-Dichloroethane, Chapter 9.

EG
See Ethylene glycol, Chapter 43.

EGME
See Methyl Celiosolve®, Chapter 42.

Fthane dichloride
See 1,2-Dichloroethane, Chapter 9.

1,2-Ethanediol
See Ethylene glycol, Chapter 43.

Ethinyl trichloride
See Trichloroethylene, Chapter 16.

Ethyl benzene
See Chapter 20.

Ethyl benzol
See Ethyl benzene, Chapter 20.

Ethyl chloride
See Chloroethane, Chapter 7.

Ethylene chloride
See 1,2-Dichloroethane, Chapter 9.

Ethylene dibromide
See Chapter 45.

Ethylene dichloride
See 1,2-Dichloroethane, Chapter 9.

Ethylene glycol
See Chapter 43.

Ethylene glycol methyl ether
See Methyl Cellosolve ®, Chapter 42.

Ethylene glycol monomethyl ether
See Methyl Cellosolve ®, Chapter 42.

Ethylene tetrachloride
See Tetrachloroethylene, Chapter 17.

Ethylene trichloride
See Trichloroethylene, Chapter 16.

2-Ethylhexyl phthalate
See Di(2-ethylhexyl)phthalate, Chapter 31.

Ethylidene chloride
See 1,1-Dichloroethane, Chapter 8.

Ethylidene dichloride
See 1,1-Dichloroethane, Chapter 8.

Ethyl methyl ketone
See Methyl ethyl ketone, Chapter 41.

Ethyl phthalate
See Diethyl phthalate, Chapter 29.

F11
See Trichlorofluoromethane, Chapter 5.

Fenoprop
See 2,4,5-TP, Chapter 62.

Fluorocarbon 11
See Trichlorofluoromethane, Chapter 5.

Fluorocarbon 1011
See Bromochloromethane, Chapter 44.

Fluorochloroform
See Trichlorofluoromethane, Chapter 5.

Fluorotrichloromethane
See Trichlorofluoromethane, Chapter 5.

Formyl trichloride
See Chloroform, Chapter 4.

Forron
See 2,4,5-T, Chapter 61.

Freon 11
See Trichlorofluoromethane, Chapter 5.

Fuel oils
See Chapter 66.

Gamma-benzene hexachloride
See Lindane, Chapter 47.

Gamma-BHC
See Lindane, Chapter 47.

Gamma-HCH
See Lindane, Chapter 47.

Glycol alcohol
See Ethylene glycol 43.

Glycol dibromide
See Ethylene dibromide, Chapter 45.

Glycol dichloride
See 1,2-Dichloroethane, Chapter 9.

Home heating oil
See Fuel oils, Chapter 66.

Hydraulic fluid
See Chapter 68.

Hydrazine
See Chapter 55.

Hydrazine, anhydrous
See Hydrazine, Chapter 55.

Hydrazine base
See Hydrazine, Chapter 55.

Hydrochloric ether
See Chloroethane, Chapter 7.

Hydrocyanic acid, ion
See Cyanide, Chapter 56.

Hydroxybenzene
See Phenol, Chapter 36.

2-Hydroxychlorobenzene
See o-Chlorophenol, Chapter 37

1-Hydroxy-2,4-dimethyl benzene
See 2,4-Dimethylphenol, Chapter 22

Jet fuel 4
See JP-4, Chapter 64.

JP-1
See Fuel oils, Chapter 66.

JP-4
See Chapter 64.

Kerosene
See Fuel oils, Chapter 66.

Levoxine
See Hydrazine, Chapter 55.

Lindane
See Chapter 47.

Malathion
See Chapter 50.

MCB
See 1,3-Dichlorobenzene, Chapter 26.

MEK
See Methyl ethyl ketone, Chapter 41.

Methane dichloride
See Methylene chloride, Chapter 1.

Methane tetrachloride
See Carbon tetrachloride, Chapter 6.

Methane trichloride
See Chloroform, Chapter 4.

2-Methoxyethanol
See Methyl Cellosolve®, Chapter 42.

Methyl acetal
See Acetone, Chapter 40.

Methyl acetone
See Methyl ethyl ketone, Chapter 41.

Methyl benzene
See Toluene, Chapter 19.

Methyl benzol
See Toluene, Chapter 19

Methyl Cellosolve ®
See Chapter 42

Methyl chloroform
See 1,1,1-Trichloroethane, Chapter 10.

2-Methyl-1,3-dinitrobenzene
See 2,6-Dinitrotoluene, Chapter 23.

Methylene bichloride
See Methylene chloride, Chapter 1.

Methylene bromide
See Dibromomethane, Chapter 2.

Methylene chloride
See Chapter 1.

Methylene chlorobromide
See Bromochloromethane, Chapter 44.

Methylene dibromide
See Dibromomethane, Chapter 2.

Methylene dichloride
See Methylene chloride, Chapter 1.

Methyl ethyl ketone
See Chapter 41.

Methyl glycol
See Methyl Cellosolve ®, Chapter 42.

Methyl ketone
See Acetone, Chapter 40.

N-Methyl-n-nitrosomethanamine
See N-Nitrosodimethylamine, Chapter 34.

Methyl trichloride
See Chloroform, Chapter 4.

Mineral base crankcase oil
See Chapter 69.

Mineral spirits
See Stoddard solvent, Chapter 67.

Monochlorobenzene
See Chlorobenzene, Chapter 24.

Monochlorodibromomethane
See Dibromochloromethane, Chapter 3.

Monochloroethane
See Chloroethane, Chapter 7.

Moth balls
See Naphthalene, Chapter 32.

Motor spirits
See Automotive gasoline, Chapter 65.

Muriatic ether
See Chloroethane, Chapter 7.

Naphthalene
See Chapter 32.

Naphthene
See Naphthalene, Chapter 32.

Navy special fuel oil
See Fuel oils, Chapter 66.

NDPA
See N-Nitrosodiphenylamine, Chapter 35.

N-Nitrosodimethylamine
See Chapter 34.

N-Nitrosodiphenylamine
See Chapter 35.

N-Nitroso-n-phenylaniline
See N-Nitrosodiphenylamine, Chapter 35.

N-Nitroso-N-phenyl-benzenamine
See N-Nitrosodiphenylamine, Chapter 35.

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.

ODB
See 1,2-Dichlorobenzene, Chapter 25.

O,O-Diethyl-O-(6-methyl-2-(1-methyethyl)-4-pyrimidinyl) phosphorothioate
See Diazinon®, Chapter 51.

1,1'-Oxybis(2-chloro)-ethane
See Bis(2-chloroethyl)ether, Chapter 33.

Paradichlorobenzene
See 1,4-Dichlorobenzene, Chapter 27.

PCB
See Aroclor®, Chapter 52.

PCE
See Tetrachloroethylene, Chapter 17.

PCP
See Pentachlorophenol, Chapter 39.

PDB
See 1,4-Dichlorobenzene, Chapter 27

Penchlorol
See Pentachlorophenol, Chapter 39

Penta
See Pentachlorophenol, Chapter 39

Pentachlorophenate
See Pentachlorophenol, Chapter 39.

Pentachlorophenol
See Chapter 39

Perc
See Tetrachloroethylene, Chapter 17.

Perchloroethene
See Tetrachloroethylene, Chapter 17.

Perchloroethylene
See Tetrachloroethylene, Chapter 17.

Perchloromethane
See Carbon tetrachloride, Chapter 6.

Permanent anti-freeze
See Ethylene glycol, Chapter 43

Petrol
See Automotive gasoline, Chapter 65.

Phenic acid
See Phenol, Chapter 36.

Phenoclor DP6
See Aroclor ® 1260, Chapter 52.

Phenol
See Chapter 36.

Phenox
See 2,4-D, Chapter 60.

Phenyl chloride
See Chlorobenzene, Chapter 24.

m-Phenylene dichloride
See 1,3-Dichlorobenzene, Chapter 26.

Phenylethane
See Ethyl benzene, Chapter 20.

Phenyl hydride
See Benzene, Chapter 18.

Phenyl hydroxide
See Phenol, Chapter 36.

Phenylic acid
See Phenol, Chapter 36.

Phenylmethane
See Toluene, Chapter 19.

Phosphoric acid, tris (2-methylphenyl) ester
See Tri-o-cresyl phosphate, Chapter 49.

Phthalic acid, butyl benzyl ester
See Butyl benzyl phthalate, Chapter 46.

Phthalic acid, dibutyl ester
See Di-n-butyl phthalate, Chapter 30.

Phthalic acid, diethyl ester
See Diethyl phthalate, Chapter 29.

Phthalic acid, dioctyl ester
See Di(2-ethylhexyl)phthalate, Chapter 31.

2-Propanone
See Acetone, Chapter 40.

Propellant 11
See Trichlorofluoromethane, Chapter 5.

Propylene chloride
See 1,2-Dichloropropane, Chapter 12.

Propylene dichloride
See 1,2-Dichloropropane, Chapter 12.

Pyroacetic acid
See Acetone, Chapter 40.

Pyroacetic ether
See Acetone, Chapter 40.

Pyrobenzol
See Benzene, Chapter 18.

R11
See Trichlorofluoromethane, Chapter 5.

Range oil
See Fuel oils, Chapter 66.

RCRA Waste Number U068
See Dibromomethane, Chapter 2.

RCRA Waste Number U082
See 2,6-Dichlorophenol, Chapter 38.

Refrigerant 11
See Trichlorofluoromethane, Chapter 5.

Residual fuel oil No. 2
See Fuel oils, Chapter 66.

Residual fuel oil No. 4
See Fuel oils, Chapter 66.

Residual fuel oil No. 5
See Fuel oils, Chapter 66.

Residual fuel oil No. 6
See Fuel oils, Chapter 66.

Silvex
See 2,4,5-TP, Chapter 62.

Sodium chromate
See Chapter 53.

Solvent naphtha
See Stoddard solvent, Chapter 67.

Stoddard solvent
See Chapter 67.

Synthetic crankcase oil
See Chapter 70.

2,4,5-T
See Chapter 61.

Tar camphor
See Naphthalene, Chapter 32.

TCB
See 1,2,4-Trichlorobenzene, Chapter 28.

2,3,7,8-TCDD
See 2,3,7,8-Tetrachlorodibenzo-p-dioxin, Chapter 63.

TCE
See Trichloroethylene, Chapter 16.

TDE
See DDD, Chapter 58.

TEL
See Tetraethyl lead, Chapter 54.

Tetrachlorocarbon
See Carbon tetrachloride, Chapter 6.

2,3,7,8-Tetrachlorodibenzo(b,e)(1,4)dioxin
See 2,3,7,8-tetrachlorodibenzo-p-dioxin, Chapter 63.

2,3,7,8-Tetrachlorodibenzo-p-dioxin
See Chapter 63.

Tetrachlorodiphenylethane
See DDD Chapter 58.

Tetrachloroethane
See 1,1,2,2-Tetrachloroethane, Chapter 11.

1,1,2,2,-Tetrachloroethane
See Chapter 11.

sym-Tetrachloroethane
See 1,1,2,2-Tetrachloroethane, Chapter 11.

Tetrachloroethene
See Tetrachloroethylene, Chapter 17.

Tetrachloroethylene
See Chapter 17.

Tetrachloromethane
See Carbon tetrachloride, Chapter 6.

Tetraethyl lead
See Chapter 54.

Tetraethyl plumbane
See Tetraethyl lead, Chapter 54.

TOCP
See Tri-o-cresyl phosphate, Chapter 49.

Toluene
See Chapter 19.

Toluol
See Toluene, Chapter 19.

TOTP
See Tri-o-cresyl phosphate, Chapter 49.

2,4,5-TP
See Chapter 62.

Tri
See Trichloroethylene, Chapter 16.

1,2,4-Trichlorobenzene
See Chapter 28.

unsym-Trichlorobenzene
See 1,2,4-Trichlorobenzene, Chapter 28.

1,2,4-Trichlorobenzol
See 1,2,4-Trichlorobenzene, Chapter 28.

1,1,1-Trichloro-2,2-bis(p-chlorophenyl)ethane
See DDT, Chapter 57.

Trichloroethane
See 1,1,1-Trichloroethane, Chapter 10.

alpha-Trichloroethane
See 1,1,1-Trichloroethane, Chapter 10.

1,1,1-Trichloroethane
See Chapter 10.

Trichloroethene
See Trichloroethylene, Chapter 16.

Trichloroethylene
See Chapter 16.

1,1-(2,2,2-Trichloroethylidene)bis(4-chlorobenzene)
See DDT, Chapter 57.

Trichlorofluoromethane
See Chapter 5.

Trichloromethane
See Chloroform, Chapter 4.

2,4,5-Trichlorophenoxy acetic acid
See 2,4,5-T, Chapter 61.

Alpha-(2,4,5-trichlorophenoxy)propanoic acid
See 2,4,5-TP, Chapter 62.

2-(2,4,5-Trichlorophenoxy)propanoic acid
See 2,4,5-TP, Chapter 62.

Tri-o-cresyl phosphate
See Chapter 49.

Tri-o-tolyl phosphate
See Tri-o-cresyl phosphate, Chapter 49.

VC
See Vinyl chloride, Chapter 13.

VCM
See Vinyl chloride, Chapter 13.

VDC
See 1,1-Dichloroethylene, Chapter 14.

Vinyl chloride
See Chapter 13.

Vinylidine dichloride
See 1,1-Dichloroethylene, Chapter 14.

White spirits
See Stoddard solvent, Chapter 67.

White tar
See Naphthalene, Chapter 32.

Xylene
See Chapter 21.

m-Xylenol
See 2,4-Dimethylphenol, Chapter 22.

2,4-Xylenol
See 2,4-Dimethylphenol, Chapter 22.

Xylol
See Xylene, Chapter 21.

INDEX 2

MOLECULAR FORMULA INDEX

The arrangement used in this index is based on the general molecular formula:
C_xH_y 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.

CCl_3F
Trichlorofluoromethane. See Chapter 5.

CCl_4
Carbon tetrachloride. See Chapter 6.

CN
Cyanide. See Chapter 56.

$CHBr_2Cl$
Dibromochloromethane. See Chapter 3.

$CHCl_3$
Chloroform. See Chapter 4.

CH_2BrCl
Bromochloromethane. See Chapter 44.

CH_2Br_2
Dibromomethane. See Chapter 2.

CH_2Cl_2
Methylene chloride. See Chapter 1.

C_2Cl_2
Tetrachloroethylene. See Chapter 17.

C_2HCl_3
Trichloroethylene. See Chapter 16.

$C_2H_2Cl_2$
1,1-Dichloroethylene. See Chapter 14.
trans-1,2-Dichloroethylene. See Chapter 15.
1,2-Dichloroethylene, mixed isomers. See Chapter 15.
cis-1,2-Dichloroethylene. See Chapter 15.

$C_2H_2Cl_4$
1,1,2,2-Tetrachloroethane. See Chapter 11.

C_2H_3Cl
Vinyl chloride. See Chapter 13.

$C_2H_3Cl_3$
1,1,1-Trichloroethane. See Chapter 10.

$C_2H_4Br_2$
Ethylene dibromide. See Chapter 45.

$C_2H_4Cl_2$
1,1-Dichloroethane. See Chapter 8.
1,2-Dichloroethane. See Chapter 9.

C_2H_5Cl
Chloroethane. See Chapter 7.

$C_2H_6N_2O$
N-Nitrosodimethylamine. See Chapter 34.

$C_2H_6O_2$
Ethylene glycol. See Chapter 43.

$C_3H_6Cl_2$
1,2-Dichloropropane. See Chapter 12.

C_3H_6O
Acetone. See Chapter 40.

$C_3H_8O_2$
Methyl Cellosolve®. See Chapter 42.

$C_4H_8Cl_2O$
Bis(2-chloroethyl)ether. See Chapter 33.

C_4H_8O
Methyl ethyl ketone. See Chapter 41.

C_6HCl_5O
Pentachlorophenol. See Chapter 39.

$C_6H_3Cl_3$
1,2,4-Trichlorobenzene. See Chapter 28.

$C_6H_4Cl_2$
1,2-Dichlorobenzene. See Chapter 25.
1,3-Dichlorobenzene. See Chapter 26.
1,4-Dichlorobenzene. See Chapter 27.

$C_6H_4Cl_2O$
2,6-Dichlorophenol. See Chapter 38.

C_6H_5Cl
Chlorobenzene. See Chapter 24.

C_6H_5ClO
o-Chlorophenol. See Chapter 37.

C_6H_6
Benzene. See Chapter 18.

$C_6H_6Cl_6$
Lindane. See Chapter 47.

C_6H_6O
Phenol. See Chapter 36.

$C_7H_6N_2O_4$
2,6-Dinitrotoluene. See Chapter 23.

C_7H_8
Toluene. See Chapter 19.

$C_8H_5Cl_3O_3$
2,4,5-T. See Chapter 61.

$C_8H_6Cl_2O_3$
2,4-D. See Chapter 60.

C_8H_{10}
Ethyl benzene. See Chapter 20.
o-Xylene. See Chapter 21.

m-Xylene. See Chapter 21.
p-Xylene. See Chapter 21.
Xylenes, mixed. See Chapter 21.

$C_8H_{10}O$
2,4-Dimethylphenol. See Chapter 22.

$C_8H_{20}Pb$
Tetraethyl lead. See Chapter 54.

$C_8H_7Cl_3O_3$
2,4,5-TP. See Chapter 62.

$C_{10}H_6Cl_8$
Chlordane. See Chapter 48.

$C_{10}H_8$
Naphthalene. See Chapter 32.

$C_{10}H_{19}O_6PS_2$
Malathion. See Chapter 50.

$C_{12}H_4Cl_4O_2$
2,3,7,8-Tetrachlorodibenzo-p-dioxin. See Chapter 63.

$C_{12}H_{10}N_2O$
N-Nitrosodiphenylamine. See Chapter 35.

$C_{12}H_{14}O_4$
Diethyl phthalate. See Chapter 29.

$C_{12}H_{21}N_2O_3PS$
Diazinon® See Chapter 51.

$C_{14}H_8Cl_4$
DDE. See Chapter 59.

$C_{14}H_9Cl_5$
DDT. See Chapter 57.

$C_{14}H_{10}Cl_4$
DDD. See Chapter 58.

$C_{16}H_{22}O_4$
Di-n-butyl phthalate. See Chapter 30.

$C_{19}H_{20}O_4$
Butyl benzyl phthalate. See Chapter 46.

$C_{21}H_{21}O_4P$
Tri-o-cresyl phosphate. See Chapter 49.

$C_{24}H_{38}O_4$
Di(2-ethylhexyl)phthalate. See Chapter 31.

Molecular Formula Unknown

Aroclor ® congeners
See Chapter 52.

Automotive gasoline
See Chapter 65.

Fuel oils
See Chapter 66.

Hydraulic fluid
See Chapter 68.

JP-4
See Chapter 64.

Mineral base crankcase oil
See Chapter 69.

Stoddard solvent
See Chapter 67.

Synthetic crankcase oil
See Chapter 70.

INDEX 3

CAS NUMBER INDEX

CAS Number	See Chapter
50-29-3	57
56-23-5	6
57-12-5	56
57-74-9	48
58-89-9	47
62-75-9	34
67-64-1	40
67-66-3	4
71-43-2	18
71-55-6	10
72-54-8	58
72-55-9	59
74-90-8	56
74-95-3	2
74-97-5	44
75-00-3	7
75-01-4	13
75-09-2	1
75-34-3	8
75-35-4	14
75-69-4	5
78-00-2	54
78-30-8	49
78-87-5	12
78-93-3	41
79-01-6	16
79-34-5	11
84-66-2	29
84-74-2	30
85-68-7	46
86-30-6	35
87-65-0	38
87-86-5	39
91-20-3	32
93-72-1	62
93-76-5	61
94-75-7	60
95-47-6	21
95-50-1	25
95-57-8	37

CAS Number	See Chapter
100-41-4	20
105-67-9	22
106-42-3	21
106-46-7	27
106-93-4	45
107-06-2	9
107-21-1	43
108-38-3	21
108-88-3	19
108-90-7	24
108-95-2	36
109-86-4	42
111-44-4	33
117-81-7	31
120-82-1	28
121-75-5	50
124-48-1	3
127-18-4	17
143-33-9	56
151-50-8	56
156-59-2	15
156-60-5	15
302-01-2	55
333-41-5	51
540-59-0	15
541-73-1	26
606-20-2	23
1330-20-7	21
1746-01-6	63
7775-11-3	53
8006-61-9	65
8008-20-6	66
8052-41-3	67
11096-82-5	52
11097-69-1	52
12674-11-2	52
53469-21-9	52
68476-30-2	66
68476-31-3	66
68553-00-4	66

No CAS Number Assigned:

Hydraulic fluid	See Chapter 68
JP-4	See Chapter 64
Mineral base crankcase oil	See Chapter 69
Synthetic crankcase oil	See Chapter 70

*Numeric designation assigned by the American Chemical Society's Chemical Abstracts Service which uniquely identifies a specific chemical compound.

INDEX 4

NIOSH NUMBER INDEX

NIOSH Number	See Chapter
AG6825000	60
AJ8400000	61
AL3150000	40
CY1400000	18
CZ0175000	24
CZ4499000	26
CZ4500000	25
CZ4550000	27
DA0700000	20
DC2100000	28
EL6475000	41
FG4900000	6
FS9100000	4
GB2955000	53
GS7175000	56
GV4900000	47
HP3500000	63
HZ1800000	66
IQ0525000	34
JJ9800000	35
KH7525000	7
KH9275000	45
KI0175000	8
KI0525000	9
Ki0700000	58
KI8575000	11
KJ2975000	10
KJ3325000	57
KL5775000	42
KN0875000	33
KU9625000	13
KV9360000	15
KV9400000	15
KV9422000	15
KV9450000	59
KW2975000	43
KX3850000	17
KX4550000	16
LS8950000	66
LX3300000	65
MU7155000	55

NIOSH Number	See Chapter
MW6825000	56
OA5500000	66
PA5250000	44
PA6360000	3
PA7350000	2
PA8050000	1
PB6125000	5
PB9800000	48
QJ0525000	32
SJ3325000	36
SK2625000	37
SK8750000	38
SM3000000	39
TD0350000	49
TF3325000	51
TH9990000	46
TI0875000	30
TI1050000	29
TI1925000	31
TP4550000	54
TQ1315100	52
TQ1356000	52
TQ1360000	52
TQ1362000	52
TS8760000	56
TX9625000	12
UF8225000	62
VZ7525000	56
WJ8925000	67
WM8400000	50
XS5250000	19
XT1925000	23
YZ8061000	14
ZE2100000	21
ZE2190000	21
ZE2275000	21
ZE2450000	21
ZE2625000	21
ZE5600000	22

No NIOSH Number Assigned:

Hydraulic fluid	See Chapter 68
JP-4	See Chapter 64
Mineral base crankcase oil	See Chapter 69
Synthetic crankcase oil	See Chapter 70

*A unique nine-position accession number (two letters and seven numerals) assigned alphabetically to each substance in the Registry of Toxic Effects of Chemical Substances published by the National Institute for Occupational Safety and Health (Reference 47).

INDEX 5

QUICK INDEX

CHEMICAL	VOLUME:CHAPTER-PAGE
ACETONE	3:40-1
AROCLOR 1016	3:52-1
AROCLOR 1242	3:52-1
AROCLOR 1260	3:52-1
AROCLOR 1254	3:52-1
AUTOMOTIVE GASOLINE	4:65-1
BENZENE	2:18-1
BROMOCHLOROMETHANE	3:44-1
BUTYL BENZYL PHTHALATE	3:46-1
DI-N-BUTYL PHTHALATE	2:30-1
CARBON TETRACHLORIDE	1:6-1
CHLORDANE	3:48-1
CHLOROBENZENE	2:24-1
CHLOROETHANE	1:7-1
BIS(2-CHLOROETHYL)ETHER	2:33-1
CHLOROFORM	1:4-1
O-CHLOROPHENOL	3:37-1
CYANIDE (CN)	4:56-1
CYANIDE (HCN)	4:56-1
CYANIDE (KCN)	4:56-1
CYANIDE (NaCN)	4:56-1
2,4-D	4:60-1
DDD	4:58-1
DDE	4:59-1
DDT	4:57-1
DIAZINON	3:51-1
DIBROMOCHLOROMETHANE	1:3-1
DIBROMOETHANE	1:2-1
1,2-DICHLOROBENZENE	2:25-1
1,3-DICHLOROBENZENE	2:26-1
1,4-DICHLOROBENZENE	2:27-1
1,1-DICHLOROETHANE	1:8-1
1,2-DICHLOROETHANE	1:9-1
1,1-DICHLOROETHYLENE	1:14-1
1,2-DICHLOROETHYLENE (CIS)	1:15-1
1,2-DICHLOROETHYLENE (MIXTURE)	1:15-1
1,2-DICHLOROETHYLENE (TRANS)	1:15-1
2,6-DICHLOROPHENOL	3:38-1
1,2-DICHLOROPROPANE	1:12-1
DIETHYL PHTHALATE	2:29-1

QUICK INDEX (Cont.)

CHEMICAL	VOLUME:CHAPTER-PAGE
2,4-DIMETHYLPHENOL	2:22-1
2,6-DINITROTOLUENE	2:23-1
ETHYL BENZENE	2:20-1
ETHYLENE DIBROMIDE	3:45-1
ETHYLENE GLYCOL	3:43-1
DI(2-ETHYLHEXYL)PHTHALATE	2:31-1
FUEL OILS 1	4:66-1
FUEL OILS 4	4:66-1
FUEL OILS 2	4:66-1
FUEL OILS 6	4:66-1
HYDRAULIC FLUID	4:68-1
HYDRAZINE	4:55-1
JP-4	4:64-1
LINDANE	3:47-1
MALATHION	3:50-1
METHYL CELLOSOLVE	3:42-1
METHYLENE CHLORIDE	1:1-1
METHYL ETHYL KETONE	3:41-1
MINERAL BASE CRANKCASE OIL	4:69-1
NAPHTHALENE	2:32-1
N-NITROSODIMETHYLAMINE	2:34-1
N-NITROSODIPHENYLAMINE	2:35-1
PENTACHLOROPHENOL	3:39-1
PHENOL	2:36-1
SODIUM CHROMATE	3:53-1
STODDARD SOLVENT	4:67-1
SYNTHETIC CRANKCASE OIL	4:70-1
2,4,5-T	4:61-1
2,3,7,8-TETRACHLORODIBENZO-P-DIOXIN	4:63-1
1,1,2,2-TETRACHLOROETHANE	1:11-1
TETRACHLOROETHYLENE	2:17-1
TETRAETHYL LEAD	3:54-1
TOLUENE	2:19-1
2,4,5-TP	4:62-1
1,2,4-TRICHLOROBENZENE	2:28-1
1,1,1-TRICHLOROETHANE	1:10-1
TRICHLOROETHYLENE	1:16-1
TRICHLOROFLUROMETHANE	1:5-1
TRI-O-CRESYL PHOSPHATE	3:49-1
VINYL CHLORIDE	1:13-1
XYLENE	2:21-1