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TOXICOLOGICAL PROFILE FOR 1,2-DICHLOROETHENE

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Agency for Toxic Substances and Disease Registry

August 1996

DISCLAIMER

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UPDATE STATEMENT

A Toxicological Profile for 1,2-dichloroethene was released in December 1990. This edition supersedes any previously released draft or final profile.

Toxicological profiles are revised and republished as necessary, but no less than once every three years. For information regarding the update status of previously released profiles, contact ATSDR at:

Agency for Toxic Substances and Disease Registry
Division of Toxicology/Toxicology Information Branch
1600 Clifton Road NE, E-29
Atlanta, Georgia 30333

FOREWORD

This toxicological profile is prepared in accordance with guidelines* developed by the Agency for Toxic Substances and Disease Registry (ATSDR) and the Environmental Protection Agency (EPA). The original guidelines were published in the *Federal Register* on April 17, 1987. Each profile will be revised and republished as necessary.

The ATSDR toxicological profile succinctly characterizes the toxicologic and adverse health effects information for the hazardous substance described therein. Each peer-reviewed profile identifies and reviews the key literature that describes a hazardous substance's toxicologic properties. Other pertinent literature is also presented, but is described in less detail than the key studies. The profile is not intended to be an exhaustive document; however, more comprehensive sources of specialty information are referenced.

The focus of the profiles is on health and toxicologic information; therefore, each toxicological profile begins with a public health statement that describes, in nontechnical language, a substance's relevant toxicological properties. Following the public health statement is information concerning levels of significant human exposure and, where known, significant health effects. The adequacy of information to determine a substance's health effects is described in a health effects summary. Data needs that are of significance to protection of public health are identified by ATSDR and EPA.

Each profile includes the following:

(A) The examination, summary, and interpretation of available toxicologic information and epidemiologic evaluations on a hazardous substance to ascertain the levels of significant human exposure for the substance and the associated acute, subacute, and chronic health effects;

(B) A determination of whether adequate information on the health effects of each substance is available or in the process of development to determine levels of exposure that present a significant risk to human health of acute, subacute, and chronic health effects; and

(C) Where appropriate, identification of toxicologic testing needed to identify the types or levels of exposure that may present significant risk of adverse health effects in humans.

The principal audience for the toxicological profiles is health professionals at the Federal, State, and local levels; interested private sector organizations and groups; and members of the public.

This profile reflects ATSDR's assessment of all relevant toxicologic testing and information that has been peer-reviewed. Staff of the Centers for Disease Control and Prevention and other Federal scientists have also reviewed the profile. In addition, this profile has been peer-reviewed by a nongovernmental panel and was made available for public review. Final responsibility for the contents and views expressed in this toxicological profile resides with ATSDR.

David Satcher, M.D., Ph.D.
Administrator
Agency for Toxic Substances and
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*Legislative Background

The toxicological profiles are developed in response to the Superfund Amendments and Reauthorization Act (SARA) of 1986 (Public Law 99-499) which amended the Comprehensive Environmental Response, Compensation, and Liability Act of 1980 (CERCLA or Superfund). This public law directed ATSDR to prepare toxicological profiles for hazardous substances most commonly found at facilities on the CERCLA National Priorities List and that pose the most significant potential threat to human health, as determined by ATSDR and the EPA. The availability of the revised priority list of 275 hazardous substances was announced in the *Federal Register* on April 29, 1996 (61 FR 18744). For prior versions of the list of substances, see *Federal Register* notices dated April 17, 1987 (52 FR 12866); October 20, 1988 (53 FR 41280); October 26, 1989 (54 FR 43619); October 17,1990 (55 FR 42067); October 17, 1991 (56 FR 52166); October 28, 1992 (57 FR 48801); and February 28, 1994 (59 FR 9486). Section 104(I)(3) of CERCLA, as amended, directs the Administrator of ATSDR to prepare a toxicological profile for each substance on the list.

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THE PROFILE HAS UNDERGONE THE FOLLOWING ATSDR INTERNAL REVIEWS:

1. Green Border Review. Green Border review assures consistency with ATSDR policy.

2. Health Effects Review. The Health Effects Review Committee examines the health effects chapter of each profile for consistency and accuracy in interpreting health effects and classifying end points.

3. Minimal Risk Level Review. The Minimal Risk Level Workgroup considers issues relevant to substance-specific minimal risk levels (MRLs), reviews the health effects database of each profile, and makes recommendations for derivation of MRLs.

PEER REVIEW

A peer review panel was assembled for 1,2-dichloroethene. The panel consisted of the following members:

1. Dr. Frederick Guengerich, Vanderbilt University School of Medicine, Department of Biochemistry, Nashville, Tennessee;

2. Dr. Derek Hodgson, Provost and Vice President of Academic Affairs, Mississippi State University, Mississippi State, Mississippi;

3. Dr. Norman Trieff, Professor of Environmental Toxicology, University of Texas Medical Branch, Galveston, Texas; and

4. Dr. Benjamin Van Duuren, Private Consultant, New York, New York.

These experts collectively have knowledge of 1,2-dichloroethene's physical and chemical properties, toxicokinetics, key health end points, mechanisms of action, human and animal exposure, and quantification of risk to humans. All reviewers were selected in conformity with the conditions for peer review specified in Section 104(i)(13) of the Comprehensive Environmental Response, Compensation, and Liability Act, as amended.

Scientists from the Agency for Toxic Substances and Disease Registry (ATSDR) have reviewed the peer reviewers' comments and determined which comments will be included in the profile. A listing of the peer reviewers' comments not incorporated in the profile, with a brief explanation of the rationale for their exclusion, exists as part of the administrative record for this compound. A list of databases reviewed and a list of unpublished documents cited are also included in the administrative record.

The citation of the peer review panel should not be understood to imply its approval of the profile's final content. The responsibility for the content of this profile lies with the ATSDR.

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1. PUBLIC HEALTH STATEMENT

This public health statement tells you about 1,2-dichloroethene and the effects of exposure.

The Environmental Protection Agency (EPA) identifies the most serious hazardous waste sites in the nation. These sites make up the National Priorities List (NPL) and are the sites targeted for long-term federal cleanup activities. Cis-1,2-dichloroethene has been found in at least 146 of the 1,430 current or former NPL sites. Trans- 1,2-dichloroethene has been found in at least 563 of the 1,430 current or former NPL sites. In 336 of the NPL sites, 1,2-dichloroethene was found but the isomer was not specified. However, it's unknown how many NPL sites have been evaluated for this substance. As more sites are evaluated, the sites with 1,2-dichloroethene may increase. This information is important because exposure to this substance may harm you and because these sites may be sources of exposure.

When a substance is released from a large area, such as an industrial plant, or from a container, such as a drum or bottle, it enters the environment. This release does not always lead to exposure. You are exposed to a substance only when you come in contact with it. You may be exposed by breathing, eating, or drinking the substance or by skin contact.

If you are exposed to 1,2-dichloroethene, many factors determine whether you'll be harmed. These factors include the dose (how much), the duration (how long), and how you come in contact with it. You must also consider the other chemicals you're exposed to and your age, sex, diet, family traits, lifestyle, and state of health.

1. PUBLIC HEALTH STATEMENT

1 .1 WHAT IS 1,2-DICHLOROETHENE?

1,2-Dichloroethene is also called 1,2-dichloroethylene. It is a highly flammable, colorless liquid with a sharp, harsh odor. You can smell very small amounts of 1,2-dichloroethene in air (beginning at a level of about 17 parts per million or ppm). There are two forms of 1,2-dichloroethene; one form is called cis-1,2-dichloroethene and the other is called trans- 1,2-dichloroethene. Sometimes both forms are present as a mixture. 1,2-Dichloroethene is used most often to produce solvents and in chemical mixtures.

1,2-Dichloroethene enters the environment through industrial activity of people. This chemical has been found in air, water, and soil. 1,2-Dichloroethene is released to the environment from chemical factories that make or use this chemical, from landfills and hazardous waste sites containing this chemical, from chemical spills, from burning of objects made of vinyl, and from breakdown of other chlorinated chemicals.

1.2 WHAT HAPPENS TO 1,2-DICHLOROETHENE WHEN IT ENTERS THE ENVIRONMENT?

1,2-Dichloroethene evaporates rapidly. When released to moist soil surfaces or to lakes, rivers, and other bodies of water, most of it evaporates into the air. Once in the air, it usually takes about 5-12 days for half of any amount of it to break down (half-life in air). 1,2-Dichloroethene that is below soil surfaces in landfills or hazardous waste sites may dissolve in water, seep deeper into the soil, and possibly contaminate groundwater. Some 1,2-dichloroethene may escape as a vapor. Once in groundwater, it takes about 13-48 weeks for half of a given amount to break down (half-life in water). There is a slight chance that small amounts of the 1,2-dichloroethene found in landfills will eventually break down into vinyl chloride, which is believed to be a more hazardous chemical.

1. PUBLIC HEALTH STATEMENT

1.3 HOW MIGHT I BE EXPOSED TO 1,2-DICHLOROETHENE?

You might be exposed to 1,2-dichloroethene by breathing contaminated air or by drinking contaminated tap water. If the tap water in your home is contaminated, you could also be breathing 1,2-dichloroethene vapors while cooking, bathing, or washing dishes. There are no known products you can buy that contain 1,2-dichloroethene. People who are most likely to be exposed live near landfills and hazardous waste sites that contain this chemical, work at factories where this chemical is made or used, work at 1,2-dichloroethene contaminated landfills, or work as firefighters. Job-related exposure results from breathing in 1,2-dichloroethene from workplace air or from touching contaminated chemicals or materials. According to a survey conducted between 1981 and 1983 by the National Institute for Occupational Safety and Health (NIOSH), an estimated 215 people in the United States may have been exposed to 1,2-dichloroethene while working.

People who live in cities or suburbs are more likely to be exposed than people living in rural areas. Most people who are exposed to 1,2-dichloroethene through air or water are exposed to very low levels, in the range of parts per million (ppm) to parts per billion (ppb).

1.4 HOW CAN 1,2-DICHLOROETHENE ENTER AND LEAVE MY BODY?

1,2-Dichloroethene can enter the body through your lungs when you breathe air contaminated with it, through your stomach and intestines when you eat food or drink water contaminated with it, or through your skin upon contact with the chemical.

When 1,2-dichloroethene enters the body, the blood and other tissues absorb it. It is broken down to other compounds in the liver. Animal studies have looked at how quickl.y the compound enters and leaves the body and what may happen to it in the body. These animal studies describe effects at levels far greater than those levels at which most people would be exposed. No studies show specifically how 1,2-dichloroethene enters a person’s body and how it is changed or removed by the body.

1. PUBLIC HEALTH STATEMENT

1.5 HOW CAN 1,2-DICHLOROETHENE AFFECT MY HEALTH?

Breathing high levels of trans-1,2-dichloroethene can make you feel nauseous, drowsy, and tired. Breathing very high levels of its vapor can kill you. When animals breathed high levels of trans-1,2-dichloroethene for short or longer periods of time, their livers and lungs were damaged. The effects were more severe with longer exposure times. Animals that breathed very high levels of trans-1,2-dichloroethene had damaged hearts. Animals given extremely high doses of cis- or trans-1,2-dichloroethene by mouth died. Lower oral doses of cis-1,2-dichloroethene caused effects on the blood, such as decreased numbers of red blood cells, and effects on the liver.

The long-term human health effects after exposure to low concentrations of 1,2-dichloroethene are not known. Results of a recent animal study suggest that an exposed fetus may not grow as quickly as one that is not exposed. No studies have been done to see whether cancer in people or animals is caused by exposure to 1,2-dichloroethene; exposure has not been shown to affect fertility in people or animals.

1.6 IS THERE A MEDICAL TEST TO DETERMINE WHETHER I HAVE BEEN EXPOSED TO 1,2-DICHLOROETHENE?

Methods are available to measure concentrations of 1,2-dichloroethene in blood, urine, and tissues. However, these methods are not routinely used to determine whether a person has been exposed to this compound, because the expected breakdown products resulting from exposure to 1,2-dichloroethene may also result from exposure to other chemicals.

1.7 WHAT RECOMMENDATIONS HAS THE FEDERAL GOVERNMENT MADE TO PROTECT HUMAN HEALTH?

The federal government has developed regulatory standards and guidelines to protect people from possible health effects of 1,2-dichloroethene in water and air. The EPA has established

water quality guidelines to protect both aquatic life and people who eat fish and shellfish. The EPA Office of Drinking Water has set a drinking water regulation that states that water delivered to any user of a public water system shall not exceed 0.07 milligrams per liter (mg/L) for cis- 1,2-dichloroethene and 0.1 mg/L for trans- 1,2-dichloroethene. For very short term exposures (1 day) for children, EPA advises that concentrations in drinking water should not be more than 4 mg/L for cis- 1,2-dichloroethene or 20 mg/L for trans-1,2-dichloroethene. For l0-day exposures for children, EPA advises that drinking water concentrations should not be more than 3 mg/L for cis-1,2-dichloroethene or 2 mg/L for trans-1,2-dichloroethene. For industrial or waste disposal sites, any release of 1,000 pounds or more must be reported to the EPA.

The National Institute for Occupational Safety and Health (NIOSH) and the American Conference of Governmental Industrial Hygienists (ACGIH) have established guidelines for occupational exposure to cis- or trans- 1,2-dichloroethene. Average concentrations should not exceed 200 ppm in the air.

1.8 WHERE CAN I GET MORE INFORMATION?

If you have any more questions or concerns, contact your community or state health or environmental quality department or:

Agency for Toxic Substances and Disease Registry
Division of Toxicology
1600 Clifton Road NE, E-29
Atlanta, Georgia 30333
Phone: 404-639-6000

This agency can also tell you where to find occupational and environmental health clinics. These clinics specialize in recognizing, evaluating, and treating illness resulting from exposure to hazardous substances.

2. HEALTH EFFECTS

2.1 INTRODUCTION

The primary purpose of this chapter is to provide public health officials, physicians, toxicologists, and other interested individuals and groups with an overall perspective of the toxicology of 1,2-dichloroethene. It contains descriptions and evaluations of toxicological studies and epidemiological investigations and provides conclusions, where possible, on the relevance of toxicity and toxicokinetic data to public health.

There are two geometric isomers of 1,2-dichloroethene, the cis form and the trans form. Isomers of an organic substance are different structures with the same molecular formula. In this case, the cis and trans forms have the chlorine atoms in different positions around the double bond. Each of these geometric isomeric forms has slightly different physical, chemical, and biological properties, because of their different molecular structures. These properties determine how the compound may affect the health of exposed individuals and how 1,2 dichloroethene behaves in air, water, and soil. The trans isomer is the more common industrial product.

A glossary and list of acronyms, abbreviations, and symbols can be found at the end of this profile.

2.2 DISCUSSION OF HEALTH EFFECTS BY ROUTE OF EXPOSURE

To help public health professionals and others address the needs of persons living or working near hazardous waste sites, the information in this section is organized first by route of exposure -inhalation, oral, and dermal; and then by health effect--death, systemic, immunological, neurological, reproductive, developmental, genotoxic, and carcinogenic effects. These data are discussed in terms of three exposure periods-acute (14 days or less), intermediate (15-364 days), and chronic (365 days or more).

Levels of significant exposure for each route and duration are presented in tables and illustrated in figures. The points in the figures showing no-observed-adverse-effect levels (NOAELs) or lowest observed-adverse-effect levels (LOAELs) reflect the actual doses (levels of exposure) used in the studies. LOAELS have been classified into “less serious” or “serious” effects. “Serious” effects are

those that evoke failure in a biological system and can lead to morbidity or mortality (e.g., acute respiratory distress or death). “Less serious” effects are those that are not expected to cause significant dysfunction or death, or those whose significance to the organism is not entirely clear. ATSDR acknowledges that a considerable amount of judgment may be required in establishing whether an end point should be classified as a NOAEL, “less serious” LOAEL, or “serious” LOAEL, and that in some cases, there will be insufficient data to decide whether the effect is indicative of significant dysfunction. However, the Agency has established guidelines and policies that are used to classify these end points. ATSDR believes that there is sufficient merit in this approach to warrant an attempt at distinguishing between “less serious” and “serious” effects. The distinction between “less serious” effects and “serious” effects is considered to be important because it helps the users of the profiles to identify levels of exposure at which major health effects start to appear. LOAELs or NOAELs should also help in determining whether or not the effects vary with dose and/or duration, and place into perspective the possible significance of these effects to human health.

The significance of the exposure levels shown in the LSE tables and figures may differ depending on the user’s perspective. Public health officials and others concerned with appropriate actions to take at hazardous waste sites may want information on levels of exposure associated with more subtle effects in humans or animals (LOAEL) or exposure levels below which no adverse effects (NOAELs) have been observed. Estimates of levels posing minimal risk to humans (Minimal Risk Levels or MRLs) may be of interest to health professionals and citizens alike.

Estimates of exposure levels posing minimal risk to humans (Minimal Risk Levels or MRLs) have been made for 1,2-dichloroethene. An MRL is defined as an estimate of daily human exposure to a substance that is likely to be without an appreciable risk of adverse effects (noncarcinogenic) over a specified duration of exposure. MRLs are derived when reliable and sufficient data exist to identify the target organ(s) of effect or the most sensitive health effect(s) for a specific duration within a given route of exposure. MRLs are based on noncancerous health effects only and do not consider carcinogenic effects, MRLs can be derived for acute, intermediate, and chronic durationexposures for inhalation and oral routes. Appropriate methodology does not exist to develop MRLs for dermal exposure.

Although methods have been established to derive these levels (Barnes and Dourson 1988; EPA 1990a), uncertainties are associated with these techniques. Furthermore, ATSDR acknowledges

additional uncertainties inherent in the application of the procedures to derive less than lifetime MRLs. As an example, acute inhalation MRLs may not be protective for health effects that are delayed in development or are acquired following repeated acute insults, such as hypersensitivity reactions, asthma, or chronic bronchitis. As these kinds of health effects data become available and methods to assess levels of significant human exposure improve, these MRLs will be revised.

A User's Guide has been provided at the end of this profile (see Appendix B). This guide should aid in the interpretation of the tables and figures for Levels of Significant Exposure and the MRLs.

2.2.1 Inhalation Exposure

2.2.1.1 Death

A single fatality was reported to have occurred after inhalation of 1,2dichloroethene vapor in a small enclosure (Hamilton 1934). Neither the level and duration of exposure associated with the fatality nor the symptoms of toxicity were reported. The isomeric composition of the vapor was not reported. No further information regarding lethal effects in humans following inhalation of 1,2-dichloroethene could be located in the literature.

The lethality of a single exposure by inhalation of trans-1,2-dichloroethene has been determined in mice (Gradiski et al. 1978). The lethal concentration resulting in 50% fatalities (LC_{50}) was 21,723 ppm trans-1,2-dichloroethene, presented in Table 2-l and in Figure 2-1, and was for a single 6-hour exposure. The cause of death was not reported.

No other studies were located regarding lethality following inhalation exposure to cis- or trans- 1 ,2dichloroethene in any animal species.

2.2.1.2 Systemic Effects

No studies were located regarding gastrointestinal, endocrine, dermal, or ocular effects in humans or animals after inhalation exposure to cis- or trans-1,2-dichloroethene. The highest NOAEL values and all LOAEL values from each reliable study for each systemic effect in each species and duration category are recorded in Table 2-1 and plotted in Figure 2-l.

Table 2-1. Levels of Significant Exposure to 1,2-Dichloroethene - Inhalation

Key to figure[a]	Species (strain)	Exposure/ duration/ frequency	System	NOAEL (ppm)	LOAEL Less serious (ppm)	LOAEL Serious (ppm)	Reference
	ACUTE EXPOSURE						
	Death						
1	Mouse (OF1,SPF)	6 hr				21723 F (LC_{50})	Gradiski et al. 1978 trans
	Systemic						
2	Rat (Wistar SPF)	8 hr	Resp		200 F (slight hyperemia of lung with alveolar septum distention in 6/6)		Freundt et al. 1977 trans
			Cardio	1000 F		3000 F (severe fibrous swelling and hyperemia, barely maintained striation in 2/6)	
			Hemato	200 F	1000 F (decreased erythrocyte count)		
			Musc/skel	3000 F			
			Hepatic		200 b F (slight fatty degeneration)	1000 F (slight to severe fatty degeneration of lobules in 2/6)	
			Renal	3000 F			
3	Rat (Wistar SPF)	1-2 wk 5 d/wk 8 hr/d	Resp		200 F (slight capillary hyperemia and alveolar septum distention in all rats)		Freundt et al. 1977 trans
			Cardio	200 F			
			Musc/skel	200 F			
			Hepatic		200 F (slight fatty accumulation in liver lobule)		
			Renal	200 F			

Table 2-1. Levels of Significant Exposure to 1,2-Dichloroethene - Inhalation (continued)

Key to figure[a]	Species (strain)	Exposure/ duration/ frequency	System	NOAEL (ppm)	LOAEL Less serious (ppm)	LOAEL Serious (ppm)	Reference
4	Rat (CD,BR)	10 d Gd 7-16 6 hr/d	Bd Wt	2000 F	6000 F (reduced body weight gain of dams of 13%)	12000 F (reduced body weight gain of 33%)	Hurtt et al. 1993 trans
			Other		2000 F (reduced food consumption of dams on gestational days 13-15)		
Immunological/Lymphoreticular							
5	Rat (Wistar SPF)	8 hr		200 F	1000 F (slight degeneration of Kuppfer cells in 2/6)		Freundt et al. 1977 trans
6	Rat (Wistar SPF)	1-2 wk 5 d/wk 8 hr/d			200 F (slight fatty accumulation in Kupffer cells)		Freundt et al. 1977 trans
7	Rat (Wistar SPF)	8 hr			200 F (decreased leukocyte count)		Freundt et al. 1977 trans
Neurological							
8	Rat (CD,BR)	10 d Gd 7-16 6 hr/d		6000 F	12000 F (lethargy and salivation)		Hurtt et al. 1993 trans
9	Mouse (Swiss OF1)	4 hr		1582 M	1720M (45% decreased duration of immobility in behavioral despair swimming test)		De Ceaurriz et al. 1983 NS
Developmental							
10	Rat (Crl: CDBR)	10 d Gd 7-16 6 hr/d		6000		12000 (significant decrease in mean fetal weight)	Hurtt et al. 1993 trans

Table 2-1. Levels of Significant Exposure to 1,2-Dichloroethene - Inhalation (continued)

Key to figure[a]	Species (strain)	Exposure/ duration/ frequency	System	NOAEL (ppm)	LOAEL Less serious (ppm)	LOAEL Serious (ppm)	Reference
INTERMEDIATE EXPOSURE							
Systemic							
11	Rat (Wistar SPF)	8 or 16 wk 5 d/wk 8 hr/d	Resp		200 F (slight capillary hyperemia and alveolar system distention)		Freundt et al. 1977 trans
			Cardio	200 F			
			Musc/skel	200 F			
			Hepatic		200 c F (slight fatty accumulation in liver lobules)		
			Renal	200 F			
Immunological/Lymphoreticular							
12	Rat (Wistar SPF)	8 or 16 wk 5 d/wk 8 hr/d			200 F (slight fatty accumulation in Kupffer cells)		Freundt et al. 1977 trans

[a]The number corresponds to entries in Figure 2-1.

[b]Used to derive an acute inhalation minimal risk level (MRL) of 0.2 ppm. Concentration is adjusted by an uncertainty factor of 1,000 (10 for use of a LOAEL, 10 for extrapolation from animals to humans, and 10 for human variability).

[c]Used to derive an intermediate inhalation MRL of 0.2 ppm. Concentration is adjusted by an uncertainty factor of 1,000 (10 for use of a LOAEL, 10 for extrapolation from animals to humans, and 10 for human variability).

Bd Wt = body weight; Cardio = cardiovascular; d = day(s); F = female; Gd = gestational day; Hemato = hematological; hr = hour(s); LC_{50} = lethal concentration, 50% kill; LOAEL = lowest-observable-adverse-effect level; M = male; Musc/skel = musculoskeletal; NOAEL = no-observable-adverse-effect level; Resp = respiratory; wk = week(s).

Figure 2-1. Levels of Significant Exposure to 1,2-Dichloroethene - Inhalation

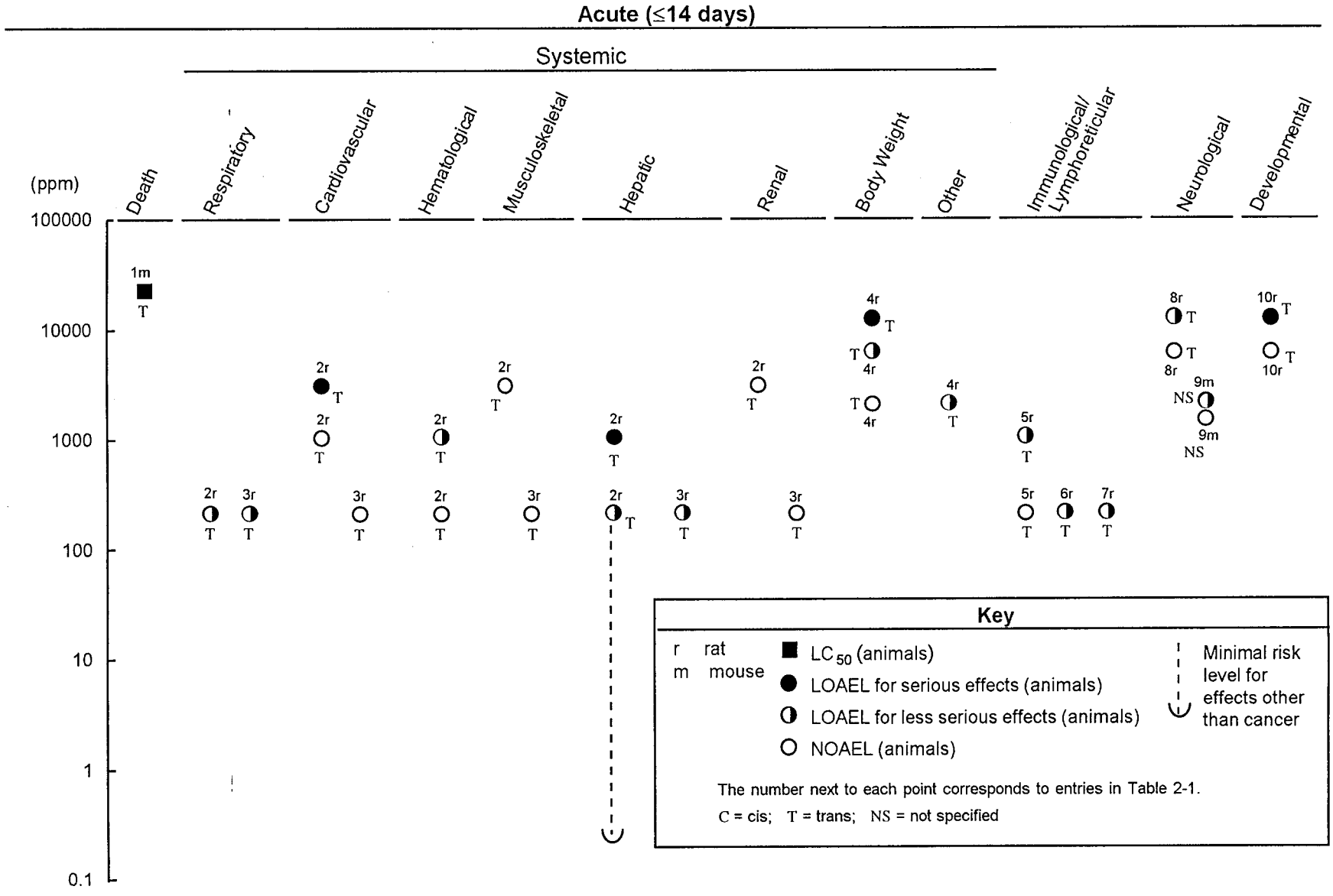
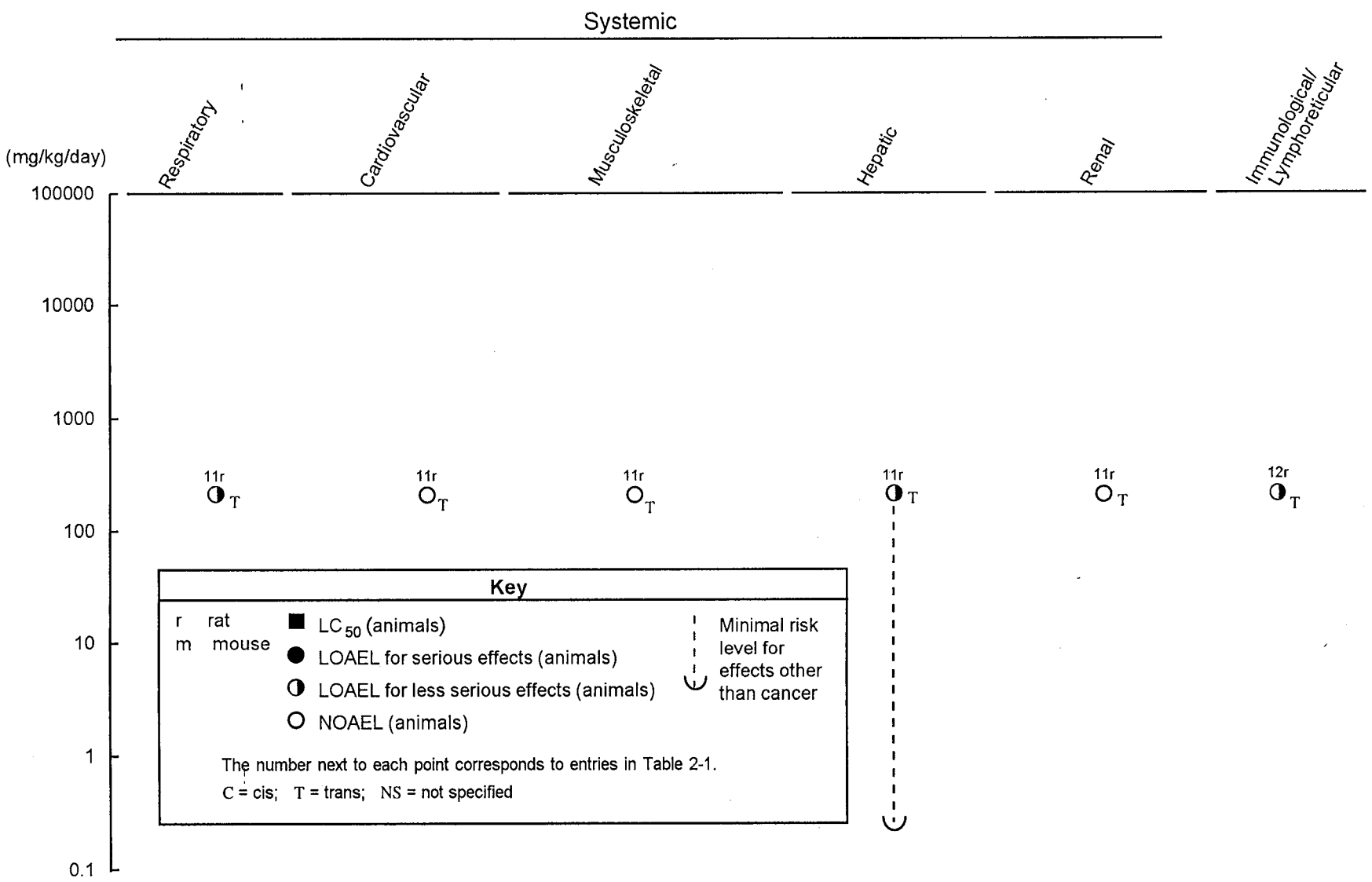


Figure 2-1. Levels of Significant Exposure to 1,2-Dichloroethene - Inhalation (continued)

Intermediate (15-364 days)



2. HEALTH EFFECTS

Respiratory Effects. No studies were located regarding respiratory effects in humans following inhalation exposure to cis- or trans-1,2-dichloroethene.

Pathologic changes in the lung have been described in rats exposed to trans-1,2-dichloroethene (Freundt et al. 1977). The pathology consisted of pulmonary capillary hyperemia, and alveolar septal distention. As shown in Table 2-l and Figure 2-1, after repeated exposure to 200 ppm effects in the lung were more severe than effects that occurred after a single exposure. This is the only reported study of lung pathology in animals exposed to trans-1,2-dichloroethene. This study had several weaknesses: several of the control rats also developed pulmonary capillary hyperemia and alveolar septal distention, a small number of animals were examined, and the upper respiratory tract was not examined for pathology. Also, a statistical evaluation of the histological data was not presented. Corroborative evidence for toxicity of trans-1,2-dichloroethene to the lung has not been reported.

No studies were located regarding the effects of cis-1,2-dichloroethene on the respiratory tract of any animal species.

Cardiovascular Effects. No studies were located regarding cardiovascular effects in humans following inhalation exposure to cis- or trans-1,2-dichloroethene.

Pathological changes in the heart have been observed in rats exposed to trans-1,2-dichloroethene (Freundt et al. 1977). The changes were described as severe fibrous swelling of the myocardium and hyperemia. As shown in Table 2-l and Figure 2- 1, the effects were evident after an 8-hour exposure to 3,000 ppm but not after exposures to lower levels. Corroborative evidence for heart toxicity of trans-1,2-dichloroethene has not been reported.

No studies were located regarding the effects of cis-1,2-dichloroethene on the cardiovascular system of any animal species.

Hematological Effects. No studies were located regarding hematological effects in humans following inhalation of cis- or trans-1 ,2dichloroethene.

Effects on composition of the blood and plasma have been observed in rats exposed to trans-1,2-dichloroethene (Freundt et al. 1977). A reduction in the number of erythrocytes was

observed after an 8-hour exposure to 1,000 ppm trans-1,2-dichloroethene. No studies were located regarding hematological effects in animals after inhalation exposure to cis- 1,2dichloroethene.

Musculoskeletal Effects. No studies were located regarding musculoskeletal effects in humans following inhalation exposure to cis- or trans-1,2-dichloroethene.

Histological examination of muscle tissue revealed no compound-related effects in rats exposed to 200, 1,000 or 3,000 ppm trans-1,2dichloroethene for up to 16 weeks (Freundt et al. 1977).

Hepatic Effects. No studies were located regarding hepatic effects in humans following inhalation of cis- or trans-1,2-dichloroethene.

Pathological changes in the liver, consisting of fatty accumulation of liver lobules and Kupffer cells, have been observed in a small group of rats exposed to trans-1,2-dichloroethene (Freundt et al. 1977). Five of six rats exposed to 200 ppm for 8 hours had livers that appeared normal when stained for fat accumulation, but one rat showed evidence of fat deposition. Although fat accumulation was not observed in the control rats for the 200 ppm exposure group, control rats for other exposure groups also showed histopathological evidence of fat accumulation in Kupffer cells. However, the incidence and severity of fat accumulation did increase with increasing exposure levels and duration. This study is the basis of an acute-duration inhalation MRL of 0.2 ppm for trans-1,2-dichloroethene, as explained in the footnote to Table 2-l and in Appendix A. In the same study, rats were exposed to 200 ppm trans-1,2-dichloroethene for 8 hours per day, 5 days per week for either 8 or 16 weeks. Fatty accumulation was found in hepatocytes (liver lobules). This LOAEL of 200 is the basis for the intermediate-duration inhalation MRL of 0.2 ppm for trans-1,2-dichloroethene, as explained in the footnote to Table 2-l and in Appendix A.

A single 8-hour exposure to cis- or trans-1,2-dichloroethene at 200 ppm has been shown to increase hexobarbital sleeping time and zoxazolamine paralysis time in rats (Freundt and Macholz-1978). These effects were more pronounced at higher 1,2-dichloroethene concentrations; the effects due to the cis isomer are stronger than those of the trans isomer. These effects suggest inhibition of the mixed function oxidase system.

2. HEALTH EFFECTS

Renal Effects. No studies were located regarding renal effects in humans following inhalation exposure to cis- or trans- 1,2-dichloroethene.

Histological examination of the kidney revealed no compound-related effects in rats exposed to 200, 1,000 or 3,000 ppm trans-1,2-dichloroethene for up to 16 weeks (Freundt et al. 1977). No studies were located regarding renal effects in animals after inhalation exposure to cis-1,2-dichloroethene.

Body Weight Effects. No studies were located regarding body weight effects in humans following inhalation of cis- or trans-1,2-dichloroethene.

Weight gain in pregnant rats was inversely related to dose from 2,000 to 12,000 ppm trans-1,2-dichloroethene, and was concomitant with the reduced food consumption of dams at 2,000 ppm on gestational days 13-15 in the developmental study of Hurtt et al. (1993). No studies were located regarding body weight effects in animals after inhalation exposure to cis-1,2-dichloroethene.

Other Systemic Effects. No studies were located regarding other systemic effects in humans following inhalation of cis- or trans-1,2-dichloroethene.

Several other systemic effects were found in the study of Hurtt et al. (1993). Brown-stained periocular hair was observed in all rats exposed to trans-1,2-dichloroethene at concentrations of 2,000-12,000 ppm. This effect was also observed in 1 of 24 control rats. Reduced food consumption of dams was observed on gestational days 13-15 at a concentration of 2,000 ppm. No studies were located regarding other systemic effects in animals after inhalation exposure to cis-1 ,2dichloroethene.

2.2.1.3 Immunological and Lymphoreticular Effects

Detailed studies were not located regarding the immunological or lymphoreticular effects-in humans or animals after inhalation exposure to cis- or trans-1 ,2dichloroethene.

Freundt et al. (1977), however, reported that inhalation exposure of rats to trans-1,2-dichloroethene at a concentration of 200 ppm or greater caused slight to severe fatty degeneration of Kupffer cells. Kupffer cells are highly phagocytic macrophages involved in protecting the systemic circulation from

gastrointestinal bacteria. In addition, decreased leukocyte (white blood cell) counts were observed in rats after an 8-hour exposure to 200 and 1,000 ppm trans-1 ,2dichloroethene, and pneumonic infiltration was observed after 8 and 16 weeks exposure to 200 ppm, suggesting that inhalation of trans- 1,2-dichloroethene may have adverse immunological effects.

2.2.1.4 Neurological Effects

Inhalation of high concentrations of vaporized trans-1,2-dichloroethene depresses the central nervous system in humans. Low levels of trans-1,2dichloroethene have been reported to cause neurological effects (Lehmann and Schmidt-Kehl 1936). Inhalation of 6.8-8.8 mg/L (1,700-2,220 ppm) of trans-1,2-dichloroethene for 5 minutes, or of 4.8 mg/L (1,200 ppm) for 10 minutes, reportedly caused nausea, drowsiness, fatigue, vertigo, and intracranial pressure in two human subjects. It is uncertain whether the human subjects were exposed to a vapor or an aerosol; however, based on information on the volatility of trans-1,2-dichloroethene, it was likely a vapor (see Chapter 3). Also, the degree of purity of the trans isomer and the precise concentrations are unclear.

The effects of inhaled cis- or trans-1,2-dichloroethene on the nervous system have not been extensively examined in animals. Hurtt et al. (1993) reported increased incidences of lethargy and salivation in pregnant rats exposed to 12,000 ppm trans-1,2-dichloroethene. Behavioral changes have been observed in mice exposed acutely (4 hours) to 1,2dichloroethene (form not specified) (De Ceaurriz et al. 1983). The reported changes consisted of a dose-related decrease in the duration of immobility in the “behavioral despair” swimming test. A 45% decrease in the total duration of immobility occurred at a concentration of 1,720 ppm. The neurological significance of changes in the duration of swimming immobility is not known. Frantik et al. (1994) studied inhibition of propagation and maintenance of the electrically evoked seizure discharge in rats and mice. The air concentration evoking a 30% depression in the duration of hindlimb tonic extension in rats was 1,810 ppm and the air concentration evoking a 30% increase in the latency for hindlimb tonic extension in mice was
3,400 pp.

2.2.1.5 Reproductive Effects

No studies were located regarding reproductive effects in humans after inhalation exposure to cis- or trans- 1,2-dichloroethene.

Significant increases in the mean number of resorptions per litter were seen in rats exposed to 6,000 and 12,000 ppm of trans-1,2-dichloroethene for 6 hours per day on days 7-16 of gestation (Hurtt et al. 1993). The authors interpreted this increase as not being treatment related because resorption values were within the range of historical controls. No studies were located regarding reproductive effects in animals after inhalation exposure to cis-1,2-dichloroethene.

2.2.1.6 Developmental Effects

No studies were located regarding developmental effects in humans after inhalation exposure to cis- or trans- 1,2-dichloroethene.

Inhalation exposure to trans-1,2-dichloroethene has been shown to affect fetal weight in animals. Hurtt et al. (1993) administered trans-1,2-dichloroethene to pregnant rats 6 hours daily, on days 7-16 of gestation, at 0, 2,000, 6,000, or 12,000 ppm. Mean fetal weights were significantly reduced in the litters of the dams exposed to 12,000 ppm. However, the reduced mean fetal weights probably resulted from reduced food consumption and reduced weight gain, which were seen in the pregnant rats in this study. No studies were located regarding developmental effects in animals after inhalation exposure to cis-1,2-dichloroethene.

2.2.1.7 Genotoxic Effects

No studies were located regarding in vivo genotoxic effects in humans or animals after inhalation exposure to cis- or trans- 1,2-dichloroethene.

Genotoxicity studies (*in vitro*) are discussed in Section 2.5.

2.2.1.8 Cancer

No studies were located regarding cancer in humans or animals after inhalation exposure to cis- or trans-1,2-dichloroethene.

2. HEALTH EFFECTS

2.2.2 Oral Exposure

2.2.2.1 Death

No studies were located regarding lethality in humans from ingestion of cis- or trans-1,2-dichloroethene. Lethal effects of orally-administered trans-1,2-dichloroethene in rats and mice have been investigated. Acute-duration dose levels exceeding 1,000 mg/kg are lethal in both species: 7 of 10 rats died following exposure to 1,130 mg/kg/day trans-1,2-dichloroethene (Freundt et al. 1977), and 2 of 6 rats died following exposure to 4,900 mg/kg/day cis-1,2-dichloroethene (McMillan 1986). In mice, LD_{50} values ranging from 2,200 mg/kg/day (males) to 2,400 mg/kg/day (females) were reported from trans-1,2-dichloroethene exposure (Munson et al. 1982). The difference in these values among and between rats and mice could be attributable to a number of different factors, including species differences, strain differences, age of animals, physiological status (e.g., fasting), experimental conditions, and vehicle used to dissolve the chemical. Symptoms associated with lethal oral doses included decreased activity, ataxia, suppressed or total loss of righting reflex, and depressed respiration (Barnes et al. 1985; Hayes et al. 1987). Necropsy revealed severe pulmonary capillary hyperemia and alveolar septal distension, along with fibrous swelling and hyperemia of cardiac muscle in several rats (Hayes et al. 1987), and hyperemia of the mucosal surface of the stomach and small intestine in mice (Barnes et al. 1985). In a 16day study, increased mortality was observed in rats exposed to 970 mg/kg/day cis-1,2-dichloroethene; 2 of 20 rats died within the first week of dosing (McCauley et al. 1990). Although the cause of death was not reported, the rats displayed central nervous system depression and secretions around the nose and mouth. In a 90-day study of cis-1,2-dichloroethene, 3 of 10 male rats treated with 290 mg/kg/day, 4 of 10 male rats treated with 870 mg/kg/day, and 1 of 10 female rats treated with both 32 and 97 mg/kg/day died within the first week of dosing. The incidence of these deaths was not statistically significant when compared with controls (l/20); no other rats died during the 90-day treatment, and the authors could not specifically relate the death to the chemical exposure (McCauley et al. 1990). The LD_{5O} values, the highest NOAEL values, and all reliable LOAEL values for death in each species in the acute-duration category are recorded in Table 2-2 and plotted in Figure 2-2.

Table 2-2. Levels of Significant Exposure to 1,2-Dichloroethene - Oral

Key to figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Specific Route)	System	NOAEL (mg/kg/day)	LOAEL		Reference
					Less Serious (mg/kg/day)	Serious (mg/kg/day)	
	ACUTE EXPOSURE						
	Death						
1	Rat (Wistar SPF)	once (GO)				1130 F (7/10 died)	Freundt et al. 1977 trans
2	Rat (Sprague-Dawley)	once (GO)				7900 M (LD_{50})	Hayes et al. 1987 trans
						10000 F (LD_{50})	
3	Rat (Sprague-Dawley)	7 d 1x/d (GO)				970 (2/20 died)	McCauley et al. 1990 cis
4	Rat (Sprague-Dawley)	once (GO)				4900 M (2/6 died)	McMillan 1986 cis
5	Mouse (CD-1)	once (G)				2100 M (LD_{50})	Barnes et al. 1985 trans
						2400 F (LD_{50})	
6	Mouse (CD-1)	once (G)				2200 M (LD_{50})	Munson et al. 1982 trans
						2400 F (LD_{50})	

Table 2-2. Levels of Significant Exposure to 1,2-Dichloroethene - Oral (continued)

Key to figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Specific Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference
	Systemic						
7	Rat (Wistar SPF)	once (GO)	Resp	940 F		1130 F (pulmonary capillary hyperemia and alveolar septal distention in 2/10)	Freundt et al. 1977 trans
			Cardio	940 F		1130 F (fibrous swelling and hyperemia, disorganization of striated pattern of cardiac muscle in 2/10)	
			Musc/skel	1600 F			
			Hepatic	1600 F			
			Renal	1600 F			
8	Rat (Sprague-Dawley)	14 d 1x/d (GO)	Resp	1900			McCauley et al. 1990 cis
			Cardio	1900			
			Gastro	1900			
			Hemato	1900 M 97[b] F		290 F (significant decreases in hematocrit and in erythrocyte count)	
			Musc/skel	1900			
			Hepatic	1900 M 97 F		290 F (significant decrease in blood urea nitrogen)	
			Renal	970 M 290 F	1900 M 970 F (increase absolute & relative kidney weights)		
			Endocr	1900			
			Dermal	1900			
			Bd Wt	1900			
			Metabolic	290M	970M (significant increase in serum calcium)		

Table 2-2. Levels of Significant Exposure to 1,2-Dichloroethene - Oral (continued)

Key to figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Specific Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference
9	Rat (Sprague-Dawley)	once (GO)	Hepatic		2500M (56% increase in plasma sorbitol dehydrogenase activity)		McMillan 1986 cis
10	Mouse (CD-1)	14 d 1x/d (G)	Resp	210M			Barnes et al. 1985 trans
			Hemato		210M (12% decrease in fibrinogen levels and 7% decrease in prothrombin time)		
			Hepatic	210M			
			Renal	210M			
			Bd Wt	210M			
	Neurological						
11	Rat (Sprague-Dawley)	14 d 1x/d (GO)		970		1900 (CNS depression)	McCauley et al. 1990 cis
12	Mouse (CD-1)	once (G)		1200	1600 (decreased activity)	2800 (ataxia and loss of righting reflex)	Barnes et al. 1985 trans
13	Mouse (CD-1)	7 d 1x/d (G)		100M	300M (taste aversion)		Kallman et al. 1983 cis and trans

Table 2-2. Levels of Significant Exposure to 1,2-Dichloroethene - Oral (continued)

Key to figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Specific Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference
	INTERMEDIATE EXPOSURE						
	Systemic						
14	Rat (Sprague-Dawley)	90 d ad lib (W)	Resp	3114 M 2809 F			Hayes et al. 1987 trans
			Hemato	3114 M 2809 F			
			Hepatic	3114 M 2809 F			
			Renal	3114 M 353 F	1257 F (12% increase in kidney weight)		
			Bd Wt	3114 M 2809 F			

Table 2-2. Levels of Significant Exposure to 1,2-Dichloroethene - Oral (continued)

Key to figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Specific Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference
15	Rat (Sprague-Dawley)	90 d 1x/d (GO)	Resp	870			McCauley et al. 1990 cis
			Cardio	870			
			Gastro	870			
			Hemato	32[c] M 97 F	97 M (decreased hematocrit) 290 F (decreased hematocrit)		
			Musc/skel	870			
			Hepatic	32	97 (significant increase relative liver weight)		
			Renal	290 M 870 F	870 M (significant increase relative kidney weight & decrease blood urea nitrogen and creatinine)		
			Endocr	870 F			
			Dermal	870			
			Bd Wt	32 M 870 F	97 M (10% decreased body weight)	290 M (27% decreased body weight)	
16	Rat (Sprague-Dawley)	30 d 1x/d (GO)	Resp		480 (significantly depressed relative lung weight)		McMillan 1986 cis and trans
			Cardio	480			
			Gastro	480			
			Hemato			480 M (significantly depressed CBC, RBC, hemoglobin, and hematocrit)	
			Hepatic		480 (significantly increased relative liver weight)		
			Renal	480			
			Bd Wt	480			
			Other	480			

Table 2-2. Levels of Significant Exposure to 1,2-Dichloroethene - Oral (continued)

Key to figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Specific Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference
17	Mouse (CD-1)	90 d ad lib (W)	Resp	387 M 224 F	452 F (11% decrease relative lung weight)		Barnes et. al. 1985 trans
			Hepatic	17[d] M 452 F	175M (increased serum alkaline phosphatase & 8% increase relative liver weight)		
			Renal	452			
			Bd Wt	452			
	Immunological/Lymphoreticular						
18	Mouse (CD-1)	90 d ad lib (W)		23 F	224 F (23% increase leukocyte count & 18% decrease relative thymus weight)		Barnes et. al. 1985 trans
19	Mouse (CD-1)	90 d ad lib (W)		387 M 452 F			Shopp et al. 1985 trans

[a]The number corresponds to entries in Figure 2-2.

[b]Used to derive an acute oral minimal risk level (MRL) of 1 mg/kg/day; dose divided by an uncertainty factor of 100 (10 for extrapolation from animals to humans and 10 for human variability).

[c]Used to derive an intermediate oral MRL of 0.3 mg/kg/day for cis-1,2-dichloroethene; dose divided by an uncertainty factor of 100 (10 for extrapolation from animals to humans and 10 for human variability).

[d]Used to derive an intermediate oral MRL of 0.2 mg/kg/day for trans-1,2-dichloroethene; dose is adjusted by an uncertainty factor of 100 (10 for extrapolation from animals to humans and 10 for human variability).

ad lib = ad libitum; Bd Wt = body weight; Cardio = cardiovascular; CBC = complete blood cell (count); CNS = central nervous system; d = day(s); Endocr = endocrine; F = female (G) = gavage; Gastro = gastrointestinal; (GO) = gavage in oil; Hemato = hematological; LD_{50} = lethal dose, 50% kill; LOAEL = lowest-observable-adverse-effect level; M = male; Musc/skel = musculoskeletal; NOAEL = no-observable-adverse-effect level; NS = not specified; RBC = red blood cell (count); Resp = respiratory; wk = week(s); (W) = water

Figure 2-2. Levels of Significant Exposure to 1,2-Dichloroethene - Oral

Acute (≤14 days)

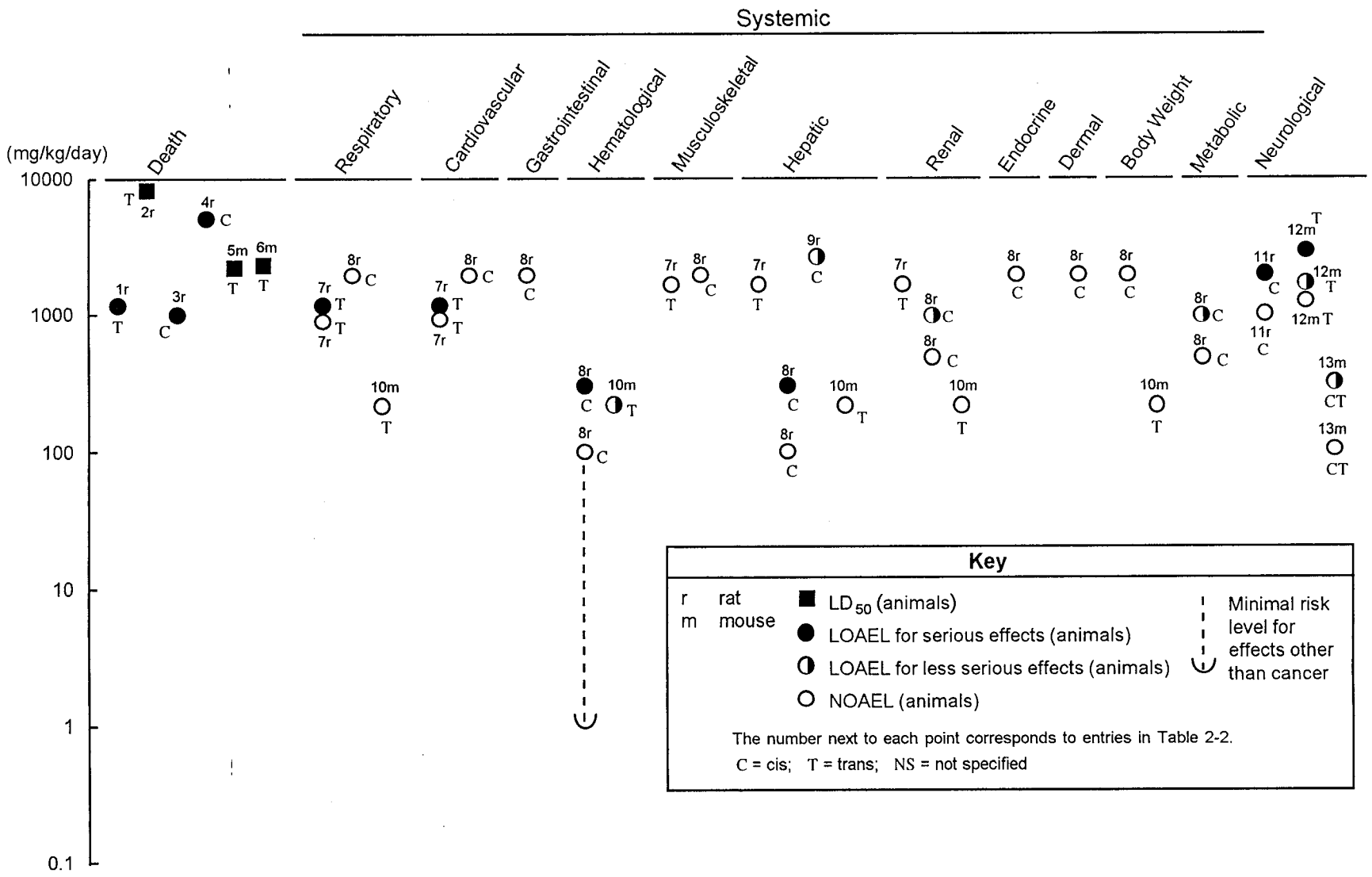
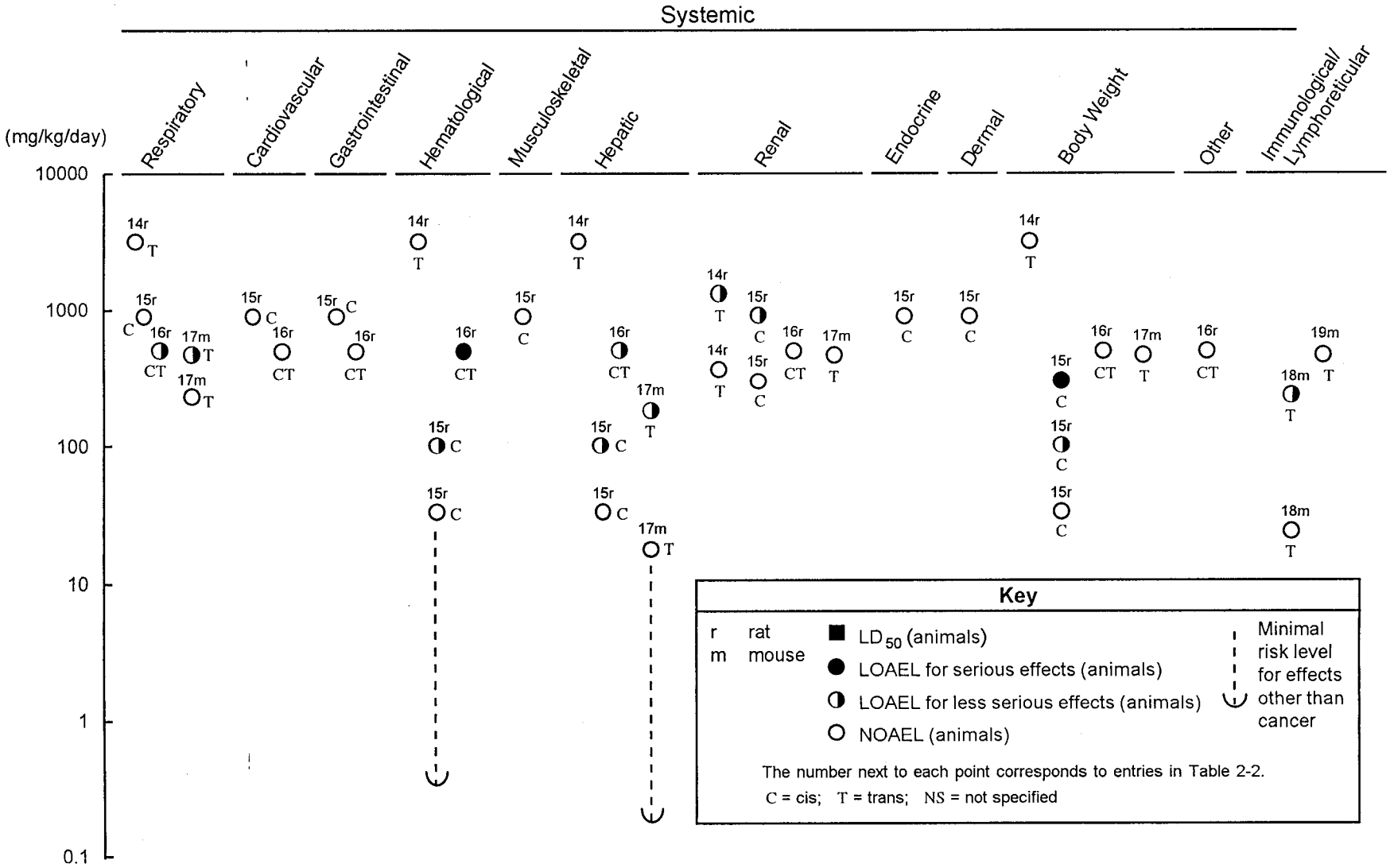


Figure 2-2. Levels of Significant Exposure to 1,2-Dichloroethene - Oral (continued)

Intermediate (15-364 days)



2.2.2.2 Systemic Effects

No studies were located regarding ocular effects in humans or animals after oral exposure to cis- or trans-1,2-dichloroethene. The highest NOAEL values and all LOAEL values from each reliable study for each systemic effect in each species and duration category are recorded in Table 2-2 and plotted in Figure 2-2.

Respiratory Effects. No studies were located regarding respiratory effects in humans following oral exposure to cis- or trans- 1,2-dichloroethene.

The effects of orally administered 1,2-dichloroethene on the respiratory tract of animals have not been examined extensively. As shown in Table 2-2 and Figure 2-2, male mice have been shown to tolerate exposure to 387 mg/kg body weight per day of trans-1,2-dichloroethene administered in drinking water for up to 90 days without developing histopathological changes in the lung (Barnes et al. 1985). The only change reported in this study was a slight decrease (11%) in lung weight in female mice at 452 mg/kg/day. No change in lung weight occurred in male rats exposed to 3,114 mg/kg/day trans-1,2dichloroethene for 90 days (Hayes et al. 1987). Pulmonary capillary hyperemia and alveolar septal distention have been observed in rats given lethal doses of trans-1,2-dichloroethene (Freundt et al. 1977). It is not clear whether this pathology represents a primary effect of the chemical on the lung or is secondary to disruption of cardiovascular function prior to death. It is notable that similar changes have been observed in rats exposed by inhalation to trans-1,2-dichloroethene (see Section 2.2.1.2).

Cardiovascular Effects. No studies were located regarding cardiovascular effects in humans following oral exposure to cis- or trans-1,2-dichloroethene.

Female rats exposed to 1,130-l ,400 mg/kg trans-1 ,2dichloroethene through oral gavage (single exposure) showed changes in cardiac muscle structure along with swelling and hyperemia (Freundt et al. 1977). No cardiovascular effects were noted in rats exposed to 1,900 mg/kg/day cis-1,2-dichloroethene for 14 days or 870 mg/kg/day cis-1,2-dichloroethene for 90 days (McCauley et al. 1990).

Gastrointestinal Effects. No studies were located regarding gastrointestinal effects in humans following oral exposure to cis- or trans- 1,2-dichloroethene.

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Mice that received lethal doses of trans- 1,2-dichloroethene had hyperemia of the stomach and small intestines (Barnes et al. 1985). No gastrointestinal effects were noted in rats exposed to 1,900 mg/kg/day cis-1,2-dichloroethene for 14 days or 870 mg/kg/day cis- 1 ,2dichloroethene for 90 days (McCauley et al. 1990).

Hematological Effects. No studies were located regarding hematological effects in humans following oral exposure to cis- or trans- 1 ,2-dichloroethene.

McMillan (1986) reported unchanged values of electrolytes, total blood cell counts, and total leukocyte counts, as compared to controls, from 14-day administration of a 50% mixture of the l,2dichloroethene cis and trans isomers (480 mg/kg/day) in rats. In contrast, the same dose, administered over 30 days, resulted in a significant depression of the total blood cell count, the red blood cell count, peripheral blood hemoglobin, and hematocrit levels.

No significant changes in hematological parameters occurred in rats (Hayes et al. 1987) or mice (Barnes et al. 1985) following oral exposure to trans-1,2-dichloroethene. As shown in Table 2-2 and Figure 2-2, rats tolerated repeated doses of 3,114 mg/kg/day (males) and 2,809 mg/kg/day (females) of trans-1 ,2dichloroethene in drinking water (emulsified with emulphor, a polyethoxylated vegetable oil) for 90 days without exhibiting significant hematological abnormalities (Barnes et al. 1985; Hayes et al. 1987). In contrast, dose-related hematotoxicity was the most evident effect in rats exposed orally by gavage to cis-1,2-dichloroethene in corn oil (McCauley et al. 1990). Decreased red blood cell count and hematocrit levels were observed in female rats exposed to 290 mg/kg/day for 14 days. No such changes were detected in female rats after exposure to 97 mg/kg/day or in male rats at all dose levels. Based on this value, an acute-duration oral MRL of 1 mg/kg/day was calculated for cis-1,2-dichloroethene as described in the footnote to Table 2-2 and in Appendix A. Similarly, decreased hematocrit levels were found in male rats exposed to 97 mg/kg/day cis-1,2-dichloroethene for 90 days and decreased hemoglobin levels were reported in both sexes at 290 mg/kg/day. The NOAEL level was 32 mg/kg/day. This. value was used for derivation of an intermediate-duration oral MRL –for cis-1,2-dichloroethene of 0.3 mg/kg/day as described in the footnote to Table 2-2 and in Appendix A.

Musculoskeletal Effects. No studies were located regarding musculoskeletal effects in humans following oral exposure to cis- or trans- 1,2-dichloroethene.

2. HEALTH EFFECTS

Histological examination of muscle tissue revealed no compound-related effects in rats exposed to 1,900 or 870 mg/kg/day of cis-1,2-dichloroethene for 14 or 90 days, respectively (McCauley et al. 1990), or in rats exposed by gavage to 1,600 mg/kg/day of trans-1,2-dichloroethene (Freundt et al. 1977).

Hepatic Effects. No studies were located regarding hepatic effects in humans following oral exposure to cis- or trans- 1,2-dichloroethene.

Liver pathology has been demonstrated in rats exposed orally to lethal or near lethal doses (e.g., 70% lethal dose) of trans- 1,2-dichloroethene. At 1,130 mg/kg/day of trans- 1,2-dichloroethene, 2 of 10 rats had severe fatty infiltration of the liver lobules and Kupffer cells; however, these effects were not seen in the rats given higher doses (Freundt et al. 1977). The pathology is similar to that observed in rats exposed by the inhalation route (i.e., fatty degeneration of the Kupffer cells and liver lobules) (Freundt et al. 1977). However, for oral exposure, the effects occurred only after exposure to lethal dose levels. As shown in Table 2-2 and Figure 2-2, repeated exposure to lower levels of trans-1,2-dichloroethene in drinking water for 90 days was tolerated by mice and did not result in liver pathology. However, at 175 mg/kg/day increased serum alkaline phosphatase was seen, indicating some degree of hepatic damage (Barnes et al. 1985).

McMillan (1986) examined the hepatic toxicity of cis- and trans-1,2-dichloroethene in rats after oral and intraperitoneal administration, respectively. At an exposure level of 4,400 mg/kg (single dose) of trans-1,2-dichloroethene, a significant increase in plasma alanine aminotransferase was noted, and at 2,500 mg/kg (single dose) of cis-1,2-dichloroethene, a significant increase in plasma sorbitol dehydrogenase activity was noted. Intermediate exposure (30 days) did not result in any treatmentrelated lesions in the liver. However, significantly elevated liver weights were noted at 480 mg/kg/day of a mixture of the cis and trans isomers for 30 days.

Biochemical changes in the liver have been reported in mice and rats exposed to cis- and trans-1,2-dichloroethene (Barnes et al. 1985; Jenkins et al. 1972). However, a connection between these biochemical changes and the pathology or impaired liver function has not been established. As such, the effects can not be classified as adverse or as being indicative of liver toxicity. Changes in hepatic alkaline phosphatase, tyrosine transaminase, glucose-6-phosphatase, and plasma alanine transaminase activities have been observed in rats exposed to single oral doses of 400 or 1,500 mg/kg

of cis- or trans-1,2dichloroethene (Jenkins et al. 1972). Although the changes observed in these enzyme activities were significant, the validity of the study is limited by the lack of dose-related patterns of the changes, the use of only three or four rats per treatment group, and the lack of reporting of animal responses to dosing. A dose-related decrease in the levels of serum glutamicoxaloacetic transaminase (SGOT) and serum glutamic-pyruvic transaminase (SGPT) was observed in female mice exposed to 23-452 mg/kg/day of trans-1,2-dichloroethene in the drinking water for 90 days (Barnes et al. 1985). Increased serum levels of these hepatic enzymes are usually indicative of liver damage; the toxicological significance of decreased levels is unknown. Increased serum alkaline phosphatase and increased relative liver weights were seen in male mice exposed to 175 mg/kg/day of trans-1,2-dichloroethene for 90 days. No such effects were noted in female mice. Based on a NOAEL of 17 mg/kg/day, an intermediate-duration oral MRL for trans-1,2-dichloroethene of 0.2 mg/kg/day was calculated as described in the footnote to Table 2-2 and in Appendix A.

The effect of 90-day exposure to trans-1,2-dichloroethene (17-452 mg/kg/day in drinking water) on hepatic microsomal drug metabolism was assessed by Barnes et al. (1985). In contrast to findings with inhalation exposure studies, oral exposure to trans-1,2-dichloroethene had no effect on the duration of hexobarbital-induced narcosis. In addition, no significant changes were found in hepatic microsomal cytochrome P-450 or cytochrome bg specific content. However, a decrease in microsomal aniline hydroxylase activity was reported in all exposed groups. A significant decrease in hepatic glutathione levels occurred in males after 90 days of exposure to 387 mg/kg/day.

A dose-related increase in relative liver weight was observed in rats exposed for 14 and 90 days to cis-1,2-dichloroethene (McCauley et al. 1990). In the 90-day study, effects were significant at 97 mg/kg/day and above. Slight increases in serum cholesterol were observed in the female rats in the 14-day study, and slight decreases in SGOT were observed in the 90-day study. The increased liver weight and biochemical changes cannot be considered adverse because they were not associated with histopathological liver lesions.

Renal Effects. No studies were located regarding renal effects in humans following oral exposure to cis- or trans- 1,2-dichloroethene.

The effects of 1,2-dichloroethene on the kidney have not been examined extensively in laboratory animals. The few studies that have been reported provide evidence to suggest that the kidney is

probably not a primary target for toxicity of trans-1,2-dichloroethene. As presented in Table 2-2 and Figure 2-2, animals tolerated repeated exposure to trans-1 ,2dichloroethene in drinking water without adverse effects on the kidney. A dose-related increase in absolute and relative kidney weight occurred in female rats treated with trans-1,2-dichloroethene for 90 days, but no histopathological lesions were identified (Hayes et al. 1987). No detectable chemically-induced changes in blood urea nitrogen or serum creatinine levels were found in animals exposed to trans-1,2-dichloroethene in either the 14-day or 90-day exposure study (Barnes et al. 1985; Hayes et al. 1987).

A significant increase in rat kidney weight was reported from a 16-day oral exposure to a 50% mixture of the 1,2-dichloroethene isomers (480 mg/kg/day) (McMillan 1986). An increase in absolute and relative kidney weight, along with a decrease in blood urea nitrogen, was also found in female rats exposed for 14 days to 970 mg/kg/day of cis-1,2-dichloroethene, and in male rats orally exposed to 1,900 mg/kg/day of cis-1,2-dichloroethene (McCauley et al. 1990). However, these changes did not occur in female rats exposed to 870 mg/kg/day of the cis isomer or less for 90 days. In male rats exposed to 870 mg/kg/day of cis-1,2-dichloroethene for 90 days, a significant increase in relative kidney weight and decreases in blood urea nitrogen and creatinine levels occurred. No changes occurred in males exposed to 1,900 mg/kg/day or less for 14 days. The toxicological significance of decreased blood urea nitrogen and creatinine levels is not clear since increases in these parameters are usually associated with renal toxicity. Furthermore, no histological evidence of kidney pathology was observed. In the absence of histological and clinical evidence of renal toxicity, the toxicological significance of the increased kidney weight is not known.

Endocrine Effects. No studies were located regarding endocrine effects in humans following oral exposure to cis-or trans-1,2-dichloroethene.

Histological examination revealed no compound-related effects in the thyroid in rats exposed to cis-1,2-dichloroethene at doses up to 1,900 or 870 mg/kg/day for 14 or 90 days, respectively (McCauley et all 1990).

Dermal Effects. No studies were located regarding dermal effects in humans following oral exposure to cis- or trans- 1,2-dichloroethene.

2. HEALTH EFFECTS

Histological examination revealed no compound-related effects on the skin of rats exposed to cis-1,2-dichloroethene at doses up to 1,900 or 870 mg/kg/day for 14 or 90 days, respectively (McCauley et al. 1990).

Body Weight Effects. No studies were located regarding body weight effects in humans following oral exposure to cis- or trans-1 ,2dichloroethene.

Body weight was not altered either by 21 or 210 mg/kg/day of trans-1,2-dichloroethene administered for 14 days to mice by gavage (Barnes et al. 1985). In rats, body weight was not altered by a 16day exposure to a 50% mixture of the 1,2-dichloroethene isomers (480 mg/kg/day) (McMillan 1986), nor by exposure to trans-1,2-dichloroethene (353-3,114 mg/kg/day) in drinking water for 90 days (Hayes et al. 1987). Significant changes in body weight gain were observed in both male and female rats treated with cis-1,2-dichloroethene for 14 days (McCauley et al. 1990). The changes were not dose-related; increased body weight gain occurred at 97 and 290 mg/kg/day and decreased body weight gain occurred at 970 and 1,900 mg/kg/day. The toxicological significance of these binodal body weight changes over a 14-day treatment period is not clear, although it could be due to decreased food intake at higher doses. In the 90-day study, only the male rats receiving the highest dose of cis-1,2-dichloroethene (870 mg/kg/day) had significantly decreased body weight gain when compared with control males.

Other Systemic Effects. No studies were located regarding other systemic effects in humans following oral exposure to cis-or trans-1,2-dichloroethene.

In female rats, a significant increase in water consumption was seen at 97 mg/kg/day. The authors stated that since cis-1,2-dichloroethene was administered by gavage, this effect must be considered to be compound-related and not associated with water palatability. They additionally noted that determining whether this effect is related to the compound's influence on the renal, central nervous system, or other-organ system will require more data (McCauley et al. 1990).

2.2.2.3 Immunological and Lymphoreticular Effects

No studies were located regarding immunological effects in humans following oral exposure to cis- or trans- 1,2-dichloroethene.

2. HEALTH EFFECTS

The effect of orally-administered trans-1,2-dichloroethene on the immune system has been investigated in rats and mice. No effects were seen on the spleen (Freundt et al. 1977; McCauley et al. 1990) or on leukocyte counts (Barnes et al. 1985; McMillan 1986; Munson et al. 1982) in rats or mice. Barnes et al. (1985) reported increased leukocyte count and decreased relative thymus weight in female mice exposed to 224 mg/kg/day of trans-1,2-dichloroethene for 90 days. Mice exposed to trans-1,2-dichloroethene (up to 220 mg/kg/day by gavage) for 14 days showed no significant changes in cell-mediated or humoral immunity (Munson et al. 1982; Shopp et al. 1985). Repeated exposure of mice to trans-1,2dichloroethene in drinking water for 90 days had no effect on the cell-mediated immune status of either sex or on the humoral immune status of females (Shopp et al. 1985). A suppression in humoral immune status, as measured by spleen cell antibody production directed against sheep erythrocytes, was observed in male mice treated with each of three doses (17, 175, and 387 mg/kg/day) of trans- 1,2-dichloroethene. Although the suppression was significant, it was not severe enough to depress the functional ability of the humoral immune system, as indicated by a normal spleen cell response to B cell mitogen lipopolysaccharide and normal hemagglutination titers. The highest NOAEL values for immunological effects in mice in each duration category are recorded in Table 2-2 and plotted in Figure 2-2.

Immunological effects were noted from exposure to 1,900 mg/kg/day of cis-1,2-dichloroethene in rats for 14 days, while an increase in absolute and relative thymus weights was noted in female rats exposed to 870 mg/kg/day for 90 days (McCauley et al. 1990).

2.2.2.4 Neurological Effects

No studies were located regarding neurological effects in humans following oral exposure to cis- or trans- 1,2-dichloroethene.

The neurological effects of cis- and trans-1,2-dichloroethene in animals have not been extensively examined, though acute exposure and stimuli/response research do provide insight. Signs of central nervous system depression have been observed in rats and mice at the terminal stages after receiving lethal doses of cis- and trans-1,2-dichloroethene (Barnes et al. 1985; Hayes et al. 1987; McCauley et al. 1990). Central nervous system depression (not further specified) was reported in rats treated with cis-1,2-dichloroethene at 1,900 mg/kg/day for 14 days (McCauley et al. 1990). The highest NOAEL

value and the LOAEL values from each reliable study with neurological end points are presented in Table 2-2 and plotted in Figure 2-2.

Dose-related conditioned taste aversion to saccharin was produced in mice exposed to a mixture of cis and trans-1,2-dichloroethene (Kallman et al. 1983). This neurobehavioral test will detect both neurological and non-neurological effects that are perceived by the test animal to be adverse. The nature of the adverse stimuli that results in taste aversion has not been identified.

2.2.2.5 Reproductive Effects

No studies were located regarding reproductive effects in humans following oral exposure to cis- or trans- 1,2-dichloroethene.

Neither acute nor intermediate exposures (14 and 90 days) have caused histological changes in reproductive organs of rats exposed to levels of cis-1,2-dichloroethene up to 1,900 mg/kg/day (McCauley et al. 1990). Rats exposed by gavage showed no treatment-related lesions in mammary glands, clitoral glands, ovaries, uterus, seminal vesicles, prostate, testes or preputial glands. No treatment-related histopathological lesions in the reproductive organs were seen in rats exposed to trans-1,2-dichloroethene for up to 90 days (Barnes et al. 1985; Hayes et al. 1987).

No studies were located regarding the following effects in humans or animals following oral exposure to cis- or trans-1,2-dichloroethene:

2.2.2.6 Developmental Effects

2.2.2.7 Genotoxic Effects

Genotoxicity studies- are discussed in Section 2.5.

2.2.2.8 Cancer

2.2.3 Dermal Exposure

2.2.3.1 Death

No studies were located regarding lethal effects in humans following dermal exposure to cis- or trans- 1.2-dichloroethene.

No deaths were reported from application of trans-1,2-dichloroethene at 5,000 mg/kg body weight on clipped, intact skin of 2 male and 3 female rabbits (Brock 1990). Table 2-3 summarizes the significant dermal exposure studies, presenting the highest NOAEL values and all LOAEL values from each important study. No studies were located regarding lethal effects in animals following dermal exposure to cis- 1,2-dichloroethene.

2.2.3.2 Systemic Effects

No dermal exposure studies of cis- or trans-1,2 dichloroethene were located regarding respiratory, cardiovascular, gastrointestinal, hematological, musculoskeletal, hepatic, renal, or endocrine effects in humans or animals.

Dermal Effects. No studies were located regarding dermal effects in humans following dermal exposure to cis- or trans- 1,2-dichloroethene.

Dermal effects have been shown in laboratory animals exposed dermally to trans-1,2-dichloroethene. Application of 170 mg/kg (0.5 mL) of trans-1,2dichloroethene for 24 hours to clipped, intact skin of 1 female and 5 male rabbits under an occlusive wrapping produced mild or moderate erythema at all observation times (24, 48 and 72 hours) (Brock 1990). In a separate experiment (Brock 1990), 5,000 mg/kg of trans-1,2-dichloroethene was applied to the clipped, intact skin of 2 male and 3 female rabbits. Severe dermal irritation was observed, but no clinical signs of toxicity other than body weight loss were found. No studies were located regarding dermal effects in animals following dermal exposure to cis- 1,2-dichloroethene.

Table 2-3. Levels of Significant Exposure to 1,2-Dichloroethene - Dermal

Species (Strain)	Exposure/ Duration/ Frequency (Specific Route)	System	NOAEL	LOAEL				Reference Chemical Form
				Less Serious		Serious		
ACUTE EXPOSURE								
Systemic								
Human	5-30 min (airborne)	Ocular	280 M ppm	830 M ppm	(slight burning of eyes)			Lehmann and Schmidt-Kehl 1936 trans
Rat (Crl: CDBR)	10 d Gd 7-16 6 hr/d (airborne)	Dermal	12000 F ppm					Hurtt et al. 1993 trans
		Ocular		2000 F ppm	(lacrimation)			
Rabbit (New Zealand White)	20 sec (eyes)	Ocular				3.3 F mg/kg	(transient severe corneal opacity, moderate iritis, and conjunctivitis)	Brock 1990 trans
Rabbit (NS)	24 hr	Dermal		170 mg/kg	(mild or moderate erythema)			Brock 1990 Abstract trans
Rabbit (NS)	24 hr	Dermal				5000 mg/kg	(severe dermal irritation)	Brock 1990 Abstract trans
		Bd Wt		5000 mg/kg	(body weight loss not otherwise specified)			

Bd Wt = body weight; d = day(s); F = female; Gd = gestational day; hr = hour(s); LOAEL = lowest-observable-adverse-effect level; M = male; min = minute(s); NOAEL = no-observable-adverse-effect level; NS = not specified; sec = second(s)

2. HEALTH EFFECTS

Ocular Effects. An early study by Lehmann and Schmidt-Kehl (1936) reported a slight burning of the eyes in two human subjects exposed for 30 minutes to concentrations between 830 and 2,220 ppm of trans-1,2-dichloroethene in air. The subjects were exposed under controlled conditions, not as an occupational accident. It is not certain whether the subjects were exposed to a vapor or to an aerosol of this chemical. The accuracy of the reported exposure levels is questionable because of the insensitivity of the methods used in 1936 to measure the concentration of 1,2dichloroethene in air. Also, the degree of purity of the trans isomer used is uncertain. No studies were located regarding ocular effects in humans following dermal exposure to cis-1,2-dichloroethene.

Severe corneal opacity, moderate iritis, conjunctivitis and lacrimation have been shown in rats after direct eye exposure to trans-1,2-dichloroethene. Trans-1,2-dichloroethene (0.01 mL) was placed in the lower conjunctival sac of two female rabbits and 20 seconds later, the eyes of one rabbit were washed with tap water while the eyes of the other rabbit remained unwashed. Severe cornea1 opacity was observed in the washed eye and moderate iritis and conjunctivitis were observed in both treated eyes; however, all irritation was resolved by day 3 (Brock 1990). Airborne exposure to trans-1,2-dichloroethene caused lacrimation in rats at 2,000 ppm (Hurtt et al. 1993). No studies were located regarding ocular effects in animals following dermal exposure to cis-1,2-dichloroethene.

Body Weight Effects. No studies were located regarding body weight effects in humans following dermal exposure to cis- or trans- 1,2-dichloroethene.

Brock (1990) applied 5,000 mg/kg trans-1,2-dichloroethene to the clipped, intact skin of 2 male and 3 female rabbits. Loss of body weight (amount unspecified) was observed. No studies were located regarding body weight effects in animals following dermal exposure to cis-1,2-dichloroethene.

2. HEALTH EFFECTS

No studies were located regarding the following effects in humans or animals following dermal exposure to cis- or trans- 1,2-dichloroethene:

2.2.3.3 Immunological and Lymphoreticular Effects

2.2.3.4 Neurological Effects

2.2.3.5 Reproductive Effects

2.2.3.6 Developmental Effects

2.2.3.7 Genotoxic Effects

Genotoxicity studies are discussed in Section 2.5.

2.2.3.8 Cancer

2.3 TOXICOKINETICS

1,2-Dichloroethene appears to be absorbed quickly by the lungs. One study reported that approximately 75% of the inhaled chemical was absorbed through the lungs in humans. 1,2-Dichloroethene is metabolized in the liver, by hepatic microsomal cytochrome P-450, to form dichloroethanol and dichloroacetic acid. Animal studies have shown that metabolism of the cis isomer occurs faster than metabolism of the trans isomer, and the cis isomer frequently inhibits activity or destroys cytochrome P-450 levels, while the trans isomer frequently increases the enzyme levels. No information is available on the excretion of 1.2-dichloroethene in humans or animals.

2.3.1 Absorption

2.3.1.1 Inhalation Exposure

In tests for partitioning between human blood and air (Gargas et al. 1989), the results show a relatively high affinity of 1,2-dichloroethene for blood (cis- 1,2-dichloroethene - blood:air partition coefficient =

9.58 [±0.70] and trans-1,2-dichloroethene = 6.04 [±0.38]). Several other studies appear to support the conclusion that 1,2dichloroethene is absorbed relatively quickly by the lungs. Sato and Nakajima (1979) reported blood:air partition coefficients (ratio concentrations in blood and air at 37 °C) of 9.2 and 5.8 for cis and trans isomers of 1,2-dichloroethene, respectively. Both isomers of 1,2-dichloroethene in inspired air achieve an equilibrium with the whole animal within 1.5-2 hours (Filser and Bolt 1979). Gargas et al. (1988, 1989) determined 1iquid:air and tissue:air partition coefficients for cis- and trans-1,2-dichloroethene. Partition coefficients were determined with 0.9% saline; olive oil; and blood, liver, muscle, and fat tissues from rats. The partition coefficients for cis-1,2-dichloroethene are: blood = 21.6 (±2.0), 0.9% saline = 3.25 (±0.12), olive oil = 278 (±6), fat = 227 (±11), liver = 15.3 (±11), and muscle = 6.09 (±1.02). The coefficients for trans-1,2-dichloroethene are: blood = 9.58 (±0.94), 0.9% saline = 1.41 (±0.04), olive oil = 178 (±6), fat = 148 (±11), liver = 8.96 (±0.61), and muscle = 3.52 (±0.54). Lehmann and Schmidt-Kehl (1936) reported that 72-75% of inhaled trans-1,2-dichloroethene is absorbed through the lungs in humans. Further insight is provided by Anderson et al. (1980), who reported that trans-1,2-dichloroethene follows mixed-form uptake kinetics, with a composite of a slow first-order and a saturable uptake process.

No studies were located regarding the rate and extent of cis- or trans-1,2dichloroethene absorption for the following:

2.3.1.2 Oral Exposure

2.3.1.3 Dermal Exposure

2.3.2 Distribution

No studies were located regarding the distribution of cis- and trans-1,2-dichloroethene following exposure by any routes.

2.3.3 Metabolism

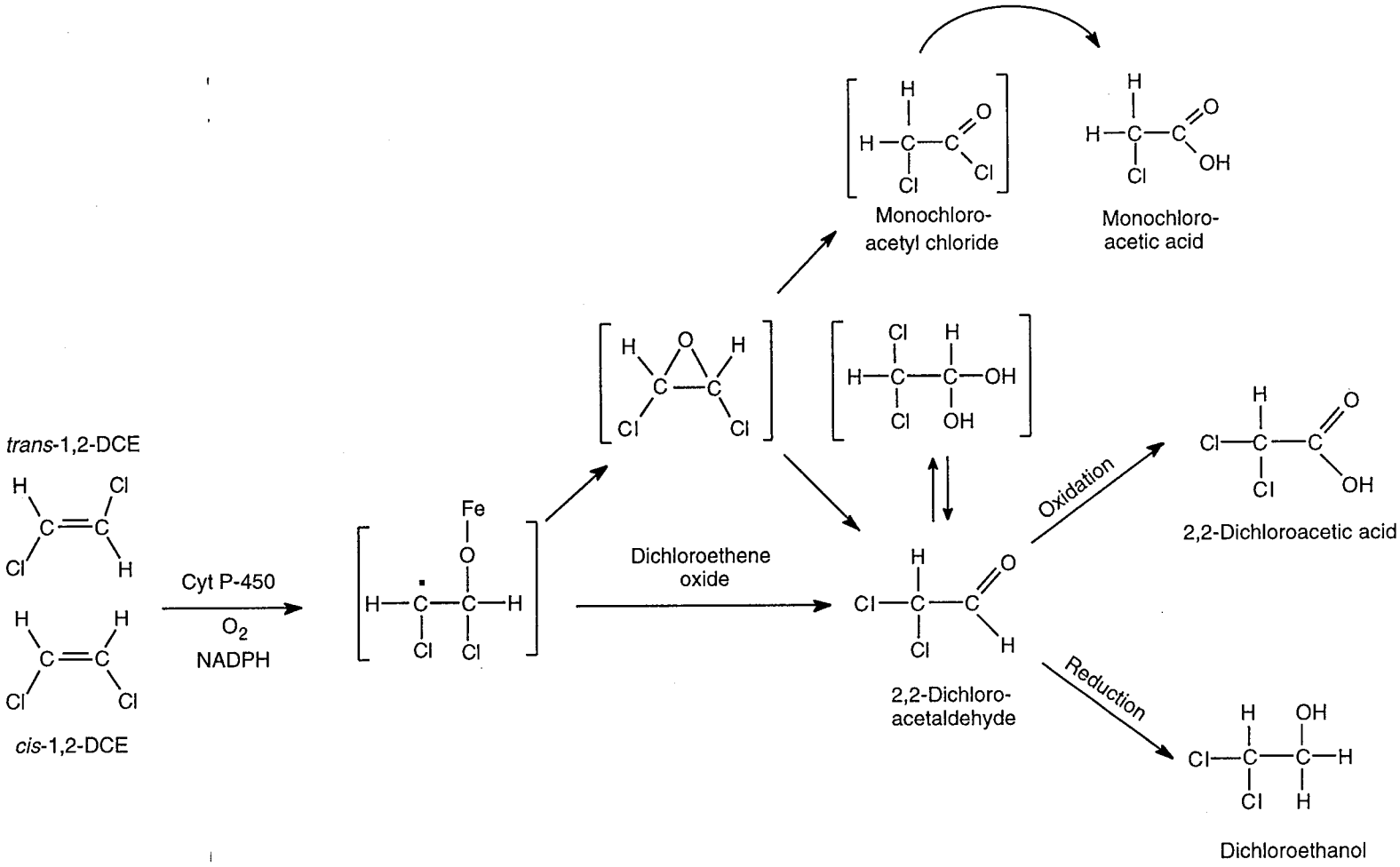
Metabolism of 1,2-dichloroethene is initially catalyzed by hepatic microsomal cytochrome P-450 (Costa and Ivanetich 1982, 1984). Although there is no direct evidence, studies on the synthesis of the epoxides suggest that this metabolism involves epoxidation of the ethylene double bond, forming

dichlorinated epoxides (Figure 2-3). Dichlorinated epoxides, in turn, can undergo a non-enzymatic rearrangement. Studies on the metabolism of 1,2-dichloroethene by hepatic microsomes and hepatocytes provide evidence to suggest that dichloroacetaldehyde is the predominant metabolite of microsomal cytochrome P-450 and that it, in turn, is extensively converted to dichloroethanol and dichloroacetate by cytosolic and/or mitochondrial aldehyde and alcohol dehydrogenases present in hepatocytes (Costa and Ivanetich 1982, 1984; Leibman and Ortiz 1977). This is consistent with the report that both the cis and trans isomers of 1,2-dichloroethene were converted to dichloroethanol and dichloroacetic acid by perfused rat liver (Bonse et al. 1975).

Similarities and differences have been observed in the metabolism of cis- and trans-1,2-dichloroethene. Both isomers have been shown to bind to the active site of hepatic cytochrome P-450 (Costa and Ivanetich 1982). In addition, classic inhibitors of cytochrome P-450 have been shown to inhibit the production of dichloroacetaldehyde from both isomers. The binding and metabolism of 1,2-dichloroethene do not appear to be specific for any one form of cytochrome P-450. The cis isomer had a 4-fold greater rate of turnover in hepatic microsomes in vitro than the trans isomer. This is consistent with studies on isolated perfused rat livers, where metabolism of the cis isomer occurred at a greater rate than metabolism of the trans isomer (Bonse et al. 1975). In addition, differences between cis- and trans-1,2-dichloroethene in the rates of formation of dichloroethanol and dichloroacetic acid have been reported in rat hepatocytes (Costa and Ivanetich 1984).

Several reports suggest that 1,2dichloroethene can alter cytochrome P-450 and mixed-function oxidase activities. McMillan (1986) reported depression of cytochrome P-450 dependent microsomal metabolism by both isomers of 1,2-dichloroethene, while Paolini et al. (1992) reported the induction of cytochrome P-450 enzymes by trans-1,2-dichloroethene. Freundt and Macholz (1978) demonstrated that each of the isomers of 1,2dichloroethene competitively inhibited the metabolism of hexobarbital in vivo following a single 8-hour inhalation exposure of rats to 200 ppm of these isomers. The effects of the cis isomer were more potent than those of the trans isomer. In addition, trans-1,2-dichloroethene competitively inhibited the oxidative *N*-demethylation of aminopyrine and the *O*-demethylation of p-nitroanisole by hepatic microsomes. Bronzetti et al. (1984) demonstrated that an intraperitoneal injection of the trans isomer can increase cytochrome P-450 levels (consistent with the work of Paolini 1992) and aminopyrine *N*-demethylase activity in mice, while injection of the cis isomer more frequently tended to inhibit activity or destroy the enzyme.

Figure 2-3. Postulated Metabolic Scheme for 1,2-Dichloroethene



Adapted from Costa and Ivanetich 1982

2. HEALTH EFFECTS

The metabolic elimination of 1,2-dichloroethene has been described as a saturable, dose-dependent process (Filser and Bolt 1979). In rats exposed to atmospheric concentrations of 1,2-dichloroethene that exceed a "point of saturation," elimination proceeds by zero-order kinetics (rate independent of the concentration of the compound); below saturation, first-order kinetics apply (Filser and Bolt 1979). Pharmacokinetic studies on 1,2dichloroethene elimination in the gas phase of a closed inhalation exposure system show that cis-1,2-dichloroethene has a higher rate of first-order clearance than the trans isomer. The cis isomer also exhibits a higher rate of metabolic elimination under saturation conditions, in comparison to the trans isomer. This observation is consistent with the higher rate of metabolism of the cis isomer relative to the trans isomer by rat liver microsomes (Costa and Ivanetich 1982) and by isolated perfused liver (Bonse et al. 1975).

2.3.4 Excretion

No studies were located regarding the excretion of 1,2-dichloroethene in humans or animals following exposure by any routes.

2.4 MECHANISMS OF ACTION

Both cis- and trans-1,2-dichloroethene are volatile, lipophilic molecules that easily move through the respiratory and gastrointestinal systems. Based on their molecular size and lipophilicity, they probably pass through membranes by simple (passive) diffusion. Toxicokinetic evidence shows they have a high affinity for lipids and blood, but little accumulation in tissues. Both the cis and trans isomers of 1,2-dichloroethene are converted to dichloroethanol and dichloroacetic acid by rat liver (Bonse et al. 1975, with the cis isomer exhibiting a higher rate of metabolism than the trans isomer (Costa and Ivanetich 1982).

1,2-Dichloroethene isomers inhibit liver enzymes involved in metabolism and may increase the "toxic" response to other chemicals (Bolt et al. 1980; McMillan 1986). Reactive metabolites of 1,2-dichloro ethene modify the heme moiety of hepatic microsomal cytochrome P-450, resulting in a loss of both cytochrome P-450 and heme (Costa and Ivanetich 1982). This modification could account for the observed *in vivo* and *in vitro* inhibition of other cytochrome P-450 substances by 1,2-dichloroethene. Compounds, such as carbon monoxide, that inactivate or inhibit the cytochrome P-450 system, should

also inhibit the metabolism of 1,2-dichloroethene. 1,2Dichloroethene is oxidized to its epoxide, which is relatively stable (Bolt et al. 1980). Its lack of genotoxicity is related to this stability.

The differences in metabolism, and possibly toxicity, between the cis and tram isomers have been partially explained by differences in the stereochemistry of the epoxides formed. The asymmetrical metabolites appear to be more electrophilic and also more mutagenic (Greim et al. 1975; Henschler 1977). The cis isomer is more actively metabolized than the tram isomer, because the trans isomer is a more stable form and the proximity of the two chlorine atoms in the cis isomer increases the binding to other molecules with which it reacts (Henschler 1977).

Physiologically based pharmacokinetic modeling (PBPK) has been used to explain metabolic rates for 1,2-dichloroethene. A model that included suicide enzyme inhibition-resynthesis has been used to describe the metabolism of 1,2-dichloroethene in the rat (Gargas et al. 1990). In this model, metabolism results in the inactivation of cytochrome P-450, which could result in an increase or decrease in the toxicity of 1,2dichloroethene.

2.5 RELEVANCE TO PUBLIC HEALTH

Inhalation, oral, and dermal routes of exposure to 1,2dichloroethene are of concern to humans because 1,2-dichloroethene has been found in air, drinking water, and soil (Shah and Singh 1988; Westrick et al. 1984; VIAR 1987). Toxicokinetic data are very limited for both human and animal exposures. Partition coefficients suggest that 1,2-dichloroethene has a much stronger affinity for blood and fats than for air. Although the compound is relatively lipophilic, there is no good evidence for accumulation in important organs such as liver, brain, kidney, and adipose tissue. Tissue saturation should not be found at anticipated exposure levels. 1,2Dichloroethene is likely to be metabolized to more hydrophilic by-products, and, therefore, eliminated quickly by the kidneys as metabolites.

The most significant effects of 1,2-dichloroethene exposure are hematological and hepatic. At high levels of exposure, clinical symptoms that have been reported in humans exposed to 1,2dichloroethene in air include nausea, drowsiness, fatigue, intracranial pressure and ocular irritation. One fatality has been reported. No information is available on oral toxicity for 1,2dichloroethene in humans. No information is available on the relative toxicities of the cis and trans isomers of 1,2dichloroethene in humans.

2. HEALTH EFFECTS

Pathological lesions of the heart, liver, and lungs have been reported in rats exposed to trans-1,2-dichloroethene in air. Ataxia and respiratory depression occur in the terminal stages prior to death in animals. Since these conditions have not been observed in humans, their relevance to public health is not known.

A variety of genotoxicity tests have been performed for 1,2-dichloroethene. The predominant results are negative, and no carcinogenicity studies were found in the literature. Federal and international agencies have given 1,2dichloroethene a non-cancer rating or a “not classifiable” rating.

Minimal Risk Levels for 1,2-Dichloroethene.

MRLs have been derived for acute and intermediate exposure to the cis and trans isomers of 1,2-dichloroethene; no chronic studies are available from which to derive MRLs for chronic exposure. The derivation of each MRL is discussed fully in Appendix A.

Inhalation MRLs.

- An MRL of 0.2 ppm has been derived for acute-duration exposure (14 days or less) and for intermediate-duration inhalation exposure (15-364 days) to trans- 1,2-dichloroethene.

The acute MRL is based on a LOAEL of 200 ppm for trans-1,2-dichloroethene over an 8-hour period that caused fatty degeneration of the liver (Freundt et al. 1977). Longer periods of exposure at 200 ppm showed increased numbers and severity of response. The intermediate MRL is based on the same study and effects (Freundt et al. 1977) in which rats were exposed to 200 ppm trans-1,2-dichloroethene for 8 hours per day, 5 days per week for 8 or 16 weeks. An uncertainty factor of 1,000 is used: 10 for using a LOAEL, 10 for extrapolation from animals to humans, and 10 for human variability.

No chronic inhalation MRL has been derived for trans-1,2-dichloroethene because no study tested 1,2-dichloroethene for a sufficiently long period of time. No acute-, intermediate- or chronic-duration MRLs have been derived for cis-1,2-dichloroethene because of lack of data.

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Oral MRLs.

Studies of oral exposure to 1,2-dichloroethene exist to develop oral MRLs for both the cis and trans isomers.

- An MRL of 1 mg/kg/day has been derived for acute-duration oral exposure (14 days or less) to cis- 1.2-dichloroethene.

This MRL for the cis isomer is based on a NOAEL of 97 mg/kg/day for decreased red blood cell counts and hematocrit levels in female rats exposed to 97 mg/kg/day cis-1,2-dichloroethene for 14 days (McCauley et al. 1990). An uncertainty factor of 100 is used: 10 for extrapolation from animals to humans, and 10 for human variability. Hematological effects have also been noted in other oral studies (Barnes et al. 1985).

No acute oral MRL has been derived for trans- 1,2-dichloroethene.

Separate intermediate-duration oral MRLs were derived for exposure to the cis and trans isomers.

- An MRL of 0.3 mg/kg/day has been derived for intermediate-duration oral exposure to

al. 1985). An uncertainty factor of 100 was developed for the MRL, using factors of 10 for animal-to-human extrapolation and 10 to protect sensitive individuals. In this study, serum alkaline phosphatase levels were significantly increased. Though the two highest doses caused increased serum alkaline phosphatase levels in a non-dose-related manner, the effects are consistent with the fatty accumulation in hepatocytes. This hepatic intermediate end point is slightly lower than a hematological NOAEL (decreased hematocrit). Other organs and end points were an order of magnitude less sensitive to cis- 1,2-dichloroethene than were hepatic and hematologic target organs.

Death. A fatality was reported to have occurred after inhalation of 1,2-dichloroethene in a small enclosure (Hamilton 1934). Details regarding the exposure levels (cis and trans) in this accident and the cause of death are not available. No reports of lethality related to oral exposure of humans to 1,2-dichloroethene were located.

Terminal symptoms in animals exposed orally to cis- or trans-1,2-dichloroethene involve central nervous system depression (e.g., ataxia and loss of righting reflex) and respiratory depression (Barnes et al. 1985; Hayes et al. 1987; McCauley et al. 1990; Munson et al. 1982). Results of studies in which animals have inhaled or ingested trans-1,2,-dichloroethene implicate the heart, liver, and lung as potential targets for toxicity (Barnes et al. 1985; Freundt et al. 1977; Hayes et al. 1987; McMillan 1986). The relative lethal potency of the cis and trans isomers to each other is not known.

Systemic Effects. Trans-1,2dichloroethene appears to be an ocular irritant in humans. Two human participants in a self-experimentation study reported mild burning of the eyes after acute exposure to either vapors or aerosols of trans-1,2-dichloroethene (Lehmann and Schmidt-Kehl 1936). No other specific systemic effects have been reported in humans. Cis- 1 ,2dichloroethene may induce a similar toxicological effect; however, no reports were located that specifically implicated cis- 1.2-dichloroethene as an ocular irritant.

Systemic effects-involving the heart, liver, and lungs have been observed in animals exposed to trans-1,2-dichloroethene. Evidence for serious adverse effects in these organs consists of only one study (Freundt et al. 1977). Effects reported in the rat include lung lesions (hyperemia and alveolar septal distension), fibrous swelling of the myocardium, and fatty degeneration of the liver. All three effects were observed after inhalation exposures to trans- 1,2-dichloroethene at concentrations of 200 ppm or greater for 8 hours. Liver and lung lesions were observed after gavage dosing, but only

after near lethal doses were administered. The treatment groups in this study were too small to establish a high degree of confidence in these findings. However, one additional serious systemic effect was found in rats-reduced weight gain for pregnant dams exposed to airborne 1,2-dichloroethene (Hurtt et al. 1993). Exposure of rats (Hayes et al. 1987) or mice (Barnes et al. 1985) to trans-1,2-dichloroethene at doses up to 3,114 mg/kg/day, in the drinking water for 90 days, did not result in adverse systemic effects.

Increased liver and kidney weights were observed in rats treated orally with cis-1,2-dichloroethene for 14 or 90 days, but these increased organ weights were not accompanied by any histopathological lesions in either organ (McCauley et al. 1990). Rats exposed to the cis isomer by gavage for 14 and 90 days showed a dose-related decrease in red blood cell count and hematocrit levels (McCauley et al. 1990). Hematotoxicity was not observed in mice or rats exposed to the trans isomer (Barnes et al. 1985; Hayes et al. 1987). The different results in the rat studies could be due to differential toxicity between the two isomers, as well as to other factors, including initial age of the rats, vehicle differences, and different exposure methods. Hayes et al. (1987) exposed rats with an initial age of 26 days to the trans isomer in a 1% emulphor drinking water suspension, while McCauley et al. (1990) treated rats with an initial age of 70 days with the cis isomer in corn oil by gavage. Data regarding toxic systemic effects of 1,2-dichloroethene in animals are too limited to draw any conclusions for human exposure.

Respiratory Effects. Pulmonary effects of inhalation and oral exposure to 1,2-dichloroethene have been shown over a range of exposure levels and for both inhalation and oral routes. No effect levels are reported from 485 to 2,000 mg/kg/day; however, several studies found pronounced respiratory effects around 1,000 mg/kg/day or 1,000 ppm (Freundt et al. 1977; McCauley et al. 1990; McMillan 1986). All these values are relatively high.

Cardiovascular Effects. The likelihood of acute exposure to 1,2-dichloroethene is quite small. Only at high levels (3,000 ppm or 1,100 mg/kg/day) is there animal evidence of swelling of heart muscle and congestion of blood in and near the heart (Freundt et al. 1977).

Hematological Effects. There are known blood effects of 1,2-dichloroethene, but these occur at exposure levels above those expected for the general population. Acute- and intermediate-exposure hematologic studies are the bases for oral MRLs for cis-1,2-dichloroethene (McCauley et al. 1990).

2. HEALTH EFFECTS

Musculoskeletal Effects. Animal studies have not reported effects on the musculoskeletal system (Freundt et al. 1977; McCauley et al. 1990). Thus, it does not appear that musculoskeletal effects are of concern for human exposure to 1,2-dichloroethene.

Hepatic Effects. Liver effects in animals include fatty degeneration of liver lobules; such effects are reasonable to anticipate among humans, though exposure levels of greater than 100 mg/kg/day are not anticipated. Higher exposure levels produced enzyme changes (decreased serum alkaline phosphatase, serum albumin and blood urea nitrogen or increased plasma enzyme activity) according to some of the available literature (Freundt et al. 1977; McMillan 1986). Acute- and intermediate-exposure hepatic studies are the bases for inhalation MRLs for trans-1,2-dichloroethene (Freundt et al. 1977) and for an oral MRL for tram-1,2dichloroethene (Barnes et al. 1985).

Renal Effects. Reduced kidney function and increased kidney weight are expected with acute high level exposure (McCauley et al. 1990; McMillan 1986); however, the public health concern is relatively small because such effects are not known to occur at chronic lower level exposure.

Dermal Effects. Acute exposure of the skin causes effects that are readily reversible. Irritation and mild effects on skin are the most frequent effects likely to be observed (Brock 1990).
Ocular Effects. Acute exposure causes readily reversible effects such as a slight burning of the eyes (Lehman and Schmidt-Kehl 1936).

Body Weight Effects. Acute- and intermediate-duration exposure has affected weight gain in pregnant and young rats (Hurtt et al. 1993; McCauley et al. 1990). In pregnant rats, reduced food consumption was observed along with reduced weight gain. Intermediate oral exposure caused smaller weight gains for growing rats.

Immunological and Lymphoreticular Effects. There are no reports of immunological effects in humans as a result of exposure to cis- or trans-1,2-dichloroethene by any route. Studies in rats and mice have not shown effects on the spleen, leukocytes, or liver Kupffer cells (Barnes et al. 1985; Freundt et al. 1977; McMillan 1986; Munson et al. 1982). Studies in mice have demonstrated perturbations of the humoral immune system (suppressed spleen cell antibody production against sheep erythrocytes) after exposure to trans-1,2-dichloroethene (Shopp et al. 1985). The observed changes in

the humoral immune system did not constitute a functional impairment of the humoral immune response and, therefore, are not considered to be adverse. The data regarding immunological effects of 1,2-dichloroethene in animals are too limited to draw any conclusion about potential immunological effects in humans.

Neurological Effects. The central nervous system depressant properties of 1 ,2dichloroethene represent an important effect in humans. Dizziness, drowsiness, vertigo, and intracranial pressure are some of the symptoms that have been reported in humans after inhalation of trans-1,2-dichloroethene (Lehmann and Schmidt-Kehl 1936). These symptoms disappeared quickly after exposure was terminated. The pharmacological basis for the 1,2-dichloroethene-mediated narcosis has not been studied.

Central nervous system depression (e.g., ataxia, loss of righting reflex) has been observed in some animal studies as well, but only at the terminal stages after the administration of lethal doses of both cis- and trans.-1,2-dichloroethene (Hayes et al. 1987; McCauley et al. 1990; Munson et al. 1982). A study in rats and mice reported on the air concentrations evoking a depression in the duration of hindlimb extension (Frantik et al. 1994). A marked species dependent effect was observed in this study. Therefore, it is difficult to draw any conclusions regarding the significance of this type of neurological effect in humans.

Reproductive Effects. There are no reports of reproductive effects in humans as a result of exposure to cis- or trans-1,2-dichloroethene by any route.

It is not known whether reproductive effects may be of concern to humans. One study showed an increase in resorption rates in rats; however, the authors interpreted this effect as not being treatment related (Hurtt et al. 1993).

Developmenta! Effects. There are no reports of developmental effects in humans as a result of exposure to cis- or trans-1,2dichloroethene by any route.

It is not known whether developmental effects may be of concern to humans. Fetal weights were reduced significantly in a developmental rat study; however, this was probably due to reduced food consumption in the pregnant rats (Hurtt et al. 1993).

Genotoxic Effects. Genotoxic effects of cis- and trans-1,2-dichloroethene in humans are unknown. Mutagenicity of 1,2dichloroethene has been examined in a variety of test systems. *In vivo* tests (Table 2-4) indicate that cis-1,2-dichloroethene, but not trans-1,2-dichloroethene, is genotoxic. The cis isomer was found to be mutagenic in the host-mediated assay using a series of Salmonella tester strains in mice (Cema and Kypenova 1977). Bronzetti et al. (1984) also found that the cis isomer was mutagenic in *Saccharomyces* cerevisiae D7 in a host-mediated assay in mice, with significant increases in convertants at the trp locus and revertants at the ilv locus. Cantelli-Forti and Bronzetti (1988) also reported that cis-1,2-dichloroethene was mutagenic in the *S. cerevisiae* D7 strain in mice. Dose-dependent toxicity increased in the presence of the mouse, S9 microsomal fraction. In addition, repeated intraperitoneal injection of cis- 1,2-dichloroethene produced chromosomal aberrations in mouse bone marrow cells (Cema and Kypenova 1977). Negative results were obtained with trans-1,2-dichloroethene in these assays.

In vitro tests of genotoxicity of the cis and trans isomers are summarized in Table 2-5. Neither isomer was genotoxic with or without metabolic activation in *Escherichia* coli K12 (Greim et al. 1973, in several strains of *S. typhimurium* in spot tests (Cema and Kypenova 1977; Mortelmans et al. 1986), or in gene mutation and gene conversion tests in S. cerevisiue D7 (Galli et al. 1982). However, Bronzetti et al. (1984) found positive results for gene mutation tests of the cis isomer in *S. cerevisiue* D7, with metabolic activation. Neither isomer produced chromosomal aberrations or sister chromatid exchanges in Chinese hamster cells (Sawada et al. 1987). The cis isomer, but not the trans isomer, induced unscheduled DNA synthesis in rat hepatocytes (Costa and Ivanetich 1984).

Cancer. To date, cancer effects of cis- and trans-1,2-dichloroethene have not been studied in humans or animals.

2.6 BIOMARKERS OF EXPOSURE AND EFFECT

Biomarkers are broadly defined as indicators signaling events in biologic systems or samples. They have been classified as markers of exposure, markers of effect, and markers of susceptibility (NAS/NRC 1989).

Table 2-4. Genotoxicity of cis- and trans-1,2-Dichloroethene *In Vivo*

Species (test system)	End point	Results	Reference
cis-1,2-Dichloroethene			
Mammalian systems:			
Mouse bone	Chromosomal aberrations	+	Cerna and Kypenova 1977
Host-mediated assays:			
Salmonella typhimurium	Gene mutation	+	Cerna and Kypenova 1977
(mouse host-mediated assay)			
Saccharomyces cerevisiae D7	Gene mutation	+	Cantelli-Forti and Bronzetti 1988
		+	Bronzetti et al. 1984
(mouse host-mediated assay)			
S. cerevisiae D7	Gene conversion	+	Bronzetti et al. 1984
(mouse host-mediated assay)		–	Cantelli-Forti and Bronzetti 1988
trans-1,2-Dichloroethene			
Mammalian systems:			
Chromosomal aberrations	Mouse bone marrow	–	Cerna and Kypenova 1977
Host-mediated assays:			
S. typhimurium	Gene mutation	–	Cerna and Kypenova 1977
(mouse host-mediated assay)		–	Cantelli-Forti and Bronzetti 1988
S. cerevisiae D7	Gene mutation	–	Bronzetti et al. 1984
(mouse host-mediated assay)			
S. cerevisiae D7	Gene conversion	–	Bronzetti et al. 1984
(mouse host-mediated assay)		–	Cantelli-Forti and Bronzetti 1988

+ = positive result; – = negative result

Table 2-5. Genotoxicity of cis- and trans-1,2-Dichloroethene *In Vitro*

Species (test system)	End point	Result		Reference
		With activation	Without activation	
cis-1,2-Dichloroethene				
Prokaryotic organisms:				
Escherichia coli K12	Gene mutation	–	–	Greim et al. 1975
Salmonella typhimurium	Gene mutation	ND	–	Cerna and Kypenova 1977
		–	–	Mortelmans et al. 1986
Eukaryotic organisms:				
Fungi:				
Saccharomyces cerevisiae D7	Gene mutation	+	–	Bronzetti et al. 1984
		–	–	Galli et al. 1982
S. cerevisiae D7	Gene conversion	–	–	Galli et al. 1982
Mammalian cells:				
Chinese hamster CHL cells	Chromosomal aberrations	–	–	Sawada et al. 1987
Chinese hamster CHL cells	Sister chromatic exchange	–	–	Sawada et al. 1987
Rat hepatocytes	Unscheduled DNA synthesis	NA	–	Costa and Ivanetich 1984
trans-1,2-Dichloroethene				
Prokaryotic organisms:				
E. coli K12	Gene mutation	–	–	Greim et al. 1975
		–	–	Cantelli-Forti and Bronzetti 1988
S. typhimurium	Gene mutation	ND	–	Cerna and Kypenova 1977

Table 2-5. Genotoxicity of cis- and trans-1,2-Dichloroethene *In Vitro* (continued)

Species (test system)	End point	Result		Reference
		With activation	Without activation	
trans-1,2-Dichloroethene (continued)				
Eukaryotic organisms:				
Fungi:				
S. cerevisiae D7	Gene mutation	–	–	Bronzetti et al. 1984
		–	–	Galli et al. 1982
S. cerevisiae D7	Gene conversion	–	–	Bronzetti et al. 1984
		–	–	Galli et al. 1982
Mammalian cells:				
Chinese hamster CHL cells	Chromosomal aberrations		–	Sawada et al. 1987
Chinese hamster CHL cells	Sister chromatid exchange	–	–	Sawada et al. 1987
Rat hepatocytes	Unscheduled DNA synthesis	NA	–	Costa and Ivenetich 1984

NA = not applicable; ND = no data; – = negative results; + = positive results.

2. HEALTH EFFECTS

Due to a nascent understanding of the use and interpretation of biomarkers, implementation of biomarkers as tools of exposure in the general population is very limited. A biomarker of exposure is a xenobiotic substance or its metabolite(s), or the product of an interaction between a xenobiotic agent and some target molecule(s) or cell(s) that is measured within a compartment of an organism (NRC 1989). The preferred biomarkers of exposure are generally the substance itself or substance-specific metabolites in readily obtainable body fluid(s) or excreta. However, several factors can confound the use and interpretation of biomarkers of exposure. The body burden of a substance may be the result of exposures from more than one source. The substance being measured may be a metabolite of another xenobiotic substance (e.g., high urinary levels of phenol can result from exposure to several different aromatic compounds). Depending on the properties of the substance (e.g., biologic half-life) and environmental conditions (e.g., duration and route of exposure), the substance and all of its metabolites may have left the body by the time samples can be taken. It may be difficult to identify individuals exposed to hazardous substances that are commonly found in body tissues and fluids (e.g., essential mineral nutrients such as copper, zinc, and selenium). Biomarkers of exposure to 1,2-dichloroethene are discussed in Section 2.6.1.

Biomarkers of effect are defined as any measurable biochemical, physiologic, or other alteration within an organism that, depending on magnitude, can be recognized as an established or potential health impairment or disease (NAWNRC 1989). This definition encompasses biochemical or cellular signals of tissue dysfunction (e.g., increased liver enzyme activity or pathologic changes in female genital epithelial cells), as well as physiologic signs of dysfunction such as increased blood pressure or decreased lung capacity. Note that these markers are not often substance specific. They also may not be directly adverse, but can indicate potential health impairment (e.g., DNA adducts). Biomarkers of effects caused by 1,2-dichloroethene are discussed in Section 2.6.2.

A biomarker of susceptibility is an indicator of an inherent or acquired limitation of an organism's ability to respond to the challenge of exposure to a specific xenobiotic substance. It can be an intrinsic genetic pr other characteristic or a preexisting disease that results in an increase in absorbed dose, a decrease in the biologically effective dose, or a target tissue response. If biomarkers of susceptibility exist, they are discussed in Section 2.8, Populations That Are Unusually Susceptible.

2. HEALTH EFFECTS

2.6.1 Biomarkers Used to Identify or Quantify Exposure to 1,2-Dichloroethene

There currently are no biomarkers available to quantify exposure to 1,2-dichloroethene.

Methods exist for determining 1,2dichloroethene in blood and biological tissues (see Chapter 6), but specific levels of 1,2-dichloroethene have not been directly correlated with exposure via any route. Acetonemia and acetone exhalation were observed in rats after inhalation exposure to halogenated ethylenes, including cis- and trans-1,2-dichloroethene (Filser et al. 1978). (Acetone is not a metabolite of 1,2dichloroethene exposure, but rather may be caused by stimulation of cellular systems that lead to increased acetone production.) Acetone exhalation occurred during exposure of rats to a concentration of trans- 1,2-dichloroethene as low as 50 ppm. This finding cannot, however, be used as a biomarker of exposure because the amount of acetone exhaled was not correlated with different exposure concentrations. Furthermore, acetone exhalation is not specific for 1 ,2dichloroethene since acetone can be found in blood and exhaled air after exposure to other chemicals such as vinyl chloride, vinylidene fluoride, and perchloroethylene (Filser and Bolt 1980), as well as in patients with diabetes, hepatic insufficiency, and other metabolic disorders.

2.6.2 Biomarkers Used to Characterize Effects Caused by 1,2-Dichloroethene

There currently are no biomarkers available to characterize effects caused by 1,2-dichloroethene in humans.

As discussed in Section 2.6.1, acetonemia and acetone exhalation were observed in rats after inhalation exposure to halogenated ethylenes, including the two isomers of 1,2-dichloroethene (Filser et al. 1978). Based on results of experiments with vinylidene fluoride, Filser and Bolt (1980) concluded that metabolites, rather than the parent compounds, were involved in invoking this response. Based on results of studies with the monohaloacetate metabolites of vinylidene fluoride and vinylidene chloride, which are known to inhibit enzymes of the citric acid cycle, Filser et al. (1982) suggested that the production of acetone by the halogenated ethylenes might also result from the inhibition-of the enzymes of the citric acid cycle. This would lead to an increase in mitochondrial acetyl-coenzyme A and, consequently, to an alteration in lipid and fatty acid metabolism and ketosis. A similar mechanism was suggested for 1,2-dichloroethene because the primary metabolite, dichloroacetate, can also increase ketone levels in the body. If such a mechanism operated, acetone exhalation could conceivably serve as a biomarker for such effects as fatty degeneration of the liver, which has been

observed in rats exposed to 1,2-dichloroethene (Freundt et al. 1977). However, acetone exhalation is extremely common and is associated with some disorders that do not obviously produce any liver degeneration.

For more information on biomarkers for renal and hepatic effects of chemicals see ATSDRKDC Subcommittee Report on Biological Indicators of Organ Damage (1990) and for information on biomarkers for neurological effects see OTA (1990).

2.7 INTERACTIONS WITH OTHER CHEMICALS

No studies were located regarding the health effects in humans or animals exposed to 1,2-dichloroethene in combination with other chemicals that are likely to be found with 1,2-dichloroethene in the environment, workplace, or at hazardous waste sites.

As mentioned in Section 2.3.3, both isomers of 1,2-dichloroethene can inhibit the cytochrome P-450-dependent metabolism of hexobarbital (Freundt and Macholz 1978). Such inhibition has also been shown to increase hexobarbital sleeping time. Costa and Ivanetich (1982) showed that multiple forms of hepatic microsomal cytochrome P-450, including the forms induced by P-naphthoflavone and phenobarbital, can bind and metabolize 1,2-dichloroethene. Thus, 1,2-dichloroethene may potentiate the toxic actions of any chemical that undergoes detoxication by cytochrome P-450-dependent metabolism by competing for binding to the active site of cytochrome P-450. Conversely, 1,2-dichloroethene may antagonize the toxic actions of any chemical that undergoes toxic activation by cytochrome-P-450-dependent metabolism.

2.8 POPULATIONS THAT ARE UNUSUALLY SUSCEPTIBLE

A susceptible population will exhibit a different or enhanced response to 1,2-dichloroethene than will most persons exposed to the same level of 1,2-dichloroethene in the environment. Reasons include genetic make-up, developmental stage, age, health and nutritional status (including dietary habits that may increase susceptibility, such as inconsistent diets or nutritional deficiencies), and substance exposure history (including smoking). These parameters result in decreased function of the detoxification and excretory processes (mainly hepatic, renal, and respiratory) or the pre-existing compromised function of target organs (including effects or clearance rates and any resulting

end-product metabolites). For these reasons we expect the elderly with declining organ function and the youngest of the population with immature and developing organs will generally be more vulnerable to toxic substances than healthy adults. Populations who are at greater risk due to their unusually high exposure are discussed in Section 5.6, Populations With Potentially High Exposure.

While no populations with unusual susceptibility to the health effects of 1,2-dichloroethene could be identified, based on the available literature, certain diabetics may be unusually susceptible because of impairment of glucose metabolism and increased production of acetone. In addition, individuals with impaired livers, such as alcoholics, and those with exposure to other halogenated hydrocarbons may be unusually susceptible to 1,2-dichloroethene exposure.

2.9 METHODS FOR REDUCING TOXIC EFFECTS

This section will describe clinical practice and research concerning methods for reducing toxic effects of exposure to 1,2-dichloroethene. However, because some of the treatments discussed may be experimental and unproven, this section should not be used as a guide for treatment of exposures to 1,2dichloroethene. When specific exposures have occurred, poison control centers and medical toxicologists should be consulted for medical advice.

2.9.1 Reducing Peak Absorption Following Exposure

1,2-Dichloroethene is available commercially as the cis or trans isomer or as a mixture. Human exposure to 1,2dichloroethene may occur by inhalation, ingestion, or by dermal contact. There are conflicting data regarding the relative toxicity of the two isomers. Vapors are extremely irritating to the eyes and upper respiratory tract, and once absorbed can cause central nervous system and respiratory depression. 1,2-Dichloroethene was used as a general anesthetic in humans, and central nervous system depression is one of its toxic effects (ACGIH 1991). It is recommended that exposed individuals be moved to fresh air and administered 100% humidified supplemental oxygen. The potential risk of aspiration, especially for infants, leading to airway and pulmonary damage, usually outweighs the potential benefit of administering syrup of ipecac to induce emesis (TOMES 1994). Once in the care of a health professional, gastric lavage can be useful if administered within 1 hour of the exposure to reduce the amount of absorbed solvent.

Following ocular contamination, the eyes should be irrigated with copious amounts of room temperature water or normal (0.9%, w/v, isotonic) saline, for at least 15 minutes. Reversible, corneal opacification has been described after exposure to 1,2-dichloroethene vapor, and ophthalmologic consultation should generally be sought after ocular contamination to evaluate the potential ocular damage (Gosselin 1984).

Following acute exposure to many chlorinated solvents, hypotension and cardiac arrhythmias due to myocardial sensitization have led to ventricular fibrillation and death (TOMES 1994). Unfortunately there is no specific treatment for 1,2dichloroethene exposure except for supportive measures to combat the effects of central nervous system, respiratory depression, and cardiac irritability.

2.9.2 Reducing Body Burden

The body does not retain significant amounts of 1,2-dichloroethene. It is largely excreted through the lungs; thus, prompt and adequate ventilation is the only known way to reduce body burden (ACGIH 1991). There is no currently recognized treatment to enhance elimination, and orthodox treatment for ingestion is entirely supportive.

2.9.3 Interfering with the Mechanism of Action for Toxic Effects

Clinical effects caused by acute exposure to 1,2-dichloroethene include central nervous system and respiratory depression, eye and upper respiratory irritation, nausea, vomiting, weakness, tremors, and epigastric cramps, all of which may resolve rapidly after the exposure ceases. There is one reported industrial fatality caused by inhalation of vapor in a small enclosure, but the level of exposure, symptoms of toxicity, and isomeric composition are unknown (ACGIH 1991). Muscular cramping and vomiting have been relieved by intravenous administration of calcium gluconate (Gosselin 1984). The mechanism of action for the central nervous system effects of 1,2-dichloroethene has not been clearly established, but may be related to solvent effects on cellular membranes. Neurotransmitter effects have also been demonstrated for some solvents, and it is reasonable to speculate that these effects on neurotransmitters might be mitigated by pharmacologic intervention. However, no such interventions are currently available for clinical use.

Fatty degeneration of the liver has been reported in animal studies, but 1,2-dichloroethene appears to have less hepatic and renal toxicity than many other chlorinated hydrocarbons (ACGIH 1991).

However, ethanol in alcoholic beverages may compete with or enhance the metabolic activation of solvents and can increase the severity of health effects, particularly liver toxicity. Alcoholic beverages should be avoided following exposure to 1,2dichloroethene and other solvents.

2.10 ADEQUACY OF THE DATABASE

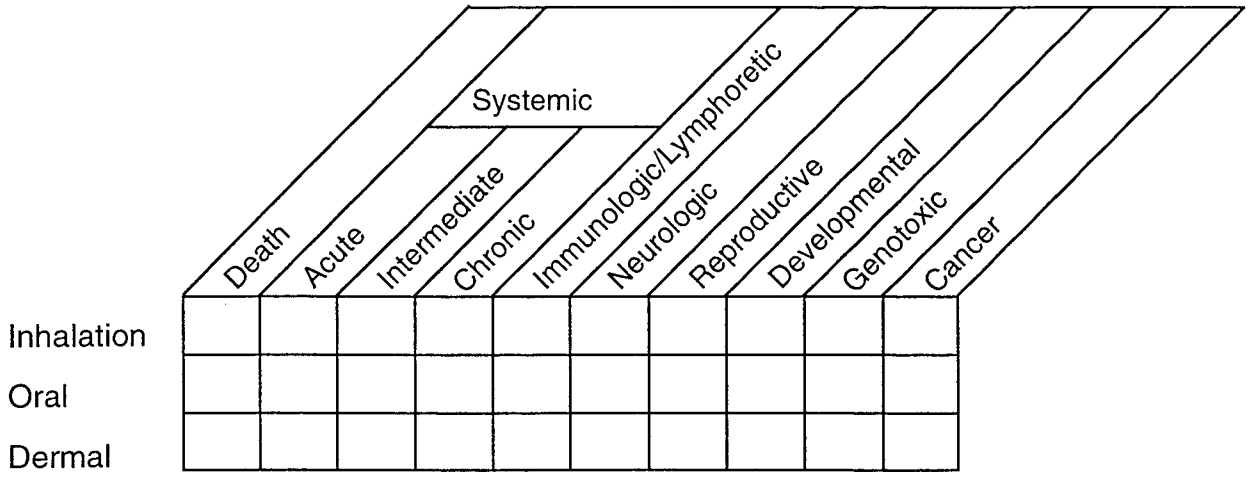
Section 104(i)(5) of CERCLA, as amended, directs the Administrator of ATSDR (in consultation with the Administrator of EPA and agencies and programs of the Public Health Service) to assess whether adequate information on the health effects of 1,2-dichloroethene is available. Where adequate information is not available, ATSDR, in conjunction with the National Toxicology Program (NTP), is required to assure the initiation of a program of research designed to determine the health effects (and techniques for developing methods to determine such health effects) of 1,2-dichloroethene.

The following categories of possible data needs have been identified by a joint team of scientists from ATSDR, NTP, and EPA. They are defined as substance-specific informational needs that if met would reduce the uncertainties of human health assessment. This definition should not be interpreted to mean that all data needs discussed in this section must be filled. In the future, the identified data needs will be evaluated and prioritized, and a substance-specific research agenda will be proposed.

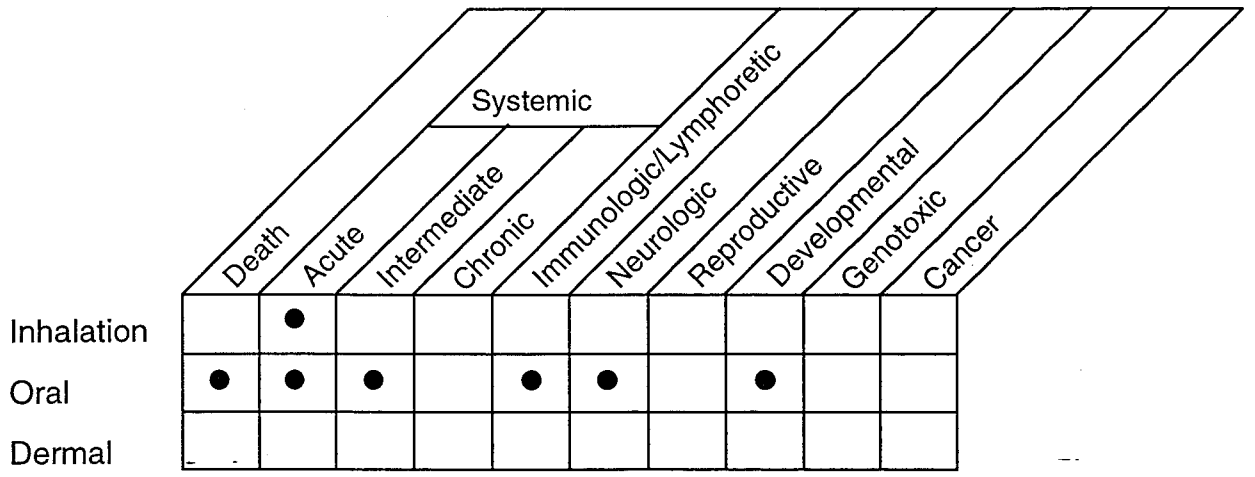
2.10.1 Existing Information on Health Effects of 1,2-Dichloroethene

The existing data on health effects of inhalation, oral, and dermal exposure of humans and animals to 1,2-dichloroethene are summarized in Figures 2-4 and 2-5. The purpose of these figures is to illustrate the existing information concerning the health effects of 1,2-dichloroethene. Each dot in the figure indicates that one or more studies provide information associated with that particular effect. The dot does not necessarily imply anything about the quality of the study or studies, nor should missing information in this figure be interpreted as a "data need." A data need, as defined in ATSDR's *Decision Guide for Identifying Substance-Specific Data Needs Related to Toxicological Profiles* (ATSDR 1989),-is substance-specific information necessary to conduct comprehensive public health assessments. Generally, ATSDR defines a data gap more broadly as any substance-specific information missing from the scientific literature.

Figure 2-4. Existing Information on Health Effects of cis-1,2-Dichloroethene



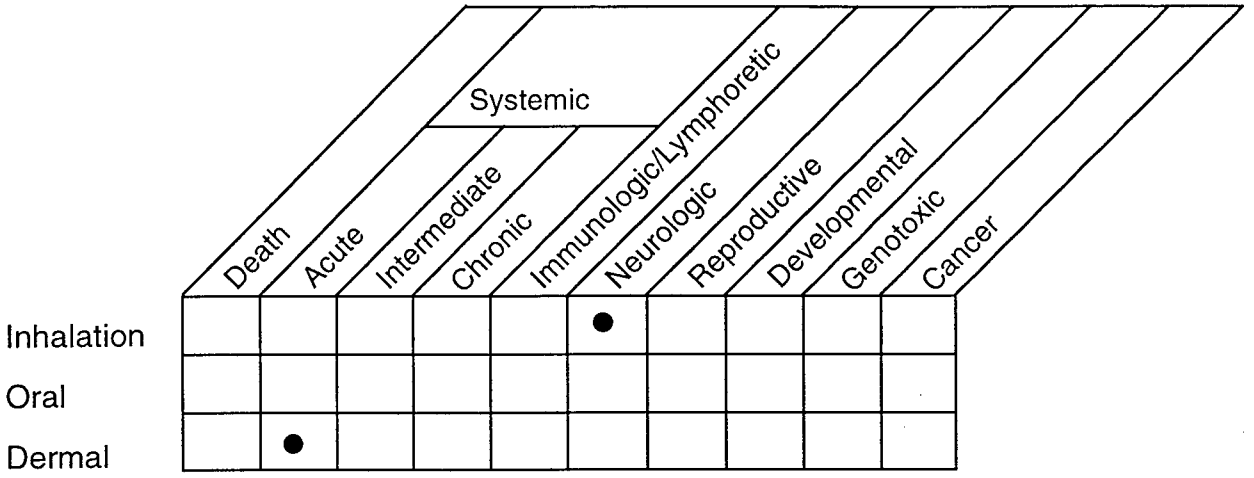
Human



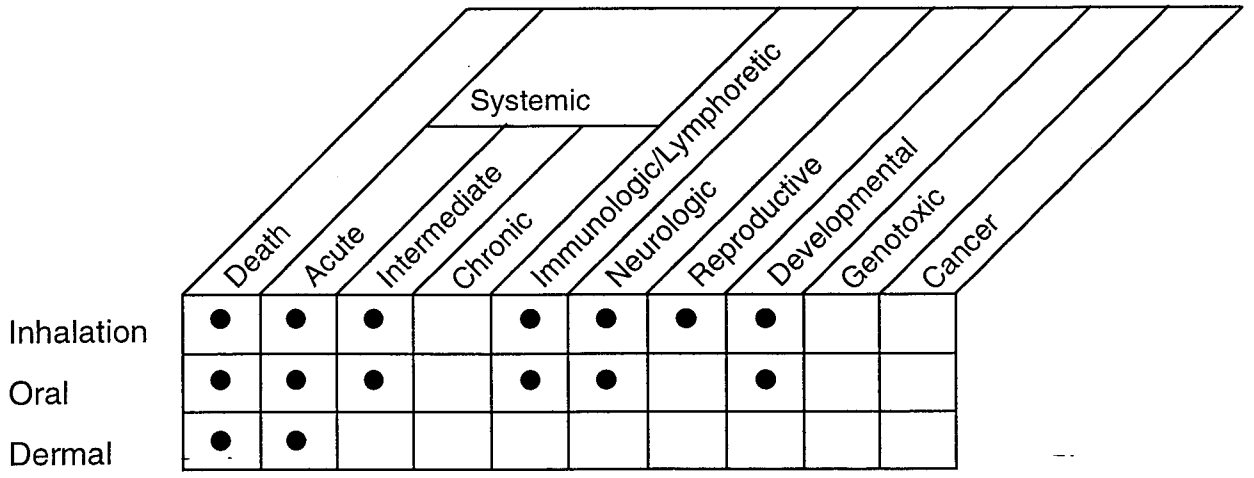
Animal

● Existing Studies

Figure 2-5. Existing Information on Health Effects of trans-1,2-Dichloroethene



Human



Animal

● Existing Studies

2. HEALTH EFFECTS

There are very few studies or case reports of human exposure to 1,2-dichloroethene by any route of exposure. One report describes neurologic symptoms in humans following acute inhalation of trans-1,2-dichloroethene. This property of depressing the central nervous system is an important effect of 1,2-dichloroethene exposure. Another study reported an industrial fatality related to accidental inhalation exposure to 1,2-dichloroethene (isomeric composition unknown).

Information has been reported regarding the lethality and toxic effects of trans-1,2-dichloroethene in animals exposed by the inhalation and oral routes for acute and intermediate durations. For inhalation and oral exposure routes, toxicity to the heart, liver, blood, and lung has been reported. Central nervous system depression has been reported in animals given lethal doses of trans-1,2-dichloroethene by the oral route. Several studies examined the effects of either cis- or trans-1,2-dichloroethene on the immune systems of mice exposed by inhalation or oral routes. A 14-day and a 90-day gavage study of cis-1,2-dichloroethene found hematological effects in rats. No information is available on the toxic effects of chronic exposure to either cis- or trans-1,2-dichloroethene by any route. In addition to central nervous system effects, inhalation exposure to trans- 1,2-dichloroethene appears to affect development of the fetus and development of the newborn and young. When inhaled, there also may be effects on reproduction because of reduced maternal weight gain and reduced litter size. As shown in Figures 2-4 and 2-5, no information on carcinogenic effects in animals by inhalation, oral, or dermal exposure is available for either cis- or trans-1,2-dichloroethene. No studies were located regarding genotoxic effects in humans or animals after inhalation, oral, or dermal exposure to 1,2-dichloroethene, but studies in mice injected intraperitoneally indicate that the cis isomer may be genotoxic; the trans isomer has shown no indication of being genotoxic.

2.10.2 Identification of Data Needs

Acute-Duration Exposure. Reliable health effects data for human exposure by any route to 1,2-dichloroethene were not located. One human fatality was reported, but the cause of death, the length of exposure, and the concentration and isomeric identity of 1,2-dichloroethene in the air were not described (Hamilton 1934). Two human volunteers reported mild burning of the eyes after acute dermal exposure to trans-1,2-dichloroethene (Lehmann and Schmidt-Kehl 1936). However, the methods used in 1936 to generate and test for exposure levels were relatively insensitive, and it is unclear whether the 1,2-dichloroethene was in an aerosol or gaseous state. No information was located for systemic toxicity in humans after oral exposure or for the relative toxicities of the cis and trans

isomers of 1,2-dichloroethene in humans. The acute lethal levels of trans-1,2-dichloroethene were established after inhalation exposure in mice and after oral exposure in mice and rats (Barnes et al. 1985; Freundt et al. 1977; Gradiski et al. 1978; Hayes et al. 1987; Kallman et al. 1983; McMillan 1986; Munson et al. 1982). An acute-duration inhalation MRL was derived from the Freundt et al. (1977) study, based on the hepatic effect of fatty degeneration of the liver seen at 200 ppm in rats. A wide range of LD_{50} values for the trans isomer, 1,300-10,000 mg/kg/day, exists in the present literature. Inhalation LC_{50} and oral LD_{50} values for cis-1,2-dichloroethene are not well defined. One study suggests an LD_{50} around 5,000 mg/kg/day for the cis isomer (McMillan 1986). Pathological lesions in the heart, liver, and lungs were reported in rats after acute inhalation exposure to trans-1,2-dichloroethene; however, the study was limited in size and scope (Freundt et al. 1977). Neurological problems, such as narcosis, lethargy, and behavioral changes, have been shown with acute inhalation of both cis and trans isomers (De Ceaurriz et al. 1983; Hurtt et al. 1993). Oral exposure to 1,2-dichloroethene is also associated with central nervous system depression and other neurological effects (Barnes et al. 1985; Hayes et al. 1987). The finding of acetone in the air exhaled by 1,2-dichloroethene-exposed rats indicates possible alterations in lipid and fatty acid metabolism at high exposure levels (Filser and Bolt 1980). This may support the observation of fatty infiltration of liver in the rat inhalation study. Evidence of target effects for oral acute exposure exists for both the cis and trans isomers. Hematotoxicity after acute oral exposure to cis- and trans-1,2-dichloroethene was reported in rats and mice and included adverse effects of decreases in fibrinogen levels, hematocrit, and erythrocyte counts (Barnes et al. 1985; McCauley et al. 1990). The NOAEL value for decreased hematocrit in female rats was used for the derivation of an acute oral MRL for cis-1,2-dichloroethene. Serious respiratory, cardiovascular, and hepatic effects were also noted in rats exposed orally. Along with the serious responses of pulmonary and fibrous hyperemia, alveolar distention, cardiac muscle changes, and decreases in blood urea nitrogen, milder hepatic changes were recorded (Barnes et al. 1985; Freundt et al. 1977; McCauley et al. 1990; McMillan 1986). Limited data were located for dermal exposure to trans-1,2-dichloroethene indicating mild to moderate, reversible, dermal and ocular effects (Brock 1990; Hurtt et al. 1993; Lehmann and Schmidt-Kehl 1936). The available toxicity data do not allow a definitive conclusion regarding the relative toxicity of the cis and tram isomers. However, *in vivo* and *in vitro* studies suggest differences in the metabolism of the two isomers (Filser et al. 1978, 1979, 1982; Gargas et al. 1988, 1989, 1990; Sato and Nakajima 1979). Furthermore, pharmacokinetic data are insufficient to identify target organs for either isomer across routes of exposure. Further studies to identify target organs of cis- and trans-1,2-dichloroethene toxicity and to assess dose-response relationships would be particularly useful

for inhalation and dermal exposure routes. Additional oral exposure studies would increase the possibilities of assessing dose-response relationships and target organs. The information is important for populations living near hazardous waste sites that might be exposed to 1,2-dichloroethene for brief periods of time.

Intermediate-Duration Exposure. No studies were located regarding intermediate-duration exposure to 1,2-dichloroethene in humans by any route of exposure. Liver and lung toxicity of trans-1,2-dichloroethene in rats, similar to that found with acute exposure, was observed after intermediate-duration inhalation exposure (Freundt et al. 1977). The exposure level that was associated with capillary hyperemia, alveolar distention and pneumonic infiltration, and fatty accumulation in liver lobules and Kupffer cells was the same as that tested with acute exposure; therefore, an intermediate inhalation MRL at the same level as the acute inhalation MRL was derived. Studies in rats and mice exposed orally to trans-1,2-dichloroethene at doses ranging from 17 to 3,100 mg/kg/day (Barnes et al. 1985; Hayes et al. 1987; McCauley et al. 1990; McMillan 1986; Shopp et al. 1985) have examined many target organs including the blood, liver, kidneys, lungs, heart and immune system. Respiratory (lung weight), hematological (blood cell counts), and body weight effects were reported at doses of 100 to 400 mg/kg/day (Barnes et al. 1985; McCauley et al. 1990; McMillan 1986). Hepatic effects in male mice at 175 mg/kg/day and a NOAEL at 17 mg/kg/day are the basis for an intermediate-duration oral MRL for trans-1,2-dichloroethene (Barnes et al. 1985). Hematologic effects at 97 mg/kg/day and a NOAEL at 32 mg/kg/day are the basis of an intermediate-duration oral MRL for cis-1,2-dichloroethene. A 60-day oral study of trans-1,2-dichloroethene in rats, available as an abstract, indicated that the lungs, spleen, and kidney are targets (see Section 2.10.3). The full published report may provide dose-response data when it becomes available. The differences in the observed effects of cis- and trans-1,2-dichloroethene that were seen in rats in the oral 90-day studies may be due to differences in toxicity of these isomers as discussed above (see acute-duration exposure) (Barnes et al. 1985; Hayes et al. 1987; McCauley et al. 1990; McMillan 1986; Shopp et al. 1985). No studies were located regarding 1,2-dichloroethene toxicity in animals after dermal exposure. Additional studies regarding 1,2-dichloroethene toxicity after inhalation exposure are necessary, with a specific need for inhalation studies using the cis isomer. Because people living near hazardous waste sites may be exposed for longer periods of time, more dose-response data for intermediate-duration exposures by all routes are important. The target organs-liver, blood, and lungs-should be emphasized.

2. HEALTH EFFECTS

Chronic-Duration Exposure and Cancer. No human or animal data were located regarding health effects of long-term (chronic) exposure to 1,2-dichloroethene by inhalation, oral, or dermal routes. Therefore, no chronic MRLs could be derived. There is a need to conduct chronic animal studies with the isomers of 1,2-dichloroethene by inhalation, oral and dermal routes. These studies could provide information on subtle toxicological changes in organs/systems and on dose-response relationships associated with 1,2-dichloroethene toxicity. Furthermore, there are communities around hazardous sites that may be exposed to low levels of 1,2-dichloroethene for long periods of time.

No studies were located regarding the carcinogenic potential of 1,2-dichloroethene in humans and animals following inhalation, oral, or dermal exposure. However, genotoxicity studies revealed mutagenic activity of the cis isomer in the host-mediated assay (Cantelli-Forti and Bronzetti 1988; Cema and Kypenova 1977; Galli et al. 1982; Greim et al. 1975; Sawada et al. 1987). Furthermore, a 60-day oral study of trans-1,2-dichloroethene in rats, which was available in abstract form, indicated a high incidence of lymphosarcoma in the lungs (see Section 2.10.3). Although this study has not yet been published, it raises a concern about the carcinogenicity of 1,2-dichloroethene, which should be further investigated in long-term oral and inhalation studies of both isomers. In humans, dermal exposure is less likely than oral or inhalation exposure; however, dermal studies could add valuable insights about 1 ,2dichloroethene toxicity.

Genotoxicity. No study was located regarding 1,2-dichloroethene genotoxicity in humans. Neither isomer of 1,2-dichloroethene was mutagenic in in vitro experiments with *E. coli, S. typhimurium*, and S. cerevisiae (Cantelli-Forti and Bronzetti 1988; Cema and Kypenova 1977; Galli et al. 1982; Greim et al. 1975). Neither isomer produced chromosomal aberrations or sister chromatid exchanges in Chinese hamster cells (Sawada et al. 1987). Reductions in numbers of convertants and revertants (positive results) were obtained with the cis isomer, but not the trans isomer, in host-mediated assays in mice (Cantelli-Forti and Bronzetti 1988). Furthermore, repeated intraperitoneal injections of the cis isomer induced chromosomal aberrations in mouse bone marrow cells (Cema and Kypenova 1977); thus, cis-1,2-dichloroethene may be a potential mutagen in animals. The weight of evidence ef genotoxicity is still small; additional studies would help to confirm the existing information or uncover unknown genetic effects. Chronic animal studies might elucidate the potential for, or isomeric differences in, cancer development. If an appropriate group of exposed workers could be identified, cytogenetic testing might help determine 1 ,2dichloroethene's genotoxic potential in humans.

2. HEALTH EFFECTS

Reproductive Toxicity. No studies were located regarding reproductive toxicity of 1,2-dichloroethene in humans by inhalation, oral, or dermal exposure. No studies were located regarding reproductive toxicity of 1,2-dichloroethene in animals following dermal exposure. An inhalation study published in 1993 (Hurtt et al. 1993) is the sole report to address the reproductive effects of 1,2-dichloroethene. In this study, maternal weight gain was reduced, proportional to dose, and possible increases in resorption were reported. In other studies, histopathological examination of the reproductive organs of animals exposed orally for 90 days to 1,2-dichloroethene has not shown effects on reproductive organs (Hayes et al. 1987; McCauley et al. 1990). Further investigation of reproductive effects, including results of dermal exposure, are necessary for understanding possible effects suggested by the existing evidence on the reproductive system.

Developmental Toxicity. No studies were located regarding developmental effects in humans after inhalation, oral, or dermal exposure to cis- or trans-1,2-dichloroethene. No data are available on developmental effects in animals after oral or dermal exposure to 1,2-dichloroethene. Fetal weights appear to be reduced after exposure to 1,2-dichloroethene, as shown in an inhalation study (Hurtt et al. 1993). During critical developmental stages (days 7-16 in rats), trans-1,2-dichloroethene exposure was associated with reduced weight gain in rat pups at a level of 12,000 ppm. Additional developmental toxicity studies in animals by inhalation, oral, and dermal exposure may provide relevant information for humans exposed near hazardous waste sites.

Immunotoxicity. No information about 1,2-dichloroethene toxicity to the human immune system was located. Findings of fatty degeneration of Kupffer cells, decreased numbers of white blood cells, and pneumonic infiltration in rats after inhalation exposure to trans-1,2-dichloroethene (Freundt et al. 1977), and of suppressed humoral immune status in male mice exposed to trans.-1,2-dichloroethene in drinking water for 90 days, as measured by mouse spleen cell antibody production (Shopp et al. 1985), suggest that 1,2-dichloroethene may be immunotoxic. Immunological studies of cis- 1 ,2dichloroethene and additional studies of trans-1,2-dichloroethene would help determine more definitely the immunotoxic potential and possible differences between the isomers. No immunotoxicity-data in animals were located for the dermal route of exposure. New dermal studies would be valuable, both because no such studies have been reported and because of the potential immuno-dermal effects of dermal exposure.

2. HEALTH EFFECTS

Neurotoxicity. Symptoms of central nervous system depression (vertigo, drowsiness, intracranial pressure, nausea) were observed in two human volunteers during a 30-minute inhalation exposure to 1,2-dichloroethene. The symptoms disappeared after discontinuation of exposure (Lehmann and Schmidt-Kehl 1936). No information was located regarding neurotoxicity after exposure by other routes of exposure in humans. In animals, inhalation exposure to 1,2dichloroethene was associated with behavioral changes, narcosis, and lethargy at levels ranging from 1,700 to 12,000 ppm (De Caurriz et al. 1983; Hurtt et al. 1993). Similarly, symptoms of central nervous system depression were observed in rodents after acute oral exposure to 1,2-dichloroethene (Barnes et al. 1985; Hayes et al. 1987; McCauley et al. 1990; Munson et al. 1982). The observations were restricted to behavioral tests. Further information regarding 1 ,2dichloroethene neurotoxicity in animals after exposure by inhalation, oral, and dermal routes would be valuable. Animal studies of the effects of 1,2-dichloroethene on the morphology of neurons, glial and myelinated cells, and on the synthesis and degradation of neurotransmitters would permit more accurate assessment of neurotoxic potential of this chemical.

Epidemiological and Human Dosimetry Studies. No epidemiologic studies of populations exposed to 1,2-dichloroethene were located. The general population might be exposed to low levels of 1,2-dichloroethene in contaminated urban air or in contaminated drinking water, or possibly by dermal contact. The occupationally exposed population is relatively small (285 individuals) (NIOSH 1988). The confounding exposure to other related compounds makes it difficult to perform an epidemiological study for 1,2-dichloroethene. Animal studies suggest that hematological, hepatic, neurological and reproductive effects would be the end points of concern (Barnes et al. 1985; Freundt et al. 1977; Hurtt et al. 1993; McCauley et al. 1990; McMillan 1986). Therefore, if a worker or a population with appropriate exposure can be identified, epidemiological studies could be designed to study the possibility that similar effects may be observed in humans. Studies that correlate exposure with blood or urine levels of biomarkers and/or with effects would be useful in establishing causality. The knowledge of a dose-effect relationship would be useful for monitoring individuals near hazardous waste sites for preventive purposes.

Biomarkers of Exposure and Effect.

Exposure. Methods exist for determining 1,2-dichloroethene in blood and biological tissues (Ashley et al. 1992; Hara et al. 1980; Lin et al. 1982; Raymer et al. 1990; Streete et al. 1992; Uehori et al. 1987), but specific levels of 1,2-dichloroethene have not been correlated with exposure. Exhalation of

acetone and the presence of acetone in blood have been noted in rats after inhalation exposure to cis and trans-1,2-dichloroethene, but the amounts exhaled or the levels in blood have not been correlated with exposure levels (Freundt et al. 1977). Furthermore, acetonemia is not specific for 1,2-dichloroethene; increased acetone levels were found after exposure to other chemicals (e.g., vinyl chloride and perchlorethylene) and in patients with diseases such as diabetes (Filser and Bolt 1980). Studies focusing on correlating blood or urine levels of 1,2-dichloroethene or its metabolites with exposure levels would be useful to facilitate future medical surveillance that can lead to early detection.

Effect. No known biomarkers are currently used to characterize effects caused by 1,2-dichloroethene. Rats exposed by inhalation to halogenated ethylenes, including cis- and trans-1,2-dichloroethene, were shown to exhale acetone (Filser et al. 1978, 1980; Freundt et al. 1977). Based on these studies, a possible mechanism for the production of acetone was suggested, whereby a metabolite (dichloroacetate for 1,2-dichloroethene) inhibits the enzymes of the citric acid cycle, which would lead to an increase in mitochondrial acetyl-coenzyme A and, consequently, to an alteration in lipid and fatty acid metabolism to form ketone bodies (Filser et al. 1982). Further studies that support this hypothesis might determine whether acetone exhalation could serve as a biomarker for such effects as fatty degeneration of the liver, which was observed in rats exposed by inhalation to trans-1,2-dichloroethene (Freundt et al. 1977).

Absorption, Distribution, Metabolism, and Excretion. The absorption, distribution, metabolism and excretion of a chemical can influence its toxicity. Several inhalation studies have examined the absorption of l,2dichloroethene, and they indicate that 1,2-dichloroethene vapors can be absorbed through the lung (Filser and Bolt 1979; Gargas et al. 1988, 1989; Lehmann and Schmidt-Kehl 1936). Studies by Gargas et al. (1988, 1989) and Sato and Nakajima (1979) determined 1,2-dichloroethene partition coefficients between a number of body tissues and show differences between the cis and trans isomers. The cis isomer has higher partition coefficients (tissue:air) and, therefore, greater affinity or absorption in biological tissue. These are important properties that influence toxicological effects. Absorption by the dermal route has not been investigated, although the lipophilic properties of this chemical make it likely. According to an ongoing study, trans-1,2-dichloroethene was quickly absorbed from the gastrointestinal tract of rats after oral exposure (see Section 2.10.3). No other studies on the absorption of 1,2-dichloroethene following oral exposure were located. The few oral toxicity studies support this conclusion (McCauley et al. 1990; McMillan

1986). No studies were located regarding the distribution and excretion of 1,2dichloroethene after inhalation, oral, or dermal exposure.

Cytochrome P-450 has been implicated in the initial step of metabolism of 1,2-dichloroethene in the liver. Subsequent steps are believed to be catalyzed by cytosolic and/or mitochondrial aldehyde and alcohol dehydrogenases or related enzymes (Costa and Ivanetich 1982, 1984). Differences in the metabolism rate and the metabolite profile have been reported for the cis and trans isomers, for example, the cis isomer had a 4-fold greater turnover rate in hepatic microsomes *in vitro* than the trans isomer (Bonse et al. 1975; Costa and Ivanetich 1982, 1984). The metabolism of 1,2-dichloroethene has not been extensively studied in tissues other than the liver. Distribution studies of cis- and trans-1,2-dichloroethene and metabolites would help identify those tissues, if any, that accumulate them. Excretion studies of 1,2-dichloroethene and its breakdown products would be useful for understanding the metabolic fate of this chemical and determining major routes and rates of excretion. One important question to be addressed is the difference in metabolism and excretion at low and high exposure levels.

Comparative Toxicokinetics. Although there are relatively few existing studies for comparative purposes, some general conclusions can be drawn. The human exposure studies consist of two inhalation studies from the 1930s, one of which is too sketchy to use in making any comparisons (Hamilton 1934; Lehmann and Schmidt-Kehl 1936). When two volunteers were exposed for 30 minutes to an unknown ratio of cis:trans 1,2-dichloroethene (Lehmann and Schmidt-Kehl 1936), their neurological responses were consistent with animal studies that show lethargy and drowsiness. No human toxicokinetic or dosimetry data were located. Among the animal species there is general consistency for both inhalation and oral exposure routes in the end points identified. Hepatic, hematological, and neurological end points are found in both rats and mice (Barnes et al. 1985; De Ceaurriz et al. 1983; McCauley et al. 1990; McMillan 1986). Investigation of 1,2-dichloroethene toxicokinetics in different animal species and comparison of detected metabolites with those detected in occupationally exposed individuals would be useful for determining an appropriate animal model for studying the toxicokinetics of 1,2-dichloroethene.

Methods for Reducing Toxic Effects. General recommendations for reducing the absorption and metabolic responses to 1,2-dichloroethene are based on limited mitigation studies and reports found in the primary and review/consensus literature. Few individuals have received intense exposure

to 1 ,2-dichloroethene, whether accidental, clinical or occupational. Its neurological, hepatic, hematic, and respiratory effects are similar to those of other solvents, and therefore, generalized interventions have been drawn from experience with these other solvents. Supportive measures to combat the effects of central nervous system, respiratory depression, and cardiac irritability are the clinical recommendations (TOMES 1994). There is no specific treatment for 1 ,2dichloroethene exposure, partly because its mechanisms of action are not well defined and the numbers of exposed individuals needing treatment are small.

2.10.3 Ongoing Studies

Several abstracts of studies in progress were located. A high incidence of lymphosarcoma in the lungs and histopathological lesions in the spleen and kidneys was reported in rats after 60 days of oral treatment with l/2, l/20, and l/200 of the reported LD_{50} for trans-1 ,2dichloroethene (Witmer et al. 1990). Absorption of trans-1,2-dichloroethene has been studied in rats after intravenous and oral applications (Manning et al. 1990). In these studies, trans-1,2-dichloroethene was quickly absorbed from the gastrointestinal tract reaching peak blood concentrations in 2-6 minutes after exposure.

3. CHEMICAL AND PHYSICAL INFORMATION

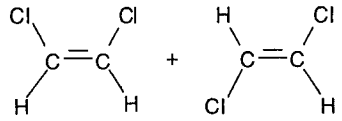
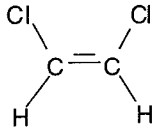
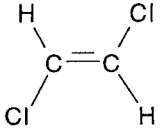
3.1 CHEMICAL IDENTITY

Information regarding the chemical identity of 1,2-dichloroethene is located in Table 3-l.

3.2 PHYSICAL AND CHEMICAL PROPERTIES

Information regarding the physical and chemical properties of 1,2dichloroethene is located in Table 3-2. There are two isomers of 1,2-dichloroethene, the cis form and the trans form. Some important characteristics of the two forms are that they possess a high vapor pressure and the vapor is heavier than air (HSDB 1995). The trans form is sufficiently volatile that 50% evaporates from water in 22 minutes when stirred at 25 °C; the cis form is similarly volatile (HSDB 1995). Experiments have shown that the degradation of the trans form is relatively slow due to ultraviolet irradiation, unless lamps of approximately 15-20 watts are used (Guertler et al. 1994) to allow greater relative stability of the vapor form in the environment.

Table 3-1. Chemical Identity of 1,2-Dichloroethene

Characteristic	Information[a]		
	mixture	cis	trans
Chemical name	1,2,-Dichloroethene	cis-1,2-Dichloroethene	trans-1,2-Dichloroethene
Synonym(s)	Acetylene dichloride;[a,b] 1,2-dichloroethene;[a,c] 1,2-dichloroethylene; sym-1,2-dichloroethylene 1,2-DCE	(Z)-1,2-dichloroethene;[a,b] (Z)-1,2-dichloroethylene;[a,c] cis-acetylene dichloride; cis-1,2-dichloroethylene; cis-dichloroethylene	(E)-1,2-dichloroethene;[a,b] (E)-1,2-dichloroethylene; trans-acetylene dichloride; trans-1,2-dichloroethylene; trans-dichloroethylene
Registered trade name(s)	Dioform[d]	Not available	Not available
Chemical formula	$C_2H_2Cl_2$[a,e]	$C_2H_2Cl_2$[a,e]	$C_2H_2Cl_2$[a,e]
Chemical structure[f]			
Identification numbers:			
CAS registry	540-59-0[a,e]	156-59-2[a,e]	156-60-5[a,e]
NIOSH RTECS	KV9360000[a,g]	KV9420000[a,g]	KV9400000[a,g]
EPA hazardous waste	U079*	Not available	U079
OHM/TADS	8300194[h]	8300194[h]	8300194[h]
DOT/UN/NA/IMO shipping	UN 1150; dichloroethylene IMO 3.2; dichloroethylene	UN 1150; dichloroethylene IMO 3.2; dichloroethylene	UN 1150; 1,2-dichloroethylene IMO 3.2; 1,2-dichloroethylene
HSDB	149	5656	6361
NCI	C56031[a,c]	Not available	Not available

*This number, U079, applies to trans-1,2-dichloroethene and to the generic 1,2-dichloroethene; 1,2-dichloroethene is a mixture containing trans-1,2-dichloroethene (HSDB 1995). In effect, the hazardous waste number U079 refers to a mixture containing trans-1,2-dichloroethene.

[a]All information obtained from HSDB 1995, except where noted.
[b]SANSS 1994
[c]Chemline 1988
[d]Bennett 1981
[e]CAS 1994
[f]Merck 1989
[g]RTECS 1994
[h]OHM/TADS 1988

CAS = Chemical Abstracts Service; DOT/UN/NA/IMO = Dept. of Transportation/United Nations/ North America/International Maritime Dangerous Goods Code; EPA = Environmental Protection Agency; HSDB = Hazardous Substances Data Bank; NCI = National Cancer Institute; NIOSH = National Institute for Occupational Safety and Health; OHM/TADS = Oil and Hazardous Materials/Technical Assistance Data System; RTECS = Registry of Toxic Effects of Chemical Substances

Table 3-2. Physical and Chemical Properties of cis- and trans-1,2-Dichloroethene

Property	Information		Reference
	cis	trans	
Molecular weight	96.95	96.95	Weast 1983; Merck 1989
Color	Colorless	Colorless	Hawley 1981; HSDB 1995
Physical state	Liquid	Liquid	Hawley 1981; HSDB 1995
Melting point	-81.5 °C -80.5 °C	-49.4 °C -50.0 °C	Weast 1983; Merck 1989 HSDB 1995
Boiling point	59.6 °C @ 745 mm Hg 60.3 °C @ 760 mm Hg	47.2 °C 745 mm Hg 48.0–48.5 °C @ 760 mm Hg	Weast 1983; Merck 1989
Density at 20/4 °C	1.2837	1.2565	Weast 1983; HSDB 1995
Odor	Ethereal, slightly acrid Sweet pleasant	Ethereal, slightly acrid Sweet pleasant	Merck 1989; HSDB 1995 HSDB 1995
Odor threshold:			
Water	No data	0.26 ppm	HSDB 1995
Air	No data	17 ppm v/v 0.084 ppm	Amoore and Hautala 1983 HSDB 1995
Solubility:			
Water at 25 °C	3.5 g/L	6.3 g/L	Horvath 1982; HSDB 1995
Organic solvents	Soluble in ether, alcohol, benzene, acetone, chloroform	Soluble in ether, alcohol, benzene, acetone, chloroform	Weast 1983; HSDB 1995
Partition coefficients:			
Log K_{ow}	1.86	2.09 (recommended value) 2.06	Hansch and Leo 1985; HSDB 1995
Log K_{oc}	1.69 (estimated)	1.56 (estimated)	HSDB 1995
Vapor pressure at 20 °C	180 mm Hg	265 mm Hg	Stevens 1979
Vapor pressure at 30 °C	273 mm Hg; 250 mm Hg	395 mm Hg; 410 mm Hg	HSDB 1995; Stevens 1979

TABLE 3-2. Physical and Chemical Properties of cis- and trans-1,2-Dichloroethene (continued)

Property	Information		Reference
	cis	trans	
Henry's law constant at 24.8 °C	4.08×10^{-3} atm-m^3/mol	9.38×10^{-3} atm-m^3/mol	Gossett 1987
	3.37×10^{-3} atm-m^3/mol	6.72×10^{-3} atm-m^3/mol	HSDB 1995
Autoignition temperature	460 °C	460 °C	Sax 1979
Flashpoint	6 °C	2–4 °C	Stevens 1979; HSDB 1995
Flammability limits in air	9.7–12.8 volume %	9.7–12.8 volume %	HSDB 1995
Conversion factors:			
ppm (v/v) to mg/m^3 in air at 25 °C	1 ppm (v/v) = 3.96 mg/m^3	1 ppm (v/v) = 3.96 mg/m^3	
mg/m^3 to ppm (v/v) in air at 25 °C	1 mg/m^3 = 0.25 ppm (v/v)	1 mg/m^3 = 0.25 ppm (v/v)	
Explosive limits	9.7–12.8% in air	9.7–12.8% in air	HSDB 1995; Stevens 1979

HSDB = Hazardous Substances Data Bank; v/v = volume per volume

4. PRODUCTION, IMPORT/EXPORT, USE, AND DISPOSAL

4.1 PRODUCTION

1,2-Dichloroethene has been produced as a commercial end product by the direct chlorination of acetylene at about 40 °C or by a technique involving the dehydrochlorination of l,l,2trichloroethane at 500 °C (HSDB 1995). Such commercial preparations are mixtures of cis- and trans-l,2dichloroethene. The trans isomer is preferred in most industrial applications, which has tended to limit sales of the commercially available mixtures (HSDB 1995). 1,2-Dichloroethene is highly flammable and extremely corrosive, and yields the explosive compound chloroacetylene in the presence of copper or heated alkaline solutions (HSDB 1995).

Industrial quantities of 1,2-dichloroethene are produced for on-site use in the production of other chlorinated compounds, which are the final commercial product. Columbia Organics of South Carolina, and Aldrich Chemical of Milwaukee, Wisconsin, sell research quantities of 1,2-dichloroethene (cis, trans, and mixture); Columbia Organics also sells cis-1,2-dichloroethene in 55-gallon drums (Kuney 1988; Van 1988). Complete data about the volume and trends of 1,2-dichloroethene production in the United States are not available (HSDB 1995). As with many chemicals, especially those whose production or use involves proprietary information, quantitative estimates of production are virtually impossible to obtain (Bason and Colbom 1992). Table 4-l lists the facilities in each state that manufacture or process 1,2-dichloroethene, the intended use, and the range of maximum amount of 1,2-dichloroethene that is stored at the site. The data listed in Table 4-l are derived from the Toxics Release Inventory (TR193 1995). Only certain types of facilities were required to report and therefore this is not an exhaustive list. Twelve facilities were identified as producers or processors of 1,2-dichloroethene, with most of the producers located in Gulf Coast states (Louisiana and Texas).

4.2 IMPORT/EXPORT

No data were found on U.S. imports or exports of 1,2-dichloroethene (HSDB 1995).

Table 4-1. Facilities That Manufacture or Process 1,2-Dichloroethene

Facility	Location[a]	Range of maximum amounts on site in pounds	Activities and uses
VULCAN CHEMICALS	WICHITA, KS	10,000-99,999	Produce; As a by-product; As a reactant
WESTLAKE MONOMERS CORP.	CALVERT CITY, KY	100,000-999,999	Produce; For on-site use/processing; As a reactant
VULCAN MATERIALS CO.	GEISMAR, LA	1,000-9,999	Produce; For on-site use/processing; As a by-product; As an impurity; As a reactant
NA	LA	100,000-999,999	Produce; As a by-product
PPG IND. INC.	LAKE CHARLES, LA	100,000-999,999	Produce; For sale/distribution; As a by-product; As an impurity
NA	LA	100,000-999,999	Produce; As a by-product
DOW CHEMICAL CO.	LA	10,000-99,999	Produce; As a by-product; As an impurity
DOW CHEMICAL CO.	FREEPORT, TX	100,000-999,999	Produce; For on-site use/processing; As a by-product; As an impurity; As a chemical processing aid
UNION CARBIDE CORP.	TEXAS CITY, TX	No Data	Produce; As a by-product
OCCIDENTAL PETROLEUM CORP.	TX	10,000-99,999	Produce; As a by-product
GEON CO.	LA PORTE, TX	1,000-9,999	Produce
OCCIDENTAL PETROLEUM CORP.	TX	10,000-99,999	Produce; As a by-product

Source: TRI93 1995

[a] Post office state abbreviations used

NA = not available

4. PRODUCTION, IMPORT/EXPORT, USE, AND DISPOSAL

4.3 USE

1,2-Dichloroethene is used primarily as a chemical intermediate in the synthesis of chlorinated solvents and compounds. It has also been used as a solvent for waxes, resins, acetylcellulose, perfumes, dyes, lacquers, thermoplastics, fats, and phenols. It is used in the extraction of rubber, as a refrigerant, in the manufacture of pharmaceuticals and artificial pearls, and in the extraction of oils and fats from fish and meat (HSDB 1995). It has also been used as a low-temperature extraction solvent for organic materials such as decaffeinated coffee (HSDB 1995). No information is available about how much, if any, 1,2-dichloroethene is currently used for solvent purposes. The trans isomer is more widely used in industry than either the cis isomer or the commercial mixture (Gosselin et a1.1984).

4.4 DISPOSAL

1,2-Dichloroethene may be released from industries in waste water streams; however, these compounds can be removed from waste water by air stripping (Dilling 1977; Gossett 1987; Shen 1982a). Improved waste water treatment methods at publicly owned treatment works (POTWs) now use air stripping processes to remove most 1,2-dichloroethene and other volatile organic compounds (VOCs) from final effluents and deposit them in sludges or release them in air emissions (Bennett 1989). Product residues and sorbent media containing 1,2-dichloroethene may be packaged in epoxy-lined drums and disposed of at an EPA-approved landfill (OHM/TADS 1988). 1,2-Dichloroethene is a potential candidate for rotary kiln incineration at 820-1,600 °C with residence times of seconds for liquids and gases, and longer for solids; fluidized bed incineration at 450-980 °C with residence times of seconds for liquids and gases, and longer for solids; and liquid injection incineration at 650-1,600 °C with residence times of 0.1-2 seconds (HSDB 1995). Care must be exercised to assure complete combustion to prevent the formation of phosgene. Acid scrubbers are required to control air emissions. Information regarding the amount disposed of by each method is not available.

Experiments using a vacuum-ultraviolet excimer flow-through reactor to degrade chloro-organic compounds in water have had promising results (Baum and Oppenlander 1995). After 60 minutes of irradiation at 172 nm, the level of 1,2-dichloroethene in contaminated groundwater was reduced from 25 mg/L to below the detection limit of 0.1 mg/L. After 180 minutes of irradiation, more than 93% of the originally organic- bound chlorine atoms were converted to inorganic chloride ions.

4. PRODUCTION, IMPORT/EXPORT, USE, AND DISPOSAL

The EPA has identified trans- 1,2dichloroethene as a hazardous waste; its disposal is regulated under the Resource Conservation and Recovery Act (RCRA). Cis-1,2-dichloroethene has not been identified as a hazardous waste by the EPA. Specific information on federal regulations concerning hazardous waste disposal by land treatment, landfilling, incineration, thermal treatment, chemical/physical/biological treatment, underground injection and deep sea injection appears in the Code of Federal Regulations (40 CFR 190 to 399). Release of trans-1,2-dichloroethene in waste water is regulated under the Clean Water Act by the National Pollutant Discharge Elimination System (NPDES). Information regarding effluent guidelines and standards for trans-1 ,2dichloroethene can be found in 40 CFR 122, 40 CFR 125, 40 CFR 413.02(i), 40 CFR 414, and 40 CFR 433.11(e).

Pursuant to RCRA Section 3004(g)(5), EPA has restricted the land disposal of trans-1,2-dichloroethene (EPA 1988b). It may be disposed on land only if prior treatment standards have been met, or if disposal occurs in units that satisfy the statutory no-migration standard (EPA 1988b). Proper guidelines and standards are outlined in the Code of Federal Regulations (EPA 1988b). Current criteria for land treatment or burial are subject to significant revision; prior to implementing land disposal of waste residue (including waste sludge) environmental regulatory agencies should be consulted for guidance on acceptable disposal practices (HSDB 1995; OHM/TADS 1988).

Rules and regulations regarding disposal practices are discussed in Chapter 7.

5. POTENTIAL FOR HUMAN EXPOSURE

5.1 OVERVIEW

1,2-Dichloroethene is a compound produced by human industrial activities. Sources of environmental exposure to 1,2-dichloroethene include: process and fugitive emissions from its production and use as a chemical intermediate; evaporation from waste water streams, landfills, and solvents; emissions from combustion or heating of polyvinyl chloride and some vinyl copolymers; formation via anaerobic biodegradation of some chlorinated solvents; and leaching from landfills. Most of the l,2dichloroethene released in the environment will eventually enter the atmosphere or groundwater, where it may be subject to further biotic or abiotic degradation processes.

1 ,2-Dichloroethene is removed from the atmosphere chiefly through reaction with photochemically-generated oxygenated species (e.g., hydroxyl radicals). The estimated atmospheric lifetimes for cis- and trans-1,2-dichloroethene due to this removal process are 12 and 5 days, respectively (Goodman et al. 1986). Precipitation may also remove it; however, most 1,2-dichloroethene thus removed will probably reenter the atmosphere by volatilization. When released to surface water, volatilization is expected to be the primary fate process, with an estimated half-life of about 3-6 hours in a model river (Thomas 1982). When released to soil, 1,2-dichloroethene volatilizes rapidly from moist soil surfaces and leaches through subsurface soil, where it could become a groundwater contaminant. In groundwater, 1,2-dichloroethene is susceptible to anaerobic biodegradation. Experimental data indicate that the anaerobic biodegradation half-life of 1,2-dichloroethene is about 13-48 weeks (Barrio-Lage et al. 1986). Aerobic or facultative biodegradation processes have also been documented (Vannelli et al. 1990). Since 1,2-dichloroethene will often be found in mixtures with other chlorinated solvents, half-lives for degradation processes can be estimated only approximately.

The general population may be exposed to low levels (0.013-0.076 ppb) of 1,2-dichloroethene through inhalation of contaminated air in urban areas (EPA 1983a). These exposure levels correspond to an average daily intake of l-6 μg/day assuming an average daily intake of 20 m^3 of air. Additional exposure may occur from contaminated tap water, through consumption, inhalation during showering, and dermal contact. Occupational exposure may occur by inhalation and/or dermal contact. According to a 1981-1983 NIOSH survey, an estimated 215 workers in the United States are

potentially exposed to 1,2-dichloroethene in the workplace (NIOSH 1988). This figure does not include firefighters and landfill workers.

Cis-1,2-dichloroethene has been identified in at least 146 of the 1,430 current or former EPA National Priorities List (NPL) hazardous waste sites and trans-1,2-dichloroethene has been identified in at least 563 of the current or former NPL sites. In 336 of the NPL sites, 1,2-dichloroethene was identified but the isomer was not specified (HazDat 1996). However, the number of sites evaluated for 1,2-dichloroethene is not known. The frequency of these sites can be seen in Figures 5-1, 5-2, and 5-3, for cis, trans, and unspecified, respectively. Two of the sites where trans-1,2-dichloroethene was found are located in the Commonwealth of Puerto Rico (not shown) and all other sites are located in the United States.

5.2 RELEASES TO THE ENVIRONMENT

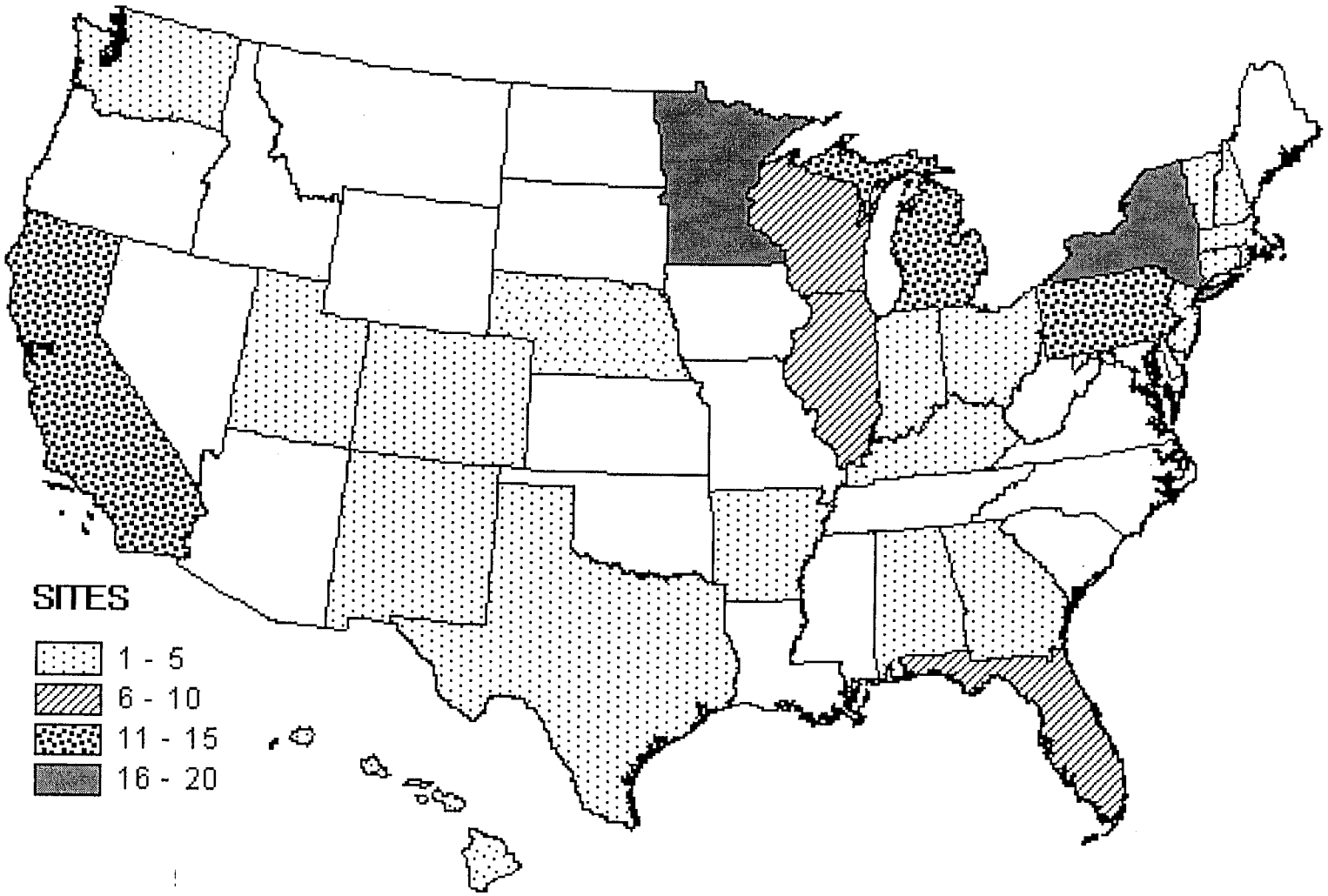
5.2.1 Air

1,2Dichloroethene may be released to the atmosphere in emissions from production facilities, contaminated waste waters, contaminated waste disposal sites, and the pyrolysis and combustion of polyvinyl chloride and some vinyl copolymers. It may also be released during its use as a solvent and extractant, in organic synthesis, and in the manufacture of perfumes, lacquers, and thermoplastics. (HSDB 1995; Michal 1976; Shen 1982b). Not enough data are currently available to estimate the total amount of 1,2-dichloroethene released to the atmosphere.

According to the Toxics Release Inventory (TRI), an estimated total of 29,478 pounds of 1,2-dichloroethene representing >99.9% of the total environmental release was discharged to air from manufacturing and processing facilities in the United States in 1993 (TR193 1995). Table 5-l lists the amounts released from each of these identified facilities. The TRI data should be used with caution since only certain types of facilities are required to report. Therefore, this is not an exhaustive list.

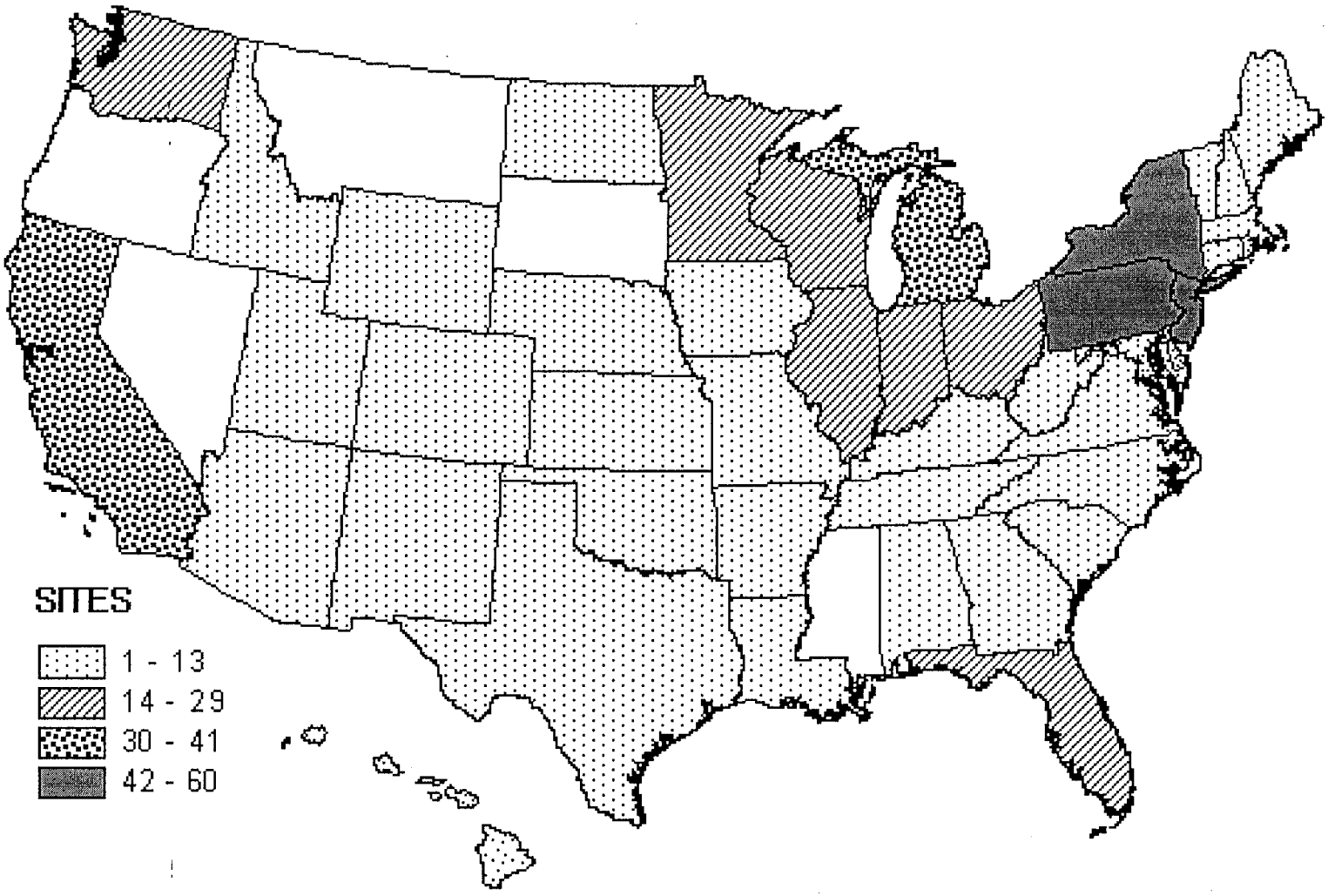
There is a potential for atmospheric release of 1,2-dichloroethene from hazardous waste sites. Cis-1,2-dichloroethene has been detected in air samples from 3 of the 146 NPL sites where cis-1,2-dichloroethene has been identified in some medium (HazDat 1996). Tram+1,2-dichloroethene

Figure 5-1. Frequency of Sites with cis-1,2-Dichloroethene Contamination



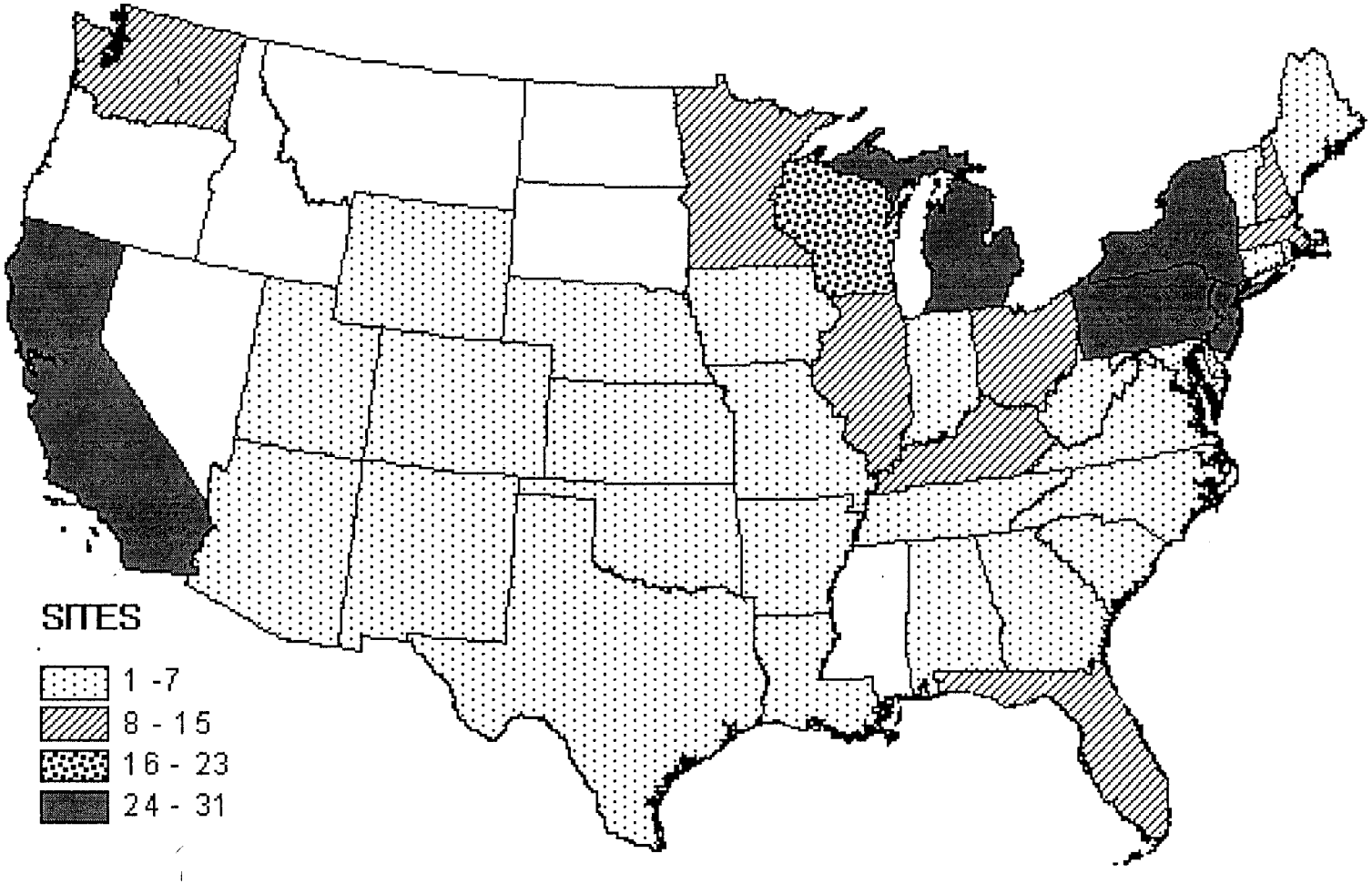
Derived from HazDat 1996

Figure 5-2. Frequency of Sites with trans-1,2-Dichloroethene Contamination



Derived from HazDat 1996

Figure 5-3. Frequency of Sites with 1,2-Dichloroethene (Unspecified) Contamination



Derived from HazDat 1996

Table 5-1. Releases to the Environment from Facilities That Manufacture or Process 1,2-Dichloroethene

State[a]	City	Facility	Reported amounts released in pounds per year						
			Air	Water	Land	Underground injection	Total environment[b]	POTW transfer	Off-site waste transfer
KS	WICHITA	VULCAN CHEMICALS	385				385		
KY	CALVERT CITY	WESTLAKE MONOMERS CORP.	40				40		2,110
LA	GEISMAR	VULCAN MATERIALS CO.	970	8			978		500
LA	LAKE CHARLES	PPG IND. INC.	19,900	3			19,903		11
LA	NA	NA							2
LA	NA	NA	1,528				1,528		
LA	NA	DOW CHEMICAL CO.		12			12		
TX	FREEPORT	DOW CHEMICAL CO.	4,808	5			4,813		
TX	LA PORTE	GEON CO.	44				44		
TX	NA	OCCIDENTAL PETROLEUM CORP.							
TX	NA	OCCIDENTAL PETROLEUM CORP.	190				190		
TX	TEXAS CITY	UNION CARBIDE CORP.	1,613				1,613		
		Totals	29,478	28			29,506		2,623

Source: TRI93 1995

[a] Post office state abbreviations used
[b] The sum of all releases of the chemical to air, land, water, and underground injection wells by a given facility

NA = not available; POTW = publicly owned treatment works

has been detected in air samples from 17 of the 563 NPL sites where trans-1,2-dichloroethene has been identified in some medium (HazDat 1996). 1,2-Dichloroethene (isomer unspecified) has been detected in air samples from 15 of the 336 NPL sites where 1,2-dichloroethene has been identified, without specifying the isomer, in some medium (HazDat 1996).

While there is disagreement in the literature on the persistence of 1,2-dichloroethene released to the atmosphere, the half-lives would likely be measured in days, allowing for transport over large regional or even continental areas (Hall et al. 1989; Winer and Atkinson 1987). However, areas like southern California, where 1,2-dichloroethene is not commonly used as an end product or a chemical intermediate, have not shown detectable levels of 1,2dichloroethene in ambient air.

5.2.2 Water

1,2-Dichloroethene may be released to surface waters via surface runoff from contaminated waste disposal sites, waste water from a variety of industrial sources, and from some publicly owned treatment works (POTWs). 1,2-Dichloroethene may be found in effluents from manufacturing and processing sites and from industries involved in its use as a solvent and extractant, in its use in organic synthesis, and in its use in the manufacture of perfumes, lacquers, and thermoplastics (Hawley 1981). As part of a comprehensive EPA survey of industrial facilities and POTWs, 4,000 samples of waste water were analyzed. The findings indicate that cis- or trans.-1,2-dichloroethene is sometimes found in waste water from: petroleum refining; coal mining; foundries; nonferrous metal manufacture; POTWs; paint and ink formulation; rubber processing; steam electricity generation; leather tanning; iron and steel manufacture; textile mills; auto and other laundries; explosives factories; and production of inorganic chemicals, mechanical products, plastics and synthetics, electrical components and electronics, pharmaceuticals, organic chemicals and plastics, and transportation equipment (EPA 1980b; Shackelford et al. 1983). Effluents from iron, steel, and nonferrous metal manufacturing; and organics, plastics, and rubber processing exceeded 100 ppb of cis-1,2-dichloroethene. Effluents of iron and steel manufacturing, electronics, and POTWs also contained trans- 1,2-dichloroethene (see Section 5.4.2) (Shackelford et al. 1983). It has been estimated that between 1982 and 1984, trans-l,2dichloro-ethene was loaded into the Niagara River at an average of 13.6 pounds per day (Spagnoli 1986). Insufficient data are available to estimate the amount of 1,2-dichloroethene released to other surface waters in the United States.

5. POTENTIAL FOR HUMAN EXPOSURE

During the 1980s as steady progress was made in negotiating final discharge permits for POTWs under EPA's National Pollutant Discharge Elimination System (NPDES) permitting program, the incidence of 1,2-dichloroethene inputs to surface waters from point source discharges may have substantially decreased. Improved levels of waste treatment have the potential to remove virtually all VOCs from final effluents. These materials will become air emissions or become immobilized in sludges (Bennett 1989).

According to TRI93 (TRI93 1995), an estimated total of only 28 pounds of 1,2-dichloroethene, Representing <0.1% of the total environmental release, was discharged to water from manufacturing and processing facilities in the United States in 1993. Table 5-l lists the amounts released to water from each of the identified facilities. The TRI data should be used with caution since only certain types of facilities are required to report; therefore, this is not an exhaustive list.

1,2-Dichloroethene may be released to groundwater as a result of leaching from contaminated waste disposal sites, and by anaerobic degradation of other more highly chlorinated ethenes and ethanes present in groundwater (Cline and Viste 1985; HSDB 1995; Parsons et al. 1984; Smith and Dragun 1984). Barber et al. (1988) reported 280 ppb of 1,2-dichloroethene (isomer unspecified) in groundwater under a sandy rapid infiltration site that had received secondary sewage effluent since 1936.

1,2-Dichloroethene in drinking water may result from raw water source contamination (Otson et al. 1982). There is very little documentation of direct 1,2dichloroethene contamination of groundwater. Research suggests that most 1,2-dichloroethene detections in groundwater involve biodegradation processes related to primary pollution from trichloroethylene (TCE) or tetrachloroethylene (PCE) (see Section 5.3).

In addition to spills or leachates from waste disposal sites, groundwater may be contaminated by cracked sewer interceptors carrying industrial wastes. Especially after rains, substantial loadings may leave the interceptor system through infiltration and inflow (I&I) processes and enter groundwater supplies. Such phenomena have been documented in Europe (Milde et al. 1988) and similar I&I problems are common in most older U.S. cities.

There is also a potential for release of 1,2-dichloroethene to water from hazardous waste sites. Cis-1,2-dichloroethene has been detected in groundwater samples collected at 130 of the 146 NPL sites, in surface water samples collected at 14 of the 146 NPL sites, and in leachate samples collected at 8 of the 146 NPL sites where cis-1,2-dichloroethene has been identified in some medium (HazDat 1996). Trans-1,2-dichloroethene has been detected in groundwater samples collected at 487 of the 563 NPL sites, in surface water samples collected at 137 of the 563 NPL sites, and in leachate samples collected at 48 of the 563 NPL sites where trans-1,2-dichloroethene has been identified in some medium (HazDat 1996). 1,2-dichloroethene (isomer unspecified) has been detected in groundwater samples collected at 263 of the 336 NPL sites, in surface water samples collected at 57 of the 336 NPL sites, and in leachate samples collected at 29 of the 336 NPL sites where 1,2-dichloroethene (isomer unspecified) has been identified in some medium (HazDat 1996).

5.2.3 Soil

Cis- and trans-1,2-dichloroethene are released to soil from the disposal of waste materials containing these compounds (Barber et al. 1988; Fain et al. 1987). They also may be formed in landfills, aquifers, or sediments as anaerobic biodegradation products of tetrachloroethene, trichloroethene, 1,l ,l - trichloroethane, and 1,1,2,2-tetrachloroethane, solvents commonly found in municipal and industrial landfills (Parsons et al. 1984; Smith and Dragun 1984). In muck and sediment microcosms, tetrachloroethylene is converted to 1,2-dichloroethene with a preponderance of the cis isomer (Parsons et al. 1984). Cis-1,2-dichloroethene apparently is the more common isomer found, although it may be mistakenly reported as the trans isomer. Because it is a priority pollutant, the trans isomer is more commonly analyzed for, and the analytical procedures used generally do not distinguish between isomers (Cline and Viste 1995). Insufficient data are available to estimate the amount of 1,2-dichloroethene released to soil.

According to TRI93 (TRI93 1995), no 1,2-dichloroethene was released to land from manufacturing and processing facilities in the United States in 1993. Table 5-l lists the amounts released from these facilities. The TRI data should be used with caution since only certain types of facilities are required to report; therefore, this is not a comprehensive list.

Available information for aquatic sediments is also very limited. Some researchers feel that the subsurface behavior of 1,2-dichloroethene would be similar in groundwater, soils, and sediments (Yeh

and Kastenberg 1991). Most empirical information, however, derives from groundwater remediation studies, usually involving controlled laboratory microcosm studies. For some highly polluted waterbodies, for instance the Delaware and Raritan Canal, 1,2-dichloroethene detections in the water column probably reflect extensive contamination with chlorinated toxics in the sediments (Granstrom et al. 1984). Analyzing cause-source pathways in such complicated systems can be extremely difficult.

There is also a potential for release of 1,2-dichloroethene to soils and sediments from hazardous waste sites. Cis-1,2-dichloroethene has been detected in soil samples collected at 12 of the 146 NPL sites, in sediment samples collected at 1 of the 146 NPL sites where cis-1,2-dichloroethene has been identified in some medium (HazDat 1996). Trans-1,2-dichloroethene has been detected in soil samples collected at 179 of the 563 NPL sites, in sediment samples collected at 61 of the 563 NPL sites, in sludge samples collected at 14 of the 563 NPL sites where trans-1,2-dichloroethene has been identified in some medium (HazDat 1996). 1,2-Dichloroethene (isomer unspecified) has been detected in soil samples collected at 76 of the 336 NPL sites, in sediment samples collected at 30 of the 336 NPL sites where 1,2-dichloroethene (isomer unspecified) has been identified in some medium (HazDat 1996).

5.3 ENVIRONMENTAL FATE

5.3.1 Transport and Partitioning

Occurrence of 1,2-dichloroethene in rainwater samples (Kawamura and Kaplan 1983) indicates thatthis compound may be removed from the atmosphere by precipitation; however, most of the1,2dichloroethene so removed is likely to reenter the atmosphere by volatilization. Organics with avapor pressure of $>10^{-4}$ mmHg should exist almost entirely in the vapor phase in the atmosphere(Eisenreich et al. 1981). Thus, cis- and trans-1,2-dichloroethene, which have vapor pressures of 215 and 336 mmHg at 25 °C, respectively (Stevens 1979), are not expected to partition from the vapor phase to particulates in the atmosphere. Because it is relatively long-lived in the atmosphere, significant transport from source areas should occur (HSDB 1995).

The dominant removal mechanism for 1,2-dichloroethene in surface waters is volatilization (EPA 1979). Henry's Law constants are 4.08×10^{-3} atm-m^3/mol at 24.8 °C for cis-1,2-dichloroethene and 9.38×10^{-3} atm-m^3/mol at 24.8 °C for trans-1,2-dichloroethene (Gossett 1987). Based on these values, the volatilization half-life from a model river 1 m deep, flowing 1 m/second with a wind speed of

3 m/second is estimated to be 3 hours, using the method of Thomas (1982). Dilling (1977) experimentally determined that the volatilization half-life in an open beaker containing 1 ppm of test compound at a solution depth of 6.5 cm under continuous stirring (200 rpm) was 19 minutes for the cis isomer and 24 minutes for the trans isomer. These values correspond to volatilization half-lives of 5.0 and 6.2 hours, respectively, from a body of water 1 m deep.

In fish, bioconcentration factors (BCFs) ranging between 5 and 23 have been estimated for the 1,2-dichloroethene isomers using linear regression equations based on log K_{ow}, and water solubility data (Bysshe 1982; Hansch and Leo 1985; Horvath 1982; Lyman et al. 1982). A BCF value of 6 for the fathead minnow (*Pimephales promelas*) was estimated in ASTER (1994) using the method of Veith and Kosian (1983). These estimated BCFs suggest that 1,2-dichloroethene does not bioconcentrate significantly in aquatic organisms. Based on this information, there is little potential for biomagnification within aquatic food chains.

Soil adsorption coefficients (K_{oc}) of 32-49 were estimated for the 1,2-dichloroethene isomers using a linear regression equation based on water solubility data (Lyman 1982) and the structure-activity relationship developed by Sabljic (1984). These K_{oc} values suggest that adsorption of the 1,2-dichloroethene isomers to soil, sediment, and suspended solids in water is not a significant fate process. Without significant adsorption to soil, 1,2-dichloroethene can leach into groundwater where very slow biodegradation should occur (HSDB 1995). The presence of 1,2-dichloroethene in groundwater, especially under sandy soil (Barber et al. 1988), substantiates its leachability. The relatively low K_{oc} and high vapor pressure of 1,2-dichloroethene indicate that this compound should also readily volatilize from moist soil surfaces (Swann et al. 1983).

5.3.2 Transformation and Degradation

5.3.2.1 Air

The dominant atmospheric removal process for 1,2-dichloroethene is predicted to be reaction with photochemically generated oxygenated species (e.g., hydroxyl radicals) in the troposphere. The estimated atmospheric lifetimes for cis- and trans-1,2-dichloroethene due to this removal process are 12 and 5 days, respectively (Goodman et al. 1986). These estimates are based on experimentally determined hydroxyl reaction rate constants of 2.0×10^{-12} cm^3/molecules-sec at 25 °C for the cis

isomer and $4.5x10^{-12}$ cm^3/molecules-sec at 25 °C for the trans isomer. Formyl chloride has been positively identified as a product of this reaction. Experimental data indicate that the reaction of cis and trans-1,2-dichloroethene with ozone, nitrate radicals, or singlet oxygen in the troposphere is too slow to be environmentally significant (Atkinson and Carter 1984; Sanhueza and Heicklen 1975a, 1975b). The half-life resulting from ozone attack of the double bond is 44 days for the trans isomer and 129 days for the cis isomer (Tuazon et al. 1984). There also is evidence that cis-1 ,2-dichloroethene will be scavenged by rain (HSDB 1995)

The primary ultraviolet (UV) absorption band for cis-1,2-dichloroethene is at 190 nm, which extends to about 240 nm (Ausbel and Wijnen 1975). The primary UV absorption band for the trans isomer also extends to about 240 nm (Dahlberg 1969). A minute amount of light is absorbed in the environmentally significant range (wavelengths greater than 290-380 nm). However, such absorption is insufficient for direct photolysis to be a significant fate process in the atmosphere.

Gtirtler et al. (1994) investigated the photochemical decomposition and oxidation of the chloroethenes in the gas phase by irradiation with a low-pressure mercury lamp in an oxygen atmosphere. Trans-1,2-dichloroethene slowly disappears after several hours of irradiation at 254 nm. After a period of restrained degradation, sudden decomposition is observed, probably resulting from the start of a chain mechanism. Trans-1,2-dichloroethene decomposes more slowly at low concentrations than at high ones. The primary photooxidation products are formyl chloride and, in small amounts, monochloro-acetyl chloride and dichloroacetaldehyde. Further photooxidation leads to the formation of phosgene, additional formyl chloride, formaldehyde, carbon monoxide, carbon dioxide, and hydrochloric acid.

In polluted urban airsheds, photolytic processes are a major factor in generating free radicals. Several studies summarized in Hall et al. (1989) emphasize that 1,2-dichloroethene degradation will proceed 2-4 times faster in polluted urban air exposed to UV radiation than with “pure air” contained no free radical precursors. Tuazon et al. (1988) and Jeffers et al. (1989) provide other convenient summaries of the reaction chemistry of chloroethenes and OH radicals.

5.3.2.2 Water

There is relatively little literature dealing with 1,2dichloroethene fate and transport in surface waters. Since 1,2-dichloroethene is appreciably volatile, the usual assumption is that 1 ,2dichloroethene introduced into surface waters will rapidly be transferred to the atmosphere (see Section 5.3.1). Chemical hydrolysis and oxidation are probably not environmentally important fate processes for 1,2-dichloroethene (EPA 1979, 1981a, 1984). Kinetic data pertaining specifically to the abiotic degradation of the 1,2-dichloroethene isomers in the environment were not located. Direct photolysis of 1,2dichloroethene is also not likely to be important in sunlit natural waters (EPA 1979) (see Section 5.3.2.1).

When dealing with surface waters, 1,2-dichloroethene and other chlorinated ethenes generally resist biodegradation under aerobic conditions (Fogel et al. 1986; Mudder 1981; Mudder and Musterman 1982). However, in one study, the 1,2-dichloroethene isomers were susceptible to aerobic biodegradation. In this study (Tabak et al. 1981), settled domestic waste water was used as the inoculum with 5 ppm each of the cis and trans isomers. Losses in 7 days were 54% of the cis isomer and 67% of the trans isomer. Losses due to volatilization over a lo-day period were 34 and 33% for the cis and tram isomers, respectively. The inoculum may have contained a facultative methanotroph capable of degrading the dichloroethenes (Fogel et al. 1986). No information was found regarding biodegradation in biological waste treatment plants.

There is a growing body of literature dealing with fate and transport processes in groundwater. These studies are related to programs under the EPA Safe Drinking Water Act that address health risks from VOC contaminants in community drinking water systems, and to efforts to mitigate pollution at older waste disposal sites and remediate areas showing smaller-scale spills. While work through the early 1980s focussed on the biodegradation of 1,2-dichloroethene itself, it quickly became apparent that 1,2dichloroethene contamination at many sites was part of a complicated series of biotransformations where such solvents- as trichloroethylene or tetrachloroethylene were the principle driving-forces (Vogel et al. 1987).

1,2-Dichloroethene undergoes slow reductive dechlorination under anaerobic conditions (Barrio-Lage et al. 1986; Fogel et al. 1986). In one study, anoxic microcosms containing uncontaminated organic sediment and water to simulate the groundwater environment were spiked with 5 mg/L of test

compound. First-order rate constants were obtained that correspond to half-lives of 88-339 and 132-147 days for the cis and trans isomers, respectively. No degradation occurred in sterile microcosms; thus, loss of the compounds was assumed to be due entirely to anaerobic biodegradation. The cis isomer degraded to chloroethane and vinyl chloride (a human carcinogen), while the tram isomer degraded to vinyl chloride only (Barrio-Lage et al. 1986). When cis- and trans-1,2-dichloroethene were incubated with methanogenic aquifer material from a site near a landfill, at least 16 weeks passed before trans isomer degradation began (Wilson et al. 1986). During the same time, the cis isomer was reduced to <2% of the concentration in the autoclaved control, and vinyl chloride appeared after only l-2 weeks incubation; therefore, the cis isomer degrades more rapidly. After 40 weeks, the tram isomer concentration fell to 18% of that in the autoclaved control containing the trans isomer. Trace amounts of the cis isomer remained in the unsterilized microcosm beyond 40 weeks. Tandoi et al. (1994) found that an anaerobic enrichment culture, using methanol as an electron donor, rapidly metabolized cis-1 ,2dichloroethene to vinyl chloride with near zero-order kinetics and apparent inhibition of subsequent vinyl chloride dechlorination. Trans- 1 ,2dichloroethene was converted to vinyl chloride more slowly with first order kinetics and an estimated half-life of 9.5 hours and did not inhibit vinyl chloride dechlorination.

Hopkins and McCarty (1995) performed an evaluation of the aerobic cometabolism of dichloroethene isomers, using phenol and toluene as the primary substrates, in a shallow aquifer at a pilot test facility. In an earlier study, a methane substrate was highly successful at transforming trans-1,2-dichloroethene in groundwater, but removal efficiency was rather low for cis-1,2-dichloroethene. Phenol was found to be superior to methane for *in situ* degradation of cis-1,2-dichloroethene, providing up to 90% removal in one pass at concentrations up to 1 mg/L. Removal of trans-1,2-dichloroethene was 74% when phenol was used. Semprini (1995) also demonstrated in pilot scale field studies of aerobic cometabolic transformations that indigenous microbes grown on phenol are more effective at degrading cis- 1,2-dichloroethene than are microbes grown on methane.

A study was performed on a sand aquifer at an industrial site near the town of St. Joseph; Michigan, to improve the understanding of the distribution of chlorinated aliphatic hydrocarbons (CAHs) years after contamination occurred (Semprini 1995). Groundwater concentrations varied significantly with depth. Relatively high concentrations of CAHs existed at all locations within 20 m of the center of the plume. The dominant dichloroethene isomer present was the cis isomer, with maximum

concentrations of the cis and trans isomers of 133 and 3.9 mg/L, respectively. Cis-1,2-dichloroethene was observed in a transition zone between high and decreasing trichloroethene concentrations.

Anaerobic biotransformation by methanogenic bacteria was the earliest documented research on the biodegradation of 1,2-dichloroethene. In addition to studies in the United States (Barrio-Lage at al. 1986; Ehlke et al. 1992; Parsons et al. 1984; Silka and Wallen 1988), there has been good documentation of similar phenomena in sandy aquifers near Berlin, Germany (Kastner 1991; Leschber et al. 1990) and in groundwater supplies near a landfill in Ottawa, Canada (Lesage et al. 1990). In addition to anaerobic pathways, laboratory studies suggest that ammonia-oxidizing aerobic bacteria (Vannelli et al. 1990) and facultative sulfur-bacteria (Bagley and Gossett 1990) can biodegrade chlorinated aliphatic hydrocarbons. Burback and Perry (1993) demonstrated that 1,2-dichloroethene, when added singly to groundwater, is catabolized by *Mycobacterium vaccae*. At 100 ppm, 1,2dichloroethene was catabolized <50%. A wide range of estimates for reaction rates and pollutant half-lives have been reported. The biodegradation processes appear to be highly site specific, and influenced by the types of bacteria present, the presence of aerobic or anaerobic conditions, the presence of other substrates such as methane or sulfide, and the toxicity impacts from the various metabolites (Janssen et al. 1988).

5.3.2.3 Sediment and Soil

Studies showing that cis- and trans-1,2-dichloroethene degrade in nonsterile groundwater microcosms (Barrio-Lage et al. 1986; Wilson et al. 1986) suggest that these compounds undergo anaerobic biodegradation in soil and that this process may be the sole mechanism by which 1,2-dichloroethene degrades in soil. Hallen et al. (1986) found that when cis- and trans-1,2-dichloroethene were incubated in a system inoculated with anaerobic sludge from a municipal digester to simulate anaerobic conditions in a landfill, vinyl chloride appeared within 6 weeks. Biodegradation of trans- 1,2-dichloroethene was studied in microcosms containing uncontaminated organic sediment from the Everglades and allowed to stand to ensure oxygen depletion. Under these anoxic conditions, 50% of the chemical was lost within 6 months (Barrio-Lage et al. 1986). The fact that ethyl chloride as well as vinyl chloride are produced indicates that there are different pathways in the sequential dechlorination of cis- 1,2-dichloroethene.

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There are no transformation and degradation studies dealing with sediments. 1,2-Dichloroethene does not show significant bioconcentration or bioaccumulation tendencies, and outside groundwater would tend to volatilize and move to the atmosphere. Some researchers feel that the behavior of 1,2dichloroethene in sediments would be similar to patterns documented for soils or groundwater (Yeh and Kastenberg 1991).

5.4 LEVELS MONITORED OR ESTIMATED IN THE ENVIRONMENT

5.4.1 Air

1,2Dichloroethene has been frequently detected in air samples from urban locations throughout the United States and in landfill gas. Data in Table 5-2 represent available air monitoring data for 1,2-dichloroethene. Only one rural air monitoring study was located (Grimsrud and Rasmussen 1975). Maximum 1,2-dichloroethene concentrations detected in landfill gas ranged from 3,260 ppb (Vogt and Walsh 1985) in a municipal landfill simulator to 75,600 ppb at two Long Island landfills (Lipsky and Jacot 1985).

In 1986, EPA carried out an update to its National Ambient Database, with a focus on updating the coverage for VOCs (Shah and Singh 1988). Based on information from 161 data points, outdoor 1,2-dichloroethene daily ambient air concentrations averaged 0.326 ppb, with a median of 0.037 ppb and with 75% of the values falling below a concentration of 0.113 ppb.

With steady improvements in the efficiency of waste water treatment plants, the loadings of various toxics to receiving waters has substantially decreased over the last decade (Bennett 1989). However, reductions to surface water loadings have often resulted in increased emission to the atmosphere as volatile constituents of the waste influents are removed through techniques such as air stripping. Wastes, including organics like 1,2-dichloroethene, will also be transferred to sludges generated from biotic digestion processes or the use of chemical coagulants. Where sludge drying beds are located. close to waste water plants, volatile constituents in the residuals will be vented to the air. These phenomena can present toxic exposure risks to workers at the treatment plants and to populations living close to these facilities.

Table 5-2. Air Monitoring Data for 1,2-Dichloroethene

Media	Location	Sampling date	Isomer	Concentration (ppb)[a]	Comments	Reference
Ambient air	Houston, TX		cis	0.071 (mean)	General urban atmosphere	EPA 1983a
	St. Louis, MO	May 1980		0.039 (mean)		
	Denver, CO	May-June 1980		0.076 (mean)		
	Riverside, CA	June 1980		0.060 (mean)		
	Staten Island, NY	July 1980		0.018 (mean)		
	Pittsburgh, PA	March-April 1981		0.013 (mean)		
	Chicago, IL	April-May 1981		0.019 (mean)		
	Edison, NJ	NS	NS	1.3 (max.)	Kin-Buc disposal site	Pellizzari 1978
	Tulsa, OK	NS	NS	<0.1		Pellizzari 1978
	Kanawha Valley, WV			0.08		
	Front Royal, VA			0.1		
	So. Charleston, WV			<0.08		
	Birmingham, AL			<0.1		
	Baton Rouge, LA			<0.1		
	Upland, CA			<0.1		
	Magna, VT			0.08		
	Grand Canyon, AZ			0.065		
	Geismar, LA			2.6 (max.)		
	Niagara Falls, NY	1978	NS	trace	Detected in air outside 3 of homes in Old Love Canal hazardous waste site (detection limit not stated)	Barkley et al. 1980
	New Jersey	NS	NS	NS	4 NPL sites and 1 municipal landfill; detected in air samples collected at 3 of 5 sites; occurred in 75 to 100% of samples collected at these sites (detection limit ≥0.1 ppb)	LaRegina et al. 1986

Table 5-2. Air Monitoring Data for 1,2-Dichloroethene (continued)

Media	Location	Sampling date	Isomer	Concentration (ppb)[a]	Comments	Reference
Ambient Air	Edison, NJ	NS	trans	0.93		Brodzinsky and Singh 1982
	Urban/suburban (669 sites)	NS	cis	0.068 (median) 3.5 (max)		
	Source areas (101 sites)	NS	cis	0.3 (median) 6.7 (max)		
	Pullman, WA (rural area)	December 1974 to February 1975	NS	ND	Detection limit 5 ppt	Grimsrud and Rasmussen 1975
Indoor air	Niagara Falls, NY	1978	NS	0.015	Air in a basement of a home in Old Love Canal	Barkley et al. 1980
	Knoxville, TN	Winter 1982	NS	8.1 (mean)	Detected in 16 of 16 samples (detection limit not stated)	Gupta et al. 1984
Landfill gas	Selected U.S. landfills	NS	NS	70 (mean) 3,600 (max.)	Secondary source	Vogt and Walsh 1985
	Municipal landfill simulator	February 1983 to February 1984	NS	210 (mean) 3,260 (max.)	Simulation	Vogt and Walsh 1985
	Long Island, NY	NS	trans	75,600 (max.)	Air samples collected from methane vents at 2 sanitary landfills	Lipsky and Jacot 1985
	California	NS	trans	59,000 (max.)	20 class II landfills	Wood and Porter 1987

[a] Unless otherwise specified.

ND = Not detected; NS = Not stated

5.4.2 Water

1,2-Dichloroethene has been detected in surface, ground, and drinking waters, as well as in industrial and municipal effluents, urban runoff, and leachate from landfills throughout the United States. Table 5-3 shows the available monitoring data for 1,2dichloroethene in these media. In some of the studies, only one of the 1,2-dichloroethene isomers was monitored; while in several of the studies the authors did not mention the specific isomer monitored. Concentrations of 1,2-dichloroethene detected in surface water ranged from 0.43 ppb in the Quinipiac River in Connecticut (Hall 1984) to 1,307.5 ppb in New Jersey (Table 5-3).

1,2-Dichloroethene has been detected in groundwater in several states and U.S. territories including Colorado, Connecticut, Florida, Maryland, Michigan, Nebraska, New Jersey, Pennsylvania, Puerto Rico, Washington, and Wisconsin (Table 5-3). Concentrations of 1,2dichloroethene isomers detected in groundwater ranged from 0.25 to 0.28 ppb (range of average concentrations) from 6 areas near Miami, Florida (Singh and Orban 1987) to a maximum of 500,000 ppb in Southington, Connecticut (Hall 1984). Groundwater contamination has been reported at numerous waste disposal sites in the United States. In a detailed study, the Wisconsin Department of Natural Resources sampled groundwater at 20 municipal and 6 industrial landfills in Wisconsin. 1,2Dichloroethene was detected in samples from 5 of 26 landfills at a maximum concentration of 3,900 ppb, and in leachate from 8 of 26 landfills at a maximum concentration of 310 ppb (Friedman 1988).

Since 1,2-dichloroethene can be produced from biodegradation of a variety of VOCs, screening tests for VOCs or tests for such widely used solvents as TCE or PCE can provide useful screening tools for follow-up testing for 1,2-dichloroethene. For instance, a study of 19 landfill sites in Wisconsin showed that while the incidence of 1,2-dichloroethene in all test wells was 19%, approximately two-thirds of the wells showing detectable VOCs also showed detectable 1,2dichloroethene (Battista and Connelly 1989). In a study of a western Connecticut manufacturing plant that used large quantities of high quality trichloroethylene for degreasing, it was found that 7 of 9 monitoring wells contained 1.2-320.9 ppb of trans-1,2-dichloroethene (Stuart 1983). More localized problems from leaking underground storage tanks or chemical spills may also show up in screens for VOCs (Stenzel and Gupta 1985). Where pollution levels are not excessive, remediation or permanent treatment technologies involving combinations of granular activated carbon or air stripping can remove over

Table 5-3. Water Monitoring Data for 1,2-Dichloroethene

Media	Location	Sampling date	Isomer	Concentration (ppb)	Comments	Reference
Surface water	Hylebos Waterway in the Puget Sound	1979	NS	0.8–2.4		Riley et al. 1980
	Potomac River in Quantico, VA	Spring 1986	trans	<2	1 sample analyzed (detection limit not reported)	Hall et al. 1987
	12 sites in the Delaware and Raritan Canal in New Jersey	August 1979 to January 1980	NS	ND	Detection limit not reported	Granstrom et al. 1984
	Indian River in Vero Beach, FL	May 1981 to May 1982	NS	ND	13 samples (detection limit 4.0 µg/L)	Wang et al. 1985b
	Drainage canal discharging into the Indian River in Vero Beach, FL	May 1981 to May 1982	NS	4.0–48.1 15.7 (mean)	Canal receiving contaminated groundwater; detected in 23 of 39 samples (detection limit 4.0 µg/L)	Wang et al. 1985b
	New Jersey	1977–1979	trans	1307.5 (max.)	Detected in 172 of 273 samples (detection limit not reported)	Page 1981
	Quinipiac River in Southington, CT	1980	trans	0.43 (mean)	Detected in 4 of 5 samples (detection limit not reported)	Hall 1984
	Wilson Creek (adjacent to hazardous waste site in Bullit County, KY	February 1979	NS	75 (max.)		Stonebraker and Smith 1980
Groundwater	178 CERCLA sites (Comprehensive Environmental Repose, Compensation, and Liability Act)	1981–1984	trans	NS	Frequency of detection = 29.1%	Plumb 1987
	New Jersey	1977–1979	trans	818.6 (max.)	Detected in 193 of 378 samples	Page 1981
	Wisconsin	Sampling results as of June 30, 1984	NS	NS	Detected in 5 of 1174 community wells and 12 of 617 private wells (detection limit 1.0–5.0 µg/L)	Krill and Sonzogni 1986
	Wausau, WI	NS	cis	83.3	Raw well water	Hand et al. 1986

Table 5-3. Water Monitoring Data for 1,2-Dichloroethene (continued)

Media	Location	Sampling date	Isomer	Concentration (ppb)	Comments	Reference
	Wisconsin	1985–1987	NS	3,900 (max.)	Detected at 5 of 26 sites	Friedman 1988
Groundwater (cont.)	Montgomery County, MO	1983	trans	27–320 158 (mean)	Detected in 4 samples	Dever 1986
	Southington, CT	1980	trans	50,000 (max.) 16 (median)	Detected in 29 of 35 samples (detection limit not reported)	Hall 1984
	Potomac-Raritan-Mogathy aquifer system (adjacent to the Delaware River	1980–1982	trans	NS	Detected in 12 of 179 wells in the outcrop area and not detected in 115 wells in the downdip of the outcrop (detection limit 1 µg/L)	Fusillo et al. 1985
	Nebraska	Summer 1982	NS	2.1 (max.) 0.50 (median)	Detected in 3 of 63 samples (detection limit 0.2 µg/L); private wells	Goodenkauf and Atkinson 1986
	Nebraska	1983–1984	NS	2.9	Detected in 1 of 97 samples; sources for public water system	Goodenkauf and Atkinson 1986
	Western CT manufacturing plant	NS	trans	1.2 to 320.9	Detected in 7 of 9 monitoring wells	Stuart 1983
	Biscayne aquifer, Miami, FL	November 1982 and March 1983	trans	0.25–28 (range of average concentration fron the mix areas)	12 total samples from 6 geographical areas defined within the study area	Singh and Orban 1987
	Miami Drum Services in Miami, FL	1981	cis	839 (max.)	Hazardous waste site	Myers 1983
	Biscayne aquifer in vicinity of Miami Drum site	1983	NS	19 (mean)	Detected in 2 of 3 samples (detection limit not reported)	Myers 1983
	Piper Aircraft Corp. in Vero Beach, FL	April 1981 to December 1983	NS	1000–4000	At site of a leaking subsurface trichloroethylene storage tank	Wang et al. 1985a
	Lakewood, WA	December 1983	trans	250–435 330 (mean)	Detected in 11 of 11 samples; in the vicinity of an NPL site	Wolf and Gorelik 1984

Table 5-3. Water Monitoring Data for 1,2-Dichloroethene (continued)

Media	Location	Sampling date	Isomer	Concentration (ppb)	Comments	Reference
	Western Processing, Kings County, WA	November 1982	trans	Qualitatively identified	Hazardous waste site	Aldis et al. 1983
Groundwater (cont.)	Marshall landfill in Boulder County, CO	NS	trans	530 (onsite) 66 (offsite)	NPL site	EPA 1986f
	Minnesota	NS	cis	0.5 - 20000	Detected in contaminated groundwater from 7 of 13 sites	Sabel and Clark 1984
			trans	0.6 to 98	Detected in contaminated groundwater from 3 of 13 sites	
	Forest Waste Disposal site in Otisville, MI	NS	trans	100 (max.)	NPL site	EPA 1986b
	Lang Property site in Pemberton Township, NJ	NS	trans	942 (mean) 2,500 (max.)	NPL site	EPA 1987a
	Vega Alta Public Supply Wells in Puerto Rico	NS	NS	74 (max.)	NPL site; detected in 89 of 168 samples (detection limit not reported)	EPA 1988a
	Ponders Corner in Pierce County, WA	1984–1985	trans	85 (max.)	NPL site	EPA 1986c
	Hollinsworth Solderless Terminal Co. in Fort Lauderdale, FL	1983	NS	2,160 (max.)	NPL site; level of dichloroethene (there was no indication whether this was 1,1- or 1,2-dichloroethene)	EPA 1986d
	Lakewood Utility District near Tacoma, WA	NS	trans	200	Production wells near a commercial facility	Boateng et al. 1984
Drinking water (using ground-water sources)	United States	NS	NS	2.0 (max.)	Detected in samples collected from 16 of 466 randomly selected sites using groundwater as a raw water source (detection limit 0.2 µg/L)	Westrick et al. 1984
Drinking water	Miami, FL	NS	trans	1		EPA 1980d

Table 5-3. Water Monitoring Data for 1,2-Dichloroethene (continued)

Media	Location	Sampling date	Isomer	Concentration (ppb)	Comments	Reference
Drinking water (Private wells)	Winnebago Co., IL	NS	trans	ND - 64 (8 median)	5 homes tested	Wehrmann 1985
Drinking water (Private wells) (cont.)	Philadelphia, PA	February 1975 to January 1977	NS	NS	Detected in 1 of 17 samples (detection limit not reported)	Suffet et al. 1980
	5 U.S. cities	1975	cis and trans	NS	U.S. EPA National Organics Reconnaissance Survey; cis isomer positively identified in samples from Miami, FL, Philadelphia, PA, and Cincinnati, OH; trans isomer positively identified in samples from Miami, FL	EPA 1975a
Raw and treated drinking water	10 potable water treatment plants in Canada	July 1982 to July 1983	NS	trace	Positively identified in 3 raw and 3 treated water samples (detection limit not reported)	Otson 1987
Leachate	30 potable water treatment plants in Canada	August 1979 to December 1979	NS	raw water - 23 (max.) treated water - 32 (max.)	Positively identified in 2 raw and 11 treated water samples	Otson et al. 1982
	NS (landfill containing mixed industrial waste)	NS	trans	45 - 800 (average concentration of leachates)	Detected in 2 of 8 leachates (detection limit not reported)	Ghassemi et al. 1984
	Minnesota	NS	cis	1.4 - 470	Detected in leachate from 5 of 6 sites (detection limit not reported)	Sabel and Clark 1984
			trans	3.8 - 88	Detected in leachate from 3 of 6 sites (detection limit not reported)	Sabel and Clark 1984
	Lyon, MN, municipal landfill	NS	trans	3.8 (mean)		Brown and Donnelly 1988

Table 5-3. Water Monitoring Data for 1,2-Dichloroethene (continued)

Media	Location	Sampling date	Isomer	Concentration (ppb)	Comments	Reference
	Meeker, MN, municipal landfill	NS	cis	190 (mean)		Brown and Donnelly 1988
Leachate (cont.)			trans	170 (mean)		Brown and Donnelly 1988
	Rochester, MN, municipal landfill	NS	cis	470 (mean)		Brown and Donnelly 1988
	Rochester, MN, municipal landfill	NS	trans	88 (mean)		Brown and Donnelly 1988
	Wisconsin, 20 municipal and industrial landfills	1985–1987	NS	310	Detected in leachate from 8 of 26 sites	Friedman 1988
Aqueous lagoon	Forest Waste Disposal site in Otisville, MI	NS	trans	50	NPL site; estimate level (compound detected below quantification limit)	EPA 1986b
Urban storm water runoff	15 U.S. cities	as of July 1982	trans	1–3 (in positive samples)	Detected in runoff from Little Rock, AR, and Eugene, OR	Cole et al. 1984
Waste water	Los Angeles, CA	NS	NS	5.2 (mean)	Effluent from a county sewage treatment plant	Gossett et al. 1983
	NS	1980/1981	trans	untreated: 52–60 effluent: 31–43	Municipal sewage treatment plant; detected in 5 of 5 samples	Lao et al. 1982
	Chicago, IL	NS	trans	<50	Effluent from a municipal sewage treatment plant	Lue-Hing et al. 1981
	NS	NS	trans	20 (max.)	Treated effluent from a petroleum refinery	Snider and Manning 1982
	Owensboro, KY	August 1975	cis	NS	Chemical plant effluent	EPA 1976
	Calvert City, KY	October 1975	cis	NS	Chemical plant effluent	EPA 1976

Table 5-3. Water Monitoring Data for 1,2-Dichloroethene (continued)

Media	Location	Sampling date	Isomer	Concentration (ppb)	Comments	Reference
	United States	NS			Industry:	EPA 1980d
			trans	10 (max.)	coal mining	
			trans	46 (max.)	electrical electronic components	
			trans	10 (max.)	foundries	
			trans	10 (max.)	pharmaceutical manufacturing	
Waste water (cont.)			trans	75 (max.)	nonferrous metals manufacturing	
			trans	12 (mean)	organic chemicals and plastics manufacturing	
			trans	190 (max.)	paint and ink formulation	
			trans	<10 (max.)	petroleum refining	
			trans	290 (max.)	rubber processing	
			cis	1.6	steam electric (detected in 1 sample)	Shackelford et al. 1983
			cis	3.3	leather tanning (detected in 1 sample)	
			cis	1400.8 (median)	iron and steel manufacturing	Shackelford et al. 1983
			trans	2265.9 (median)	(detected in 2 samples)	
			cis	314.6	nonferrous metal (detected in 1 sample)	
	United States	NS	cis	121.5 (median)	organics and plastics [(detected in	Shackleford et al. 1983
			trans	14.6 (median)	2 samples) (cis) and 3 samples	
			trans	3.9	(trans)]	
					inorganic chemicals (detected in 2 samples)	
			cis	8.3	textile mill (detected in 1 sample)	
			cis	20.1 (median)	plastics and synthetics (detected in 3 samples)	
			cis	712.0	rubber processing	

Table 5-3. Water Monitoring Data for 1,2-Dichloroethene (continued)

Media	Location	Sampling date	Isomer	Concentration (ppb)	Comments	Reference
			trans	19.0 (median)	[detected in 1 sample (cis) and 2 samples (trans)]	
			trans	60.6	auto and other laundries (detected in 1 sample)	
Waste water (cont.)			cis trans	1.5 3.9	explosives (detected in 1 sample)	
			trans	140.7 (medium)	electronics (detected in 7 samples)	
			trans	13.7 (median)	mechanical products (detected in 2 samples)	Shackelford et al. 1983
			trans	29.3	transportation equipment (detected in 1 sample)	
			trans	16.3 (median)	publicly owned treatment works (POTW)(detected in 63 samples)	Shackelford et al. 1983
	NS	NS	trans	260 (mean) 1700 (max)	metal finishing	EPA 1980b
			trans	2200 (max)	photographic equipment/supplies	
			trans	75 (mean) 260 (max)	non-ferrous metal manufacturing	
			trans	150 (mean) 290 (max)	rubber processing	
Rain water	UCLA campus, Los Angeles, CA	3/26/82	NS	0.230	1 sample	Kawamura and Kaplan 1983

ND = Not detected; NS = Not stated

96% of VOCs such as cis-1,2-dichloroethene (Clark et al. 1988; Lee et al. 1988; Stenzel and Gupta 1985).

In a comprehensive survey of United States drinking water derived from groundwater, 16 of 466 randomly selected sites and 38 of 479 purposely selected sites contained 1,2-dichloroethene. The maximum concentration was 2 ppb at random sites and 120 ppb at the nonrandom sites (Westrick et al. 1984). Trans-1,2-dichloroethene was found in Miami, Florida, drinking water at 1 ppb. Cis-1,2-dichloroethene was found in Miami drinking water at 16 ppb; and in Cincinnati, Ohio, and Philadelphia, Pennsylvania, drinking water at 0.1 ppb; but was not detected in 7 other drinking waters surveyed (EPA 1980d).

In a four-city study (Cincinnati, Ohio; St. Louis, Missouri; Atlanta, Georgia; Hartford, Connecticut) to determine the major source type of priority pollutants in tap water and POTW influents, it was found that 43, 38, and 28% of commercial sources, industrial sources, and POTW influents, respectively, contained trans- 1 ,2dichloroethene (EPA 198 lc). The average concentrations from the industrial sources were between 10 and 100 ppb while the others were <10 ppb. Industrial effluent monitoring data from Shackelford et al. (1983) was obtained from a database of a comprehensive EPA survey of 4,000 effluent samples from industries and POTWs. This survey was conducted in response to the consent decree between the National Resources Defense Council and the EPA on June 7, 1976. Data from this study are presented in Table 5-3.

Over the last decade, the Safe Drinking Water Act has focussed attention on improved controls over VOC contamination (including 1,2-dichloroethene) of community drinking water systems. Based on available national statistics, 1,2-dichloroethene has been found in detectable concentrations at less than 5% of the community systems using surface water sources. The figures jumped to 21%, however, for community systems relying on groundwater (Coniglio et al. 1980). No comparable figures are available for noncommunity systems, such as truck stops or highway convenience stores in rural areas, or for domestic groundwater wells.

5.4.3 Sediment and Soil

Available data on 1,2-dichloroethene in soil are limited to those obtained through hazardous waste site monitoring (Aldis et al. 1983; EPA 1986c, 1987a; Pennington 1983; VIAR 1987). Soil gas pollutants

in a shallow, unconfined aquifer receiving waste water from metal-plating operations at Picattinny Arsenal in Morris County, New Jersey, were found to have a maximum cis-1,2-dichloroethene concentration of 33 ppb in the vadose zone (Smith 1988). 1,2-Dichloroethene has been detected, but not quantified, in sediment samples at Love Canal, New York (HSDB 1995).

Recent summaries related to data on 1,2dichloroethene in sediments have not been located. In the early 1980s 1,2-dichloroethene was found at a concentration of >5 ppb (wet weight) in sediment at 4% of 361 stations reported in EPA's STORET database (Staples et al. 1985). No further summary information was located on the occurrence of 1,2-dichloroethene in sediments. EPA is in the process of consolidating all available information on toxics in sediments to comply with provisions of the Water Resources Development Act of 1992. This will lead to the creation of a National Sediment Inventory, which should eventually facilitate custom data retrievals and encourage research studies to analyze available sediment monitoring results (EPA 1993).

5.4.4 Other Environmental Media

Trans-1,2dichloroethene concentrations ranging from 22 to 55 g/L have been detected in municipal sludge from various treatment plants throughout the United States (Feiler et al. 1980; Naylor and Loehr 1982).

Few reports exist of 1,2-dichloroethene in biota from U.S. waters. This is because 1,2-dichloroethene is not a typical biota contaminant (Staples et al. 1985). Nicola et al. (1987) reported mean and maximum 1,2dichloroethene levels of 0.04 and 0.05 ppm, respectively, in fish tissue from Commencement Bay in Tacoma, Washington. No fish obtained at the 95 stations in EPA's STORET database contained detectable levels of 1,2-dichloroethene (Staples et al. 1985). A BCF of 6 was estimated for fathead minnows (ASTER 1995) using the method of Veith and Kosian (1983). Using a log octanol/water partition coefficient of 2.06 for trans-1,2-dichloroethene and a recommended regression equation (Lyman et al. 1982), a BCF of 22 has been estimated (HSDB 1995). Based on these estimated BCFs, 1,2-dichloroethene is not expected to bioaccumulate to any appreciable extent.

5. POTENTIAL FOR HUMAN EXPOSURE

The general population is exposed to 1,2-dichloroethene in urban air and drinking water, with higher possibilities of exposure in community systems relying on groundwater supplies. Contaminated tap water can cause exposure via ingestion, inhalation, and dermal contact during showering and bathing. Inhalation is the most probable route of exposure. 1,2-Dichloroethene has been detected in urban air at average concentrations of 0.013-0.076 ppb (0.052-0.30 μg/m^3) (EPA 1983a). These exposure levels correspond to an average daily intake of l-6 μg 1,2-dichloroethene, assuming an average daily intake of 20 m^3 of air. Risks from inhalation exposures may be of more concern to populations in regions such as Gulf Coast states that have substantial production facilities for chlorinated polymers (Hall et al. 1989). An average daily intake of 0.5-5.4 μg from water is calculated assuming a concentration of 0.23-2.7 ppb (HSDB 1995). Data are insufficient for estimating 1,2-dichloroethene intake via other routes of exposure.

Ashley et a1.(1994) determined the internal dose of 32 volatile organic compounds in 600 or more people in the United States who participated in the Third National Health and Nutrition Survey (NHANES III). Detectable concentrations of cis- and tram-1,2-dichloroethene were found in fewer than 10% of the samples examined. Their detection limits were 0.013 and 0.014 ppb, respectively.

According to a National Occupational Exposure Survey (NOES) conducted by NIOSH between 1981 and 1983, an estimated 215 workers in the United States are potentially exposed to 1,2-dichloroethene (mixture of cis and trans isomers); an estimated 61 workers in the United States are potentially exposed to cis-1,2-dichloroethene (NIOSH 1988). These tentative estimates will be updated as additional information on trade name compounds containing 1 ,2dichloroethene becomes available. There was no NOES estimate for the trans isomer. Occupational exposure is by dermal contact with the vapor and liquid or by inhalation (HSDB 1995). Common operations in which there is potential industrial exposure to 1,2-dichloroethene include: use as a low-temperature solvent for heat-sensitive substances in extraction of caffeine, perfume oils, and fats from animal flesh; in rubber and dye industries in extraction and application; as a direct solvent in gums, waxes, etc.; in solvent mixtures for ester and ether derivatives, lacquers, resins, thermoplastics, and artificial fibers; in organic synthesis for polymers and telomeres; and in miscellaneous applications as a liquid dry cleaning agent, cleaning agent for printed circuit boards, food packaging adhesive, and germicidal fumigant (NIOSWOSHA 1978). The extent of continuing use of 1,2-dichloroethene in these operations is unknown.

Firefighters and workers at landfill sites may also be exposed to 1,2dichloroethene (Michal 1976; NIOSWOSHA 1978; Vogt and Walsh 1985). No information was located on exposure levels in other occupational settings.

5.6 POPULATIONS WITH POTENTIALLY HIGH EXPOSURES

Other than individuals who are occupationally exposed, populations with potentially high exposure include those living near production and processing facilities, hazardous waste sites, municipal waste water treatment plants, and municipal landfills. Near production and processing facilities, certain hazardous waste sites, and municipal landfills, potential exists for exposure to elevated levels of dichloroethene in air downwind of the sites and in contaminated drinking water from groundwater downgradient of the sites. Potential exposure levels cannot be estimated with the data available.

5.7 ADEQUACY OF THE DATABASE

Section 104(i)(5) of CERCLA, as amended, directs the Administrator of ATSDR (in consultation with the Administrator of EPA and agencies and programs of the Public Health Service) to assess whether adequate information on the health effects of 1,2-dichloroethene is available. Where adequate information is not available, ATSDR, in conjunction with the NTP, is required to assure the initiation of a program of research designed to determine the health effects (and techniques for developing methods to determine such health effects) of 1,2-dichloroethene.

The following categories of possible data needs have been identified by a joint team of scientists from ATSDR, NTP, and EPA. They are defined as substance-specific informational needs that if met would reduce the uncertainties of human health assessment. This definition should not be interpreted to mean that all data needs discussed in this section must be filled. In the future, the identified data needs will be evaluated and prioritized, and a substance-specific research agenda will be proposed.

5.7.1 Identification of Data Needs

Physical and Chemical Properties. The physical and chemical properties of both cis- and trans-1,2-dichloroethene are well characterized (see Table 3-2) and allow prediction of the transport

and transformation of the chemicals in the environment. Therefore, no data needs have been identified at this time.

Current production and import/export volumes and usage data are presently unavailable in the literature. Much of the information regarding 1,2dichloroethene may be difficult to obtain because many manufacturing companies maintain confidentiality. In 1977, the estimated production of cis-1,2-dichloroethene was 500 metric tons. No information was available for the trans isomer or for the mixture (HSDB 1995). Also, information about future domestic production, and past, present and future imports and exports is lacking. Furthermore, determining the percentage of 1,2dichloroethene that is used as a captive intermediate (i.e., the 1,2dichloroethene consumed in closed processes in which the compound is not isolated), as opposed to its use as a solvent, is critical to estimating the amount released to the environment. Differences in toxicity and environmental fate also suggest that isomer-specific information on use and consumption is important. Determination of the levels of 1,2-dichloroethene in consumer products is essential for estimating the exposure of the general population.

With up-to-date and accurate production, import/export, and use data, the extent of release into the environment and the potential for human exposure could be more realistically determined. Disposal methods have been described and appear to be satisfactory.

Because the EPA identified trans-1,2-dichloroethene as a hazardous waste, its disposal is regulated under the Resource Conservation and Recovery Act (RCRA). Specific information on federal regulations concerning hazardous waste disposal by land treatment, landfilling, incineration, thermal treatment, chemical/physical/biological treatment, underground injection, and deep sea injection appears in the Code of Federal Regulations (40 CFR 190 to 399). Release of trans-1 ,2dichloroethene in waste water is regulated under the Clean Water Act by the National Pollutant Discharge Elimination System (NPDES). Information regarding effluent guidelines and standards for trans-1,2-dichloroethene can be found in 40 CFR 122, 40 CFR 125, 40 CFR 413.02(i), 40 CFR 414, and 40 CFR433.1l(e).

Environmental Fate. 1,2Dichloroethene released to the environment partitions mainly to the atmosphere (Eisenreich et al. 1981; Swann et al. 1983; Thomas 1982). It is primarily found in the atmosphere and groundwater (HSDB 1995; TR193 1995). Important sources of 1,2dichloroethene include industrial releases and degradation products from other solvents such as trichloroethene,

tetrachlorethene, and vinyl chloride (Parsons et al. 1984; Shen 1982b; Smith and Dragun 1984; Vogel et al. 1987). 1,2Dichloroethene isomers have predicted atmospheric half-lives of 12 days (cis) and 5 days (trans) (Goodman et al. 1986). Both isomers react with hydroxyl radicals in the atmosphere, forming formy1 chloride, but atmospheric ozone, nitrate radicals and singlet oxygen have little environmental effect (Atkinson and Carter 1984). In surface waters, the isomers of 1,2dichloroethene are rapidly volatized; half-lives of 5-6.2 hours are estimated for water 1 m deep (Dilling 1977). The compound is not significantly bound to soils or sediments (Barber et al. 1988). Soil-groundwater degradation processes are anaerobic and may involve multiple pathways. Additional information about the long-term atmospheric fate would be useful, because of the importance of this pathway and the uncertainty of atmospheric degradation processes.

Bioavailability from Environmental Media. No specific information is available regarding human inhalation, oral, or dermal absorption of 1,2-dichloroethene from air, water, food, or soil. Exposure via contaminated drinking water is particularly relevant to humans. Since 1,2-dichloroethene is a neutral lipophilic chemical with a low molecular weight, it probably is readily absorbed through the lungs and gastrointestinal tract. The few available toxicity studies of animals exposed to 1,2-dichloroethene support this contention (Filser and Bolt 1979; Gargas et al. 1988, 1989). No information about human exposure to 1,2-dichloroethene in the environment and the resulting concentrations in human tissue was located. Studies of absorption of 1,2dichloroethene from air, water, food, and soil in contaminated environments near hazardous waste sites would allow for determination of the rate and extent of absorption from each of these media and for comparison of the potential hazards posed by 1,2-dichloroethene within these media.

Food Chain Bioaccumulation. Few data are available describing the food chain bioaccumulation of 1,2dichloroethene. Experimental data are unavailable; therefore, it is not known if the bioconcentration potential is consistent with estimated values obtained from regression equations. The estimated BCF of 6 for fathead minnows (ASTER 1995; Veith and Kosian 1983) suggests that the potential for 1,2dichloroethene to bioconcentrate is low for aquatic organisms. Therefore, further studies on bioaccumulation are not recommended. However, biomagnification studies would enable scientists to assess the dangers of human exposure to 1,2dichloroethene from fish and seafood.

Data describing exposure levels in air, surface water, drinking water, groundwater, and soil are limited. 1,2-Dichloroethene has been detected in urban and rural air, air near hazardous waste sites, and indoor

air (Grimsrud and Rasmussen 1975; Lipsky and Jacot 1985; Shah and Singh 1988; Vogt and Walsh 1985). Where it is used as a dry cleaning agent and in the manufacture of other chemicals, indoor air concentrations of 1,2-dichloroethene are likely to be greater than concentrations in outdoor air. Information concerning the number of persons potentially exposed to 1,2-dichloroethene near waste sites, manufacturing and production facilities, and use facilities, however, is not available. In these areas and in areas of widespread use, the potential for human exposure is high. Monitoring data that showed the existence of 1,2-dichloroethene in food could not be located. 1,2-Dichloroethene has been detected infrequently in drinking water supplies. Reliable estimates of human intake of 1,2-dichloroethene via air, water, and food are not available. Therefore, it is recommended that further studies on human intake of 1,2-dichloroethene from air, water, and food, particularly around hazardous waste sites, be undertaken.

Exposure Levels in Humans. 1,2-Dichloroethene is not a naturally occurring substance. Monitoring data pertaining to the presence of 1,2-dichloroethene in human urine, breast milk, blood, or adipose tissue were not located in the available literature. Information on biological media monitoring of the general populations, particularly populations near waste sites, is necessary for assessing the need to conduct health studies on these populations.

Exposure Registries. No exposure registries for 1,2-dichloroethene were located. This substance is not currently one of the compounds for which a subregistry has been established in the National Exposure Registry. The substance will be considered in the future when chemical selection is made for subregistries to be established. The information that is amassed in the National Exposure Registry facilitates the epidemiological research needed to assess adverse health outcomes that may be related to exposure to this substance.

Production, Import/Export, Use, Release, and Disposal. According to the Emergency Planning and Community Right-to-Know Act of 1986, 42 U.S.C. Section 11023, industries are required to submit substance release and off-site transfer information to the EPA. The Toxics Release Inventory (TRI), which contains this information for 1993, became available in 1995. This database will be updated yearly and should provide a list of industrial production facilities and emissions.

Exposure Levels in Environmental Media. Reliable monitoring data for the levels of 1,2dichloroethene in contaminated media at hazardous waste sites are needed so that the information

obtained on levels of 1,2-dichloroethene in the environment can be used in combination with the known body burden of 1,2-dichloroethene to assess the potential risk of adverse health effects in populations living in the vicinity of hazardous waste sites.

5.7.2 Ongoing Studies

As part of the Third National Health and Nutrition Evaluation Survey (NHANES III), the Environmental Health Laboratory Sciences Division of the National Center for Environmental Health, Centers for Disease Control and Prevention, will be analyzing human blood samples for 1,2-dichloroethene and other volatile organic compounds. These data will give an indication of the frequency of occurrence and background levels of these compounds in the general population.

No studies on the environmental fate of 1,2dichloroethene are in progress. NIOSH is now updating its occupational exposure estimates with additional information about exposure to trade name compounds. No other ongoing studies that would address data needs on general population and worker exposure to 1,2-dichloroethene were found.

6. ANALYTICAL METHODS

The purpose of this chapter is to describe the analytical methods that are available for detecting, and/or measuring, and/or monitoring 1,2-dichloroethene, its metabolites, and other biomarkers of 1,2-dichloroethene exposure and effect. The intent is not to provide an exhaustive list of analytical methods. Rather, the intention is to identify well-established methods that are used as the standard methods of analysis. Many of the analytical methods used for environmental samples are the methods approved by federal agencies and organizations such as EPA and the National Institute for Occupational Safety and Health (NIOSH). Other methods presented in this chapter are those that are approved by groups such as the Association of Official Analytical Chemists (AOAC) and the American Public Health Association (APHA). Additionally, analytical methods are included that modify previously used methods to obtain lower detection limits, and/or to improve accuracy and precision.

To determine dichloroethenes in various matrixes, most approaches involve purge procedures. Since these analytes are volatile (bp: 60.3 °C cis; 48.0-48.5 °C trans), removing them from an often complex matrix has very distinct advantages, particularly for biological and environmental samples. Virtually all standard methods use purge and trap procedures, in which the compounds are volatilized by passing an inert gas through a sample solution or suspension and the purged components are trapped on a solid sorbent for subsequent removal and analysis by gas chromatography (GC). Because of the presence of halogens, dichloroethenes can be selectively detected using devices such as electron capture, Hall electrolytic conductivity, or photoionization detectors. The most common detection technique specified by the standard methods is mass spectrometry (MS), which can readily achieve a high degree of selectivity and sensitivity.

6.1 BIOLOGICAL SAMPLES

Methods of analysis for 1 ,2dichloroethene in biological materials are presented in Table 6- 1. The purge and trap method of Lin et al. (1982) is a suitable method for extraction and measurement of cisand trans- 1,2-dichloroethene in body tissues. However, recovery of trans- 1,2-dichloroethene varies with the type of body tissue. This finding generally agrees with those of the investigators who have attempted to measure levels of volatile halocarbons in body tissues. In addition to purge and trap, the headspace analysis methods of Hara et al. (1980) and Uehori et al. (1987) allow qualitative

Table 6-1. Analytical Methods for Determining 1,2-Dichloroethene in Biological Samples

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Adipose, kidney, and brain tissue	Mince and purge tissue at 60 °C; trap on Tenax®; thermal desorption	GC/HECD	50 pg	93.3±12.4[a](adipose) 53.4±2.4[a](kidney) 62.6±2.6[a] (brain)	Lin et al. 1982
Blood	Heat in a closed vial	GC/FID	No data	No data	Uehori et al. 1987
Blood	Mix with water; heat in a closed vial at 40 °C; headspace analysis	GC/MS	10–20 pg	No data	Hara et al. 1980
Blood	Purge and trap with antifoaming agent; thermal desorption	GC/MS	20 ppt	~ 125	Ashley et al. 1992
Blood, urine, solid tissue	Sample in sealed vial heated to 65 °C; headspace analysis	GC/FID GC/ECD	No data	No data	Streete et al. 1992
Body tissue	Homogenize and mix tissue with water; heat in a closed vial at 40 °C; headspace analysis	GC/MS	10–20 pg	No data	Hara et al. 1980
Breath	Portable spirometer into canisters	GC/MS	No data	99 (trans) 90 (cis)	Raymer et al. 1990

[a]For trans-1,2-dichloroethene

ECD = electron capture detector; FID = flame ionization detector; GC = gas chromatography; HECD = Hall electroconductivity detection; MS = mass spectrometry

identification of 1,2-dichloroethene in biological materials. A combination of detectors enabled Streete et al. (1992) to determine dichloroethenes in the headspace of blood, urine, and solid tissues. Dichloroethenes in breath can be determined by GUMS after collection with a portable spirometer (Raymer et al. 1990). In this approach, recoveries exceeded 90% for the dichloroethene isomers. The detection limit for dichloroethenes in human blood has been extended to part-per-trillion levels by Ashley et al. (1992), using an automated purge and trap technique that suppresses sample foaming with an antifoaming agent. High resolution GUMS can be used to enhance the contaminant separation abilities of gas chromatography on blood samples (Ashley et al. 1992; Bonin et al. 1992).

6.2 ENVIRONMENTAL SAMPLES

Analytical methods for determining cis- and trans- 1,2 dichloroethene in environmental samples are presented in Table 6-2. Analysis of 1,2 dichloroethene in workplace air samples can be determined by NIOSH method 1003 (NIOSH 1987).

Methodologies appearing in the literature for sampling 1,2-dichloroethene in air are essentially the same with minor variations. Capillary columns are versatile in separating contaminants of interest, and usually offer superior resolution and limits of detection (Oxenford et al. 1989). Various detectors are used, such as flame ionization detectors (FID), electron capture detectors (ECD), Hall electroconductivity detectors (HECD), and mass spectrometers. Multiple detectors are often employed in series or in parallel to increase the number and types of compounds detectable by purge and trap methods (Ho 1989; Kessels et al. 1992). Of the four listed, the FID is the least sensitive to halogenated hydrocarbons, yet it is sensitive enough for environmental samples.

For 1,2-dichloroethene, adsorption to the solid sorbent is a significant analytical concern because of its volatility. It may be difficult to completely remove highly volatile compounds such as 1,2-dichloroethene from the air stream. Solid sorbents other than charcoal appear in some analytical methods; the most popular is the resin, Tenax® GC. In addition to Tenax, Mehran et al. (1990) usedCarbosieve® with capillary chromatography to decrease the analysis time for EPA method 502.2. Pollack and coworkers (1991) provide for automating the collection and analysis of cis-1,2-dichloroethene by focusing the sample on a trap consisting of Carbopack-B and Carbosieve S-III instead of on glass beads. Substituting spray and trap for purge and trap enhances extraction efficiencies by a factor of 2-5 and eliminates difficulties associated with sample foaming (Matz and Kesners 1993).

Table 6-2. Analytical Methods for Determining 1,2-Dichloroethene in Environmental Samples

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Air	Charcoal tube collection and CS_2 desorption	GC/FID	16 ppm	No data	NIOSH 1987
Air	Stainless steel canister (modified EPA method TO-14)	GC/MS	0.3 ppb (cis)	No data	McClenny et al. 1991
Air	Gas sampling loop	Fast GC/FID	4.3 ppb (cis)	No data	Ke et al. 1992b
Drinking water	Purge and trap onto adsorbent; backflush to cryogenically-cooled trap	GC/HECD	0.002 µg/L	80±7	EPA 1986e
Drinking water	Automated purge and trap; thermal desorption	GC/PID; GC/HECD (capillary)	No data	No data	Ho et al. 1989
Drinking water	Purge and trap (modified EPA method 524.2)	GC/ITD (capillary)	<0.2 µg/L	100 (cis) 92 (trans)	Eichelberger et al. 1990
Drinking water	Purge and trap (modified EPA method 524.2)	GC/FID; GC/ECD (capillary)	0.01 µg/L (trans)[a] 0.03 µg/L (cis)[a]	100 (trans) 99 (cis)	Kessels et al. 1992
Water	Purge and trap; thermal desorption	GC/MS (method 6210)	1.6 µg/L (trans)	1.05*C*+0.03[b] (trans)	APHA/AWWA/WEF 1992 (Standard Methods)
Water	Purge and trap onto adsorbent; thermal desorption	GC/HECD (method 6230)	0.10 µg/L (trans)	0.97*C*-0.16 (trans)	APHA/AWWA/WEF 1992 (Standard Methods)
Water	Flow injection	MIMS (uses ion trap MS)	0.5 ppt (trans)	No data	Bauer and Solyom 1994; Soni et al. 1995
Groundwater, soil, sediment, solid waste	Purge and trap onto adsorbent; thermal desorption	GC/MS (SW846 method 8240B)	5 µg/L (trans)	1.05*C*+0.03	EPA 1986
Groundwater, soil, sediment, solid waste	Purge and trap onto adsorbent; thermal desorption	GC/MS (SW846 method 8260A)	60 ng/L (trans), 120 ng/L (cis)	93±5.2 (trans), 101±6.7 (cis)	EPA 1986

Table 6-2. Analytical Methods for Determining 1,2-Dichloroethene in Environmental Samples (continued)

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Groundwater, soil, sediment, solid waste	Purge and trap onto adsorbent; thermal desorption	GC/HECD (SW846 method 8010B)	2 ng/L (optimum conditions for trans)	0.97*C*-0.16 (trans)	EPA 1986
Groundwater, soil, sediment, solid waste	Purge and trap onto adsorbent; thermal desorption	GC/PID GC/HECD (SW846 method 8021A)	50 ng/L (trans) 60 ng/L (trans)	93±3.7 (trans) 99±3.7 (trans)	EPA 1986
Wastewater	Purge and trap onto adsorbent; backflush to cryogenically-cooled trap	GC/HECD (EPA 601)	0.1 µg/L	91±19	EPA 1982
Wastewater	Purge and trap onto adsorbent; backflush to cryogenically-cooled trap	GC/MS (EPA 624)	1.6 µg/L	99±12	EPA 1982
Wastewater	Purge and trap (EPA Master Analytical Scheme)	GC/MS (capillary)	~1 ppb	No data	Michael et al. 1991
Landfill leachate	Homogenized sample; heated at 40 °C; headspace sampled	GC/MS (qual.) GC/FID (quant.)	~1 ppb	No data	Först et al. 1989
Soil	Purge and trap onto adsorbent; rapid heating desorption	GC/MS	5 µg/kg	No data	EPA 1987b
Food	Headspace with solid-phase microextraction	GC/HECD	~100 µg/kg	No data	Page and Lacroix 1993
Food	Homogenize sample in alcohol	GC/MCD	No data	No data	AOAC 1990a

[a]ECD
[b]This formula has concentration entered as µg/L in place of *C* (true concentration) then calculated as a percentage.
Example: For 0.97*C*-0.16 at a concentration of 10 µg/L: (0.97×10) - 0.16 = 9.54. 9.54 of 10 is equivalent to 95.4% recovery.

AOAC = Association of Official Analytical Chemists; APHA = American Public Health Association; AWWA = American Water Works Association; ECD = electron capture detection; EPA = Environmental Protection Agency; FID = flame ionization detection; GC = gas chromatography; HECD = Hall electrolytic conductivity detection; ITD = ion trap detection; MCD = microcoulometric detection; MIMS = membrane introduction mass spectrometry; MS = mass spectrometry; NIOSH = National Institute of Occupational Safety and Health; PID = photoionization detection; WEF = Water Environment Federation

6. ANALYTICAL METHODS

EPA method 601 (purgeable halocarbons) and EPA method 524 (purgeables) describe analysis of 1,2-dichloroethene in municipal and industrial waste water (EPA 1982). In both methods, a 5 mL grab sample of water is connected to a purging chamber. This chamber allows an inert gas to bubble through the water sample; the gas flow is directed through an adsorbent tube. In EPA method 601, nitrogen or helium.is the purging gas, and the adsorbent column consists of two different adsorbents and a drying agent. In EPA method 624, helium is the purging gas, and the adsorbent column is made up of one adsorbent and a drying agent. The collected organics are liberated from the sorbent by heating the sorbent column while backflushing with an inert gas; these organics are then introduced into the gas chromatograph. EPA methods 601 and 624 were developed to analyze volatile priority pollutants. In EPA method 601, analysis by GC uses a Carbopack B column, a Poracil C column, and a HECD detector. In EPA method 624, analysis by GC uses a Carbopack B column and a mass spectrometer. Since trans-1,2-dichloroethene is a priority pollutant and cis- 1,2-dichloroethene is not, only the trans isomer is mentioned in this method.

EPA method 502.1 is used to analyze 1,2-dichloroethene in finished or raw source water (EPA 1986e). This method is similar to EPA method 601. However, once the compound has been purged from the water sample to the adsorbent tube, the compound is introduced to the gas chromatograph by rapidly heating the adsorbent tube, with no intermediate cryogenic trapping.

Numerous researchers have applied modifications of the EPA methods to environmental samples. EPA's Master Analytical Scheme (Michael et al. 1991) incorporates automated purge and trap and capillary chromatography into method 624 to achieve sensitivity of 1 ppb. Method 624 was compared to purgeable organic chloride analysis by Barber et al. (1992) and found to be superior by virtue of its contaminant identification capabilities. Eichelberger et al. (1990) modified method 524 by using a capillary column and an ion trap detector (ITD) to achieve detection levels below 200 ppt. Headspace sampling coupled with capillary GUMS offers a promising screening tool since it requires minimal sample preparation (Gryder-Boutet and Kennish 1988). Headspace GUMS can also been used for determining dichloroethenes in landfill leachate (Forst et al. 1989).

Purge and trap methodology sometimes involves direct trapping of the bubbled compound cryogenically. Water contamination can become a problem in this method. The cryogenic trap described in EPA methods 601 and 624 is a specialized item and may not be adaptable to all gas

chromatographs. The considerations discussed above regarding use of different columns and detectors also apply here.

The EPA guidelines for contract laboratories include methodology for water and soil sample analysis (EPA 1987c). The method listed in Table 6-2 is identical to EPA method 502.1 for the purpose of this discussion (except for the use of a mass spectrometer as the detector). The procedure for analyzing low-level contamination in soil is also similar to EPA method 502.1, except that the purging gas passes through a soil sample rather than a water sample. For higher-level soil contamination, the soil sample is first extracted with methanol. An aliquot of the extract is diluted with water; then the purge and trap methodology is followed. With respect to dichloroethene recoveries, Hewitt et al. (1991) found a headspace technique that is comparable to EPA SW-846 method 8240 for soil. It is practical for sample screening where contaminant identities were not required. The various SW-846 methods for 1,2-dichloroethene presented in Table 6-2 are similar except for detection method.

EPA method TO-14 uses an evacuated stainless steel canister to collect ambient air samples. Sample aliquots are analyzed by GUMS. McClenny et al. (1991) report a method detection limit of 0.3 ppb for this method. A method which represents a significant departure from more traditional methods for environmental samples is solid-phase microextraction (SPME). Solid phase microextraction uses a coated fused-silica fiber to collect contaminants from air and water samples. Chai et al. (1993) describe a simple non-purge and trap technique for determining dichloroethenes in air and water using this approach. The contaminants on the coated fused-silica fiber can then be thermally desorbed directly into the gas chromatograph for analysis. Page and Lacroix (1993) show the utility of headspace sampling coupled with fused-silica fiber adsorption in determining dichloroethenes at the 100 ppt level in foods. Their method satisfies the detection limit requirements of EPA method 524.2 for chloroethenes. Bauer and Solyom (1994) have developed a method to directly analyze waters in an ion trap mass spectrometer and have achieved a limit of detection for trans-1,2-dichloroethene of 0.5 ppt using single ion monitoring of *m/z* 96 (Soni et al. 1995).

6.3 ADEQUACY OF THE DATABASE

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information is not available, ATSDR, in conjunction with the NTP, is required to assure the initiation of a program of research designed to determine the health effects (and techniques for developing methods to determine such health effects) of 1,2-dichloroethene.

The following categories of possible data needs have been identified by a joint team of scientists from ATSDR, NTP, and EPA. They are defined as substance-specific informational needs that if met would reduce the uncertainties of human health assessment. This definition should not be interpreted to mean that all data needs discussed in this section must be filled. In the future, the identified data needs will be evaluated and prioritized, and a substance-specific research agenda will be proposed.

6.3.1 Identification of Data Needs

Methods for Determining Biomarkers of Exposure and Effect. The available database provides several analytical methods adequate for the measurement of cis- and trans- 1,2dichloroethene in body tissue (see Section 6.1). Accuracy measurements for 1,2dichloroethene by Lin et al. (1982) show excellent recovery from adipose tissue but marginal recoveries from kidney and brain tissues. 1,2Dichloroethene was recovered at 88-150% from blood (Ashley et al. 1992). Limits of detection for all biological matrices ranged from 10 to 50 pg. Additional recovery data in all condensed biological media are needed. Other than the parent compounds, there are no known biomarkers of exposure or the effects of exposure that are unique to 1,2-dichloroethene. Consequently, biomarkers of exposure or the effect of exposure should be identified; standardized analytical methods for their determination should be identified or developed in response. These biomarkers could allow an easier route for identification of exposure, especially for some tissues where bioconcentration of 1,2-dichloroethene does not occur.

Methods for Determining Parent Compounds and Degradation Products in Environmental Media. Numerous analytical methods exist for analysis of cis- and trans-1,2-dichloroethene in environmental matrices (see Section 6.2). These analytical methods may be used to identify areas of 1,2-dichloroethene contamination, and to determine the potential threat to human health of 1,2-dichloroethene in the environment. Standardized methods exist for the analysis of drinking water, waste water, soil and air (APHA 1992; EPA 1986, 1987b; NIOSH 1987). Standardized methods for analyzing other media such as sediments and surface water will aid in establishing levels of human exposure to 1,2-dichloroethene. Inhalation is the most probable route of

exposure, and atmospheric exposure is likely to be of greatest concern to humans. However, the standardized methods for detecting 1,2-dichloroethene in air appear to be weak. For example, its detection limit of 16 ppm, outlined by the NIOSH technique (NIOSH 1987), is relatively high. Conversely, the stainless steel canister method of McClenny et al. (1991) purports to have a detection limit of 0.3 ppb and although not rigorously standardized, shows promise in detecting ambient background levels of 1,2-dichloroethene. Information regarding the recovery efficiencies of the NIOSH (1987), McClenny (1991), and Ke et al. (1992b) procedures for detecting 1,2-dichloroethene in air were lacking. Additional data is needed to assess both accuracy and precision in the analysis of 1,2-dichloroethene in air.

Contamination of surface water, groundwater, and foods in the vicinity of waste sites poses a threat to humans through oral exposure to 1,2-dichloroethene. Near quantitative recoveries and <.02 ppb detection limits were reported by Eichelberger et al. (1990). Low part-per-trillion detection limits were reported by Kessels et al. (1992) and an 0.5 ppt detection limit was reported by Soni et al. (1995). These recoveries and detection limits for 1,2-dichloroethene in water, coupled with the specificity offered by capillary gas chromatography and selective detection used by these researchers provide a means for determining 1,2-dichloroethene at very low levels in water.

Currently, no viable method exists for determining 1,2-dichloroethene in food. The detection limit of 100 μg/kg reported by Page and Lacroix (1993) is at least two orders of magnitude higher than what is required to be comparable to existing air and water methods for 1,2-dichloroethene. Appreciable additional work is needed in this area.

6.3.2 Ongoing Studies

The Environmental Health Laboratory Sciences Division of the National Center for Environmental Health, Centers for Disease Control and Prevention, is developing methods for the analysis of both cisand trans-1,2-dichloroethene and other volatile organic compounds in blood. These methods use purge and trap methodology, high resolution gas chromatography, and magnetic sector mass spectrometry which gives detection limits in the low parts per trillion (ppt) range.

Ongoing studies for developing new analytical methods for 1,2-dichloroethene in environmental matrices could not be located.

7. REGULATIONS AND ADVISORIES

The international, national, and state regulations and guidelines regarding 1,2-dichloroethene in air, water, and other media are summarized in Table 7-l.

ATSDR has derived an MRL of 0.2 ppm for both acute-duration inhalation exposure (14 days or less) and intermediate-duration inhalation exposure (15-365 days) to trans- 1,2-dichloroethene based on a study by Freundt et al. (1977) that found fatty degeneration of the liver. The acute MRL is based on an LOAEL of 200 ppm over an 8-hour period, and the intermediate MRL is based on an LOAEL of 200 ppm for 8 hours per day, 5 days per week for 8 or 16 weeks.

ATSDR has derived oral MRLs for both acute- and intermediate-duration exposure. For acute oral exposure, data supported the derivation of an MRL for cis-1,2-dichloroethene of 1 mg/kg/day; however, no acute-duration MRL was derived for trans-1,2-dichloroethene. The acute oral MRL for cis-1,2-dichloroethene is based on a study by McCauley et al. (1990) that found hematological effects at 290 mg/kg/day and reported a NOAEL of 97 mg/kg/day.

Intermediate-duration oral exposure MRLs were derived for both the cis and trans isomers. The intermediate duration oral MRL for cis-1,2-dichloroethene is 0.3 mg/kg/day based on a hematological study (McCauley et al. 1990). For trans-1,2-dichloroethene, the intermediate oral MRL is 0.2 mg/kg/day, based on hepatic effects (Barnes et al. 1985).

EPA has given cis-1,2-dichloroethene a non-cancer rating or a “not classifiable” rating (D) (IRIS 1995). No National Toxicology Program (NTP) or IARC classifications exists.

OSHA requires employers of workers who are occupationally exposed to a mixture of trans- and cis-1,2-dichloroethene (CAS No. 540-59-0) to institute engineering controls and work practices to reduce exposure-to and maintain employee exposure at or below permissible exposure limits (PEL). The employer must use engineering and work practice controls, if feasible, to reduce exposure to or below an g-hour time-weighted average (TWA) of 200 ppm (790 mg/m^3). Respirators must be provided during the time period necessary to install or implement feasible engineering and work practice controls (OSHA 1989).

7. REGULATIONS AND ADVISORIES

1,2-Dichloroethene is regulated by the Clean Water Effluent Guidelines as stated in Title 40, Section 400-475, of the Code of Federal Regulations. The point source category for which 1,2-dichloroethene is controlled as a Total Toxic Organic is electroplating (EPA 1981).

The Resource Conservation and Recovery Act (RCRA) identifies 1,2-dichloroethene as a hazardous waste when it is discarded as a commercial chemical product, off-spec species, container residue, or spill residue (EPA 1980a).

Table 7-1. Regulations and Guidelines Applicable to trans- and cis-1,2-Dichloroethene

Agency	Description	Information trans	Information cis	Reference
INTERNATIONAL				
WHO		NAp	NAp	
IARC	Group (cancer ranking)	None	None	
NATIONAL				
Regulations:				
a. Water:				
EPA/OW	Ambient Water Quality Criterion	$1.16x10^{+4}$ µg/L (aquatic organisms)	$3.3x10^{-2}$ µg/L (human health)	IRIS 1995 45 FR 79318 (11/28/80)
	Method 601-Purgeable Halocarbons	Yes	NAp	40 CFR 136 EPA 1973
	Method 624-Purgeables	Yes	NAp	40 CFR 136 EPA 1973
	Method 1624 Revision B - Volatile Organic Compounds by Isotope Dilution GC/MS	Yes	NAp	40 CFR 136 EPA 1973
	Hazardous Waste Injection Restrictions (Proposed rule)	Yes	NAp	40 CFR 148 60 FR 11702 EPA 1995
EPA-ODW	Public Notification	Yes	NAp	40 CFR 141.32 EPA 1975a
	Maximum Contaminant Levels for Organic Contaminants	0.1 mg/L	0.1 mg/L	40 CFR 141.61 EPA 1975a
b. Other:				
CPSC	Consumer product limits	Nap	NAp	
EPA/OERR	Reportable Quantity	1,000 lb.	NAp	40 CFR 302.4 EPA 1985
EPA/OSW	Municipal Solid Waste Landfills: Appendix I - Constituents for Detection Monitoring	Yes	Yes	40 CFR 258 EPA 1991
	Municipal Solid Waste Landfills: Appendix II - List of Hazardous Inorganic and Organic Constituents	0.5–5 µg/L (Practical Quantitation Limits for 3 Methods)	same	40 CFR 258 EPA 1991
	Discarded Commercial Chemical Products, Off-specification Species, Container Residues, and Spill Residues Thereof	Yes	NAp	40 CFR 261.33 EPA 1980a
	Identification and Listing of Hazardous Wastes: Appendix VIII - Hazardous Constituents	Yes	NAp	40 CFR 261 EPA 1980a
	Standards for Owners and Operators of Hazardous Waste Treatment, Storage, and Disposal Facilities: Appendix IX - Ground-water Monitoring List	1-5 µg/L (Practical Quantitation Limits for 2 Methods)	NAp	40 CFR 264 EPA 1980

Table 7-1. Regulations and Guidelines Applicable to trans- and cis-1,2-Dichloroethene (continued)

Agency	Description	Information trans	Information cis	Reference
NATIONAL (cont.)				
	Treatment Standards - Applicability	Yes	Nap	40 CFR 268.40 EPA 1987
	Treatment Standards Expressed as Waste Concentrations	0.054 mg/L (waste waters); 33 mg/kg (non-waste waters)	NAp	40 CFR 268.43 EPA 1988
	Land Disposal Restrictions: Appendix III - List of Halogenated Organic Compounds Regulated Under 268.32	Yes	NAp	40 CFR 268 EPA 1986
	Universal Treatment Standards (proposed)	0.054 mg/L	Nap	40 CFR 268.48 EPA 1995b 60 FR 242
Guidelines:				
a. Air:				
ACGIH	Ceiling Limit for Occupational Exposure (TLV-TWA)	200 ppm (790 mg/m^3) (CAS No. 540-59-0)		ACGIH 1994
NIOSH	Recommended Exposure Limit for Occupational exposure (TWA)	200 ppm (790 mg/m^3) TWA (CAS No. 540-59-0)		NIOSH 1992
b. Water:				
EPA	1-d Health Advisory	20 mg/L (child)	4 mg/L (child)	EPA 1995c
	10-d Health Advisory	2 mg/L (child)	3 mg/L (child)	EPA 1995c
	Lifetime Health Advisory	0.1 mg/L (adult)	0.07 mg/L (adult)	EPA 1995c
	Longer-term Health Advisory	6 mg/L (adult) 2 mg/L (child)	11 mg/L (adult) 3 mg/L (child)	EPA 1995c
	Maximum Contaminant Level	0.1 mg/L	0.07 mg/L	EPA 1995c
	Maximum Contaminant Level Guideline	0.1 mg/L	0.07 mg/L	EPA 1995c
c. Other:				
EPA	Cancer classification	None	D[a]	IRIS 1995
NTP	Cancer classification	None	None	

Table 7-1. Regulations and Guidelines Applicable to trans- and cis-1,2-Dichloroethene (continued)

Agency	Description	Information trans	Information cis	Reference
STATE				
Regulations and Guidelines a. Air:				
	Acceptable Ambient Air Concentration Guidelines or Standards[b]			NATICH 1992
AZ	1 hr avg. time		$2.38 \times 10^{+4}$ $\mu g/m^3$ (6.00 ppm)	
	24 hr avg. time		$6.30 \times 10^{+3}$ $\mu g/m^3$ (1.60 ppm)	
CT	8 hr avg. time	$1.58 \times 10^{+4}$ $\mu g/m^3$ (3.99 ppm)		
FL-PINELLA	8 hr avg. time	$2.90 \times 10^{+3}$ $\mu g/m^3$ (0.731 ppm)		
	24 hr avg. time	$6.96 \times 10^{+2}$ $\mu g/m^3$ (0.176 ppm)		
MA	24 hr avg. time	$2.16 \times 10^{+2}$ $\mu g/m^3$ (0.054 ppm)		
	Annual avg. time	$1.08 \times 10^{+2}$ $\mu g/m^3$ (0.027 ppm)		
ND	8 hr avg. time	7.93 mg/m^3 (2.00 ppm)		
NV	8 hr avg. time	$1.88 \times 10^{+1}$ mg/m^3 (4.74 ppm)		
NY	Annual avg. Time	3.6×10^{2} $\mu g/m^3$ (0.091 ppm)	1.9×10^{3} $\mu g/m^3$ (0.479 ppm)	Sittig 1994
OK	24 hr avg. time	$7.93 \times 10^{+4}$ $\mu g/m^3$ (20.00 ppm)		NATICH 1992
TX	30 min avg. time	$7.93 \times 10^{+3}$ $\mu g/m^3$ (2.00 ppm)		

Table 7-1. Regulations and Guidelines Applicable to trans- and cis-1,2-Dichloroethene (continued)

Agency	Description	Information trans	Information cis	Reference
STATE (Cont.)				
	Annual avg. time	$7.90x10^{+2}$ $\mu g/m^3$ (0.199 ppm)		
	30 min avg. time		$7.90x10^{+3}$ $\mu g/m^3$ (2.00 ppm)	
	Annual avg. time		$7.90x10^{+2}$ $\mu g/m^3$ (0.199 ppm)	
VA	24 hr avg. time	$1.30x10^{+4}$ $\mu g/m^3$ (3.28 ppm)		
VT	8 hr avg. time	$7.90x10^{+4}$ $\mu g/m^3$ (19.93 ppm)		
WA-SWEST	24 hr avg. time	$2.63x10^{+3}$ $\mu g/m^3$ (0.663 ppm)		
b. Water:				
	Water Quality: Human Health			CELDs 1993
AZ	Domestic water source	100 µg/L	70 µg/L	
	Fish consumption	13,000 µg/L		
CA	Drinking water guideline	10 µg/L	6 µg/L	FSTRAC 1990
CT	Listed but no values			CELDs 1993
DE	Freshwater fish ingestion only	130.0 mg/L		
	Freshwater fish & water ingestion	700 µg/L		
	Marine, estuarine fish/shellfish ingestion	19.0 mg/L		
FL	Domestic/Drinking water	100 µg/L	70 µg/L	Sittig 1994
KS	Drinking water guideline	70 µg/L	70 µg/L	FSTRAC 1990
MA	Drinking water guideline	70 µg/L	70 µg/L	
ME	Drinking water guideline	70 µg/L	70 µg/L	
MI	Domestic/Drinking water	120 µg/L	77 µg/L	Sittig 1994
MN	Drinking water guideline	70 µg/L	70 µg/L	FSTRAC 1990

Table 7-1. Regulations and Guidelines Applicable to trans- and cis-1,2-Dichloroethene (continued)

Agency	Description	Information trans	Information cis	Reference
STATE (Cont.)				
MO	Fish consumption	140,000 µg/L		CELDs 1993
	Drinking water supply	700 µg/L		
NH	Drinking water guideline	100 µg/L	70 µg/L	FSTRAC 1990
NJ	Drinking water standard: generic	100 µg/L	10 µg/L	Sittig 1994
NY	Domestic/Drinking water	5 µg/L		
OR	Generic: Water & fish ingestion	0.033 µg/L		CELDs 1993
	Domestic/Drinking water	100 µg/L	70 µg/L	Sittig 1994
	Fish consumption only	1.85 µg/L		CELDs 1993
RI	Drinking water guideline	70 µg/L		FSTRAC 1990
TN	Domestic/Drinking water	100 µg/L	70 µg/L	Sittig 1994
TX	Domestic/Drinking water		70 µg/L	
VT	Drinking water guideline: generic	70 µg/L		FSTRAC 1990
WI	Drinking water guideline	100 µg/L	100 µg/L	
	Water Quality: Aquatic			CELDs 1993
AL	Listed but no value			
AZ	Acute-cold water fishery	68,000 µg/L		
	Acute-warm water fishery	68,000 µg/L		
	Acute-effluent dominated water	68,000 µg/L		
	Chronic-cold water fishery	3,900 µg/L		
	Chronic-warm water fishery	3,900 µg/L		
	Chronic-effluent dominated water	3,900 µg/L		
NJ	Generic "Dichloroethylenes" (1,2 dce listed as subset but no value) - Acute-freshwater (max)	11,600		
	Acute-saltwater (max)	224,000		
OH	Exceptional modified, & seasonal warm water; outside mixing zone; max	7000 µg/L		
	Exceptional modified, & seasonal warm water; outside mixing zone; max; 30-d avg.	310 µg/L		
	Exceptional modified, & seasonal warm water; outside mixing zone; inside mixing zone; maximum	14,000 µg/L		

Table 7-1. Regulations and Guidelines Applicable to trans- and cis-1,2-Dichloroethene (continued)

Agency	Description	Information trans	Information cis	Reference
STATE (Cont.)				
	Cold water & limited resource warmwater; outside mixing zone; maximum	7,000 µg/L		
	Coldwater & limited resource warmwater; 30-d avg.	310 µg/L		
	Cold water & limited resource warmwater; inside mixing zone; max	14,000 µg/L		
OR	Generic: Acute-freshwater	11,600 µg/L		
	Acute-marine	224,000µg/L		
	Water Quality: Recreational Use			CELDs 1993
AZ	Full body contact	2,800 µg/L		
	Partial body contact	2,800 µg/L		
	Groundwater Quality Standards			CELDs 1993
MO		700 µg/L		
NC	Class GS		0.07 mg/L	
	Class GS	0.07 mg/L		
WI	Enforcement standard		100 µg/L	
	Preventive action limit		10 µg/L	
	Enforcement standard	100 µg/L		
	Preventive action limit	20 µg/L		
	Groundwater Monitoring Parameter			CELDs 1993
CO	Generic	Yes		
IL		Yes		
LA		Yes		
MN		Yes		
VA		Yes		
WI		Yes		
	MCLG's = MCLs or Action Levels			
WI		0.1 mg/L	0.07 mg/L	
SD	Surfacewater Discharge Permit Application Requirements: Testing Requirements for Organic Toxic Pollutants	Yes		
NJ	NPDES Permits: Testing Requirements for Organic Toxic Pollutants	Yes		

Table 7-1. Regulations and Guidelines Applicable to trans- and cis-1,2-Dichloroethene (continued)

Agency	Description	Information trans	Information cis	Reference
STATE (Cont.)				
WI	Toxic Discharge	Yes		
c. Other:				
	Hazardous Waste			CELDs 1993
CO		Yes (LDR)		
IL		Yes		
	Generic	Yes		
LA		Yes		
MA		Yes (LDR)		
	Hazardous Waste Constituents			CELDs 1993
CO		Yes		
IL		Yes		
LA		Yes		
	Generic	Yes		
	Generic	Yes		
MN	Generic	Yes		
ND	Generic	Yes		
WV	Generic	Yes (App. VIII)		
WI	Generic	Yes (App. IV)		

NOTE: Update of drinking water guidelines and other areas in progress.
Units in table reflect values and units of measure designated by each agency in its regulations or advisories.

[a] Not classifiable as to human carcinogenicity

[b] Additional Guidelines or Standards for a mixture of cis- and trans-1,2-dichloroethene (CAS No. 540-59-0)

ACGIH = American Conference of Governmental and Industrial Hygienists; CAS = Chemical Abstracts Services; CELDs = Computer-aided Environmental Legislative Database; CFR = Code of Federal Regulations; CPSC = Consumer Product Safety Commission; EPA = Environmental Protection Agency; FR = Federal Register; FSTRAC = Federal State Toxicology and Regulatory Alliance Committee; GC/MS = Gas Chromatography/Mass Spectrometry; IARC = International Agency for Research on Cancer; IRIS = Integrated Risk Information System; LDR = Land Disposal Restrictions; MCL = Maximum Contaminant Level; MCLG = Maximum Contaminant Level Goal; NA = Not available at the present time; NAp = Not applicable; NATICH = National Air Toxics Information Clearinghouse; NIOSH = National Institute of Occupational Safety and Health; NPDES = National Pollutant Discharge Elimination System; ODW = Office of Drinking Water ;OERR = Office of Emergency and Remedial Response; OSW = Office of Solid Waste; OW = Office of Water; TLV = Threshold Limit Value; TWA = Time Weighted Average; WHO = World Health Organization

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9. GLOSSARY

Acute Exposure -- Exposure to a chemical for a duration of 14 days or less, as specified in the Toxicological Profiles.

Adsorption Coefficient (Koc) -- The ratio of the amount of a chemical adsorbed per unit weight of organic carbon in the soil or sediment to the concentration of the chemical in solution at equilibrium.

Adsorption Ratio (Kd) -- The amount of a chemical adsorbed by a sediment or soil (i.e., the solid phase) divided by the amount of chemical in the solution phase, which is in equilibrium with the solid phase, at a fixed solid/solution ratio. It is generally expressed in micrograms of chemical sorbed per gram of soil or sediment.

Bioconcentration Factor (BCF) -- The quotient of the concentration of a chemical in aquatic organisms at a specific time or during a discrete time period of exposure divided by the concentration in the surrounding water at the same time or during the same period.

Cancer Effect Level (CEL) -- The lowest dose of chemical in a study, or group of studies, that produces significant increases in the incidence of cancer (or tumors) between the exposed population and its appropriate control.

Carcinogen -- A chemical capable of inducing cancer.

Ceiling Value -- A concentration of a substance that should not be exceeded, even instantaneously.

Chronic Exposure -- Exposure to a chemical for 365 days or more, as specified in the Toxicological Profiles.

Developmental Toxicity -- The occurrence of adverse effects on the developing organism that may result from exposure to a chemical prior to conception (either parent), during prenatal development, or postnatally to the time of sexual maturation. Adverse developmental effects may be detected at any point in the life span of the organism.

Embryotoxicity and Fetotoxicity -- Any toxic effect on the conceptus as a result of prenatal exposure to a chemical; the distinguishing feature between the two terms is the stage of development during which the insult occurred. The terms, as used here, include malformations and variations, altered growth, and in utero death.

EPA Health Advisory -- An estimate of acceptable drinking water levels for a chemical substance based on health effects information. A health advisory is not a legally enforceable federal standard, but serves as technical guidance to assist federal, state, and local officials.

Immediately Dangerous to Life or Health (IDLH) -- The maximum environmental concentration of a contaminant from which one could escape within 30 min without any escape-impairing symptoms or irreversible health effects.

Intermediate Exposure -- Exposure to a chemical for a duration of 15-364 days, as specified in the Toxicological Profiles.

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Immunologic Toxicity -- The occurrence of adverse effects on the immune system that may result from exposure to environmental agents such as chemicals.

In Vitro -- Isolated from the living organism and artificially maintained, as in a test tube.

In Vivo -- Occurring within the living organism.
Lethal Concentration IO)

Lethal Concentration $_{(LO)}$ (LC_{LO}) -- The lowest concentration of a chemical in air which has been reported to have cause death in humans or animals.

Lethal Concentration($_{50}$) (LC_{50}) -- A calculated concentration of a chemical in air to which exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population.

Lethal Dose($_{LO}$) (LD_{LO}) -- The lowest dose of a chemical introduced by a route other than inhalation that is expected to have caused death in humans or animals.

Lethal Dose($_{50}$) (LT_{50}) -- The dose of a chemical which has been calculated to cause death in 50% of a defined experimental animal population.

Lethal Time($_{50}$) (LT_{50}) -- A calculated period of time within which a specific concentration of a chemical is expected to cause death in 50% of a defined experimental animal population.

Lowest-Observed-Adverse-Effect Level (LOAEL) -- The lowest dose of chemical in a study, or group of studies, that produces statistically or biologically significant increases in frequency or severity of adverse effects between the exposed population and its appropriate control.

Malformations -- Permanent structural changes that may adversely affect survival, development, or function.

Minimal Risk Level -- An estimate of daily human exposure to a dose of a chemical that is likely to be without an appreciable risk of adverse noncancerous effects over a specified duration of exposure.

Mutagen -- A substance that causes mutations. A mutation is a change in the genetic material in a body cell. Mutations can lead to birth defects, miscarriages, or cancer.

Neurotoxicity -- The occurrence of adverse effects on the nervous system following exposure to chemical.

No-Observed-Adverse-Effect Level (NOAEL) -- The dose of chemical at which there were no statistically or biologically significant increases in frequency or severity of adverse effects seen between the exposed population and its appropriate control. Effects may be produced at this dose, but they are not considered to be adverse.

Octanol-Water Partition Coefficient (K_{ow}) -- The equilibrium ratio of the concentrations of a chemical in n-octanol and water, in dilute solution.

Permissible Exposure Limit (PEL) -- An allowable exposure level in workplace air averaged over an 8-hour shift.

9. GLOSSARY

q_1* -- The upper-bound estimate of the low-dose slope of the dose-response curve as determined by the multistage procedure. The q_1* can be used to calculate an estimate of carcinogenic potency, the incremental excess cancer risk per unit of exposure (usually μg/L for water, mg/kg/day for food, and $\mu g/m^3$ for air).

Reference Dose (RfD) -- An estimate (with uncertainty spanning perhaps an order of magnitude) of the daily exposure of the human population to a potential hazard that is likely to be without risk of deleterious effects during a lifetime. The RfD is operationally derived from the NOAEL (from animal and human studies) by a consistent application of uncertainty factors that reflect various types of data used to estimate RfDs and an additional modifying factor, which is based on a professional judgment of the entire database on the chemical. The RfDs are not applicable to nonthreshold effects such as cancer.

Reportable Quantity (RQ) -- The quantity of a hazardous substance that is considered reportable under CERCLA. Reportable quantities are (1) 1 pound or greater or (2) for selected substances, an amount established by regulation either under CERCLA or under Sect. 311 of the Clean Water Act. Quantities are measured over a 24-hour period.

Reproductive Toxicity -- The occurrence of adverse effects on the reproductive system that may result from exposure to a chemical. The toxicity may be directed to the reproductive organs and/or the related endocrine system. The manifestation of such toxicity may be noted as alterations in sexual behavior, fertility, pregnancy outcomes, or modifications in other functions that are dependent on the integrity of this system.

Short-Term Exposure Limit (STEL) -- The maximum concentration to which workers can be exposed for up to 15 min continually. No more than four excursions are allowed per day, and there must be at least 60 min between exposure periods. The daily TLV-TWA may not be exceeded.

Target Organ Toxicity -- This term covers a broad range of adverse effects on target organs or physiological systems (e.g., renal, cardiovascular) extending from those arising through a single limited exposure to those assumed over a lifetime of exposure to a chemical.

Teratogen -- A chemical that causes structural defects that affect the development of an organism.

Threshold Limit Value (TLV) -- A concentration of a substance to which most workers can be exposed without adverse effect. The TLV may be expressed as a TWA, as a STEL, or as a CL.

Time-Weighted Average (TWA) -- An allowable exposure concentration averaged over a normal S-hour workday or 40-hour workweek.

Toxic Dose (TD_{50}) -- A calculated dose of a chemical, introduced by a route other than inhalation, which is expected to cause a specific toxic effect in 50% of a defined experimental animal population.

Uncertainty Factor (UF) -- A factor used in operationally deriving the RfD from experimental data. UFs are intended to account for (1) the variation in sensitivity among the members of the human population, (2) the uncertainty in extrapolating animal data to the case of human, (3) the uncertainty in extrapolating from data obtained in a study that is of less than lifetime exposure, and (4) the uncertainty in using LOAEL data rather than NOAEL data. Usually each of these factors is set equal to 10.

APPENDIX A

ATSDR MINIMAL RISK LEVEL

The Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA) [42 U.S.C. 9601 et seq.], as amended by the Superfund Amendments and Reauthorization Act (SARA) [Pub. L. 99-4991, requires that the Agency for Toxic Substances and Disease Registry (ATSDR) develop jointly with the U.S. Environmental Protection Agency (EPA), in order of priority, a list of hazardous substances most commonly found at facilities on the CERCLA National Priorities List (NPL); prepare toxicological profiles for each substance included on the priority list of hazardous substances; and assure the initiation of a research program to fill identified data needs associated with the substances.

The toxicological profiles include an examination, summary, and interpretation of available toxicological information and epidemiologic evaluations of a hazardous substance. During the development of toxicological profiles, Minimal Risk Levels (MRLs) are derived when reliable and sufficient data exist to identify the target organ(s) of effect or the most sensitive health effect(s) for a specific duration for a given route of exposure. An MRL is an estimate of the daily human exposure to a hazardous substance that is likely to be without appreciable risk of adverse noncancer health effects over a specified duration of exposure. MRLs are based on noncancer health effects only and are not based on a consideration of cancer effects. These substance-specific estimates, which are intended to serve as screening levels, are used by ATSDR health assessors to identify contaminants and potential health effects that may be of concern at hazardous waste sites. It is important to note that MRLs are not intended to define clean-up or action levels.

MRLs are derived for hazardous substances using the no-observed-adverse-effect level/uncertainty factor approach. They are below levels that might cause adverse health effects in the people most sensitive to such chemical-induced effects. MRLs are derived for acute (1-14 days), intermediate (15-364 days), and chronic (365 days and longer) durations and for the oral and inhalation routes of exposure. Currently, MRLs for the demal route of exposure are not derived because ATSDR has not yet identified a method suitable for this route of exposure. MRLs are generally based on the most sensitive chemical-induced end point considered to be of relevance to humans. Serious health effects (such as irreparable damage to the liver or kidneys, or birth defects) are not used as a basis for establishing MRLs. Exposure to a level above the MRL does not mean that adverse health effects will occur.

APPENDIX A

ATSDR MINIMAL RISK LEVEL

MRLs are intended only to serve as a screening tool to help public health professionals decide where to look more closely. They may also be viewed as a mechanism to identify those hazardous waste sites that are not expected to cause adverse health effects. Most MRLs contain a degree of uncertainty because of the lack of precise toxicological information on the people who might be most sensitive (e.g., infants, elderly, nutritionally or immunologically compromised) to the effects of hazardous substances. ATSDR uses a conservative (i.e., protective) approach to address this uncertainty consistent with the public health principle of prevention. Although human data are preferred, MRLs often must be based on animal studies because relevant human studies are lacking. In the absence of evidence to the contrary, ATSDR assumes that humans are more sensitive to the effects of hazardous substance than animals and that certain persons may be particularly sensitive. Thus, the resulting MRL may be as much as a hundredfold below levels that have been shown to be nontoxic in laboratory animals.

Proposed MRLs undergo a rigorous review process: Health Effects/MRL Workgroup reviews within the Division of Toxicology, expert panel peer reviews, and agencywide MRL Workgroup reviews, with participation from other federal agencies and comments from the public. They are subject to change as new information becomes available concomitant with updating the toxicological profiles. Thus, MRLs in the most recent toxicological profiles supersede previously published levels. For additional information regarding MRLs, please contact the Division of Toxicology, Agency for Toxic Substances and Disease Registry, 1600 Clifton Road, Mailstop E-29, Atlanta, Georgia 30333.

MINIMAL RISK LEVEL (MRL) WORKSHEET

Chemical name: trans- 1,2-dichloroethene
CAS number: 156-60-5
Date: August 1996
Profile status: Final
Route: [x] Inhalation [ ] Oral
Duration: [x] Acute [IIntermediate [ ] Chronic
Key to figure: 2
Species: Rat

MRL: 0.2 [ ] mg/kg/day [x] ppm [ ] mg/m^3

Reference: Freundt, KJ, Liebaldt, GP, and Lieberwirth, E. 1977. Toxicity Studies on Trans-1,2-Dichloroethylene. Toxicology, 7, pp. 141-153.

Experimental design

- l Female, mature SPF Wistar Rats; 180-200 g.
- l Exposure for 8 hours; 0, 200, 1,000, and 3,000 ppm of trans-1,2-dichloroethene by inhalation.
- 6 rats/group.
- Animals were sacrificed immediately following exposure and examined for gross pathology including lung, heart, liver, kidney, spleen, brain, quadriceps muscle and sciatic nerve. Standard hematological tests, clinical chemistry tests, and tests of clearance of bromosulphthalein in bile were carried out.

Effects noted in study and corresponding doses:

- Slight to severe fatty degeneration of the hepatic lobules and Kupffer cells was seen in all dosing groups (except controls). At 200 ppm fatty degeneration and fatty accumulation in Kupffer cells was seen in l/6 rats; at 1,000 and 3,000 ppm 1 or 2/6 rats showed similar liver and Kupffer cell changes.
- Slight increases in capillary hyperaemia and alveolar septum distention were noted.
- Fibrous swelling, hyperemia and modified muscular striation were found in the cardiac muscles at 3,000 ppm in 2/6 rats.
- No pathological changes were seen in the kidneys, spleen, brain, or peripheral nerves. No central nervous system depression was seen.

Dose endpoint used for MRL derivation:

Fatty degeneration of liver cells: LOAEL = 200 ppm

[ ] NOAEL [x] LOAEL

APPENDIX A

Uncertainty factors used in MRL derivation:

[ ] 1 [ ] 3 [x] 10 (for use of a LOAEL)
[ ] 1 [ ] 3 [xl 10 (for extrapolation from animals to humans)
[ ] 1 [ ] 3 [x] 10 (for human variability)

Was a conversion factor used from ppm in food or water to a mg/body weight dose? No.
If so, explain:

If an inhalation study in animals, list conversion factors used in determining human eauivalent dose: The NOAEL $_{(HEC)}$ was calculated for a gas:extrarespiratory effect in rats assuming periodicity was attained, using the following equation: NOAEL $_{(HEC)}$ = NOAEL $_{(adj.)}$ x λ_A/λ_H, where: NOAEL $_{(HEC)}$ = the NOAEL human equivalent concentration; NOAEL $_{(adj)}$ = the NOAEL adjusted for continuous exposure (e.g., adjusted for exposure regimen by h hours/24 hours and d days/7 days); λ_A/λ_H, = the ratio of the blood to air partition coefficient of the chemical for the animal species to the human value, used only if λ_A/λ_H . For the situation in which $\lambda_A > \lambda_H$, and in the case where I values are unknown, the default value of λ_A/λ_H, = 1 is recommended. For 1,2-dichloroethene, λ_A = 9.58 and λ_H = 6.04, therefore $\lambda_A > \lambda_H$, and a default value of 1 was used.

Was a conversion used from intermittent to continuous exposure? No.
If so, explain:

Other additional studies or pertinent information that lend support to this MRL:

McCauley et al. (1990), Barnes et al. (1985), and McMillan (1986) also reported hepatic effects, from oral exposure to cis- or trans-1,2-dichloroethene.

Agency Contact (Chemical Manager): Carolyn Harper

APPENDIX A

MINIMAL RISK LEVEL WORKSHEET

Chemical name:trans-1,2-dichloroethene
CAS number: 156-60-5
Date: August 1996
Profile status: Final
Route: [x] Inhalation [ ] Oral
Duration: [ ] Acute [x] Intermediate [ ] Chronic
Key to figure: 11
Species: Rat

MRL: 0.2 [ ] mg/kg/day [xl ppm [ ] mg/m^3

Reference: Freundt, KI, Liebaldt, GP, and Lieberwirth, E. 1977. Toxicity Studies on Trans-1,2-Dichloroethylene. Toxicology, 7, pp. 141-153.

Experimental design

- Female, mature SPF Wistar Rats; 180-200 g.
- Exposure for g-hour periods, 5 days per week, for either 8 or 16 weeks, at or 200 ppm of trans-1,2-dichloroethene by inhalation.
- 6 rats/group.
- Animals were sacrificed immediately following exposure and examined for gross pathology including lung, heart, liver, kidney, spleen, brain, quadriceps muscle and sciatic nerve.

Effects noted in study and corresuonding doses:

- In the 8-week experiment, slight fatty degeneration of the hepatic lobules was observed in 316 exposed rats and severe fatty accumulation in the Kupffer cells was seen in 3/6 exposed rats (200 ppm). In the16-week experiment, slight (2/6 exposed) and severe (3/6 exposed) fatty accumulation in the liver lobule was seen and slight fatty accumulation in the Kupffer cells was seen in 5/6 exposed rats (200 PPm).
- Slight increases in capillary hyperaemia and alveolar septum distention were seen.
- No pathological changes were seen in the kidneys, spleen, brain, striated muscle, or peripheral nerves. No central nervous system depression was seen.

Dose endpoint used for MRL derivation:

Fatty degeneration of liver cells: LOAEL = 200 ppm

[ ] NOAEL [x] LOAEL

Uncertainty factors used in MRL derivation:

[] 1 [] 3 [x] lO(foruseofaLOAEL)
[ ] 1 [ ] 3 [x] 10 (for extrapolation from animals to humans)
[ ] 1 [ ] 3 [x] 10 (for human variability)

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If an inhalation study in animals. list conversion factors used in determining. human equivalent dose: The NOAEL $_{(HEC)}$ was calculated for a gas:extrarespiratory effect in rats assuming periodicity was attained, using the following equation: NOAEL $_{(HEC)}$ = NOAEL $_{(adj.)}$ x λ_A/λ_H, where: NOAEL $_{(HEC)}$ = the NOAEL human equivalent concentration; NOAEL $_{(adj)}$ = the NOAEL adjusted for continuous exposure (e.g., adjusted for exposure regimen by h hours/24 hours and d days/7 days); λ_A/λ_H, = the ratio of the blood to air partition coefficient of the chemical for the animal species to the human value, used only if λ_A/λ_H . For the situation in which $\lambda_A > \lambda_H$, and in the case where I values are unknown, the default value of λ_A/λ_H, = 1 is recommended. For 1,2-dichloroethene, λ_A = 9.58 and λ_H = 6.04, therefore $\lambda_A > \lambda_H$, and a default value of 1 was used.

Was a conversion used from intermittent to continuous exposure? No.
If so, explain:

Other additional studies or pertinent information that lend support to this MRL:
McCauley et al. (1990), Barnes et al. (1985), and McMillan (1986) also reported hepatic effects, from oral exposure to cis- or trans-1,2-dichloroethene.

Agency Contact (Chemical Manager): Carolyn Harper

APPENDIX A

MINIMAL RISK LEVEL WORKSHEET

Chemical name: cis- 1,2-dichloroethene
CAS number: 156-60-5
Date: August 28, 1996
Profile status: Final
Route: [ ] Inhalation [x]Oral
Duration: [x] Acute [ ]Intermediate [ ] Chronic
Key to figure: 8
Species: rat

MRL: 1 [x] mg/kg/day [ ] ppm [ ] mg/m^3

Reference: McCauley et al. 1990. The effects of subacute and subchronic oral exposure to cis- 1,2-dichloroethylene in rats. Health Effects Research Laboratory, U.S. EPA, Cincinnati, OH and Air Force Aerospace Medical Research Laboratory, Wright-Patterson AFB, OH.

Experimental design :

- Male and female Sprague-Dawley-derived Charles River rats.
- Doses: 1.0, 3.0, 10.0,20.0 n-M/kg/day (97, 290,970, 1,900 mg/kg/day)
- Administration was in corn oil via gavage for 14 days.
- 10 rats/sex/group.
- Food and water were available ad libitum, body weights were taken weekly. At the end of the exposure
  period, all animals were sacrificed and specimens were collected for clinical chemistry, hematology, and histopathology studies.

Effects noted in study and corresnonding doses:

- Mortality was observed in rats treated with 970 mg/kg/day (2/20) and 1,900 mg/kg/day (5/20).
- CNS depression was observed at 1,900 mg/kg/day.
- Increased absolute and relative liver weights in treated males and female rats at 97 mg/kg/day.
- Increased absolute and relative kidney weights in females at doses greater than or equal to 970 mglkglday.
- Decreased blood urea nitrogen at 290 mg/kg/day and increased serum cholesterol in females at 1,900 mg/kg/day.
- Decreased hematocrit levels and erythrocyte counts in females at doses greater than or equal to 290 mg/kg/day.
- Increased serum calcium levels in males at doses greater or equal to 970 mg/kg/day.

Dose endnoint used for MRL derivation:

Decreased hematocrit in females NOAEL = 97 mg/kg/day.

[x] NOAEL [ ]LOAEL

APPENDIX A

Uncertainty factors used in MRL derivation:
[] 1 []3 [] l0(for use of a LOAEL)
[ ] 1 [ ] 3 [x] 10 (for extrapolation from animals to humans)
[ ] 1 [ ] 3 [x] 10 (for human variability)

Was a conversion factor used from ppm in food or water to a mg/body weight dose?
If so, explain: No

If an inhalation study in animals, list conversion factors used in determining human equivalent dose:

Was a conversion used from intermittent to continuous exposure?
If so, explain: No

Other additional studies or pertinent information that lend support to this MRL:
Hematological effects have also been noted in other oral studies. Barnes et al. (1985) reported a 12% decrease in fibrinogen levels and a 7% decrease in prothrombin time in mice exposed to 210 mg/kg/day trans- 1,2-dichloroethene.

Agency Contact (Chemical Manager): Carolyn Harper

APPENDIX A

MINIMAL RISK LEVEL WORKSHEET

Chemical name: cis- 1,2-dichloroethene
CAS number: 156-60-5
Date: August 28, 1996
Profile status: Final
Route: [ ] Inhalation [x]Oral
Duration: [ ] Acute [x]Intermediate [ ] Chronic
Key to figure: 15
Species: rat

MRL: 0.3 [x] mg/kg/day [I ppm [I mg/m^3

Reference: McCauley et al. 1990. The effects of subacute and subchronic oral exposure to cis-1,2-dichloroethylene in rats. Health Effects Research Laboratory, U.S. EPA, Cincinnati, OH and Air Force Aerospace Medical Research Laboratory, Wright-Patterson AFB, OH.

Experimental design:

- Male and female Sprague-Dawley-derived Charles River rats.
- Doses: 0.33, 1.0, 3.0, and 9.0 mM/kg/day (32, 97, 290, 870 mg/kg/day)
- Administration was in corn oil via gavage for 90 days.
- 10 rats/sex/group.
- Food and water were available ad libitum, body weights were taken weekly. At the end of the exposure
  period, all animals were sacrificed and specimens were collected for clinical chemistry, hematology, and histopathology studies.

Effects noted in study and corresponding doses:

- Mortality was observed in the control group and all four treatment groups within the first week: l/20, l/20, l/20, 3/20,4/20 respectively.
- Increased relative kidney weight in male rats at 870 mg/kg/day and increased relative liver weights in male and female rats given greater than or equal to 97 mg/kg/day were observed.
- Increased relative thymus weights were observed in females treated at 870 mg/kg/day.
- A dose related decrease in blood urea nitrogen and serum creatinine was observed at 870 mg/kg/day.
- Decreased hematocrit levels in males at doses greater than or equal to 97 mg/kg/day and in females at doses greater than or equal to 290 mg/kg/day was observed.
- Decreased hemoglobin levels in males at doses greater than or equal to 290 mg/kg/day and in females at 290 mg/kg/day was noted.
- A 27% decrease in body weight was observed in males at 290 mg/kg/day and a 10% decrease in body weight was observed in males at 97 mg/kg/day.

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Dose endpoint used for MRL derivation:

Decreased hematocrit and hemoglobin: NOAEL = 32 mg/kg/day.

[x] NOAEL [ ]LOAEL

Uncertainty factors used in MRL derivation:

[] 1 []3 [] l0(for use of a LOAEL)
[ ] 1 [ ] 3 [x] 10 (for extrapolation from animals to humans)
[ ] 1 [ ] 3 [x] 10 (for human variability)

Was a conversion factor used from ppm in food or water to a mg/body weight dose?
If so, explain: No

If an inhalation study in animals. list conversion factors used in determining human equivalent dose:

Was a conversion used from intermittent to continuous exposure?
If so, explain: No

Other additional studies or pertinent information that lend support to this MRL:
Hematological effects have also been noted in other oral studies. Barnes et al. (1985) reported a 12% decrease in fibrinogen levels and a 7% decrease in prothrombin time in mice exposed to 210 mg/kg/day trans- 1,2-dichloroethene.

Agency Contact (Chemical Manager): Carolyn Harper

APPENDIX A

MINIMAL RISK LEVEL WORKSHEET

Chemical name:trans- 1,2-dichloroethene
CAS number: 156-60-5
Date: August 28, 1996
Profile status: Final
Route: [ ] Inhalation [x] Oral
Duration: [ ] Acute [x] Intermediate [ ] Chronic
Key to figure: 17
Species: Mouse

MRL: 0.2 [x] mg/kg/day [ ] ppm [ ] mg/m^3

Reference:

Barnes DW, Sanders VM, White KL Jr, Shopp GM, and Munson AE. 1985. Toxicology of trans-1,2-Dichloroethylene in the Mouse. Drug and Chemical Toxicology 8(5):373-392.

Experimental design:

- 90-day study with 260 male and 260 female mice in the control group and 140 mice of each sex in groups exposed to drinking water with 0.1, 1.0, or 2.0 mg trans-1,2-dichlorethene/mL (males: 0, 17, 175, 387 mg/kg/day; females: 0,23, 224,452 mg/kg/day).
- Exposure was averaged over the 90 days.
- Trans-1,2-dichloroethene was maintained in solution using a 1% emulphor (vegetable oil) and deionized water.

Effects noted in study and corresponding doses:

- No trans-1,2-dichloroethene-induced changes in terminal body weight or gross pathology.
- Male mice showed an increase in relative liver weights (8%) and increased serum alkaline phosphatase at 175 mg/kg/day.
- Glucose levels were elevated in all exposure groups for both sexes and males showed decreased glutathione levels at 387 mg/kg/day.
- An 11% decrease in relative lung weight was seen in female mice at 452 mg/kg/day.
- No effects were noted on hematocrit, hemoglobin, or erythrocyte and platelet counts.

Dose endpoint used for MRL derivation:

Increased serum alkaline phosphatase NOAEL = 17 mg/kg/day
[x] NOAEL [ ]LOAEL

APPENDIX A

Uncertainty factors used in MRL derivation:

[] 1 [] 3 [] l0(for use of a LOAEL)
[ ] 1 [ ] 3 [x] 10 (for extrapolation from animals to humans)
[ ] 1 [ ] 3 [x] 10 (for human variability)

Was a conversion factor used from ppm in food or water to a mg/body weight dose? Author provided.
If so, explain:

If an inhalation study in animals, list conversion factors used in determining human equivalent dose:
Was a conversion used from intermittent to continuous exposure? No.
If so, explain:

Other additional studies or pertinent information that lend support to this MRL:
McCauley et al. (1990) and McMillan (1986) also reported hepatic effects from oral exposure to trans- 1,2-dichloroethene.

Agency Contact (Chemical Manager): Carolyn Harper

APPENDIX B

USER'S GUIDE

Chapter 1

Public Health Statement

This chapter of the profile is a health effects summary written in non-technical language. Its intended audience is the general public especially people living in the vicinity of a hazardous waste site or chemical release. If the Public Health Statement were removed from the rest of the document, it would still communicate to the lay public essential information about the chemical.

The major headings in the Public Health Statement are useful to find specific topics of concern. The topics are written in a question and answer format. The answer to each question includes a sentence that will direct the reader to chapters in the profile that will provide more information on the given topic.

Chapter 2

Tables and Figures for Levels of Significant Exposure (LSE)

Tables (2-1, 2-2, and 2-3) and figures (2-l and 2-2) are used to summarize health effects and illustrate graphically levels of exposure associated with those effects. These levels cover health effects observed at increasing dose concentrations and durations, differences in response by species, minimal risk levels (MRLs) to humans for noncancer endpoints, and EPA's estimated range associated with an upperbound individual lifetime cancer risk of 1 in 10,000 to 1 in 10,000,000. Use the LSE tables and figures for a quick review of the health effects and to locate data for a specific exposure scenario. The LSE tables and figures should always be used in conjunction with the text. All entries in these tables and figures represent studies that provide reliable, quantitative estimates of No-Observed-Adverse-Effect Levels (NOAELs), Lowest-Observed-Adverse-Effect Levels (LOAELs), or Cancer Effect Levels (CELs).

The legends presented below demonstrate the application of these tables and figures. Representative examples of LSE Table 2- 1 and Figure 2-l are shown. The numbers in the left column of the legends correspond to the numbers in the example table and figure.

LEGEND

See LSE Table 2-l

(1) Route of Exposure One of the first considerations when reviewing the toxicity of a substance using these tables and figures should be the relevant and appropriate route of exposure. When sufficient data exists, three LSE tables and two LSE figures are presented in the document. The three LSE tables present data on the three principal routes of exposure, i.e., inhalation, oral, and dermal (LSE Table 2-1, 2-2, and 2-3, respectively). LSE figures are limited to the inhalation (LSE Figure 2-l) and oral (LSE Figure 2-2) routes. Not all substances will have data on each route of exposure and will not therefore have all five of the tables and figures.

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(2) Exposure Period Three exposure periods - acute (less than 15 days), intermediate (15-364 days), and chronic (365 days or more) are presented within each relevant route of exposure. In this example, an inhalation study of intermediate exposure duration is reported. For quick reference to health effects occurring from a known length of exposure, locate the applicable exposure period within the LSE table and figure.

(3) Health Effect The major categories of health effects included in LSE tables and figures are death, systemic, immunological, neurological, developmental, reproductive, and cancer. NOAELs and LOAELs can be reported in the tables and figures for all effects but cancer. Systemic effects are further defined in the "System" column of the LSE table (see key number 18).

(4) Key to Figure Each key number in the LSE table links study information to one or more data points using the same key number in the corresponding LSE figure. In this example, the study represented by key number 18 has been used to derive a NOAEL and a Less Serious LOAEL (also see the 2 "18r" data points in Figure 2-l).

(5) Species The test species, whether animal or human, are identified in this column. Section 2.5, "Relevance to Public Health," covers the relevance of animal data to human toxicity and Section 2.3, "Toxicokinetics," contains any available information on comparative toxicokinetics. Although NOAELs and LOAELs are species specific, the levels are extrapolated to equivalent human doses to derive an MRL.

(6) Exposure Frequency/Duration The duration of the study and the weekly and daily exposure regimen are provided in this column. This permits comparison of NOAELs and LOAELs from different studies. In this case (key number 18), rats were exposed to toxaphene via inhalation for 6 hours per day, 5 days per week, for 3 weeks. For a more complete review of the dosing regimen refer to the appropriate sections of the text or the original reference paper, i.e., Nitschke et al. 1981.

(7) System This column further defines the systemic effects. These systems include: respiratory, cardiovascular, gastrointestinal, hematological, musculoskeletal, hepatic, renal, and dermal/ocular. "Other" refers to any systemic effect (e.g., a decrease in body weight) not covered in these systems. In the example of key number 18, 1 systemic effect (respiratory) was investigated.

(8) NOAEL A No-Observed-Adverse-Effect Level (NOAEL) is the highest exposure level at which no harmful effects were seen in the organ system studied. Key number 18 reports a NOAEL of 3 ppm for the respiratory system which was used to derive an intermediate exposure, inhalation MRL of 0.005 ppm (see footnote "b").

(9) LOAEL A Lowest-Observed-Adverse-Effect Level (LOAEL) is the lowest dose used in the study that caused a harmful health effect. LOAELs have been classified into "Less- Serious" and "Serious" effects. These distinctions help readers identify the levels of exposure at which adverse health effects first appear and the gradation of effects with increasing dose. A brief description of the specific endpoint used to quantify the adverse effect accompanies the LOAEL. The respiratory effect reported in key number 18 (hyperplasia) is a Less serious LOAEL of 10 ppm. MRLs are not derived from Serious LOAELs.

(10) Reference The complete reference citation is given in chapter 8 of the profile.

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(11) CEL A Cancer Effect Level (CEL) is the lowest exposure level associated with the onset of carcinogenesis in experimental or epidemiologic studies. CELs are always considered serious effects. The LSE tables and figures do not contain NOAELs for cancer, but the text may report doses not causing measurable cancer increases.

(12) Footnotes Explanations of abbreviations or reference notes for data in the LSE tables are found in the footnotes. Footnote "b" indicates the NOAEL of 3 ppm in key number 18 was used to derive an MRL of 0.005 ppm.

LEGEND

See Figure 2-1

LSE figures graphically illustrate the data presented in the corresponding LSE tables. Figures help the reader quickly compare health effects according to exposure concentrations for particular exposure periods.

(13) Exposure Period The same exposure periods appear as in the LSE table. In this example, health effects observed within the intermediate and chronic exposure periods are illustrated.

(14) Health Effect These are the categories of health effects for which reliable quantitative data exists. The same health effects appear in the LSE table.

(15) Levels of Exposure concentrations or doses for each health effect in the LSE tables are graphically displayed in the LSE figures. Exposure concentration or dose is measured on the log scale "y" axis. Inhalation exposure is reported in mg/m^3 or ppm and oral exposure is reported in mg/kg/day .

(16) NOAEL In this example, 18r NOAEL is the critical endpoint for which an intermediate inhalation exposure MRL is based. As you can see from the LSE figure key, the open-circle symbol indicates to a NOAEL for the test species-rat. The key number 18 corresponds to the entry in the LSE table. The dashed descending arrow indicates the extrapolation from the exposure level of 3 ppm (see entry 18 in the Table) to the MRL of 0.005 ppm (see footnote "b" in the LSE table).

(17) CEJ Key number 38r is 1 of 3 studies for which Cancer Effect Levels were derived. The diamond symbol refers to a Cancer Effect Level for the test species-mouse. The number 38 corresponds to the entry in the LSE table.

(18) Estimated Upper-Bound Human Cancer Risk Levels This is the range associated with the upper-bound for lifetime cancer risk of 1 in 10,000 to 1 in 10,000,000. These risk levels are derived from the EPA's Human Health Assessment Group's upper-bound estimates-of the slope of the cancer dose response curve at low dose levels (ql*).

(19) Key to LSE Figure The Key explains the abbreviations and symbols used in the figure.

SAMPLE

1 →

TABLE 2-1. Levels of Significant Exposure to [Chemical x] – Inhalation

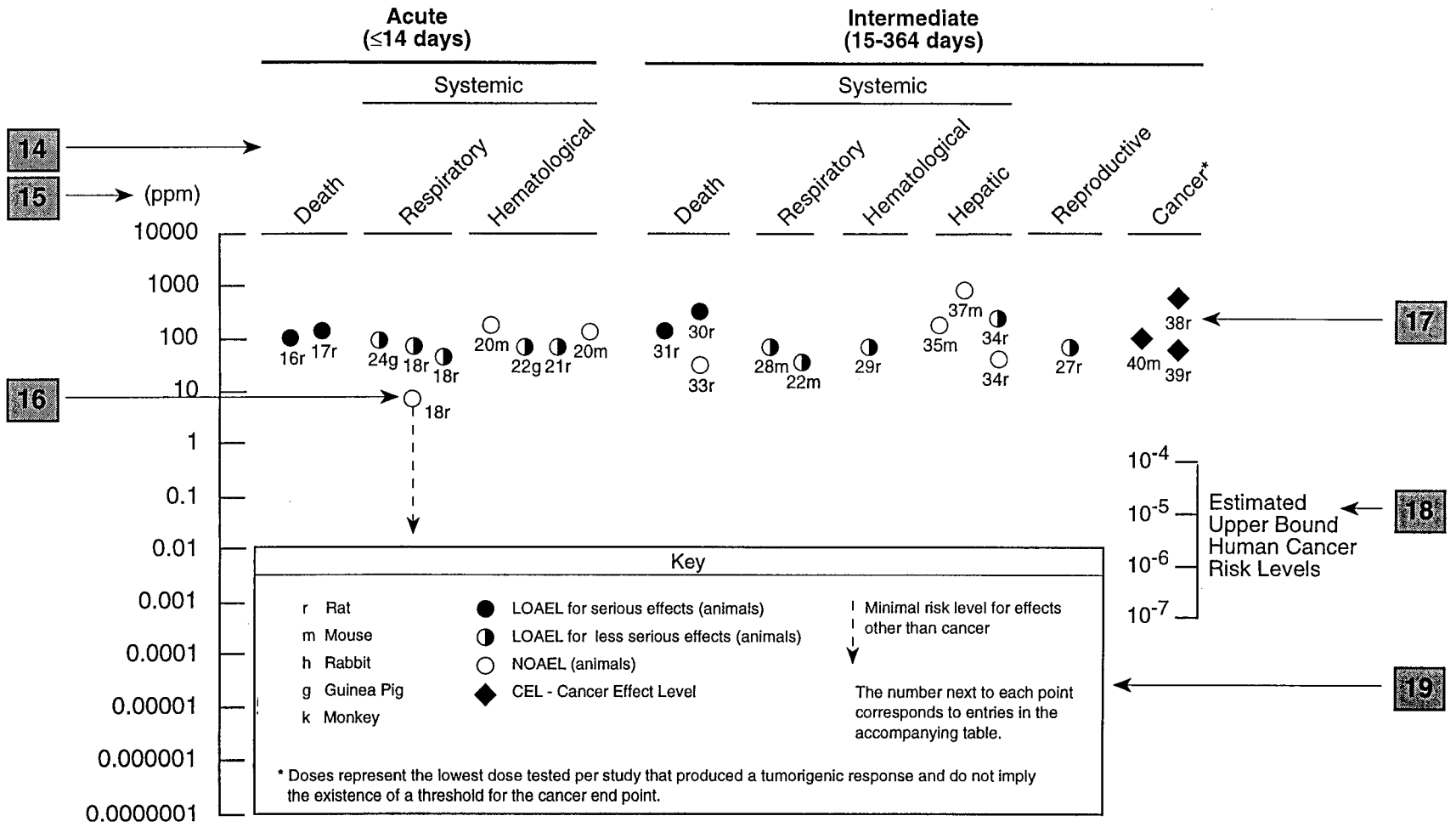
Key to figure[a]	Species	Exposure frequency/ duration	System	NOAEL (ppm)	LOAEL (effect)		Reference
					Less serious (ppm)	Serious (ppm)	
2 → INTERMEDIATE EXPOSURE							
	5	6	7	8	9		10
3 → Systemic	↓	↓	↓	↓	↓		↓
4 → 18	Rat	13 wk 5d/wk 6hr/d	Resp	3[b]	10 (hyperplasia)		Nitschke et al. 1981
CHRONIC EXPOSURE							
					11		
Cancer					↓		
38	Rat	18 mo 5d/wk 7hr/d			20	(CEL, multiple organs)	Wong et al. 1982
39	Rat	89–104 wk 5d/wk 6hr/d			10	(CEL, lung tumors, nasal tumors)	NTP 1982
40	Mouse	79–103 wk 5d/wk 6hr/d			10	(CEL, lung tumors, hemangiosarcomas)	NTP 1982

[a] The number corresponds to entries in Figure 2-1.

12 → [b] Used to derive an intermediate inhalation Minimal Risk Level (MRL) of 5 x 10^{-3} ppm; dose adjusted for intermittent exposure and divided by an uncertainty factor of 100 (10 for extrapolation from animal to humans, 10 for human variability).

SAMPLE

13 → **Figure 2-1. Levels of Significant Exposure to [Chemical X] – Inhalation**



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Chapter 2 (Section 2.5)

Relevance to Public Health

The Relevance to Public Health section provides a health effects summary based on evaluations of existing toxicologic, epidemiologic, and toxicokinetic information. This summary is designed to present interpretive, weight-of-evidence discussions for human health endpoints by addressing the following questions.

1. What effects are known to occur in humans?

2. What effects observed in animals are likely to be of concern to humans?

3. What exposure conditions are likely to be of concern to humans, especially around hazardous waste sites?

The section covers endpoints in the same order they appear within the Discussion of Health Effects by Route of Exposure section, by route (inhalation, oral, dermal) and within route by effect. Human data are presented first, then animal data. Both are organized by duration (acute, intermediate, chronic). *In vitro* data and data from parenteral routes (intramuscular, intravenous, subcutaneous, etc.) are also considered in this section. If data are located in the scientific literature, a table of genotoxicity information is included.

The carcinogenic potential of the profiled substance is qualitatively evaluated, when appropriate, using existing toxicokinetic, genotoxic, and carcinogenic data. ATSDR does not currently assess cancer potency or perform cancer risk assessments. Minimal risk levels (MRLs) for noncancer endpoints (if derived) and the endpoints from which they were derived are indicated and discussed.

Limitations to existing scientific literature that prevent a satisfactory evaluation of the relevance to public health are identified in the Data Needs section.

Interpretation of Minimal Risk Levels

Where sufficient toxicologic information is available, we have derived minimal risk levels (MRLs) for inhalation and oral routes of entry at each duration of exposure (acute, intermediate, and chronic). These MRLs are not meant to support regulatory action; but to acquaint health professionals with exposure levels at which adverse health effects are not expected to occur in humans. They should help physicians and public health officials determine the safety of a community living near a chemical emission, given the concentration of a contaminant in air or the estimated daily dose in water. MRLs are based largely on toxicological studies in animals and on reports of human occupational exposure.

MRL users should be familiar with the toxicologic information on which the number is based. Chapter 2.5, “Relevance to Public Health,” contains basic information known about the substance. Other sections such as 2.7, “Interactions with Other Substances,” and 2.8, “Populations that are Unusually Susceptible” provide important supplemental information.

MRL users should also understand the MRL derivation methodology. MRLs are derived using a modified version of the risk assessment methodology the Environmental Protection Agency (EPA) provides (Barnes and Dourson 1988) to determine reference doses for lifetime exposure (RfDs).

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To derive an MRL, ATSDR generally selects the most sensitive endpoint which, in its best judgement, represents the most sensitive human health effect for a given exposure route and duration. ATSDR cannot make this judgement or derive an MRL unless information (quantitative or qualitative) is available for all potential systemic, neurological, and developmental effects. If this information and reliable quantitative data on the chosen endpoint are available, ATSDR derives an MRL using the most sensitive species (when information from multiple species is available) with the highest NOAEL that does not exceed any adverse effect levels. When a NOAEL is not available, a lowest-observed-adverse-effect level (LOAEL) can be used to derive an MRL, and an uncertainty factor (UF) of 10 must be employed. Additional uncertainty factors of 10 must be used both for human variability to protect sensitive subpopulations (people who are most susceptible to the health effects caused by the substance) and for interspecies variability (extrapolation from animals to humans). In deriving an MRL, these individual uncertainty factors are multiplied together. The product is then divided into the inhalation concentration or oral dosage selected from the study. Uncertainty factors used in developing a substance-specific MRL are provided in the footnotes of the LSE Tables.

APPENDIX C

ACRONYMS, ABBREVIATIONS, AND SYMBOLS

ACGIH	American Conference of Governmental Industrial Hygienists
ADME	Absorption, Distribution, Metabolism, and Excretion
atm	atmosphere
ATSDR	Agency for Toxic Substances and Disease Registry
BCF	bioconcentration factor
BSC	Board of Scientific Counselors
C	Centigrade
CDC	Centers for Disease Control
CEL	Cancer Effect Level
CERCLA	Comprehensive Environmental Response, Compensation, and Liability Act
CFR	Code of Federal Regulations
CLP	Contract Laboratory Program
cm	centimeter
CNS	central nervous system
d	day
DHEW	Department of Health, Education, and Welfare
DHHS	Department of Health and Human Services
DOL	Department of Labor
ECG	electrocardiogram
EEG	electroencephalogram
EPA	Environmental Protection Agency
EKG	see ECG
F	Fahrenheit
F_1	first filial generation
FAO	Food and Agricultural Organization of the United Nations
FEMA	Federal Emergency Management Agency
FIFRA	Federal Insecticide, Fungicide, and Rodenticide Act
fpm	feet per minute
ft	foot
FR	Federal Register
g	gram
GC	gas chromatography
gen	generation
HPLC	high-performance liquid chromatography
hr	hour
IDLH	Immediately Dangerous to Life and Health
IARC	International Agency for Research on Cancer
ILO	International Labor Organization
in	inch
Kd	adsorption ratio
kg	kilogram
kkg	metric ton
K_{oc}	organic carbon partition coefficient
K_{ow}	octanol-water partition coefficient

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L	liter
LC	liquid chromatography
LC_{Lo}	lethal concentration, low
LC_{50}	lethal concentration, 50% kill
LD_{Lo}	lethal dose, low
LD_{50}	lethal dose, 50% kill
LOAEL	lowest-observed-adverse-effect level
LSE	Levels of Significant Exposure
m	meter
mg	milligram
min	minute
mL	milliliter
mm	millimeter
mmHg	millimeters of mercury
mmol	millimole
mo	month
mppcf	millions of particles per cubic foot
MRL	Minimal Risk Level
MS	mass spectrometry
NIEHS	National Institute of Environmental Health Sciences
NIOSH	National Institute for Occupational Safety and Health
NIOSHTIC	NIOSH's Computerized Information Retrieval System
ng	nanogram
nm	nanometer
NHANES	National Health and Nutrition Examination Survey
nmol	nanomole
NOAEL	no-observed-adverse-effect level
NOES	National Occupational Exposure Survey
NOHS	National Occupational Hazard Survey
NPL	National Priorities List
NRC	National Research Council
NTIS	National Technical Information Service
NTP	National Toxicology Program
OSHA	Occupational Safety and Health Administration
PEL	permissible exposure limit
pg	picogram
pmol	picomole
PHS	Public Health Service
PMR	proportionate mortality ratio
ppb	parts per billion
ppm	parts per million
ppt	parts per trillion
REL	recommended exposure limit
RfD	Reference Dose
RTECS	Registry of Toxic Effects of Chemical Substances
sec	second
SCE	sister chromatid exchange
SIC	Standard Industrial Classification
SMR	standard mortality ratio

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STEL	short term exposure limit
STORET	STORAGE and RETRIEVAL
TLV	threshold limit value
TSCA	Toxic Substances Control Act
TRI	Toxics Release Inventory
TWA	time-weighted average
U.S.	United States
UF	uncertainty factor
yr	year
WHO	World Health Organization
wk	week

>	greater than
≥	greater than or equal to
=	equal to
<	less than
≤	less than or equal to
%	percent
α	alpha
β	beta
δ	delta
γ	gamma
μm	micron
μg	microgram

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