TOXICOLOGICAL PROFILE FOR
1,1-DICHLOROETHANE

Agency for Toxic Substances and Disease Registry
U.S. Public Health Service

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The use of company or product name(s) is for identification only and does not imply endorsement by the Agency for Toxic Substances and Disease Registry.

FOREWORD

The Superfund Amendments and Reauthorization Act (SARA) of 1986 (Public Law 99-499) extended and amended the Comprehensive Environmental Response, Compensation, and Liability Act of 1980 (CERCLA or Superfund). This public law directed the Agency for Toxic Substances and Disease Registry (ATSDR) to prepare toxicological profiles for hazardous substances which are most commonly found at facilities on the CERCLA National Priorities List and which pose the most significant potential threat to human health, as determined by ATSDR and the Environmental Protection Agency (EPA). The lists of the 250 most significant hazardous substances were published in the Federal Register on April 17, 1987, on October 20, 1988, on October 26, 1989, and on October 17, 1990.

Section 104(i)(3) of CERCLA, as amended, directs the Administrator of ATSDR to prepare a toxicological profile for each substance on the list. Each profile must include the following content:

(A) An examination, summary, and interpretation of available toxicological information and epidemiological evaluations on the hazardous substance in order 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 which present a significant risk to human health of acute, subacute, and chronic health effects, and

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

This toxicological profile is prepared in accordance with guidelines developed by ATSDR and EPA. The original guidelines were published in the Federal Register on April 17, 1987. Each profile will be revised and republished as necessary, but no less often than every three years, as required by CERCLA, as amended.

The ATSDR toxicological profile is intended to characterize succinctly the toxicological and adverse health effects information for the hazardous substance being described. Each profile identifies and reviews the key literature (that has been peer-reviewed) that describes a hazardous substance's toxicological properties. Other pertinent literature is also presented but 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.

Foreword

Each toxicological profile begins with a public health statement, which describes in nontechnical language a substance's relevant toxicological properties. Following the public health statement is information concerning significant health effects associated with exposure to the substance. The adequacy of information to determine a substance's health effects is described. Data needs that are of significance to protection of public health will be identified by ATSDR, the National Toxicology Program (NTP) of the Public Health Service, and EPA. The focus of the profiles is on health and toxicological information; therefore, we have included this information in the beginning of the document.

The principal audiences for the toxicological profiles are health professionals at the federal, state, and local levels, interested private sector organizations and groups, and members of the public.

This profile reflects our assessment of all relevant toxicological testing and information that has been peer reviewed. It has been reviewed by scientists from ATSDR, the Centers for Disease Control, the NTP, and other federal agencies. It has also been reviewed by a panel of nongovernment peer reviewers and is being made available for public review. Final responsibility for the contents and views expressed in this toxicological profile resides with ATSDR.

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1. PUBLIC HEALTH STATEMENT

This Statement was prepared to give you information about l,l-dichloroethane and to emphasize the human health effects that may result from exposure to it. The Environmental Protection Agency (EPA) has identified 1,177 sites on its National Priorities List (NPL). l,l-Dichloroethane has been found at 189 of these sites. However, we do not know how many of the 1,177 NPL sites have been evaluated for l,l-dichloroethane. As EPA evaluates more sites, the number of sites at which l,l-dichloroethane is found may change. The information is important for you because l,l-dichloroethane may cause harmful health effects and because these sites are potential or actual sources of human exposure to l,l-dichloroethane.

When a chemical 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 as a chemical emission. This emission, which is also called a release, does not always lead to exposure. You can be exposed to a chemical only when you come into contact with the chemical. You may be exposed to it in the environment by breathing, eating, or drinking substances containing the
chemical or from skin contact with it.

If you are exposed to a hazardous substance such as l,l-dichloroethane several factors will determine whether harmful health effects will occur and what the type and severity of those health effects will be. These factors include the dose (how much), the duration (how long), the route or pathway by which you are exposed (breathing, eating, drinking, or skin contact), the other chemicals to which you are exposed, and your individual characteristics such as age, sex, nutritional status, family traits, life style, and state of health.

1.1 WHAT IS l,l-DICHLOROETHANE?

l,l-Dichloroethane is a colorless, oily, man-made liquid. It evaporates quickly at room temperature and has an odor like ether. l,l-Dichloroethane burns easily. When l,l-dichloroethane is released to the environment, it usually exists as a vapor rather than a liquid. It is used primarily to make l,l,l-trichloroethane and a number of other chemicals. It is also used to dissolve other substances such as paint, varnish and finish removers, and to remove grease. l,l-Dichloroethane was used as a surgical anesthetic, but is no longer.

Almost all of the l,l-dichloroethane from industrial sources that is released goes into the air. l,l-Dichloroethane can also be found in the environment as a breakdown product of l,l,l-trichloroethane in landfills where no air comes in contact with the l,l,l-trichloroethane. l,l-Dichloroethane does not dissolve easily in water. The small amounts released to water can

evaporate easily into the air. l,l-Dichloroethane remains as a vapor in the air for about 2 months and dissolved in water for about 5 days. The vapor in air can be washed out by rain or broken down by sunlight. l,l-Dichloroethane in water will evaporate. Small amounts of l,l-dichloroethane released to soil can also evaporate into the air or move through the soil to enter groundwater. It is not known how long l,l-dichloroethane remains in the soil. Although it does not dissolve easily in water, low levels can be found in water.

More information on the chemical and physical properties of l,l-dichloroethane can be found in Chapter 3, on its production and uses in Chapter 4, and on its occurrence and fate in the environment in Chapter 5.

1.2 HOW MIGHT I BE EXPOSED TO 1,1-DICHLOROETHANE?

You can be exposed to l,l-dichloroethane by breathing air containing its vapors in the outdoor air or in your workplace, or by drinking water contaminated with it. Releases from industrial processes are the main source of this chemical in the air. Some members of the general population may be exposed to low levels of l,l-dichloroethane from this source (0.08-0.14 parts per billion [l part l,l-dichloroethane per 1 billion parts of air, or ppb]). Levels in . this range have been measured around industrial plants in Magna, Utah (0.082 ppb); Iberville, Louisiana (0.12 ppb); Deer Park, Texas (0.14 ppb); and Baton Rouge (0.058 ppb) and Geismary, Louisiana (0.14 ppb). You may be part of a much smaller population of workers who could be exposed to higher levels of l,l-dichloroethane in your workplace, if you are employed in the chemical, rubber and plastic, electrical, or oil and gas industries. However, since current levels of production and use are not known, it is difficult to predict how often exposure might occur from these sources of l,l-dichloroethane. Exposure can also occur near sites where the chemical was improperly disposed of or spilled on the ground.

The average concentration of l,l-dichloroethane in the air across the United States is reported to be 55 parts of l,l-dichloroethane per one trillion parts of air (ppt). These ambient levels may be from chlorinated water or building materials. The air levels of l,l-dichloroethane are usually lower in rural areas and higher in industrialized areas. Higher levels have been found in the air around some small sources of release, such as hazardous waste sites. l,l-Dichloroethane has been found in drinking water (that is, water that has usually been treated and that comes out of your tap) in the United States at levels that range from trace amounts to 4.8 parts of l,l-dichloroethane per one billion parts of water (ppb). l,l-Dichloroethane has not been detected in any surface water samples from rivers, lakes, or ponds. No information is available on background levels of l,l-dichloroethane in soil or food.

Additional information on the levels of l,l-dichloroethane in the environment and human exposure to l,l-dichloroethane can be found in Chapter 5.

1.3 HOW CAN 1,1-DICHLOROETHANE ENTER AND LEAVE MY BODY?

l,l-Dichloroethane can enter your body if you breathe contaminated air or drink contaminated water. l,l-Dichloroethane is believed to rapidly enter your body when it is breathed or swallowed. It is not known what factors affect how quickly l,l-dichloroethane enters your body. Studies in animals show that it is likely that l,l-dichloroethane can also enter your body through your skin.

The most common way you could be exposed to l,l-dichloroethane released from hazardous waste sites would be by breathing contaminated air around the site. Soil and water in and around hazardous waste sites are not likely to contain high concentrations of l,l-dichloroethane because it escapes quickly into the air. Therefore, though this route of exposure cannot be ruled out completely, exposure of the skin from soil or water contaminated with l,l-dichloroethane is much less likely.

Experiments in animals indicate that the l,l-dichloroethane that is inhaled or swallowed may go to many organs of the body, depending on the amount taken in. However, most of the l,l-dichloroethane taken in is usually removed unchanged from the body in the breath within 2 days. A small part of the l,l-dichloroethane taken in is broken down, and these breakdown products are quickly removed in the breath or urine.

Additional information on how l,l-dichloroethane can enter and leave the body is presented in Chapter 2.

1.4 HOW CAN l,l-DICHLOROETHANE AFFECT MY HEALTH?

Reliable information on how l,l-dichloroethane affects the health of humans is not available. Because brief exposures to l,l-dichloroethane in the air at very high levels have caused death in animals (16,000 ppm), it is likely that exposure to such high levels of l,l-dichloroethane in the air can also cause death in humans. Some studies in animals have shown that l,l-dichloroethane can cause kidney disease after long-term, high-level exposure in the air. l,l-Dichloroethane caused cancer in animals given very high doses (over 3,000 mg/kg/day) by mouth for a lifetime. Delayed growth was observed in the offspring of animals who breathed high concentrations of l,l-dichloroethane during pregnancy. The severity of these effects may increase when people or animals are exposed to increased levels of l,l-dichloroethane. Since these effects were seen in animals at high doses, it is also possible that they could occur in humans exposed to high levels of l,l-dichloroethane. However, we have no information to indicate that these effects do occur in humans. More information on health effects associated with exposure to l,l-dichloroethane can be found in Chapter 2.

1.5 WHAT LEVELS OF EXPOSURE HAVE RESULTED IN HARMFUL HEALTH EFFECTS?

There is no reliable information on what levels of exposure to l,l-dichloroethane have resulted in harmful health effects in humans. l,l-Dichloroethane is deadly to animals if large enough quantities are breathed or swallowed. Tables l-1 through l-4 show the relationship between exposure to l,l-dichloroethane and known health effects in humans and animals. l,l-Dichloroethane can be smelled when it is present in the air at levels of 120 to 200 parts of l,l-dichloroethane per one million parts of air (ppm).

1.6 IS THERE A MEDICAL TEST TO DETERMINE WHETHER I HAVE BEEN EXPOSED TO l,l-DICHLOROETHANE?

Tests are available that measure l,l-dichloroethane in urine, blood, breath and body tissues. Because urine, blood, and breath samples are easily obtained, these samples are examined to determine if a person has been exposed to l,l-dichloroethane. These tests are not routinely available at a doctor's office and would require special equipment for sampling and detection of the compound. Since most of the l,l-dichloroethane that is taken into the body leaves within two days, these tests must be done soon after exposure occurs. Although these tests can confirm that a person has been exposed to l,l-dichloroethane, it is not yet possible to use the test results to predict the type or severity of any health effects that might occur or the level of exposure that may have occurred. Because exposure to l,l-dichloroethane at hazardous waste sites is likely to include exposure to other similar chemicals at the same time, levels of l,l-dichloroethane measured through these types of medical tests may not reflect exposure to l,l-dichloroethane alone. Information regarding tests for the detection of 1,1-dichloroethane in the body is presented in Chapters 2 and 6.

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

There are no regulatory standards or advisories for l,l-dichloroethane in drinking water and food. The Environmental Protection Agency (EPA) has determined that any release to the environment in excess of 1,000 pounds should be reported.

Rules and regulations have been developed to protect individuals from the potential health effects of l,l-dichloroethane in air. The American Conference of Governmental Industrial Hygienists (ACGIH) has set a threshold limit value (TLV) of 810 mg/m^3 (200 ppm) l,l-dichloroethane in workroom air to protect workers during an S-hour shift over a 40-hour work week. The Occupational Safety and Health Administration (OSHA) has issued a permissible exposure limit (PEL) of 400 mg/m^3 (98.9 ppm).

For more information on criteria and standards for l,l-dichloroethane exposure, see Chapter 7.

TABLE 1-1. Human Health Effects from Breathing 1,1-Dichloroethane*

Short-term Exposure (less than or equal to 14 days)		
Levels in Air (ppm)	Length of Exposure	Description of Effects
		The health effects resulting from short-term exposure of humans to air containing specific levels of 1,1-dichloroethane are not known.
Long-term Exposure (greater than 14 days)		
Levels in Air (ppm)	Length of Exposure	Description of Effects
		The health effects resulting from long-term exposure of humans to air containing specific levels of 1,1-dichloroethane are not known.

*See Section 1.2 for a discussion of exposures encountered in daily life.

TABLE 1-2. Animal Health Effects from Breathing 1,1-Dichloroethane

Short-term Exposure (less than or equal to 14 days)		
Levels in Air (ppm)	Length of Exposure	Description of Effects*
1,750	10 days	Birth defects in rats.
Long-term Exposure (greater than 14 days)		
Levels in Air (ppm)	Length of Exposure	Exposure of Effects*
		The health effects resulting from long-term exposure of animals to air containing specific levels of 1,1-dichloroethane are not known.

*These effects are listed at the lowest level at which they were first observed. They may also be seen at higher levels.

TABLE 1-3. Human Health Effects from Eating or Drinking 1,1-Dichloroethane*

Short-term Exposure (less than or equal to 14 days)		
Levels in Food (ppm)	Length of Exposure	Description of Effects
		The health effects resulting from short-term exposure of humans to food containing specific levels of 1,1-dichloroethane are not known.
Levels in Water (ppm)		
		The health effects resulting from short-term exposure of humans to water containing specific levels of 1,1-dichloroethane are not known.
Long-term Exposure (greater than 14 days)		
Levels in Food (ppm)	Length of Exposure	Description of Effects
		The health effects resulting from long-term exposure of humans to food containing specific levels of 1,1-dichloroethane are not known.
Levels in Water (ppm)		
		The health effects resulting long-term exposure of humans to water containing specific levels of 1,1-dichloroethane are not known.

*See Section 1.2 for a discussion of exposures encountered in daily life.

TABLE 1-4. Animal Health Effects from Eating or Drinking 1,1-Dichloroethane

Short-term Exposure (less than or equal to 14 days)		
Levels in Food (ppm)	Length of Exposure	Description of Effects
		The health effects resulting from short-term exposure of animals to food containing specific levels of 1,1-dichloroethane are not known.
Levels in Water (ppm)		
		The health effects resulting from short-term exposure of animals to water containing specific levels of 1,1-dichloroethane are not known.
Long-term Exposure (greater than 14 days)		
Levels in Food (ppm)	Length of Exposure	Description of Effects*
7,640	2 years	Death in rats.
9,500	2 years	Cancer in rats.
Levels in Water (ppm)		
		The health effects resulting from long-term exposure of animals to water containing specific levels of 1,1-dichloroethane are not known.

*These effects are listed at the lowest level at which they were first observed. They may also be seen at higher levels.

1.8 WHERE CAN I GET MORE INFORMATION?

If you have any more questions or concerns not covered here, please contact your State Health or Environmental Department or:

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

This agency can also give you information on the location of the nearest occupational and environmental health clinics. Such clinics specialize in the recognizing, evaluating, and treating illnesses that result from exposure to hazardous substances.

2. HEALTH EFFECTS

2.1 INTRODUCTION

This chapter contains descriptions and evaluations of studies and interpretation of data on the health effects associated with exposure to l,l-dichloroethane. Its purpose is to present levels of significant exposure for l,l-dichloroethane based on toxicological studies, epidemiological investigations, and environmental exposure data. This information is presented to provide public health officials, physicians, toxicologists, and other interested individuals and groups with (1) an overall perspective of the toxicology of l,l-dichloroethane and (2) a depiction of significant exposure levels associated with various adverse health effects.

2.2 DISCUSSION OF HEALTH EFFECTS BY ROUTE OF EXPOSURE

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

Levels of significant exposure for each exposure route and duration (for which data exist) 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. These distinctions are intended to help the users of the document identify the levels of exposure at which adverse health effects start to appear, determine whether or not the intensity of the effects varies 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 on the tables and graphs may differ depending on the user's perspective. For example, physicians concerned with the interpretation of clinical findings in exposed persons or with the identification of persons with the potential to develop such disease may be interested in levels of exposure associated with "serious" effects. Public health officials and project managers concerned with response actions at Superfund sites may want information on levels of exposure associated with more subtle effects (LOAEL) in humans or animals or exposure levels below which no adverse effects (NOAEL) have been observed. Estimates of levels posing minimal risk to humans (Minimal Risk Levels, MRLs) are of interest to health professionals and citizens alike.

2. HEALTH EFFECTS

Estimates of exposure posing minimal risk to humans (MRLs) have been made, where data were believed reliable, for the most sensitive noncancer end point for each exposure duration. MRLs include adjustments to reflect human variability and, where appropriate, the uncertainty of extrapolating from laboratory animal data to humans. Although methods have been established to derive these levels (Barnes et al. 1987; EPA 1986a; EPA 1989), uncertainties are associated with the techniques.

2.2.1 Inhalation Exposure

Very little information is available regarding the health effects of l,l-dichloroethane following inhalation exposure in humans or animals. l,l-Dichloroethane was used in the past as an anesthetic at a pressure of 0.026 atm, which is approximately equivalent to a concentration of 105,000 mg/m^3 (26,000 ppm) (Miller et al. 1965). This use was discontinued when it was discovered that this compound induced cardiac arrhythmias at anesthetic doses (Browning 1965).

ATSDR, in consultation with EPA, is evaluating the inhalation exposure database for development of inhalation MRLs. The evaluation process will be completed following the public comment period for this document.

Table 2-l and Figure 2-l describe the health effects observed in laboratory animals associated with inhalation exposure levels at varying time and exposure durations.

2.2.1.1 Death

No studies were located regarding death in humans following inhalation exposure to l,l-dichloroethane. No deaths were observed in rats exposed to 4,000 ppm for 8 hours, but an 8-hour exposure to 16,000 ppm was lethal (Smyth 1956). It has been reported in the early literature that the lethal exposure level of l,l-dichloroethane in mice was 17,500 ppm (Browning 1965). These values were reported in a secondary source and it is therefore impossible to assess their validity. Subchronic intermittent exposure to 500 ppm of l,l-dichloroethane for 13 weeks followed by l,000 ppm of l,l,-dichloroethane for an additional 13 weeks was not lethal to rats, rabbits, guinea pigs, or cats (Hofmann et al. 1971). Based on these limited data in laboratory animals, it would appear that l,l-dichloroethane causes death in animals at high concentrations (16,000 ppm).

The highest NOAEL values for death in each species and duration category are recorded in Table 2-l and plotted in Figure 2-l.

2.2.1.2 Systemic Effects

One study of the subchronic effects of inhaled l,l-dichloroethane in animals was located. No adverse clinical effects were noted in rats, rabbits,

TABLE 2-1. Levels of Significant Exposure to 1,1-Dichloroethane - Inhalation

Figure Key	Species	Exposure Frequency/ Duration	Effect	NOAEL (ppm)	LOAEL (Effect) Less Serious (ppm)	LOAEL (Effect) Serious (ppm)	Reference
ACUTE EXPOSURE							
Developmental							
1	Rat	10 d Gd6-15 7hr/d		3800		6000[a] (skeletal anomalies)	Schwetz et al. 1974
INTERMEDIATE EXPOSURE							
Death							
2	Rat	13 wk 6hr/d 5d/wk		1000			Hofmann et al. 1971
3	Gn Pig	13 wk 5d/wk 6hr/d		1000			Hofmann et al. 1971
4	Rabbit	13 wk 5d/wk 6hr/d		1000			Hofmann et al. 1971
5	Cat	13 wk 6hr/d 5d/wk		1000			Hofmann et al. 1971
Systemic							
6	Rat	13 wk 6hr/d 5d/wk	Hemato Hepatic Other (body wt)	1000 1000 1000			Hofmann et al. 1971
7	Gn Pig	13 wk 5d/wk 6hr/d	Hemato Hepatic Renal Other (body wt)	1000 1000 1000 1000			Hofmann et al. 1971

TABLE 2-1 (Continued)

Figure Key	Species	Exposure Frequency/ Duration	Effect	NOAEL (ppm)	LOAEL (Effect) Less Serious (ppm)	LOAEL (Effect) Serious (ppm)	Reference
8	Rabbit	13 wk 5d/wk 6hr/d	Hemato Hepatic Renal Other (body wt)	1000 1000 1000 1000			Hofmann et al. 1971
9	Cat	13 wk 6hr/d 5d/wk	Hemato Hepatic Renal Other (body wt)	500 500 500 500	1000 (decreased body wt)	1000 (enzyme changes, histopathology)	Hofmann et al. 1971

[a]Adjusted for intermittent exposure and presented in Table 1-2.

d = day; wk = week; min = minute; Gd = gestational day; hemato = hematological; wt = weight

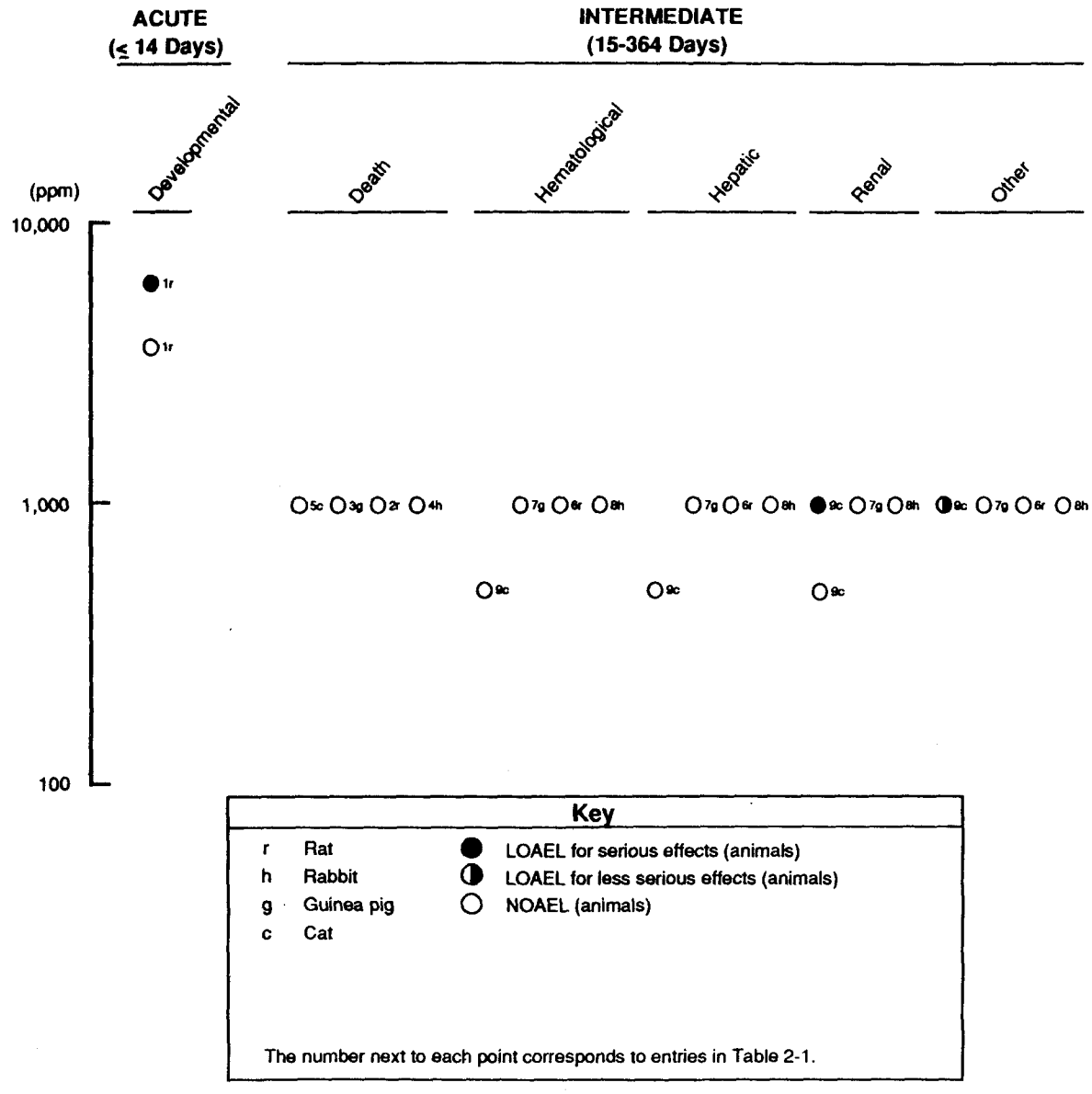


FIGURE 2-1. Levels of Significant Exposure to 1,1-Dichloroethane - Inhalation

or guinea pigs exposed to 1000 ppm l,l-dichloroethane for 13 weeks, which followed a prior 13 week exposure to 500 ppm of l,l-dichloroethane (Hofmann et al. 1971). Histological examination of the liver and kidneys after 26 weeks revealed no treatment-related lesions. These NOAELs are recorded in Table 2-l and plotted in Figure 2-l. However, this study is limited in that an inadequate number of animals was tested. Also, it is not clear how the lack of effects observed in these experiments relates to continuous exposure to 1000 ppm l,l-dichloroethane over a 26-week period. This is particularly relevant for humans living in the vicinity of hazardous waste sites since exposure to l,l-dichloroethane in this situation is expected to be continuous. No studies were located regarding respiratory, gastrointestinal, hematological, musculoskeletal, or dermal/ocular effects in humans or animals following inhalation exposure to l,l-dichloroethane.

Cardiovascular Effects. A cardiostimulatory effect resulting in arrhythmias prompted the discontinuance of the use of l,l-dichloroethane as an anesthetic in humans (Browning 1965). This effect was noted at the relatively high dose used to induce anesthesia (0.026 atm, which is approximately equivalent to 105,000 mg/m^3, or 26,000 ppm) (Miller et al. 1965). No studies were located regarding cardiovascular effects in animals following inhalation exposure to l,l-dichloroethane.

Hepatic Effects. No studies were located regarding hepatic effects in humans following inhalation exposure to l,l-dichloroethane. Rats, rabbits, guinea pigs and cats experienced no change in serum glutamic oxaloacetic transaminase (SGOT) or serum glutamic pyruvic transaminase (SGPT) activity after intermittent 6-hour inhalation exposure to 500 ppm l,l-dichloroethane for 13 weeks followed by 13 weeks of exposure 6 hours per day to 1,000 ppm l,l-dichloroethane (Hofmann et al. 1971). Furthermore, no treatment-related histopathological lesions were noted in the livers of these animals after this 26 week exposure regimen. Six days after the tenth and last daily 7-hour exposure to 6,000 ppm l,l-dichloroethane, female rats exhibited a slight but statistically significant increase in relative liver weight (Schwetz et al. 1974). However, there was no increase in SGPT activity over control values and no changes in the gross appearance of the liver were noted at necropsy in these animals. These results indicate that under the conditions of these studies, l,l-dichloroethane is not hepatotoxic.

Renal Effects. No studies were located regarding renal effects in humans following inhalation exposure to l,l-dichloroethane. Renal injury was apparent in cats intermittently exposed 6 hours daily to 1,000 ppm l,l-dichloroethane for 13 weeks following 13 weeks of intermittent exposure to 500 ppm l,l-dichloroethane (Hofmann et al. 1971). Serum urea and creatinine were increased in these animals. One cat was so severely affected that it had to be removed from the study. Histopathological lesions in the kidney tubules (including crystalline precipitates and dilation) were noted at necropsy. The ill health of these animals was also manifest by a progressive decrease in

body weight. Rats, rabbits, and guinea pigs similarly exposed to l,l-dichloroethane exhibited no adverse effects. Thus, based on the results of this study, cats appear to be uniquely sensitive to the nephrotoxic effects of l,l-dichloroethane. This study is limited in that only four cats were used and it is not clear how the effects observed in this experiment relate to continuous exposure to 1000 ppm l,l-dichloroethane over a 26-week period. A NOAEL of 500 ppm was identified for cats. However, the observation that all cats exhibited a high degree of renal toxicity suggests that these findings were toxicologically significant.

2.2.1.3 Immunological Effects

No studies were located regarding immunological effects in humans or animals after inhalation exposure to l,l-dichloroethane.

2.2.1.4 Neurological Effects

Since l,l-dichloroethane was once used as a gaseous anesthetic, it can be inferred that it causes central nervous system depression upon acute exposure. No information is available on the long-term neurologic effects of inhaled l,l-dichloroethane in humans.

No studies were located regarding neurologic effects in animals after inhalation exposure to l,l-dichloroethane.

2.2.1.5 Developmental Effects

No studies were located regarding developmental effects in humans following inhalation exposure to l,l-dichloroethane.

In the only animal study located, retarded fetal development without any significant toxic effects was observed following inhalation exposure 7 hours daily to l,l-dichloroethane in pregnant rats during days 6 through 15 of gestation (Schwetz et al. 1974). Except for a significant increase in the incidence gf fetuses with delayed ossification of sternebrae at an exposure level of 6,000 ppm, no other malformations were observed. The use of only two exposure levels precluded the assessment of a dose-dependent response. Maternal food consumption and body weight were significantly reduced in the treated animals during the exposure period but returned to normal by day 21 of gestation. No other adverse effects were noted in the dams. This study showed that l,l-dichloroethane is only slightly fetotoxic, though not teratogenic, in rats following inhalation exposure to high levels of the chemical, and it is not likely that humans would experience adverse developmental effects as a result of low-level exposure to l,l-dichloroethane. Based on the observed effects, the LOAEL value for the developmental toxicity of l,l-dichloroethane in rats was 6,000 ppm; the NOAEL was 3,800 ppm. These values are listed in Table 2-1 and plotted in Figure 2-1.

2.2.1.6 Reproductive Effects

No studies were located regarding reproductive effects in humans or animals following inhalation exposure to l,l-dichloroethane.

2.2.1.7 Genotoxic Effects

No studies were located regarding genotoxic effects in humans or animals after inhalation exposure to l,l-dichloroethane.

2.2.1.8 Cancer

No studies were located regarding cancer in humans or animals after inhalation exposure to l,l-dichloroethane.

2.2.2 Oral Exposure

Two studies were located that investigated the health effects associated with oral exposure to l,l-dichloroethane in rats and mice (Klaunig et al. 1986; NCI 1977). With the exception of body weight depression observed in one subchronic range-finding study, neither one provided any conclusive evidence of adverse toxic effects associated with oral exposure to l,l-dichloroethane.

Table 2-2 and Figure 2-2 describe the health effects observed in laboratory animals associated with oral exposure levels at varying time and exposure durations. No MRLs to humans for adverse effects (other than cancer) were calculated for the oral route of exposure because of the limited database.

2.2.2.1 Death

No studies were located regarding death in humans following oral exposure to l,l-dichloroethane.

Secondary sources report the following oral LD_{50} in rats: 725 mg/kg (RTECS 1988) and 14.1 g/kg (Grayson 1978). Since these values were obtained from secondary sources, no details were available to assess the quality of these data. Survival was poor in both treated and control rats and mice in the chronic bioassay conducted by NCI (1977), but a significant dose-related trend for mortality was noted in the male rats and mice. The deaths could not be attributed to cancer or any other non-neoplastic lesions, though pneumonia was observed in a large percentage of the rats, and this was thought to be related to the increased mortality (NCI 1977).

The highest NOAEL values and all reliable LOAEL values for death in each species and duration category are recorded in Table 2-2 and plotted in Figure 2-2.

TABLE 2-2. Levels of Significant Exposure to 1,1-Dichloroethane - Oral

Figure Key	Species	Route	Exposure Frequency/ Duration	Effect	NOAEL (mg/kg/day)	LOAEL (Effect) Less Serious (mg/kg/day)	LOAEL (Effect) Serious (mg/kg/day)	Reference
INTERMEDIATE EXPOSURE								
Death								
1	Rat	(G)	6 wk 5d/wk 1x/d		M:5620		F:3160	NCI 1977
2	Mouse	(G)	6 wk 5d/wk 1x/d		3160		5620	NCI 1977
Systemic								
3	Rat	(G)	6 wk 5d/wk 1x/d	Other		M:562 (decreased body weight) F:1780		NCI 1977
4	Mouse	(G)	6 wk 5d/wk 1x/d	Other (body weight)	10000			NCI 1977
CHRONIC EXPOSURE								
Death								
5	Rat	(G)	78 wk 5d/wk 1x/d				[a]M:382 F:475	NCI 1977
6	Mouse	(W)	52 wk ad lib		475			Klaunig et al. 1986
7	Mouse	(G)	78 wk 5d/wk 1x/d		M:1442 F:1665		M:2885 F:3331	NCI 1977

TABLE 2-2 (Continued)

Figure Key	Species	Route	Exposure Frequency/ Duration	Effect	NOAEL (mg/kg/day)	LOAEL (Effect) Less Serious (mg/kg/day)	LOAEL (Effect) Serious (mg/kg/day)	Reference
Systemic								
8	Rat	(G)	78 wk 5d/wk 1x/d	Resp	M:764 F:950			NCI 1977
				Cardio	M:764 M:950			
				Gastro	M:764 M:950			
				Hemato	M:764 M:950			
				Hepatic	M:764 M:950			
				Renal	M:764 M:950			
				Other (body weight)	M:764 F:950			
9	Mouse	(G)	78 wk 5d/wk 1x/d	Resp	M:2885 F:3331			NCI 1977
				Cardio	M:2885 M:3331			
				Gastro	M:2885 F:3331			
				Hemato	M:2885 F:3331			
				Hepatic	M:2885 F:3331			
				Renal	M:2885 F:3331			
				Other (body weight)	M:2885 F:3331			

TABLE 2-2 (Continued)

Figure Key	Species	Route	Exposure Frequency/ Duration	Effect	NOAEL (mg/kg/day)	LOAEL (Effect) Less Serious (mg/kg/day)	LOAEL (Effect) Serious (mg/kg/day)	Reference
10	Mouse	(W)	52 wk ad lib	Resp	475			Klaunig et al. 1986
				Hepatic	475			
				Renal	475			
				Other (body weight)	475			
Cancer								
11	Rat	(G)	78 wk 5d/wk 1x/d				[b]F:475 (CEL) (blood vessels, mammary glands)	NCI 1977
12	Mouse	(G)	78 wk 5d/wk 1x/d				F: (CEL) 3331 (uterus)	NCI 1977

[a]Converted to an equivalent concentration of 7,640 ppm in food for presentation in Table 1-4.

[b]Converted to an equivalent concentration of 9,500 ppm in food for presentation in Table 1-4.

d = day; wk = week; min = minute; M = male; F = female; G = gavage; W = water; ad lib = ad libitum; CEL = cancer effect level; Resp = respiratory; Cardio = cardiovascular; Gastro = gastrointestinal; Hemato = hematological.

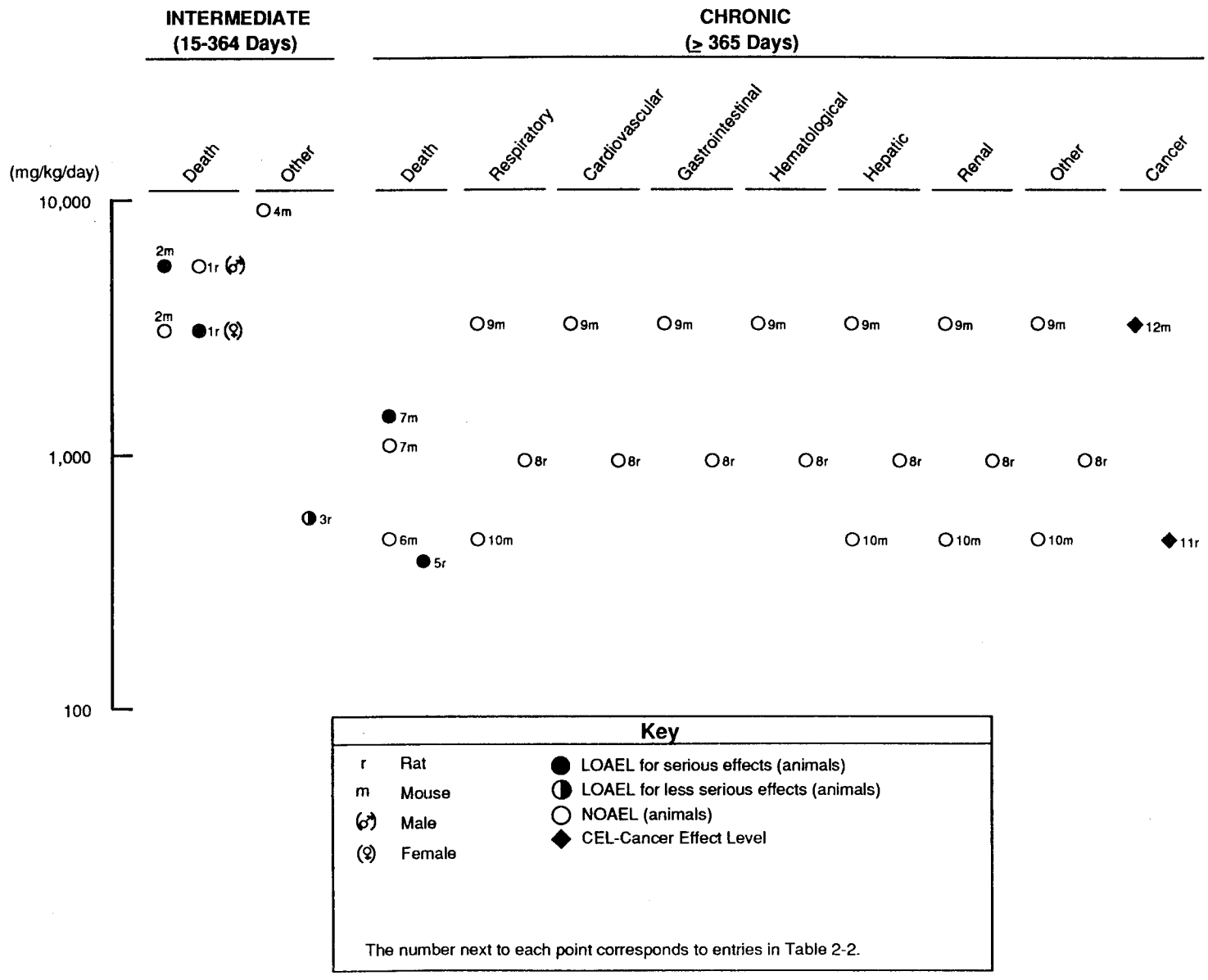


FIGURE 2-2. Levels of Significant Exposure to 1,1-Dichloroethane - Oral

2.2.2.2 Systemic Effects

No studies were located regarding respiratory, cardiovascular, gastrointestinal, hematological, musculoskeletal, hepatic, renal, or dermal/ocular effects in humans or animals following oral exposure to l,l-dichloroethane. There were no treatment-related histopathological changes in the liver, kidneys, or other tissues of the rats examined in the NCI (1977) study. Similarly, no histopathological alterations were noted in the liver, kidneys, or lungs of male mice that ingested relatively high levels of l,l-dichloroethane in drinking water (up to 2500 mg/L) for 52 weeks (Klaunig et al. 1986).

No studies were located regarding the following health effects in humans or animals following oral exposure to l,l-dichloroethane.

2.2.2.3 Immunological Effects

2.2.2.4 Neurological Effects

2.2.2.5 Developmental Effects

2.2.2.6 Reproductive Effects

2.2.2.7 Genotoxic Effects

2.2.2.8 Cancer

No studies were located regarding carcinogenic effects in humans following oral exposure to l,l-dichloroethane. The results of the bioassay conducted by NCI (1977) suggest carcinogenic effects induced by l,l-dichloroethane in rats and mice. A significant positive dose-related trend was observed for the incidence of hemangiosarcomas and mammary adenocarcinomas in female rats, hepatocellular carcinoma in male mice, and endometrial stromal polyps in female mice. However, only the incidence of endometrial stromal polyps in female mice was significantly increased over the corresponding control animals. There are several limitations to this study. Survival was poor in both treated and control animals, thereby limiting the validity of these results. Although it appears that the maximum tolerated dose (MTD) had been reached (475 mg/kg/day for rats; 3,331 mg/kg/day for mice), it is not clear that the increase in mortality was treatment-related. Furthermore, there were no other treatment-related effects on body weight, clinical signs, or the incidence of non-neoplastic lesions. Because of the high mortality in both the treated and control animals, the authors concluded that not enough animals survived to be at risk for late-developing tumors. Thus, though the results of this bioassay suggest that l,l-dichloroethane is carcinogenic to rats and mice, the evidence is not conclusive.

The carcinogenicity of l,l-dichloroethane was studied in mice chronically exposed to 475 mg/kg/day of the compound in the drinking water (Klaunig et al. 1986). A two-stage carcinogenesis protocol was also employed in this study to assess the ability of l,l-dichloroethane to act as a tumor promoter. Neither l,l-dichloroethane-treated animals initiated with diethylnitrosamine (DENA) or animals treated with l,l-dichloroethane without initiation showed a significant increase in the incidence of lung or liver tumors over their corresponding controls. The authors concluded that l,l-dichloroethane was not carcinogenic to mice and that it did not act as a tumor promoter following initiation with DENA under the conditions of this study. This was generally a well-conducted study: the MTD was used (as demonstrated in preliminary rangefinding studies), an adequate number of animals was used, and the appropriate clinical, gross, and microscopic observations were made. However, the conclusion that l,l-dichloroethane is not a tumor promoter may not be entirely justified since a maximal response was observed in terms of tumor incidence in the DENA-alone-treated mice (100% tumor incidence at 52 weeks). Therefore, an increase in the incidence of liver tumors due to l,l-dichloroethane following DENA initiation, if it existed, could not have been detected. Furthermore, since measurement of water consumption and replenishment were only done once a week, there was no way to determine the extent, if any, evaporation contributed to loss of the test chemical and affected the reported level of exposure. However, precautions were taken to minimize the loss of test chemical during the l-week period; amber bottles with Teflon stoppers and double sipper tubes were used. Since l,l-dichloroethane is a volatile chemical, this may present a limitation to the interpretation of results obtained from drinking water administration.

The difference in results (e.g., induction of liver tumors) between the NC1 (1977) and Klaunig et al. (1986) studies may be due to the method of administration, vehicle, and/or doses used. The pharmacokinetics of l,l-dichloroethane may vary considerably when administered in drinking water ad libitum over a week as compared to bolus doses given in corn oil. Evidence obtained with carbon tetrachloride indicates that corn oil likely acts as a reservoir in the gut to delay and diminish the systemic absorption of the lipophilic chemical, while such a chemical is probably rapidly absorbed when ingested in water (Kim et al. 1990a,b). Furthermore, the doses given to mice by gavage were approximately six times higher than the drinking water concentrations. Species differences in susceptibility may also have played a role, as rats used in the NC1 study showed adverse effects at a dose that was without effect in the Klaunig et al. (1986) study. Sufficient information is not available to assess the contributions of these factors to the apparently disparate responses; i.e., the finding of 475 mg/kg/day as a LOAEL in the NC1 study and the same dose as a NOAEL in the Klaunig study.

2.2.3 Dermal Exposure

No studies were located regarding the following health effects in humans or animals after dermal exposure to l,l-dichloroethane.

2.2.3.1 Death

2.2.3.2 Systemic Effects

2.2.3.3 Immunological Effects

2.2.3.4 Neurological Effects

2.2.3.5 Developmental Effects

2.2.3.6 Reproductive Effects

2.2.3.7 Genotoxic Effects

2.2.3.8 Cancer

2.3 TOXICOKINETICS

2.3.1 Absorption

2.3.1.1 Inhalation Exposure

No studies were located in humans or animals regarding the absorption of inhaled l,l-dichloroethane. However, its use as a gaseous anesthetic agent in humans provides evidence of its absorption. Furthermore, the volatile and lipophilic nature of l,l-dichloroethane favors pulmonary absorption. Structurally related chlorinated aliphatics and gaseous anesthetics are known to be rapidly and extensively absorbed from the lung. The total amount absorbed from the lungs will be directly proportional to the concentration in inspired air, the duration of exposure, the blood/air partition coefficient of l,l-dichloroethane, its solubility in tissues, and the individual's ventilation rate and cardiac output. One of the most important factors controlling pulmonary absorption is the blood/air partition coefficient of the chemical. The concentration of the chemical and the duration of exposure are also important determinants of the extent of systemic absorption.

It is known that an isomer of l,l-dichloroethane, 1,2-dichloroethane, is well-absorbed following inhalation exposure. However, the blood/air partition coefficient for 1,2-dichloroethane is approximately four times that of l,l-dichloroethane. This suggests that l,l-dichloroethane would not be absorbed into the blood from air as readily as 1,2-dichloroethane, but it will still be well absorbed from the lung (Sato and Nakajima 1987). However, the excretion of metabolites in the urine indicated that l,l-dichloroethane was absorbed following inhalation exposure, though the rate or extent of dichloroethane absorption is not known, since this represents theoretical estimates rather than actual data (Sato and Nakajima 1987).

2.3.1.2 Oral Exposure

No studies were located that quantitated the absorption of ingested l,l-dichloroethane in humans or animals. However, when 700 mg [^{14}C]- l,l-dichloroethane/kg was orally administered to rats and mice, absorption was evidenced by the presence of radiolabel in expired air and the presence of radiolabeled metabolites in urine, though there was no quantitative assessment made of the extent or rate of absorption (Mitoma et al. 1985).

2.3.1.3 Dermal Exposure

No studies were located regarding the absorption of l,l-dichloroethane in humans or animals following dermal exposure. However, Browning (1965) reported evidence that l,l-dichloroethane penetrates the skin. l,l-Dichloroethane was applied to the shaved abdominal skin of rabbits that were fitted with masks to prevent inhalation of the compound. Exhaled air from the rabbits was passed into pure alcohol, and the presence of halogen was tested by flaming a copper wire introduced into it. The green color observed after 1 hour indicated that the halogen ion was absorbed into the bloodstream, though no quantitative assessment of the extent or rate of absorption was possible.

2.3.1.4 Other Routes of Exposure

Binding of radiolabeled l,l-dichloroethane or its metabolites to macromolecules (e.g. DNA, RNA, and proteins) in the liver, stomach, lung, and kidney of rats and mice following intraperitoneal injection is evidence that absorption of l,l-dichloroethane occurs (Colacci et al. 1985).

2.3.2 Distribution

2.3.2.1 Inhalation Exposure

No studies were located in humans or animals regarding the distribution of l,l-dichloroethane following inhalation exposure. Hoyever, since this chemical was once used as a gaseous anesthetic, it can be assumed that it is distributed to the central nervous system as well as to the other tissues of the body. Tissue uptake of halocarbons such as l,l-dichloroethane is governed by the affinity of each tissue for the lipophilic chemical (i.e. the higher the lipid content of a tissue, the greater its uptake of l,l-dichloroethane) (Sato and Nakajima 1987)

2.3.2.2 Oral Exposure

No studies were located regarding the distribution of l,l-dichloroethane following oral exposure in humans or animals.

2.3.2.3 Dermal Exposure

No studies were located regarding the distribution of l,l-dichloroethane following dermal exposure in humans or animals.

2.3.2.4 Other Routes of Exposure

Rats and mice were intraperitoneally injected with 1.2 mg [^{14}C]- l,l-dichloroethane/kg and sacrificed 22 hours later. l,l-Dichloroethane was covalently bound to proteins, RNA, and DNA of liver, kidney, lung, and stomach. The extent of binding was greatest in the tissue proteins and least in the DNA. Binding to rat and mouse DNA was greatest in the stomach and liver, respectively (Colacci et al. 1985). Although distribution of l,l-dichloroethane very likely occurs to other tissues, the liver, kidney, lung, and stomach were the only tissues analyzed in this study.

2.3.3 Metabolism

The metabolism of l,l-dichloroethane has not been extensively characterized. In vivo studies of the metabolism of l,l-dichloroethane in humans and animals are very limited. Elucidation of l,l-dichloroethane's metabolic scheme to date is primarily based on in vitro studies. In general, the identification of specific metabolites and the monitoring of enzyme activities indicate that the biotransformation of l,l-dichloroethane is mediated by hepatic microsomal cytochrome P-450 system.

Large portions of orally administered l,l-dichloroethane are excreted unchanged by rats and mice in the expired air (Table 2-3). Forty-eight hours after oral administration of quite high doses of [^{14}C]-1,1-dichloroethane, 7.4% and 29.3% of the dose was metabolized by rats and mice, respectively. The predominant metabolite in both species was [^{14}C]-CO_2 (Mitoma et al. 1985). It is likely that the ingested radiolabeled l,l-dichloroethane underwent first-pass extraction by the liver. It has been suggested that high doses such as those used in this study exceed the capacity of the animals to metabolize l,l-dichloroethane (Bruckner 1989). The radiolabeled compound that was not excreted unchanged in the expired air was probably largely metabolized in the liver, followed by subsequent redistribution of labeled metabolites to other organs prior to their excretion.

l,l-Dichloroethane was added to phenobarbital-induced and uninduced hepatic microsomes from rats, and P-450 enzyme activity was monitored by measuring the production of metabolite spectrophotometrically. Induction with phenobarbital significantly stimulated the binding, as well as hepatic microsomal NADPH oxidation, demonstrating the involvement of the P-450 system. Increased P-450 levels resulted in an increased affinity of enzyme for l,l-dichloroethane, thus increasing the rate of metabolism. ,6-naphthaflavone, an agent that specifically induces P-448, had no effect on the extent of l,l-dichloroethane binding, suggesting that P-448 is not involved in

TABLE 2-3. Metabolic Disposition of Radiolabeled 1,1-Dichloroethane in Rats and Mice[a]

Dose	Rat (700 mg/kg)	Mouse (1,800 mg/kg)
Expired air	86.1	70.4
Carbon dioxide (a)	5.1	25.2
Excreta (b)	0.9	1.6
Carcass (c)	1.4	2.4
% Metabolized (a)+(b)+(c)	7.4	29.2
Recovery	93.5	99.6

[a]Reported as % of the administered dose.

Source: Mitoma et al. 1985.

l,l-dichloroethane metabolism (McCall et al. 1983). The rate and extent of l,l-dichloroethane metabolism was increased 6.3 times in the hepatic microsomes of rats that were induced by chronic ethanol consumption (Sato et al. 1980). Chronic ethanol consumption increased the levels of P-450, supporting the role of cytochrome P-450 in the metabolism of l,l-dichloroethane.

Colacci et al. (1985) reported that l,l-dichloroethane binds to nucleic acids and proteins in vivo and in vitro. This binding is also mediated by the liver cytochrome-P-450 system. Phenobarbital enhances the extent of covalent macromolecular binding. Hence, metabolites of l,l-dichloroethane bind to the DNA, RNA, and tissue proteins. The involvement of P-450 was confirmed by a reduction in binding when rats were pretreated with SKF-525-A, a P-450 inhibitor. Liver microsomes are the only tissue microsomes that are efficient in bioactivating l,l-dichloroethane. Therefore, binding to macromolecules of various organs in vivo could be due to an hepatic metabolite that is sufficiently stable to reach extrahepatic organs. Addition of GSH to the microsomal system suppresses the extent of binding and minimizes the potential for toxic effects.

Metabolism of l,l-dichloroethane by hepatic microsomes resulted in the production of acetic acid as the major metabolite and 2,2-dichloroethanol, mono-, and dichloroacetic acid as minor metabolites (Table 2-4) (McCall et al. 1983). On the basis of these results, pathways for the metabolism of l,l-dichloroethane were proposed (Figure 2-3). The initial steps in the metabolism of l,l-dichloroethane were proposed to involve cytochrome P-450- dependent hydroxylations at either carbon. Hydroxylation at C-l would result in the production of an unstable alpha-haloalcohol, which can lose HCl to yield acetyl chloride. An alternative, but less favorable reaction, would be a chlorine shift to yield chloroacetyl chloride. These acyl chlorides can react with water to generate free acids or react with cellular constituents. Hydroxylation at C-2 would produce 2,2-dichloroethanol, which would undergo subsequent oxidation to dichloroacetaldehyde and dichloroacetic acid (McCall et al. 1983).

Chloroethanes have been shown to undergo dechlorination by an enzyme system that is similar to the hepatic microsomal mixed function oxidase system (Van Dyke and Wineman 1971). Dechlorination was inducible by phenobarbital and required oxygen and NADPH. However, dechlorination also required a factor from the cytosolic fraction of the liver homogenate for optimal dechlorinating activity. In terms of structural requirements, dechlorination was enhanced if the carbon atom containing the chlorine had only one hydrogen. In a microsomal incubation, 13.5% of the ^{36}C1 of l,l-dichloroethane was enzymatically removed after 30 minutes, while less than 0.5% of the ^{36}C1 of 1,2-dichloroethane was removed (Van Dyke and Wineman 1971).

Under hypoxic conditions, l,l-dichloroethane gives rise to free radicals. However, its ability to develop free radicals is much less when compared to

TABLE 2-4. Production of Metabolites from l,l-Dichloroethane with Hepatic Microsomes from Phenobarbital-Induced Rats

Metabolites	Metabolite Production[a] (nmoles/mg microsomal proteion/20 min)
Acetic acid	179 (15)
2,2-Dichloroethane	0.12 (0.02)
Chloroacetic acid	0.22 (0.08)
Dichloroacetic acid	0.048 (0.005)
Chloroacetaldehyde	<0.07 (0.03)

[a]Values represent means (SD) for determinations in triplicate on three to five separate preparations of hepatic microsomes.

Source: McCall et al. 1983.

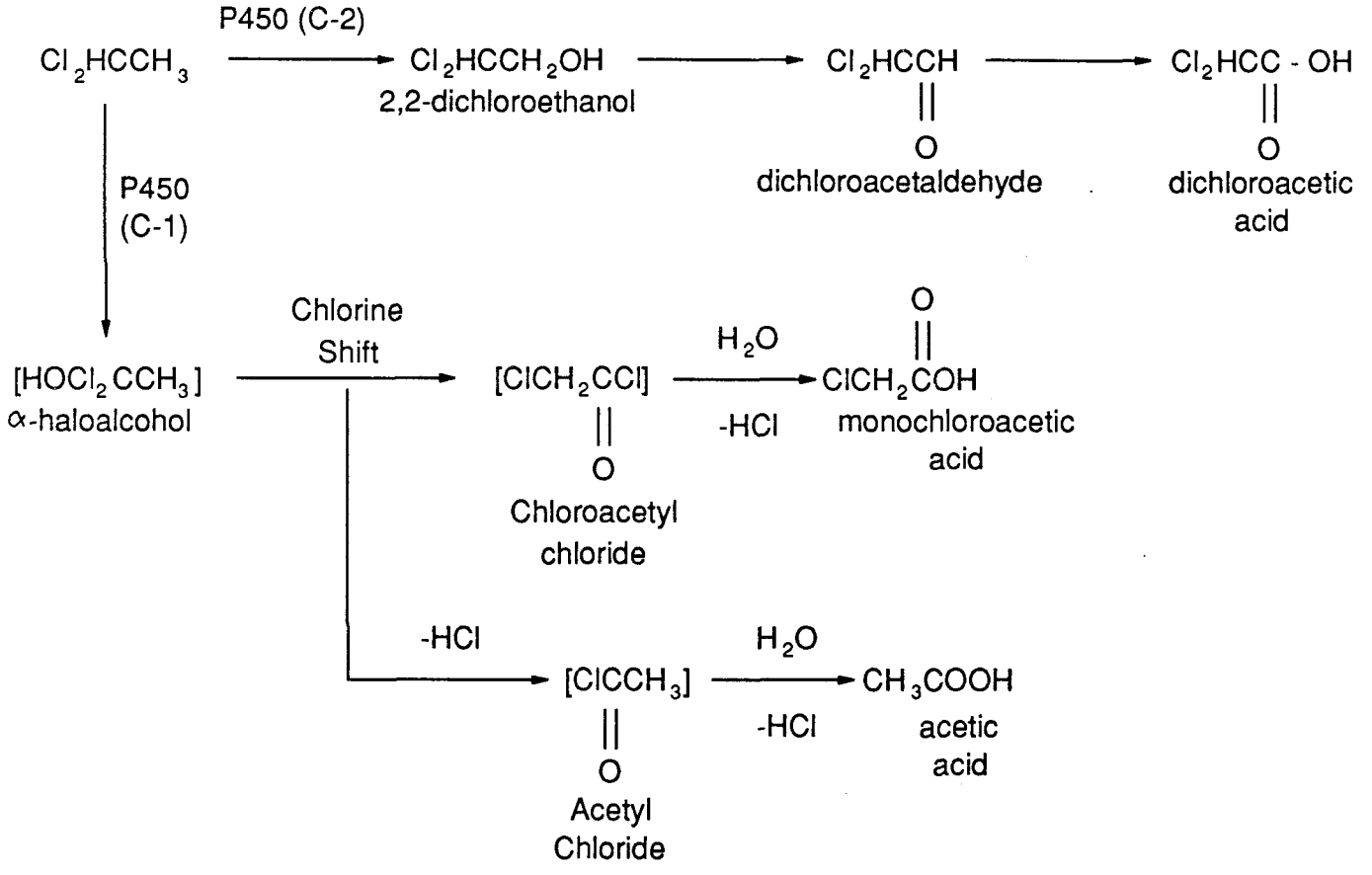


FIGURE 2-3. Proposed Metabolic Scheme for 1,1-Dichloroethane

Source: McCall et al. 1983

other chlorinated hydrocarbons like trichloroethane and carbon tetrachloride. It has been suggested that these free radicals possess the potential to induce toxic and carcinogenic effects. There is no correlation between the ease of free radical activation, covalent binding formation, or carcinogenic potency (Tomasi et al. 1984).

2.3.4 Excretion

One study was located regarding the extent or rate of l,l-dichloroethane excretion in humans (Sato and Nakajima 1987). They reported that 59% of the l,l-dichloroethane inhaled was metabolized and excreted in the urine and 41% was excreted in expired air. This amount of inhaled l,l-dichloroethane that was metabolized and excreted in the urine was considerably less than the 88% of inhaled 1,2-dichloroethane that was metabolized and excreted in the urine. However, these values are theoretical and not actual.

A study conducted by Mitoma et al. (1985) indicated that more than 90% of an oral dose in rats (700 mg/kg) and mice (1,800 mg/kg) was excreted unchanged or as carbon dioxide within 48 hours after administration. However, no blood, urine, or tissue concentrations were monitored over time to determine the elimination kinetic parameters. No studies were located in humans or animals regarding excretion of l,l-dichloroethane following dermal exposure.

2.4 RELEVANCE TO PUBLIC HEALTH

Relatively little information is available on the health effects of l,l-dichloroethane in humans or animals. However, the limited data available in animals indicate that it is less toxic than its isomer, 1,2-dichloroethane, and most other chlorinated aliphatics (Bruckner 1989). Chlorinated aliphatics as a class are known to cause central nervous system depression, and respiratory tract and dermal irritation when humans are exposed by inhalation to sufficiently high levels (Parker et al. 1979).

The available data in animals suggest that inhaled l,l-dichloroethane may be nephrotoxic. However, this finding is limited to one species (cat) and was not observed in three other species tested under the same conditions. Another effect observed in animals but not humans following inhalation exposure to l,l-dichloroethane exposure is fetotoxicity. Suggestive, but inconclusive, evidence of carcinogenicity was obtained in an oral chronic bioassay of l,l-dichloroethane in rats and mice.

Death. No reports of death in humans following exposure to l,l-dichloroethane were found. Death has been observed in laboratory animals following inhalation and oral exposure to l,l-dichloroethane. No reliable LC_{50} or LD_{50} data were found, but lethal doses of l,l-dichloroethane are perhaps 5 to 10 times higher than those required to produce death following exposure to 1,2-dichloroethane or tetrachlorocarbons (EPA 1985; Hofmann et

al. 1971; Smyth 1956). Thus, it is likely that l,l-dichloroethane can be fatal to humans, if exposure to high enough levels occurs.

The cause of death in animals following exposure to l,l-dichloroethane has not been well-defined, but Plaa and Larson (1965) reported that deaths observed following intraperitoneal injection of this compound appeared to be due to fatal central nervous system depression.

Systemic Effects. The use of l,l-dichloroethane as an anesthetic was discontinued when it was discovered that this compound induced cardiac arrhythmias in humans at anesthetic doses (approximately 105,000 mg/m^3, or 26,000 ppm). The mechanism of action for the induction of cardiac arrhythmias by l,l-dichloroethane is not known. However, when the cardiac muscle is markedly depressed, it is more susceptible to the effects of catecholamines. Secretion of catecholamines is increased in this situation by compensatory and other mechanisms, resulting in excessive spontaneous contractions of the heart. This is an effect common to exposure to other chlorinated aliphatics at high concentrations (Reinhardt et al. 1971). Cardiovascular toxicity has not been reported in animals following exposure to l,l-dichloroethane.

No reports of adverse renal effects in humans following exposure to l,l-dichloroethane were found. Nephrotoxicity has been observed in cats following subchronic inhalation exposure to l,l-dichloroethane. However, rats, rabbits, and guinea pigs exposed under the same conditions failed to exhibit any toxic effects on the kidney (Hofmann et al. 1971). Plaa and Larson (1965) tested renal function in mice following intraperitoneal injection of l,l-dichloroethane, and found that adverse effects on the kidney were only observed at lethal doses. These effects included increased glucose and protein in the urine and tubular swelling. Though data obtained following intraperitoneal injection provides information on potential health effects, data from oral, inhalation and dermal experiments are more relevant to possible exposures in humans. No histopathological changes in the kidney were noted after chronic ingestion of l,l-dichloroethane by rats and mice (Klaunig et al. 1986; NCI 1977). The toxicological significance of the nephrotoxicity observed in cats and the mice with regard to human health is not known given the small number of animals tested (cats), the lack of a nephrotoxic effect in other species and in other studies where l,l-dichloroethane was administered orally, and the fact that nephrotoxicity is not an effect commonly attributed to the halogenated hydrocarbons.

Immunological Effects. No studies were located regarding immunologic effects in humans or animals following exposure to l,l-dichloroethane, and it is not known if l,l-dichloroethane is immunotoxic in humans.

Neurological Effects. Chlorinated aliphatics as a class are known to cause central nervous system depression following high-level exposure in humans and animals. No reliable dose-response data were found on the central

nervous system depression induced by l,l-dichloroethane, though l,l-dichloroethane was once used as an anesthetic agent in humans. However, Plaa and Larson (1965) attributed deaths observed in mice following intraperitoneal injection to fatal central nervous system depression. Neurologic effects associated with long-term exposure to l,l-dichloroethane in humans or animals have not been reported.

Developmental Effects. Adverse developmental effects in humans associated with exposure to l,l-dichloroethane have not been reported. One study in rats indicated that inhalation exposure to l,l-dichloroethane resulted in retarded fetal development (delayed ossification of vertebrae) in the absence of significant maternal toxicity (Schwetz et al. 1974). The absence of maternal toxicity implies a direct effect on the fetus, rather than effects due to illness in the dam. The implications of the findings from one study with regard to potential developmental effects in humans are not known.

Reproductive Effects. No studies were located regarding reproductive effects in humans or animals following exposure to l,l-dichloroethane, and it is not known if l,l-dichloroethane has the potential to cause adverse reproductive effects in humans.

Genotoxic Effects. No studies were located regarding in vivo genotoxic effects in humans. The genotoxic potential of l,l-dichloroethane has been investigated in vitro in Salmonella tvphimurium (Riccio et al. 1983; Simmon et al. 1977), Saccharomyces cerevisiae (Bronzetti et al. 1987; Simmon et al. 1977), and Syrian hamster embryo cells (Hatch et al. 1983). In addition in vitro and in vivo assays have been conducted using rat and mouse organs (Colacci et al. 1985). Results of these studies are summarized in Table 2-5. Results from three studies conducted in S. typhimurium tester strains were conflicting. l,l-Dichloroethane was nonmutagenic in yeast cells even in the presence of metabolic activation system. However, because of insufficient reporting of data by Bronzetti et al. (1987) and Simmon et al. (1977), no assessment of the genotoxic potential of l,l-dichloroethane in S. cerevisiae can be made. The available data from the remaining studies indicate that, although l,l-dichloroethane did not induce cell transformation in BALB/c-3T3 cells (Tu et al. 1985), it increased the frequency of transformations induced by Simian adenovirus (SA7) in hamster embryo cells (Hatch et al. 1983).

In the Ames assay, l,l-dichloroethane was nonmutagenic in Salmonella strains TA97, TA98, Ta100, and TA102 (Nohmi et al. 1985). The compound was tested with and without metabolic activation. The highest dose was toxic to all strains of bacteria. In contrast, l,l-dichloroethane was mutagenic to strains TA1537, TA98, TA100, and TA1535 exposed to its vapor in a desiccator in the presence and absence of S9 mix (Riccio et al. 1983). Although the tests were conducted using three dose levels, the authors did not report the actual doses tested, and therefore the presence of a dose-dependent response could not be assessed. Simmon et al. (1977) on the other hand obtained

TABLE 2-5. Genotoxicity of 1,1-Dichloroethane In Vitro

End Point	Species (Test System)	Results: With Activation	Results: Without Activation	Reference
Prokaryotic organisms:				
Gene mutation	Salmonella typhimurium (Ames assay)	-	-	Nohmi et al. 1986
	S. typhimurium (Dessicator assay; vapor exposure)	+	+	Riccio et al. 1983
	S. typhimurium (Dessicator assay; vapor exposure)	-	No data	Simmon et al. 1977
Eukaryotic organisms:				
Gene mutation	Saccharomyces cerevisiae D7	-	-	Bronzetti et al. 1987
	S. cerevisiae D3 (Suspension assay)	-	No data	Simmon et al. 1977
Mammalian cells:				
DNA viral transformation	Syrian hamster embryo (cell transformation assay; vapor exposure)	No data	+	Hatch et al. 1983
Cell transformation	BALB/C-3T3 (cell transformation assay; exposure in sealed chamber)	No data	-	Tu et al. 1985
Macromolecular binding	Rat and mouse organs	+[a]	No data	Colacci et al. 1985

- = negative result; + = positive result;

[a]Pretreatment with phenobarbitone enhanced the extent of binding to DNA, microsomal RNA and proteins while addition of GSH suppressed the binding.

negative results using the same strains of Salmonella and a similar protocol. The concentrations of l,l-dichloroethane tested were not reported. Because the reporting of data was insufficient in studies by Riccio et al. (1983) and Simmon et al. (1977), the discrepancies in their reported results cannot be explained at this time.

l,l-Dichloroethane was nonmutagenic in yeast strains D3 and D7, even in the presence of S9 mix (Bronzetti et al. 1987; Simmon et al. 1977). Bronzetti et al. (1987) conducted an assay using strain D7 of Saccharomvces cerevisiae from the stationary and logarithmic growth phase. The cells harvested from the log phase cultures contained cytochrome P-450 and were capable of metabolizing promutagens to genetically active products. Both studies lacked details regarding doses of l,l-dichloroethane tested, though conflicting results may also be due to impurities in the chemicals used.

Tu et al. (1985) exposed BALB/c-3T3 cells to l,l-dichloroethane in a sealed chamber for 24 hours. No cell transformation was detected. This lack of effect may be due to the short period of exposure. However, l,l-dichloroethane increased the frequency of transformation induced by SA-7 virus in Syrian hamster embryo cells (Hatch et al. 1983). Embryo cell cultures were exposed in a sealed treatment chamber to volatilized l,l-dichloroethane for 20 hours and then treated with SA7 virus for 3 hours. l,l-Dichloroethane treatment significantly increased the viral transformation frequency in cells in a dose-dependent manner. The highest concentration (1,000 µg/mL) was cytotoxic. These results reflect the capacity of l,l-dichloroethane to interact with cellular DNA in hamster embryo cells.

In an in vivo study by Colacci et al. (1985) l,l-dichloroethane (98% purity) was found covalently bound to nucleic acids and proteins from liver, lung, kidney, and stomach of male rats and mice 22 hours following a single intraperitoneal injection of approximately 1.2 mg/kg. In vitro binding of l,l-dichloroethane to nucleic acids and proteins was mediated by liver P-450 dependent microsomal mixed function oxidase system. Glutathione-s-transferase shifted the equilibrium of the enzymatic reaction and thereby decreased binding, presumably by reducing the amount of toxic metabolite available for binding to macromolecules. On the other hand, phenobarbital increased binding by increasing cytochrome P-450 activity, thus generating more toxic metabolites available for binding to macromolecules. Presumably the metabolites generated from P-450 enzymatic action on l,l-dichloroethane bind to cellular macromolecules. Lung microsomes were weakly effective whereas kidney and stomach microsomal fractions were ineffective. Therefore, the binding to macromolecules of various organs detected in vivo may have been due to a stable hepatic metabolite that was circulated to reach extrahepatic organs. Pretreatment with phenobarbital enhanced the binding to DNA, microsomal RNA and proteins while addition of glutathione-s-transferase (GSH) to the microsomal systems caused suppression of binding. Because only radioactivity was measured it is difficult to determine whether the µmole bound represents l,l-dichloroethane or its metabolite(s). However, the fact

that binding is enhanced with induction of P-450 suggests that it represents the metabolite(s). Thus, GSH appears to play a detoxification role in the metabolism of l,l-dichloroethane. The fact that l,l-dichloroethane binds to nucleic acid suggests that it may have a potential to produce mutation in a mammalian system.

Cancer. There is inconclusive evidence that l,l-dichloroethane may be carcinogenic in humans. A significant positive dose-related trend was observed for the incidence of hemangiosarcomas and mammary adenocarcinomas in female rats, hepatocellular carcinoma in male mice, and endometrial stromal polyps in female mice. However, only the incidence of endometrial stromal polyps in female mice was significantly increased over the corresponding control animals. Limitations in this study (e.g., poor survival in both treated and control animals) preclude the consideration of these results as conclusive evidence of carcinogenicity (NCI 1977).

Results of a recently reported drinking water bioassay in mice indicated that l,l-dichloroethane is not carcinogenic (Klaunig et al. 1986). Possible differences in the pharmacokinetics of l,l-dichloroethane between the NCI (1977) and Klaunig et al. (1986) studies because of the different methods of administration and different vehicle and/or differences in dose levels employed may account for the disparate results. An in vitro assay of carcinogenicity initiation also yielded negative results for l,l-dichloroethane (Herren-Freund and Pereira 1986).

The induction of γ-glutamyltranspeptidase (GTP) foci, which are putative preneoplastic lesions, in isolated rat liver hepatocytes correlates well with carcinogenicity. l,l-Dichloroethane failed to induce GTP foci in liver hepatocytes obtained from rats and mice treated with l,l-dichloroethane for 7 days followed by promotion with phenobarbital (Herren-Freund and Pereira 1986). This suggests that l,l-dichloroethane is not carcinogenic, though these results are not conclusive.

There is limited evidence that neither confirms or dispels the carcinogenic potential of l,l-dichloroethane. Thus, these results are inconclusive as to whether it poses a cancer threat for humans. The EPA has classified l,l-dichloroethane as a Class C chemical which is defined as a possible human carcinogen (IRIS 1990).

2.5 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).

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 or cell that is measured within a compartment of an organism (NAS/NRC 1989). The preferred biomarkers of exposure are generally the substance itself or substance-specific metabolites in readily obtainable body fluid 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 (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 biologic 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 l,l-dichloroethane are discussed in Section 2.5.1.

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 (NAS/NRC 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 often not substance specific. They also may not be directly adverse, but can indicate potential health impairment (e.g., DNA adducts). Biomarkers of effects caused by l,l-dichloroethane are discussed in Section 2.5.2.

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. It can be an intrinsic genetic or other characteristic or a preexisting disease that results in an increase in absorbed dose, biologically effective dose, or target tissue response. If biomarkers of susceptibility exist, they are discussed in Section 2.7, "POPULATIONS THAT ARE UNUSUALLY SUSCEPTIBLE."

2.5.1 Biomarkers Used to Identify or Quantify Exposure to l,l-Dichloroethane

Although analytical methods are available to determine levels of l,l-dichloroethane in blood, urine, and expired breath, no information was located on levels of l,l-dichloroethane found in human tissues following exposure to measured quantities of this chemical.

2.5.2 Biomarkers Used to Characterize Effects Caused by l,l-Dichloroethane

l,l-Dichloroethane was used as an anesthetic in the early part of this century (Browning 1965; Konietzko 1984). However, no information was

available on blood levels associated with anesthesia or the occurrence of anesthesia-induced cardiac arrhythmias.

2.6 INTERACTIONS WITH OTHER CHEMICALS

No information was located regarding toxic interactions of l,l-dichloroethane with other xenobiotics. Evidence exists to indicate that l,l-dichloroethane is detoxified by glutathione (Colacci et al. 1985). Thus, it is likely that other substances that deplete glutathione stores such as other chlorinated hydrocarbons (e.g. l,l-dichloroethene and 1,2-dichloroethane), acetaminophen, and bromobenzene may enhance the toxicity of l,l-dichloroethane. Substances that alter the activity of the microsomal enzymes that are responsible for the metabolism of l,l-dichloroethane may also affect the toxicity of this chemical. For example, it has been shown that ethanol increases the metabolism of l,l-dichloroethane in vitro (Sato et al. 1980).

2.7 POPULATIONS THAT ARE UNUSUALLY SUSCEPTIBLE

No populations unusually susceptible to l,l-dichloroethane or chlorinated ethanes in general have been identified. NIOSH (1978) has identified the following individuals as possibly being at increased risk from exposure to l,l-dichloroethane: (1) Individuals with skin disease because of the purported dermal irritant effects induced by l,l-dichloroethane. (2) Individuals with liver disease because of the role of this organ in the biotransformation and detoxification of xenobiotics such as l,l-dichloroethane. (3) Individuals with impaired renal function because of the limited evidence that l,l-dichloroethane is nephrotoxic in animals. (4) Individuals with chronic respiratory disease because of the purported respiratory irritant effects induced by l,l-dichloroethane. Although there are no data to substantiate this, additional populations that may be unusually susceptible to l,l-dichloroethane include children and the elderly because of immature or compromised metabolic capabilities, and phenobarbital or alcohol consumers because of the ability of these substances to alter the activity of the cytochrome P-450 system.

It should be noted that no reliable data were found regarding dermal or respiratory irritant effects of l,l-dichloroethane.

2.8 ADEQUACY OF THE DATABASE

Section 104(i)5 of CERCLA 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 l,l-dichloroethane is available. Where adequate information is not available, ATSDR, in conjunction with 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 l,l-dichloroethane.

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 or eliminate the uncertainties of human health assessment. In the future, the identified data needs will be evaluated and prioritized, and a substance-specific research agenda will be proposed.

2.8.1 Existing Information on the Health Effects of l,l-Dichloroethane

The existing data on health effects of inhalation, oral, and dermal exposure of humans and animals to l,l-dichloroethane are summarized in Figure 2-4. The purpose of this figure is to illustrate the existing information concerning the health effects of l,l-dichloroethane. Each dot in the figure indicates that one or more studies provide information associated with that particular effect. The dot does not imply anything about the quality of the study or studies. Gaps in this figure should not be interpreted as "data needs" information.

Figure 2-4 graphically depicts the information that currently exists on the health effects of l,l-dichloroethane. The literature reviewed concerning the health effects of l,l-dichloroethane in humans consisted solely of an anecdotal report describing the occurrence of cardiac arrhythmias when this compound was used as a gaseous anesthetic. Chlorinated aliphatics as a class are known to cause central nervous system depression. Respiratory tract and dermal irritation also result when humans are exposed by inhalation to sufficiently high levels. It has been inferred that l,l-dichloroethane causes these latter effects, but no reliable data were found that verified this activity.

The database for the health effects of l,l-dichloroethane in experimental animals is lacking, and the studies reviewed consisted primarily of one subchronic inhalation study, one inhalation developmental toxicity study, and two oral chronic bioassays. No information is available on the effects of l,l-dichloroethane following dermal exposure. The limited information available in animals suggests that l,l-dichloroethane may be nephrotoxic, fetotoxic, and possibly carcinogenic. The data also indicate that l,l-dichloroethane is considerably less toxic than 1,2-dichloroethane and the tetrachlorinated aliphatics.

2.8.2 Identification of Data Needs

Acute-Duration Exposure. No reliable information is available on the effects of single-dose exposures in humans and animals. LD_{50} values are available in secondary sources, but no details are available to assess the

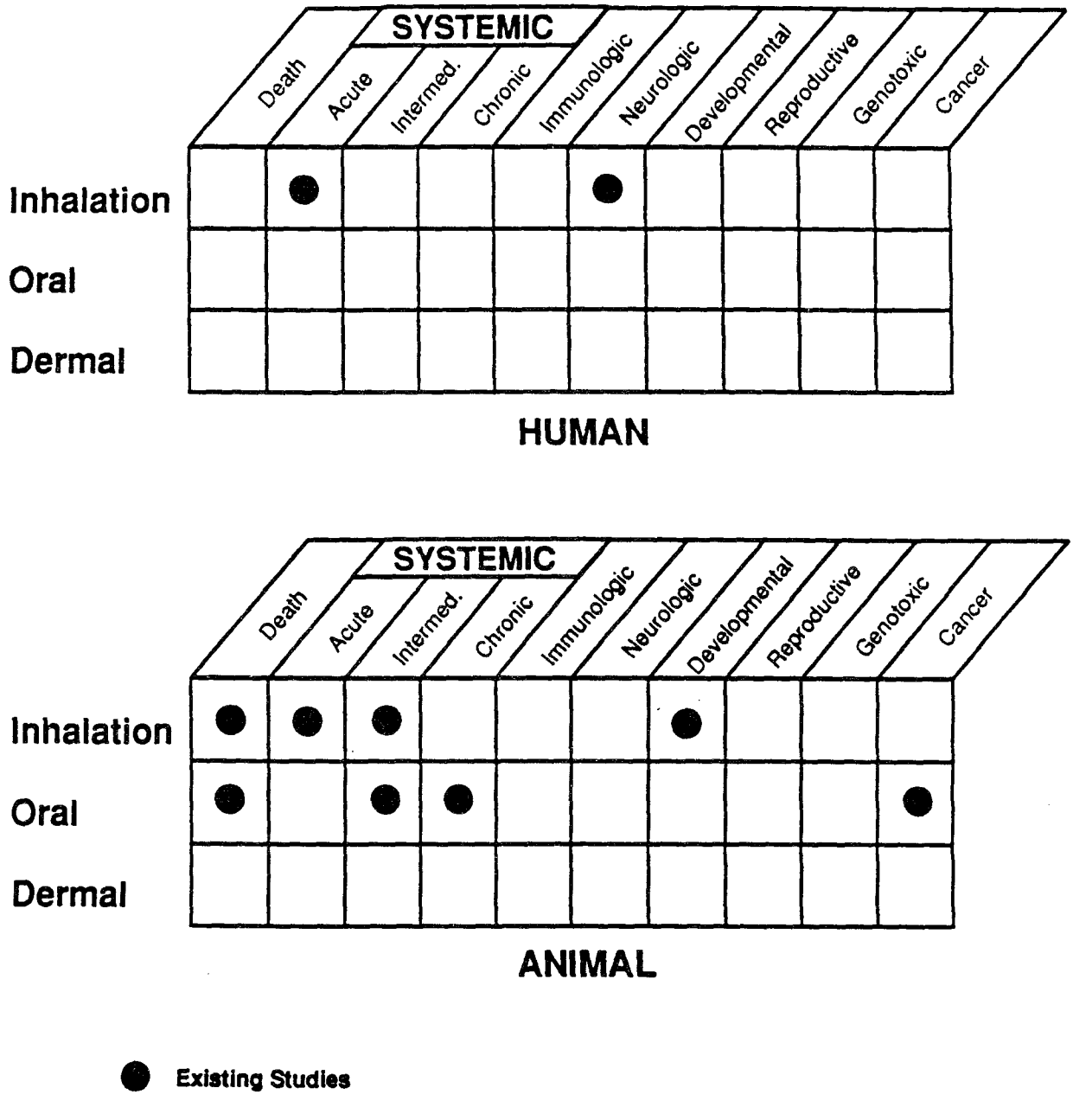


FIGURE 2-3. Existing Information on Health Effects of 1, 1-Dichloroethane

quality of these data. Therefore, an acute MRL for systemic effects can not be derived because of insufficient data. Since the chlorinated aliphatics in general are known to cause central nervous system depression and irritation of respiratory and ocular mucosal epithelium following single high-level exposures, more information on the effects of single-dose exposures to 1,1-dichloroethane by all routes would be useful to assess more fully the acute hazards of this chemical. Single-dose inhalation studies are of a higher priority, since inhalation is the most likely exposure pathway for this chemical although disposal may be by buried storage drums so soil and groundwater contamination from leakage is also possible. Though the relative potential for a high level of exposure via contaminated air is probably remote, there is a need to determine the threshold exposure level for effects caused by acute inhalation exposure.

Intermediate-Duration Exposure. No reliable information is available on the effects of repeated-dose exposure in humans. Limited information is available on the effects of repeated inhalation and oral exposures to 1,1-dichloroethane in animals. The studies reviewed indicate that 1,1-dichloroethane is possibly nephrotoxic, but this effect has only been demonstrated at high doses in one of several species tested. No other toxic effects have been attributed to 1,1-dichloroethane following repeated-dose exposures in animals. An intermediate MRL could not be derived for any routes of exposure. More information on the systemic effects of repeated-dose exposures in animals, particularly by the inhalation route since this is the most likely route of human exposure, would be useful to determine whether nephrotoxic effects observed in one study are an actual result of exposure to 1,1-dichloroethane, to determine if 1,1-dichloroethane reacts like other chlorinated aliphatics (e.g., causes neuro- and liver toxicity), and to more fully assess potential human health hazards from repeated exposure to 1,1-dichloroethane. This latter justification is particularly important since repeated exposure to low levels of 1,1-dichloroethane may be of more concern than short-term exposure to very high levels based on the current use and/or disposal of this chemical.

Chronic-Duration Exposure and Cancer. No information is available on the effects of chronic exposure to 1,1-dichloroethane in humans. The NCI study reported histopathological examinations for endpoints of systemic toxicity in addition to the neoplastic effects in rats and mice. No MRL can be derived for long-term exposure. Additional chronic toxicity studies particularly by the inhalation route would be useful to fully assess potential human health hazard from long-term exposure to 1,1-dichloroethane. This justification is important since chronic exposure to low levels of 1,1-dichloroethane may be of more concern than short-term exposure to very high levels based on the current use and/or disposal of this chemical.

Two bioassays were reviewed that investigated the potential carcinogenic effect of 1,1-dichloroethane by the oral route of exposure in animals. One

study provided suggestive evidence of carcinogenicity, but because there was poor survival in this study and the statistical significance of the cancer incidence is uncertain, the results could not be considered conclusive. The other bioassay yielded negative results for l,l-dichloroethane. No chronic toxic effects other than lethality were noted in either bioassay. The possibility that significant differences between the two studies could be due to administering l,l-dichloroethane in drinking water as compared to bolus doses in corn oil needs to be evaluated. Given the limitations present in the one study, the fact that 1,2-dichloroethane and certain other chlorinated aliphatics are carcinogenic and hepatotoxic, and the observations that l,l-dichloroethane possibly forms DNA adducts and metabolizes to free radicals, more information obtained from well-conducted carcinogenicity studies would be useful to assess more fully the carcinogenic potential of l,l-dichloroethane in humans and animals. Studies conducted by the inhalation route would be useful.

Genotoxicity. With one exception, the genotoxic potential of l,l-dichloroethane has been investigated almost exclusively using in vitro assays. Though the available data are conflicting, l,l-dichloroethane is generally considered to be nongenotoxic. l,l-Dichloroethane has been observed to enhance cell transformation in Syrian hamster embryo cells and results suggest that l,l-dichloroethane or a metabolite can bind to cellular macromolecules such as DNA. More information on the genotoxic effects of l,l-dichloroethane in animals both in vitro and in vivo would be useful to resolve the discrepancies in the present data and to assess the genotoxic hazard of this chemical in humans.

Reproductive Toxicity. No information on the reproductive effects of l,l-dichloroethane in humans or animals is available. Reproductive toxicity studies in animals would be useful particularly by the inhalation route since this is the most likely route of human exposure.

Developmental Toxicity. No information on the developmental effects of l,l-dichloroethane in humans Is available. One study was located that investigated the developmental effects of inhaled l,l-dichloroethane in animals. The results from this study indicated that l,l-dichloroethane is fetotoxic in rats, causing retarded fetal development (i.e., delayed ossification of the vertebrae) in the absence of significant maternal toxicity. Additionally, well-conducted developmental toxicity studies on l,l-dichloroethane, particularly by the inhalation route since this is the most likely route of human exposure, would be useful to verify the data from the single study that suggest this compound may cause adverse developmental effects. Data that compared the effects caused from different routes of exposure in mammalian species would also be useful to determine the likeliness of effects in humans.

Immunotoxicity. No information is available on the immunotoxic effects of l,l-dichloroethane in humans or animals. Immunotoxicity studies in animals, particularly by the inhalation route since this is the most likely route of human exposure, would be useful to assess the potential risk for l,l-dichloroethane-induced adverse immunologic effects in humans.

Neurotoxicity. Chlorinated aliphatics as a class are known to cause central nervous system depression in humans exposed by inhalation to sufficiently high levels. l,l-Dichloroethane can also cause this effect, evidenced by its former use as an anesthetic. However, no reliable data were found that indicated a threshold level for this effect. No data (behavioral, histopathological, neurochemical, or neurophysiological) are available on possible neurotoxic effects of long-term low level exposures to l,l-dichloroethane. More information on potential short- and long-term neurotoxic effects of inhaled l,l-dichloroethane would be useful to determine whether this compound can produce neurotoxic effects following low level, long-term exposures, and to determine the threshold exposure level for l,l-dichloroethane-induced central nervous system depression.

Epidemiological and Human Dosimetry Studies. No epidemiological studies were located on l,l-dichloroethane. Well-controlled epidemiological studies of people living in close proximity to areas where l,l-dichloroethane contamination of surface water and groundwater or air is known to have occurred, people living near hazardous waste sites, and of occupationally exposed people could add to the limited database and clarify health effects in humans induced by l,l-dichloroethane. However, while this information would be useful, it is unlikely that it could be easily obtained from occupational studies. Other short-chain halogenated hydrocarbons are usually encountered in the same facilities where l,l-dichloroethane is manufactured or used, thus confounding the results obtained in such a study.

Biomarkers of Exposure and Effect. For high exposure to l,l-dichloroethane, the levels of this compound in the blood, urine, and breath may be used for biomarkers of exposure. However, these methods should be more sensitive and quantitative. The development of methods for detecting metabolites in the fluids and tissue of humans is needed to indicate l,l-dichloroethane exposure.

Biomarkers of effect would be useful for identifying l,l-dichloroethanespecific injury (e.g., hepatotoxicity, renal toxicity, neurotoxicity) for short-, intermediate- and long-term exposure. Presently, no biomarkers of effect are available; however, DNA adducts may be useful for indicating carcinogenicity in animals or humans following chronic exposure to l,l-dichloroethane.

Absorption, Distribution, Metabolism, and Excretion. Studies of the pharmacokinetics of l,l-dichloroethane are very limited. Much of the

information regarding the disposition of l,l-dichloroethane is based on indirect evidence. Pharmacokinetic data are useful for providing information on mechanisms of toxicity and can often support findings of toxicity studies.

Absorption of l,l-dichloroethane occurs following exposure via all routes. The presence of a l,l-dichloroethane metabolite in urine and expired air and its binding to tissue macromolecules provide evidence of its absorption. Studies regarding the direct analysis of the extent and rate of l,l-dichloroethane absorption are lacking and would provide useful information on the potential health hazards associated with exposure to l,l-dichloroethane via inhalation of contaminated air or ingestion of contaminated water.

Studies in humans and animals regarding tissue distribution of l,l-dichloroethane are not available. Its lipophilicity suggests that the compound would be well absorbed and distributed to tissues according to their lipid content. Binding studies conducted in rats following intraperitoneal injection indicate that l,l-dichloroethane localizes in the liver, kidney, lung, and stomach. However, analysis has been limited to these tissues. Distribution studies using routes of administration relevant to human exposure (inhalation, oral) would provide useful information on potential target organs of l,l-dichloroethane-induced toxicity in humans.

Characterization of l,l-dichloroethane's metabolism relies heavily on in vitro data. These studies reveal that the biotransformation process is mediated by cytochrome P-450 with hepatic microsomes being the most effective. Identification of products in these microsomal studies allows for the prediction of metabolic pathways. However, exposure to l,l-dichloroethane under in vivo conditions may alter substrate availability and consequently alter the metabolic scheme. In vivo studies would provide a better understanding of the rate and extent of l,l-dichloroethane metabolism and a more realistic perspective of its metabolic fate. This information would allow more accurate prediction of the potential of l,l-dichloroethane to induce toxic effects, and aid in devising methods to detoxify exposed persons.

Studies regarding the excretion of l,l-dichloroethane by humans were not available. One study was located in animals regarding the extent or rate of l,l-dichloroethane excretion. Studies monitoring levels in blood and excretion would be useful to estimate pharmacokinetic parameters.

Comparative Toxicokinetics. The absorption, distribution, metabolism, and excretion data for l,l-dichloroethane are all derived from animal studies. It is likely that human disposition would follow a scheme similar to that found in animals, but this conclusion is highly speculative. However, similar results obtained in vivo across several animal species would provide supportive evidence for the assumption that l,l-dichloroethane is handled in a similar manner in humans.

2.8.3 On-going Studies

No on-going studies were identified that explored the health effects or toxicokinetics of l,l-dichloroethane or attempted to associate l,l-dichloroethane levels in human tissues with effects.

3. CHEMICAL AND PHYSICAL INFORMATION

3.1 CHEMICAL IDENTITY

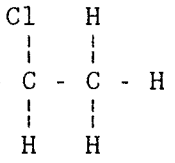
The synonyms, and identification numbers for l,l-dichloroethane are listed in Table 3-l.

3.2 PHYSICAL AND CHEMICAL PROPERTIES

Important physical and chemical properties of l,l-dichloroethane are listed in Table 3-2.

3. CHEMICAL AND PHYSICAL INFORMATION

TABLE 3-1. Chemical Identity of 1,1-Dichloroethane

	Value	Reference
Chemical name	1,1-Dichloroethane	CAS 1988
Synonyms	alpha alpha-Dichloroethane; asymmetrical dichloroethane; chlorinated hydrochloric ether; S-dichloroethane; Dutch oil; ethane, 1,1,-dichloro-(9CI); ethylidene chloride; ethylidene dichloride; 1,1-ethylidene dichloride	Grayson 1978; Weiss 1986
Trade names	No data	
Chemical formula	$C_2H_4Cl_2$	Weiss 1986; Windholz 1983
Chemical structure		
Identification numbers:		
CAS registry	75-34-3	Grayson 1978
NIOSH RTECS	KI0175000	HSDB 1988
EPA hazardous waste	U076	HSDB 1988
OHM-TADS	No data	
DOT/UN/NA/IMCO	DOT 2362; UN 2362; IMCO 3.2	HSDB 1988; Weiss 1986
HSDB	64	HSDB 1988
NCI	No data	
STCC	No data	

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

TABLE 3-2. Physical and Chemical Properties of 1,1-Dichloroethane

Property	Value	Reference
Molecular weight	98.97	Windholz 1983
Color	Colorless	
Physical state	Liquid	Weiss 1986
Melting point	-96.7°C	Grayson 1978
Boiling point	57.3°C	Grayson 1978; Windholz 1983
Density at 20°C	1.1747 g/cm^3	Grayson 1978
Odor	Aromatic ethereal; chloroform-like	
Odor threshold:		
Air	120 ppm; 200 ppm	Verschueren 1983
Water	No data	
Solubility:		
Water at 20°C	0.55 g/100 g	Grayson 1978
Organic solvents	Miscible with most organic solvents, including other chlorinated solvents	
Partition coefficients:		
log K_{ow}	1.79	EPA 1985
log K_{oc}	1.76	EPA 1985
Vapor pressure at 20°C	182 mmHg	EPA 1985
at 25°C	230 mmHg	HSDB 1988
Henry's law constant	4.2×10^{-2} atm-m^3/mol	EPA 1985
Autoignition temperature	457.8°C	HSDB 1988; Weiss 1986
Flashpoint:		
Closed cup	-8.33°C	ACGIH 1986; HSDB 1988;
Open cup	-5.56°C	NIOSH 1985
Flammability limits	Lower 5.6%; upper 11.4%	Weiss 1986
Conversion factors	1 ppm x 4.05 = 1 mg/m^3 1 mg/m^3 x 0.25 = 1 ppm	

4. PRODUCTION, IMPORT, USE, AND DISPOSAL

4.1 PRODUCTION

l,l-Dichloroethane is produced commercially through the reaction of hydrogen chloride and vinyl chloride at 20°-55°C in the presence of an aluminum, ferric, or zinc chloride catalyst (Grayson 1978). Other production methods include the direct chlorination of ethane, the reaction of PCl, with acetaldehyde as a by-product during the manufacture of chloral (Browning 1965)) and as an intermediate in the production of vinyl chloride and l,l,l-trichloroethane by photochlorination (Windholz 1983).

Information regarding the volume of l,l-dichloroethane production is limited. At least 4.55×10^{10} grams were produced in 1977 (HSDB 1988). No information was found regarding U.S. production volumes after this date.

Major companies producing l,l-dichloroethane within the United States include PPG Industries, Inc., Continental Oil Company, and Vulcan Materials, all based in Louisiana, and Dow Chemical located in Texas. Each of these companies manufactures l,l-dichloroethane primarily to be used as an intermediate in the manufacture of l,l,l-trichloroethane.

4.2 IMPORT

No information was found concerning U.S. imports and exports of l,l-dichloroethane.

4.3 USE

The largest individual use of l,l-dichloroethane is as an intermediate in the manufacture of other products such as vinyl chloride, l,l,l-trichloroethane, and to a lesser extent high vacuum rubber. It also has limited use as a solvent for plastics, oils, and fats, and thus is employed as both a cleaning agent and a degreaser. In the past, l,l-dichloroethane was used as an anesthetic, but that use has been discontinued. Other uses of l,l-dichloroethane include fabric spreading, varnish and finish removers, organic synthesis, ore flotation, and as a fumigant and insecticide spray (EPA 1985; Grayson 1978; HSDB 1988). No information is available regarding the use proportions among these categories.

4.4 DISPOSAL

l,l-Dichloroethane may be disposed of by atomization within a combustion chamber equipped with an appropriate effluent gas cleaning device, by hightemperature incineration with a hydrochloric acid scrubber, or by placing product residues and sorbent media into 17H epoxy-lined drums and disposing of

them at an EPA-approved site. However, the criteria for treatment or sanitary landfill disposal practices are currently undergoing revision. Consultation with environmental regulatory agencies is advised (HSDB 1988; NIOSH 1978; OHMTADS 1988).

5. POTENTIAL FOR HUMAN EXPOSURE

5.1 OVERVIEW

The primary disposition of l,l-dichloroethane in the environment is related to the production, storage, consumption, transport, and disposal of l,l-dichloroethane used as a chemical intermediate, solvent, finish remover, and degreaser. Releases from industrial processes are almost exclusively to the atmosphere. Releases of the compound to surface waters and soils are expected to partition rapidly to the atmosphere through volatilization. Hydrolysis, photolysis, and biodegradation do not appear to be important processes in determining the environmental fate of l,l-dichloroethane. It has been detected at generally low levels in ambient air, surface water, groundwater, drinking water, and human breath. Concentrations in environmental media are greatest near source areas (e.g., industrial point sources, hazardous waste sites).

Inhalation of l,l-dichloroethane in ambient or workpiace air is generally the main route of human exposure to the compound. Estimates of populations potentially exposed to l,l-dichloroethane in workplace environments range from 715 to 1,957 workers (NIOSH 1976, 1984). Inhalation of ambient air and ingestion of contaminated drinking water may also be important routes of exposure for populations living near industrial facilities and hazardous waste sites.

5.2 RELEASES TO THE ENVIRONMENT

There are no known natural sources of l,l-dichloroethane, but McCarty et al. (1986) reported that l,l,l-trichloroethane is biodegraded in anaerobic methanogenic environments, such as those found in landfills, to form l,l-dichloroethane. Laboratory studies designed to elucidate the degradation reactions of chloroethenes and chloroethanes have been described by Hallen et al. (1986) and Vogel and McCarty (1987). Hallen et al. (1986) observed that dechlorination reactions appear to be reversible, and'chlorinated ethanes can be converted to chlorinated ethenes. Releases of the compound to the environment result from industrial manufacturing and use processes. Additional sources of environmental release are fugitive emissions from storage, distribution, and disposal; use as an extraction solvent and fumigant; and as a constituent of medicines and stone, clay, and glass products (Infante and Tsongas 1982).

EPA has identified 1,177 NPL sites. We do not know how many of the 1,177 NPL sites have been evaluated for 1,1-dichloroethane. l,l-Dichloroethane has been found at 248 of the total number of sites evaluated for that compound. As more sites are evaluated by EPA, this number may change (VIEW 1989). The frequency of these sites within the United States can be seen in Figure 5-l.

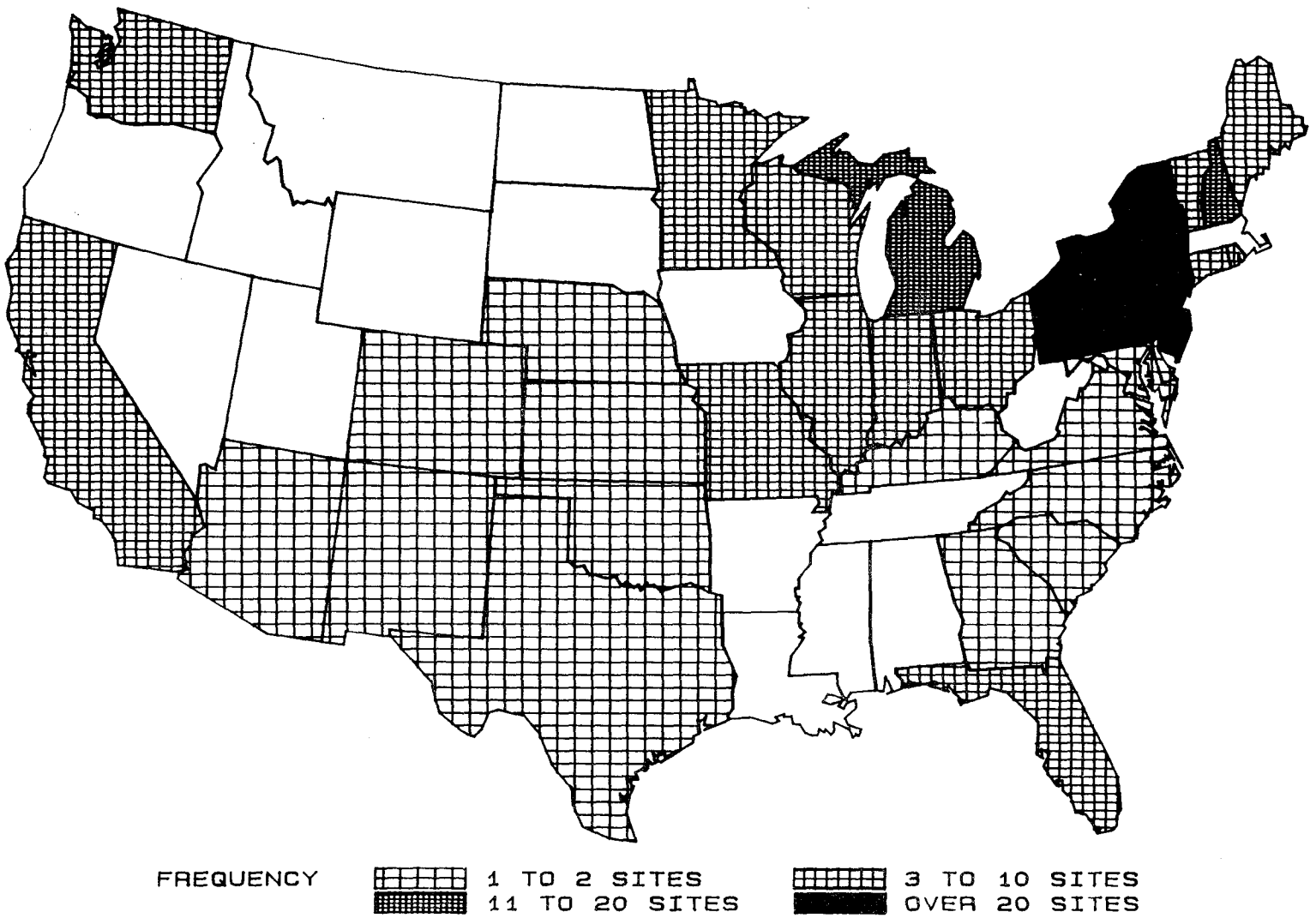


FIGURE 5-1. FREQUENCY OF SITES WITH 1,1-DICHLOROETHANE CONTAMINATION

5.2.1 Air

Emissions to the atmosphere comprise more than 99% of all releases of l,l-dichloroethane to the environment (Perwak et al. 1982). l,l-Dichloroethane released in the production of l,l,l-trichloroethane accounts for about 52% of the atmospheric releases, with the production of 1,2-dichloroethane accounting for about 35%. Pellizzari (1982) reported the presence of low levels of l,l-dichloroethane in ambient air of the Baton Rouge industrial area and at the Kin-Buc waste disposal site outside Edison, New Jersey. Approximately 52,000 kg of l,l-dichloroethane are released to the atmosphere by privately owned treatment work facilities (POTWs) each year (EPA 1980).

5.2.2 Water

Industrial releases of l,l-dichloroethane, to surface waters are minor in comparison to releases to the atmosphere. Releases from solvent use and POTWs account for only 2,000 kg annually (Perwak et al. 1982). Industrial processes involving the use of l,l-dichloroethane as a chemical intermediate or cleaning solvent are believed to be the largest sources of surface water releases, Young et al. (1983) reported l,l-dichloroethane in the primary, secondary, and final effluents from municipal wastewater treatment plants. Approximately 1,000 kg of l,l-dichloroethane are discharged in effluent from POTWs each year (EPA 1980).

l,l-Dichloroethane has been detected in groundwater samples taken at an estimated 9% of the NPL hazardous water sites participating in the Contract Laboratories Program (CLP) at a geometric mean concentration of 23.1 ppb for the positive samples (CLP 1989). The compound was also detected in surface water samples taken at an estimated 2% of the NPL hazardous waste sites participating in the CLP at a geometric mean concentration of 24 ppb for the positive samples. Note that these data from the CLP Statistical Database represent frequency of occurrence and concentration information of NPL sites only.

5.2.3 Soil

Little information was found regarding releases of l,l-dichloroethane to soils. Solvent use and POTWs are the only identified sources of l,l-dichloroethane releases to the land, with 6,000 kg released in 1978 (Perwak et al. 1982). Approximately 4,000 kg of l,l-dichloroethane from POTWs are dispersed on land each year as sludge (EPA 1980).

l,l-Dichloroethane has been detected in soil samples taken at an estimated 0.7% of the NPL hazardous waste sites participating in the Contract Laboratory Program (CLP) at a geometric mean concentration of 40.8 ppb for the positive samples (CLPSD 1989). Note that these data from the CLP Statistical

Database represent frequency of occurrence and concentration information for NPL sites only.

5.3 ENVIRONMENTAL FATE

5.3.1 Transport and Partitioning

Releases of l,l-dichloroethane to the environment as a result of industrial activity are expected to be primarily to the atmosphere (see Section 5.2). l,l-Dichloroethane released to the atmosphere may be transported long distances before being washed out in precipitation. For example, Pearson and McConnell (1975) attributed the presence of chlorinated organic compounds, including l,l-dichloroethane, in upland waters to longrange aerial transport and deposition in precipitation. Perwak et al. (1982) discussed the atmospheric fate of l,l-dichloroethane in the Gulf Coast area, where there is a high percentage of cloudy days. Increased atmospheric losses due to washout in frequent, heavy rains could occur, although much of the l,l-dichloroethane could be revolatilized. Dichloroethanes released in this area could be transported north by the prevailing winds to populated areas before significant photochemical degradation could occur.

Cupitt (1980), however, considered the loss of 1,2-dichloroethane from the atmosphere by dissolution into rain drops or adsorption onto aerosols insignificant compared with loss from chemical degradation based on mathematical calculations. Since l,l-dichloroethane has higher volatility and lower aqueous solubility than the 1,2-isomer, physical removal of l,l-dichloroethane from the atmosphere would be even less likely to be important (EPA 1985). Pellizzari et al. (1979) measured actual concentrations of airborne contaminants in the vicinity of known emission sources of l,l-dichloroethane, making aerial transport the logical source of downwind concentrations.

Henry's law constant value for l,l-dichloroethane ($4.2x10^{-2}$ atm-m^3/mol) suggests that it should partition rapidly to the atmosphere. Evaporation half-life depends on a number of factors: wind speed and mixing conditions of the receiving waters are particularly important. Dilling et al. (1975) and Dilling (1977) estimated a volatilization half-life of 22 minutes for l,l-dichloroethane present at 1 ppm concentration in an open water column held at 25°C and stirred at 200 rpm. Under these conditions 90% of the compound was removed within 109 minutes. Volatilization half-lives determined in the laboratory are related to actual environmental situations by a correction factor that takes into account the oxygen reaeration rate ratio. The reaeration rate ratio has been determined to be 0.55 for l,l-dichloroethane (Cadena et al. 1984). Using the values of Mabey et al. (1981) for oxygen reaeration rates in ponds and rivers (0.19 and 0.96 day^{-1}, respectively), the evaporation half-life of l,l-dichloroethane is estimated to be approximately five times longer for ponds than for rivers (more than 1 day for river water and more than 6 days for pond water). Therefore, evaporation may be the most

significant means of removal of l,l-dichloroethane from aquatic media (EPA 1985).

No information was found regarding partitioning of l,l-dichloroethane from the water column onto sediments. However, analogs of the compound (i.e., dichloromethane, trichloromethane, and l,l,l-trichloroethane) have not been found to concentrate selectively onto sediments (Dilling et al. 1975; Pearson and McConnell 1975). The K_{OC} values for these compounds are similar to the K_{OC} for l,l-dichloroethane; therefore, adsorption onto sediments would not be considered significant for l,l-dichloroethane (EPA 1985).

l,l-Dichloroethane released to land surfaces in spills would rapidly volatilize to the atmosphere, but l,l-dichloroethane remaining on soil surfaces would be available for transport into groundwater, since the compound does not sorb to soil particulates unless the organic content of the soil is high. Experimentally derived K_{OC} values for a silt loam soil also indicate that little sorption of l,l-dichloroethane to low organic content soil is expected. Wilson et al. (1981) found that although 50% of the applied l,l-dichloroethane volatilized to the atmosphere, the remainder percolated rapidly through a sandy soil, suggesting ready availability to groundwater transport processes. Environmental surveys conducted by EPA have detected l,lcdichloroethane in groundwater sources in the vicinity of contaminated sites (EPA 1985).

Gossett et al. (1983) analyzed the tissues of several species of aquatic organisms for l,l-dichloroethane near the discharge of the Los Angeles County wastewater treatment plant. The concentration of l,l-dichloroethane in the effluent was 3.5 ppb, however none was found in the animal tissues (detection limit of 0.3-0.5 ppb). These results may be evidence that the potential for l,l-dichloroethane to bioconcentrate is low in aquatic organisms. EPA (1984) estimated the bioconcentration factor from the K_{OW} as 6.6, indicating that bioconcentration would not be expected.

5.3.2 Transformation and Degradation

5.3.2.1 Air

In the atmosphere, l,l-dichloroethane is oxidized by reaction with hydroxyl radicals. The residence time of the compound in the atmosphere has been estimated by several investigators to be 44 days (Singh et al. 1981; Howard and Evenson 1976).

5.3.2.2 Water

l,l-Dichloroethane in surface water is expected to be lost to the atmosphere through volatilization before undergoing any significant chemical or biological degradation. The hydrolytic half-life of l,l-dichloroethane at pH 7 and 25°C has been estimated to be 60 years (Jeffers et al. 1989).

According to McCarty et al. (1986), l,l-dichloroethane appears to be produced by biodegradation of l,l,l-trichloroethane in groundwater. Further degradation could also occur. In the absence of oxygen and in the presence of anaerobic, methane-producing bacteria, halocarbons are transformed by reductive dehydrohalogenation in a step-wise manner: l,l,l-trichloroethane -> l,l-dichloroethane → chloroethane → ethanol → carbon dioxide. Under aerobic conditions, Tabak et al. (1981) reported about 50% degradation of l,l-dichloroethane by unadapted microorganisms isolated from municipal waste water inoculum after 7 days, which was increased to 78% degradation by adapted organisms in the same time period. l,l-Dichloroethane has been reported to be resistant to biological degradation by bacteria isolated from shallow aquifer aerobic groundwater after 8-16 weeks incubation (Wilson et al. 1983).

Data from landfill sites with a documented contamination history were examined by Cline and Viste (1984). They observed that l,l-dichloroethane was detected in groundwater at sites where the compound had not been handled or disposed of and concluded that l,l-dichloroethane had been produced by anaerobic degradation of other compounds present, particularly l,l,l-trichloroethane.

5.3.2.3 Soil

l,l-Dichloroethane in soils is expected to volatilize to the atmosphere or be transported to groundwater before undergoing significant abiotic transformation; the compound is not expected to sorb to soils of low organic content. As in surface waters, direct photolysis of l,l-dichloroethane on soil surfaces is not expected. The rate of biodegradation of l,l-dichloroethane in soils is unknown. In subsurface soil, the loss of l,l-dichloroethane through biodegradation is expected to be insignificant (Wilson et al. 1983). The biodegradation half-life of l,l,l-trichloroethane under anaerobic conditions has been reported to be about 16 days, whereas the half-life of l,l-dichloroethane has been reported to be greater than 30-60 days (Wood et al. 1985).

5.4 LEVELS MONITORED OR ESTIMATED IN THE ENVIRONMENT

l,l-Dichloroethane has been detected in ambient urban and rural air, in waste gas generated from garbage dumps, and in surface water, groundwater, and drinking water. Quantitative concentration information is presented in the following sections by environmental medium.

5.4.1 Air

l,l-Dichloroethane was not seen at a detection limit of 5 ppt in ambient rural air samples taken in southeastern Washington state (Grimsrud and Rasmussen 1975). It has been found at higher concentrations in ambient air samples from urban areas of the United States. Brodzinsky and Singh (1983) tabulated atmospheric levels at urban, rural, and industrial sites across the

United States and reported a median concentration of 55 ppt. Pellizzari (1982) reported the detection of low levels (unspecified concentrations) of the compound in the vicinity of the Baton Rouge industrial area. Singh et al. (1983) reported that the average concentration of the compound in the air of seven urban locations in 1980-1981 ranged from 0.1 to 1.5 ppb. It has also been detected in samples of ambient air collected in the vicinity of hazardous waste disposal sites, such as the Kin-Buc site near Edison, New Jersey, at a level of 23 $\mu g/m^3$ (5.68 ppm) (Pellizzari 1982). Hoefler et al. (1982) found a level of 1.1 mg/kg of the compound in waste gas generated at a garbage dump. Pellizzari (1978) tabulated analytical results for l,l-dichloroethane in the ambient air of various locations generally in close proximity to industrial plants, including Magna, Utah (0.082 ppb); Iberville, Louisiana (0.12 ppb); Deer Park, Texas (0.14 ppb); and Baton Rouge (0.058 ppb) and Geismar, Louisiana (0.14 ppb).

Barkley et al. (1980) found no l,l-dichloroethane in the ambient air surrounding nine houses bordering the old Love Canal. Gupta et al. (1984) found l,l-dichloroethane at higher levels indoors (mean concentration of 3.2 ppb) than outdoors (not detected) in residences in suburban Knoxville, Tennessee, and concluded that there must be a source of the compound inside the home. Possible sources were not identified except to suggest building materials or chlorinated water.

5.4.2 Water

Perwak et al. (1982) summarized data from EPA's STORET database, where reported concentrations of l,l-dichloroethane range from undetected (<l0 ppb) to 1,900 ppb, with the highest reading in the Upper Mississippi River basin at Alton, Illinois. However, they observed that monitoring results reported for l,l-dichloroethane in surface waters are almost always below the detection limit (generally 10 ppb). The compound has also been found in samples of urban runoff from Long Island, New York, and Eugene, Oregon, at concentrations of 1.5 and 3 ppb, respectively (Cole et al. 1984). Coniglio et al. (1980) summarized groundwater monitoring data obtained by numerous state agencies and reported that l,l-dichloroethane was found in 18% of the wells tested, with a maximum concentration of 11,330 ppb. They cautioned that the state data may have been biased since the monitoring was generally conducted by the states in areas where contamination was suspected. However, l,l- dichloroethane has been detected in groundwater sampled during random testing of water supplies (see further discussion).

Finished water supplies obtained from groundwater sources were tested by EPA for contaminants. It was reported that up to 10.8% of 158 nonrandom sample sites from across the United States contained detectable levels of l,l-dichloroethane. The maximum concentration was 4.2 ppb (Westrick et al. 1984). l,l-Dichloroethane was detected at a maximum concentration of 220 ppb in samples from 193 private wells in Rhode Island analyzed over a period of nine years (RIDH 1989). A maximum concentration of 40 ppb l,l-dichloroethane

was detected in 6 public drinking water systems in Rhode Island between April 1982, and April 1989 (RIDH 1989).

Drinking water samples from a number of urban and rural locations in the United States have been reported to be contaminated with l,l-dichloroethane. Unspecified levels of the compound have been detected in drinking water samples taken from Philadelphia (Suffet et al. 1980). Private drinking water wells in Wisconsin were found to contain unspecified levels of l,l-dichloroethane in 11 of 617 wells surveyed (Krill and Sonzogni 1986). Concentrations of l-3 ppb were reported in four public well water supplies in Iowa (Kelley 1985).

Groundwater samples taken from 178 hazardous waste disposal sites were found to contain l,l-dichloroethane at 18% frequency (Plumb 1987), with an average concentration of 0.31 ppm and a maximum of 56.1 ppm (Yang and Rauckman 1987). Using the STORET database, Staples et al. (1985) reported median concentrations of less than 0.1 ppb in 8,716 samples of ambient water (3% detectable values), less than 1.0 ppb in 1,375 effluent samples (5% detectable values), less than 5.0 ppb in 354 sediment samples (0.6% detectable values), and less than 0.05 ppb in 94 biota samples (no detectable values). Also using the STORET database, Perwak et al. (1982) reported that l,l-dichloroethane was not found in the sediment of the lower Mississippi or the western Gulf of Mexico; however, a maximum concentration of 5 ppb was detected in sediment samples from the Pacific Northwest.

5.4.3 Soil

No information was found on the ambient concentrations of l,l-dichloroethane in soil, or on the current disposal of waste products containing the compound in landfills. The compound has more commonly been detected in ambient air and groundwater samples taken at hazardous waste sites, and it is expected that the lack of available soil monitoring data is at least in part due to rapid partitioning of l,l-dichloroethane released to soils to these other media.

5.4.4 Other Media

Little information was found on the levels of l,l-dichloroethane in other media. Ferrario et al. (1985) measured 33 ppb wet weight of l,l-dichloroethane in oysters from Lake Pontchartrain near New Orleans, Louisiana, however, l,l-dichloroethane was not detected in 2 types of clams. Kallonen et al. (1985) detected l,l-dichloroethane in the effluent gases of burning polyester fiber fill. Data on concentrations in human breath are presented in Section 5.5.

5.5 GENERAL POPULATION AND OCCUPATIONAL EXPOSURE

The greatest source of exposure to l,l-dichloroethane for most of the U.S. population is inhalation of the compound in contaminated air. Another potential route of human exposure is ingestion of the compound in contaminated drinking water. There have been no reports of adverse effects associated with occupational inhalation of l,l-dichloroethane in humans, and amounts dermally absorbed are reported to be insufficient to cause systemic injury (ACGIH 1971). Industrial exposures can result from the use of l,l-dichloroethane as a chemical intermediate, solvent, and a component of fumigant formulations (ACGIH 1971).

The National Occupational Hazard Survey (NOHS), conducted by NIOSH from 1972 to 1974, estimated that 715 workers in 143 plants were potentially exposed to l,l-dichloroethane in the workplace in 1970 (NIOSH 1976). These estimates were derived from observations of the actual use of l,l-dichloroethane (90% of total estimate) and the use of trade name products known to contain l,l-dichloroethane (10%). The exposed workers were in the rubber and plastic, chemical and allied products, electrical equipment and supply, medical and other health services, miscellaneous business services, and oil and gas extraction industries. The occupational groups with exposed workers we're assemblers, agricultural and biological technicians, chemists, electrical and electronic engineering technicians, therapists, geologists, and machine operators.

Preliminary data from a second workplace survey, the National Occupational Exposure Survey (NOES), conducted by NIOSH from 1980 to 1983, indicated that 1,957 workers, including 272 women, were potentially exposed to l,l-dichloroethane in the workplace in 1980 (NIOSH 1984). The exposed workers were employed in the chemical and allied products and business service industries, as chemical technicians; plumbers, pipefitters, and steamfitters; supervisors in production occupations; electricians; machinists; chemical engineers; and welders and cutters. The estimates were based on direct observation by the surveyor of the actual use of the compound (100%).

Neither the NOHS nor the NOES databases contain information on the frequency, level, or duration of exposure of workers to any of the chemicals listed therein. They provide only estimates of workers potentially exposed to the chemicals.

NIOSH (1978) noted that there was a large potential for exposure to l,l-dichloroethane in the workplace during its use as a dewaxer of mineral oils, extractant for heat-sensitive substances, or fumigant, and in the manufacture of vinyl chloride and high-vacuum rubber and silicon grease.

Zweidinger et al. (1982) and Wallace et al. (1982) conducted a study of the levels of l,l-dichloroethane in the inhaled and exhaled air and drinking water of college students in Texas and North Carolina. Low levels (<0.49 ppb)

of l,l-dichloroethane were found in the personal air quality monitors of the Texas students, whose campus bounded a petrochemical manufacturing area, but none was detected in the exhaled breath samples. l,l-Dichloroethane was not detected in the breathing zone air of the North Carolina students.

Barkley et al. (1980) found a trace of l,l-dichloroethane in the expired breath of one resident whose home bordered the old Love Canal, but none was detected in ambient air. Wallace et al. (1984) found a trace of l,l-dichloroethane in the expired breath and drinking water of one resident of New Jersey).

Assuming a median ambient air level of 55 ppt reported by Brodzinsky and Singh (1983) and a theoretical average inhalation of 20 m^3 of air per day, the average inhalation exposure to l,l-dichloroethane for an individual in the United States is estimated at 4 μg/day (EPA 1985).

5.6 POPULATIONS WITH POTENTIALLY HIGH EXPOSURES

Human exposure to l,l-dichloroethane is expected to be highest among certain occupational groups (e.g., chemical and allied products industry workers) and members of the general population living in the vicinity of industrial point emission sources (EPA 1985) and hazardous waste sites. The compound has been detected in both ambient air and water in low concentrations, with substantially higher concentrations in localized areas around industrial and disposal sites. No information was found regarding the number of people potentially exposed around hazardous waste sites.

5.7 ADEQUACY OF THE DATABASE

Section 104(i) of CERCLA 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 l,l-dichloroethane is available. Where adequate information is not available, ATSDR, in conjunction with 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 l,l-dichloroethane.

The following categories of data needs have been identified by a joint team of scientists from ATSDR, NTP, and EPA. They are defined as substancespecific informational needs that, if known, would reduce or eliminate the uncertainties of human health assessment. Each data need discussion highlights the availability, or absence, of the relevant exposure information. A statement that reflects the importance of identified data needs is also included. In the future, these 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/chemical properties of l,l-dichloroethane are sufficiently well characterized to enable assessment of the environmental fate of this compound.

Production, Use, Release, and Disposal. Based on its industrial use, l,l-dichloroethane is primarily released to the atmosphere, and humans are potentially exposed to this chemical through the inhalation or ingestion of contaminated air or water. However, because the data available on production, import, export, use, and disposal are limited, it is difficult to estimate whether or not the potential for human exposure to l,l-dichloroethane may be substantial. Data concerning the production and use of l,l-dichloroethane both within the United States and worldwide are extremely limited. Information regarding possible disposal methods, criteria, and regulations are available; however, the present criteria may undergo revision in the near future. Information on current production levels, quantities imported and exported, proportions allocated to various uses, and proportions and efficiencies associated with differing modes of disposal is not available. This information would be useful in identifying potential sources and levels of exposure, thus enabling identification of exposed populations.

Environmental Fate. Releases from industrial processes are almost exclusively to the atmosphere, and releases of the compound to surface waters and soils are expected to partition rapidly to the atmosphere through volatilization. l,l-Dichloroethane released to the atmosphere may be transported long distances before being washed out in precipitation. Although l,l-dichloroethane released to land surfaces in spills would rapidly volatilize to the atmosphere, the l,l-dichloroethane remaining on soil surfaces would be available for transport into groundwater. The atmospheric residence time of l,l-dichloroethane is about 44 days. The dominant removal mechanism is reaction with hydroxyl free radicals. Hydrolysis and biodegradation do not appear to be important processes in the environmental fate of this compound. Data are lacking on the partitioning of l,l-dichloroethane from the water column onto sediments. Additional information on the atmospheric transformation and on the rate of biodegradation of l,l-dichloroethane in soils would be useful in the determination of its environmental fate.

Bioavailability from Environmental Media. Data are incomplete on the bioavailability of l,l-dichloroethane from environmental media. Animal data on l,l-dichloroethane exposure via inhalation and oral administration in drinking water suggest that the compound is bioavailable following inhalation of ambient air and ingestion of drinking water. Additional information on the bioavailability of l,l-dichloroethane from air, water, soil, and sediment would be useful in determining actual risks associated with exposure to environmental levels of l,l-dichloroethane.

Food Chain Bioaccumulation. The information located on the potential for bioconcentration of l,l-dichloroethane in plants, aquatic organisms, or animals is limited. An analysis of animal tissues from several species of aquatic organisms near the discharge of a wastewater treatment plant did not detect l,l-dichloroethane in the animal tissues, although the compound was found in the effluent. However, l,l-dichloroethane has been detected in oysters (33 ppb wet weight). An estimated bioconcentration potential of less than 1 from the K_{OW} suggests that bioconcentration would not be expected. Very little information was found regarding the biomagnification of l,l-dichloroethane among food chain trophic levels. Additional information on bioconcentration and biomagnification would be useful in determining if food chain bioaccumulation is an important source of,human exposure.

Exposure Levels in Environmental Media. Limited information is available regarding ambient concentrations of l,l-dichloroethane in soils. Based on a median ambient air level reported in 1982, the average inhalation exposure to l,l-dichloroethane for an individual in the United States has been estimated to be 4 μg/day. The information on foodstuffs is limited to the detection of l,l-dichloroethane in oysters (33 ppb wet weight). Additional site-specific concentration data for ambient air, drinking water, soil, and biota would be helpful in estimating potential exposure of the general population as well as populations in the vicinity of hazardous waste sites.

Exposure Levels in Humans. Although relatively recent estimates of the size of the population occupationally exposed to l,l-dichloroethane are available from NIOSH, monitoring data on workplace exposures are generally limited, with a few observations about l,l-dichloroethane included in detailed studies of 1,2-dichloroethane. A study of the levels of l,l-dichloroethane in the inhaled and exhaled air and drinking water of college students in Texas and North Carolina found low levels (<0.49 ppb) of l,l-dichloroethane in the personal air quality monitors of the Texas students, whose campus bounded a petrochemical manufacturing area, but none in samples of their exhaled breath. Additional information on the availability of biomarkers that could be used to indicate human exposure to l,l-dichloroethane would be helpful.

Exposure Registries. No exposure registries for l,l-dichloroethane were located. This compound is not currently one of the compounds for which a subregistry has been established in the National Exposure Registry. The compound 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 the exposure to this compound.

5.7.2 On-going Studies

Long-term research studies on the environmental fate of l,l-dichloroethane have not been identified. The data generated as a result of the remedial investigation/feasibility studies of the 189 sites on the National Priority List (NPL) known to be contaminated with l,l-dichloroethane should add to the current knowledge regarding the environmental transport and fate of the compound.

As part of the Third National Health and Nutrition Evaluation Survey (NHANES III), the Environmental Health Laboratory Sciences Division of the Center for Environmental Health and Injury Control, Centers for Disease Control, will be analyzing human blood samples for l,l-dichloroethane 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.

6. ANALYTICAL METHODS

The purpose of this chapter is to describe the analytical methods that are available for detecting and/or measuring and monitoring l,l-dichloroethane in environmental media and in biological samples. The intent is not to provide an exhaustive list of analytical methods that could be used to detect and quantify l,l-dichloroethane. Rather, the intention is to identify wellestablished methods that are used as the standard methods of analysis by various Federal agencies. Many of the analytical methods used to detect l,l-dichloroethane in environmental samples are methods approved by federal agencies such as EPA and NIOSH. Other methods presented in this chapter are those that are approved by trade associations such as the Association of Official Analytical Chemists (AOAC) and the American Public Health Association (APHA). A third category of analytical methods emphasizes research and development activities, where efforts are underway to refine previously used methods, to obtain lower detection limits, and to increase accuracy and precision.

The analytical methods used to quantify l,l-dichloroethane in biological and environmental samples are summarized below. Table 6-l lists the applicable analytical methods used for determining l,l-dichloroethane in biological fluids and tissues, and Table 6-2 lists the methods used for determining l,l-dichloroethane in environmental samples.

6.1 BIOLOGICAL MATERIALS

The determination of trace levels of l,l-dichloroethane in biological tissues and fluids has been restricted to gas chromatography (GC) equipped with mass spectrometry (MS) or flame ionization detection (FID).

Recent work conducted by Cramer and co-workers (1988) showed that l,l-dichloroethane can be detected at nanogram per liter (ppt) levels in whole human blood using a dynamic headspace analyzer and GC/MS technique. A disadvantage of the GC/MS technique is that only limited mass scanning can be employed to obtain better sensitivity of target volatile organic compounds at ppt levels. This is because of the inherent differences in sensitivity between the full-scan MS and the limited mass scanning MS techniques (Cramer et al. 1988).

Hara et al. (1980) employed GC/MS for the analysis of trace amounts of mixed halogenated compounds in the blood and tissue of humans. Identification and quantitative analysis of various compounds was achieved by monitoring the mass fragments for selectively molecular, abundant or characteristic ions for each compound. Thus, the monitoring ion (m/z) for quantification of l,l-dichloroethane was set at 83 [$(M)^{+}$-CH_3]. A lower detection limit of 20 to 20 pg per sample was achieved.

TABLE 6-1. Analytical Methods for Determining 1,1-Dichloroethane in Biological Materials

Sample Matrix	Sample Preparation	Analytical Method	Sample Detection Limit	Accuracy	Reference
Blood and tissue specimen	Warm sample and inject vapor phase into GC column	GC/MS	0.01-0.02 ng/sample	<6% relative standard deviation	Hara et al. 1980
Blood	Vaporize blood sample in a headspace vial and inject into GC column	GC/FID	ng range	No data	Uehori et al. 1987
Whole blood	Purge-and-trap on Tenax adsorbent	GC/MS	100 ng/L	76-110% recovery	Cramer et al. 1988
Blood and urine	Heat biological sample; purge-and-trap volatile compounds on Tenax GC adsorbent	GC/MS	No data	No data	Barkley et al. 1980
Breath	Collect human breath sample by means of a spirometer and analyze	GC/MS	Not detected	No data	Barkley et al. 1980

GC/MS = gas chromatography/mass spectrometry; GC/FID = gas chromatography/flame ionization detector.

TABLE 6-2. Analytical Methods for Determining 1,1-Dichloroethane in Environmental Samples

Sample Matrix	Sample Preparation	Analytical Method	Sample Detection Limit	Accuracy	Reference
Groundwater	Purge-and-trap on absorbent	GC/MS	<1 μg/L	~ 90% recovery	Krasner et al. 1981
	Purge-and-trap on absorbent	GC/MS	0.0001-0.02 μg/sample	<±5% RSD	Lopez-Avila et al. 1987a
	Purge-and-trap on absorbent	GC/PID-FID	No data	No data	Driscoll et al. 1987
Groundwater and soil	Purge-and-trap on adsorbent	GC/EICD-PID	water = 0.1 to 0.9 μg/L; soil = 1 to 5 μg/L	83 to 102% recovery	Lopez-avila et al. 1987b
Drinking Water	Heat water sample; purge-and-trap volatile compounds on Tenax GC absorbent	GC/MS	Not detected	No data	Barkley et al. 1980
	Pass sample through XAD-2 macroreticular resin and extract continuously with ether	GC/MS	<1 μg/L	No data	Suffet et al. 1986
	Purge-and-trap water sample	GC/MS	0.2 μg/L	94% recovery	Otson and Chan 1987
	Extract sample in hexane and analyze	GC/EICD	<1 μg/L	No data	Otson and Chan 1987
	Purge-and-trap on Tenax absorbent	GC/EICD-FID	<1 μg/L	>75% recovery	Otson and Williams 1982
	Purge-and-trap water sample	GC/EICD	80 μg/L	84% recovery	Comba and Kaiser 1983
	Purge-and-trap water sample	GC/EICD-PID	0.1 to 0.5 μg/L	No data	Kingsley et al. 1983
Wastewater	Collect water sample through a permeation cell membrane and direct into G.C.	GC/FID	μg/L (ppb) range	<6% RSD	Blanchard and Hardy 1986
	Collect sample through a permeation cell membrane; adsorb onto charcoal; extract with carbon disulfide	GC/FID	74 to 16800 μg/L	No data	Blanchard and Hardy 1985
Wastewater and sludge	Purge-and-trap on adsorbent	GC/MS	No data	No data	Giabbaie et al. 1983

TABLE 6-2 (Continued)

Sample Matrix	Sample Preparation	Analytical Method	Sample Detection Limit	Accuracy	Reference
Air (ambient)	Purge-and-trap on charcoal absorbent; extract with carbon disulfide	GC/ECD	0.001 ppm range	No data	Bruner et al. 1978
	Collect air sample on Tenax adsorbent; vaporize thermally and analyze	GC/MS	23 $\mu g/m^3$	No data	Pellizari 1982
	Collect air particulates on a glass fiber filter and Tenax GC adsorbent; extract with MeOH pentane	GC/MS	Not detected	No data	Barkley et al. 1980
	Adsorb air sample onto charcoal tube; extract with carbon disulfide	GC/FID	ppm range	No data	NIOSH 1987 (method 1003)
Air (Space cabin)	Dehydrohalogenate air sample with lithium hydroxide and analyze by GC/MS	GC/MS	0.5 to 4.0 ppm	No data	Spain et al. 1985
Air (high humidity atmosphere)	Collect vapor sample in a Tedlar gas bag	Portable Organic Vapor Analyzer with PID	25 ppm	0.998 correlation coefficient	Barsky et al. 1985
Garbage dump	Collect sample on headspace cold trap system	GC/MS and GC/ECD	0.12 μg/ sample	No data	Hoefler et al. 1986
Various food (e.g., diary products, meat, vegetables and soda)	Food containing <70% fat: add sample to acetone: isooctane (10:1) and 1% phosphoric acid, shake and add MeOH; clean-up on florisil column Food containing >70% fat: dissolve sample in isooctane and shake; clean-up on florisil column	GC/ECD-EICD	ng/g range	~70% recovery	Daft 1988
Compound formulation	Prepare dilute solution of sample in MeoH; introduce into headspace trap	GC/PID	20 pg	No data	Jerpe and Davis 1987

TABLE 6-2 (Continued)

Sample Matrix	Sample Preparation	Analytical Method	Sample Detection Limit	Accuracy	Reference
Fish tissue	Add water to fish sample; homogenize and extract ultrasonically; purge-and-trap on adsorbent	GC/MS	0.01 μg/g	77% recovery	Easley et al. 1981
	Freeze fish sample; homogenize in liquid nitrogen; distil in vacuum	GC/MS equipped with fused-silica capillary column	No data	No data	Hiatt 1983
	Warm sample,purge-and-trap volatiles on activated carbon adsorbent; extract with carbon disulfide	GC/FID	No data	~32% recovery	Reinert et al. 1983
Whole fish	Freeze fish sample and homogenize; add MeOH and extract ultrasonically; purge-and-trap on adsorbent	GC/MS equipped with fused silica capillary column	$7.5x10^{-4}$ μg/g	6.2% RSD	Dreisch and Munson 1983
Fish and sediment	Add water containing acrolein and acrylonitrile to sample; freeze sample, extract in vacuum	GC/MS	0.025 μg/g	Sediment matrix 101% recovery. Fish matrix 90% recovery	Hiatt 1981

GC = gas chromatography; GC/MS = gas chromatography/mass spectrometry; GC/EICD = gas chromatography/electrolytic conductivity detector; GC/PID = gas chromatography/photoionization detector; GC/ECD = gas chromatography/electron captive detector; GC/FID = gas chromatography/flame ionization detector; RSD = relative standard deviation; ppb = part per billion; ppt = parts per trillion.

Uehori and co-workers (1987) developed a retention index in GC to screen and quantify volatile organic compounds in blood. A dynamic headspace analyzer and GC/FID with retention indices were employed for the detection of l,l-dichloroethane at nanogram levels. Uehori and co-workers noted that this method is simple, reliable and requires little or no sample preparation.

Gas purging-and-trapping on a Tenax GC adsorbent and GC/MS technique has been employed by Barkley et al. (1980) for the determination of trace levels of volatile halogenated compounds (including l,l-dichloroethane) in water, human blood, and urine.

6.2 ENVIRONMENTAL SAMPLES

A GC equipped with an appropriate detector is the most frequently used analytical technique for determining the concentrations of l,l-dichloroethane in air, water, soil, fish, diary products, and various foods. Volatile organic compounds in environmental samples may exist as complex mixtures or at very low concentrations (ppt to ppb range). Subsequently, the GC technique must be supplemented by some method of sample preconcentration.

Gas purging-and-trapping is the generally accepted method for the isolation, concentration, and determination of volatile organic compounds in water and various environmental samples (Bellar et al. 1977; EPA 198613, 1987; Krasner et al. 1981; Lopez-Avila et al. 1987a, 1987b; Reding 1987; Wylie 1987, 1988). This method appears to be most adaptable for use with almost any GC detector -- MS, FID, electron capture detector (ECD), and electrolytic conductivity detector (EICD). In addition, the method offers an important preliminary separation of highly volatile compounds from often highly complex samples prior to GC analysis. Detection limits at less than 1 μg of l,l-dichloroethane per liter of sample have been achieved by this method (Dreisch and Munson 1983; Kingsley et al. 1983; Krasner et al. 1981; Lopez- Avila et al. 1987a, 1987b; Otson and Williams 1982). Bruner et al. (1978) employed purge-and-trap technique on charcoal adsorbent and GC/ECD for determination at ppt levels of volatile halo organic compounds in air. A major problem is that some of the halocarbons in the atmosphere are present as ultra-trace impurities in highly pure commercial inert gases. Subsequently, these impurities may interfere with the quantitative and qualitative analysis of l,l-dichloroethane in environmental samples.

Recently, Badings et al. (1985) and Pankow and Rosen (1988) employed the purge-and-trap technique with cryogenic trapping (cryofocusing) of volatile organic compounds in water samples as an effective concentration method prior to capillary GC analysis. The purge-and-trap technique offers advantages over other techniques in that it allows easy isolation and concentration of target compounds, which reduces interference, thereby improving overall limits of detection and recovery of sample (Otson and Chan 1987). Among the other advantages of the purge-and-trap technique with cryofocusing are its

simplicity and therefore its reliability; the low background contamination since no sorbent traps are needed; and the relatively short time of sample analysis (Pankow and Rosen 1988).

Dynamic headspace analyzer GC has been used for the analysis and identification of l,l-dichloroethane in water and fish tissue (Comba and Kaiser 1983; Mehran et al. 1985, 1986; Otson and Williams 1982; Reinert et al. 1983; Trussell et al. 1983). The analytic sample is placed in a sealed flask connected to the headspace analyzer, which is directly interfaced with the injection port of the GC system. This arrangement allows for a greater proportion of compound contained in a sample to be analyzed. This method is simple and does not require any sample preparation (Mehran et al. 1985). Detection limits of less than 1 μg l,l-dichloroethane/L water and less than 1 μg l,l-dichloroethane/g fish tissue were achieved (Mehran et al. 1986; Otson and Williams 1982; Reinert et al. 1983; Trussel et al. 1983). A disadvantage of this technique is that the inherent volatility of the halo organic compounds gives rise to an excessive foaming in the headspace system, thereby forming low yields and causing interference with the GC quantification. The typical yield of l,l-dichloroethane was approximately 32% (Reinart et al. 1983). The authors indicated that use of an antifoaming agent such as silicone surfaces greatly reduced the foam, but extraneous chromatographic comp.Fnents and peak masking problems were encountered.

Pellizzari (1982) initiated the development and evaluation of trace levels of volatile organic compounds in industrial and chemical waste disposal sites. Ambient air samples were collected by a sampler equipped with Tenax GC adsorbent cartridges. Compounds were thermally removed from the adsorbent and analyzed by capillary GC/MS. The detection limit was at the $\mu g/m^3$ level (Pellizzari 1982).

Blanchard and Hardy (1985, 1986) developed a method that allows for continuous monitoring or intermittent analysis of volatile organic priority pollutants in environmental media. The method is based on permeation of volatile organic compounds through a silicone polycarbonate membrane from wastewater sample matrix, into an inert gas stream and directed into a capillary GC/FID via a sampling loop (Blanchard and Hardy 1986). Advantages of this procedure are that it is simple, it does not require time-consuming preconcentration steps, and it can be used either in the field or in the laboratory.

The liquid-liquid extraction procedure provides a simple, rapid, screening method for semiquantitative determination of l,l-dichloroethane in aqueous samples containing limited number of volatile organic compounds. It is less effective for aqueous samples containing large numbers of volatile organic compounds, Furthermore, interference from the organic (hexane) extraction solvent makes it more difficult to identify completely all compounds (Otson and Williams 1981). GC/EICD was employed by Otson and

Williams (1981) for the detection of trace amounts (less than 1 μg/L of sample) of l,l-dichloroethane in drinking water.

Daft (1988) employed a photoionization detector and an electrolytic conductivity detector connected in series to a capillary GC to detect l,l-dichloroethane at rig/g levels in fumigants and industrial chemical residues of various foods (e.g., diary products, meat, vegetables, and soda). Typically, foods were extracted with isooctane and injected in GC column for analysis. However, foods containing lipid and fat were subjected to further clean-up on micro-florisil column prior to GC analysis.

A procedure was developed by Hiatt (1983) and Dreisch and Munson (1983) to identify and quantify 1,1-dichloroethane in fish tissue samples by GC/MS, employing a fused-silica capillary column (FSCC) and vacuum distillation (extraction). An advantage of the vacuum extraction is that the system does not require elevated temperatures or the addition of reagents, which could produce unwanted degradation products (Hiatt 1981). The FSCC provides a more attractive approach than packed column for chromatographic analysis of volatile organic compounds, because FSCC can be heated to a higher-temperature (350°C) than that recommended for packed column thereby improving the resolution (at the ng/g level) of compounds at a lesser retention time. A physical limitation for compounds that can be detected, however, is that the vapor pressure of the compounds must be greater than 0.78 torr (approximately 50°C) in the sample chamber (Hiatt 1983).

6.3 ADEQUACY OF THE DATABASE

Section 104(i) of CERCLA 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 l,l-dichloroethane is available. Where adequate information is not available, ATSDR, in conjunction with 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 l,l-dichloroethane.

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 or eliminate the uncertainties of human health assessment. 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. Reliable methods are available for detecting and quantifying l,l-dichloroethane in the

tissues and body fluids of humans. GC/MS or GC/FID has been employed to detect l,l-dichloroethane at nanogram to picogram levels in blood and tissue samples of humans. No additional analytical methods for determining trace levels of l,l-dichloroethane in the blood of humans are needed. However, the report by Hara et al. (1980) did not identify what tissues were analyzed to detect l,l-dichloroethane by GC/MS. Also, no detection limits for detecting l,l-dichloroethane in urine samples by GC/MS were indicated by Barkley et al. (1980). Therefore, additional research and development of sensitive and selective methods for detecting and quantifying the levels of l,l-dichloroethane and its metabolites in the tissues and urine of humans would be useful. If methods were available, it would assist investigators in determining whether specific levels of l,l-dichloroethane found in the tissues/fluids of exposed persons correlate with any adverse health effects.

Methods for Determining Parent Compounds and Degradation Products in Environmental Media. Analytical methods are available to detect l,l-dichloroethane in environmental samples. GC/ECD and GC/MS have been used to detect and quantify l,l-dichloroethane in air and water samples at ppt and ppb levels [EPA methods 5030, 8240 (1986); method 601, 624, 1624 (1987)]. GC equipped with FID, PID, or EICD has also been used to detect and quantify l,l-dichloroethane in air, water, milk, vegetables, and fish at parts-per-billion levels NIOSH [method 1003 (1987)]. No additional analytical methods for determining track levels of l,l-dichloroethane in environmental media are needed.

6.3.2 On-going Studies

No on-going studies concerning methods for measuring and determining l,l-dichloroethane in biological and environmental samples were reported.

The Environmental Health Laboratory Sciences Division of the Center for Environmental Health and Injury Control, Centers for Disease Control, is developing methods for the analysis of l,l-dichloroethane and other volatile organic compounds in blood. These methods use purge and trap methodology and magnetic mass spectrometry which gives detection limits in the low parts per trillion range.

7. REGULATIONS AND ADVISORIES

The international, national, and state regulations and advisories pertaining to l,l-dichloroethane in air, water, and food are summarized in Table 7-1.

7. REGULATIONS AND ADVISORIES

TABLE 7-1. Regulations and Guidelines Applicable to 1,1-Dichloroethane

Agency	Description	Value	References
	National		
Regulations:			
a. Air:			
OSHA	PEL TWA	400 mg/m^3	OSHA 1988b (29 CFR 1910.1000)
b. Water:			
EPA	MCL	No data	
c. Other:			
EPA OERR	Reportable quantity	1,000 lb	EPA 1988b (40 CFR 302)
Guidelines:			
a. Air:			
ACGIH	TLV TWA	810 mg/m^3	ACGIH 1986
	STEL	1,010 mg/m^3	
NIOSH	IDLH	4,000 ppm	NIOSH 1985
	State		
a. Air:			
	Acceptable ambient air concentration guidelines and standards		NATICH 1987
Connecticut		8,000 μg/m^3 (8 hr)	
Nevada		19.3 μg/m^3 (8 hr)	
North Dakota		8.1 mg/m^3	
Virginia		13,500 μg/m^3 (24 hr)	
b. Water:			
	Drinking water standards		FSTRAC 1988
New Mexico		25 mg/L	
	Drinking water guidelines		
California		28 μg/L	
Illinois		1 μg/L	
Vermont		70 μg/L	
Wisconsin		850 μg/L	

OSHA = Occupational Safety and Health Administration; PEL = Permissible Exposure Limit; TWA = Time Weighted Average; EPA = Environmental Protection Agency; MCL = Maximum Contaminant Level; OERR = Office of Emergency and Remedial Response; ACGIH = American Conference of Governmental Industrial Hygienists; TLV = Threshold Limit Value; STEL = Short Term Exposure Limit; NIOSH = National Institute for Occupational Safety and Health; IDLH = Immediately Dangerous to Life or Health.

8. REFERENCES

*ACGIH. 1971. American Industrial Hygiene Association, Hygienic Guide Series. Am Ind Hyg Assoc J 32:67-71. (Retrieval in progress).

ACGIH. 1971. Documentation of the threshold limit values for substances in workroom air. 3rd ed. American Conference of Governmental Industrial Hygienists,Cincinnati, OH, 79.

*ACGIH. 1986. Documentation of the threshold limit values and biological exposure indices. 5th ed. American Conference of Governmental Industrial Hygienists, Inc., Cincinnati, OH, 184.

Aldis H, Osborn J, Wolf F. 1983. Investigation of soil and water contamination at Western Processing, King County, Washington. National Conference on Management of Uncontrolled Hazardous Waste Sites:43-53.

Anonymous. 1978. [Reagent hazards]. A&R 16:458-463. (Japanese).

Anonymous. 1981. The central plant of the St. Louis County Water Company. Aqua 4:20-24.

*Badings HT, de Jong C, Dooper RPM. 1985. Automatic system for rapid analysis of volatile compounds by purge-and- cold-trapping/capillary gas chromatography. Journal of High Resolution Chromatography and Chromatography Communications 8:755-763.

Baird R, Gute J, Jacks C, et al. 1980. Health effects of water reuse: A combination of toxicological and chemical methods for assessment. Water Chlorination: Environmental Impact and Health Effects 3:925-935.

Barbari TA, King CJ. 1982. Equilibrium distribution coefficients for extraction of chlorinated hydrocarbons and aromatics from water into undecane. Environ Sci Technol 16:624-627.

*Barkley J, Bunch J, Bursey JT, et al. 1980. Gas chromatography mass spectrometry computer analysis of volatile halogenated hydrocarbons in man and his environment - a multimedia environmental study. Biomed Mass Spectrom 7:139-147.

Barlow SM, Sullivan FM. 1982. Reproductive hazards of industrial chemicals. An evaluation of animal and human data. London, England: Academic Press Ltd., 273.

*Cited in text

8. REFERENCES

*Barnes D, Bellin J, DeRosa C, et al. 1987. Reference dose (RfD): Description and use in health risk assessments. Volume 1, Appendix A: Integrated risk information system supportive documentation. Cincinnati, OH: US Environmental Protection Agency, Office of Health and Environmental Assessment. EPA 600/a-86/0322.

*Barsky JB, Hee SSQ, Clark CS. 1985. An evaluation of the response of some portable, direct-reading 10.2 electron volt and 11.8 electron volt photoionization detectors and a flame ionization gas chromatograph for organic vapors in high humidity atmospheres. Am Ind Hyg Assoc J 46:9-14.

Bayer CW, Black MS, Galloway LM. 1988. Sampling and analysis techniques for trace volatile organic emissions from consumer products. J Chromatogr Sci 26:168-173.

*Bellar TA, Budde WL, Eichelberger JW. 1979. The identification and measurement of volatile organic compounds in aqueous environmental samples. IN: Schuetzle D, ed. Monitoring toxic substances. American Chemical Society Symposium Series No. 94. Washington, DC: American Chemical Society, 49-62. ISBM o-8412-0480-2.

*Blanchard RD, Hardy JK. 1985. Use of a permeation sampler in the collection of 23 volatile organic priority pollutants. Anal Chem 57:2349-2351.

*Blanchard RD, Hardy JK. 1986. Continuous monitoring device for the collection of 23 volatile organic priority pollutants. Anal Chem 58:1529-1532.

Brass HJ. 1982. Procedures for analyzing organic contaminants in drinking water. Am Water Works Assoc J 74:107-112.

*Brodzinsky R, Singh HB. 1983. Volatile organic chemicals in the atmosphere: An assessment of available data. Menlo Park, CA: Atmospheric Science Center. SRI International. Report to U.S. Environmental Protection Agency, Environmental Sciences Research Laboratory, Research Triangle Park, N.C. by SRI International, Atmospheric Sciences Center, Menlo Park, CA.

*Bronzetti G, Galli A, Vellosi R, et al. 1987. Genetic activity of chlorinated ethanes [Abstract]. Eur J Cancer Clin Oncol 23:1737-1738.

Brown JR. 1970. The effect of environmental and dietary stress on the concentration of l,l-bis(4-chlorophenyl)-2,2,2-trichloroethane in rats. Toxic Appl Pharmacol 17:504-510.

*Browning E. 1965. Toxicity and metabolism of industrial solvents. New York, NY: Elsevier Science Publishing Co., Inc., 247-252.

8. REFERENCES

*Bruckner JV. 1989. Written communication (June 2). Peer review comments on the Toxicological Profile for l,l-Dichloroethane.

*Bruner F, Bertoni G, Crescentini G. 1978. Critical evaluation of sampling and gas chromatographic analysis of halocarbons and other organic air pollutants. J Chromatogr 167:399-407.

Callahan MA, Ehreth DJ, Levins PL. 1979. Sources of toxic pollutants found in influent to sewage treatment plants. Proceedings of the National Conference on Municipal Sludge Management 8:55-61.

CASR. 1989. Chemical Activity Status Report. US Environmental Protection Agency, Chemical Information System (CIS), Baltimore, MD. December 9, 1988.

Castello G, Gerbino TC, Kanitz S. 1982. Gas chromatographic analysis of halocarbons in drinking water by headspace extraction and mixed column separation. J Chromatogr 247:263-272.

Castello G, Gerbino TC, Kanitz S. 1986. Sensitivity and linearity of headspace and liquid-liquid extraction techniques for gas chromatographic analysis of halocarbons in water. J Chromatogr 351:165-175.

Chang LW, Pereira MA, Klaunig JE. 1985. Cytotoxicity of halogenated alkanes in primary cultures of rat hepatocytes from normal, partially hepatectomized, and preneoplastic/neoplastic liver. Toxic01 Appl Pharmacol 80:274-283.

CHEMFATE. 1988. CHEMFATE Database. Syracuse Research Corporation, Syracuse, NY. December 9, 1988.

CHEMLINE. 1988. National Library of Medicine, National Toxicology Information Program, Bethesda, MD. December 9, 1988.

CHRIS. 1984. l,l-Dichloroethane. Hazard assessment handbook. Vol. 1, Washington, DC: US Coast Guard, Department of Transport.

Clement Associates I. 1985. l,l-Dichloroethane. In: Chemical, physical and biological properties of compounds present at hazardous waste sites Report to US Environmental Protection Agency, Office Response.

*Cline PV, Viste DR. 1985. Migration and degradation patterns of volatile organic compounds. Waste Management and Research 3:351-360.

*CLP. 1989. Contract laboratory program statistical database. US Environmental Protection Agency, August 17, 1988

*Colacci A, Arfellini G, Mazzullo M, et al. 1985. Genotoxicity of l,l-dichloroethane. Research Communications in Chemical Pathology and Pharmacology 49:243-254.

8. REFERENCES

*Cole RH, Frederick RE, Healy RP, et al. 1984. Preliminary findings of the priority pollutant monitoring project of the Nationwide Urban Runoff Program. J Water Pollut Control Fed 56:898-908.

*Comba ME, Kaiser KLE. 1983. Determination of volatile contaminants at the ng.l-1 level in water by capillary gas chromatography with electron capture detection. Int J Environ Anal Chem 16:17-31.

*Coniglio WA, Miller K, MacKeever D. 1980. The occurrence of volatile organics in drinking water. Briefing for the Deputy Assistant Administrator for Drinking water, March 1980. (Retrieval in progress).

Conkle JP, Camp BJ, Welch BE. 1975. Trace composition of human respiratory gas. Arch Env Health 30:290-295.

*Contract Laboratory Program Statistical Database. 1988. US Environmental Protection Agency, Contract Laboratory Program, Washington, DC.

*Cramer PH, Boggess K, Hosenfeld JM, et al. 1988. Determination of organic chemicals in human whole blood: Preliminary method development for volatile organics. Bull Environ Contam Toxic01 40:612-618.

*Daft JL. 1988. Rapid determination of fumigant and industrial chemical residues in food. J Assoc Off Anal Chem 71:748-760.

Dallenback-Toelke K, Nyiredy S, Meier B, et al. 1986. Optimization of overpressured layer chromatography of polar, naturally occurring compounds by the "PRISMA" model. J Chromatogr 365:63-72.

Deneer JW, Sinnige TL, Seinen W, et al. 1988. The joint acute toxicity to Daphnia magna of industrial organic chemicals. Aquatic Toxicology 12:33-38;

Dever RJ. 1986 Responding to industrial contamination of groundwater. A case study. J Am Water Works Assoc 78:82-86.

de Zeeuw J, de Nijs RCM, Henrick LT. 1987. Adsorption chromatography on PLOT (porous-layer open-tubular) columns: A new look at the future of capillary GC. J Chromatogr Sci 25:71-83.

*Dilling WL. 1977. Interphase transfer processes. II. Evaporation rates of chloromethanes, ethanes, ethylenes, propanes, and propylenes from dilute aqueous solutions. Comparisons with theoretical predictions. Environ Sci Technol 11:405-409.

*Dilling WL, Tefertiller NB, Kallos GJ. 1975. Evaporation rates and reactivities of methylene chloride, chloroform, l,l,l-trichloroethane, trichloroethylene, tetrachloroethylene, and other chlorinated compounds in dilute aqueous solutions. Environ Sci Technol 9:833-837.

8. REFERENCES

*DiVincenzo GD, Krasavage WJ. 1974. Serum ornithine carbamyl transferase as a liver response test for exposure. Am Ind Hyg Assoc J 35:21-29.

*Dreisch FA, Munson TO. 1983. Purge-and-trap analysis using fused silica capillary column gas chromatography-mass spectrometry. J Chromatogr Sci 21:111-118.

*Driscoll JN, Duffy M, Pappas S, et al. 1987. Analysis for purgeable organics in water by capillary GC/PID-EICD. J Chromatogr Sci 25:369-375.

Easley DM, Kleopfer RD, Carasea AM. 1981. Gas chromatographic-mass spectrometric determination of volatile organic compounds in fish. J Assoc Off Anal Chem 64:653-656.

Elskamp DMW. 1981. Toxicology of 1,1-dichloroethane. NTIS no PB82-182809.

*EPA 1980. Ambient water quality criteria for chlorinated ethanes. Washington, DC: US Environmental Protection Agency, Office of Water Regulations and Standards, Criteria and Standards Division. EPA 440/5-80-029.

EPA. 1980 . Water sample analysis-vinyl acetate spill pump-out well with attached it enviroscience analytical report HK-239. Environmental Protection Agency, Washington, DC: US Office of Transportation and Safety. EPA/OTS no 88-8000345.

EPA. 1982. Fate and effects of methylene chloride in activated sludge. Washington, DC: US Environmental Protection Agency, Office of Transportation and Safety. EPA/OTS no 87821130.

EPA. 1984. Health effects assessment for 1,1-dichloroethane. Cincinnati, OH: US Environmental Protection Agency, Office of Research and Development. EPA 540/l-86/027.

*EPA. 1985. Health and environmental effects profile for dichloroethane. Cincinnati, OH: US Environmental Assessment. EPA 600/X-85/359.

EPA. 1985. Results of analytical data with attached tables. Washington, DC: US Environmental Protection Agency, Office of Transportation and Safety. FYI-OTS-0185-0375.

EPA. 1985. Comments to reports of groundwater contamination at Pfaudler plant site with attached hydrogeologic report. Washington, DC: US Environmental Protection Agency, Office of Transportation and Safety. FYI-OTS-0485-0375.

*EPA. 1986a. Reference values for risk assessment (final draft). Cincinnati, OH: US Environmental Protection Agency. ECAO-CIN-477.

8. REFERENCES

*EPA. 1986b. Test methods for evaluating solid waste: Physical and chemical methods. Washington, DC: US Environmental Protection Agency, Office of Solid Waste and Emergency Response. EPA SW-846., 8010.1--8010.4; 8240.1--8240.6.

*EPA. 1987. US Environmental Protection Agency. Code of Federal Regulations. 40 CFR 136.

*EPA. 1988. US Environmental Protection Agency. Code of Federal Regulations. 40 CFR 302.

EPA. 1988a. US Environmental Protection Agency. Code of Federal Regulations. 40 CFR 261.

EPA. 1988. US Environmental Protection Agency. Federal Register., 22300-22325.

EPA. 1989. Health effects assessment summary tables. Washington, DC: US Environmental Protection Agency, Office of Solid Waste and Emergency Response. March, 1989.

*EPA. 1989. Interim Methods for Development of Inhalation Reference Doses. US Environmental Protection Agency, Office of Health and Environmental Assessment. Washington, DC. DPA 600/8-88/066F.

Fabbri A, Crescentini G, Mangani F, et al. 1987. Advances in the determination of volatile organic solvents and other organic pollutants by gas chromatography with thermal desorption sampling and injection. Chromatographia 23:856-860.

Fabricant JD, Chalmers JH Jr. 1980. Evidence of the mutagenicity of ethylene dichloride and structurally related compounds. IN: Ames B, Infante P, Reitz R, ed. Ethylene dichloride: A potential health risk. Cold Spring Harbor, NY: Cold Spring Harbor Laboratory, 309-322.

*Ferrario JB, Lawler GC, DeLeon IR, et al. 1985. Volatile organic pollutants in biota and sediments of Lake Pontchatrain. Bull Environ Contam Toxicol 34:246-255.

Fielding M, Gibson TM, James HA, et al. 1981. Organic micropollutants in drinking water. Medminham, England: Water Research Centre. Technical Report 159., 49.

*FSTRAC. 1988. Summary of state and federal drinking water standards and guidelines. Chemical Communication Subcommittee, Federal-State Toxicology and Regulatory Alliance Committee (FSTRAC) data base, Washington, DC, March 1988.

Fusillo TV, Hochreiter JJ Jr, Lord DG. 1985. Distribution of volatile organic compounds in a New Jersey coastal plain aquifer system. Ground Water 23:354-360.

8. REFERENCES

Garman JR, Freund T, Lawless EW. 1987. Testing for groundwater contamination at hazardous waste sites. J Chromatogr Sci 25:328-337.

Gentry SJ, Walsh PT. 1987. Eight-hour TWA personal monitoring using a diffusive sampler and short-term stain tube. Am Ind Hyg Assoc J 48:287-292.

*Giabbai M, Roland L, Chian ESK. 1983. Trace analysis of organic priority pollutants by high-resolution gas chromatography and selective detectors (FID, ECD, NPD, and MS-DS): Application to municipal wastewater and sludge samples. Chromatography in Biochemistry Medicine and Environmental Research 13:41-52.

Gombar VK. 1987. Quantitative structure-activity relationship studies: Acute toxicity of environmental contaminants. QSAR in Environmental Toxicology, Proceedings of the International Workshop 2:125-133.

Gossett JM. 1987. Measurement of Henry's law constant for Cl and C2 chlorinated hydrocarbons. Environ Sci Technol 21:202-206.

*Gossett RW, Brown DA, Young DR. 1983. Predicting the bioaccumulation of organic compounds in marine organisms using octanol/water partition coefficients. Marine Pollution Bulletin 14:387-392.

Gould JP, Ramsey RE, Giabani M, et al. 1983. Formation of volatile haloorganic compounds in the chlorination of municipal landfill leachates. Water Chlorination, Environmental Impact and Health Effects 4:525-539.

*Grayson M. 1978. Kirk-Othmer encyclopedia of chemistry and technology. Vol. 5, 3rd ed. New York, NY: John Wiley and Sons, Inc., 722.

Griesemer R-4, Cueto C Jr. 1980. Toward a classification scheme for degrees of experimental evidence for the carcinogenicity of chemicals for animals. Molecular and cellular aspects of carcinogen screening tests. Vol. 27, Lyon, France: IARC Scientific Publications, 259-281.

Grilli S, Colacci A, Mazzullo M, et al, 1985. Binding of l,l-dichloroethane to macromolecules of rat and mouse organs [Abstract]. Eur J Cancer Clin Oncol 21:1385.

*Grimsrud EP, Rasmussen RA. 1975. Survey and analysis of halocarbons in the atmosphere by gas chromatography- mass spectrometry. Atmos Environ 9:1014-1017.

Gryder-Boutet DE, Kennish JM. 1987. Trace volatile organic analysis of water and wastewater utilizing headspace sampling with capillary column GC/MS. Proceeding -- Water Quality Technology Conference 14:679-688.

*Gupta KC, Ulsamer AG, Gammage R. 1984. Volatile organic compounds in residential air: Levels, sources and toxicity. Proceedings of the 77th Air Pollution Control Association Annual Meeting 1:9.

8. REFERENCES

Hall DW. 1984. Volatile organic contamination in an alluvial aquifer, Southington, Connecticut. Hazardous Wastes Environmental Emergency: Management, Prevention, Cleanup Control. Silver Spring, MD: Hazardous Materials Control Research Institute, 190-197.

*Hallen RT, Pyne JR Jr., Molton PM. 1986. Transformation of chlorinated ethenes and ethanes by anaerobic microorganisms. In: Proceedings of 192nd national meeting: ACS Division of Environmental Chemistry, Vol. 26, 344-346.

Hamilton A, Hardy HL ed. 1974. Industrial Toxicology. 3rd ed. Acton, MA: Publishing Sciences Group, Inc., 284.

*Hara K, Nagata T, Kishimoto E, et al. 1980. Gas chromatographic/mass spectrometric demonstration of chlorinated aliphatic hydrocarbons in biological materials. Nippon Hoigaku Zasshi 34:507-512.

Harkov R, Jenks J, Ruggeri C. 1987. Volatile organic compounds in the ambient air near a large, regional sewage plant in New Jersey. Proceedings of the 80th Air Pollution Control Association Annual Meeting., l-16.

*Hatch GG, Mamay PD, Ayer ML, et al. 1983. Chemical enhancement of viral transformation in Syrian hamster embryo cells. Cancer Research 43:1945-1950.

Hatch G, Anderson T, Elmore E, et al. 1983. Status of enhancement of DNA viral transformation for determination of mutagenic and carcinogenic potential of gaseous and volatile compounds [Abstract]. Environ Mutag 5:422.

Hauser TR, Bromberg SM. 1982. EPA's monitoring program at Love Canal 1980. Environmental Monitoring and Assessment 2:249-271.

*Herren-Freund SL, Pereira MA. 1986. Carcinogenicity of by-products of disinfection in mouse and rat liver. Environ Health Perspect 69:59-65.

Hess AF, Jakob PG, Hurlburt V et al. 1986. Protecting the Fort Lauderdale wellfields from groundwater contamination. Proceedings of the Annual Conference of american Water Works Association:565-571.

*Hiatt MH. 1981. Analysis of fish and sediment for volatile priority pollutants. Anal Chem 53:1541-1543.

*Hiatt MH. 1983. Determination of volatile organic compounds in fish samples by vacuum distillation and fused silica capillary gas chromatography/mass spectrometry. Anal Chem 55:506-516.

*Hoefler F, Schneider J, Moeckel HJ 1986. Analytical investigations on the composition of gaseous effluents from a garbage dump. I. General data, sampling technique, and analysis of low boiling halogenated compounds. Fresnius Z Anal Chem 325:365-368.

8. REFERENCES

*Hofmann HT, Birnstiel H, Jobst P. 1971. [Inhalation toxicity of l,l- and 1,2-dichloroethane]. Arch Toxikol 27:248-265. (German).

Hoerner G, Kuehn W, Leonhardt D. 1982. [Continuous monitoring of water using process chromatography - determination of halogenated hydrocarbons]. Vom Wasser 59:115-128. (German).

*Howard CJ, Evenson KM. 1976. Rate constants for the reactions of OH with ethane and some halogen substituted ethanes at 296 K. J Chem Phys 64:4303-4306.

*HSDB. 1988. Hazardous Substances Databank. National Library of Medicine, National Toxicology Information Program, Bethesda, MD. December 9, 1988.

Ichibashi M. 1979. [The real status of air pollution. 2. Atmospheric organic compounds in Kawasaki]. Kanagawa-ken Taiki Osen Chosa Kenkyu Hokoku 21:131-143. (Japanese).

*Infante PF, Tsongas TA. 1982. Mutagenic and oncogenic effects of chloromethanes. Chloromethanes and halogenated analogues of vinyl chloride. Enyironmental Science Research 25:301-327.

International Technical Information Institute (ITII). Toxic and hazardous industrial chemicals safety manual. Tokyo, Japan: International Technical Information Institute, 164-165.

*IRIS. 1990. Integrated risk information systems. Environmental Protection Agency. Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, Ohio.

Jaeger RJ, Conolly RB, Reynolds ES, et al. 1975. Biochemical toxicology of unsaturated halogenated monomers. Environmental Health Perspectives 11:121-128.

*Jeffers PM, Ward LM, Woytowitch LM, Wolfe NL. 1989. Homogeneous hydrolysis rate constants for selected chlorinated methanes, ethanes, ethenes, and propanes. Environ Sci Technol 23:965-969.

Jensen S, Lange R, Berge G, et al. 1975. On the chemistry of EDC-tar and its biological significance in the sea. Proc R Sot Lond B 1989:333-346.

*Jerpe J, Davis A. 1987. Ambient capillary chromatography of volatile organics with a portable gas chromatograph. J Chromatogr Sci 25:154-157.

Josephson J. 1983. Subsurface organic contaminants. Environ Sci Technol 17:518A-521A.

8. REFERENCES

Jury WA, Winer AM, Spencer WF, et al. 1987. Transport and transformations of organic chemicals in the soil-air-water ecosystem. Reviews of Environmental Contamination and Toxicology 99:119-164.

*Kallonen R, von Wright A, Tikkanen L, et al. 1985. The toxicity of fire effluents from textiles and upholstery materials. Journal of Fire Science 3:145-160.

*Kelley RD. 1985. Synthetic organic compounds sampling survey of public water supplies. Report to US Environmental Protection Agency, Washington, DC, by Iowa Department of Water, Air, and Waste Management, Des Moines, IA. NTIS no PB85-214427., 38.

Khourey CJ, Mohr ET, Gifford G, et al. 1984. Purgeable organic compounds in northeast Ohio groundwater. Trace Substances and Environmental Health 18:397-402.

*Kim HJ, Odend'hal S, Bruckner JV. 1990a. Effect of oral dosing vehicles on the acute hepatotoxicity of carbon tetrachloride in rats. Toxic01 Appl Pharmacol 102:34-49.

*Kim HF, Bruckner JV, Dallas CE, et al. 1990b. Effect of dosing vehicles on the pharmacokinetics of orally administered carbon tetrachloride in rats. Toxic01 Appl Pharmacol 102:5060.

*Kingsley BA, Gin C, Coulson DM, et al. 1983. Gas chromatographic analysis of purgeable halocarbon and aromatic compounds. Water Chlorination: Environmental Impact and Health Effects 4:593-608.

Kinkead ER, Leahy HF. 1987. Evaluation of the acute toxicity of selected groundwater contaminants. Armstrong Aerospace Medical Research Laboratory, Wright-Patterson Air Force Base, OH. AAMRL-TR-87-021.

*Klaunig JE, Ruth RJ, Pereira MA. 1986. Carcinogenicity of chlorinated methane and ethane compounds administered in drinking water to mice. Environmental Health Perspectives 69:89-95.

Koch R. 1982. Molecular connectivity and acute toxicity of environmental pollutants. Chemosphere 11:925-931.

*Konietzko H. 1984. Chlorinated ethanes: Sources, Distribution, Environmental Impact, and Health Effects. Hazard Assessment Chemicals: Current Developments 3:401-448.

*Krasner SW, Hwang CJ, Cohen RS, et al. 1981. Development of a volatile organic analysis technique for the Orange-Los Angeles County reuse study. Chemistry of Water Reuse 2:17-31.

8. REFERENCES

Kretzschmar JG, Peperstraete H, Rymen T. 1976. Air pollution in and around Tessenderlo (the Netherlands). Extern 5:147-178.

*Krill RM, Sonzogni WC. 1986. Chemical monitoring of Wisconsin's groundwater. Journal of the American Water Works Association 78:70-75.

Krost KJ, Pellizzari ED, Walburn SG, et al. 1982. Collection and analysis of hazardous organic emissions. Anal Chem 54:810-817.

Kurosaki H, Ohizumi T, Tominaga Y, et al. 1985. Determination of low boiling organochlorine compounds in groundwater by headspace gas chromatography. Niigata Rikagaku 11127-32.

Lattanzi G, Colacci A, Grilli S, et al. 1988. Binding of hexachloroethane to biological macromolecules from rat and mouse organs. J Toxic01 Environ Health 24:403-411.

Lazarew NW. 1929. [The narcotic effect of the vapors of the chloride derivatives of methane, ethane, and ethylene]. Archiv fuer Experimentelle Pathologie und Pharmakologie 141:19-24. (German).

Leong BKJ, Schwetz BA, Gehring PJ. 1974. carbon tetrachloride, Embryo- and fetotoxicity of inhaled l,l- dichloroethane and methyl ethyl ketone in rats [Abstract]. Toxic01 Appl Pharmacol 29:123.

*Lopez-Avila V, Wood R, Flanagan M, et al. 1987a. Determination of volatile priority pollutants in water by purge and trap and capillary column gas chromatography/mass spectrometry. J Chromatogr Sci 25:286-291.

*Lopez-Avila V, Heath N, Hu A. 1987b. Determination of purgeable halocarbons and aromatics by photoionization and hall electrolytic conductivity detectors connected in series. J Chromatogr Sci 25:356-363.

*Mabey WR, Smith JH, Pod011 TT, et al. 1982. Aquatic fate process data for organic priority pollutants. Report to US Environmental Protection Agency, Office of Water Regulations and Standards,, Washington, DC, by Syracuse Research Institute Intl SO. EPA 440/4-81-014.

Matter-Muller C, Gujer W, Giger W. 1981. Transfer of volatile substances from water to the atmosphere. Water Research 15:1271-1279.

*McCall SN, Jurgens P, Ivanetich KM. 1983. Hepatic microsomal metabolism of the dichloroethanes. Biochem Pharmacol 32:207-213.

McCann J, Horn L, Girman J, et al. 1987. Potential risks from exposure to organic carcinogens in indoor air. Environmental Science Research 36:325-354.

8. REFERENCES

*McCarty PL, Siegrist H, Vogel TM, et al. 1986. Biotransformation of groundwater contaminants. Report to Fairchild Semiconductor Corporation, by Department of Civil Engineering, Stanford University, Stanford, CA. Technical Report no 298.

McDonald TJ, Kennicutt MC II, Brooks JM. 1988. Volatile organic compounds at a coastal Gulf of Mexico site. Chemosphere 17:123-136.

McNally ME, Grob RL. 1983. Determination of the solubility limits of organic priority pollutants by gas chromatographic headspace analysis. J Chromatogr 260:23-32.

McNally ME, Grob RL. 1984. Headspace determination of solubility limits of the base neutral and volatile components from the Environmental Protection Agency's list of priority pollutants. J Chromatogr 284:105-116.

Mehran MF, Cooper WJ, Jennings W. 1984. The use of coupled columns for the capillary gas chromatographic separation. Journal of High Resolution Chromatography and Chromatography Communications 7:215-217.

*Mehran M, Cooper WJ, Mehran M, et al. 1986 . Comparison of direct headspace and aqueous injection techniques for halogenated hydrocarbons in water. J Chromatogr Sci 24:142-146.

*Mehran M, Mehran MF, Cooper WJ. 1985 Application of capillary gas chromatography for water pollution analysis. Studies in Environmental Science 29:723-743.

Meyers VK. 1983. Chemicals which cause birth defects - teratogens: A special concern of research chemists. Sci Total Environ 32:1-12.

Miller HC, James RH, Dickson WR, et al. 1981. Evaluation of methodology for the survey analysis of solid wastes. American Society for Testing Materials Special Technical Publication 760:240-266.

*Miller KW, Paton WDM, Smith EB. 1965. Site of action of general anaesthetics GA. Nature 206:575-577.

Milman HA, Mitoma C, Tyson C, et al. 1986. Carcinogenicity studies with chlorinated aliphatics [Abstract]. 14th International Cancer Congress. Union Internationale Contre le Cancer, Budapest, Hungary., 305.

*Mitoma C, Steeger T, Jackson SE, et al. 1985. Metabolic disposition study of chlorinated hydrocarbons in rats and mice. Drug Chem Toxic01 8:183-194.

Morgan A, Black A, Belcher DR. 1972. Absorption of halogenated hydrocarbons and their excretion in breath using chlorine-38 tracer techniques. Ann Occup Hyg 15:273-283.

8. REFERENCES

Mosesman NH, Sidisky LM, Corman SD. 1987. Factors influencing capillary analyses of volatile pollutants. J Chromatogr Sci 25:351-355.

Muller J. 1925. [Comparative investigations of the narcotic and toxic effect of some hydrocarbon halides]. Archiv fuer Experimentelle Pathologie und Pharmakologie 109:276-294. (German).

Nakajima T, Sato A. 1979. Enhanced activity of liver drug-metabolizing enzymes from aromatic and chlorinated hydrocarbons following food deprivation. Toxicol Appl Pharmacol 50:549-556.

*NAS/NRC. 1989. Biological markers in reproductive toxicology. National Academy of Sciences/National Research Council. Washington, DC: National Academy Press, 15-35.

*NATICH. 1988. National Air Toxics Information Clearinghouse (NATICH) database. US Environmental Protection Agency, Office of Air Quality Planning and Standards, Research Triangle Park, NC. July, 1988.

*National Occupational Exposure Survey (1980-1983) Database. 1984. US Department of Health and Human Services, National Institute for Occupational Safety and Health, Cincinnati, OH.

*National Occupational Hazard Survey (1970) Database. 1976. US Department of Health and Human Services, National Institute of Occupational Safety and Health, Cincinnati, OH.

*NCI. 1977. Bioassay of l,l-dichloroethane for possible carcinogenicity. Bethesda, MD: National Cancer Institute. NIH publication No. 78-1316.

Nellor MH, Baird RB, Garrison WE. 1982. Health effects of water reuse by groundwater recharge. Proceedings of the Water Reuse Symposium 3:2138-2166.

Nelson GO, Harder CA. 1974. Respirator cartridge efficiency studies: V. Effect of solvent vapor. Amer Ind Hyg Ass J 35:391-410.

Nelson GO, Harder CA. 1976. Respirator cartridge efficiency studies: VI. Effect of concentration. Am Ind Hyg Assoc J 37:205-216.

Nikitin YS, Viryasov MB. 1986. Gas chromatography of low molecular weight halocarbons on macroporous silica modified by a thin liquid phase film. Chromatographia 21:681-686.

*NIOSH. 1978. Occupational health guidelines for l,l-dichloroethane. Occupational health guidelines for chemical hazards. Washington, DC: US Department of Labor, National Institute for Occupational Safety and Health, 1-4.

8. REFERENCES

*NIOSH. 1985. NIOSH pocket guide to chemical hazards. Cincinnati, OH: US Department of Health and Human Services, National Institute for Occupational Safety and Health, 98-99.

*NIOSH. 1987. NIOSH manual of analytical methods. Vol. l-7, 2 ed. Washington, DC: US Department of Labor, National Institute for Occupational Safety and Health, 1003.1-1003.6.

*Nohmi T, Miyata R, Yoshikawa K, et al. 1985. [Mutagenicity tests on organic chemical contaminants in city water and related compounds: I. Bacterial mutagenicity tests]. Bulletin of National Hygiene Science 103:60-64. (Japanese).

Oda J, Maeda I, Ichidkawa S, et al. 1987. [Studies on the analytical methodsof organic chemicals in air. 1. Determination and identification of volatile chlorinated organic compounds at ppb level in air by gas chromatography-mass spectrometry]. Okayama-ken Kankyo Hoken Senta Nenpo 11:60-68. (Japanese).

*OHM, TADS. 1988. Oil and Hazardous Materials/Technical Assistance Data System. US Environmental Protection Agency, Chemical Information Service (CIS), Bethesda, MD. December 9, 1988.

*OSHA. 1988. US Department of Labor, Occupational Safety and Health Administration. Code of Federal Regulations. 40 CFR 1910.1000.

OSHA . 1988. US Department of Labor, Occupational Safety and Health Administration. Code of Federal Regulations. 29 CFR 1910.20.

*Otson R, Williams DT. 1981. Evaluation of a liquid-liquid extraction technique for water pollutants. J Chromatogr 212:187-198.

*Otson R, Williams DT. 1982. Headspace chromatographic determination of water pollutants. Anal Chem 54:942-946.

*Otson R, Chan C. 1987. Sample handling and analysis for 51 volatile organics by an adapted purge and trap GC-MS technique. Int J Environ Anal Chem 30:275-287.

Otson R, Williams DT, Bothwell PD. 1982. Volatile organic compounds in water at thirty Canadian potable water treatment facilities. J Assoc Off Anal Chem 65:1370-1374.

*Pankow JF, Rosen ME. 1988. Determination of volatile compounds in water by purging directly to a capillary column with whole column cryotrapping. Environ Sci Technol 22:398-405.

*Parker JC, Casey GE, Bahlman LJ, et al. 1979. Chloroethanes: Review of Toxicity. Am Ind Hyg Assoc J 40:A46-A57.

8. REFERENCES

*Pellizzari ED. 1978. Quantification of chlorinated hydrocarbons in previously collected air samples. Report to US Environmental Protection Agency, Office of Air Quality Planning and Standards, Research Triangle Park, NC, by Research Triangle Park Institute, Research Triangle Park, NC. EPA 450/3-78-112., 151.

*Pellizzari ED. 1982. Analysis for organic vapor emissions near industrial and chemical waste disposal sites. Environ Sci Technol 16:781-785.

Pellizzari ED, Erickson MC, Zweidinger RA. 1979. Formulation of preliminary assessment of halogenated organic compounds in man and environmental media. Washington, DC: U.S. Environmental Protection Agency.

*Perwak J, Byrne M, Goyer M, et al. 1982. Exposure and risk assessment for dichloroethanes. l,l-Dichloroethane, 1,2-dichloroethane. Report to US Environmental Protection Agency, Office of Water Regulations and Standards, Washington, DC, by Arthur D. Little, Inc., Cambridge, MA. EPA 440/4-85-009.,
197.

Pfannhauser W, Thaller A. 1985. [Determination of halogenated solvent residues in water, wastewater, feeds, and food]. Fresenius Z Anal Chem 322:220-222. (German).

*Plaa GL, Larson RE. 1965. Relative nephrotoxic properties of chlorinated methane, ethane, and ethylene derivatives in mice. Toxic01 Appl Pharmacol 7:37-44.

*Plumb RI-I Jr. 1987. A comparison of groundwater monitoring data from CERCLA and RCRA sites. Ground Water Monitoring Review 7:94-100.

Potapov AA, Potapova ZG, Medvedev MA. 1976. The effect of adrenal insufficiency on the gallbladder motility. Fiziol Zh SSSR Im I M Sechenova 62:1691-1697. (Russian).

Radeleff RD, Bushland RC. 1950. Acute toxicity of chlorinated insecticides applied to livestock. J Econo Entomol 43:358-364.

Rawlings GD, Samfield M. 1979. Toxicity of secondary effluents from textile plants. Symposium Proceedings of Process Measurements for Environmental Assessment. EPA 600/7-78-168., 153-169.

*Reding R. 1987. Chromatographic monitoring methods for organic contaminants under the Safe Drinking Water Act. J Chromatogr Sci 25:338-344.

*Reinert RH, Hunter JV, Sabatino T. 1983. Dynamic heated headspace analyses of volatile organic compounds present in fish tissue samples. J Agric Food Chem 31:1057-1060.

8. REFERENCES

*Reinhardt CF, Azar A, Maxfield ME, et al. 1971. Cardiac arrhythmias and aerosol "sniffing." Arch Environ Health 22:265-279.

*Reynolds ES, Kanz MF, Chieco P, et al. 1984. l,l-Dichloroethylene: A n apoptotic hepatotoxin? Env Health Pespect 57:313-320.

*Riccio E, Griffin A, Mortelmans K, et al. 1983. A comparative mutagenicity study of volatile halogenated hydrocarbons using different metabolic activation systems. Environ Mut 5:472.

*RIDH. 1989. Written communication regarding l,l-dichloroethane detected in private well water and public drinking water. Providence, RI: Rhode Island Department of Health (June 19).

Robinson BG, Hales IB, Henniker AJ, et al. 1987. The effect of o-, p'-DDD on adrenal steroid replacement therapy requirements. Clin Enodcrinol 27:437-444.

*RTECS. 1988. Registry of Toxic Effects of Chemical Substances. National Library of Medicine, National Toxicology Information Program, Bethesda, MD. December 9, 1988.

Salmon AG, Jones RB, Mackrodt WC. 1981. Microsomal dechlorination of chloroethanes: Structure-reactivity relationships. Xenobiotica 11:723-734.

Sato A, Nakajima T. 1979. Enhanced activity of liver drug-metabolizing enzymes following chronic ethanol consumption and starvation. Arh Hig Rada Toksikol 30:645-651.

*Sato A, Nakajima T. 1987. Pharmacokinetics of organic solvent vapors in relation to their toxicity. Stand J Work Environ Health 13:81-93. Sato K, Tanaka H. 1987. Degradation and metabolism of a fungicide, 2,4,5,6-tetra-chloroisophthalonitrile (TPN) in soil. Biol Fertil Soils 3:205-209.

*Sate A, Nakajima T, Koyama Y. 1980. Effects of chronic ethanol consumption on hepatic metabolism of aromatic and chlorinated hydrocarbons in rats. Br J Ind Med 37:382-386.

Schneider M, Wolfrum J. 1986. Mechanisms of by-product formation in the dehydrochlorination of 1,2-dichloroethane. Ber Bunsen Ges Phys Chem 90:1058-1062.

*Schwetz BA, Leong BKJ, Gehring PJ. 1974. Embryo-and fetotoxicity of inhaled carbon tetrachloride, l,l-dichloroethane and methyl ethyl ketone in rats. Toxicol Appl Pharmacol 28:452-464.

Scott DR, Dunn WJ III, Emery SL. 1987. Classification and identification of hazardous organic compounds in ambient air by pattern recognition of mass spectral data. Environ Sci Technol 21:891-897.

8. REFERENCES

Seaman CV, Hill LO, Vignon BW, et al. 1983. Halogenated organic study at selected Tennessee Valley Authority fossil- fueled power plants. Environmental Impact and Health Effects, Part 1: Chemistry and Water Treatment. Proceedings of the 4th Conference, Pacific Grove, CA, October 18- 23, 1981. Ann Arbor, MI: Ann Arbor Science Publishers., 373-382.

Senser DW, Cundy VA. 1987. Gas chromatographic determination of Cl and C2 chlorinated hydrocarbon species in combustion products. Hazardous Waste and Hazardous Materials 4:99-110.

Seybold PG, May MA, Gargas ML. 1986. On the physical properties of halogenated hydrocarbons. Acta Pharm Jugosl 36:253-265.

Siddiqui MKJ, Saxena MC, Krishna Murti CR. 1981. Storage of DDT and BHC in adipose tissue of Indian males. Int J Environ Anal Chem 10:197-204.

Silverman L, Reece GM, Drinker P. 1939. A new vapor pressure instrument for determining organic solvents in air. Journal of Industrial Hygiene and Toxicology 21:270-278.

*Simmon VF, Kauhanen K, Tardiff RG. 1977. Mutagenic activity of chemicals identified in drinking water. ,I Dev Toxic01 Environ Sci 2:249-258.

Sims RC, Sims JL, DuPont RR. 1987. Human health effects assays. J Water Pollut Control Fed 59:601-614.

*Singh HB, Salas LJ, Smith AJ, et al. 1981. Measurements of some potentially hazardous organic chemicals in urban environments. Atmos Environ 15:601-612.

*Singh HB, Salas LJ, Stiles R, et al. 1983. Measurements of hazardous organic chemicals in the ambient atmosphere. Report to US Environmental Protection Agency, Office of Research and Development, Research Triangle Park, NC, by SRI International, Menlo Park, CA. EPA 600/3-83-002.

*Smyth HF Jr. 1956. Improved communication: Hygienic standards for daily inhalation. American Industrial Hygiene Association Quarterly., 129-195.

Snider EH, Manning FS. 1982. A survey of pollutant emission levels in wastewaters and residuals from the petroleum refining industry. Environment International 7:237-258.

Spain MA, Middleditch BS, Bafus DA, et al. 1985. Dehydrohalogenation of atmospheric contaminants in the space cabin. Aviat Space Environ Med 56:262-264.

Spasovski M, Stancev S, Nosko M, et al. 1984. [Changes in some biochemical indices in workers exposed to vinyl chloride and dichloroethane]. Problemi na higienata 9:50-58. (Russian).

8. REFERENCES

Spielmann H. 1986. [Evaluation of embryototoxic properties of industrial chemicals]. Geburtsh U Frauenheilk 46:335-339. (German).

*Staples CA, Werner AF, Hoogheem TJ. 1985. Assessment of priority pollutant concentrations in the United States using STORET database. Environmental Toxicology and Chemistry 4:131-142.

Stewart RD, Gay HH, Schaffer AW, et al. 1969. Experimental human exposure to methyl chloroform vapor. Arch Environ Health 19:467-472.

Stottmeister E, Hendel P, Engewald W. 1986. [Gas-chromatographic trace analysis of highly volatile halocarbons in waters with simultaneous ECD/FID detection]. Acta Hydrochim Hydrobiol 14:463-474. (German).

Stuart JD. 1983. Organics transported thru selected geologic media: Assessment of organics transported away from industrial waste disposal sites. Report to US Department of the Interior, Office of Water Research and Technology, Washington, DC, by University of Connecticut, Institute of Water Resources, Storrs, CT. NTIS PB83-224246., 37.

*Suffet IH, Brenner L, Cairo PR. 1980. Gas chromatography-mass spectrometry identification of trace organics in Philadelphia, Pennsylvania, USA, drinking waters during a 2-year period. Water Res 14:853-867.

*Tabak HH, Quave SA, Mashni CI, et al. 1981. Biodegradability studies with organic priority pollutant compounds. J Water Pollut Control Fed 53:1503-1518.

Thienes C, Haley TJ, ed. 1972. Clinical toxicology. 5th ed. Philadelphia, PA: Lea and Febiger, Co., 150.
Thompson JA, Ho B, Mastovich SL. 1984. Reductive metabolism of 1,1,1,2-tetrachloroethane and related chloroethanes. Chem Biol Interact 51:321-333.

Thompson JA, Ho B, Mastovich SL. 1985. Dynamic headspace analysis of volatile metabolites from the reductive dehalogenation of trichloro- and tetrachloroethanes by hepatic microsomes. Anal Biochem 145:376-384.

*Tomasi A, Albano E, Bini A, et al. 1984. Free radical intermediates under hypoxic conditions in the metabolism of halogenated carcinogens. Toxicol Path01 12:240-246.

Torkelson TR, Rowe VK. 1981-1982. l,l-Dichloroethane. IN: Clayton GD, Clayton FE, ed. Patty's industrial hygiene and toxicology. Vol. 2A, 2B, 2C, New York, NY: John Wiley and Sons, Inc., 3488-3490.

8. REFERENCES

Truhaut R. 1971. [Present condition of the problem of permissible or tolerable limits for potentially toxic chemicals in occupational environment]. Arch Ma1 Prof 32:353-370. (French).

*Trussell AR, Moncur JG, Lieu FY, et al. 1983. New developments in dynamic headspace analysis of halogenated organics. Water Chlorination: Environmental Impact Health Effects 4:583-592.

*Tu AS, Murray TA, Hatch KM, et al. 1985. In vitro transformation of BALB/c-3T3 cells by chlorinated ethanes and ethylenes. Cancer Lett 28:85-92. Tyson CA. 1987. Correspondence of results from hepatocyte studies with in vivo response. Toxic01 Ind Health 3:459-478.

*Uehori R, Nagata T, Kimura K, et al. 1987. Screening of volatile compounds present in human blood using retention indices in gas chromatography. J Chromatogr 411:251-257.

*Van Dyke RA, Wineman CG. 1971. Enzymatic dechlorination: Dechlorination of chloroethanes and propanes in vitro. Biochem Pharmacol 20:463-470.

*Verschueren K. 1983. Handbook of environmental data on organic chemicals. 2nd‘ ed. New York, NY: Van Nostrand Reinhold Co., 486.

*VIEW database. 1989. Agency for Toxic Substances and Disease Registry (ATSDR), Office of External Affairs, Exposure and Disease Registry Branch, Atlanta, GA. June 20, 1989. (Map based on VIEW Database, June 12, 1989).

*Wallace L, Zweidinger R, Erickson M, et al. 1982. Monitoring individual exposure. Measurements of volatile organic compounds in breathing air, drinking water, and exhaled breath. Environment International 8:269-282. (Retrieval in progress)

*Vogel TM, McCarty PL. 1987. Abiotic and biotic transformations of l,l,l-trichloroethane under methanogenic conditions. Environ Sci Technol 2i:i208-1213.

*Wallace LA, Pellizzari E, Harwell T, et al. 1984. Personal exposure to volatile organic compounds. I. Direct measurements. Environ Res 35:293-319.

Watanabe Y . 1983. [Studies on biological effects of hydrocarbons. III. Chlorinated hydrocarbons]. Kanagawa-ken Taiki Osen Chosa Kenkyu Hokoku 25:146-152. (Japanese).

Weisburger EK. 1977. Carcinogenicity studies on halogenated hydrocarbons. Environ Health Perspect 21:7-16.

*Weiss G. 1986. Hazardous chemicals databook. 2nd ed. Park Ridge, NJ: Noyes Data Corporation, 359.

8. REFERENCES

Welch RM, Levin W, Kuntzman R, et al. 1971. Effect of halogenated hydrocarbon insecticides on the metabolism and uterotropic action on estrogens in rats and mice. Toxic01 Appl Pharmacol 19:234-246.

*Westrick JJ, Mello JW, Thomas RF. 1984. The groundwater supply survey. J Amer Water Works Assoc 76:52-59.

*Wilson JT, McNabb JF, Wilson BH, et al 1983. Biotransformation of selected organic pollutants in groundwater. Dev Ind Microbiology 241225-233.

*Windholz M. 1983. The Merck index. 10th ed. Rahway, NJ: Merck and Co., Inc., 552.

*Wood PR, Lang RF, Payan IL. 1985. Anaerobic transformation, transport, and removal of volatile chlorinated organics in ground water. In: Ward CH, Giger W, ed. Ground water quality. New York, NY: John Wiley and Sons, 493- 511.

*Wylie PL. 1987. A comparison of headspace purge and trap techniques for the analysis of volatile priority pollutants. Proceedings of the Water Quality Technology Conference 14:185-202.

*Wylie PL. 1988. Comparing headspace with purge and trap for analysis of volatile priority pollutants. American Water Works Association 80:65-72.

*Yang RSH, Rauckman EJ. 1987. Toxicological studies of chemical mixtures of environmental concern at the National Toxicology Program: Health Effects of Groundwater Contaminants. Toxicology 47:15-34.

*Young DR, Gossett RW, Baird RB, et al. 1983. Wastewater inputs and marine bioaccumulation of priority pollutant organics off Southern California. Water Chlorination: Environmental Impact and Health Effects 4:871-884.

Zakhari S, Aviado DM. 1982. Cardiovascular toxicology of aerosol propellants refrigerants and related solvents. IN: Van Stee EW, ed. Cardiovascular Toxicology. New York, NY: Raven Press, 281-326.

Zaki MH. 1986. Groundwater contamination with synthetic organic compounds and pesticides. Northeastern Environmental Science 5:15-22.

*Zweidinger R, Erickson M, Cooper S, et al. 1982. Direct measurement of volatile organic compounds in breathing-zone air, drinking water, breath, blood, and urine. Research Triangle Park, NC: US Environmental Protection Agency. EPA 600/4-82-015.

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 (GEL) -- 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.

9. GLOSSARY

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.

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$_{(LO)}$(LC_{LO}) -- The lowest concentration of a chemical in air which has been reported to have caused 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 $_{(50)}$(LD_{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 chemical that is likely to be without an appreciable risk of deleterious effects (noncancerous) 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.

9. GLOSSARY

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 (Kow) -- 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.

q1* -- The upper-bound estimate of the low-dose slope of the dose-response curve as determined by the multistage procedure. The q1* can be used to calculate an estimate of carcinogenic potency, the incremental excess cancer risk per unit of exposure (usually μg/L for water, m&/kg/day for food, and pg/m^3 for air).

Reference Dose (RfD) -- An estimate (with uncertainty spanning perhaps an ordkr 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 lb 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.

9. GLOSSARY

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 8-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

PEER REVIEW

A peer review panel was assembled for l,l-dichloroethane. The panel consisted of the following members: Dr. Benjamin Van Duuren, Institute of Environmental Medicine, New York University Medical Center; Dr. James Bruckner, Department of Toxicology and Pharmacology, University of Georgia; Dr. Theodore Mill, Director, Physical Organic Chemistry Department, SRI International; Dr. Nancy Tooney, Associate Professor, Department of Chemistry, Polytechnic University, Brooklyn, New York; and Ms. Linda Massey, Private Toxicology Consultant, Santa Clara, California. These experts collectively have knowledge of l,l-dichloroethane'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 comm&ts 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 Agency for Toxic Substances and Disease Registry.