TOXICOLOGICAL PROFILE FOR 1,1-DICHLOROETHANE

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

August 2015

DISCLAIMER

Use of trade names is for identification only and does not imply endorsement by the Agency for Toxic Substances and Disease Registry, the Public Health Service, or the U.S. Department of Health and Human Services.

UPDATE STATEMENT

A Toxicological Profile for 1,1-Dichloroethane, Draft for Public Comment was released in April 2013. This edition supersedes any previously released draft or final profile.

Toxicological profiles are revised and republished as necessary. For information regarding the update status of previously released profiles, contact ATSDR at:

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Division of Toxicology and Human Health Sciences
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FOREWORD

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

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

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

Each profile includes the following:

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

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

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

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

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*Legislative Background

The toxicological profiles are developed under the Comprehensive Environmental Response, Compensation, and Liability Act of 1980, as amended (CERCLA or Superfund). CERCLA section 104(i)(1) directs the Administrator of ATSDR to "…effectuate and implement the health related authorities" of the statute. This includes the preparation of toxicological profiles for hazardous substances most commonly found at facilities on the CERCLA National Priorities List and that pose the most significant potential threat to human health, as determined by ATSDR and the EPA. Section 104(i)(3) of CERCLA, as amended, directs the Administrator of ATSDR to prepare a toxicological profile for each substance on the list. In addition, ATSDR has the authority to prepare toxicological profiles for substances not found at sites on the National Priorities List, in an effort to "…establish and maintain inventory of literature, research, and studies on the health effects of toxic substances" under CERCLA Section 104(i)(1)(B), to respond to requests for consultation under section 104(i)(4), and as otherwise necessary to support the site-specific response actions conducted by ATSDR.

QUICK REFERENCE FOR HEALTH CARE PROVIDERS

Toxicological Profiles are a unique compilation of toxicological information on a given hazardous substance. Each profile reflects a comprehensive and extensive evaluation, summary, and interpretation of available toxicologic and epidemiologic information on a substance. Health care providers treating patients potentially exposed to hazardous substances will find the following information helpful for fast answers to often-asked questions.

Primary Chapters/Sections of Interest

Chapter 1: Public Health Statement: The Public Health Statement can be a useful tool for educating patients about possible exposure to a hazardous substance. It explains a substance's relevant toxicologic properties in a nontechnical, question-and-answer format, and it includes a review of the general health effects observed following exposure.

Chapter 2: Relevance to Public Health: The Relevance to Public Health Section evaluates, interprets, and assesses the significance of toxicity data to human health.

Chapter 3: Health Effects: Specific health effects of a given hazardous compound are reported by type of health effect (death, systemic, immunologic, reproductive), by route of exposure, and by length of exposure (acute, intermediate, and chronic). In addition, both human and animal studies are reported in this section.
NOTE: Not all health effects reported in this section are necessarily observed in the clinical setting. Please refer to the Public Health Statement to identify general health effects observed following exposure.

Pediatrics: Four new sections have been added to each Toxicological Profile to address child health issues:

Chapter 1	**How Can (Chemical X) Affect Children?**
Chapter 1	**How Can Families Reduce the Risk of Exposure to (Chemical X)?**
Section 3.7	**Children's Susceptibility**
Section 6.6	**Exposures of Children**

Other Sections of Interest:

Section 3.8	**Biomarkers of Exposure and Effect**
Section 3.11	**Methods for Reducing Toxic Effects**

ATSDR Information Center

Phone: 1-800-CDC-INFO (800-232-4636) or 1-888-232-6348 (TTY)
Internet: http://www.atsdr.cdc.gov

The following additional material is available online at www.atsdr.cdc.gov:

Case Studies in Environmental Medicine—Case Studies are self-instructional publications designed to increase primary care provider's knowledge of a hazardous substance in the environment and to aid in the evaluation of potentially exposed patients.

Managing Hazardous Materials Incidents is a three-volume set of recommendations for on-scene (prehospital) and hospital medical management of patients exposed during a hazardous materials incident. Volumes I and II are planning guides to assist first responders and hospital emergency department personnel in planning for incidents that involve hazardous materials. Volume III—*Medical Management Guidelines for Acute Chemical Exposures*—is a guide for health care professionals treating patients exposed to hazardous materials.

Fact Sheets (ToxFAQs™) provide answers to frequently asked questions about toxic substances.

Other Agencies and Organizations

The National Center for Environmental Health (NCEH) focuses on preventing or controlling disease, injury, and disability related to the interactions between people and their environment outside the workplace. Contact: NCEH, Mailstop F-29, 4770 Buford Highway, NE, Atlanta, GA 30341-3724 • Phone: 770-488-7000 • FAX: 770-488-7015.

The National Institute for Occupational Safety and Health (NIOSH) conducts research on occupational diseases and injuries, responds to requests for assistance by investigating problems of health and safety in the workplace, recommends standards to the Occupational Safety and Health Administration (OSHA) and the Mine Safety and Health Administration (MSHA), and trains professionals in occupational safety and health. Contact: NIOSH, 395 E Street, S.W., Suite 9200, Patriots Plaza Building, Washington, DC 20201 • Phone: (202) 245-0625 or 1-800-CDC-INFO (800-232-4636).

The National Institute of Environmental Health Sciences (NIEHS) is the principal federal agency for biomedical research on the effects of chemical, physical, and biologic environmental agents on human health and well-being. Contact: NIEHS, PO Box 12233, 104 T.W. Alexander Drive, Research Triangle Park, NC 27709 • Phone: 919-541-3212.

Clinical Resources

The Association of Occupational and Environmental Clinics (AOEC) has developed a network of clinics in the United States to provide expertise in occupational and environmental issues. Contact: AOEC, 1010 Vermont Avenue, NW, #513, Washington, DC 20005 • Phone: 202-347-4976 • FAX: 202-347-4950 • e-mail: AOEC@AOEC.ORG • Web Page: http://www.aoec.org/.

The American College of Occupational and Environmental Medicine (ACOEM) is an association of physicians and other health care providers specializing in the field of occupational and environmental medicine. Contact: ACOEM, 25 Northwest Point Boulevard, Suite 700, Elk Grove Village, IL 60007-1030 • Phone: 847-818-1800 • FAX: 847-818-9266.

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THE PROFILE HAS UNDERGONE THE FOLLOWING ATSDR INTERNAL REVIEWS:

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

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

3. Data Needs Review. The Environmental Toxicology Branch reviews data needs sections to assure consistency across profiles and adherence to instructions in the Guidance.

4. Green Border Review. Green Border review assures the consistency with ATSDR policy.

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PEER REVIEW

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

1. Gary Stoner, Ph.D., Department of Medicine, Division of Hematology and Oncology, Medical College of Wisconsin, Milwaukee, Wisconsin;

2. G.A. Shakeel Ansari, Ph.D., Department of Human Biological Chemistry & Genetics and Pathology, University of Texas Medical Branch, Galveston Texas;

3. Hermann Bolt, Ph.D., Institut für Arbeitsphysiologie an der Universität Dortmund (IfADo), Leibniz Research Centre for Working Environment and Human Factors, Dortmund, Germany.

These experts collectively have knowledge of 1,1-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 comments will be included in the profile. A listing of the peer reviewers' comments not incorporated in the profile, with a brief explanation of the rationale for their exclusion, exists as part of the administrative record for this compound.

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

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1. PUBLIC HEALTH STATEMENT FOR 1,1-DICHLOROETHANE

This Public Health Statement summarizes the Division of Toxicology and Human Health Science's findings on 1,1-dichloroethane, tells you about it, the effects of exposure, and describes what you can do to limit that exposure.

The U.S. Environmental Protection Agency (EPA) identifies the most serious hazardous waste sites in the nation. These sites make up the National Priorities List (NPL) and are sites targeted for long-term federal clean-up activities. U.S. EPA has found 1,1-dichloroethane in at least 673 of the 1,699 current or former NPL sites. The total number of NPL sites evaluated for 1,1-dichloroethane is not known. But the possibility remains that as more sites are evaluated, the sites at which 1,1-dichloroethane is found may increase. This information is important because these future sites may be sources of exposure, and exposure to 1,1-dichloroethane may be harmful.

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

WHAT IS 1,1-DICHLOROETHANE?

1,1-Dichloroethane is a colorless oily liquid with a chloroform-like odor. 1,1-Dichloroethane is a chemical used mostly as an intermediate in the manufacture of 1,1,1-trichloroethane (1,1,1-TCE). 1,1-Dichloroethane is also used in limited amount as a solvent for cleaning and degreasing, and in the manufacture of plastic wrap, adhesives, and synthetic fiber.

More information on the chemical and physical properties as well as the production and uses of 1,1-dichloroethane is presented in Chapters 4 and 5 of this profile.

WHERE IS 1,1-DICHLOROETHANE FOUND?

1,1-Dichloroethane can be released into the air, water, and soil at places where it is produced or used as a solvent. The majority of the monitoring data for 1,1-dichloroethane focuses on air and water, specifically

at hazardous waste sites. Minimal data are available for concentrations of 1,1-dichloroethane measured in soil. It is expected that the lack of available soil data is, in part, due to the rapid partitioning of 1,1-dichloroethane to air and water from soil or sediment. 1,1-Dichloroethane has been detected and measured in air samples at concentrations ranging from parts per trillion (ppt) to parts per million (ppm). In the air, 1,1-dichloroethane is slow to break down and has the potential for long-range transport.

1,1-Dichloroethane has been detected in drinking water and groundwater. 1,1-Dichloroethane does not degrade quickly in water, but it can evaporate from the water into the air. Minimal information was found on concentrations of 1,1-dichloroethane in soil, releases of 1,1-dichloroethane to land surfaces, or the disposal of waste products containing 1,1-dichloroethane into landfills. 1,1-Dichloroethane released to soil surfaces would rapidly evaporate to the air. Residual 1,1-dichloroethane remaining on soil surfaces would be available for transport into groundwater, since it is not expected to bind to soil particulates unless the organic content of the soil is high. Minimal information was found on the levels of 1,1-dichloroethane in other media.

In a survey of 234 table ready foods evaluated for the presence of volatile organic compounds (VOCs), 1,1-dichloroethane was not found in any of the samples. It was detected in three peanut butter samples at levels of 1.1, 1.9, and 3.7 micrograms per kilogram (µg/kg); however, the compound was not found in several other foods that were analyzed.

More information on levels of 1,1-dichorethane found in the environment is presented in Chapter 6 of this profile.

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

The use of 1,1-dichloroethane as a solvent, cleaning agent, and degreaser, and its use in manufacturing of other compounds, such as 1,1,1-TCE, may result in releases to the environment. 1,1-Dichloroethane has been detected in ambient air and water. Exposure to 1,1-dichloroethane occurs mainly by breathing air near contaminated areas or by drinking water contaminated with 1,1-dichloroethane. However, most people who are exposed to 1,1-dichloroethane through air or water are exposed to very low levels, in the range of ppm to ppt. People may be exposed to higher levels of 1,1-dichloroethane if they smoke cigarettes or are exposed to cigarette smoke. People may also be exposed to 1,1-dichloroethane by using consumer products that contain this compound.

Job-related exposure of 1,1-dichloroethane results from breathing in workplace air or from touching contaminated chemicals or materials at workplaces where 1,1-dichloroethane is used. According to a survey conducted between 1980 and 1983 by the National Institute for Occupational Safety and Health (NIOSH), an estimated 1,957 people in the United States may have been exposed to 1,1-dichloroethane while working. In general, people who work with 1,1-dichloroethane or live near industrial emission sources and hazardous waste sites containing 1,1-dichloroethane are more likely to be exposed.

Additional information on levels in the environment and potential for human exposure is presented in Chapter 6 of the toxicological profile.

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

If you breathe air containing 1,1-dichloroethane, it will enter your body through your lungs. 1,1-Dichloroethane in your drinking water will enter your body through the digestive tract. We do not know how much will be absorbed; studies with similar compounds suggested that 1,1-dichloroethane will be rapidly and extensively absorbed.

1,1-Dichloroethane leaves your body in the breath or is broken down into other chemicals, which leave your body in the breath or in the urine.

HOW CAN 1,1-DICHLOROETHANE AFFECT MY HEALTH?

No information is available in humans on the health effects associated with occupational or environmental exposure to 1,1-dichloroethane. 1,1-Dichloroethane was used as an anesthetic; however, it is no longer used for this purpose because of the heart effects that also occurred at these very high concentrations.

Kidney effects have been observed in cats exposed to 1,1-dichloroethane in air for long periods. However, kidney effects have not been observed in other animal species following long-term inhalation or oral exposure.

The results of a study in rats and mice suggest that 1,1-dichloroethane may cause cancer. However, the study had several flaws and the results are not conclusive. Another long-term study of mice that drank water containing 1,1-dichloroethane did not find cancer.

The U.S. Department of Health and Human Services (DHHS) and The International Agency for Research on Cancer (IARC) have not evaluated the carcinogenic potential of 1,1-dichloroethane. The U.S. EPA has determined that 1,1-dichloroethane is a possible human carcinogen.

See Chapters 2 and 3 for more information on 1,1-dichloroethane health effects.

HOW CAN 1,1-DICHLOROETHANE AFFECT CHILDREN?

This section discusses potential health effects of 1,1-dichloroethane exposure in humans from when they're first conceived to 18 years of age, and how you might protect against such effects.

No available studies have described the effects of exposure to 1,1-dichloroethane on children or young animals. Although we think that children would likely show the same health effects as adults, we don't know whether children are more susceptible than are adults to 1,1-dichloroethane effects.

We don't know whether 1,1-dichloroethane can harm an unborn child. Minor skeletal problems were observed in the fetuses of rats exposed to 1,1-dichloroethane in the air; decreases in body weight were also observed in the mothers.

HOW CAN FAMILIES REDUCE THE RISK OF EXPOSURE TO 1,1-DICHLOROETHANE?

If your doctor finds that you have been exposed to significant amounts of 1,1-dichloroethane, ask whether your children might also be exposed. Your doctor might need to ask your state health department to investigate.

1,1-Dichloroethane can enter your body from air, water, or consumer products containing this substance. Contact local drinking water authorities and follow their advice if you have any concerns about the presence of 1,1-dichloroethane in your tap water. 1,1-Dichloroethane has the potential to contaminate foods, although the levels found in food are generally low. 1,1-Dichloroethane can also be present in groundwater and soil underneath a building or a home, resulting in above-ground vapors through vapor intrusion (movement of vapors from groundwater or soil into air). To minimize risks associated with breathing in contaminated vapors, ensure that the area is well ventilated. If you think that you may have groundwater contaminated with 1,1-dichloroethane, contact your local state health department. Follow instructions on product labels to minimize exposure to 1,1-dichloroethane. Storing these items in a shed or an outside location may reduce exposure and decrease the impact on indoor air.

ARE THERE MEDICAL TESTS TO DETERMINE WHETHER I HAVE BEEN EXPOSED TO 1,1-DICHLOROETHANE?

1,1-Dichloroethane and its breakdown products (metabolites) can be measured in blood and urine. However, the detection of 1,1-dichoroethane or its metabolites cannot predict the kind of health effects that might develop from that exposure. Because 1,1-dichloroethane and its metabolites leave the body fairly rapidly, the tests need to be conducted within days after exposure.

For more information on the different substances formed by 1,1-dichloroethane breakdown and on tests to detect these substances in the body, see Chapters 3 and 7.

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

The federal government develops regulations and recommendations to protect public health. Regulations can be enforced by law. Federal agencies that develop regulations for toxic substances include the Environmental Protection Agency (EPA), the Occupational Safety and Health Administration (OSHA), and the Food and Drug Administration (FDA). Recommendations provide valuable guidelines to protect public health but cannot be enforced by law. Federal organizations that develop recommendations for toxic substances include the Agency for Toxic Substances and Disease Registry (ATSDR) and the National Institute for Occupational Safety and Health (NIOSH).

Regulations and recommendations can be expressed as “not-to-exceed” levels; that is, levels of a toxic substance in air, water, soil, or food that do not exceed a critical value usually based on levels that affect animals; levels are then adjusted to help protect humans. Sometimes these not-to-exceed levels differ among federal organizations. Different organizations use different exposure times (an 8-hour workday or a 24-hour day), different animal studies, or emphasize some factors over others, depending on their mission.

Recommendations and regulations are also updated periodically as more information becomes available. For the most current information, check with the federal agency or organization that issued the regulation or recommendation.

OSHA set a legal limit of 100 ppm 1,1-dichloroethane in workplace air averaged over an 8-hour work day. NIOSH recommends a limit of 100 ppm 1,1-dichloroethane in workplace air averaged over a 10-hour work day.

WHERE CAN I GET MORE INFORMATION?

If you have any questions or concerns, please contact your community or state health or environmental quality department, or contact ATSDR at the address and phone number below. ATSDR can also provide publically available information regarding medical specialists with expertise and experience recognizing, evaluating, treating, and managing patients exposed to hazardous substances.

- Call the toll-free information and technical assistance number at 1-800-CDCINFO (1-800-232-4636) or

- Write to:
  Agency for Toxic Substances and Disease Registry
  Division of Toxicology and Human Health Sciences
  1600 Clifton Road NE
  Mailstop F-57
  Atlanta, GA 30329-4027

Toxicological profiles and other information are available on ATSDR's web site: http://www.atsdr.cdc.gov.

2. RELEVANCE TO PUBLIC HEALTH

2.1 BACKGROUND AND ENVIRONMENTAL EXPOSURES TO 1,1-DICHLOROETHANE IN THE UNITED STATES

The production and use of 1,1-dichloroethane as a solvent, cleaning agent, and degreaser, and in the manufacture of 1,1,1-trichloroethane, vinyl chloride, and high vacuum rubber may result in its release to the environment. Volatilization is expected to be high based on its vapor pressure and Henry's Law constant. Atmospheric photooxidation occurs slowly in the environment, as does biodegradation and hydrolysis. 1,1-Dichloroethane has high mobility in soil and has the potential to leach from surface soils into groundwater. The bioaccumulation potential of 1,1-dichloroethane is low.

Monitoring data indicate that the general population may be exposed to 1,1-dichloroethane via inhalation for people living near source areas, ingestion of contaminated drinking water, and use of consumer products such as paint removers, which may contain this compound. Ingestion of food sources contaminated with 1,1-dichloroethane is not an important exposure pathway.

A National Health and Nutrition Survey of the U.S. population in 2003–2004 screened for 1,1-dichloroethane in blood from 1,367 participants (670 males and 679 females) in the age range of 20–59 years old. The portion of the data below the limit of detection (LOD) was too high to provide valid results.

2.2 SUMMARY OF HEALTH EFFECTS

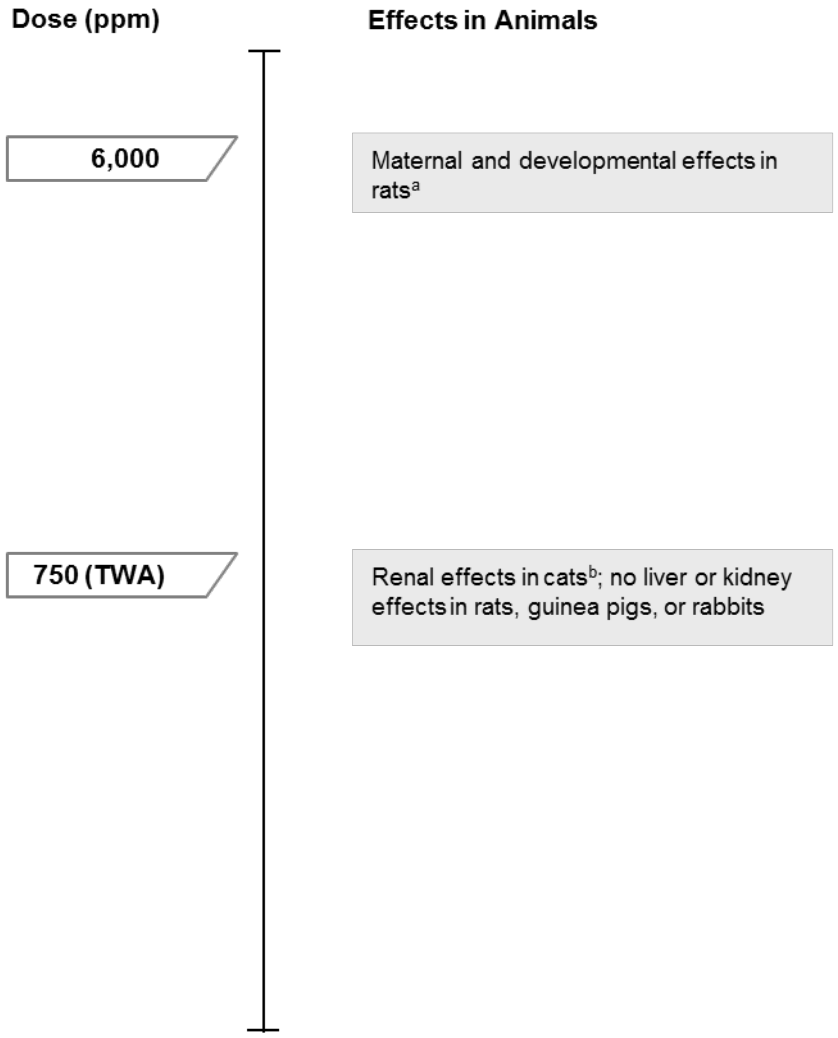
Relatively little information is available on the health effects of 1,1-dichloroethane in humans or animals. Chlorinated aliphatics as a class are known to cause central nervous system depression and respiratory tract and dermal irritation when humans are exposed by inhalation to sufficiently high levels. In the past, 1,1-dichloroethane was used as an anesthetic; however, this use was discontinued due to the risk of cardiac arrhythmia induction in humans at anesthetic doses (approximately 26,000 ppm). A small number of animal studies have examined the toxicity and carcinogenicity of 1,1-dichloroethane; these studies have failed to conclusively identify the critical targets of toxicity. Nonneoplastic effects are limited to renal toxicity in cats, maternal and fetal toxicity in rats, and alterations in body weight gain. Crystal precipitations and obstruction in the renal tubule lumina and increases in serum urea and creatinine were observed in cats exposed to 500 ppm for 13 weeks followed by a 13-week exposure to 1,000 ppm for 13 weeks. However, these effects were not observed in rats, guinea pigs, or rabbits similarly exposed to 1,1-dichloroethane, and renal effects have not been observed following gavage administration of 764 or

950 mg/kg/day in rats or 2,885 or 3,331 mg/kg/day in mice 5 days/week for 78 weeks or in mice exposed to 465 mg/kg/day 1,1-dichloroethane in drinking water for 52 weeks. Kidney effects have also been observed in mice administered a lethal intraperitoneal injection of 1,1-dichloroethane; the effects included increased glucose and protein in the urine and tubular swelling. 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 1,1-dichloroethane was administered orally.

The liver is the only other organ that has been examined in multiple studies; no hepatic effects have been reported following intermediate-duration inhalation exposure of rats, guinea pigs, rabbits, or cats, intermediate-duration oral exposure of mice, or chronic-duration exposure of rats and mice. The potential reproductive toxicity, immunotoxicity, and neurotoxicity of 1,1-dichloroethane have not been examined following inhalation, oral, or dermal exposure. A single developmental toxicity study reported retarded fetal development (delayed ossification of vertebrae) in rats at 6,000 ppm (7 hours/day on gestation days 6–15); an 11% decrease in maternal body weight gain and a decrease in maternal food consumption were also reported at this concentration. There is inconclusive evidence that 1,1-dichloroethane may be carcinogenic in rodents. A significant positive dose-related trend was observed for the incidence of hemangiosarcomas and mammary adenocarcinomas in female rats, hepatocellular carcinomas 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, particularly the poor survival in treated and control animals, preclude the consideration of these results as conclusive evidence of carcinogenicity. A 52-week drinking water study, testing much lower doses, did not find increases in the incidence of lung, liver, or kidney tumors in mice. Based on the available carcinogenicity data for 1,1-dichloroethane and supporting data on 1,2-dichloroethane, the EPA has classified 1,1-dichloroethane as a possible human carcinogen (group C). Neither the Department of Health and Human Services nor the International Agency for Research on Cancer have classified the carcinogenic potential of 1,1-dichloroethane.

An overview of these data is presented in Figures 2-1 and 2-2.

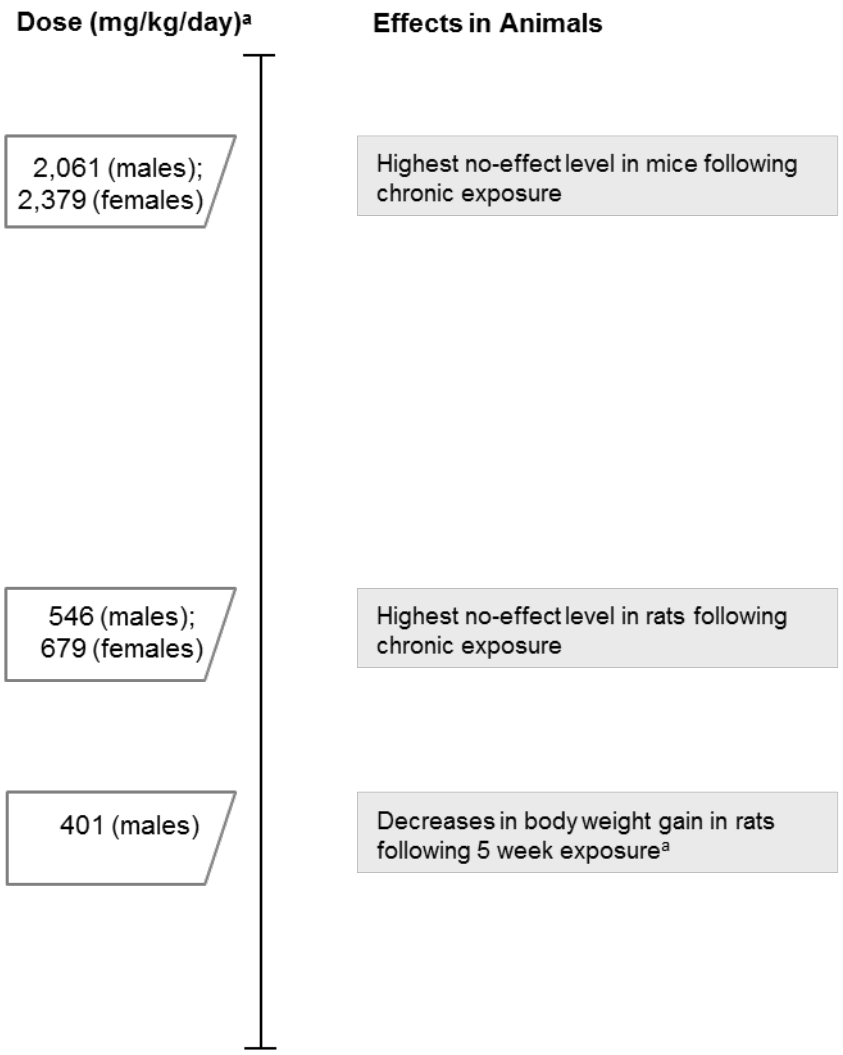
Figure 2-1. Health Effects for Following Inhalation Exposure to 1,1-Dichloroethane



[a]11% decrease in maternal body weight gain and increased incidence of fetuses with delayed ossification
[b]Increased serum urea and creatinine levels, crystal precipitations and obstruction in tubule lumina and dilatation of proximal section of renal tubules

TWA = time-weighted average

Figure 2-2. Health Effects for Following Oral Exposure to 1,1-Dichloroethane



[a]Doses adjusted for intermittent exposure (5 days/week)

2.3 MINIMAL RISK LEVELS (MRLs)

Inhalation MRLs

There are limited data to derive inhalation MRLs for 1,1-dichloroethane; the database consists of two inhalation studies. Hofmann et al. (1971) examined the potential for 1,1-dichloroethane to induce liver and/or kidney effects in rats, guinea pigs, rabbits, and cats exposed to 500 ppm 6 hours/day, 5 days/week for 13 weeks followed by a second 13-week exposure period to 1,000 ppm. No adverse effects were observed in the rats, guinea pigs, or rabbits. In three of four cats, increases in serum urea and creatinine levels and renal tubular effects (crystalline precipitates, obstruction of lumina, and dilatation) were observed at the end of the 26-week period. Tubular degeneration and periglomerular fibrosis were also noted; however, it is not known if this was observed in all affected cats. In a developmental toxicity study (Schwetz et al. 1974), decreases in maternal body weight gain and decreases in maternal food consumption were observed in rats exposed to 3,800 or 6,000 ppm 1,1-dichloroethane on gestation days 6–15 (7 hours/day); the magnitude of the decrease in weight gain was 8 and 11%, respectively. Increases in the incidence of fetuses with delayed ossification of sternebrae were also observed at 6,000 ppm. No other developmental effects, including alterations in fetal resorptions, fetal growth, or incidences of gross or soft tissue anomalies, were observed.

These studies examined a limited number of end points and there is a great deal of uncertainty regarding the primary targets of toxicity following inhalation exposure. The lowest adverse effect level that has been identified is 750 ppm (time-weighted average) for renal effects in cats following a 26-week exposure (Hofmann et al. 1971). However, this effect has not been corroborated in other species following inhalation (Hofmann et al. 1971) or oral (Klaunig et al. 1986; NCI 1977) exposure. Additionally, it is not known if cats are a good model for 1,1-dichloroethane-induced crystal formation and tubular damage and there is uncertainty regarding the threshold concentration for these renal effects due to the exposure protocol, which involved increasing the exposure concentration mid-way through the study. Both maternal and fetal growth retardation were observed at 6,000 ppm in an acute-duration study; however, it is not known if systemic or neurological effects would occur at lower concentrations. 1,1-Dichloroethane has anesthetic properties at fairly high concentrations (approximately 26,000 ppm) (Miller et al. 1965), a concentration also associated with cardiac arrhythmias (Reid and Muianga 2012). It is not known if exposure to lower concentrations would also result in central nervous system depressive effects or cardiotoxic effects because these end points have not been examined. Uncertainties associated with

identification of the most sensitive target and the associated concentration-response relationships, precludes deriving inhalation MRLs for 1,1-dichloroethane.

Oral MRLs

Two studies have examined the oral toxicity of 1,1-dichloroethane following intermediate- or chronic-duration exposure. No lung, liver, or kidney effects were observed in mice exposed to doses as high as 465 mg/kg/day 1,1-dichloroethane in drinking water for 52 weeks (Klaunig et al. 1986); no other potential targets were examined. Similarly, no nonneoplastic effects were noted in major tissues and organs of rats and mice administered 1,1-dichloroethane in corn oil 5 days/week for 78 weeks (NCI 1977). The highest doses tested were 764 and 950 mg/kg/day, respectively, in male and female rats and 2,885 and 3,331 mg/kg/day, respectively, in male and female mice. A 6-week study found decreases in body weight gain (>16%) in male rats administered 562 mg/kg/day and female rats administered 1,780 mg/kg/day 1,1-dichloroethane 5 days/week in corn oil (NCI 1977). No additional information was reported, and the cause of the decreased weight gain is not known. The chronic-duration rat study did not find significant alterations in body weight gain at higher concentrations in the male rats. Thus, the oral studies have not identified a target of toxicity, precluding the derivation of oral MRLs for 1,1-dichloroethane.

3. HEALTH EFFECTS

3.1 INTRODUCTION

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

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

3.2 DISCUSSION OF HEALTH EFFECTS BY ROUTE OF EXPOSURE

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

Levels of significant exposure for each route and duration are presented in tables and illustrated in figures. The points in the figures showing no-observed-adverse-effect levels (NOAELs) or lowest-observed-adverse-effect levels (LOAELs) reflect the actual doses (levels of exposure) used in the studies. LOAELs have been classified into "less serious" or "serious" effects. "Serious" effects are those that evoke failure in a biological system and can lead to morbidity or mortality (e.g., acute respiratory distress or death). "Less serious" effects are those that are not expected to cause significant dysfunction or death, or those whose significance to the organism is not entirely clear. ATSDR acknowledges that a considerable amount of judgment may be required in establishing whether an end point should be classified as a NOAEL, "less serious" LOAEL, or "serious" LOAEL, and that in some cases, there will be insufficient data to decide whether the effect is indicative of significant dysfunction. However, the Agency has established guidelines and policies that are used to classify these end points. ATSDR believes that there is sufficient merit in this approach to warrant an attempt at distinguishing between "less serious" and "serious" effects. The distinction between "less serious" effects and "serious" effects is considered to be important because it helps the users of the profiles to identify levels of exposure at which major health effects start to appear. LOAELs or NOAELs should also help in determining whether or not

the effects vary with dose and/or duration, and place into perspective the possible significance of these effects to human health.

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

3.2.1 Inhalation Exposure

Very little information is available regarding the health effects of 1,1-dichloroethane following inhalation exposure in humans or animals. 1,1-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 (Reid and Muianga 2012).

Table 3-1 and Figure 3-1 describe the health effects observed in laboratory animals associated with inhalation exposure levels at varying time and exposure durations.

3.2.1.1 Death

No studies were located regarding death in humans following inhalation exposure to 1,1-dichloroethane. In a review paper, Smyth (1956) reported that 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. It has been reported in the early literature that the lethal exposure level of 1,1-dichloroethane in mice was 17,500 ppm (Reid and Muianga 2012). These values were reported in a secondary source and it is therefore impossible to assess their validity. Subchronic intermittent exposure to 500 ppm of 1,1-dichloroethane for 13 weeks followed by 1,000 ppm of 1,1-dichloroethane for an additional 13 weeks was not lethal to rats, rabbits, guinea pigs, or cats (Hofmann et al. 1971).

The highest NOAEL values for death in each species and duration category are recorded in Table 3-1 and plotted in Figure 3-1.

3.2.1.2 Systemic Effects

No studies were located regarding respiratory, gastrointestinal, hematological, musculoskeletal, or dermal/ocular effects in humans or animals following inhalation exposure to 1,1-dichloroethane.

Cardiovascular Effects. A cardiostimulatory effect resulting in arrhythmias prompted the discontinuance of the use of 1,1-dichloroethane as an anesthetic in humans (Reid and Muianga 2012). 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 1,1-dichloroethane.

Hepatic Effects. No studies were located regarding hepatic effects in humans following inhalation exposure to 1,1-dichloroethane. Rats, rabbits, guinea pigs, and cats experienced no change in serum alanine aminotransferase or aspartate aminotransferase activity after intermittent 6-hour inhalation exposure to 500 ppm 1,1-dichloroethane for 13 weeks followed by 13 weeks of exposure 6 hours/day to 1,000 ppm 1,1-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 termination of a 10-day exposure to 6,000 ppm 1,1-dichloroethane (7 hours/day), a slight but statistically significant increase in relative liver weight (26% higher than controls) was observed in female Sprague-Dawley rats (Schwetz et al. 1974). However, there was no increase in aspartate aminotransferase activity over control values, and no changes in the gross appearance of the liver were noted at necropsy in these animals; the slight increase in liver weight was not considered adverse.

Renal Effects. No studies were located regarding renal effects in humans following inhalation exposure to 1,1-dichloroethane. Renal injury was apparent in cats intermittently exposed 6 hours/day to 1,000 ppm 1,1-dichloroethane for 13 weeks following 13 weeks of intermittent exposure to 500 ppm 1,1-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 in three of four cats at necropsy; renal tubular degenerations without preliminary lumen displacement and periglomerular fibrosis and tubule destruction were also observed. The ill health of these animals was also manifest by a progressive decrease in body weight. Rats, rabbits, and guinea pigs similarly exposed to 1,1-dichloroethane exhibited no adverse effects.

Table 3-1 Levels of Significant Exposure to 1,1-Dichloroethane - Inhalation

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (ppm)	LOAEL Less Serious (ppm)	LOAEL Serious (ppm)	Reference Chemical Form	Comments
ACUTE EXPOSURE								
Systemic								
1	Rat (Sprague-Dawley)	7 hr/d 10 d	Hepatic	6000 F			Schwetz et al. 1974	
Developmental								
2	Rat (Sprague-Dawley)	7 hr/d Gd 6-15		3000 F	6800 F (Increased incidence of delayed ossification)		Schwetz et al. 1974	
INTERMEDIATE EXPOSURE								
Systemic								
3	Rat (Sprague-Dawley)	6 hr/d 5 d/wk 26 wk	Hepatic	750			Hofmann et al. 1971 1,1-DCE	
			Renal	750				
			Bd Wt	750				
4	Gn Pig (Firbright-White)	6 hr/d 5 d/wk 26 wk	Hepatic	750			Hofmann et al. 1971 1,1-DCE	
			Renal	750				
			Bd Wt	750				
5	Rabbit (Brunte)	6 hr/d 5 d/wk 26 wk	Hepatic	750			Hofmann et al. 1971 1,1-DCE	
			Renal	750				
			Bd Wt	750				

Table 3-1 Levels of Significant Exposure to 1,1-Dichloroethane - Inhalation (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (ppm)	LOAEL Less Serious (ppm)	LOAEL Serious (ppm)	Reference Chemical Form	Comments
6	Cat (NS)	6 hr/d 5 d/wk 26 wk	Hepatic	750			Hofmann et al. 1971 1,1-DCE	
			Renal		750 (crystal precipitation and obstruction in tubule lumina)			
			Bd Wt	750				

a The number corresponds to entries in Figure 3-1.

Bd Wt = body weight; d = day(s); F = Female; Gd = gestational day; Gn pig = guinea pig; hr = hour(s); LOAEL = lowest-observed-adverse-effect level; NOAEL = no-observed-adverse-effect level; NS = not specified; wk = week(s)

Figure 3-1 Levels of Significant Exposure to 1,1-Dichloroethane - Inhalation

Acute (≤14 days)

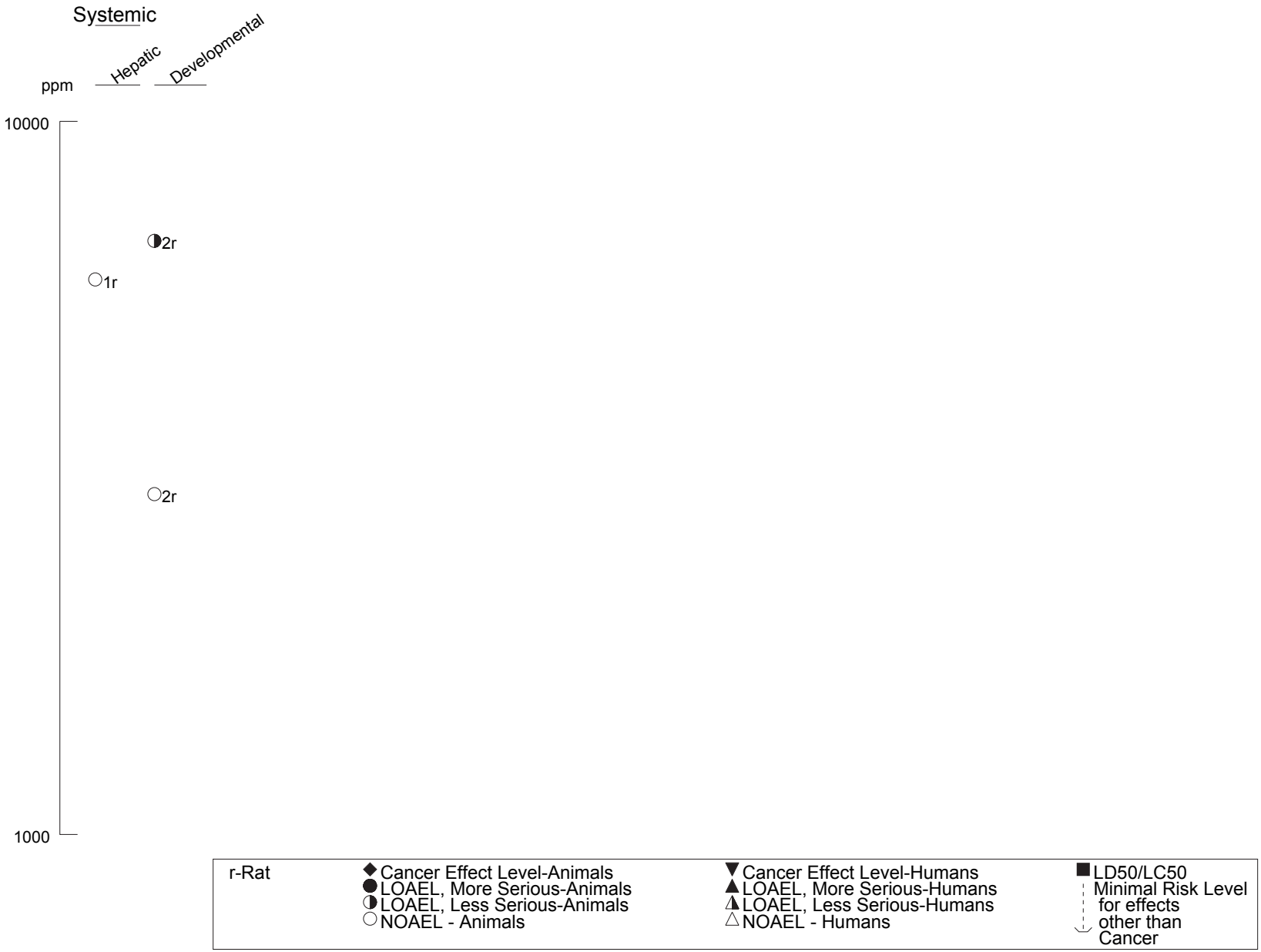
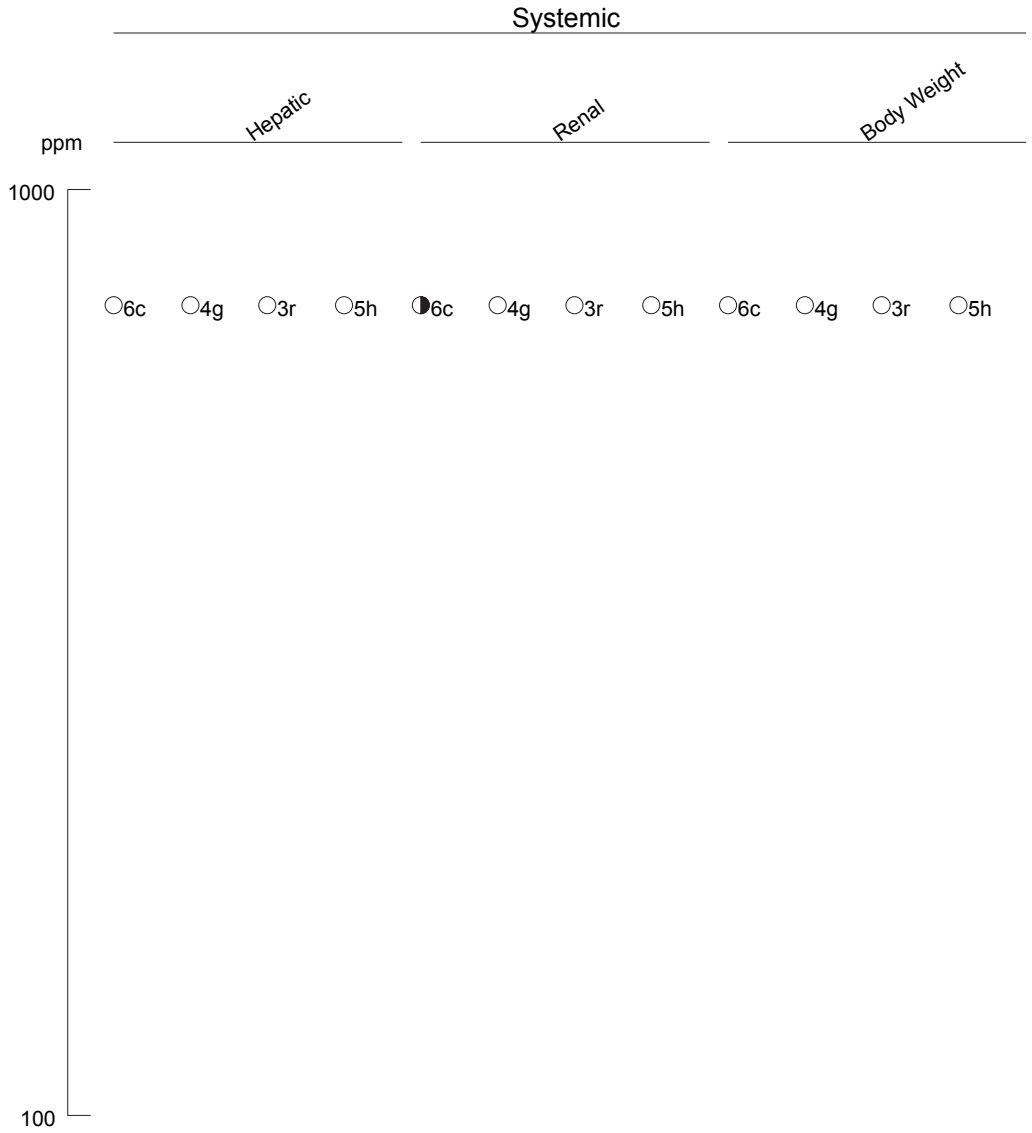


Figure 3-1 Levels of Significant Exposure to 1,1-Dichloroethane - Inhalation *(Continued)*

Intermediate (15-364 days)



c-Cat
r-Rat
h-Rabbit
g-Guinea Pig

◆ Cancer Effect Level-Animals
● LOAEL, More Serious-Animals
◑ LOAEL, Less Serious-Animals
○ NOAEL - Animals

▼ Cancer Effect Level-Humans
▲ LOAEL, More Serious-Humans
◭ LOAEL, Less Serious-Humans
△ NOAEL - Humans

■ LD50/LC50
Minimal Risk Level for effects other than Cancer

3.2.1.3 Immunological and Lymphoreticular Effects

No studies were located regarding immunological effects in humans or animals after inhalation exposure to 1,1-dichloroethane.

3.2.1.4 Neurological Effects

Since 1,1-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 1,1-dichloroethane in humans.

No studies were located regarding neurologic effects in animals after inhalation exposure to 1,1-dichloroethane.

3.2.1.5 Reproductive Effects

No studies were located regarding developmental effects in humans or animals following inhalation exposure to 1,1-dichloroethane.

3.2.1.6 Developmental Effects

No studies were located regarding reproductive effects in humans following inhalation exposure to 1,1-dichloroethane.

One study examined the developmental toxic potential of 1,1-dichloroethane following inhalation exposure. No alterations in litter size, fetal resorptions, fetal growth, or incidences of gross or soft tissue anomalies were observed in the offspring of Sprague-Dawley rats exposed to 3,800 or 6,000 ppm 7 hours/day on gestation days 6–15 (Schwetz et al. 1974). A significant increase in the incidence of fetuses with delayed ossification of sternebrae was observed at 6,000 ppm. 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; on gestation day 3, dams in the 3,800 and 6,000 ppm groups weighed 8 and 11% less than controls, respectively. No other adverse effects were noted in the dams. Based on the observed effects, the LOAEL value for the developmental toxicity of 1,1-dichloroethane in rats was 6,000 ppm; the NOAEL was 3,800 ppm. These values are listed in Table 3-1 and plotted in Figure 3-1.

3.2.1.7 Cancer

No studies were located regarding cancer in humans or animals after inhalation exposure to 1,1-dichloroethane.

3.2.2 Oral Exposure

Two studies were located that investigated the health effects associated with oral exposure to 1,1-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 1,1-dichloroethane.

Table 3-2 and Figure 3-2 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.

3.2.2.1 Death

No studies were located regarding death in humans following oral exposure to 1,1-dichloroethane.

Secondary sources report the following oral LD_{50} values in rats: 725 mg/kg (Lewis 2004) and 14.1 g/kg (Archer 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 the National Cancer Institute (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, although 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 3-2 and plotted in Figure 3-2.

Table 3-2 Levels of Significant Exposure to 1,1-Dichloroethane - Oral

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
INTERMEDIATE EXPOSURE								
Death								
1	Rat (Osborne-Mendel)	5 d/wk 6 wk (GO)				3160 F (2/5 rats died)	NCI 1977 1,1-DCE	
2	Mouse (B6C3F1)	5 d/wk 6 wk (GO)				5620 (4/10 deaths)	NCI 1977 1,1-DCE	
Systemic								
3	Rat (Osborne-Mendel)	5 d/wk 6 wk (GO)	Bd Wt		562 M (16% decreased body weight gain)	1000 M (29% decreased body weight gain)	NCI 1977 1,1-DCE	
4	Mouse (B6C3F1)	daily 52 wk (W)	Resp	465 M			Klaunig et al. 1986 1,1-DCE	
			Hepatic	465 M				
			Renal	465 M				
			Bd Wt	465 M				
5	Mouse (B6C3F1)	5 d/wk 6 wk (GO)	Bd Wt	2885 M			NCI 1977 1,1-DCE	

Table 3-2 Levels of Significant Exposure to 1,1-Dichloroethane - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
CHRONIC EXPOSURE								
Systemic								
6	Rat (Osborne-Mendel)	5 d/wk 78 wk (GO)	Resp	764 M			NCI 1977 1,1-DCE	
			Cardio	764 M				
			Hemato	764 M				
			Musc/skel	764 M				
			Hepatic	764 M				
			Renal	764 M				
			Endocr	764 M				
			Dermal	764 M				
			Bd Wt	764 M				
7	Mouse (B6C3F1)	5 d/wk 78 wk (GO)	Resp	2885 M			NCI 1977 1,1-DCE	
			Cardio	2885 M				
			Gastro	2885 M				
			Musc/skel	2885 M				
			Hepatic	2885 M				
			Renal	2885 M				
			Endocr	2885 M				
			Dermal	2885 M				
			Bd Wt	2885 M				

a The number corresponds to entries in Figure 3-2.

Bd Wt = body weight; Cardio = cardiovascular; d = day(s); Endocr = endocrine; F = Female; Gastro = gastrointestinal; (GO) = gavage in oil; Hemato = hematological; hr = hour(s); LOAEL = lowest-observed-adverse-effect level; M = male; Musc/skel = musculoskeletal; NOAEL = no-observed-adverse-effect level; NS = not specified; Resp = respiratory; (W) = drinking water; wk = week(s)

Figure 3-2 Levels of Significant Exposure to 1,1-Dichloroethane - Oral

Intermediate (15-364 days)

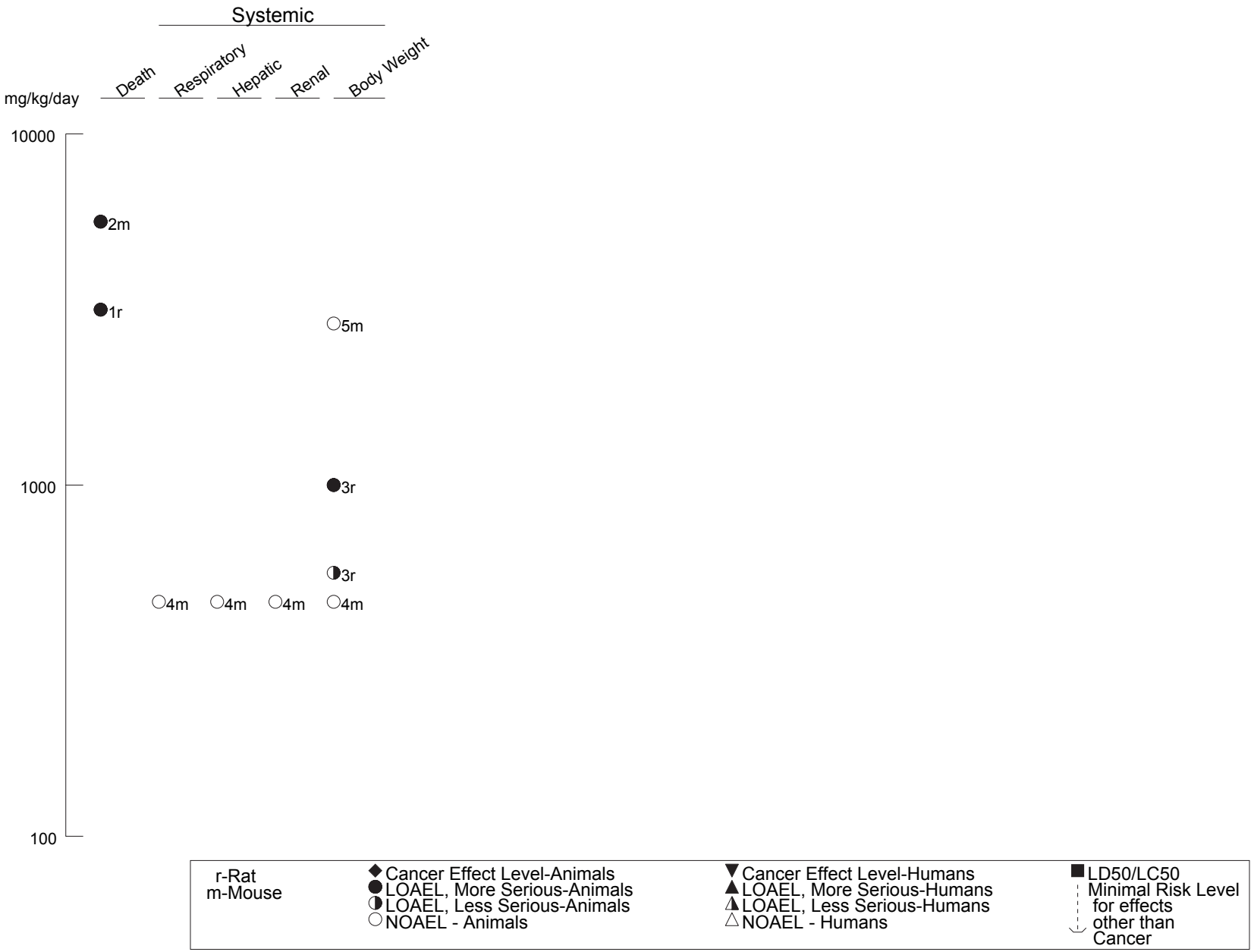
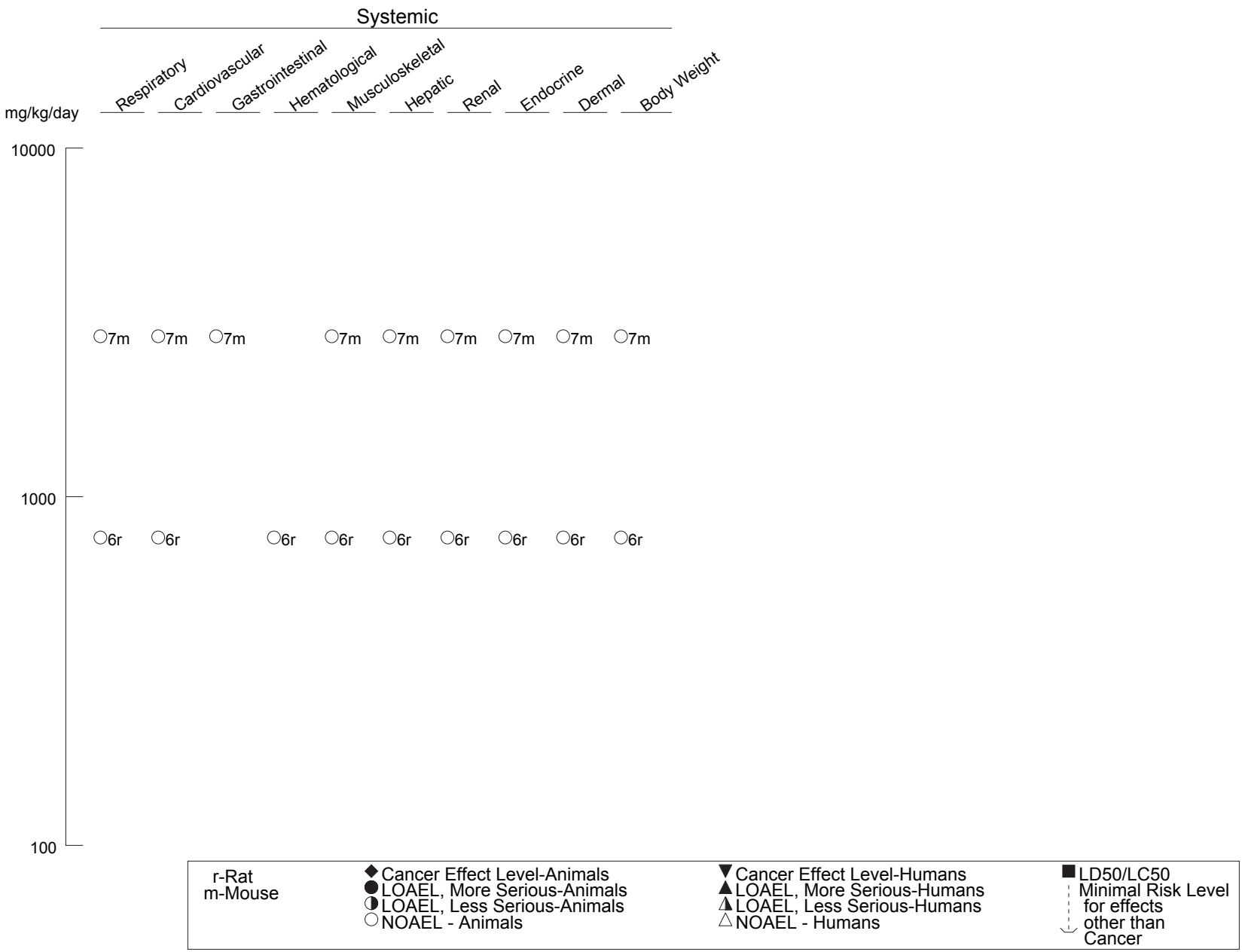


Figure 3-2 Levels of Significant Exposure to 1,1-Dichloroethane - Oral *(Continued)*

Chronic (≥365 days)



3.2.2.2 Systemic Effects

No studies were located regarding systemic effects in humans following oral exposure to 1,1-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 1,1-dichloroethane in drinking water (up to 2500 mg/L) for 52 weeks (Klaunig et al. 1986).

Respiratory Effects. No histological alterations were observed in the lungs of mice exposed to 465 mg/kg/day 1,1-dichloroethane in drinking water for 52 weeks (Klaunig et al. 1986). Similarly, no significant alterations in respiratory tract lesions were observed in rats or mice chronically exposed to 1,1-dichloroethane for 78 weeks (NCI 1977). The highest gavage doses were 764 and 950 mg/kg/day (5 days/week) in male and female rats, respectively, and 2,885 and 3,331 mg/kg (5 days/week) in male and female mice, respectively.

Cardiovascular Effects. The NCI (1977) chronic-duration gavage study did not find significant alterations in the incidence of lesions in the cardiovascular system.

Gastrointestinal Effects. No gastrointestinal effects were reported in rats or mice administered gavage doses of 1,1-dichloroethane for 78 weeks (NCI 1977).

Hematological Effects. No histological alterations were observed in hematological tissues in rats or mice chronically exposed to 1,1-dichloroethane (NCI 1977); however, the study did not examine the potential for alterations in erythrocyte or leukocyte counts or hemoglobin levels.

Musculoskeletal Effects. No musculoskeletal alterations were reported in the NCI (1977) chronic study of rats and mice.

Hepatic Effects. No nonneoplastic alterations were observed in mice exposed to 465 mg/kg/day via drinking water for 52 weeks (Klaunig et al. 1986) or in rats or mice administered 764/950 mg/kg/day or

2,885/3,331 mg/kg/day 1,1-dichloroethane, respectively, via gavage 5 days/week for 78 weeks (NCI 1977).

Renal Effects. Intermediate-duration drinking exposure of mice (Klaunig et al. 1986) or chronic gavage administration to rats and mice (NCI 1977) did not result in significant alteration in the occurrence of renal lesions.

Endocrine Effects. No histological alterations in endocrine tissues were observed in rats or mice chronically administered 1,1-dichloroethane (NCI 1977).

Dermal Effects. No dermal effects were noted in rats or mice administered 1,1-dichloroethane for 78 weeks (NCI 1977).

Ocular Effects. No eye damage was noted in rats or mice following chronic administration of 1,1-dichloroethane (NCI 1977).

Body Weight Effects. Administration of doses as high as 562 mg/kg/day in male rats and 1,780 mg/kg/day in female rats 5 days/week for 6 weeks resulted in decreases in body weight gain (≥16%) (NCI 1977); no alterations in body weight were observed in mice similarly exposed to doses as high as 10,000 mg/kg/day (NCI 1977). This study did not find significant decreases in body weight gain following 78 weeks of exposure (5 days/week) to 764 and 950 mg/kg/day, respectively, in male and female rats and 2,885 and 3,331 mg/kg/day, respectively, in male and female mice (NCI 1977). Similarly, no alterations in body weight gain were observed in mice exposed to 465 mg/kg/day in drinking water for 52 weeks (Klaunig et al. 1986).

No studies were located regarding the following health effects in humans or animals following oral exposure to 1,1-dichloroethane:

3.2.2.3 Immunological and Lymphoreticular Effects
3.2.2.4 Neurological Effects
3.2.2.5 Reproductive Effects
3.2.2.6 Developmental Effects

3.2.2.7 Cancer

No studies were located regarding carcinogenic effects in humans following oral exposure to 1,1-dichloroethane. The results of the bioassay conducted by NCI (1977) suggest carcinogenic effects induced by 1,1-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 exposed to 3,331 mg/kg/day, 5 days/week was significantly increased over the corresponding control animals. When only male mice surviving at least 52 weeks were examined, there was a significant increase in the incidence of hepatocellular carcinomas in the 2,885 mg/kg/day group. There are several limitations to this study. Survival was poor in both treated and control animals, thereby limiting the validity of these results. Although survival was significantly lower in the exposed groups, 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 1,1-dichloroethane is carcinogenic to rats and mice, the evidence is not conclusive.

The carcinogenicity of 1,1-dichloroethane was also examined in mice exposed to 155 or 465 mg/kg/day of the compound in the drinking water for 52 weeks (Klaunig et al. 1986). A two-stage carcinogenesis protocol was also employed in this study to assess the ability of 1,1-dichloroethane to act as a tumor promoter. Neither 1,1-dichloroethane-treated animals initiated with diethylnitrosamine (DENA) or animals treated with 1,1-dichloroethane without initiation showed a significant increase in the incidence of lung or liver tumors over their corresponding controls. However, the conclusion that 1,1-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 1,1-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 1-week period; amber bottles with Teflon stoppers and double sipper tubes were used. Since 1,1-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 NCI (1977) and Klaunig et al. (1986) studies may be due to the method of administration, vehicle, and/or doses used. The pharmacokinetics of 1,1-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, 1990b). Furthermore, the doses given to mice by gavage were approximately 6 times higher than the drinking water concentrations. Sufficient information is not available to assess the contributions of these factors to the apparently disparate responses.

Milman et al. (1988) examined the carcinogenic potential of 1,1-dichloroethane in initiation and promotion assays. In partially hepatectomized Osborne-Mendel rats receiving a single gavage dose of 700 mg/kg 1,1-dichloroethane in corn oil followed by dietary exposure to phenobarbitol for 7 weeks, there were no alterations in gamma-glutamyltranspeptidase (GGT)-altered foci. However, in the promotion assay in which partially hepatecomized Osborne-Mendel rats received an intraperitoneal dose of diethylnitrosamine followed by gavage administration of 700 mg/kg 1,1-dichloroethane in corn oil 5 days/week for 7 weeks, there was an increase in the total number of GGT-altered foci.

3.2.3 Dermal Exposure

No studies were located regarding the following health effects in humans or animals after dermal exposure to 1,1-dichloroethane:

3.2.3.1 Death
3.2.3.2 Systemic Effects
3.2.3.3 Immunological and Lymphoreticular Effects
3.2.3.4 Neurological Effects
3.2.3.5 Reproductive Effects
3.2.3.6 Developmental Effects
3.2.3.7 Cancer

Table 3-3. Genotoxicity of 1,1-Dichloroethane *In Vitro*

Species (test system)	End point	Results		Reference
		With activation	Without activation	
Prokaryotic organisms:				
Salmonella typhimuriu,m strains TA97, TA98, TA100, and TA102 (Ames assay)	Gene mutation	–	–	Nohmi et al. 1986
S. typhimurium, strains TA1535, TA1537, TA1538, TA98, and TA100 (Ames assay)	Gene mutation	–	–	Simmon et al. 1977
S. typhimurium, strains TA1537, TA98, TA100, and TA1535 (dessicator assay; vapor exposure)	Gene mutation	+	+	Riccio et al. 1983
S. typhimurium, strains TA1535, TA98, and TA100 (Ames assay; dessicator)	Gene mutation	+	+	Milman et al. 1988
Eukaryotic organisms:				
Saccharomyces cerevisiae D7	Gene mutation	–	–	Bronzetti et al. 1987
Mammalian cells				
Syrian hamster embryo (cell transformation assay; vapor exposure)	DNA viral transformation	No data	+	Hatch et al. 1983
Osborne-Mendel rat and B6C3F1 mouse hepatocytes	DNA repair	No data	+	Milman et al. 1988
BALB/C-3T3 (cell transformation assay; exposure in sealed chamber)	Cell transformation	No data	–	Tu et al. 1985
BALB/C-3T3 (cell transformation assay; exposure in sealed chamber)	Cell transformation	No data	–	Milman et al. 1998
Chinese hamster lung fibroblasts (chromosomal aberration assay; exposure in sealed chamber)	Chromosomal aberrations	–	–	Matsuoka et al. 1998)

— = negative result; + = positive result; ± = weakly positive

3.3 GENOTOXICITY

A limited number of studies have examined the genotoxicity of 1,1-dichloroethane. No studies were located regarding *in vivo* genotoxic effects in humans. The genotoxic potential of 1,1-dichloroethane has been investigated *in vitro* in bacteria, fungus, and mammalian systems; the results of these studies are summarized in Table 3-3. 1,1-Dichloroethane did not result in an increase in reverse mutations in *Salmonella typhimurium* strains with or without metabolic activation in Ames assays (Nohmi et al. 1985; Simmon et al. 1977). In contrast, Riccio et al. (1983, as reported in an abstract) and Milman et al. (1988) reported positive mutagenic alterations in *S. typhimurium* exposed to 1,1-dichloroethane vapor in a desiccator assay in the presence and absence of S9 mix. Negative findings for mutagenicity were observed in *Saccharomyes cerevisiae* exposed to 1,1-dichloroethane, with or without metabolic activation (Bronzetti et al. 1987).

Similarly, negative genotoxicity results have been observed in mammalian cell assays. *In vitro* exposure to 1,1-dichloroethane did not induce increases in cell transformations in BALB/C-3T3 cells (Milman et al. 1988; Tu et al. 1985) or chromosomal aberrations in Chinese hamster lung fibroblasts (Matsuoka et al. 1998). However, an increase in Simian adenovirus (SA7)-induced transformations was observed in Syrian hamster embryo cells (Hatch et al. 1983) and an increase in DNA repair was found in hepatocytes from Osborne-Mendel rats and B6C3F1 mice (Milman et al. 1988).

In an *in vivo* study by Colacci et al. (1985), 1,1-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 1,1-dichloroethane to nucleic acids and proteins was mediated by liver P-450 dependent microsomal mixed function oxidase system. Glutathione-S-transferase (GSH) 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, phenobarbitone 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 1,1-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 phenobarbitone enhanced the binding to DNA, microsomal RNA and proteins while addition of glutathione-s-transferase to the microsomal systems caused

suppression of binding. Because only radioactivity was measured it is difficult to determine whether the μmole bound represents 1,1-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 1,1-dichloroethane. The fact that 1,1-dichloroethane binds to nucleic acid suggests that it may have a potential to produce mutation in a mammalian system.

3.4 TOXICOKINETICS

3.4.1 Absorption

3.4.1.1 Inhalation Exposure

No studies were located in humans or animals regarding the absorption of inhaled 1,1-dichloroethane. However, its use as a gaseous anesthetic agent in humans provides evidence of its absorption. Furthermore, the volatile and lipophilic nature of 1,1-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 1,1-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 1,1-dichloroethane, 1,2-dichloroethane, is well-absorbed following inhalation exposure. However, the blood/air partition coefficient for 1,2-dichloroethane is approximately 4 times that of 1,1-dichloroethane. This suggests that 1,1-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).

3.4.1.2 Oral Exposure

No studies were located that quantitated the absorption of ingested 1,1-dichloroethane in humans or animals. However, when 700 mg [^{14}C]-1,1-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, although there was no quantitative assessment made of the extent or rate of absorption (Mitoma et al. 1985).

3.4.1.3 Dermal Exposure

No studies were located regarding the absorption of 1,1-dichloroethane in humans or animals following dermal exposure. However, Reid and Muianga (2012) reported evidence that 1,1-dichloroethane penetrates the skin. 1,1-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, although no quantitative assessment of the extent or rate of absorption was possible.

3.4.2 Distribution

3.4.2.1 Inhalation Exposure

No studies were located in humans or animals regarding the distribution of 1,1-dichloroethane following inhalation exposure. However, 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 1,1-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 1,1-dichloroethane) (Sato and Nakajima 1987).

3.4.2.2 Oral Exposure

No studies were located regarding the distribution of 1,1-dichloroethane following oral exposure in humans or animals.

3.4.2.3 Dermal Exposure

No studies were located regarding the distribution of 1,1-dichloroethane following dermal exposure in humans or animals.

3.4.2.4 Other Routes of Exposure

Rats and mice were intraperitoneally injected with 1.2 mg [^{14}C]-1,1-dichloroethane/kg and sacrificed 22 hours later. 1,1-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 1,1-dichloroethane very likely occurs to other tissues, the liver, kidney, lung, and stomach were the only tissues analyzed in this study.

3.4.3 Metabolism

The metabolism of 1,1-dichloroethane has not been extensively characterized. *In vivo* studies of the metabolism of 1,1-dichloroethane in humans and animals are very limited. Elucidation of 1,1-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 1,1-dichloroethane is mediated by hepatic microsomal cytochrome P-450 system.

In rats and mice orally administered 700 or 1,800 mg/kg, respectively, 1,1-dichloroethane (5 days/week for 4 weeks followed by a single dose of radiolabelled 1,1-dichloroethane), most of the radiolabel was detected in expired air; the investigators assumed that this was parent compound (Mitoma et al. 1985). Forty-eight hours after oral administration, 7.4 and 29.3% of the radiolabel was detected in the urine, carcass, or expired carbon dioxide. The investigators assumed that this represented metabolized 1,1-dichloroethane; however, only radiolabel was measured in the carcass. It is likely that the ingested radiolabeled 1,1-dichloroethane underwent first-pass extraction by the liver. It is possible that high doses used in this study exceeded the capacity of the animals to metabolize 1,1-dichloroethane. 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.

An *in vitro* study demonstrated cytochrome P450 metabolism of 1,1-dichloroethane. McCall et al. (1983) demonstrated 1,1-dichloroethane binding to hepatic microsomal cytochrome P450 from rats; as compared to microsomes from untreated rats, cytochrome P450 binding was 2.25 times higher, per mole of cytochrome, in microsomes from phenobarbital-stimulated rats. Administration of β-naphthaflavone had no effect on the extent of 1,1-dichloroethane binding to cytochrome P450 binding. *In vitro* exposure of hepatic microsomal to 1,1-dichloroethane also stimulated NADPH oxidation. The rate and extent of

1,1-dichloroethane metabolism was increased 6.3 times in the hepatic microsomes of rats that were induced by chronic ethanol consumption (Sato et al. 1980).

Metabolism of 1,1-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 3-4) (McCall et al. 1983). On the basis of these results, pathways for the metabolism of 1,1-dichloroethane were proposed (Figure 3-3). The initial steps in the metabolism of 1,1-dichloroethane were proposed to involve cytochrome P-450-dependent hydroxylations at either carbon. Hydroxylation at C-1 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}Cl of 1,1-dichloroethane was enzymatically removed after 30 minutes, while <0.5% of the ^{36}Cl of 1,2-dichloroethane was removed (Van Dyke and Wineman 1971).

Under hypoxic conditions, 1,1-dichloroethane gives rise to free radicals. However, its ability to develop free radicals is much less when compared to 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).

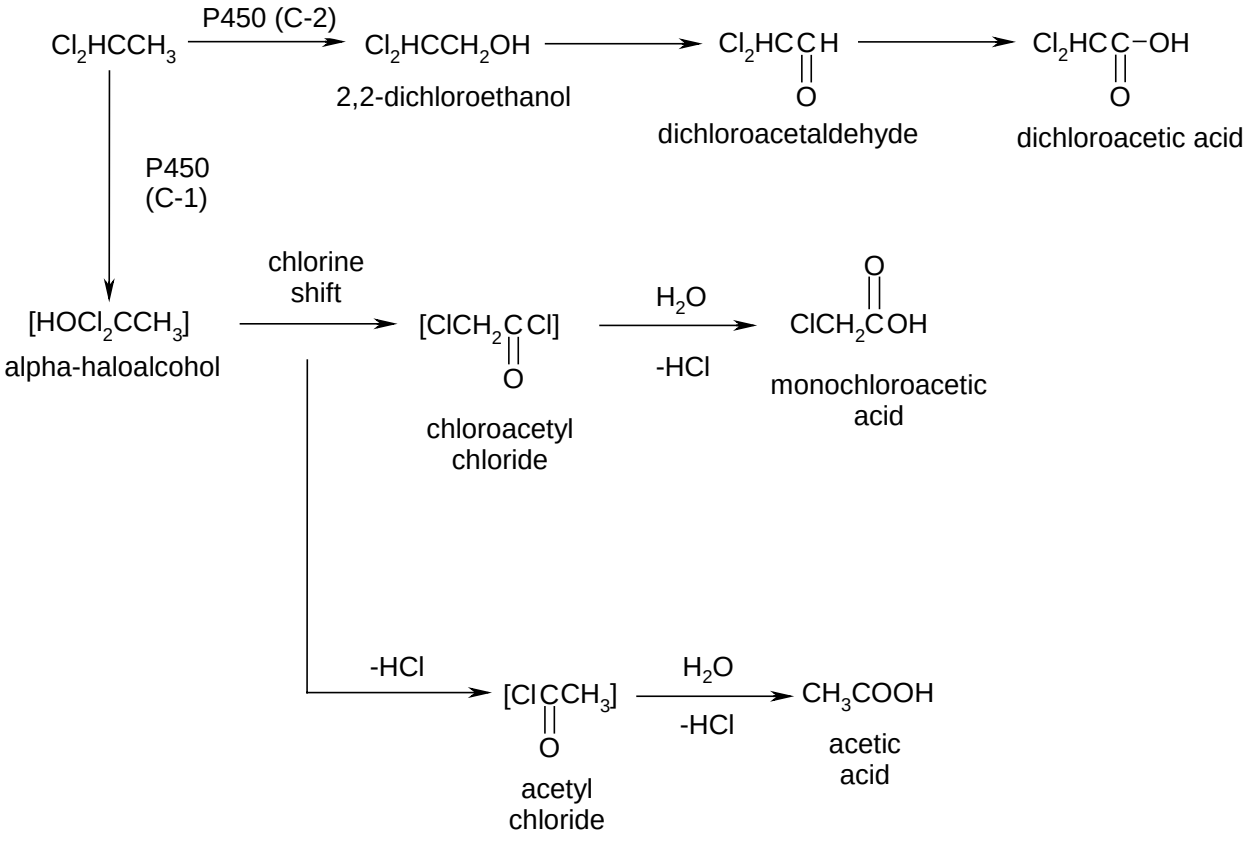
Table 3-4. Production of Metabolites from 1,1-Dichloroethane with Hepatic Microsomes from Phenobarbital-Induced Rats

Metabolites	Metabolic production[a] (nmoles/mg microsomal protein/20 minutes)
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 (standard deviation) for determinations in triplicate on three to five separate preparations of hepatic microsomes.

Source: McCall et al. 1983

Figure 3-3. Proposed Metabolic Scheme for 1,1-Dichloroethane



Source: McCall et al. 1983

3.4.4 Elimination and Excretion

3.4.4.1 Inhalation Exposure

No empirical data on the elimination of excretion of 1,1-dichloroethane in humans or animals were identified. Sato and Nakajima (1987) predicted that 59% of inhaled 1,1-dichloroethane would be metabolized and excreted in the urine and 41% would be eliminated in expired air.

3.4.4.2 Oral Exposure

Mitoma et al. (1985) examined excretion of 1,1-dichloroethane in rats and mice administered 1,1-dichloroethane via gavage 700 or 1,800 mg/kg, respectively, 5 days/week for 4 weeks followed by a single dose of radiolabelled 1,1-dichloroethane. In the rats, 86% of the administered dose was excreted in expired air 5% expired as carbon dioxide and 0.9% was detected in the urine. In mice, 70% was excreted in expired air, 25% was expired as carbon dioxide, and 1.6% was detected in urine. Because rats and mice were administered different doses, a determination cannot be made as to whether the differences in excretion and metabolism are due to species differences or are a reflection of different doses.

3.4.4.3 Dermal Exposure

No studies were located in humans or animals regarding excretion of 1,1-dichloroethane following dermal exposure

3.4.5 Physiologically Based Pharmacokinetic (PBPK)/Pharmacodynamic (PD) Models

Physiologically based pharmacokinetic (PBPK) models use mathematical descriptions of the uptake and disposition of chemical substances to quantitatively describe the relationships among critical biological processes (Krishnan et al. 1994). PBPK models are also called biologically based tissue dosimetry models. PBPK models are increasingly used in risk assessments, primarily to predict the concentration of potentially toxic moieties of a chemical that will be delivered to any given target tissue following various combinations of route, dose level, and test species (Clewell and Andersen 1985). Physiologically based pharmacodynamic (PBPD) models use mathematical descriptions of the dose-response function to quantitatively describe the relationship between target tissue dose and toxic end points.

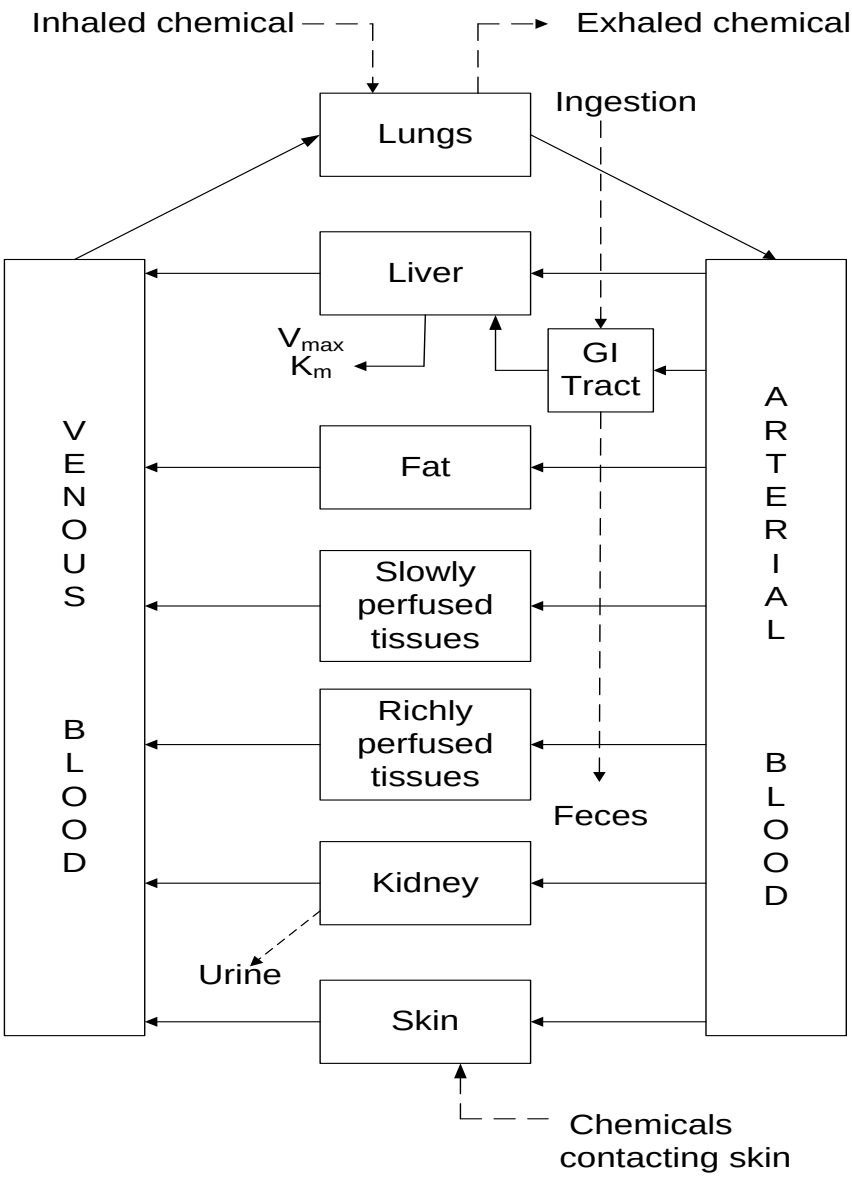
PBPK/PD models refine our understanding of complex quantitative dose behaviors by helping to delineate and characterize the relationships between: (1) the external/exposure concentration and target tissue dose of the toxic moiety, and (2) the target tissue dose and observed responses (Andersen and Krishnan 1994; Andersen et al. 1987). These models are biologically and mechanistically based and can be used to extrapolate the pharmacokinetic behavior of chemical substances from high to low dose, from route to route, between species, and between subpopulations within a species. The biological basis of PBPK models results in more meaningful extrapolations than those generated with the more conventional use of uncertainty factors.

The PBPK model for a chemical substance is developed in four interconnected steps: (1) model representation, (2) model parameterization, (3) model simulation, and (4) model validation (Krishnan and Andersen 1994). In the early 1990s, validated PBPK models were developed for a number of toxicologically important chemical substances, both volatile and nonvolatile (Krishnan and Andersen 1994; Leung 1993). PBPK models for a particular substance require estimates of the chemical substance-specific physicochemical parameters, and species-specific physiological and biological parameters. The numerical estimates of these model parameters are incorporated within a set of differential and algebraic equations that describe the pharmacokinetic processes. Solving these differential and algebraic equations provides the predictions of tissue dose. Computers then provide process simulations based on these solutions.

The structure and mathematical expressions used in PBPK models significantly simplify the true complexities of biological systems. If the uptake and disposition of the chemical substance(s) are adequately described, however, this simplification is desirable because data are often unavailable for many biological processes. A simplified scheme reduces the magnitude of cumulative uncertainty. The adequacy of the model is, therefore, of great importance, and model validation is essential to the use of PBPK models in risk assessment.

PBPK models improve the pharmacokinetic extrapolations used in risk assessments that identify the maximal (i.e., the safe) levels for human exposure to chemical substances (Andersen and Krishnan 1994). PBPK models provide a scientifically sound means to predict the target tissue dose of chemicals in humans who are exposed to environmental levels (for example, levels that might occur at hazardous waste sites) based on the results of studies where doses were higher or were administered in different species. Figure 3-4 shows a conceptualized representation of a PBPK model.

Figure 3-4. Conceptual Representation of a Physiologically Based Pharmacokinetic (PBPK) Model for a Hypothetical Chemical Substance



Note: This is a conceptual representation of a physiologically based pharmacokinetic (PBPK) model for a hypothetical chemical substance. The chemical substance is shown to be absorbed via the skin, by inhalation, or by ingestion, metabolized in the liver, and excreted in the urine or by exhalation.

Source: adapted from Krishnan and Andersen 1994

If PBPK models for 1,1-dichloroethane exist, the overall results and individual models are discussed in this section in terms of their use in risk assessment, tissue dosimetry, and dose, route, and species extrapolations.

No PBPK models were identified for 1,1-dichloroethane.

3.5 MECHANISMS OF ACTION

3.5.1 Pharmacokinetic Mechanisms

No information was identified on the pharmacokinetic mechanisms of action of 1,1-dichloroethane.

3.5.2 Mechanisms of Toxicity

There are limited data to identify the critical targets of 1,1-dichloroethane toxicity or to elucidate the mode of action for the observed effects.

3.5.3 Animal-to-Human Extrapolations

The inhalation study by Hofmann et al. (1971) found species differences in the renal toxicity of 1,1-dichloroethane. Crystalline precipitations and tubular obstruction were observed in cats, but not in rats, rabbits, or guinea pigs. There are insufficient data to determine whether this would also be a relevant end point in humans and whether humans would be as sensitive to this effect as cats.

3.6 TOXICITIES MEDIATED THROUGH THE NEUROENDOCRINE AXIS

Recently, attention has focused on the potential hazardous effects of certain chemicals on the endocrine system because of the ability of these chemicals to mimic or block endogenous hormones. Chemicals with this type of activity are most commonly referred to as *endocrine disruptors*. However, appropriate terminology to describe such effects remains controversial. The terminology *endocrine disruptors*, initially used by Thomas and Colborn (1992), was also used in 1996 when Congress mandated the EPA to develop a screening program for "...certain substances [which] may have an effect produced by a naturally occurring estrogen, or other such endocrine effect[s]...". To meet this mandate, EPA convened a panel called the Endocrine Disruptors Screening and Testing Advisory Committee (EDSTAC), and in 1998, the EDSTAC completed its deliberations and made recommendations to EPA concerning *endocrine disruptors*. In 1999, the National Academy of Sciences released a report that referred to these same types

of chemicals as *hormonally active agents*. The terminology *endocrine modulators* has also been used to convey the fact that effects caused by such chemicals may not necessarily be adverse. Many scientists agree that chemicals with the ability to disrupt or modulate the endocrine system are a potential threat to the health of humans, aquatic animals, and wildlife. However, others think that endocrine-active chemicals do not pose a significant health risk, particularly in view of the fact that hormone mimics exist in the natural environment. Examples of natural hormone mimics are the isoflavinoid phytoestrogens (Adlercreutz 1995; Livingston 1978; Mayr et al. 1992). These chemicals are derived from plants and are similar in structure and action to endogenous estrogen. Although the public health significance and descriptive terminology of substances capable of affecting the endocrine system remains controversial, scientists agree that these chemicals may affect the synthesis, secretion, transport, binding, action, or elimination of natural hormones in the body responsible for maintaining homeostasis, reproduction, development, and/or behavior (EPA 1997). Stated differently, such compounds may cause toxicities that are mediated through the neuroendocrine axis. As a result, these chemicals may play a role in altering, for example, metabolic, sexual, immune, and neurobehavioral function. Such chemicals are also thought to be involved in inducing breast, testicular, and prostate cancers, as well as endometriosis (Berger 1994; Giwercman et al. 1993; Hoel et al. 1992).

No studies were located regarding endocrine disruption in [humans and/or animals] after exposure to 1,1-dichloroethane.

No *in vitro* studies were located regarding endocrine disruption of 1,1-dichloroethane.

3.7 CHILDREN'S SUSCEPTIBILITY

This section discusses potential health effects from exposures during the period from conception to maturity at 18 years of age in humans, when all biological systems will have fully developed. Potential effects on offspring resulting from exposures of parental germ cells are considered, as well as any indirect effects on the fetus and neonate resulting from maternal exposure during gestation and lactation. Relevant animal and *in vitro* models are also discussed.

Children are not small adults. They differ from adults in their exposures and may differ in their susceptibility to hazardous chemicals. Children's unique physiology and behavior can influence the extent of their exposure. Exposures of children are discussed in Section 6.6, Exposures of Children.

Children sometimes differ from adults in their susceptibility to hazardous chemicals, but whether there is a difference depends on the chemical (Guzelian et al. 1992; NRC 1993). Children may be more or less susceptible than adults to health effects, and the relationship may change with developmental age (Guzelian et al. 1992; NRC 1993). Vulnerability often depends on developmental stage. There are critical periods of structural and functional development during both prenatal and postnatal life, and a particular structure or function will be most sensitive to disruption during its critical period(s). Damage may not be evident until a later stage of development. There are often differences in pharmacokinetics and metabolism between children and adults. For example, absorption may be different in neonates because of the immaturity of their gastrointestinal tract and their larger skin surface area in proportion to body weight (Morselli et al. 1980; NRC 1993); the gastrointestinal absorption of lead is greatest in infants and young children (Ziegler et al. 1978). Distribution of xenobiotics may be different; for example, infants have a larger proportion of their bodies as extracellular water, and their brains and livers are proportionately larger (Altman and Dittmer 1974; Fomon 1966; Fomon et al. 1982; Owen and Brozek 1966; Widdowson and Dickerson 1964). The fetus/infant has an immature (developing) blood-brain barrier that past literature has often described as being leaky and poorly intact (Costa et al. 2004). However, current evidence suggests that the blood-brain barrier is anatomically and physically intact at this stage of development, and the restrictive intracellular junctions that exist at the blood-CNS interface are fully formed, intact, and functionally effective (Saunders et al. 2008, 2012).

However, during development of the blood-brain barrier, there are differences between fetuses/infants and adults which are toxicologically important. These differences mainly involve variations in physiological transport systems that form during development (Ek et al. 2012). These transport mechanisms (influx and efflux) play an important role in the movement of amino acids and other vital substances across the blood-brain barrier in the developing brain; these transport mechanisms are far more active in the developing brain than in the adult. Because many drugs or potential toxins may be transported into the brain using these same transport mechanisms—the developing brain may be rendered more vulnerable than the adult. Thus, concern regarding possible involvement of the blood-brain barrier with enhanced susceptibility of the developing brain to toxins is valid. It is important to note however, that this potential selective vulnerability of the developing brain is associated with essential normal physiological mechanisms; and not because of an absence or deficiency of anatomical/physical barrier mechanisms.

The presence of these unique transport systems in the developing brain of the fetus/infant is intriguing; as it raises a very important toxicological question as to whether these mechanisms provide protection for the developing brain or do they render it more vulnerable to toxic injury. Each case of chemical exposure

should be assessed on a case-by-case basis. Research continues into the function and structure of the blood-brain barrier in early life (Kearns et al. 2003; Saunders et al. 2012; Scheuplein et al. 2002).

Many xenobiotic metabolizing enzymes have distinctive developmental patterns. At various stages of growth and development, levels of particular enzymes may be higher or lower than those of adults, and sometimes unique enzymes may exist at particular developmental stages (Komori et al. 1990; Leeder and Kearns 1997; NRC 1993; Vieira et al. 1996). Whether differences in xenobiotic metabolism make the child more or less susceptible also depends on whether the relevant enzymes are involved in activation of the parent compound to its toxic form or in detoxification. There may also be differences in excretion, particularly in newborns who have a low glomerular filtration rate and have not developed efficient tubular secretion and resorption capacities (Altman and Dittmer 1974; NRC 1993; West et al. 1948). Children and adults may differ in their capacity to repair damage from chemical insults. Children also have a longer remaining lifetime in which to express damage from chemicals; this potential is particularly relevant to cancer.

Certain characteristics of the developing human may increase exposure or susceptibility, whereas others may decrease susceptibility to the same chemical. For example, although infants breathe more air per kilogram of body weight than adults breathe, this difference might be somewhat counterbalanced by their alveoli being less developed, which results in a disproportionately smaller surface area for alveolar absorption (NRC 1993).

Information on children's susceptibility to the toxic effects of 1,1-dichloroethane is limited to a developmental toxicity study in rats (Schwetz et al. 1974) that found an increase in the incidence of delayed ossifications in the fetuses of dams exposed to 6,000 ppm 1,1-dichloroethane on gestation days 6–15. An *in vitro* study (Andrews et al. 2002; only available as an abstract) utilizing rat whole embryo cultures reported eye defects in at 17.9 mM; this concentration also reported in 35% embryolethality.

3.8 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).

The National Report on Human Exposure to Environmental Chemicals provides an ongoing assessment of the exposure of the U.S. population to environmental chemicals using biomonitoring. This report is available at http://www.cdc.gov/exposurereport/. The biomonitoring data for 1,1-dichloroethane from this report is discussed in Section 6.5. A biomarker of exposure is a xenobiotic substance or its metabolite(s) or the product of an interaction between a xenobiotic agent and some target molecule(s) or cell(s) that is measured within a compartment of an organism (NAS/NRC 1989). The preferred biomarkers of exposure are generally the substance itself, substance-specific metabolites in readily obtainable body fluid(s), or excreta. However, several factors can confound the use and interpretation of biomarkers of exposure. The body burden of a substance may be the result of exposures from more than one source. The substance being measured may be a metabolite of another xenobiotic substance (e.g., high urinary levels of phenol can result from exposure to several different aromatic compounds). Depending on the properties of the substance (e.g., biologic half-life) and environmental conditions (e.g., duration and route of exposure), the substance and all of its metabolites may have left the body by the time samples can be taken. It may be difficult to identify individuals exposed to hazardous substances that are commonly found in body tissues and fluids (e.g., essential mineral nutrients such as copper, zinc, and selenium). Biomarkers of exposure to 1,1-dichloroethane are discussed in Section 3.8.1.

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 not often substance specific. They also may not be directly adverse, but can indicate potential health impairment (e.g., DNA adducts). Biomarkers of effects caused by 1,1-dichloroethane are discussed in Section 3.8.2.

A biomarker of susceptibility is an indicator of an inherent or acquired limitation of an organism's ability to respond to the challenge of exposure to a specific xenobiotic substance. It can be an intrinsic genetic or other characteristic or a preexisting disease that results in an increase in absorbed dose, a decrease in the biologically effective dose, or a target tissue response. If biomarkers of susceptibility exist, they are discussed in Section 3.10, Populations That Are Unusually Susceptible.

3.8.1 Biomarkers Used to Identify or Quantify Exposure to 1,1-Dichloroethane

As summarized in Section 6.5, 1,1-dichloroethane was not detected in blood samples collected from the National Health and Nutrition Examination Survey (2003–2004). No other biomarkers that could be used to identify or quantify exposure to 1,1-dichloroethane were identified.

3.8.2 Biomarkers Used to Characterize Effects Caused by 1,1-Dichloroethane

1,1-Dichloroethane was used as an anesthetic in the early part of the 20th century (Konietzko 1984; Reid and Muianga 2012). No information was available on blood levels associated with anesthesia or the occurrence of anesthesia-induced cardiac arrhythmias.

3.9 INTERACTIONS WITH OTHER CHEMICALS

No information was located regarding toxic interactions of 1,1-dichloroethane with other xenobiotics. Evidence exists to indicate that 1,1-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., 1,1-dichloroethene and 1,2-dichloroethane), acetaminophen, and bromobenzene may enhance the toxicity of 1,1-dichloroethane. Substances that alter the activity of the microsomal enzymes that are responsible for the metabolism of 1,1-dichloroethane may also affect the toxicity of this chemical. For example, it has been shown that ethanol increases the metabolism of 1,1-dichloroethane *in vitro* (Sato et al. 1980).

3.10 POPULATIONS THAT ARE UNUSUALLY SUSCEPTIBLE

A susceptible population will exhibit a different or enhanced response to 1,1-dichloroethane than will most persons exposed to the same level of 1,1-dichloroethane in the environment. Reasons may include genetic makeup, age, health and nutritional status, and exposure to other toxic substances (e.g., cigarette smoke). These parameters result in reduced detoxification or excretion of 1,1-dichloroethane, or compromised function of organs affected by 1,1-dichloroethane. Populations who are at greater risk due to their unusually high exposure to 1,1-dichloroethane are discussed in Section 6.7, Populations with Potentially High Exposures.

No populations unusually susceptible to 1,1-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 1,1-dichloroethane: (1) individuals with skin disease because of the purported dermal irritant effects induced by 1,1-dichloroethane; (2) individuals with liver disease because of the role of this organ in the biotransformation and detoxification of xenobiotics such as 1,1-dichloroethane; (3) Individuals with impaired renal function because of the limited evidence that 1,1-dichloroethane is nephrotoxic in animals; and (4) individuals with chronic respiratory disease because of the purported respiratory irritant effects induced by 1,1-dichloroethane. Although there are no data to substantiate this, additional populations that may be unusually susceptible to 1,1-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 1,1-dichloroethane.

3.11 METHODS FOR REDUCING TOXIC EFFECTS

This section will describe clinical practice and research concerning methods for reducing toxic effects of exposure to 1,1-dichloroethane. However, because some of the treatments discussed may be experimental and unproven, this section should not be used as a guide for treatment of exposures to 1,1-dichloroethane. When specific exposures have occurred, poison control centers and medical toxicologists should be consulted for medical advice. No texts providing specific information about treatment following exposures to 1,1-dichloroethane were identified.

3.11.1 Reducing Peak Absorption Following Exposure

No information specific to 1,1-dichloroethane was identified.

3.11.2 Reducing Body Burden

No information specific to 1,1-dichloroethane was identified.

3.11.3 Interfering with the Mechanism of Action for Toxic Effects

The mechanisms of toxicity have not been identified for 1,1-dichloroethane.

3.12 ADEQUACY OF THE DATABASE

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

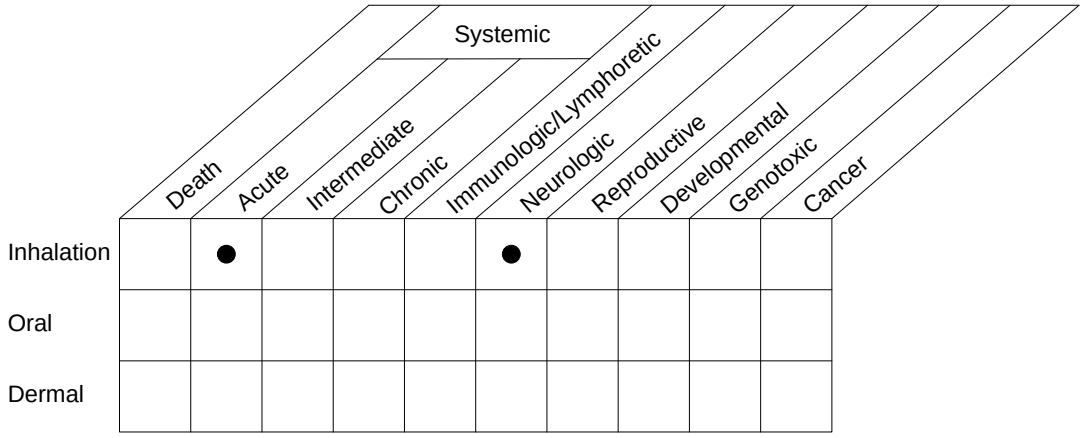
The following categories of possible data needs have been identified by a joint team of scientists from ATSDR, NTP, and EPA. They are defined as substance-specific informational needs that if met would reduce the uncertainties of human health assessment. This definition should not be interpreted to mean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

3.12.1 Existing Information on Health Effects of 1,1-Dichloroethane

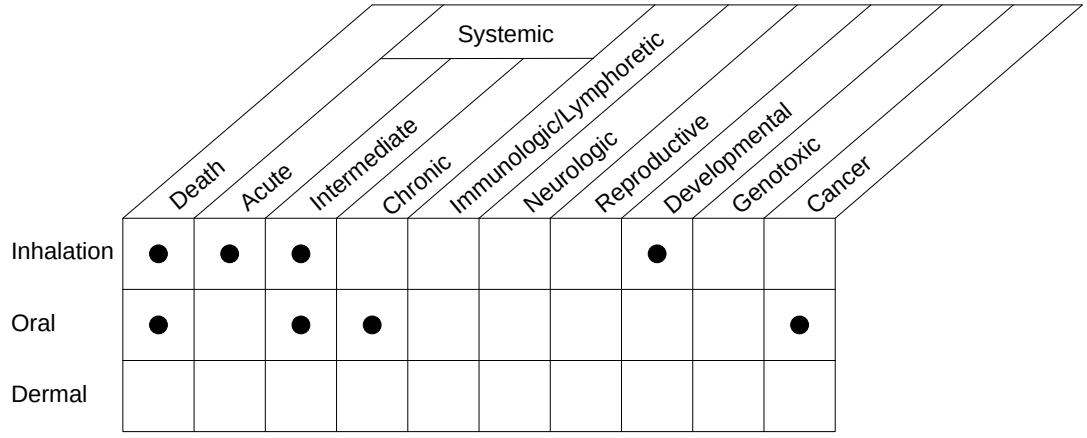
The existing data on health effects of inhalation, oral, and dermal exposure of humans and animals to 1,1-dichloroethane are summarized in Figure 3-5. The purpose of this figure is to illustrate the existing information concerning the health effects of 1,1-dichloroethane. Each dot in the figure indicates that one or more studies provide information associated with that particular effect. The dot does not necessarily imply anything about the quality of the study or studies, nor should missing information in this figure be interpreted as a "data need". A data need, as defined in ATSDR's *Decision Guide for Identifying Substance-Specific Data Needs Related to Toxicological Profiles* (Agency for Toxic Substances and Disease Registry 1989), is substance-specific information necessary to conduct comprehensive public health assessments. Generally, ATSDR defines a data gap more broadly as any substance-specific information missing from the scientific literature.

Figure 3-5 graphically depicts the information that currently exists on the health effects of 1,1-dichloroethane. The literature reviewed concerning the health effects of 1,1-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, and respiratory tract and dermal irritation when humans are exposed

Figure 3-5. Existing Information on Health Effects of 1,1-Dichloroethane



Human



Animal

● Existing Studies

by inhalation to sufficiently high levels. It has been inferred that 1,1-dichloroethane causes these effects, but no reliable data were found that verified this activity.

The database for the health effects of 1,1-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 1,1-dichloroethane following dermal exposure. The limited information available in animals suggests that 1,1-dichloroethane may be nephrotoxic, fetotoxic, and possibly carcinogenic. The data also indicate that 1,1-dichloroethane is considerably less toxic than 1,2-dichloroethane and the tetrachlorinated aliphatics.

3.12.2 Identification of Data Needs

Acute-Duration Exposure. No reliable information is available on the effects of acute exposure to 1,1-dichloroethane in humans. Information on the lethality of 1,1-dichloroethane following inhalation or oral exposure of animals comes from secondary sources (Archer 1978; Smyth 1956). One study examined the nonlethal toxicity of 1,1-dichloroethane following inhalation exposure (Schwetz et al. 1974); this study reported decreases in maternal weight gain and delayed ossification in the fetuses. Because the potential systemic toxicity of 1,1-dichloroethane has not been evaluated following acute inhalation or dermal exposure, the database was not considered adequate for derivation of acute-duration inhalation or oral MRLs for 1,1-dichloroethane.

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 acute-duration exposures to 1,1-dichloroethane by all routes would be useful to assess more fully the acute hazards of this chemical.

Intermediate-Duration Exposure. No reliable information is available on the effects of repeated 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 cats, but not in rats, guinea pigs, or rabbits (Hofmann et al. 1971). No other toxic effects have been attributed to 1,1-dichloroethane following intermediate-duration inhalation exposures in animals. The lack of supporting toxicity or mechanistic data precluded using this study as the basis on an intermediate-duration inhalation MRL. 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 neurotoxicity and liver toxicity), and to more fully assess potential human health hazards from repeated exposure to 1,1-dichloroethane. Two studies have examined the intermediate-duration oral toxicity of 1,1-dichloroethane. In a limited reported study, NCI (1977) found alterations in body weight gain in rats, but not mice, administered 1,1-dichloroethane for 6 weeks. In the second study, no adverse effects were observed in mice exposed to 1,1-dichloroethane in drinking water for 52 weeks (Klaunig et al. 1986). Additional oral studies are needed to identify sensitive targets of toxicity and establish dose-response relationships. Dermal studies are also necessary to evaluate the toxicity of this compound.

Chronic-Duration Exposure and Cancer. No information is available on the effects of chronic exposure to 1,1-dichloroethane in humans. No chronic-duration inhalation or dermal exposure studies were identified. In chronic-duration oral exposure studies in rats and mice (NCI1977), no nonneoplastic alterations were observed. Without information on the targets of toxicity and dose-response relationships, inhalation and oral MRLs cannot be derived. 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.

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 (NCI 1977). The other bioassay yielded negative results for 1,1-dichloroethane (Klaunig et al. 1986). Given the limitations (high mortality) present in the NCI (1977) study and the observations that 1,1-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 1,1-dichloroethane in humans and animals. Studies conducted by the inhalation route would be useful.

Genotoxicity. The genotoxic potential of 1,1-dichloroethane has been investigated in *in vitro* assays; *in vivo* genotoxicity studies are necessary to evaluate the genotoxic potential of this chemical. In general, these studies provide suggestive evidence that 1,1-dichloroethane is not genotoxic. 1,1-Dichloroethane has been observed to enhance cell transformation in Syrian hamster embryo cells (Hatch et al. 1983) and results suggest that 1,1-dichloroethane or a metabolite can bind to cellular macromolecules such as DNA

(Colacci et al. 1985). More information on the genotoxic effects of 1,1-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 1,1-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 1,1-dichloroethane in humans is available. One study was located that investigated the developmental effects of inhaled 1,1-dichloroethane in animals (Schwetz et al. 1974). The results from this study indicated that 1,1-dichloroethane is fetotoxic in rats, causing retarded fetal development (i.e., delayed ossification of the vertebrae) in the presence of decreases in maternal food consumption and body weight gain. Additionally, well-conducted developmental toxicity studies on 1,1-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.

Immunotoxicity. No information is available on the immunotoxic effects of 1,1-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 1,1-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. 1,1-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 1,1-dichloroethane. More information on potential short- and long-term neurotoxic effects of inhaled 1,1-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 1,1-dichloroethane-induced central nervous system depression.

Epidemiological and Human Dosimetry Studies. No epidemiological studies were located on 1,1-dichloroethane. Well-controlled epidemiological studies of people living in close proximity to areas

where 1,1-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 1,1-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 1,1-dichloroethane is manufactured or used, thus confounding the results obtained in such a study.

Biomarkers of Exposure and Effect. For high exposure to 1,1-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 formation of DNA adducts has been suggested, and if they do occur *in vivo*, they may serve to identify long-term exposure to 1,1-dichloroethane. The development of methods for detecting metabolites in the fluids and tissue of humans is needed to indicate 1,1-dichloroethane exposure.

Biomarkers of effect would be useful for identifying 1,1-dichloroethane-specific 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 1,1-dichloroethane.

Absorption, Distribution, Metabolism, and Excretion. Studies of the toxicokinetics of 1,1-dichloroethane are very limited. Much of the information regarding the disposition of 1,1-dichloroethane is based on indirect evidence. Toxicokinetic data are useful for providing information on mechanisms of toxicity and can often support findings of toxicity studies.

Absorption of 1,1-dichloroethane occurs following exposure via all routes. The presence of a 1,1-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 1,1-dichloroethane absorption are lacking and would provide useful information on the potential health hazards associated with exposure to 1,1-dichloroethane via inhalation of contaminated air or ingestion of contaminated water.

Studies in humans and animals regarding tissue distribution of 1,1-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

1,1-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 1,1-dichloroethane-induced toxicity in humans.

Characterization of 1,1-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 1,1-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 1,1-dichloroethane metabolism and a more realistic perspective of its metabolic fate. This information would allow more accurate prediction of the potential of 1,1-dichloroethane to induce toxic effects, and aid in devising methods to detoxify exposed persons.

Studies regarding the excretion of 1,1-dichloroethane by humans were not available. One study was located in animals regarding the extent or rate of 1,1-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 1,1-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 1,1-dichloroethane is handled in a similar manner in humans.

Methods for Reducing Toxic Effects. Limited information regarding methods for reducing the toxic effects of 1,1-dichloroethane were identified. Additional information regarding the toxicity of 1,1-dichloroethane is needed prior to research on mitigating the toxicity of this compound.

Children's Susceptibility. Data needs relating to both prenatal and childhood exposures, and developmental effects expressed either prenatally or during childhood, are discussed in detail in the Developmental Toxicity subsection above.

No data were identified on children's susceptibility to the toxic effects of 1,1-dichloroethane and whether there are toxicokinetic differences in the metabolism of this chemical between adults and children. As noted previously, one developmental toxicity study (Schwetz et al. 1974) reported altered fetal growth.

Child health data needs relating to exposure are discussed in Section 6.8.1, Identification of Data Needs: Exposures of Children.

3.12.3 Ongoing Studies

No ongoing studies sponsored by NIH, NTP, or EPA were identified for 1,1-dichloroethane.

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4. CHEMICAL AND PHYSICAL INFORMATION

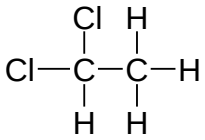
4.1 CHEMICAL IDENTITY

The synonyms, and identification numbers for 1,1-dichloroethane are listed in Table 4-1.

4.2 PHYSICAL AND CHEMICAL PROPERTIES

Important physical and chemical properties of 1,1-dichloroethane are listed in Table 4-2.

Table 4-1. Chemical Identity of 1,1-Dichloroethane

Characteristic	Information[a]	Reference
Chemical name	1,1-Dichloroethane[b]	
Synonym(s)	Alpha,alpha-dichloroethane; asymmetrical dichloroethane; S-dichloroethene; Dutch oil; ethane, 1,1-dichloro-; ethylidene chloride; ethylidene dichloride; 1,1-ethylidene dichloride[c]	
Registered trade name(s)	No data	
Chemical formula	$C_2H_4Cl_2$[b]	
Chemical structure		
Identification numbers:		
CAS registry	75-34-3[b]	
NIOSH RTECS	KI0175000	
EPA hazardous waste	U076	
OHM/TADS	No data	
DOT/UN/NA/IMDG shipping	DOT 2362; UN 2362; IMO 3.2	
HSDB	64	
NCI	C04535[d]	

[a]All information obtained from HSDB 2012, except where noted
[b]O'Neil et al. 2006
[c]Archer 1978; Weiss 1986
[d]ChemIDPlus Lite 2012

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

Table 4-2. Physical and Chemical Properties of 1,1-Dichloroethane

Property	Information	Reference
Molecular weight	98.97	HSDB 2012
Color	Colorless	
Physical state	Oily liquid	O'Neil et al. 2006
Melting point	-96.9 °C	HSDB 2012
Boiling point	57.3 °C	O'Neil et al. 2006
Density at 20 °C	1.175 g/cm^3	HSDB 2012
Odor	Aromatic ethereal; chloroform-like	
Odor threshold:		
Water	No data	
Air	120 ppm; 200 ppm	Verschueren 1983
Solubility:		
Water at 20 °C	0.55 g/100 g	HSDB 2012
Organic solvents	Miscible with oxygenated and chlorinated solvents	
Partition coefficients:		
Log K_{ow}	1.79	HSDB 2012
Log K_{oc}	1.48	HSDB 2012
Vapor pressure at 25 °C	230 mmHg	HSDB 2012
Henry's law constant at 24 °C	5.62x10^{-3} atm-m^3/mol 5.51x10^{-3} atm-m^3/mol	HSDB 2012 Chen et al. 2012
Autoignition temperature	457.8 °C	HSDB 2012
Flashpoint	Closed cup -12 °C; open cup 14 °C	HSDB 2012
Flammability limits	Lower 5.4%; upper 11.4%	HSDB 2012
Conversion factors	1 ppm x 4.05 = 1 mg/m^3 1 mg/m^3 x 0.25 = 1 ppm	
Explosive limits	Lower explosive limit: 5.6%; moderate explosion hazard when exposed to heat or flame	HSDB 2012

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

5.1 PRODUCTION

Table 5-1 lists the number of facilities in each state that manufacture or process 1,1-dichloroethane, the activities and uses, and the range of maximum amounts of 1,1-dichloroethane that are stored on site. The data listed in Table 5-1 are derived from the Toxics Release Inventory (TRI13 2014). Based on the TRI information from 2013, there are 19 facilities that produce or process 1,1-dichloroethane in the United States. The TRI data should be used with caution since only certain types of facilities were required to report. This is not an exhaustive list.

1,1-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 (HSDB 2012). Other production methods include the direct chlorination of ethane, addition of hydrogen chloride to acetylene, the reaction of ethylene and chlorine in the presence of calcium chloride, and the reaction of phosphorus chloride and acetaldehyde (HSDB 2012). 1,1-Dichloroethane can also be produced as a byproduct during the manufacture of chloral, as a byproduct in the production of vinyl chloride via ethylene oxychlorination (HSDB 2012; Marshall 2003), and as an intermediate in the production of 1,1,1-trichloroethane by thermal or photochemical chlorination of vinyl chloride (Cowfer 2006). It has been reported that 1,1-dichloroethane often occurs as an unwanted byproduct in numerous chlorination and oxychlorination processes of C2 hydrocarbons (HSDB 2012).

Information regarding the production volume of 1,1-dichloroethane in the United States is not reported in SRI Directory of Chemical Producers (SRI 2011). Additionally, no data are reported for U.S. production volume in the Hazardous Substance Data Bank (HSDB 2012).

Data from the Chemical Data Reporting (CDR) information system indicates that three companies within the United States manufactured or imported 1,1-dichloroethane (EPA 2014a). The Dow Chemical Company reported 0 pounds/year for imported and exported data, confidential business information (CBI) for manufactured data, 0 pounds/year for volume used on site and ‘CBI’ for past production volume data. 1,1-Dichloroethane is reported to be used as an intermediate, a substance used to form another compound by the Dow Chemical Company. The Shin Etsu Company reports ‘withheld’ for imported data, 1,844,512 pounds/year for exported data, ‘withheld’ for manufactured data, 2,629,704 pounds/year for volume used on site data, and 2,959,696 pounds/year for past production volume data (EPA 2014a). The

Table 5-1. Facilities that Produce, Process, or Use 1,1-Dichloroethane

State[a]	Number of facilities	Minimum amount on site in pounds[b]	Maximum amount on site in pounds[b]	Activities and uses[c]
KY	1	10,000	99,999	1, 3, 6
LA	9	0	9,999,999	1, 2, 3, 4, 5, 6, 8, 12, 13
NY	1	100	999	12
OH	1	1,000	9,999	12
SC	1	100	999	12
TX	6	1,000	999,999	1, 2, 3, 5, 6, 8, 12, 13, 14

[a]Post office state abbreviations used.
[b]Amounts on site reported by facilities in each state.
[c]Activities/Uses:

1. Produce
2. Import
3. Onsite use/processing
4. Sale/Distribution
5. Byproduct
6. Reactant
7. Formulation Component
8. Article Component
9. Repackaging
10. Chemical Processing Aid
11. Manufacturing Aid
12. Ancillary/Other Uses
13. Manufacturing Impurity
14. Process Impurity

Source: TRI13 2014 (Data are from 2013)

Shin Etsu Company reports use of 1,1-dichloroethane as 'not reasonably known or ascertainable.' The national production volume ranged between 1,000,000 and 10,000,000 pounds/year. There are no data reported for consumer products or consumer uses.

According to EPA Inventory Update Rule (IUR) records, in 2006, two companies in the United States produced 1,1-dichloroethane in 2006: Oxy Vinyls in La Porte, Texas and The Dow Chemical Company in Plaquemine, Louisiana (EPA 2010). Both of these companies manufactured 1,1-dichloroethane primarily to be used as an intermediate, a substance used to form another compound. Production volume data were not provided for each specific company. Aggregated national production volumes reported in 2006 were in the range of 500,000–<1 million pounds (EPA 2010).

5.2 IMPORT/EXPORT

No information was found concerning U.S. imports and exports of 1,1-dichloroethane.

5.3 USE

The largest individual use of 1,1-dichloroethane is as an intermediate in the manufacture of 1,1,1-trichloroethane (Dreher et al. 2014; HSDB 2012). 1,1-Dichloroethane also has limited use as a solvent for plastics, oils, and fats, and is thus employed as both a cleaning agent and a degreaser (O'Neil et al. 2006). In the past, 1,1-dichloroethane was used as an anesthetic (HSDB 2012; O'Neil et al. 2006). Other uses of 1,1-dichloroethane include fabric spreading, varnish and finish removers, organic synthesis, ore flotation, and as a fumigant and insecticide spray (HSDB 2012). 1,1-Dichloroethane is also used in the manufacture of plastic wrap, adhesives, and synthetic fiber (USGS 2006a). No information is available regarding the use proportions among these categories.

5.4 DISPOSAL

1,1-Dichloroethane may be disposed of by atomization within a combustion chamber equipped with an appropriate effluent gas cleaning device, by high-temperature 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. Waste water treatment technologies investigated by the EPA include concentration processes such as stripping, solvent extraction, activated carbon, and resin adsorption.

Consultation with environmental regulatory agencies is advised (HSDB 2012; Marshall 2003; NIOSH 1978).

6. POTENTIAL FOR HUMAN EXPOSURE

6.1 OVERVIEW

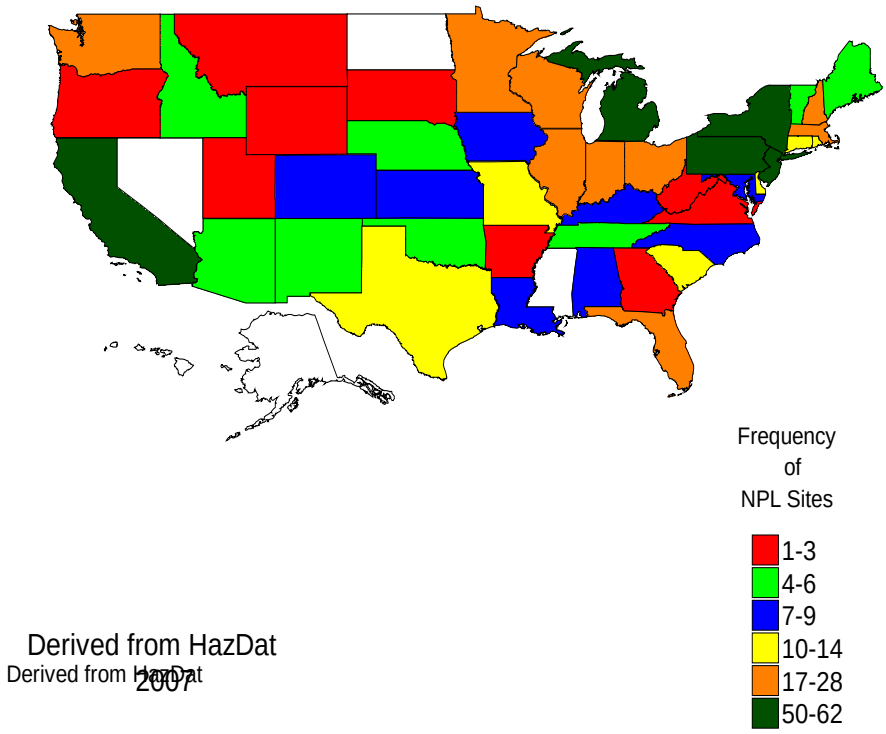
1,1-Dichloroethane has been identified in at least 673 of the 1,699 hazardous waste sites that have been proposed for inclusion on the EPA National Priorities List (NPL) (HazDat 2007). However, the number of sites evaluated for 1,1-dichloroethane is not known. The frequency of these sites can be seen in Figure 6-1.

1,1-Dichloroethane has been identified in at least 400 of the 1,760 proposed (51), final (1,323), and deleted (386) hazardous waste sites listed on the EPA Superfund NPL under the synonym 1,1-dichloroethene (CASRN: 75-34-3) and at least 26 of the 1,760 EPA Superfund NPL sites under the synonym ethylidene dichloride (CASRN: 75-34-3) (EPA 2015c; NLM 2015). However, the number of sites evaluated for 1,1-dichloroethane is not known.

1,1-Dichloroethane in the environment is mainly related to the production, storage, consumption, transport, and disposal of 1,1-dichloroethane used as a chemical intermediate, solvent, finish remover, and degreaser. 1,1-Dichloroethane may occur in the environment as a biodegradation product of 1,1,1-trichloroethane. In addition, 1,1-dichlrooethane was reported as a constituent in the gaseous emissions of cigarette smoke. 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 1,1-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).

The main route of human exposure to 1,1-dichloroethane is through inhalation of 1,1-dichloroethane in ambient or workplace air. Estimates of populations potentially exposed to 1,1-dichloroethane in workplace environments in the 1980s ranged from 715 to 1,957 workers (EPA 2001c). Ingestion of contaminated drinking water may also be an important route of exposure for populations living near industrial facilities and hazardous waste sites. Boman and Maibach (1996) concluded that exposure to skin results in very little absorption due to the compound’s volatility; in addition, the concentration levels greatly diminish in properly ventilated areas.

Figure 6-1. Frequency of NPL Sites with 1,1-Dichloroethane Contamination



6.2 RELEASES TO THE ENVIRONMENT

The Toxics Release Inventory (TRI) data should be used with caution because only certain types of facilities are required to report (EPA 2005). This is not an exhaustive list. Manufacturing and processing facilities are required to report information to the TRI only if they employ 10 or more full-time employees; if their facility is included in Standard Industrial Classification (SIC) Codes 10 (except 1011, 1081, and 1094), 12 (except 1241), 20–39, 4911 (limited to facilities that combust coal and/or oil for the purpose of generating electricity for distribution in commerce), 4931 (limited to facilities that combust coal and/or oil for the purpose of generating electricity for distribution in commerce), 4939 (limited to facilities that combust coal and/or oil for the purpose of generating electricity for distribution in commerce), 4953 (limited to facilities regulated under RCRA Subtitle C, 42 U.S.C. section 6921 et seq.), 5169, 5171, and 7389 (limited S.C. section 6921 et seq.), 5169, 5171, and 7389 (limited to facilities primarily engaged in solvents recovery services on a contract or fee basis); and if their facility produces, imports, or processes ≥25,000 pounds of any TRI chemical or otherwise uses >10,000 pounds of a TRI chemical in a calendar year (EPA 2005).

Of the 21,526 TRI facilities reporting nationwide, 1,1-dichloroethane (CASRN: 75-34-3), has been reported in 0 onsite TRI releases for the reporting year 2013. Of these TRI facilities reporting nationwide, 1,1-dichloroethane, under the synonym ethylidene dichloride (CASRN: 75-34-3), has been reported in 18 onsite TRI releases for the reporting year 2013 (NLM 2015).

Section 112 of the Clean Air Act (CAA) lists 1,1-dicloroethane as one of 188 hazardous air pollutants (HAPs) known to cause or suspected of causing cancer or other serious human health effects or ecosystem damage (EPA 2000). EPA's National Emission Inventory (NEI) database contains data regarding sources that emit criteria air pollutants and their precursors, and HAPs for the 50 United States, Washington DC, Puerto Rico, and the U.S. Virgin Islands (prior to 1999, criteria pollutant emission estimates were maintained in the National Emission Trends [NET] database and HAP emission estimates were maintained in the National Toxics Inventory [NTI] database). The NEI database derives emission data from multiple sources including: state and local environmental agencies; the TRI database; computer models for on-road and off-road emissions; databases related to EPA's Maximum Achievable Control Technology (MACT) programs to reduce emissions of hazardous air pollutants. Using composite data from the NTI database from 1990 to 1993, it was estimated that the annual emissions of 1,1-dichloro-ethane in the United States was approximately 274 tons per year during that time frame (EPA 2000).

Data downloaded from the 2005 NEI indicated that the total emission of 1,1-dichloroethane was approximately 387 tons, with the biggest source arising from point source waste disposal (EPA 2012c).

There are no known natural sources of 1,1-dichloroethane. It has been reported that 1,1,1-trichloroethane is rapidly biodegraded in anaerobic methanogenic environments, such as those found in landfills, to form 1,1-dichloroethane as the major product, with slow, yet complete anaerobic degradation of 1,1-dichloroethane to carbon dioxide also indicated (deBest et al. 1997; van Eekert et al. 1999; Vogel and McCarty 1987). 1,1,1-Trichloroethane occurs in the environment as a result of accidental spills, industrial manufacturing, and use processes. 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 1,1-dichloroethane to the environment are a result of industrial manufacturing use processes and from the degradation of 1,1,1-trichloroethane. Additional sources of environmental release are fugitive emissions from storage, distribution, and disposal; use as an extraction solvent and fumigant or insecticide spray and in paints, varnish, and paint removers; as a constituent of medicines and stone, clay, and glass products; and in ore floatation (EPA 2001c; Infante and Tsongas 1982).

6.2.1 Air

Estimated releases of 20,972 pounds (~9.51 metric tons) of 1,1-dichloroethane to the atmosphere from 19 domestic manufacturing and processing facilities in 2013, accounted for about 90.1% of the estimated total environmental releases from facilities required to report to the TRI (TRI13 2014). These releases are summarized in Table 6-1.

Emissions to the atmosphere comprise >98% of all releases of 1,1-dichloroethane to the environment (TRI10 2012). 1,1-Dichloroethane released in the production of 1,1,1-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 1,1-dichloroethane in ambient air of the Baton Rouge industrial area and at the Kin-Buc waste disposal site outside Edison, New Jersey. Eitzer (1995) observed low levels of 1,1-dichloroethane ($\leq$1 $\mu g/m^3$) in at least one of eight municipal solid waste sites sampled in the United States.

Table 6-1. Releases to the Environment from Facilities that Produce, Process, or Use 1,1-Dichloroethane[a]

		Reported amounts released in pounds per year[b]							
							Total release		
State[c]	RF[d]	Air[e]	Water[f]	UI[g]	Land[h]	Other[i]	On-site[j]	Off-site[k]	On- and off-site
KY	1	56	0	0	0	0	56	0	56
LA	9	20,612	80	0	11	0	20,692	11	20,703
NY	1	2	0	0	0	0	2	0	2
OH	1	4	0	0	10	0	4	10	14
SC	1	1	0	0	0	0	1	0	1
TX	6	297	2	2,200	0	0	2,498	0	2,498
Total	19	20,972	82	2,200	21	0	23,254	21	23,275

[a]The TRI data should be used with caution since only certain types of facilities are required to report. This is not an exhaustive list. Data are rounded to nearest whole number.
[b]Data in TRI are maximum amounts released by each facility.
[c]Post office state abbreviations are used.
[d]Number of reporting facilities.
[e]The sum of fugitive and point source releases are included in releases to air by a given facility.
[f]Surface water discharges, waste water treatment-(metals only), and publicly owned treatment works (POTWs) (metal and metal compounds).
[g]Class I wells, Class II-V wells, and underground injection.
[h]Resource Conservation and Recovery Act (RCRA) subtitle C landfills; other onsite landfills, land treatment, surface impoundments, other land disposal, other landfills.
[i]Storage only, solidification/stabilization (metals only), other off-site management, transfers to waste broker for disposal, unknown
[j]The sum of all releases of the chemical to air, land, water, and underground injection wells.
[k]Total amount of chemical transferred off-site, including to POTWs.

RF = reporting facilities; UI = underground injection

Source: TRI13 2014 (Data are from 2013)

Approximately 52,000 kg of 1,1-dichloroethane are released to the atmosphere by privately owned treatment work facilities (POTWs) each year (EPA 1980).

In 2002, air emissions from point, area, and mobile sources in the Great Lakes region were calculated. Data from Illinois, Indiana, Michigan, Minnesota, New York, Ontario, Pennsylvania, and Wisconsin were evaluated. Total emissions of 1,1-dichloroethane in the Great Lakes region were calculated to be 27,110 pounds from point sources and 1,360 pounds from area sources. All states reported only point source emissions for the compound with the exception of Minnesota, which reported 341 pounds from point sources and 1,360 pounds from area sources. Ontario and Illinois accounted for the majority of the emissions (41 and 33%, respectively). The other states each accounted for 1–9% of the emissions (Great Lakes Commission 2006).

1,1-Dichloroethane was detected with the VOCs emanating from a low-level radioactive waste disposal facility at the U.S. Geological Survey (USGS) Amargosa Desert Research Site in Nevada (Baker et al. 2012). The study quantified VOCs being emitted over an 11-year period and estimated the yearly vertical diffusive flux of the detected VOCs to the atmosphere. Concentrations decreased as the distance from the site increased. Samples taken at the site contained 29.9, 33.6, and 66 mg dichloroethane/m^2 per year, while samples taken 100 m from the site along the north south transect contained 2.8, 3.6, and 9.7 mg dichloroethane/m^2 per year in 2001, 2003, and 2005 respectively. At distances of 200 and 300 m, concentrations were reported as 0.0 mg dichloroethane/m^2 for 2001, 2003, and 2005. Table 6-2 summarizes the estimates obtained from locations along the north-south transect at distances of 0–400 m from the facility.

Emissions from six commercial cigarette brands were examined in a chamber study; five cigarettes per brand were smoked for approximately 6 minutes (Wang et al. 2012). The amount of 1,1-dichloroethane emitted during smoking ranged between 51 and 110 µg/cigarette. The average concentration of 1,1-dichloroethane during smoking ranged from 12 to 26 µg/m^3 and the average concentration during the post-smoking period ranged from 7.9 to 17 µg/m^3.

In 2011, 1,1-dichloroethane was detected in the gaseous emissions of a commercial poultry farm in Poland (Witkowska 2013). The farm consisted of five buildings that had mechanical ventilation systems. Measurements were taken over the turkey's rearing period, from week 4 to 19. The average concentrations detected in the turkey houses at week 4, 7, 10, and 13 were 1.15±0.55, 1.08±0.82,

Table 6-2. Estimated Yearly Emissions of 1,1-Dichloroethane (mg/m^2 per Year)

Distance from landfill (m)	2001	2003	2005
0	29.9	33.6	66
25	22.6	31.8	51.5
50	18.4	17.9	Not reported
75	Not reported	16.4	Not reported
100	2.8	3.6	9.7
150	Not reported	0.1	Not reported
200	0.0	0.0	0.0
300	0.0	0.0	0.0
400	0.0	Not reported	Not reported

Source: Baker et al. 2012

1.57±0.45, and 1.33±0.55 ppm, respectively. Reported concentrations for week 16 and 19 were 0.00 ppm.

6.2.2 Water

Estimated releases of 82 pounds (~0.037 metric tons) of 1,1-dichloroethane to surface water from 15 domestic manufacturing and processing facilities in 2013, accounted for <1% of the estimated total environmental releases from facilities required to report to the TRI (TRI13 2014). This estimation includes surface water discharges, waste water treatment (metal only), and POTWs (metal and metal compounds) (TRI13 2014). These releases are summarized in Table 6-1.

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

6.2.3 Soil

Estimated releases of 21 pounds (~0.009 metric tons) of 1,1-dichloroethane to soils from eight domestic manufacturing and processing facilities in 2013, accounted for <0.01% of the estimated total environmental releases from facilities required to report to the TRI (TRI13 2014). An additional 2,200 pounds (~1.0 metric tons), constituting about 9.46% of the total environmental emissions, were released via underground injection (TRI13 2014). These releases are summarized in Table 6-1.

Little information was found regarding releases of 1,1-dichloroethane to soils. Approximately 4,000 kg of 1,1-dichloroethane from POTWs are dispersed on land each year as sludge (EPA 1980).

6.3 ENVIRONMENTAL FATE

6.3.1 Transport and Partitioning

Releases of 1,1-dichloroethane to the environment as a result of industrial activity are expected to be primarily to the atmosphere (see Section 6.2). 1,1-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 1,1-dichloroethane, in upland waters to long-range aerial transport and deposition in precipitation. EPA (1982b) discussed the atmospheric fate of 1,1-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 1,1-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 1,1-dichloroethane has higher volatility and lower aqueous solubility than the 1,2-isomer, physical removal of 1,1-dichloroethane from the atmosphere would be even less likely to be important. Pellizzari et al. (1979) measured actual concentrations of airborne contaminants in the vicinity of known emission sources of 1,1-dichloroethane, making aerial transport the logical source of downwind concentrations.

The Henry's law constant value for 1,1-dichloroethane ($5.51x10^{-3}$ atm-m^3/mol) suggests that it should partition rapidly to the atmosphere. The 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 1,1-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 re-aeration rate ratio. The re-aeration rate ratio has been determined to be 0.55 for 1,1-dichloroethane (Cadena et al. 1984). Using the values of Mabey et al. (1982) for oxygen re-aeration rates in ponds and rivers (0.19 and 0.96 day^{-1}, respectively), the evaporation half-life of 1,1-dichloroethane is estimated to be approximately 5 times longer for ponds than for rivers (>1 day for river water and >6 days for pond water).

Little information was found regarding partitioning of 1,1-dichloroethane from the water column onto sediments. According to DeWulf et al. (1996), 1,1-dichloroethane does not really accumulate on marine sediment and it will therefore not be an important sink for this compound. Analogs of the compound (i.e., dichloromethane, trichloromethane, and 1,1,1-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 1,1-dichloroethane; therefore, partitioning to sediment from the water column is not likely to be an important environmental fate process for 1,1-dichloroethane.

1,1-Dichloroethane released to land surfaces in spills would rapidly volatilize to the atmosphere, but 1,1-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 1,1-dichloroethane to low organic content soil is expected. Goodin and Webber (1992) conducted studies of several volatile organic compounds (VOCs), including 1,1-dichloroethane, to determine their fate in soils. It was determined that the compounds were lost from the soils mainly by volatilization, with first-order disappearance half-lives ranging from 1 to 949 hours. Wilson et al. (1981) found that although 50% of the applied 1,1-dichloroethane volatilized to the atmosphere, the remainder percolated rapidly through a sandy soil, suggesting ready availability to groundwater transport processes.

Gossett et al. (1983) analyzed the tissues of several species of aquatic organisms for 1,1-dichloroethane near the discharge of the Los Angeles County waste water treatment plant. The concentration of 1,1-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 1,1-dichloroethane to bioconcentrate is low in aquatic organisms. An estimated bioconcentration factor of 5 indicates that bioconcentration would be low (HSDB 2012).

6.3.2 Transformation and Degradation

6.3.2.1 Air

In the atmosphere, 1,1-dichloroethane is oxidized by reaction with hydroxyl radicals. The rate constant for the vapor-phase reaction is 2.74×10^{-13} cm^3/molecule-second at 25 °C (HSDB 2012). The residence time of the compound in the atmosphere has been estimated to be 49 days (HSDB 2012).

6.3.2.2 Water

1,1-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 1,1-dichloroethane at pH 7 and 25 °C has been estimated to be 60 years (Jeffers et al. 1989).

As summarized in Klecka et al. (1990), 1,1-dichloroethane is produced by biodegradation of 1,1,1-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: 1,1,1-trichloroethane → 1,1-dichloroethane → chloroethane. van Eeker et al. (1999) reported 31.1% anaerobic degradation of 1,1-dichloroethane to mainly chloroethane (14.5%) in living sludge after 25 days. Under aerobic conditions, Tabak et al. (1981) reported about 50% degradation of 1,1-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. 1,1-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 (1985). They observed that 1,1-dichloroethane was detected in groundwater at sites where the compound had not been handled or disposed of and concluded that 1,1-dichloroethane had been produced by anaerobic degradation of other compounds present, particularly 1,1,1-trichloroethane. Washington and Cameron (2001) used well monitoring data, from a landfill with a contamination history, to calculate a degradation rate constant for 1,1-dichloroethane. Under sulfate-reducing conditions at 10 °C, the rate constant was found to be 6.0×10^{-3} L/day with a half-life of 115 days.

6.3.2.3 Sediment and Soil

1,1-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 1,1-dichloroethane on soil surfaces is not expected. The rate of biodegradation of 1,1-dichloroethane in soils is unknown. In subsurface soil, the loss of 1,1-dichloroethane through biodegradation is expected to be insignificant (Wilson et al. 1983). The biodegradation half-life of 1,1,1-trichloroethane under anaerobic conditions has been reported to be about 16 days, whereas the half-life of 1,1-dichloroethane has been reported to be >30–60 days (Wood et al. 1985).

Hamonts et al. (2012) monitored chlorinated aliphatic hydrocarbons, such as 1,1-dichloroethane, in groundwater that discharges into the Zenne River over a 21-month period. The Zenne River had been

previously continuously contaminated with municipal sewage containing chlorinated aliphatic hydrocarbons. The study also evaluated microbial reductive dechlorination occurring under anaerobic conditions in the river sediments. Microbial degradation of 1,1-dichloroethane was evident in the riverbed locations in which *Dehalobactor* spp. was detected; however, in the absence of this microorganism, 1,1-dichloroethane did not appear to degrade.

6.4 LEVELS MONITORED OR ESTIMATED IN THE ENVIRONMENT

Reliable evaluation of the potential for human exposure to 1,1-dichloroethane depends in part on the reliability of supporting analytical data from environmental samples and biological specimens. Concentrations of 1,1-dichloroethane in unpolluted atmospheres and in pristine surface waters are often so low as to be near the detection limits of analytical methods. In reviewing data on 1,1-dichloroethane levels monitored or estimated in the environment, it should also be noted that the amount of chemical identified analytically is not necessarily equivalent to the amount that is bioavailable. The analytical methods available for monitoring 1,1-dichloroethane in a variety of environmental media are detailed in Chapter 7.

1,1-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.

6.4.1 Air

The Air Quality System (AQS) database is EPA's repository of criteria air pollutants and hazardous air pollutants (HAPs) containing monitoring data from over 2,600 monitoring sites across the United States. Detailed AQS ambient air monitoring data from 2013 for 1,1-dichloroethane are summarized in Table 6-3 (http://www.epa.gov/ttnamti1/toxdat.html#data*). Data for other years are available as zipped Microsoft Access database files that may be accessed directly from the EPA website. In general, the average concentration of the samples for 1,1-dichloroethane in outdoor air was approximately 0.02 µg/m^3. The highest reported concentration (4.4 µg/m^3) occurred in one sample from Kentucky. The second highest reported concentration (0.83 µg/m^3) also occurred in one sample from Kentucky. The third highest reported concentration (0.81 µg/m^3) was detected in 173 samples from Ohio. Rhode Island had the largest number of samples with detectable concentrations, 836 samples, that ranged in concentration from 0.004 to 0.12 µg/m^3. The 24-hour average concentration of 1,1-dichloroethane in outdoor air ranged from

Table 6-3. 2013 Air Monitoring Data from Air Toxics Data Ambient Monitoring Archive for 1,1-Dichloroethane

State[a]	Number of samples	Concentration range (µg/m^3)
AK	61	0
AZ	104	0
CO	61	0
FL	32	0.0081–0.18
FL	376	0
GA	237	0
IA	87	0
IL	180	0
IN	28	0.04
IN	442	0
KY	33	0.044–4.4
KY	467	0
MA	141	0.004–0.0081
MA	25	0
ME	36	0.016–0.4
ME	244	0
MI	2	0.34–0.35
MI	329	0
MN	1	0.004
MN	1,008	0
MO	61	0
MS	121	0
NC	437	0
NJ	1	0.045
NJ	239	0
NY	238	0.004–0.47
NY	483	0
OH	173	0.81
OH	243	0
OK	303	0
PA	27	0.04–0.12
PA	274	0
RI	836	0.004–0.012
RI	42	0
SC	118	0
TX	6	0.04–0.2
TX	2,355	0
UT	52	0
VA	89	0

Table 6-3. 2013 Air Monitoring Data from Air Toxics Data Ambient Monitoring Archive for 1,1-Dichloroethane

State[a]	Number of samples	Concentration range (µg/m^3)
VT	140	0
WA	57	0
WI	95	0

[a]Post office state abbreviations used.

Source: EPA 2015b

approximately 0.008 to 3.5.4 μg/m^3 (0.001–1.09 ppb). The analytical methods had detection limits that ranged between 0.0081 and 3.4 μg/m^3 (EPA, 2015b).

1,1-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. EPA (1983b) 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. EPA (1983a) 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 μg/m^3 (5.68 ppm) (Pellizzari 1982). EPA (1978) tabulated analytical results for 1,1-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 ppm); Deer Park, Texas (0.14 ppb); and Baton Rouge (0.058 ppb) and Geismar, Louisiana (0.14 ppb).

Barkley et al. (1980) found no 1,1-dichloroethane in the ambient air surrounding nine houses bordering the old Love Canal. Gupta et al. (1984) found 1,1-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.

Air monitoring data from 22 tire fire incidents across the United States were evaluated. 1,1-Dichloroethane was detected at low levels in the vicinity of several of the fires. It was noted that the source may be from something other than the burning tires (EPA 1993).

Air was monitored over a 3-week period at the Fresh Kills Landfill of Staten Island, New York. The overall air emission rate for 1,1-dichloroethane was 0.216 g/second (EPA1996a).

In 1994, 1,1-dichloroethane was not detected in six spatial sites around the Columbus metro area. Detection limits of the analysis were 0.05 ppb (Spicer 1996).

In 1996, Mohamed et al. (2002) monitored VOCs in air at 13 urban locations in the United States for 1 year. Monitoring sites were located in Louisiana, Texas, Vermont, and New Jersey. TRI reporting facilities near the monitoring sites ranged from 0 to 38 facilities. 1,1-Dichloroethane was detected at all 13 of the monitoring stations at levels <1 ppb by volume (ppbv). The detection limit of the analytical method was <0.5 ppbv.

1,1-Dichloroethane was detected in the headspace of five out of eight household bleach products at levels ranging from 0.7 to 176 µg/m^3. It was concluded that the compound was formed by the reaction of hypochlorite and the organic matter of the product's additives. In addition, 1,1-dichloroethane levels of indoor air increased during the use of bleach products, from 0.004–0.01 µg/m^3 before use, to 0.01–0.62 µg/m^3 during use, and then to 0.01–0.29 µg/m^3 after use (Odabasi 2008).

From February to December 2009, 1,1-dichloroethane was detected in ambient air samples from four sites in Seoul, Korea (Jong Ro, Yang Jae, Gwang Jin, and Gang Seo) at concentrations of 0.04–0.18, 0.03–0.08, 0.04–0.15, and 0.04–0.32 ppb, respectively (Kim et al. 2012).

6.4.2 Water

. The compound has 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 1,1-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, 1,1-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 1,1-dichloroethane. The maximum concentration was 4.2 ppb (Westrick et al. 1984).

Drinking water samples from a number of urban and rural locations in the United States have been reported to be contaminated with 1,1-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 1,1-dichloroethane in 11 of 617 wells

surveyed (Krill and Sonzogni 1986). Concentrations of 1–3 ppb were reported in four public well water supplies in Iowa (EPA 1985).

Groundwater samples taken from 178 hazardous waste disposal sites were found to contain 1,1-dichloroethane at 18% frequency (Plumb 1987), with an average concentration of 0.31 ppm and a maximum concentration of 56.1 ppm (Yang and Rauckman 1987). Using the STORET database, Staples et al. (1985) reported median concentrations of <0.1 ppb in 8,716 samples of ambient water (3% detectable values), <1.0 ppb in 1,375 effluent samples (5% detectable values), <5.0 ppb in 354 sediment samples (0.6% detectable values), and <0.05 ppb in 94 biota samples (no detectable values).

Nine shallow groundwater samples contained 1,1-dichloroethane with a maximum concentration of 2.2 μg/L, in 5.3% of 208 urban wells sampled in the United States (Kolpin et al. 1997).

1,1-Dichloroethane was detected above background levels in groundwater beneath Savannah River Site's Interim Sanitary Landfill. Several wells at the site were sampled twice each in 2005. The site was in operation from 1992 to 1998 (DOE2005).

The Aerojet-General Corporation reports that 1,1-dichloroethane is present as a groundwater contaminant just outside Sacramento, California, in varying concentrations in several separate domestic and industrial well water samples and test borings. Additionally, a 1996 study indicated the presence of the compound in groundwater from the Glassboro region of Southern New Jersey at a detection frequency of 5% and a concentration of >0.1 μg/L (HSDB 2012).

The Solid Waste Management Unit 12 in South Carolina was in use from the 1970s until 1981. In September 1999, water sampled from an excavation hole that contained a leaking underground storage tank (UST) contained 1,1-dichloroethane at a concentration of 84,300 μg/L. Monitoring efforts of wells surrounding the site from August 2000 to November 2007 detected 1,1-dichloroethane as a consistent contaminant in the groundwater. Groundwater samples from August 2001 indicated that the highest concentrations of contaminants in groundwater were near the UST, indicating that it was the source area. Maximum measured concentrations of 1,1-dichloroethane of 155,000 μg/L were found at that time. Natural and engineered remediation efforts have contributed to the irregular decline of contaminants. On the northern side of the facility, concentrations of 1,1-dichloroethane in groundwater at one of the wells declined from >100 μg/L in 2000 to approximately 20–30 μg/L in 2003, remained relatively unchanged in 2003–2005, and declined in 2006–2007 (USGS 2006b).

The National Water Quality Assessment Program (NAWQA) evaluated 3,496 wells nationwide for the presence of VOCs from 1985 to 2001. 1,1-Dichloroethane had an overall detection frequency of 0.86% at an assessment level of 0.2 µg/L; a detection frequency of 0.17% at an assessment level of 1 µg/L; and a detection frequency of 0.029% at an assessment level of 5 µg/L. The compound was also detected as a mixture with 1,1,1-trichloroethane in 0.71% of the samples (USGS 2006a). According to the report, there were 30 detections of 1,1-dichloroethane in 3,496 aquifer samples. More specifically, 7 detections occurred in 2,400 domestic well samples, 22 detections occurred in 1,096 public well samples, 20 detections occurred in 847 urban area shallow groundwater samples, and 1 detection occurred in 723 agricultural area shallow groundwater samples. Reported concentrations ranged from approximately 0.007 to 9 µg/L, with the bulk of the samples falling in the range of 0.02–0.2 µg/L (USGS 2006a).

1,1-Dichloroethane was detected in 2.3% of 130 groundwater well samples at a maximum concentration of 0.6 µg/L (Bi et al. 2012). Samples were collected during 2008 and 2009 from five alluvial plains in East China considered to be susceptible to contamination from human activities.

From May 3, 1999 through October 23, 2000, random samples from 954 water sources across the United States were collected. The sources included 579 groundwater and 375 surface water samples. 1,1-Dichloroethane was detected in 11 groundwater samples at levels between 0.1 and 10 µg/L (USGS 2003a).

Shallow groundwaters underlying areas of residential and commercial use in Salt Lake Valley, Utah were analyzed for VOCs such as 1,1-dichloroethane using monitoring wells at 30 separate sites (USGS 2003b). 1,1-Dichloroethane was detected in one of the samples, at an estimated concentration of 0.03 µg/L (below the laboratory reporting level of 0.07µg/L).

1,1-Dicholorethane was one of the primary VOCs detected in several water quality studies from the Snake River Plain aquifer conducted between 1987 and 2005 (USGS 2010a). In April 2007, the USGS National Water Quality Laboratory analyzed perched groundwater samples from well USGS 92 at the Radioactive Waste Management Complex in the Snake River Plain aquifer and 1,1-dichloroethane was detected at a concentration of 0.8 µg/L (USGS 2010a).

The CALEPA (2003) analysis of 13,347 California groundwater sources of drinking water found 1,1-dichloroethane in 68 samples, ranging from 0.51 to 30 ppb. 1,1-Dichloroethane was not found in any of the 754 surface water sources of drinking water sampled.

Samples from 2,948 wells across the United States were sampled between 1985 and 1995. The sources consisted of both drinking water and non-drinking water in 406 urban wells and 2,542 rural wells. The detection frequency of 1,1-dichloroethane was 6.4% in urban wells and 0.7% in rural wells. Reported concentrations were approximately 0.2–60 µg/L with a median of approximately 0.45 µg/L, and approximately 0.2–8 µg/L with a median of about 0.7 µg/L, respectively (Squillace et al. 1999).

VOCs were examined in 30 public water supply wells in the Columbia aquifer in Delaware (USGS 2010c). In 2000, 1,1-dichloroethane was detected 6 times at concentrations ranging from 0.015 to 0.149 µg/L and in 2008, the chemical was detected 4 times at concentrations of <0.04–0.135 µg/L. Active wells were resampled in a study by the Source Water Assessment and Protection Program from August through November 2008. Twenty-two of the original wells and 8 similar wells were sampled. The range of detected concentrations remained the same; however, the number of detections decreased by 1 for both years.

The USGS assessed the quality of source water from public supply wells in the United States from 1993 to 2007 (USGS 2010d). 1,1-Dichloroethane was detected in 7.7% of 832 samples, and 1.4% of the samples contained ≥0.2 µg/L (USGS 2010b). The maximum concentration of 1,1-dichloroethane detected was 4.878 µg/L.

6.4.3 Sediment and Soil

Very little information was found on the ambient concentrations of 1,1-dichloroethane in soil, or on the current disposal of waste products containing the compound in landfills. 1,1-Dichloroethane was detected, yet not quantified, in soil samples of Love Canal, New York. At a detection limit of 0.5 ppb, 1,1-dichloroethane was not detected in sediment of the submarine outfall region of the Los Angeles County (Joint Water Pollution Control Plant [JWPCP]) municipal waste water treatment plant (HSDB 2012). 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 1,1-dichloroethane released to soils to these other media.

Soil gas was monitored for the U.S. Army from October 2010 until September 2011 in Fort Gordon, Georgia (USGS 2012). Soil-gas samplers were installed at three former fuel-dispensing stations in order to assess organic soil-gas contaminants for the Resource Conservation and Recovery Act Part B Hazardous Waste Permit process. There were 55 samplers at one site, 30 samplers at a second site, and 39 samplers at a third site. 1,1-Dichloroethane was reported as not detected in all samples and the method detection limit was 0.02 µg (USGS 2012).

6.4.4 Other Environmental Media

Little information was found on the levels of 1,1-dichloroethane in other media. Ferrario et al. (1985) measured 33 ppb wet weight of 1,1-dichloroethane in oysters from Lake Pontchartrain near New Orleans, Louisiana; however, 1,1-dichloroethane was not detected in two types of clams. Kallonen et al. (1985) detected 1,1-dichloroethane in the effluent gases of burning polyester fiber fill. Data on concentrations in human breath are presented in Section 6.5. 1,1-Dichloroethane was not found in any samples in a survey of 234 table-ready foods evaluated for the presence of VOCs (Heikes et al. 1995). Page and Lacroix (1995) found 1,1-dichloroethane in three peanut butter samples at levels of 1.1, 1.9, and 3.7 µg/kg; however, the compound was not found in several other foods that were analyzed.

6.5 GENERAL POPULATION AND OCCUPATIONAL EXPOSURE

The greatest source of exposure to 1,1-dichloroethane for most of the U.S. population is inhalation of the compound in contaminated air, especially near source areas. Another potential route of human exposure is ingestion of the compound in contaminated drinking water, and use of consumer products that may contain 1,1-dichloroethane. The general population may also be exposed through inhalation of cigarette smoke (Wang et al. 2012). Occupational exposure to 1,1-dichloroethane may occur via inhalation or dermal contact at workplaces where it is produced or used (HSDB 2012).

The Fourth National Report on Human Exposures to Environmental Chemicals, published and updated by the Centers for Disease Control and Prevention (CDC 2015), reported data for 1,1-dichlorethane from the National Health and Nutrition Examination Survey (NHANES) for the survey years 2003–2004 and 2005–2006. These data are summarized in Table 6-4. Blood concentrations of 1,1-dichloroethane for male and female participants of ages 12–>60 years and various ethnicities were reported. Concentrations of 1,1-dichloroethane in all categories for all NHANES survey years were below the detection limit of the method (0.01 µg/L) (CDC 2015).

Table 6-4. Geometric Mean and Selected Percentiles of Blood Concentrations of 1,1-Dichloroethane (in ng/L) for the U.S. Population from the National Health and Nutrition Examination Survey (NHANES)

	Survey years	Geometric mean (95% CI)	Selected percentiles (95% CI)				Sample size
			50th	75th	90th	95th	
Total	2003–2004	*[a]	<LOD[b]	<LOD	<LOD	<LOD	1,367
	2005–2006	*	<LOD	<LOD	<LOD	<LOD	3,193
Age group							
12–19 years	2005–2006	*	<LOD	<LOD	<LOD	<LOD	941
20–59 years	2003–2004	*	<LOD	<LOD	<LOD	<LOD	1,367
	2005–2006	*	<LOD	<LOD	<LOD	<LOD	1,569
≥60 years	2005–2006	*	<LOD	<LOD	<LOD	<LOD	683
Gender							
Males	2003–2004	*	<LOD	<LOD	<LOD	<LOD	670
	2005–2006	*	<LOD	<LOD	<LOD	<LOD	1,510
Females	2003–2004	*	<LOD	<LOD	<LOD	<LOD	697
	2005–2006	*	<LOD	<LOD	<LOD	<LOD	1,683
Race/ethnicity							
Mexican Americans	2003–2004	*	<LOD	<LOD	<LOD	<LOD	267
	2005–2006	*	<LOD	<LOD	<LOD	<LOD	778
Non-Hispanic blacks	2003–2004	*	<LOD	<LOD	<LOD	<LOD	300
	2005–2006	*	<LOD	<LOD	<LOD	<LOD	832
Non-Hispanic whites	2003–2004	*	<LOD	<LOD	<LOD	<LOD	695
	2005–2006	*	<LOD	<LOD	<LOD	<LOD	1,347

[a]Not calculated; the proportion of results below limit of detection (LOD) was too high to provide a valid result. The [b]<LOD means less than the limit of detection, which may vary for some chemicals by year and by individual sample. LODs for survey years 2003–2004 and 2005–2006 were 0.01 and 0.01 µg/L, respectively.

CI = confidence interval

Source: CDC 2015

The National Occupational Exposure Survey (NOES), conducted by NIOSH from 1981 to 1983, indicated that 1,957 workers, including 272 women, were potentially exposed to 1,1-dichloroethane in the workplace (NOES 1990). 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.

NIOSH (1978) noted that there was a large potential for exposure to 1,1-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.

The EPA (1982a) and Wallace et al. (1982) conducted a study of the levels of 1,1-dichloroethane in the inhaled and exhaled air and drinking water of college students in Texas and North Carolina. Low levels (<0.49 ppb) of 1,1-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. 1,1-Dichloroethane was not detected in the breathing zone air of the North Carolina students.

Barkley et al. (1980) found a trace of 1,1-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 1,1-dichloroethane in the expired breath and drinking water of one resident of New Jersey).

Assuming a median ambient air level of 55 pptv reported by EPA (1983b) and a theoretical average inhalation of 20 m^3 air/day, the average inhalation exposure to 1,1-dichloroethane for an individual in the United States is estimated at 4 µg/day.

Buckley et al. (1997) reported the detection of 1,1-dichlorethane in 1 of 16 blood samples at a concentration of 0.01 µg/L. 1,1-Dichloroethane was detected in <10% of blood samples from 1,000 people between the years 1988 and 1994 (Needham et al. 1995). In October 2001, Edelman et al. (2003) analyzed blood and urine samples from World Trade Center firefighters for VOCs, including 1,1-dichloroethane; detection of the compound was insignificant. A National Health and Nutrition Survey of the U.S. population in 2003–2004 screened for 1,1-dichloroethane in blood samples at a limit of detection (LOD) concentration of 0.01 ng/mL (CDC 2015). The samples were taken from 1,367 participants in the age range of 20–59 years old, about half females (n=679) and half males (n=670). The survey included Mexican Americans (n=267), non-Hispanic blacks (n=300), and non-

Hispanic whites (n=695). The portion of the data below the LOD for 1,1-dichloroethane was too high to provide valid results (CDC 2015).

6.6 EXPOSURES OF CHILDREN

This section focuses on exposures from conception to maturity at 18 years in humans. Differences from adults in susceptibility to hazardous substances are discussed in Section 3.7, Children's Susceptibility.

Children are not small adults. A child's exposure may differ from an adult's exposure in many ways. Children drink more fluids, eat more food, breathe more air per kilogram of body weight, and have a larger skin surface in proportion to their body volume. A child's diet often differs from that of adults. The developing human's source of nutrition changes with age: from placental nourishment to breast milk or formula to the diet of older children who eat more of certain types of foods than adults. A child's behavior and lifestyle also influence exposure. Children crawl on the floor, put things in their mouths, sometimes eat inappropriate things (such as dirt or paint chips), and spend more time outdoors. Children also are closer to the ground, and they do not use the judgment of adults to avoid hazards (NRC 1993).

There are no exposure studies or body burden measurements of 1,1-dichloroethane in children. 1,1-Dichloroethane has been detected in air, as discussed in Section 6.4.1, and inhalation of contaminated air likely represents the greatest route of potential exposure for children. 1,1-Dichloroethane has also been detected in drinking water, and therefore, ingestion of contaminated water is a possible source of exposure. Dichloroethane (isomer not specified) has been detected in human milk (Urusova 1953); however, these data are not current.

6.7 POPULATIONS WITH POTENTIALLY HIGH EXPOSURES

Human exposure to 1,1-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 2001c) 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.

Smokers are exposed to higher concentrations of 1,1-dichloroethane than nonsmokers. Emissions from cigarette smoke can contain between 51 and 110 µg 1,1-dichloroethane/cigarette (Wang et al. 2012). The

average concentration of 1,1-dichloroethane at the onset of smoking and 60 minutes after smoking ranges from 7.9 to 26 μg/m^3. In addition, nonsmokers who are in close proximity to cigarette smoke are susceptible to higher exposure concentrations.

6.8 ADEQUACY OF THE DATABASE

Section 104(i)(5) of CERCLA, as amended, directs the Administrator of ATSDR (in consultation with the Administrator of EPA and agencies and programs of the Public Health Service) to assess whether adequate information on the health effects of 1,1-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 1,1-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 the uncertainties of human health assessment. This definition should not be interpreted to mean that all data needs discussed in this section must be filled. In the future, the identified data needs will be evaluated and prioritized, and a substance-specific research agenda will be proposed.

6.8.1 Identification of Data Needs

Physical and Chemical Properties. The physical/chemical properties of 1,1-dichloroethane are sufficiently well characterized to enable assessment of the environmental fate of this compound.

Production, Import/Export, Use, Release, and Disposal. According to the Emergency Planning and Community Right-to-Know Act of 1986, 42 U.S.C. Section 11023, industries are required to submit substance release and off-site transfer information to the EPA. The TRI, which contains this information for 2013, became available in October of 2014. This database is updated yearly and should provide a list of industrial production facilities and emissions.

Based on its industrial use, 1,1-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 1,1-dichloroethane may be substantial. Data concerning the production and use of 1,1-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 limited. 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. 1,1-Dichloroethane released to the atmosphere may be transported long distances before being washed out in precipitation. Although 1,1-dichloroethane released to land surfaces in spills would rapidly volatilize to the atmosphere, the 1,1-dichloroethane remaining on soil surfaces would be available for transport into groundwater. The atmospheric residence time of 1,1-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 1,1-dichloroethane from the water column onto sediments. Additional information on the atmospheric transformation and on the rate of biodegradation of 1,1-dichloroethane in soils would be useful in the determination of its environmental fate.

Bioavailability from Environmental Media. Data are incomplete on the bioavailability of 1,1-dichloroethane from environmental media. Animal data on 1,1-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 1,1-dichloroethane from air, water, soil, and sediment would be useful in determining actual risks associated with exposure to environmental levels of 1,1-dichloroethane.

Food Chain Bioaccumulation. The information located on the potential for bioconcentration of 1,1-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 waste water treatment plant did not detect 1,1-dichloroethane in the animal tissues, although the compound was found in the effluent. However, 1,1-dichloroethane has been detected in oysters (33 ppb wet weight). An estimated bioconcentration potential of <1 from the K_{ow} suggests that bioconcentration would not be expected. Very little information was found regarding the biomagnification of 1,1-dichloroethane among food chain trophic

levels. Additional information on bioconcentration and biomagnification would be useful in determining whether food chain bioaccumulation is an important source of human exposure.

Exposure Levels in Environmental Media. Reliable monitoring data for the levels of 1,1-dichloroethane in contaminated media at hazardous waste sites are needed so that the information obtained on levels of 1,1-dichloroethane in the environment can be used in combination with the known body burden of 1,1-dichloroethane to assess the potential risk of adverse health effects in populations living in the vicinity of hazardous waste sites.

Limited information is available regarding ambient concentrations of 1,1-dichloroethane in soils. Based on a median ambient air level reported in 1982, the average inhalation exposure to 1,1-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 1,1-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 1,1-dichloroethane are available from NIOSH, monitoring data on workplace exposures are generally limited, with a few observations about 1,1-dichloroethane included in detailed studies of 1,2-dichloroethane. A study of the levels of 1,1-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 1,1-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 1,1-dichloroethane would be helpful.

This information is necessary for assessing the need to conduct health studies on these populations.

Exposures of Children. A data need has been identified to conduct body burden studies of 1,1-dichloroethane in children. Measurements of 1,1-dichloroethane in blood samples for a population of adults was conducted in 2003–2004 as part of the National Health and Nutrition Examination Survey (CDC 2015). Most of the samples were below the detection limit of 0.01 ng/mL. Similar results among a group of children would demonstrate that exposure to 1,1-dichloroethane is low for both children and adults.

Child health data needs relating to susceptibility are discussed in Section 3.12.2, Identification of Data Needs: Children's Susceptibility.

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

6.8.2 Ongoing Studies

No ongoing studies regarding sponsored by NIH or EPA were identified for 1,1-dichloroethane.

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7. ANALYTICAL METHODS

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

The analytical methods used to quantify 1,1-dichloroethane in biological and environmental samples are summarized below. Table 7-1 lists the applicable analytical methods used for determining 1,1-dichloroethane in biological fluids and tissues, and Table 7-2 lists the methods used for determining 1,1-dichloroethane in environmental samples.

7.1 BIOLOGICAL MATERIALS

The determination of trace levels of 1,1-dichloroethane in biological tissues and fluids has been restricted to gas chromatography (GC) equipped with mass spectrometry (MS) or flame ionization detection (FID).

Work conducted by Cramer and co-workers (1988) showed that 1,1-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 VOCs 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).

Uehori et al. (1987) developed a retention index in GC to screen and quantify VOCs in blood. A dynamic headspace analyzer and GC/FID with retention indices were employed for the detection of 1,1-dichloroethane at nanogram levels. Uehori et al. (1987) noted that this method is simple and reliable, and requires little or no sample preparation.

Table 7-1. Analytical Methods for Determining 1,1-Dichloroethane in Biological Materials

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
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	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
Whole blood	Collect by venipuncture, store cold; inject sample into purge-and-trap apparatus	GC/MS	0.013 ppb	102–118	Ashley et al. 1992
Breath	Collect human breath sample by means of a spirometer and analyze	GC/MS	Not detected	No data	Barkley et al. 1980
Breath	Collect human breath sample by means of a spirometer and analyze	GC/MS	Not reported	No data	Raymer et al. 1990

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

Table 7-2. Analytical Methods for Determining 1,1-Dichloroethane in Environmental Samples

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Groundwater, aqueous sludges, caustic liquors, soils, sediments	Purge-and-trap (EPA method 624) or direct injection (EPA Method 5030)	GC/MS	4.7 µg/L (groundwater; 5 µg/kg (soil/sediment)	59–155%	EPA 1994a (Method 8240B), 2015a
Groundwater, surface water, waste water	Purge-and-trap (EPA method 624) or direct injection (EPA Method 5030)	GC with HECD	0.002 µg/L	47–132	EPA 1994b (Method 8010B)
Groundwater	Purge-and-trap on absorbent	GC/MS	0.0001–0.02 µg/sample	<±5 relative standard deviation	Lopez-Avila et al. 1987a
Groundwater	Purge-and-trap on absorbent	GC/FID-FID	No data	No data	Driscoll et al. 1987
Groundwater and soil	Purge-and-trap on absorbent	GC/EICD-FID	Water=0.1–0.9 µg/L; soil=1–5 µg/L	83–102	Lopez-Avila 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
Drinking water	Pass sample through XAD-2 macroreticular resin and extract continuously with ether	GC/MS	<1 µg/L	No data	Suffet et al. 1986
Drinking water	Purge-and-trap water sample	GC/MS	0.2 µg/L	94	Otson and Chan 1987
Drinking water	Extract sample in hexane and analyze	GC-EICD	<1 µg/L	No data	Otson and Chan
Drinking water	Purge-and-trap on Tenax absorbent	GC-EICD-FID	<1 µg/L	>75	Otson and Williams 1982
Drinking water	Purge-and-trap water sample	GC/EICD	80 µg/L	84	Comba and Kaiser 1983
Drinking water	Purge-and-trap water sample	GC/EICD-FID	0.1–0.5 µg/L	No data	Kingsley et al. 1983
Water (river; sea)	Inject 1 mL into flow injection analysis system	MIMS/ITD	0.2 ppb	No data	Bauer and Solyom 1994
Waste water	Collect water sample through a permeation cell membrane and direct into GC	GC/FID	µg/L (ppb) range	<6 relative standard deviation	Blanchard and Hardy 1986

Table 7-2. Analytical Methods for Determining 1,1-Dichloroethane in Environmental Samples

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Waste water	Collect sample through a permeation cell membrane; adsorb onto charcoal; extract with carbon disulfide	GC/FID	74–16,800 µg/L	No data	Blanchard and Hardy 1985
Waste water (municipal and industrial discharges)	Purge-and-trap (EPA method 601) with direct aqueous injection; the trap is backflushed and heated to desorb compounds onto column	GC/MS	0.07 µg/L	47–132	EPA 2001a
Waste water (municipal and industrial discharges)	Purge-and-trap (EPA method 624); the trap is backflushed and heated to desorb compounds onto column	GC/MS	4.7 µ/L	59–155	EPA 1999, 2015a
Waste water	Purge-and-trap with isotopic dilution (EPA method 1624); stable isotopes are added; the trap is backflushed and heated to desorb compounds onto column	GC/MS	10 µg/L	Labeled compound recovery: 23–191	EPA 2001b
Waste water and sludge	Purge-and-trap on adsorbent	GC/MS	No data	No data	Giabbaie et al. 1983
Drinking, ground, and surface water	Purge and trap water sample	GC/AED	0.17 µg/L	No data	Silgoner et al. 1997
Air (ambient)	Purge-and-trap on charcoal absorbent; extract with carbon disulfide	GC/ECD	0.001 ppm range	No data	Bruner et al. 1978
Air (ambient)	Collect air sample on Tenax adsorbent; vaporize thermally and analyze	GC/MS	23 µg/m^3	No data	Pellizari 1982
Air (ambient)	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
Air (ambient)	Adsorb air sample onto charcoal tube; extract with carbon disulfide	GC/FID	ppm range	No data	NIOSH 2003 (method 1003)

Table 7-2. Analytical Methods for Determining 1,1-Dichloroethane in Environmental Samples

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Air (space cabin)	Dehydrohalogenate air sample with lithium hydroxide and analyze	GC/MS	0.5–4.0 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
Air	Air collected in cooled trap; heated upon injection	GC/IMS	No data	No data	Simpson et al. 1996
Air (ambient)	Collection on multiadsorbent traps; automated preconcentration	Capillary GC/MS	0.71 ppbv		Oliver et al. 1996
Air	Sample collected on Tenax GC/carboxene 1000 trap, separated by capillary column	GC/PID/EICD	0.1 ppb		Maeda et al. 1998
Various food (e.g., dairy products, meat, vegetables, and soda)	Food containing >70% fat: dissolve sample in isooctane and shake; cleanup on florisil column	GC/ECD-EICD	ng/g range	~70	Daft 1988
Various food (e.g., fruit juices, soda, coffees, cream, peanut butter, and butter)	Cold liquid (4 °C) and aqueous flour-based samples injected; plunge sampling tube or needle into dry/viscous foods for injection; steam distillation; purge and trap	SD/PT/GC	0.003 µg/kg	95.2	Page and Lacroix 1995
Compound formulation	Prepare dilute solution of sample in MeOH; introduce into headspace trap	GC/PID	20 pg	No data	Jerpe and Davis 1987
Fish tissue	Add water to fish sample; homogenize and extract ultrasonically; purge-and-trap on adsorbent	GC/MS	0.01 µg/g	77	Easley et al. 1981
Fish tissue	Freeze fish sample; homogenize in liquid nitrogen; distill in vacuum	GC/MS equipped with fused-silica capillary column	No data	No data	Hiatt 1983

Table 7-2. Analytical Methods for Determining 1,1-Dichloroethane in Environmental Samples

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Fish tissue	Warm sample; purge-and-trap volatiles on activated carbon adsorbent; extract with carbon disulfide	GC/FID	No data	~32	Reinert et al. 1983
Fish tissue	Edible tissue and liver homogenized in blender; organic-free water and standard added; vial sealed and placed in ultrasonic bath; purge and trap	GC/EICD	5 pg/g	115±25	Roose and Brinkman 1998
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 relative standard deviation	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; fish matrix 90	Hiatt 1981

AED = atomic emission detection; ECD = electron captive detector; EICD = electrolytic conductivity detector; FID = flame ionization detector; GC = gas chromatography; HECD = Hall electrolytic conductivity detector; IMS = ion mobility spectrometry; ITD = ion trap detector; MIMS = membrane introduction mass spectrometry; MS = mass spectrometry; PID = photoionization detector; PT = purge-and-trap; SD = steam distillation

Gas purging-and-trapping on a Tenax GC adsorbent and GC/MS technique has been employed by Barkley et al. (1980) and Ashley et al. (1992) for the determination of trace levels of volatile halogenated compounds (including 1,1-dichloroethane) in water, human blood, and urine.

7.2 ENVIRONMENTAL SAMPLES

A GC equipped with an appropriate detector is the most frequently used analytical technique for determining the concentrations of 1,1-dichloroethane in air, water, soil, fish, dairy 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. The EPA updated Method 624 with revised quality control frequencies and improved internal standards and surrogates (EPA 2015a). GC columns were changed from packed columns to open tubular capillary columns in order to increase resolution and decrease losses due to adsorption.

Gas purging-and-trapping is the generally accepted method for the isolation, concentration, and determination of VOCs in water and various environmental samples (Bellar et al. 1979; EPA 1994a, 1994b, 1996b, 1999, 2001a, 2001b; Lopez-Avila et al. 1987a, 1987b; Page and Lacroix 1995; Reding 1987; Wylie 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 <1 µg 1,1-dichloroethane/L of sample have been achieved by this method (Dreisch and Munson 1983; Kingsley et al. 1983; Lopez-Avila et al. 1987a, 1987b; Otson and Williams 1982). Page and Lacroix (1995) successfully coupled purge-and-trap procedures with steam distillation collection methods to yield an analytical method, for various foods, with a detection limit of 0.003 µg/kg for 1,1-dichloroethane. 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 1,1-dichloroethane in environmental samples.

A purge-and-trap method with cryogenic trapping (cryofocusing) for concentrating VOCs from water samples into the headspace, for analysis by capillary GC, was described by Pankow and Rosen (1988). 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). Roose and Brinkman (1998) capitalized on these techniques to analyze fish samples in a rapid, selective, and sensitive manner. An automated GC system with dual multi-adsorbent traps was successfully operated in a mobile laboratory to collect and analyze ambient air samples. The system continuously collects air samples, uses a pre-concentration approach (cryofocusing), and recovers analytes using thermal desorption. The detection limit for 1,1-dichloroethane was reported as 0.71 ppbv (Oliver et al. 1996).

Purge-and-trap techniques have been successfully coupled with atomic emission detection (AED) for the analysis of water (Silgoner et al. 1997). Solutes eluting from the GC are atomized in a microwave-induced plasma, and individual wavelengths are measured using a photodiode array. The detection limit of this method for 1,1-dichloroethane is 0.17 µg/L. While some improvement is still needed, the purge-and-trap technique coupled with AED offers some advantages over other methods. Dynamic headspace analyzer GC has been used for the analysis and identification of 1,1-dichloroethane in water and fish tissue (Comba and Kaiser 1983; Mehran et al. 1986; Otson and Williams 1982; Reinert 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. Detection limits of <1 µg 1,1-dichloroethane/L water and <1 µg 1,1-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 1,1-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 components and peak masking problems were encountered.

Bauer and Solyom (1994) and Wong et al. (1995) reported that membrane introduction mass spectrometry (MIMS) offers measurements of trace-level organics in environmental media, including polluted seawater, without sample preparation, using a non-porous silicon membrane. A detection limit of 0.2 ppb was reported for 1,1-dichloroethane (Bauer and Solyom 1994).

Pellizzari (1982) initiated the development and evaluation of trace levels of VOCs 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 μg/m^3 level (Pellizzari 1982).

Simpson et al. (1996) developed a method that has potential for on-site monitoring of vapor-phase organics in air. GC is coupled with ion mobility spectrometry to offer high sensitivity and the ability to operate at ambient pressure. While a detection limit for 1,1-dichloroethane was not reported, detection limits for several other EPA priority pollutants ranged from 0.05 to 140 pg/second. Maeda et al. (1998) also investigated analytical methods that may be applied to on-site monitoring techniques of HAPs. The analytical methods that they employed included a Tenax GC and Carboxene 1000 trap, followed by capillary separation and either photo ionization detector (PID) or EICD detection methods. The detection limit of the system was reported as 0.1 ppb. Another method for sampling and analyzing VOCs in air is proposed to have some advantages for use in field situations and may provide satisfactory results. The method uses teraglyme as a sample enrichment tool and employs purge-and-trap methods along with GC/MS (Huybrechts et al. 2001).

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 VOCs 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 1,1-dichloroethane in aqueous samples containing limited number of VOCs. It is less effective for aqueous samples containing large numbers of VOCs. 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 (<1 μg/L of sample) of 1,1-dichloroethane in drinking water.

Daft (1988) employed a photoionization detector and an electrolytic conductivity detector connected in series to a capillary GC to detect 1,1-dichloroethane at ng/g levels in fumigants and industrial chemical residues of various foods (e.g., dairy 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 VOCs, 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 >0.78 torr (approximately 50 °C) in the sample chamber (Hiatt 1983).

7.3 ADEQUACY OF THE DATABASE

Section 104(i)(5) of CERCLA, as amended, directs the Administrator of ATSDR (in consultation with the Administrator of EPA and agencies and programs of the Public Health Service) to assess whether adequate information on the health effects of 1,1-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 1,1-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 the uncertainties of human health assessment. This definition should not be interpreted to mean that all data needs discussed in this section must be filled. In the future, the identified data needs will be evaluated and prioritized, and a substance-specific research agenda will be proposed.

7.3.1 Identification of Data Needs

Methods for Determining Biomarkers of Exposure and Effect. Reliable methods are available for detecting and quantifying 1,1-dichloroethane in the tissues and body fluids of humans. GC/MS or GC/FID has been employed to detect 1,1-dichloroethane at nanogram to picogram levels in blood and tissue samples of humans. No additional analytical methods for determining trace levels of 1,1-dichloro-

ethane in the blood of humans are needed. Also, no detection limits for detecting 1,1-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 1,1-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 1,1-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 1,1-dichloroethane in environmental samples. Purge-and-trap or direct injection followed by analysis with GC/ECD and GC/MS have been used to detect and quantify 1,1-dichloroethane in water samples at ppt and ppb levels (methods 5030, 8240, 8010B [EPA 1994a, 1994b, 1996b]; method 601, 624, 1624 [EPA 1999, 2001a, 2001b]). GC equipped with FID, PID, or EICD has also been used to detect and quantify 1,1-dichloroethane in air, water, milk, vegetables, and fish at ppb levels NIOSH (method 1003 [NIOSH 2003]). No additional analytical methods for determining trace levels of 1,1-dichloroethane in environmental media are needed.

7.3.2 Ongoing Studies

No ongoing studies regarding sponsored by NIH or EPA were identified for 1,1-dichloroethane.

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8. REGULATIONS, ADVISORIES, AND GUIDELINES

MRLs are substance specific estimates, which are intended to serve as screening levels, are used by ATSDR health assessors and other responders to identify contaminants and potential health effects that may be of concern at hazardous waste sites.

No inhalation or oral MRLs were derived for 1,1-dichloroethane.

The EPA (IRIS 2002) has not derived an oral reference dose (RfD) or an inhalation reference concentration (RfC) for 1,1-dichloroethane.

1,1-Dichloroethane appears on the list of chemicals in "The Emergency Planning and Community Right-to-Know Act of 1986" and has been assigned a reportable quantity (RQ) limit of 1,000 pounds (EPA 2014e). The RQ represents the amount of a designated hazardous substance which, when released to any environmental media, must be reported to the appropriate authority.

The international and national regulations, advisories, and guidelines regarding 1,1-dichloroethane in air, water, and other media are summarized in Table 8-1.

Table 8-1. Regulations, Advisories, and Guidelines Applicable to 1,1-Dichloroethane

Agency	Description	Information	Reference
INTERNATIONAL			
Guidelines:			
IARC	Carcinogenicity classification	No data	IARC 2015
WHO	Air quality guidelines	No data	WHO 2010
	Drinking water quality guidelines	No data[a]	WHO 2011
NATIONAL			
Regulations and Guidelines:			
a. Air			
ACGIH	TLV (8-hour TWA)	100 ppm	ACGIH 2014
AIHA	ERPGs	No data	AIHA 2014
DOE	PAC-1 and PAC-2[b]	160 ppm	DOE 2012a
	PAC-3[b]	4,000 ppm	
EPA	AEGLs	No data	EPA 2014b
	NAAQS	No data	EPA 2012b
NIOSH	REL (10-hour TWA)	100 ppm (400 mg/m^3)[c]	NIOSH 2015
	IDLH	3,000 ppm	
OSHA	PEL (8-hour TWA) for general industry	100 ppm (400 mg/m^3)	OSHA 2013 29 CFR 1910.1000, Table Z-1
	PEL (8-hour TWA) for construction	100 ppm (400 mg/m^3)	OSHA 2014a 29 CFR 1926.55, Appendix A
	PEL (8-hour TWA) for shipyards	100 ppm (400 mg/m^3)	OSHA 2014b 29 CFR 1915.1000
b. Water			
EPA	Designated as hazardous substances in accordance with Section 311(b)(2)(A) of the Clean Water Act	No data	EPA 2013a 40 CFR 116.4
	Drinking water standards and health advisories	No data	EPA 2012a
	Master Testing List	Yes[d]	EPA 2014c
	National primary drinking water standards	No data	EPA 2009
	National recommended water quality criteria: human health for the consumption of	No data	EPA 2013b
	Reportable quantities of hazardous substances designated pursuant to Section 311 of the Clean Water Act	No data	EPA 2013c 40 CFR 117.3

Table 8-1. Regulations, Advisories, and Guidelines Applicable to 1,1-Dichloroethane

Agency	Description	Information	Reference
NATIONAL *(cont.)*			
c. Food			
FDA	EAFUS[e]	No data	FDA 2013
d. Other			
ACGIH	Carcinogenicity classification	A4[f]	ACGIH 2014
EPA	Carcinogenicity classification	C[g]	IRIS 2002
	RfC	No data	
	RfD	No data	
	Identification and listing of hazardous waster	U076	EPA 2013e 40 CFR 261, Appendix VIII
	Inert pesticide ingredients in pesticide products	No data	EPA 2014d
	Superfund, emergency planning, and community right-to-know		
	Designated CERCLA hazardous substance and reportable quantity	1,000 pounds[h]	EPA 2014e 40 CFR 302.4
	Effective date of toxic chemical release reporting	01/01/1994	EPA 2014f 40 CFR 372.65
	Extremely hazardous substances and its threshold planning quantity	No data	EPA 2013d 40 CFR 355, Appendix A
	TSCA chemical lists and reporting periods		EPA 2014g 40 CFR 712.30
	Effective date	03/11/1994	
	Reporting date	05/10/1994	
	TSCA health and safety data reporting		EPA 2014h 40 CFR 716.120
	Effective date	06/01/1987	
	Reporting date	06/01/1997	
NTP	Carcinogenicity classification	No data	NTP 2014

[a]In view of the very limited database on toxicity and carcinogenicity, the Guidelines concluded that no guideline value for 1,1-dichloroethane should be proposed.
[b]Definitions of PAC terminology are available from U.S. Department of Energy (DOE 2012b).
[c]NIOSH recommends that 1,1-dichloroethane be treated in the workplace with caution because of its structural similarity to the four chloroethanes (ethylene dichloride, hexachloroethane, 1,1,2,2-tetrachloroethane, and 1,1,2-trichloroethane) shown to be carcinogenic in animals.
[d]1,-Dichloroethane was recommended to the MTL by the EPA's Office of Water and Office of Drinking Water in 1990 and was later removed in 1995. The initial chemical testing program was for prechronic toxicity (14–28 day) and subchronic toxicity (90 day) health effects.
[e]The EAFUS list of substances contains ingredients added directly to food that FDA has either approved as food additives or listed or affirmed as GRAS.
[f]A4: not classifiable as a human carcinogen
[g]C: possible human carcinogen
[h]Designated CERCLA hazardous substance pursuant to Section 307(a)of the Clean Water Act, Section 112 of the Clean Air Act, and Section 3001 of RCRA.

Table 8-1. Regulations, Advisories, and Guidelines Applicable to 1,1-Dichloroethane

Agency	Description	Information	Reference

ACGIH = American Conference of Governmental Industrial Hygienists; AEGL = acute exposure guideline levels; AIHA = American Industrial Hygiene Association; CERCLA = Comprehensive Environmental Response, Compensation, and Liability Act; CFR = Code of Federal Regulations; DOE = Department of Energy; EAFUS = Everything Added to Food in the United States; EPA = Environmental Protection Agency; ERPG = emergency response planning guidelines; FDA = Food and Drug Administration; GRAS = Generally Recognized As Safe; IARC = International Agency for Research on Cancer; IDLH = immediately dangerous to life or health; IRIS = Integrated Risk Information System; MTL = Master Testing List; NAAQS = National Ambient Air Quality Standards; NIOSH = National Institute for Occupational Safety and Health; NTP = National Toxicology Program; OSHA = Occupational Safety and Health Administration; PAC = Protective Action Criteria; PEL = permissible exposure limit; RCRA = Resource Conservation and Recovery Act; REL = recommended exposure limit; RfC = inhalation reference concentration; RfD = oral reference dose; TLV = threshold limit values; TSCA = Toxic Substances Control Act; TSD = treatment, storage, and disposal; TWA = time-weighted average; WHO = World Health Organization

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10. GLOSSARY

Absorption—The taking up of liquids by solids, or of gases by solids or liquids.

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

Adsorption—The adhesion in an extremely thin layer of molecules (as of gases, solutes, or liquids) to the surfaces of solid bodies or liquids with which they are in contact.

Adsorption Coefficient (K_{oc})—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 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.

Benchmark Dose (BMD)—Usually defined as the lower confidence limit on the dose that produces a specified magnitude of changes in a specified adverse response. For example, a BMD_{10} would be the dose at the 95% lower confidence limit on a 10% response, and the benchmark response (BMR) would be 10%. The BMD is determined by modeling the dose response curve in the region of the dose response relationship where biologically observable data are feasible.

Benchmark Dose Model—A statistical dose-response model applied to either experimental toxicological or epidemiological data to calculate a BMD.

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.

Biomarkers—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.

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

Carcinogen—A chemical capable of inducing cancer.

Case-Control Study—A type of epidemiological study that examines the relationship between a particular outcome (disease or condition) and a variety of potential causative agents (such as toxic chemicals). In a case-controlled study, a group of people with a specified and well-defined outcome is identified and compared to a similar group of people without outcome.

Case Report—Describes a single individual with a particular disease or exposure. These may suggest some potential topics for scientific research, but are not actual research studies.

Case Series—Describes the experience of a small number of individuals with the same disease or exposure. These may suggest potential topics for scientific research, but are not actual research studies.

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.

Cohort Study—A type of epidemiological study of a specific group or groups of people who have had a common insult (e.g., exposure to an agent suspected of causing disease or a common disease) and are followed forward from exposure to outcome. At least one exposed group is compared to one unexposed group.

Cross-sectional Study—A type of epidemiological study of a group or groups of people that examines the relationship between exposure and outcome to a chemical or to chemicals at one point in time.

Data Needs—Substance-specific informational needs that if met would reduce the uncertainties of human health assessment.

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.

Dose-Response Relationship—The quantitative relationship between the amount of exposure to a toxicant and the incidence of the adverse effects.

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 occurs. The terms, as used here, include malformations and variations, altered growth, and *in utero* death.

Environmental Protection Agency (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.

Epidemiology—Refers to the investigation of factors that determine the frequency and distribution of disease or other health-related conditions within a defined human population during a specified period.

Genotoxicity—A specific adverse effect on the genome of living cells that, upon the duplication of affected cells, can be expressed as a mutagenic, clastogenic, or carcinogenic event because of specific alteration of the molecular structure of the genome.

Half-life—A measure of rate for the time required to eliminate one half of a quantity of a chemical from the body or environmental media.

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

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

Immunological Effects—Functional changes in the immune response.

Incidence—The ratio of individuals in a population who develop a specified condition to the total number of individuals in that population who could have developed that condition in a specified time period.

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

***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 that 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 has been reported to have caused death in humans or animals.

Lethal Dose$_{(50)}$ (LD_{50})—The dose of a chemical that 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 exposure level 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.

Lymphoreticular Effects—Represent morphological effects involving lymphatic tissues such as the lymph nodes, spleen, and thymus.

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

Minimal Risk Level (MRL)—An estimate of daily human exposure to a hazardous substance that is likely to be without an appreciable risk of adverse noncancer health effects over a specified route and duration of exposure.

Modifying Factor (MF)—A value (greater than zero) that is applied to the derivation of a Minimal Risk Level (MRL) to reflect additional concerns about the database that are not covered by the uncertainty factors. The default value for a MF is 1.

Morbidity—State of being diseased; morbidity rate is the incidence or prevalence of disease in a specific population.

Mortality—Death; mortality rate is a measure of the number of deaths in a population during a specified interval of time.

Mutagen—A substance that causes mutations. A mutation is a change in the DNA sequence of a cell's DNA. Mutations can lead to birth defects, miscarriages, or cancer.

Necropsy—The gross examination of the organs and tissues of a dead body to determine the cause of death or pathological conditions.

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

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

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

Odds Ratio (OR)—A means of measuring the association between an exposure (such as toxic substances and a disease or condition) that represents the best estimate of relative risk (risk as a ratio of the incidence among subjects exposed to a particular risk factor divided by the incidence among subjects who were not exposed to the risk factor). An OR of greater than 1 is considered to indicate greater risk of disease in the exposed group compared to the unexposed group.

Organophosphate or Organophosphorus Compound—A phosphorus-containing organic compound and especially a pesticide that acts by inhibiting cholinesterase.

Permissible Exposure Limit (PEL)—An Occupational Safety and Health Administration (OSHA) allowable exposure level in workplace air averaged over an 8-hour shift of a 40-hour workweek.

Pesticide—General classification of chemicals specifically developed and produced for use in the control of agricultural and public health pests.

Pharmacokinetics—The dynamic behavior of a material in the body, used to predict the fate (disposition) of an exogenous substance in an organism. Utilizing computational techniques, it provides the means of studying the absorption, distribution, metabolism, and excretion of chemicals by the body.

Pharmacokinetic Model—A set of equations that can be used to describe the time course of a parent chemical or metabolite in an animal system. There are two types of pharmacokinetic models: data-based and physiologically-based. A data-based model divides the animal system into a series of compartments, which, in general, do not represent real, identifiable anatomic regions of the body, whereas the physiologically-based model compartments represent real anatomic regions of the body.

Physiologically Based Pharmacodynamic (PBPD) Model—A type of physiologically based dose-response model that quantitatively describes the relationship between target tissue dose and toxic end points. These models advance the importance of physiologically based models in that they clearly describe the biological effect (response) produced by the system following exposure to an exogenous substance.

Physiologically Based Pharmacokinetic (PBPK) Model—Comprised of a series of compartments representing organs or tissue groups with realistic weights and blood flows. These models require a

variety of physiological information: tissue volumes, blood flow rates to tissues, cardiac output, alveolar ventilation rates, and possibly membrane permeabilities. The models also utilize biochemical information, such as air/blood partition coefficients, and metabolic parameters. PBPK models are also called biologically based tissue dosimetry models.

Prevalence—The number of cases of a disease or condition in a population at one point in time.

Prospective Study—A type of cohort study in which the pertinent observations are made on events occurring after the start of the study. A group is followed over time.

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

Recommended Exposure Limit (REL)—A National Institute for Occupational Safety and Health (NIOSH) time-weighted average (TWA) concentration for up to a 10-hour workday during a 40-hour workweek.

Reference Concentration (RfC)—An estimate (with uncertainty spanning perhaps an order of magnitude) of a continuous inhalation exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious noncancer health effects during a lifetime. The inhalation reference concentration is for continuous inhalation exposures and is appropriately expressed in units of mg/m^3 or ppm.

Reference Dose (RfD)—An estimate (with uncertainty spanning perhaps an order of magnitude) of the daily exposure of the human population to a potential hazard that is likely to be without risk of deleterious effects during a lifetime. The RfD is operationally derived from the no-observed-adverse-effect level (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 the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA). Reportable quantities are (1) 1 pound or greater or (2) for selected substances, an amount established by regulation either under CERCLA or under Section 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.

Retrospective Study—A type of cohort study based on a group of persons known to have been exposed at some time in the past. Data are collected from routinely recorded events, up to the time the study is undertaken. Retrospective studies are limited to causal factors that can be ascertained from existing records and/or examining survivors of the cohort.

Risk—The possibility or chance that some adverse effect will result from a given exposure to a chemical.

Risk Factor—An aspect of personal behavior or lifestyle, an environmental exposure, or an inborn or inherited characteristic that is associated with an increased occurrence of disease or other health-related event or condition.

Risk Ratio—The ratio of the risk among persons with specific risk factors compared to the risk among persons without risk factors. A risk ratio greater than 1 indicates greater risk of disease in the exposed group compared to the unexposed group.

Short-Term Exposure Limit (STEL)—The American Conference of Governmental Industrial Hygienists (ACGIH) maximum concentration to which workers can be exposed for up to 15 minutes continually. No more than four excursions are allowed per day, and there must be at least 60 minutes between exposure periods. The daily Threshold Limit Value-Time Weighted Average (TLV-TWA) may not be exceeded.

Standardized Mortality Ratio (SMR)—A ratio of the observed number of deaths and the expected number of deaths in a specific standard population.

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)—An American Conference of Governmental Industrial Hygienists (ACGIH) concentration of a substance to which most workers can be exposed without adverse effect. The TLV may be expressed as a Time Weighted Average (TWA), as a Short-Term Exposure Limit (STEL), or as a ceiling limit (CL).

Time-Weighted Average (TWA)—An allowable exposure concentration averaged over a normal 8-hour workday or 40-hour workweek.

Toxic Dose$_{(50)}$ (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.

Toxicokinetic—The absorption, distribution, and elimination of toxic compounds in the living organism.

Uncertainty Factor (UF)—A factor used in operationally deriving the Minimal Risk Level (MRL) or Reference Dose (RfD) or Reference Concentration (RfC) 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 lowest-observed-adverse-effect level (LOAEL) data rather than no-observed-adverse-effect level (NOAEL) data. A default for each individual UF is 10; if complete certainty in data exists, a value of 1 can be used; however, a reduced UF of 3 may be used on a case-by-case basis, 3 being the approximate logarithmic average of 10 and 1.

Xenobiotic—Any chemical that is foreign to the biological system.

APPENDIX A. ATSDR MINIMAL RISK LEVELS AND WORKSHEETS

The Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA) [42 U.S.C. 9601 et seq.], as amended by the Superfund Amendments and Reauthorization Act (SARA) [Pub. L. 99–499], requires that the Agency for Toxic Substances and Disease Registry (ATSDR) develop jointly with the U.S. Environmental Protection Agency (EPA), in order of priority, a list of hazardous substances most commonly found at facilities on the CERCLA National Priorities List (NPL); prepare toxicological profiles for each substance included on the priority list of hazardous substances; and assure the initiation of a research program to fill identified data needs associated with the substances.

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

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

MRLs are intended only to serve as a screening tool to help public health professionals decide where to look more closely. They may also be viewed as a mechanism to identify those hazardous waste sites that

are not expected to cause adverse health effects. Most MRLs contain a degree of uncertainty because of the lack of precise toxicological information on the people who might be most sensitive (e.g., infants, elderly, nutritionally or immunologically compromised) to the effects of hazardous substances. ATSDR uses a conservative (i.e., protective) approach to address this uncertainty consistent with the public health principle of prevention. Although human data are preferred, MRLs often must be based on animal studies because relevant human studies are lacking. In the absence of evidence to the contrary, ATSDR assumes that humans are more sensitive to the effects of hazardous substance than animals and that certain persons may be particularly sensitive. Thus, the resulting MRL may be as much as 100-fold below levels that have been shown to be nontoxic in laboratory animals.

Proposed MRLs undergo a rigorous review process: Health Effects/MRL Workgroup reviews within the Division of Toxicology and Human Health Sciences, expert panel peer reviews, and agency-wide MRL Workgroup reviews, with participation from other federal agencies and comments from the public. They are subject to change as new information becomes available concomitant with updating the toxicological profiles. Thus, MRLs in the most recent toxicological profiles supersede previously published levels. For additional information regarding MRLs, please contact the Division of Toxicology and Human Health Sciences, Agency for Toxic Substances and Disease Registry, 1600 Clifton Road NE, Mailstop F-57, Atlanta, Georgia 30329-4027.

MRLs were not derived for 1,1-dichloroethane, as discussed in Section 2.3.

APPENDIX B. USER'S GUIDE

Chapter 1

Public Health Statement

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

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

Chapter 2

Relevance to Public Health

This chapter provides a health effects summary based on evaluations of existing toxicologic, epidemiologic, and toxicokinetic information. This summary is designed to present interpretive, weight-of-evidence discussions for human health end points by addressing the following questions:

1. What effects are known to occur in humans?

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

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

The chapter covers end points in the same order that they appear within the Discussion of Health Effects by Route of Exposure section, by route (inhalation, oral, and dermal) and within route by effect. Human data are presented first, then animal data. Both are organized by duration (acute, intermediate, chronic). *In vitro* data and data from parenteral routes (intramuscular, intravenous, subcutaneous, etc.) are also considered in this chapter.

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

Limitations to existing scientific literature that prevent a satisfactory evaluation of the relevance to public health are identified in the Chapter 3 Data Needs section.

Interpretation of Minimal Risk Levels

Where sufficient toxicologic information is available, ATSDR has derived MRLs for inhalation and oral routes of entry at each duration of exposure (acute, intermediate, and chronic). These MRLs are not meant to support regulatory action, but to acquaint health professionals with exposure levels at which adverse health effects are not expected to occur in humans.

MRLs should help physicians and public health officials determine the safety of a community living near a chemical emission, given the concentration of a contaminant in air or the estimated daily dose in water. MRLs are based largely on toxicological studies in animals and on reports of human occupational exposure.

MRL users should be familiar with the toxicologic information on which the number is based. Chapter 2, "Relevance to Public Health," contains basic information known about the substance. Other sections such as Chapter 3 Section 3.9, "Interactions with Other Substances," and Section 3.10, "Populations that are Unusually Susceptible" provide important supplemental information.

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

To derive an MRL, ATSDR generally selects the most sensitive end point which, in its best judgement, represents the most sensitive human health effect for a given exposure route and duration. ATSDR cannot make this judgement or derive an MRL unless information (quantitative or qualitative) is available for all potential systemic, neurological, and developmental effects. If this information and reliable quantitative data on the chosen end point are available, ATSDR derives an MRL using the most sensitive species (when information from multiple species is available) with the highest no-observed-adverse-effect level (NOAEL) that does not exceed any adverse effect levels. When a NOAEL is not available, a lowest-observed-adverse-effect level (LOAEL) can be used to derive an MRL, and an uncertainty factor (UF) of 10 must be employed. Additional uncertainty factors of 10 must be used both for human variability to protect sensitive subpopulations (people who are most susceptible to the health effects caused by the substance) and for interspecies variability (extrapolation from animals to humans). In deriving an MRL, these individual uncertainty factors are multiplied together. The product is then divided into the inhalation concentration or oral dosage selected from the study. Uncertainty factors used in developing a substance-specific MRL are provided in the footnotes of the levels of significant exposure (LSE) tables.

Chapter 3

Health Effects

Tables and Figures for Levels of Significant Exposure (LSE)

Tables and figures are used to summarize health effects and illustrate graphically levels of exposure associated with those effects. These levels cover health effects observed at increasing dose concentrations and durations, differences in response by species, MRLs to humans for noncancer end points, and EPA's estimated range associated with an upper- bound individual lifetime cancer risk of 1 in 10,000 to 1 in 10,000,000. Use the LSE tables and figures for a quick review of the health effects and to locate data for a specific exposure scenario. The LSE tables and figures should always be used in conjunction with the text. All entries in these tables and figures represent studies that provide reliable, quantitative estimates of NOAELs, LOAELs, or Cancer Effect Levels (CELs).

The legends presented below demonstrate the application of these tables and figures. Representative examples of LSE Table 3-1 and Figure 3-1 are shown. The numbers in the left column of the legends correspond to the numbers in the example table and figure.

LEGEND

See Sample LSE Table 3-1 (page B-6)

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

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

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

(4) Key to Figure. Each key number in the LSE table links study information to one or more data points using the same key number in the corresponding LSE figure. In this example, the study represented by key number 18 has been used to derive a NOAEL and a Less Serious LOAEL (also see the two "18r" data points in sample Figure 3-1).

(5) Species. The test species, whether animal or human, are identified in this column. Chapter 2, "Relevance to Public Health," covers the relevance of animal data to human toxicity and Section 3.4, "Toxicokinetics," contains any available information on comparative toxicokinetics. Although NOAELs and LOAELs are species specific, the levels are extrapolated to equivalent human doses to derive an MRL.

(6) Exposure Frequency/Duration. The duration of the study and the weekly and daily exposure regimens are provided in this column. This permits comparison of NOAELs and LOAELs from different studies. In this case (key number 18), rats were exposed to “Chemical x” via inhalation for 6 hours/day, 5 days/week, for 13 weeks. For a more complete review of the dosing regimen, refer to the appropriate sections of the text or the original reference paper (i.e., Nitschke et al. 1981).

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

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

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

(10) Reference. The complete reference citation is given in Chapter 9 of the profile.

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

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

LEGEND

See Sample Figure 3-1 (page B-7)

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

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

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

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

(16) NOAEL. In this example, the open circle designated 18r identifies a NOAEL critical end point in the rat upon which an intermediate inhalation exposure MRL is based. The key number 18 corresponds to the entry in the LSE table. The dashed descending arrow indicates the extrapolation from the exposure level of 3 ppm (see entry 18 in the table) to the MRL of 0.005 ppm (see footnote "b" in the LSE table).

(17) CEL. Key number 38m is one of three studies for which CELs were derived. The diamond symbol refers to a CEL for the test species-mouse. The number 38 corresponds to the entry in the LSE table.

(18) Estimated Upper-Bound Human Cancer Risk Levels. This is the range associated with the upper-bound for lifetime cancer risk of 1 in 10,000 to 1 in 10,000,000. These risk levels are derived from the EPA's Human Health Assessment Group's upper-bound estimates of the slope of the cancer dose response curve at low dose levels (q_1*).

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

SAMPLE

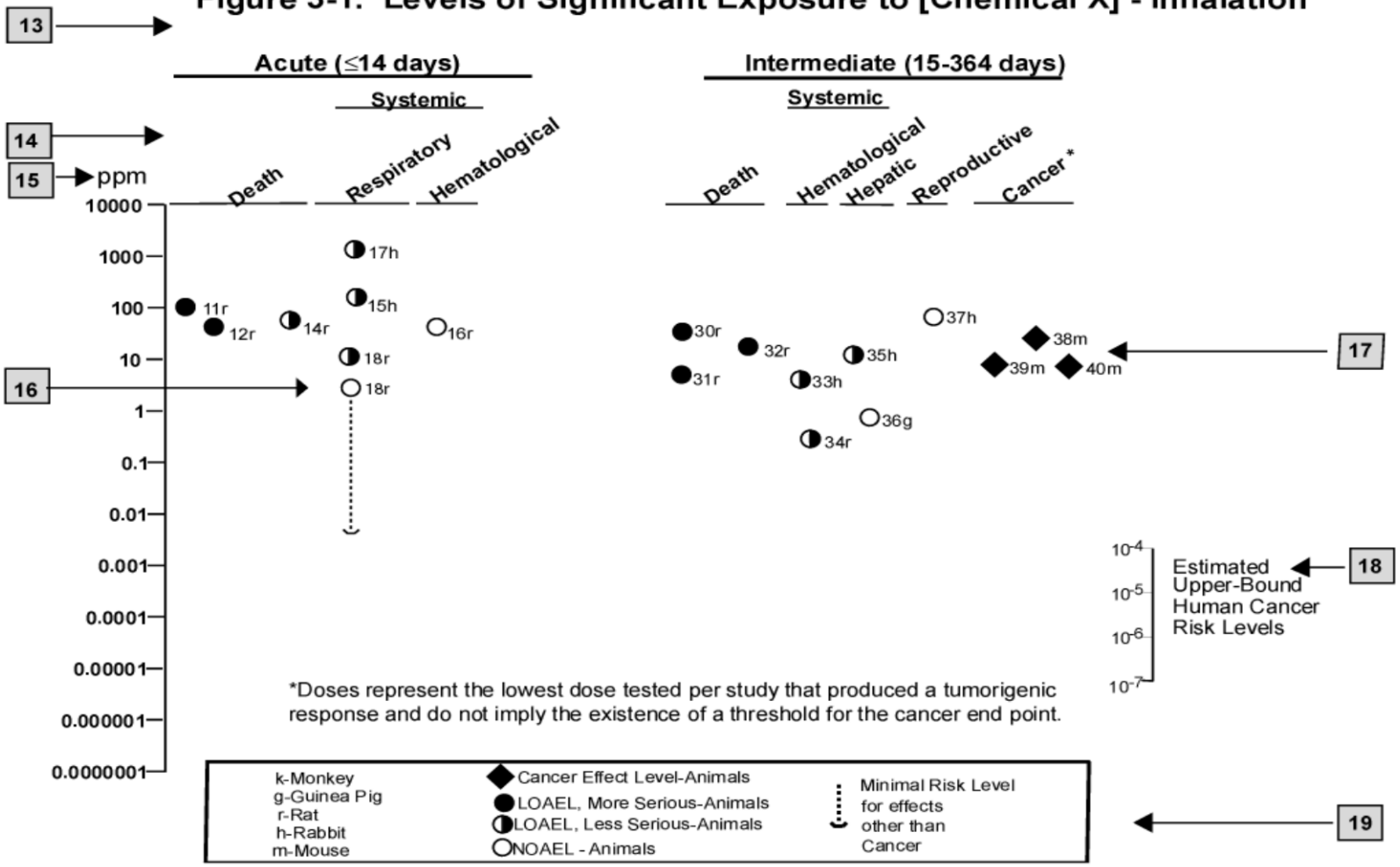
1 → **Table 3-1. Levels of Significant Exposure to [Chemical x] – Inhalation**

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

12 → [a] The number corresponds to entries in Figure 3-1.
[b] Used to derive an intermediate inhalation Minimal Risk Level (MRL) of $5x10^{-3}$ ppm; dose adjusted for intermittent exposure and divided by an uncertainty factor of 100 (10 for extrapolation from animal to humans, 10 for human variability).

SAMPLE

Figure 3-1. Levels of Significant Exposure to [Chemical X] - Inhalation



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APPENDIX C. ACRONYMS, ABBREVIATIONS, AND SYMBOLS

ACGIH	American Conference of Governmental Industrial Hygienists
ACOEM	American College of Occupational and Environmental Medicine
ADI	acceptable daily intake
ADME	absorption, distribution, metabolism, and excretion
AED	atomic emission detection
AFID	alkali flame ionization detector
AFOSH	Air Force Office of Safety and Health
ALT	alanine aminotransferase
AML	acute myeloid leukemia
AOAC	Association of Official Analytical Chemists
AOEC	Association of Occupational and Environmental Clinics
AP	alkaline phosphatase
APHA	American Public Health Association
AST	aspartate aminotransferase
atm	atmosphere
ATSDR	Agency for Toxic Substances and Disease Registry
AWQC	Ambient Water Quality Criteria
BAT	best available technology
BCF	bioconcentration factor
BEI	Biological Exposure Index
BMD/C	benchmark dose or benchmark concentration
BMD_X	dose that produces a X% change in response rate of an adverse effect
$BMDL_X$	95% lower confidence limit on the BMD_X
BMDS	Benchmark Dose Software
BMR	benchmark response
BSC	Board of Scientific Counselors
C	centigrade
CAA	Clean Air Act
CAG	Cancer Assessment Group of the U.S. Environmental Protection Agency
CAS	Chemical Abstract Services
CDC	Centers for Disease Control and Prevention
CEL	cancer effect level
CELDS	Computer-Environmental Legislative Data System
CERCLA	Comprehensive Environmental Response, Compensation, and Liability Act
CFR	Code of Federal Regulations
Ci	curie
CI	confidence interval
CL	ceiling limit value
CLP	Contract Laboratory Program
cm	centimeter
CML	chronic myeloid leukemia
CPSC	Consumer Products Safety Commission
CWA	Clean Water Act
DHEW	Department of Health, Education, and Welfare
DHHS	Department of Health and Human Services
DNA	deoxyribonucleic acid
DOD	Department of Defense
DOE	Department of Energy
DOL	Department of Labor

DOT	Department of Transportation
DOT/UN/ NA/IMDG	Department of Transportation/United Nations/ North America/Intergovernmental Maritime Dangerous Goods Code
DWEL	drinking water exposure level
ECD	electron capture detection
ECG/EKG	electrocardiogram
EEG	electroencephalogram
EEGL	Emergency Exposure Guidance Level
EPA	Environmental Protection Agency
F	Fahrenheit
F_1	first-filial generation
FAO	Food and Agricultural Organization of the United Nations
FDA	Food and Drug Administration
FEMA	Federal Emergency Management Agency
FIFRA	Federal Insecticide, Fungicide, and Rodenticide Act
FPD	flame photometric detection
fpm	feet per minute
FR	Federal Register
FSH	follicle stimulating hormone
g	gram
GC	gas chromatography
gd	gestational day
GLC	gas liquid chromatography
GPC	gel permeation chromatography
HPLC	high-performance liquid chromatography
HRGC	high resolution gas chromatography
HSDB	Hazardous Substance Data Bank
IARC	International Agency for Research on Cancer
IDLH	immediately dangerous to life and health
ILO	International Labor Organization
IRIS	Integrated Risk Information System
Kd	adsorption ratio
kg	kilogram
kkg	metric ton
K_{oc}	organic carbon partition coefficient
K_{ow}	octanol-water partition coefficient
L	liter
LC	liquid chromatography
LC_{50}	lethal concentration, 50% kill
LC_{Lo}	lethal concentration, low
LD_{50}	lethal dose, 50% kill
LD_{Lo}	lethal dose, low
LDH	lactic dehydrogenase
LH	luteinizing hormone
LOAEL	lowest-observed-adverse-effect level
LSE	Levels of Significant Exposure
LT_{50}	lethal time, 50% kill
m	meter
MA	*trans,trans*-muconic acid
MAL	maximum allowable level
mCi	millicurie

MCL	maximum contaminant level
MCLG	maximum contaminant level goal
MF	modifying factor
MFO	mixed function oxidase
mg	milligram
mL	milliliter
mm	millimeter
mmHg	millimeters of mercury
mmol	millimole
mppcf	millions of particles per cubic foot
MRL	Minimal Risk Level
MS	mass spectrometry
NAAQS	National Ambient Air Quality Standard
NAS	National Academy of Science
	National Air Toxics Information Clearinghouse
NATO	North Atlantic Treaty Organization
NCE	normochromatic erythrocytes
NCEH	National Center for Environmental Health
NCI	National Cancer Institute
ND	not detected
NFPA	National Fire Protection Association
ng	nanogram
NHANES	National Health and Nutrition Examination Survey
NIEHS	National Institute of Environmental Health Sciences
NIOSH	National Institute for Occupational Safety and Health
NIOSHTIC	NIOSH's Computerized Information Retrieval System
NLM	National Library of Medicine
nm	nanometer
nmol	nanomole
NOAEL	no-observed-adverse-effect level
NOES	National Occupational Exposure Survey
NOHS	National Occupational Hazard Survey
NPD	nitrogen phosphorus detection
NPDES	National Pollutant Discharge Elimination System
NPL	National Priorities List
NR	not reported
NRC	National Research Council
NS	not specified
NSPS	New Source Performance Standards
NTIS	National Technical Information Service
NTP	National Toxicology Program
ODW	Office of Drinking Water, EPA
OERR	Office of Emergency and Remedial Response, EPA
OHM/TADS	Oil and Hazardous Materials/Technical Assistance Data System
OPP	Office of Pesticide Programs, EPA
OPPT	Office of Pollution Prevention and Toxics, EPA
OPPTS	Office of Prevention, Pesticides and Toxic Substances, EPA
OR	odds ratio
OSHA	Occupational Safety and Health Administration
OSW	Office of Solid Waste, EPA
OTS	Office of Toxic Substances

OW	Office of Water
OWRS	Office of Water Regulations and Standards, EPA
PAH	polycyclic aromatic hydrocarbon
PBPD	physiologically based pharmacodynamic
PBPK	physiologically based pharmacokinetic
PCE	polychromatic erythrocytes
PEL	permissible exposure limit
pg	picogram
PHS	Public Health Service
PID	photo ionization detector
pmol	picomole
PMR	proportionate mortality ratio
ppb	parts per billion
ppm	parts per million
ppt	parts per trillion
PSNS	pretreatment standards for new sources
RBC	red blood cell
REL	recommended exposure level/limit
RfC	reference concentration
RfD	reference dose
RNA	ribonucleic acid
RQ	reportable quantity
RTECS	Registry of Toxic Effects of Chemical Substances
SARA	Superfund Amendments and Reauthorization Act
SCE	sister chromatid exchange
SGOT	serum glutamic oxaloacetic transaminase
SGPT	serum glutamic pyruvic transaminase
SIC	standard industrial classification
SIM	selected ion monitoring
SMCL	secondary maximum contaminant level
SMR	standardized mortality ratio
SNARL	suggested no adverse response level
SPEGL	Short-Term Public Emergency Guidance Level
STEL	short term exposure limit
STORET	Storage and Retrieval
TD_{50}	toxic dose, 50% specific toxic effect
TLV	threshold limit value
TOC	total organic carbon
TPQ	threshold planning quantity
TRI	Toxics Release Inventory
TSCA	Toxic Substances Control Act
TWA	time-weighted average
UF	uncertainty factor
U.S.	United States
USDA	United States Department of Agriculture
USGS	United States Geological Survey
VOC	volatile organic compound
WBC	white blood cell
WHO	World Health Organization

>	greater than
≥	greater than or equal to
=	equal to
<	less than
≤	less than or equal to
%	percent
α	alpha
β	beta
γ	gamma
δ	delta
μm	micrometer
μg	microgram
q_1^*	cancer slope factor
–	negative
+	positive
(+)	weakly positive result
(–)	weakly negative result