CHAPTER 6. 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 1,1,2-trichloroethane 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 adverse health effects (and techniques for developing methods to determine such health effects) of 1,1,2-trichloroethane.

Data needs are defined as substance-specific informational needs that, if met, would reduce the uncertainties of human health risk 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.

6.1 Information on Health Effects

Studies evaluating the health effects of inhalation, oral, and dermal exposure of humans and animals to 1,1,2-trichloroethane that are discussed in Chapter 2 are summarized in Figure 6-1. The purpose of this figure is to illustrate the information concerning the health effects of 1,1,2-trichloroethane. The number of human and animal studies examining each endpoint is indicated regardless of whether an effect was found and the quality of the study or studies.

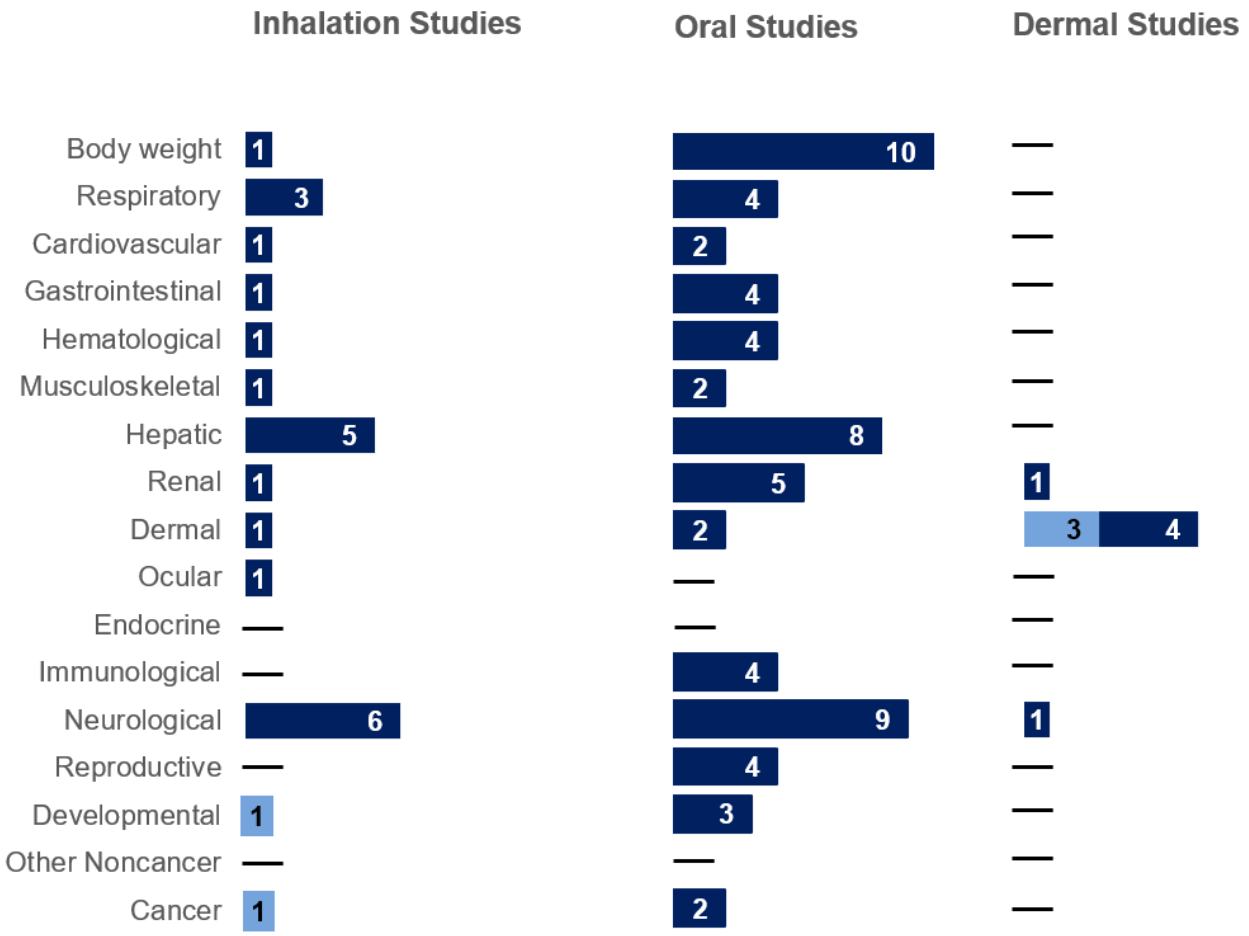
6.2 Identification of Data Needs

Missing information in Figure 6-1 should not be interpreted as a “data need”. A data need, as defined in ATSDR’s *Decision Guide for Identifying Substance-Specific Data Needs Related to Toxicological Profiles* (ATSDR 1989), is substance-specific information necessary to conduct comprehensive public health assessments. Generally, ATSDR defines a data gap more broadly as any substance-specific information missing from the scientific literature.

Studies evaluating the health effects of inhalation, oral, and dermal exposure of humans and animals to 1,1,2-trichloroethane that are discussed in Chapter 2 are summarized in Figure 6-1. The purpose of this figure is to illustrate the information concerning the health effects of 1,1,2-trichloroethane. The number of human and animal studies examining each endpoint is indicated regardless of whether an effect was found and the quality of the study or studies.

Figure 6-1. Summary of Existing Health Effects Studies on 1,1,2-Trichloroethane By Route and Endpoint[a]*

Potential body weight, liver, and neurological effects were the most studied endpoints
The majority of the studies examined oral exposure in **animals** (versus **humans**)



[a]Individual studies may have evaluated more than one of these endpoints.
*Includes studies discussed in Chapter 2; the number of studies include those finding no effect.

As illustrated in Figure 6-1, most of the data on the toxicity of 1,1,2-trichloroethane come from oral studies in laboratory animals. Five human studies were identified; three studies evaluated dermal endpoints and two epidemiology studies evaluated developmental or cancer endpoints. The most commonly examined endpoints in animal studies involving oral exposure were body weight, liver, and neurological. A smaller number of animal studies have assessed 1,1,2-trichloroethane toxicity following inhalation exposure; these studies primarily examined respiratory, hepatic, and neurological endpoints. Additionally, five animal dermal studies were identified; these studies examined a limited number of endpoints.

Acute-Duration MRLs. A number of single exposure studies have evaluated the toxicity of 1,1,2-trichloroethane following inhalation exposure. Based on these data, the most sensitive effect appears to be necrosis of the nasal olfactory epithelium in rats exposed to 58 ppm 1,1,2-trichloroethane for 4 hours (Kirkpatrick 2001). The study examined a wide range of endpoints and was considered suitable for derivation of an MRL. Repeated exposure studies examining a wide range of potential endpoints including the nasal cavity and neurological endpoints are needed to establish concentration-response relationships. Acute-duration oral studies have identified several targets of toxicity in rats, mice, and dogs. The most sensitive endpoint appears to be hepatotoxicity. The available data were considered adequate for derivation of an MRL. Additional studies, particularly studies evaluating repeated exposure, are needed to provide support for this MRL.

Intermediate-Duration MRLs. Although only one study examining the intermediate-duration inhalation toxicity of 1,1,2-trichloroethane (Kirkpatrick 2002) was located, the study examined a wide range of endpoints and was considered suitable for derivation of an MRL. Additional studies that examined the nasal cavity and neurological endpoints (most sensitive target following oral exposure) would provide support this MRL. Intermediate-duration oral studies have examined a variety of potential endpoints in rats and mice; the data suggest that hepatotoxicity, immunotoxicity, and neurotoxicity are the most sensitive effects. An intermediate-duration oral MRL was derived based on hepatotoxicity and immunotoxicity endpoints. Since only one study evaluated immune function, additional immunotoxicity studies would provide support to the MRL.

Chronic-Duration MRLs. No chronic-duration inhalation studies were identified for 1,1,2-trichloro-ethane were identified and an MRL was not derived. The database was also considered inadequate for derivation of a chronic-duration oral MRL because no adverse effects, aside from lethality and cancer, were identified. Chronic inhalation and oral studies are needed. These studies should include a wide

range of potential endpoints including the respiratory tract (inhalation studies), neurological endpoints, and immune function.

Health Effects. In addition to the inhalation and oral exposure studies identified in the discussion of MRL data needs, there is a need for dermal toxicity studies examining a wide range of potential endpoints. Toxicokinetic studies suggest that 1,1,2-trichloroethane can be absorbed through the skin (Jakobson et al. 1977; Kronevi et al. 1977) and studies are needed that would identify sensitive targets of toxicity and establish dose-response relationships.

Cancer Effects. A chronic-duration oral study (NCI 1978) reported increases in the occurrence of liver and adrenal tumors in mice exposed to 1,1,2-trichloroethane for 78 weeks; the study did not find increases in neoplastic lesions in similarly exposed rats. It is not known if a longer duration study would have also resulted in cancerous lesions in rats. Additionally, the carcinogenicity of 1,1,2-trichloroethane has not been evaluated following chronic inhalation or dermal exposure.

Immunotoxicity. The immunological effects of 1,1,2-trichloroethane have been studied following 14- and 90-day oral exposures. Several measures of both humoral and cell-mediated immune response were investigated in this study, and there was some indication that 1,1,2-trichloroethane elicited an immune response. The fact that effects were found in some tests, but not others intended to measure the same response, indicates that more studies of this type could provide worthwhile information. In addition, immune responses were different in male and female mice, and investigation of these differences might provide meaningful information. No studies were located regarding dermal sensitization by 1,1,2-trichloroethane.

Neurotoxicity. Studies of 1,1,2-trichloroethane in animals have provided information on the neurological effects produced by acute exposure to 1,1,2-trichloroethane, and the levels at which they occur. The results of one study suggested that taste aversion may be a sensitive indicator of the acute neurological effects of 1,1,2-trichloroethane. Additional neurobehavioral tests may reveal still more sensitive neurologic endpoints or provide support for use of taste aversion as an indicator of neurologic effects. Repeated exposure studies involved examination of neurological organs and tissues, but no tests of neurological function. Reliable studies of neurotoxicity by dermal exposure do not exist.

Epidemiology and Human Dosimetry Studies. There are limited epidemiology studies evaluating the toxicity or carcinogenicity of 1,1,2-trichloroethane (Brender et al. 2014; Dosemeci et al. 1999); common limitations of these studies are co-exposure to other pollutants and the lack of exposure data. In addition, experimental studies in humans have assessed dermal toxicity following short-term exposure. The evidence in animals, however, indicates that 1,1,2-trichloroethane can have effects on the nervous system, immune system, respiratory system, and liver and kidney function, and can be lethal. It is also carcinogenic in mice. These effects may also occur in humans, if they are exposed to appropriate levels of 1,1,2-trichloroethane. Epidemiological and human dosimetry studies might reveal whether humans are indeed susceptible to adverse health effects due to exposure to 1,1,2-trichloroethane.

Biomarkers of Exposure and Effect. Biomarkers do not adequately capture exposure to 1,1,2-trichloroethane. Although 1,1,2-trichloroethane and its metabolites can be measured in blood and urine, no studies have examined the possible relationship between potential biomarkers and exposure levels. No studies were located that identified biomarkers specific for 1,1,2-trichloroethane-induced effects. If epidemiological studies are performed that associate effects with exposure, it may be possible to identify alterations in blood chemistry indices or other pathological endpoints that would be useful to identify the disease state. Biomarkers for diagnosis of target organ toxicity (e.g., AST for liver damage) can provide useful information in conjunction with specific knowledge of 1,1,2-trichloroethane exposure.

Absorption, Distribution, Metabolism, and Excretion. Little information is available regarding the toxicokinetics of 1,1,2-trichloroethane in humans or animals. Information on absorption in humans comes from a brief study using two volunteers and from some studies in animals. Animal studies that specifically test the amount and rate of absorption of 1,1,2-trichloroethane would provide information as to how much 1,1,2-trichloroethane humans might be likely to absorb from various routes of exposure. For distribution, the only human data are from one briefly reported study; there are several acute-duration animal studies. More extensive and longer-term animal studies using the inhalation, oral, or dermal routes would help determine 1,1,2-trichloroethane distribution in the body. For metabolism, more animal studies would be helpful in showing what kind of metabolites might be expected to be found in the blood or urine of humans; if these could be measured, they might give an indication of amount of exposure to 1,1,2-trichloroethane. Additional metabolism studies may also reveal more definitive information on mechanisms of 1,1,2-trichloroethane toxicity and carcinogenicity. Data on excretion are fairly complete.

Comparative Toxicokinetics. No studies were located that compared human and animal toxicokinetics. Two comparative toxicokinetics studies were performed that examined the differences

between rats and mice in the types of metabolites formed, and the excretion rates from various routes. Although percent of administered dose metabolized was similar in both species, the overall rate of metabolism of 1,1,2-trichloroethane was greater in mice (Mitoma et al. 1985). The same metabolites were formed in the same proportions in both species. The difference in metabolic rate may be related to species differences in susceptibility to the toxic effects of 1,1,2-trichloroethane. More studies of this type could corroborate this theory or identify other factors that may be responsible for the species difference in toxicity.

Children's Susceptibility. There are limited data on children's susceptibility; the results of a 2-generation study suggest similar toxicity between immature and mature rats (Mylchreest 2006). However, additional animal studies are needed to examine potential differences in adults and children, particularly for more sensitive endpoints. Oral exposure studies do not suggest that 1,1,2-trichloroethane is a developmental toxicant. However, these studies did not examine potential effects on the development of the nervous system or immune system; studies in adult animals suggest that neurological and immunological endpoints are sensitive targets.

Physical and Chemical Properties. The physical and chemical properties of 1,1,2-trichloroethane have been adequately characterized (see Table 4-2).

Production, Import/Export, Use, Release, and Disposal. Data on current uses and disposal practices would be valuable in determining whether industrial activities pose an important source of human exposure to 1,1,2-trichloroethane.

Environmental Fate. Further investigation would resolve the discrepancies in the data for anaerobic degradation of 1,1,2-trichloroethane. Additional studies are needed to characterize the nature of the transformation and to clarify whether biotic, abiotic, or catalyzed abiotic reactions are involved and whether these reactions will generally occur under environmental conditions. A determination of the half-life in representative groundwater and sediment-water systems would be useful. From the available evidence, biodegradation in aerobic systems appears unlikely, although additional studies, particularly in soil, are desirable and would clarify this point.

Bioavailability from Environmental Media. Since 1,1,2-trichloroethane is expected to exist in the atmosphere as the vapor rather than adsorb to particulate matter, there would not be a competing adsorption that would impede its bioavailability via the lungs. Limited data showing the presence of

1,1,2-trichloroethane in adipose and other tissue of exposed subjects indicate that 1,1,2-trichloroethane is taken up via the lungs, gastrointestinal tract, or both. A pilot study demonstrated that similar low molecular weight chlorinated alkanes are found in human milk (Pellizzari et al. 1982). The source of these pollutants was probably ambient air, and this is the most probable route of intake for the general population.

Food Chain Bioaccumulation. 1,1,2-Trichloroethane has not been reported in food or biota, nor were any studies located in which the levels of this chemical in plants or animals were reported. The bioaccumulation potential for a chemical is most conveniently studied by measuring the BCF or the concentration of a chemical in fish divided by the concentration in water from which the chemical is taken up. The BCF of 1,1,2-trichloroethane in fish is reported to be <10 (Kawasaki 1980), indicating a very low potential for bioaccumulation in the food chain. Experimental verification of the lack of food chain bioaccumulation is not available. Such information can be obtained by studying the accumulation of 1,1,2-trichloroethane in organisms from different trophic levels that have been exposed to the chemical.

Exposure Levels in Environmental Media. The best estimates of exposure are based on monitoring data and these data add credence to emission and exposure estimates based on production and use. In the case of 1,1,2-trichloroethane, monitoring data are fragmentary and not very recent; most of the data are from the early 1980s or earlier. Information on production and use, particularly that with the largest probability for exposure, is not available. While 1,1,2-trichloroethane may be contained in some consumer products, the Dow Chemical Company is not aware of any consumer uses (Moolenaar and Olson 1989).

Exposure Levels in Humans. Estimates of general population and occupational exposure require current monitoring data or current data on production and use. This information is not available. The use pattern of 1,1,2-trichloroethane may have changed since the NOES. If this is the case, the results of the NOES could be reanalyzed in order to reflect current occupational exposures.

Exposures of Children. No studies are available to assess potential exposures of children.

6.3 Ongoing Studies

No ongoing studies were identified for 1,1,2-trichloroethane.