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 1,2-dichloropropane 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 1,2-dichloropropane.

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.

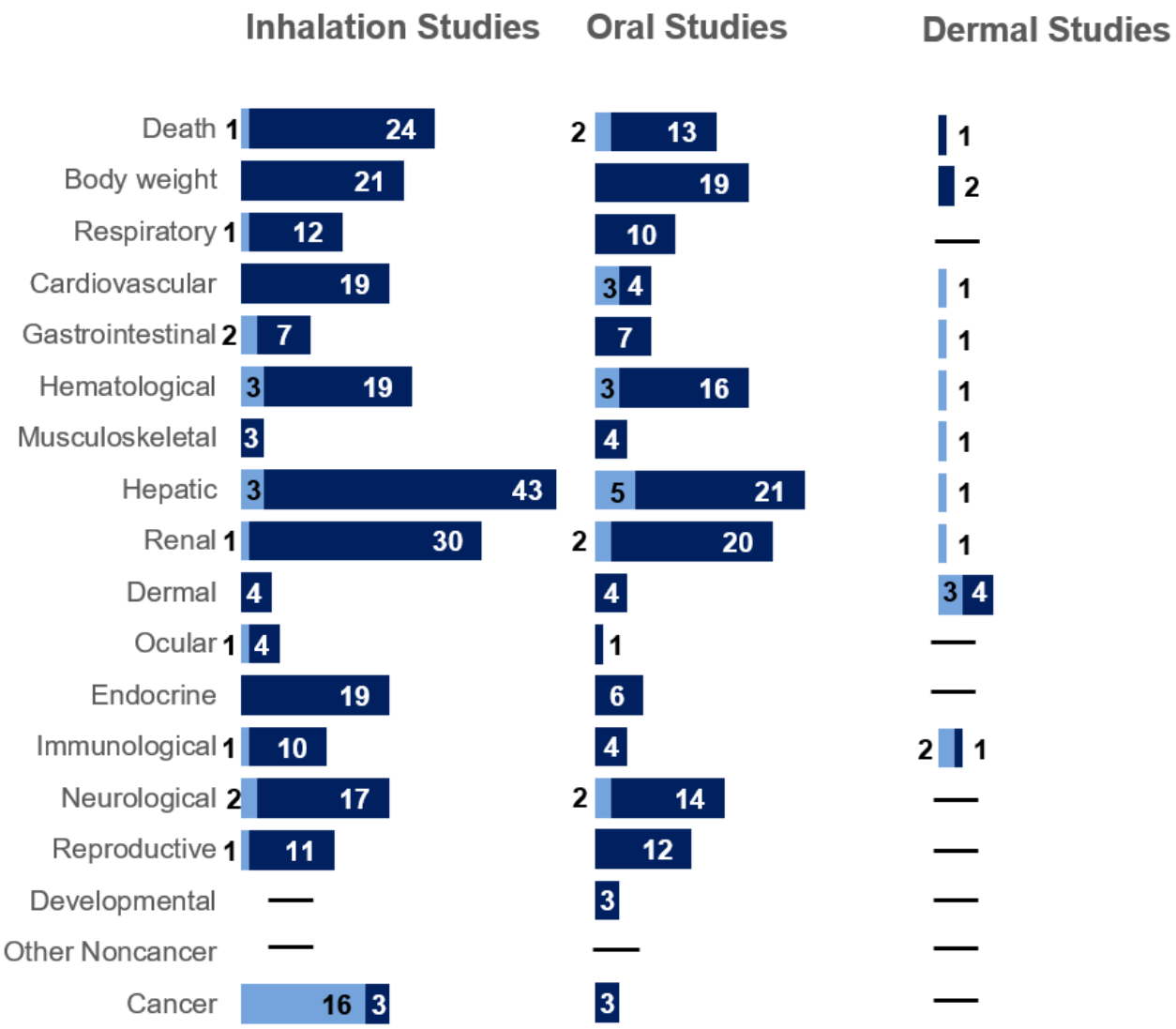
6.1 Information on Health Effects

Studies evaluating the health effects of inhalation, oral, and dermal exposure of humans and animals to 1,2-dichloropropane 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 1,2-dichloropropane. 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.

As illustrated in Figure 6-1, most of the data on the toxicity of 1,2-dichloropropane come from inhalation studies in laboratory animals, although several oral studies in laboratory animals are also available. The most commonly examined endpoints were hepatic, renal, and body weight effects. The available human studies include several epidemiological studies evaluating cancer in workers exposed to 1,2-dichloropropane, in which exposure is expected to be predominantly via inhalation. Data on noncancer effects in humans are primarily from case reports of accidental or intentional acute oral, inhalation, and/or dermal exposure to high levels of 1,2-dichloropropane. The laboratory animal dermal toxicity database consists of a small number of studies evaluating limited endpoints.

Figure 6-1. Summary of Existing Health Effects Studies on 1,2-Dichloropropane By Route and Endpoint

Potential hepatic, renal, and hematological effects were the most studied endpoints
The majority of the studies examined inhalation exposure in **animals** (versus **humans**)



*Includes studies discussed in Chapter 2. A total of 113 studies (including those finding no effect) have examined toxicity; most animal studies examined multiple endpoints.

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.

Acute-Duration MRLs. The inhalation database is adequate to derive an acute-duration inhalation MRL. Additional low-concentration studies designed to identify a NOAEL for the critical effect (upper respiratory lesions) in the most susceptible species (rat) could decrease uncertainty in the acute-duration inhalation MRL. The oral database is adequate to derive an acute-duration oral MRL.

Intermediate-Duration MRLs. The inhalation database is adequate to derive an intermediate-duration inhalation MRL. Additional low-concentration studies designed to identify a NOAEL for the critical effect (upper respiratory lesions) could decrease uncertainty in the intermediate-duration inhalation MRL. The oral database is adequate to derive an intermediate-duration oral MRL.

Chronic-Duration MRLs. The inhalation database is inadequate to derive a chronic-duration inhalation MRL. Available chronic inhalation studies identified LOAEL concentrations for the critical effect (nasal lesions) at levels >5-fold higher than the lowest LOAEL for nasal lesions identified in intermediate-duration studies. Low-concentration studies designed to identify a NOAEL for the critical effect (nasal lesions) could potentially identify a point of departure (POD) to use as the basis for a chronic-duration inhalation MRL. The oral database is inadequate to derive a chronic-duration oral MRL. Chronic studies providing data at low doses are needed.

Health Effects. Identification of data needs for health effects in animal studies is limited to targets included in the systematic review with animal data needs.

> ***Respiratory.*** The upper respiratory tract has been identified as a sensitive target following acute-, intermediate-, and chronic-duration inhalation exposure in animals; however, a NOAEL for repeated exposure has not been established. Additional low-concentration studies designed to identify a NOAEL for upper respiratory lesions are needed. Studies designed to determine the

mechanism of nasal lesion toxicity could be useful for determining the human relevance of these findings.

Renal. While human case studies indicate that the kidney may be a target of 1,2-dichloropropane toxicity, supporting animal data are inconsistent or lacking. Human epidemiological studies and/or additional animal studies designed to evaluate renal toxicity following exposure, particularly renal function, may be useful.

Developmental. Developmental toxicity data are only available from a limited number of oral studies. Additional studies evaluating specialized developmental effects (e.g., neurotoxicity) as well as developmental effects following inhalation exposure would be useful to address this data gap. Also, since available data only report developmental effects at doses that elicit parental toxicity, studies designed to assess whether developmental effects are secondary to parental toxicity may be useful.

Epidemiology and Human Dosimetry Studies. Epidemiology studies are limited to case studies of accidental or intentional exposure, one case-control study evaluating potential associations with atopic dermatitis, and occupational case studies and retrospective cohort studies evaluating cancer in Japanese printers. A common limitation of these studies is the lack of control for the presence of other chlorinated solvents, many of which have similar toxic endpoints as 1,2-dichloropropane. Additional epidemiology studies controlling confounding exposures and examining endpoints that have been shown to occur at low doses in laboratory animals (respiratory, hematological, hepatic, neurological, and developmental effects) would be useful. In the absence of additional epidemiological studies, studies designed to evaluate potential mechanisms of action (MOAs), particularly cancer MOAs, would be useful to determine the relevance of animal findings.

Biomarkers of Exposure and Effect. Available data suggest that unchanged 1,2-dichloropropane in the urine or blood or glutathione conjugated metabolites in the blood may be appropriate biomarkers of exposure. While current analytical methods used to detect unchanged 1,2-dichloropropane in the blood are not sensitive enough to detect background levels in the general population, Kirman et al. (2012) and Aylward et al. (2010) indicate that the whole blood analytical method used to collect NHANES data is sensitive enough to detect recent toxicologically relevant exposures. Additional research is needed to validate extrapolation of biomarker levels to external exposure doses.

Absorption, Distribution, Metabolism, and Excretion. The toxicokinetics of 1,2-dichloropropane in rats are relatively well characterized following oral and inhalation exposure. Additional studies following dermal exposure and/or in different species would address this data need.

Comparative Toxicokinetics. No studies were found that evaluated differences in toxicokinetics between species. Toxicokinetic studies in different species may be useful to determine if toxicokinetic differences may explain observed species differences (increased susceptibility to nasal lesions in rats, potentially increased susceptibility to renal lesions in mice). Qualitative and quantitative comparison of human metabolites with those of animals could help identify the most appropriate species to serve as a model for predicting toxic effects in humans and for studying the mechanisms of action.

Children's Susceptibility. No human data are available regarding children's susceptibility. Available data from oral developmental studies do not indicate that developing animals are uniquely susceptible to toxicity following exposure to 1,2-dichloropropane. Developmental effects have not been evaluated in animals following inhalation exposure. 1,2-Dichloropropane is primarily metabolized by CYP2E1, which is fully developed in children, but it is not known if there would be toxicodynamic differences between children and adults that might influence susceptibility. Experimental studies in young animals and/or epidemiological data for children would be useful to address these data gaps.

Physical and Chemical Properties. The physical and chemical properties of 1,2-dichloropropane have been adequately characterized (see Table 4-2). No data needs are identified.

Production, Import/Export, Use, Release, and Disposal. Information on production, uses, and releases of 1,2-dichloropropane are available and have been discussed in Chapter 5. Data indicate that use of this substance in consumer products has been diminished. 1,2-Dichloropropane is not sold for direct consumer use; this substance is mainly used onsite or as a limited transport co-product/raw material for the production of other chlorinated compounds. Limited information is available concerning U.S. imports and exports of 1,2-dichloropropane. Disposal practices are regulated by environmental regulatory agencies. Further data do not appear to be essential at this time.

Environmental Fate. Sufficient data exist to show that chemical hydrolysis and aerobic biodegradation of 1,2-dichloropropane are very slow and are not significant in determining the half-life in surface water or soil. Additional studies of anaerobic biotransformation could be useful in estimating the half-life of 1,2-dichloropropane in soil and groundwater. Experimental hydrolysis data at pH 5–9 would

be helpful for predicting the half-life of 1,2-dichloropropane in groundwater where volatilization is not significant.

Bioavailability from Environmental Media. Since 1,2-dichloropropane was phased out as a fumigant and its use in solvents has declined, recent monitoring data are needed for air, groundwater, and surface water. This is particularly important with respect to groundwater, where it is especially persistent and may be present in significant concentrations. Field monitoring studies of 1,2-dichloropropane would also be useful. This may be the only feasible way of determining the half-life of 1,2-dichloropropane in groundwater. Air monitoring and surface water studies would show the effects of changing 1,2-dichloropropane use patterns. While EPA's STORET database contains considerable water monitoring data, there are problems with the database that limit its usefulness. The detection limit is apparently recorded when no chemical is detected, so that it is impossible to say whether the 90^{th} percentile figures for surface water and groundwater provided in Section 5.3.2 represent positive determinations or merely detection limits. It would be helpful, when quantitative data cannot be obtained, if these monitoring data would indicate whether 1,2-dichloropropane was qualitatively detected in the samples.

Food Chain Bioaccumulation. 1,2-Dichloropropane has not been reported in food or in organisms collected from the environment. No studies investigating uptake of this chemical in animals were located, and experimental studies in plants are limited to a single study in potatoes. An experimentally determined BCF of 3.2 in carp, along with the estimated BCF of 9, indicate that there is a very low potential for bioaccumulation in the food chain.

Exposure Levels in Environmental Media. Monitoring data indicate a decrease of the detectable concentrations in the environment over the past few decades, most likely as a result of the discontinuation of several use categories. Section 112 of the Clean Air Act (CAA) lists 1,2-dichloropropane as one of the original 189 HAPs known to cause or suspected of causing cancer or other serious human health effects or ecosystem damage. Continued monitoring would be beneficial in assessing the potential risk for environmental exposure. There are little or no monitoring data regarding 1,2-dichloropropane on vegetation and flora; these data would be useful as there is the potential for dermal exposure to individuals handling plant material near contaminated sites that may contain 1,2-dichloropropane due to atmospheric deposition.

Exposure Levels in Humans. The use pattern of 1,2-dichloropropane has changed radically since NIOSH's NOES survey. Since the elimination of 1,2-dichloropropane from agricultural fumigants, photographic film manufacture, and paint strippers, fewer workers are exposed. While agricultural workers were not included in the survey, those engaged in the manufacture of agricultural chemicals were included. As a chemical in paint strippers, 1,2-dichloropropane would have a particularly high potential for exposing large numbers of people at high levels of exposure, since such applications are labor intensive and performed in the open. Therefore, the results of the NOES will have to be reanalyzed in light of current use patterns in order to reflect current occupational exposures. People living in the vicinity of landfills containing 1,2-dichloropropane and hazardous waste sites may be exposed to 1,2-dichloropropane present in off-gases. Not enough information is available to estimate what the level of exposure from this source might be. Data correlating levels in biological samples with media exposure levels and the subsequent development of health effects are especially needed for populations living in the vicinity of hazardous waste sites.

Exposures of Children. Children may be exposed to 1,2-dichloropropane through the same routes as adults. However, occupationally exposed workers are at greater risk of exposure to higher levels of 1,2-dichloropropane than the general U.S. population. Monitoring of children's exposure to 1,2-dichloropropane would be useful, in combination with children's health and susceptibility information, to assess the potential risk for deleterious effects.

6.3 Ongoing Studies

One ongoing epidemiological study of 1,2-dichloropropane was identified by the National Institutes of Health (NIH) (RePORTER 2020). This study, summarized in Table 6-1, is the ongoing Sister Study prospective cohort evaluating potential associations between air toxics and breast cancer.

Table 6-1. Ongoing Studies on 1,2-Dichloropropane

Investigator	Affiliation	Research description	Sponsor
Dale P. Sandler	National Institutes of Health	Potential associations between air toxics and breast cancer; Sister Study prospective cohort	NIEHS

NIEHS = National Institute of Environmental Health Sciences

Source: RePORTER 2020