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-dibromoethane 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-dibromoethane.

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-dibromoethane 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-dibromoethane. 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.

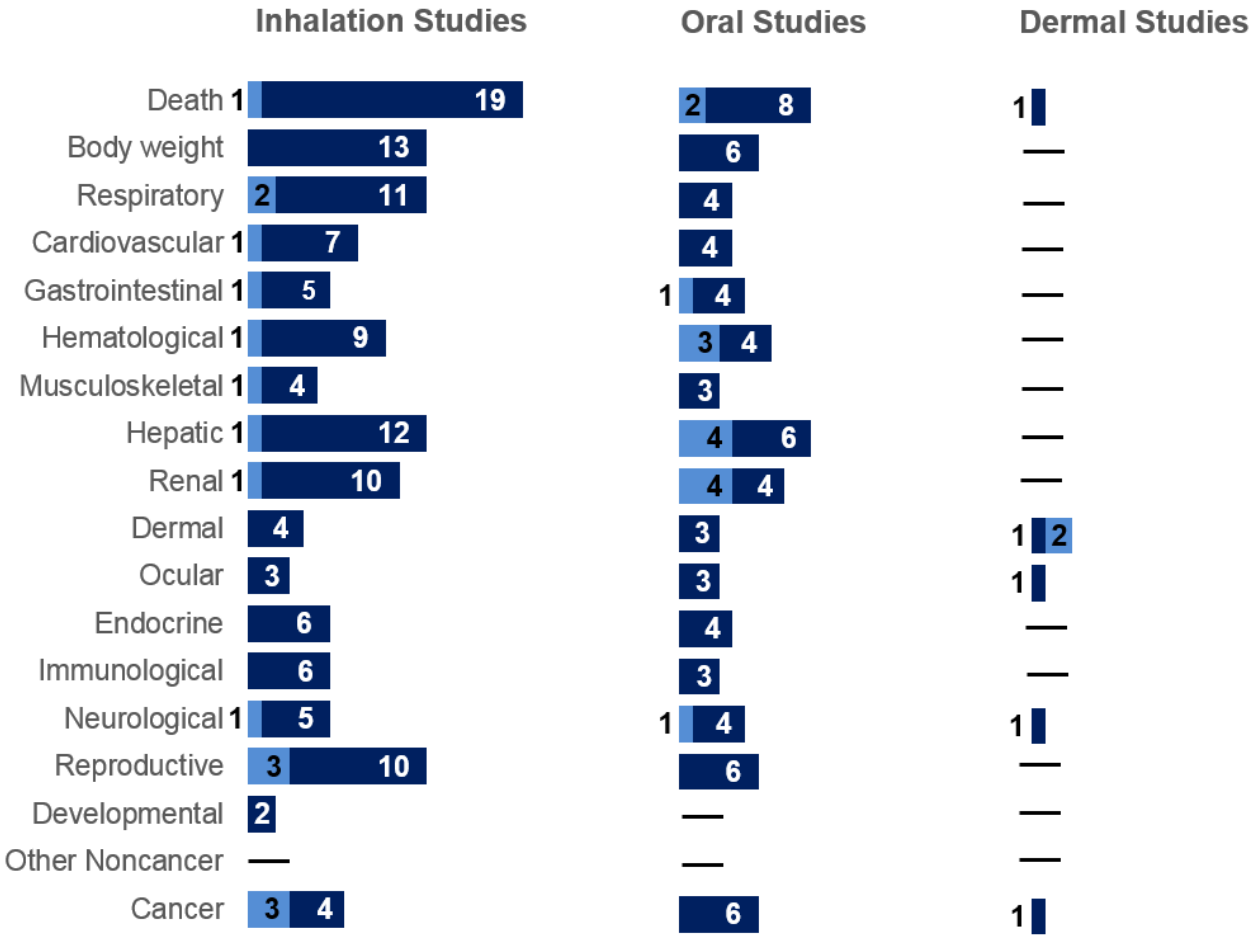
6.2 Identification of Data Needs

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.

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

Potential body weight, respiratory, hepatic, and reproductive effects were the most studied endpoints

The majority of the studies examined oral exposure in **animals** (versus **humans**)



*Includes studies discussed in Chapter 2; the number of studies include those finding no effect.

MRLs. No MRLs have been derived for 1,2-dibromoethane. For acute and chronic inhalation exposure, severe effects and mortality were observed at the lowest exposures tested and, therefore, acute- and chronic-duration inhalation MRLs were not derived. For intermediate-duration oral exposure, effects observed at the lowest exposure tested (hyperplasia of nasal turbinates) is a potentially precarcinogenic effect; thus, an intermediate-duration inhalation MRL was not derived. For oral exposure, severe effects and mortality observed at the lowest exposures tested for all exposure duration categories preclude derivation of oral MRLs. More detailed discussions of the rationale for not deriving MRLs for 1,2-dibromoethane are provided in the MRL worksheets (Appendix A). Acute-, intermediate-, and chronic-duration inhalation and oral studies conducted at lower exposures (nonlethal) could provide data to identify the most sensitive, non-serious endpoints for 1,2-dibromoethane.

Health Effects. Available studies show that 1,2-dibromoethane damages several organ systems. However, as noted above, inhalation and oral studies conducted in laboratory animals at lower (nonlethal) exposures are needed to identify NOAEL and LOAEL values for effects for comprehensive toxicological endpoints. Other specific data needs are as follows.

Reproductive. Occupational exposure studies have evaluated effects to the male reproductive system (Ratcliffe et al. 1987; Schrader et al. 1988; Ter Haar 1980; Wong et al. 1979). Several studies in laboratory animals have identified the male reproductive system as a target for 1,2-dibromoethane (NCI 1978; NTP 1982; Short et al. 1979). Very little information is available regarding reproductive performance, although one study did not observe adverse effects on fertility in rats (Shivanandappa et al. 1987). Additional studies would be important to more fully explore potential reproductive effects of 1,2-dibromoethane in males and females.

Developmental. Only one study has evaluated the potential developmental effects of 1,2-dibromoethane, with results showing incomplete skeletal ossification in rats and mice (Short et al. 1978). Additional studies investigating developmental effect are needed to fully evaluate the potential for 1,2-dibromoethane to adversely affect the developing organism.

Epidemiology and Human Dosimetry Studies. Available data in humans exposed to 1,2-dibromoethane consists of a few case reports at lethal and near-lethal exposures and a few studies in workers, with only one occupational study providing exposure data and appropriate controls (Ratcliffe et al. 1987). Additional well-controlled studies in workers or the general population would be helpful in

evaluating the chronic human health risk from 1,2-dibromoethane exposure, including the potential for 1,2-dibromoethane to induce cancer in humans.

Biomarkers of Exposure and Effect. Use of 1,2-dibromoethane biomarkers has not been well-investigated or applied.

Absorption, Distribution, Metabolism, and Excretion. Few studies have quantitatively evaluated the absorption of 1,2-dibromoethane. No studies on the distribution of dermally administered 1,2-dibromoethane in animals were identified. Studies evaluating the toxicokinetics of 1,2-dibromoethane provide information on the absorption, distribution, metabolism, and excretion of 1,2-dibromoethane in animal models with no data available in humans. A single PBPK model has been developed for rats and humans (Hissink et al. 2000). However, the model has not been evaluated for predicting toxicokinetics in humans, or for predicting toxicokinetics in rats following inhalation exposure or repeated oral exposures. Additional toxicokinetic data are important to conduct these evaluations.

Comparative Toxicokinetics. Although a PBPK model has been developed for rats and humans (Hissink et al. 2000), it has not been evaluated for use in dosimetry extrapolation. Therefore, additional toxicokinetic data to allow for dosimetry extrapolations would be useful.

Children's Susceptibility. No studies have evaluated the toxicity of 1,2-dibromoethane in children or young animals. Studies in young animals would be useful to address potential concerns that children may be more susceptible to the toxicity of 1,2-dibromoethane than adults.

Physical and Chemical Properties. The physical/chemical properties of 1,2-dibromoethane, described in Table 4-2, are sufficiently well characterized to enable assessment of the environmental fate of the compound.

Production, Import/Export, Use, Release, and Disposal. Although 1,2-dibromoethane is currently produced and used in the United States, increased government regulation and restriction on products containing the compound probably have decreased the potential for exposure of the U.S. population (Fishbein 1980; Santodonato et al. 1985). 1,2-Dibromoethane is used as a chemical intermediate. Previous uses as a gasoline additive and soil fumigant are no longer permitted (Fishbein 1979, 1980; HSDB 1989; Santodonato et al. 1985; Stenger 1978). Incineration and burial are the main disposal methods; however, there is no accounting of disposal amounts by each method (HSDB 1989).

However, more recent data describing present domestic production levels, the proportions of 1,2-dibromoethane consumed by the various uses, as well as data on export levels and the countries to which these exports are made would be helpful in providing a broader, more up-to-date picture of the U.S. 1,2-dibromoethane industry as a whole.

Environmental Fate. 1,2-Dibromoethane partitions to the atmosphere and groundwater (Windolz 1983). It is transported in the atmosphere where it undergoes degradation by hydroxyl radicals (EPA 1987a). 1,2-Dibromoethane is mobile and biodegradable in soils, although 1,2-dibromoethane sorbed to soil micropores is immobile and persistent (Pignatello 1986; Steinberg et al. 1987). Additional information is needed on the persistence of 1,2-dibromoethane in groundwater and sorbed to soil micropores. This information will be helpful in establishing the half-life of the compound in the media of most concern for human exposure.

Bioavailability from Environmental Media. 1,2-Dibromoethane can be absorbed by inhalation of contaminated ambient air, dermal contact, and ingestion of contaminated drinking water and foodstuffs (EPA 1983; Jakobson et al. 1982; Letz et al. 1984; Rowe et al. 1952; Saraswat et al. 1986; Stott and McKenna 1984). Ingestion of contaminated groundwater is the exposure route of concern. Additional information is needed on the absorption of 1,2-dibromoethane from soil following ingestion or dermal contact. This information will be useful in determining the bioavailability of residual 1,2-dibromoethane in soils.

Food Chain Bioaccumulation. 1,2-Dibromoethane is not expected to bioconcentrate in plants, aquatic organisms, or animals, or biomagnify in terrestrial or aquatic food chains as a result of its high water solubility (NIOSH 1978; Parrish 1983). Additional information is needed on bioconcentration and biomagnification of the compound to confirm this predicted environmental behavior.

Exposure Levels in Environmental Media. 1,2-Dibromoethane has been detected in ambient air, groundwater, soils, and foodstuffs (Brodzinsky and Singh 1983; Daft 1989; EPA 1983; Ewing et al. 1977; Page 1981; Pellizzari et al. 1978; Singh et al. 1981; Williams et al. 1988). However, new monitoring data are currently needed.

Exposure Levels in Humans. As of 2008, NHANES reported that 1,2-dibromoethane in blood is less than the detection limit (0.015 ng/mL) for 2,577 individuals. 1,2-Dibromoethane can be measured in

6blood and metabolites can be detected in urine (Letz et al. 1984; Nachtomi et al. 1965). However, since the compound is rapidly and extensively metabolized in mammals, and 1,2-dibromoethane metabolites do not persist in tissues, these biomarkers have not been useful in identifying or quantifying human exposure to the compound.

Exposures of Children. No studies are available to assess whether children are at a higher exposure risk than adults to 1,2-dibromoethane. Studies examining potential exposure sources for children would be useful.

6.3 Ongoing Studies

One ongoing study was identified in NIH Reporter (2017); this study is summarized in Table 6-1.

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

Investigator	Affiliation	Research description	Sponsor
Guengerich, F Peter	Vanderbilt University	Mechanism of action study on 1,2-dibromoethane crosslinks with DNA	NIEHS

DNA = deoxyribonucleic acid; NIEHS = National Institute of Environmental Health Sciences

Source: NIH Reporter 2017