CHAPTER 1. RELEVANCE TO PUBLIC HEALTH

1.1 OVERVIEW AND U.S. EXPOSURES

ATSDR's *Toxicological Profile for 1,2-Dibromoethane* was released in 1992. In order to update the literature in this profile, ATSDR conducted a literature search focused on health effects information as described in Appendix B. Chapters 2, 3, and 7 were revised to reflect the most current health effects and regulations/guidelines data. In some cases, other sections of the profile were updated as needed or for consistency with the updated health effects data. However, the focus of the update to this profile is on health effects information.

1,2-Dibromoethane ($C_2H_4Br_2$; CAS Number 106-93-4) is a colorless liquid with a mild, sweet odor. It is volatile and soluble in water. 1,2-Dibromoethane is used as an intermediate in the production of dyes, resins, gums, and waxes and as a pesticide treatment of felled logs. Previously, 1,2-dibromoethane was used as an additive to leaded gasoline and as a fumigant; however, these uses are historical only. The primary source of 1,2-dibromoethane released to the environment is from emissions into air from industrial processing facilities. 1,2-Dibromoethane is highly mobile in soil and can persist in soils and groundwater. The most likely exposure to 1,2-dibromoethane for the general population is from inhalation of air near processing facilities or ingestion of contaminated drinking water.

1.2 SUMMARY OF HEALTH EFFECTS

Little information on the effects of 1,2-dibromoethane in humans is available. Case reports of individuals exposed acutely to 1,2-dibromoethane by inhalation or ingestion at lethal or near-lethal levels identify the respiratory tract, gastrointestinal tract, liver, and kidney as targets of 1,2-dibromoethane (Letz et al. 1984; Olmstead 1960; Prakash et al. 1999; Singh et al. 2000; Saraswat et al. 1986). Cross-sectional studies of the same occupational cohort showed serious effects to the male reproductive system (Ratcliffe et al. 1987; Schrader et al. 1988).

Studies in laboratory animals have been conducted for acute-, intermediate-, and chronic-duration inhalation and oral exposures. Many studies include assessment of comprehensive toxicological endpoints, including cancer. Studies in animals provide support for the target organs observed in humans and identify additional targets, as discussed below. By all routes, tissue damage is observed at the point of contact (e.g., portal-of-entry). Most animal exposure studies had treatment-related mortality or serious adverse effects at the lowest exposures tested. Therefore, it is not possible to determine the most sensitive

effects of exposure for 1,2-dibromoethane. Effects of inhaled and oral 1,2-dibromoethane are depicted in Figures 1-1 and 1-2, respectively.

Body Weight Effects. Results of most acute-, intermediate-, and chronic-duration inhalation and intermediate- and chronic-duration oral exposure in laboratory animals consistently show marked body weight loss or reduced weight gain.

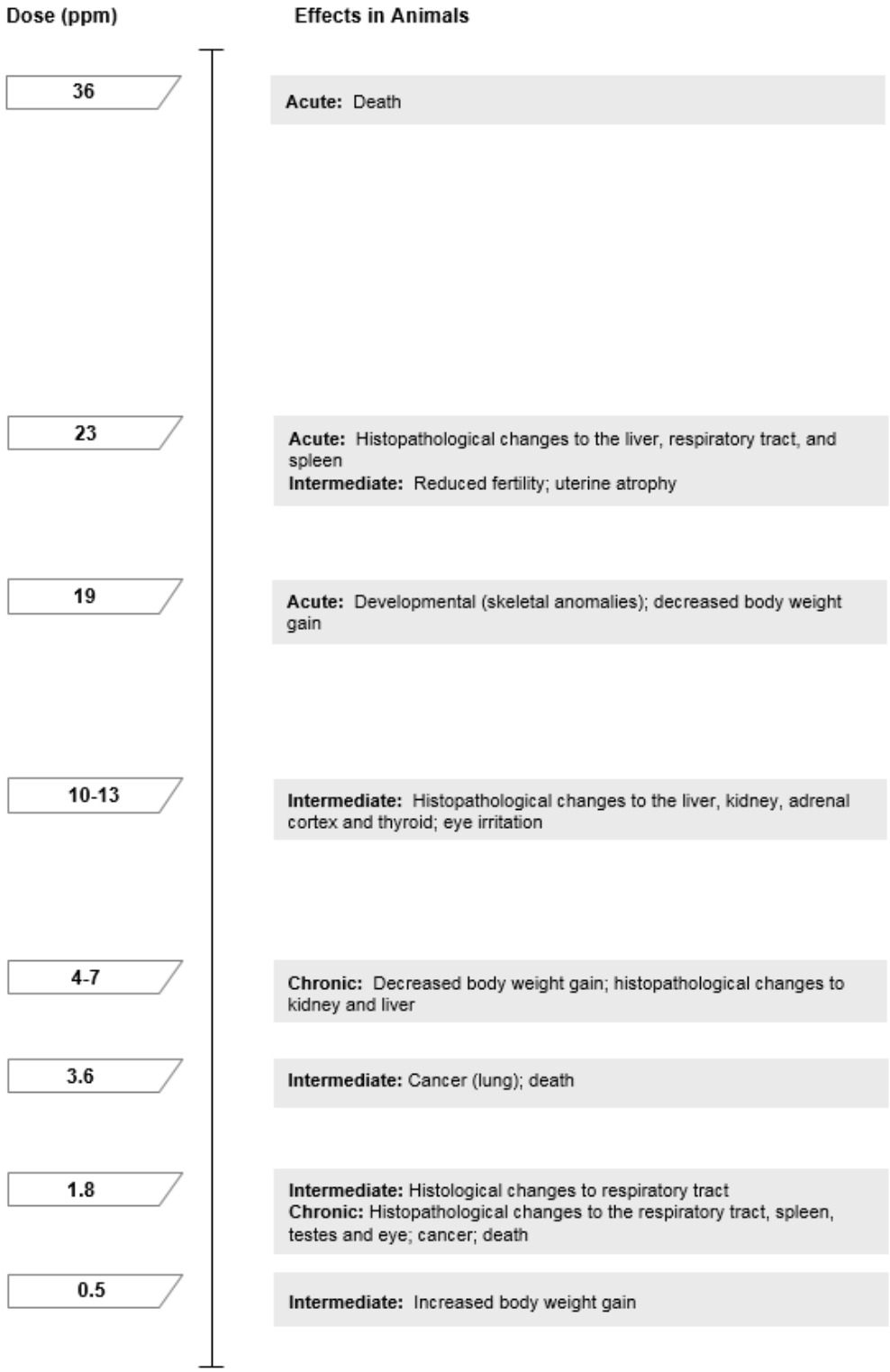
Respiratory Effects. Pulmonary edema was observed in one worker who died following dermal and inhalation exposure (exposure levels not reported). In some laboratory animals, acute-, intermediate- and chronic-duration inhalation exposure to 1,2-dibromoethane caused damage to the upper and/or lower respiratory tract. Effects in the nasal cavity include cytomegaly, hyperplasia, metaplasia and loss of cilia in rats and mice exposed for intermediate and chronic durations. Effects in the lower respiratory tract include leukocytic infiltration of the lungs and hyperplasia of the lung and bronchus in mice exposed for intermediate durations and rats and mice exposed for chronic durations.

Gastrointestinal Effects. In humans ingesting 1,2-dibromoethane, oral and pharyngeal ulceration, vomiting, and diarrhea have been observed. Acute-duration gavage exposure of rats and chronic-duration gavage exposure of mice to 1,2-dibromoethane produced damage to the forestomach, including cell proliferation, hyperkeratosis, and acanthosis.

Hematological Effects. Case studies in acutely exposed humans reported decreased hemoglobin and white blood cell count; however, because pre-exposure values for these parameters were not available, it is not possible to determine if effects were related to exposure. Histopathological changes in the spleen (hematopoiesis, hemosiderosis, and atrophy) have been observed in laboratory animals following acute- and chronic-duration inhalation exposure and chronic-duration oral exposure. Effects on hematological parameters in blood have not been observed, although few studies evaluated these parameters.

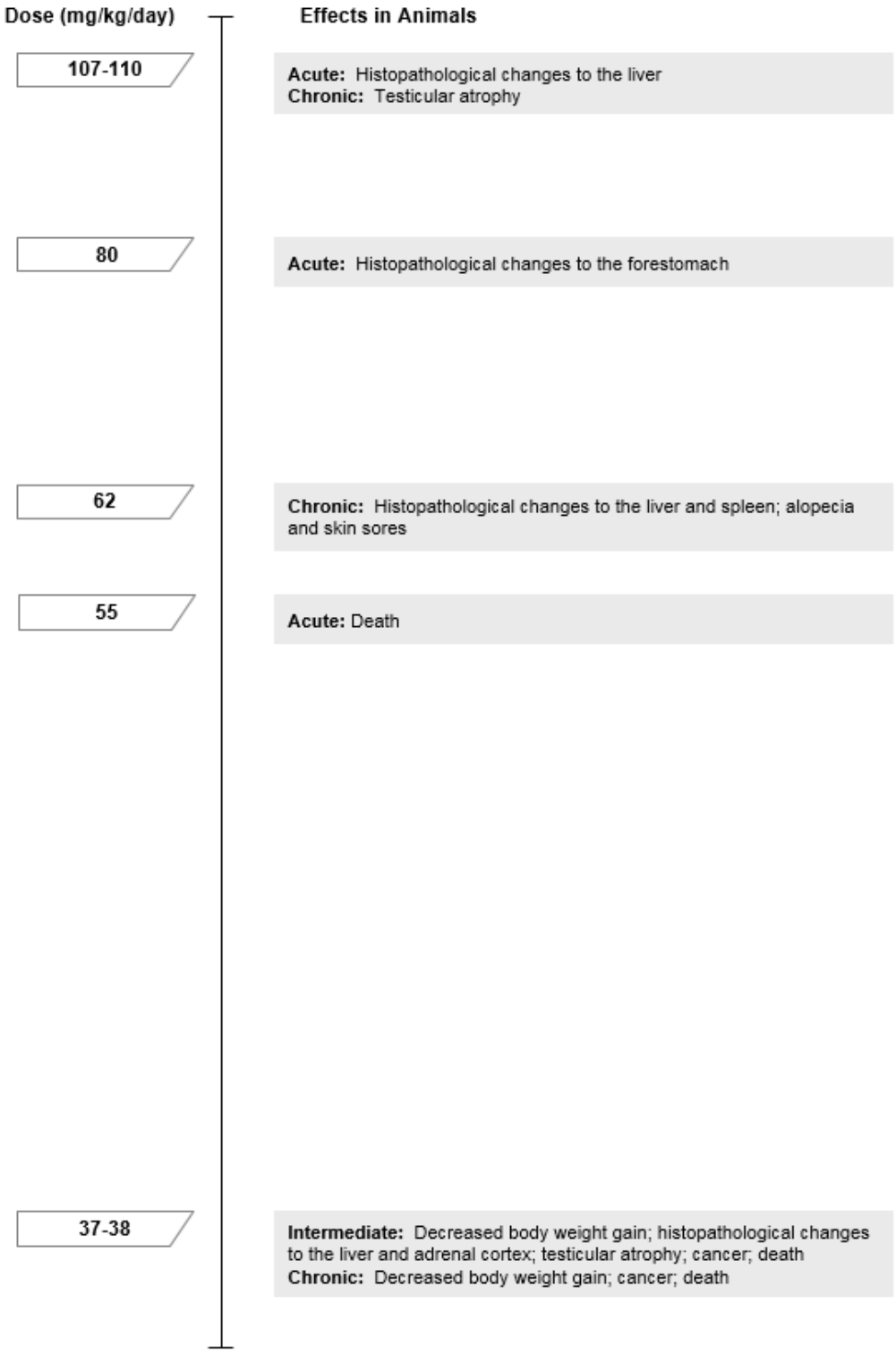
Hepatic Effects. Case reports of individuals acutely exposed to 1,2-dibromoethane at lethal or near-lethal levels by inhalation or ingestion observed acute, severe liver failure and hepatic necrosis. Oral and inhalation exposure studies in laboratory animals also show that the liver is a target organ for 1,2-dibromoethane, with studies reporting histopathological lesions (cloudy swelling, inflammation, fatty degeneration, necrosis, peliosis hepatis).

Figure 1-1. Health Effects Found in Animals Following Inhalation Exposure to 1,2-Dibromoethane*



*Doses adjusted for continuous exposure and are the lowest level found for each effect

Figure 1-2. Health Effects Found in Animals Following Oral Exposure to 1,2-Dibromoethane*



*Doses are the lowest dose found for each effect

Ocular Effects. Few studies have investigated ocular effects from 1, 2-dibromoethane in air. Eye irritation and retinal degradation occurred in an intermediate and chronic study, respectively, in which laboratory animals were exposed to 1,2-dibromoethane in air. Instillation of 1,2-dibromoethane to the eyes of laboratory animals resulted in conjunctival irritation and corneal damage.

Endocrine Effects. Degeneration of the adrenal cortex has been observed in rats following intermediate-duration oral exposure and chronic-duration inhalation exposure.

Reproductive Effects. Exposure of humans and laboratory animals to 1,2-dibromoethane produces adverse effects to the male reproductive system. A cross-sectional study in fumigant workers with combined inhalation and dermal exposure reported decreased sperm count, decreased percentages of viable and motile sperm, and increased abnormal sperm. The time-weighted (5-year) exposure concentration was 0.088 ppm. Testicular atrophy or infertility have been observed in laboratory animals exposed to inhaled and oral 1,2-dibromoethane. In female rats, reduced fertility and degeneration of the uterine epithelium were observed following intermediate-duration inhalation exposure; however, this finding has not been corroborated in other inhalation or oral exposure studies.

Developmental Effects. Developmental effects have only been evaluated in a single inhalation study in rats and mice. In both species, skeletal anomalies (incomplete ossification) were observed at the lowest exposure tested.

Cancer Effects. In laboratory animals exposed to inhaled and oral 1,2-dibromoethane for intermediate and/or chronic durations, cancers have been observed in portal-of-entry tissues (respiratory tract and forestomach). Cancers also developed in several other tissues, including spleen, adrenal gland, mesenchymal tissue, subcutaneous tissue, mammary tissue, testes, blood, and cardiovascular tissue. In addition, lung adenomas were observed in mice following chronic-duration dermal exposure. Cancer was observed at the lowest exposures tested in all studies evaluating this endpoint.

The Department of Health and Human Services classified 1,2-dibromoethane as “reasonably anticipated to be a human carcinogen” based on sufficient evidence of carcinogenicity from studies in laboratory animals (NTP 2016). EPA (2004) concluded that 1,2-dibromoethane is “likely to be carcinogenic to humans” based on strong evidence of carcinogenicity in animals and inconclusive evidence in humans. The International Agency for Research on Cancer (IARC) has classified 1,2-dibromoethane as a group 2A

chemical, “probably carcinogenic to humans” based on sufficient evidence in animals and inadequate evidence in humans (IARC 1999).

1.3 MINIMAL RISK LEVELS (MRLs)

The inhalation database was not considered adequate for deriving inhalation MRLs. As presented in Figure 1-3, the limited available data do not provide adequate information to identify the most sensitive effects of 1,2-dibromoethane, with adverse effects occurring at the lowest concentrations tested. Because mortality or serious adverse health effects were observed at the lowest concentrations tested, this precludes identification derivation of MRLs.

The oral database was not considered adequate for deriving oral MRLs; data are presented in Figure 1-4. At the lowest exposure levels evaluated in acute-, intermediate- and chronic-duration oral studies, excessive treatment-related mortality was observed (NCI 1978; NTP 1982; Rowe et al. 1952; Short et al. 1978). Therefore, MRLs could not be derived.

Inhalation and oral MRL values are summarized in Table 1-1.

Figure 1-3. Summary of Sensitive Targets of 1,2-Dibromoethane – Inhalation

Numbers in triangles and circles are the lowest LOAELs (ppm) among health effects in humans and animals, respectively.

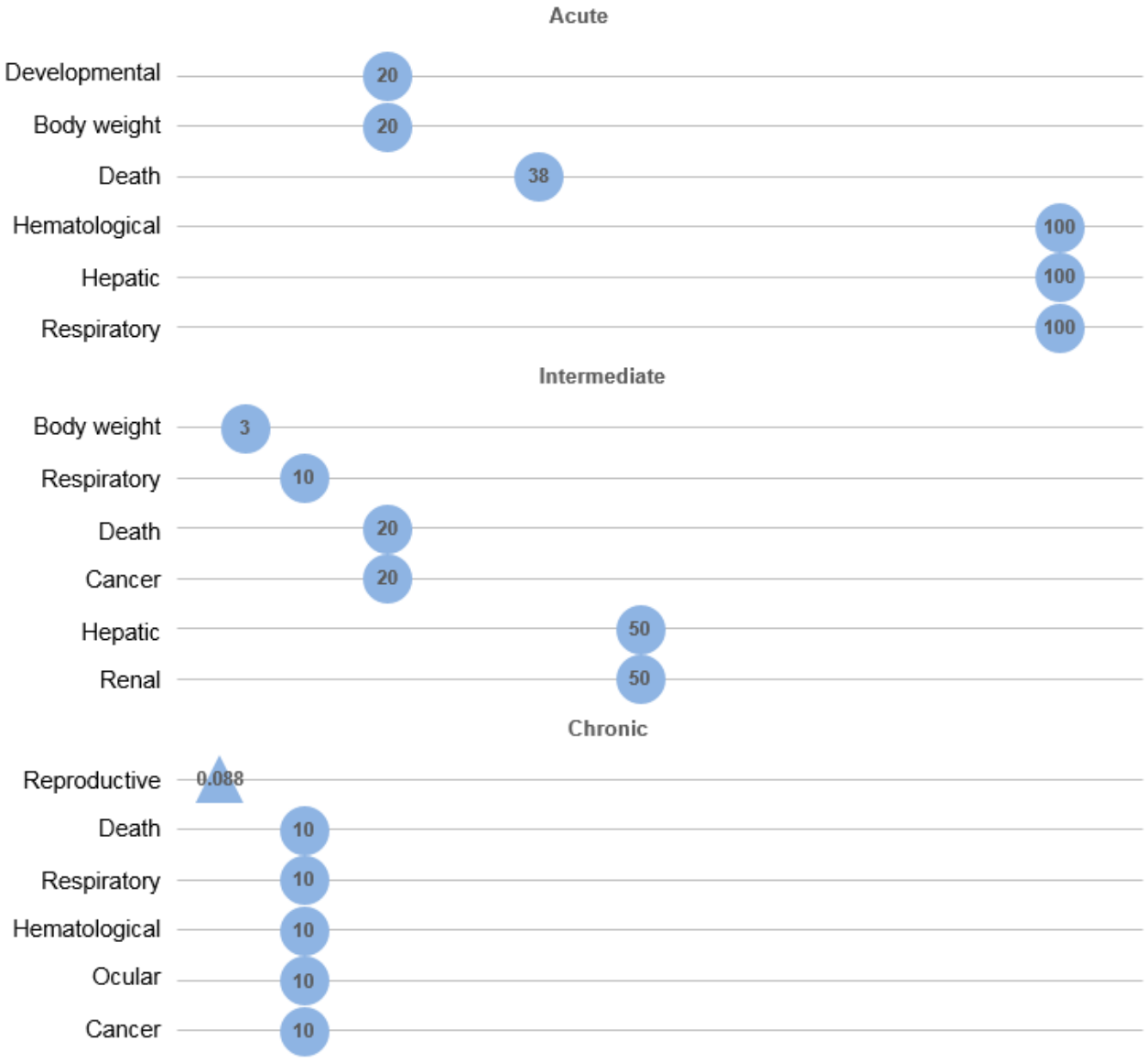


Figure 1-4. Summary of Sensitive Targets of 1,2-Dibromoethane – Oral

Numbers in circles are the lowest LOAELs (mg/kg/day) for all health effects in animals; except for case reports, no human data were identified.

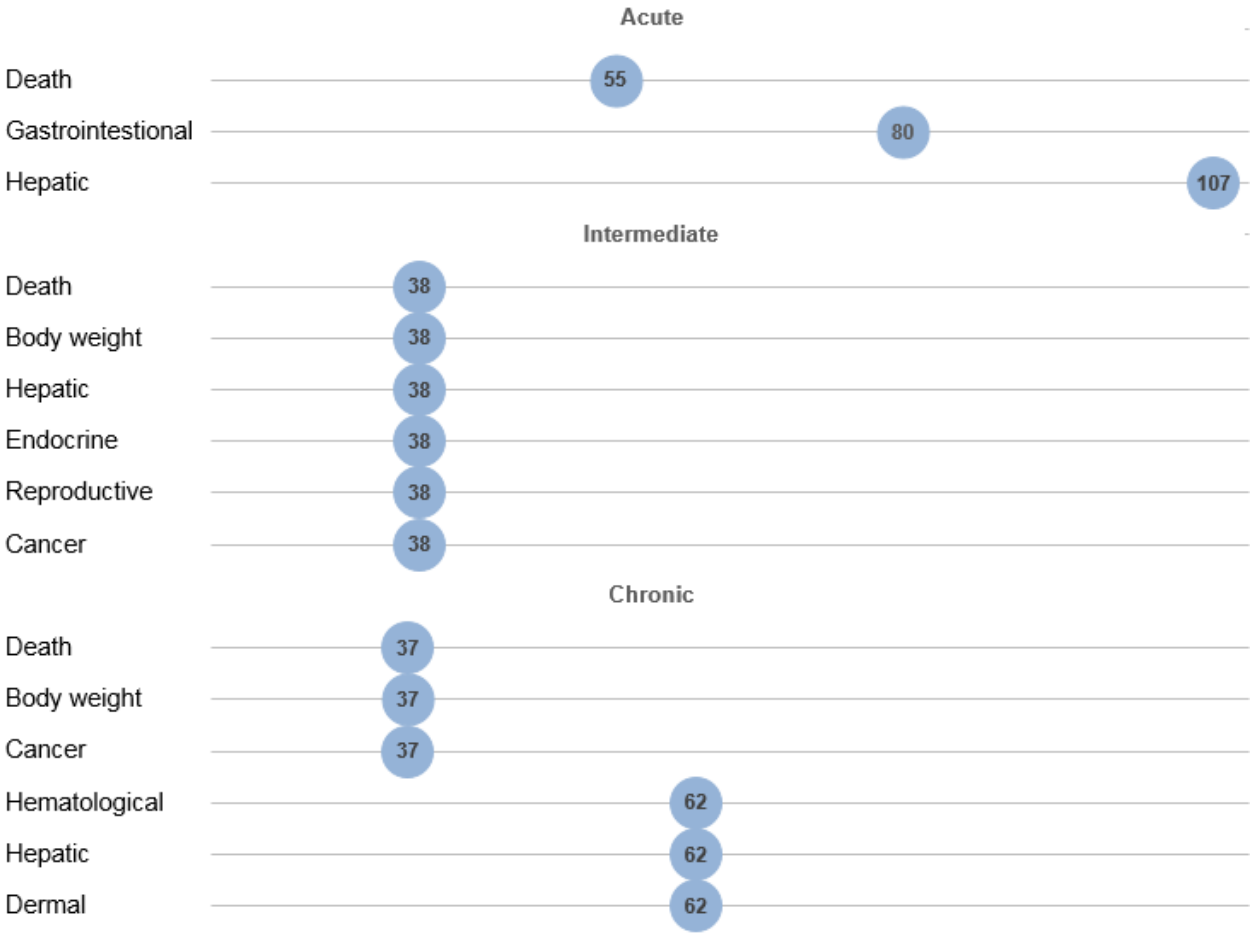


Table 1-1. Minimal Risk Levels (MRLs) for 1,2-Dibromoethane[a]

Exposure duration	MRL	Critical effect	Point of departure	Uncertainty factor	Reference
Inhalation exposure (ppm)					
Acute	Insufficient data for MRL derivation				
Intermediate	Insufficient data for MRL derivation				
Chronic	Insufficient data for MRL derivation				
Oral exposure (mg/kg/day)					
Acute	Insufficient data for MRL derivation				
Intermediate	Insufficient data for MRL derivation				
Chronic	Insufficient data for MRL derivation				

[a]See Appendix A for additional information.