CHAPTER 1. RELEVANCE TO PUBLIC HEALTH

1.1 OVERVIEW AND U.S. EXPOSURES

ATSDR's *Toxicological Profile for Bis(2-Chloromethyl)Ether* was released in 1989. 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 and 3 were revised to reflect the most current health effects 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.

Bis(chloromethyl)ether (BCME; CAS No. 542-88-1) is a colorless liquid that readily evaporates into air. BCME was used in the production of several types of polymers, resins, and textiles. However, most of these uses have been stopped and BCME is now only used in small amounts in fully enclosed systems in manufacturing facilities. BCME has a relatively short half-life in air and water, and exposure to the general population is minimal.

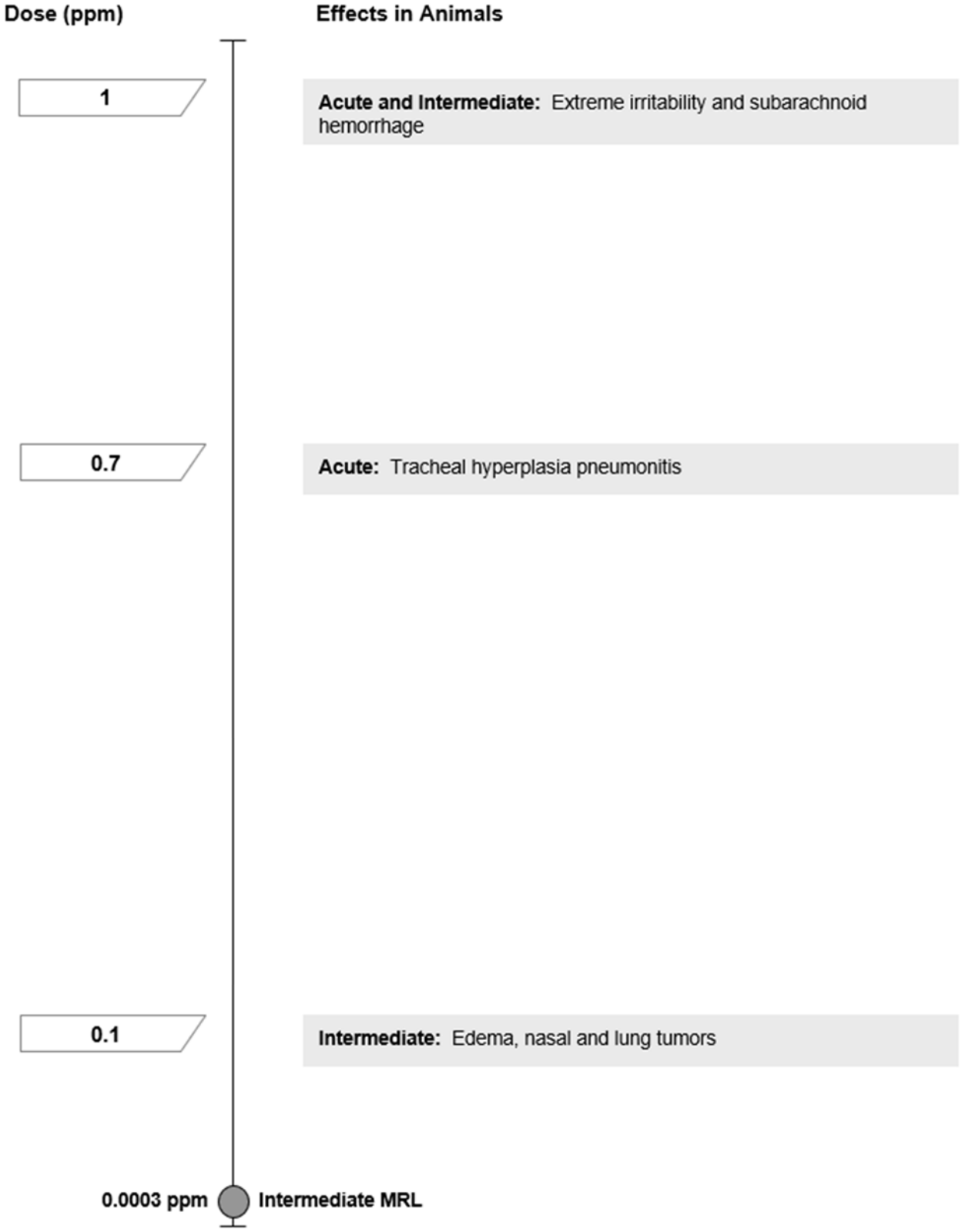
1.2 SUMMARY OF HEALTH EFFECTS

Information on the toxicity of BCME comes primarily from shorter duration inhalation studies in laboratory animals, many of which examined a limited number of potential endpoints. A number of occupational exposure studies have focused on the carcinogenicity of BCME. As illustrated in Figure 1-1, the most sensitive effects appear to be non-neoplastic respiratory effects, neurological effects, and cancer. The most sensitive target is epithelial tissues at the point of contact with BCME, which is consistent with the short half-life of BCME in aqueous media.

Respiratory Effects. A single exposure to 0.7 ppm resulted in tracheal epithelial hyperplasia in rats and pneumonitis in hamsters (Drew et al. 1975). Repeated exposure to 1 ppm resulted in signs of respiratory distress in mice (Leong et al. 1971); this concentration also resulted in increases in mortality. Gross necropsy of rats exposed to 0.1 ppm for 6 months did not find alterations in the respiratory tract (Leong et al. 1981). At lethal concentrations, lung congestion, hemorrhage, and edema have been observed.

Neurological Effects. Extreme irritability was noted in rats and hamsters exposed to 1 ppm for at least 10 exposures (Drew et al. 1975). Subarachnoid hemorrhaging was also observed in the rats. This exposure also resulted in an extreme shortening of the lifespan of the exposed rats and hamsters.

Figure 1-1. Health Effects Found in Animals Following Inhalation Exposure to Bis(Chloromethyl)Ether



Cancer Effects. Lung cancer has been observed in a number of occupational exposure studies of workers exposed to BCME or chloromethyl ether containing BCME (for example, Collingwood et al. 1987; Gowers et al. 1993; Weiss 1989; see Section 2.19 for complete citation list). Studies in laboratory animals have shown that chronic exposure is not required for BCME tumorigenesis. Nasal and/or lung tumors were reported in rats exposed to 0.1 ppm BCME for 4 weeks (Kuschner et al. 1975) or rats and mice exposed for 6 months (Leong et al. 1981).

The U.S. Department of Health and Human Services (NTP 2016), U.S. Environmental Protection Agency (EPA) (IRIS 2002), and International Agency for Research on Cancer (IARC 2012, 2017) have concluded that BCME is a human carcinogen.

1.3 MINIMAL RISK LEVELS (MRLs)

As presented in Figure 1-2, the limited available inhalation data for BCME suggest that the respiratory tract, nervous system, and cancer are sensitive targets of toxicity. The oral database is limited to an acute lethality study and was not considered adequate for deriving MRLs. The acute-duration inhalation MRL value is summarized in Table 1-1 and discussed in greater detail in Appendix A.

Figure 1-2. Summary of Sensitive Targets of Bis(Chloromethyl)Ether -- Inhalation

Cancer, the respiratory tract, and nervous system are the most sensitive targets of bis(chloromethyl)ether.

Numbers in circles are the lowest LOAELs (ppm) for all health effects in animals; no human data were identified.

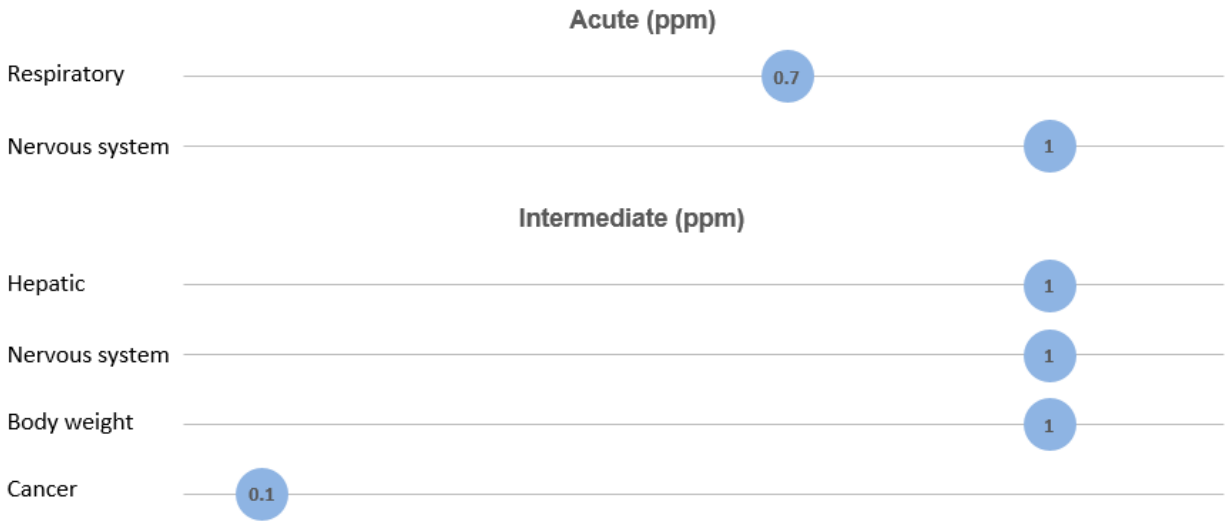


Table 1-1. Minimal Risk Levels (MRLs) for Bis(Chloromethyl)Ether[a]

Exposure duration	MRL	Critical effect	Point of departure	Uncertainty factor	Reference
Inhalation exposure (ppm)					
Acute	Insufficient data for MRL derivation				
Intermediate	0.0003	Respiratory effects	0.1 (NOAEL)	100	Leong et al. 1971
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.

NOAEL = no-observed-adverse-effect level