CHAPTER 1. RELEVANCE TO PUBLIC HEALTH

1.1 OVERVIEW AND U.S. EXPOSURES

ATSDR's *Toxicological Profile for Bis(2-Chloroethyl)Ether (BCEE)* 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(2-chloroethyl)ether (BCEE; CAS Number 111-44-4) is a colorless non-flammable liquid. BCEE is manufactured for use in the production of pesticides and other chemicals. BCEE is soluble in water and will slowly evaporate from water and soil. The most likely source of exposure for the general population is from contaminated drinking water. Populations living near facilities manufacturing or using BCEE may also be exposed via contaminated air.

1.2 SUMMARY OF HEALTH EFFECTS

A small number of studies (<10) have evaluated the toxicity of BCEE following inhalation, oral, or dermal exposure. All but one of these studies were conducted in laboratory animals. Most studies examined a limited number of potential endpoints; one intermediate-duration inhalation study examined a wide range of potential targets.

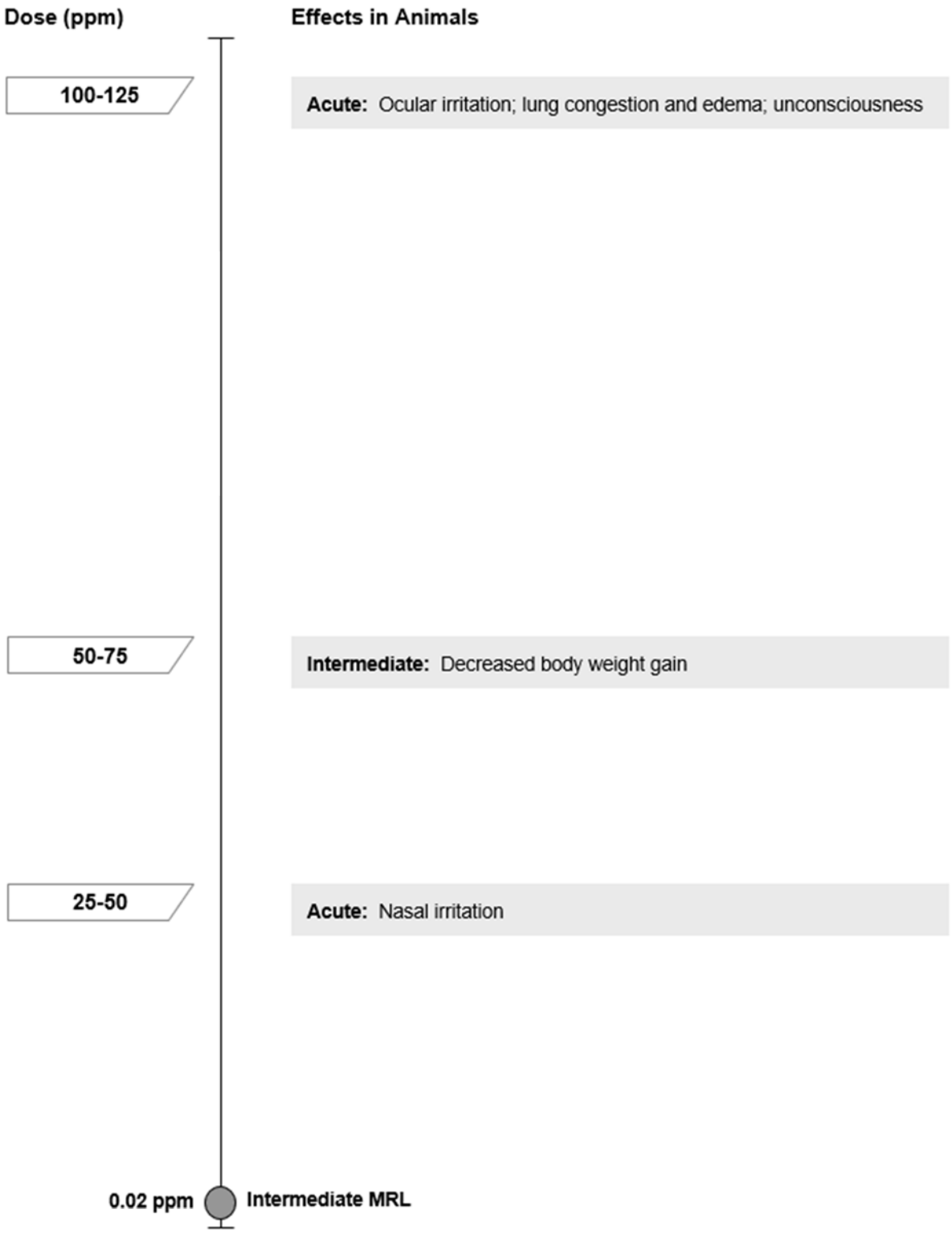
As illustrated in Figure 1-1, the most sensitive effects following inhalation exposure are respiratory and ocular irritation and damage, unconsciousness, and body weight alterations. Alterations in body weight have also been observed following chronic oral exposure. The oral exposure studies were limited in scope and were not considered sufficient for identifying critical targets of toxicity.

Respiratory Effects. Nasal irritation was reported in humans briefly exposed to BCEE in air (Schrenk et al. 1933). In guinea pigs exposed to airborne BCEE, nasal irritation was the most sensitive effect (Schrenk et al. 1933). At higher concentrations (≥105 ppm), lung congestion, edema, and hemorrhage were noted. A repeated exposure study in rats and guinea pigs did not report histological alterations in the respiratory tract (Dow Chemical 1958).

Ocular Effects. Humans briefly exposed to airborne BCEE reported eye irritation (Schrenk et al. 1933). Squinting and lacrimation were reported in guinea pigs exposed to airborne BCEE at 105 and 260 ppm, respectively (Schrenk et al. 1933).

Nervous System Effects. Loss of consciousness was observed in guinea pigs exposed to lethal concentrations of BCEE (≥105 ppm) for 13 hours (Schrenk et al. 1933). In guinea pigs exposed to airborne BCEE, nasal irritation was the most sensitive effect.

Figure 1-1. Health Effects Found in Animals Following Inhalation Exposure to Bis(2-Chloroethyl)Ether



Body Weight Effects. An intermediate-duration inhalation study (Dow Chemical 1958) and a chronic-duration oral study (Weisburger et al.1981) suggest that decreases in body weight gain may be a sensitive endpoint of BCEE toxicity.

Cancer Effects. The carcinogenic potential of BCEE has not been evaluated following inhalation exposure. In a chronic oral mouse study, BCEE exposure resulted in increases in the incidence of liver tumors (Innes et al. 1969). A second study (Weisburger et al. 1981) did not find increases in tumors in rats.

The U.S. Department of Health and Human Services (NTP 2016) and the International Agency for Research on Cancer (IARC 2017) have not categorized the carcinogenicity of BCEE. EPA categorized it as a probable human carcinogen (Group B2) (IRIS 2002).

1.3 MINIMAL RISK LEVELS (MRLs)

As presented in Figure 1-2, the limited available inhalation data for BCEE suggest that the respiratory tract, body weight, and nervous system are sensitive targets of toxicity. The oral database was not considered adequate for deriving MRLs. Available studies have only examined lethality, body weight, and carcinogenicity endpoints. The MRL values are summarized in Table 1-1 and discussed in greater detail in Appendix A.

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

The respiratory tract is the most sensitive target of bis(2-chloroethyl)ether.
Numbers in circles are the lowest LOAELs (ppm) for all health effects in animals; no reliable human data were identified.

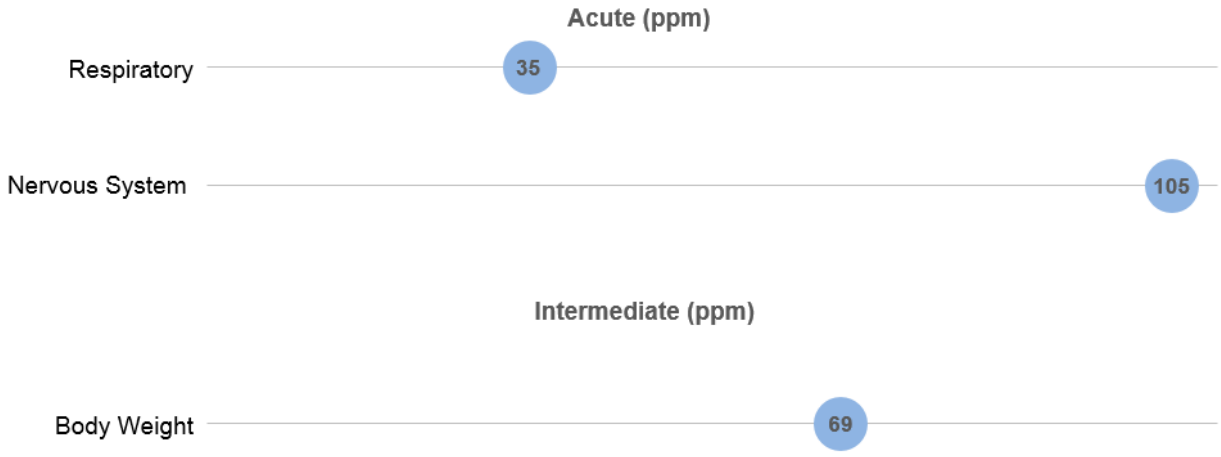


Table 1-1. Minimal Risk Levels (MRLs) for Bis(2-Chloroethyl)Ether[a]

Exposure duration	MRL	Critical effect	Point of departure	Uncertainty factor	Reference
Inhalation exposure (ppm)					
Acute	Insufficient data for MRL derivation				
Intermediate	0.02	Decreased body weight gain	69 (LOAEL)	1,000	Dow Chemical 1958
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.

LOAEL = lowest-observed-adverse-effect level