CHAPTER 1. RELEVANCE TO PUBLIC HEALTH

1.1 OVERVIEW AND U.S. EXPOSURES

1,1,1-Trichloroethane is a synthetic chemical that does not occur naturally in the environment. It is introduced into the environment by human activity. 1,1,1-Trichloroethane also is known as methyl chloroform, methyltrichloromethane, trichloromethylmethane, and α-trichloromethane. Its registered trade names are Tri-Ethane™, chloroethene NU®, and Aerothene TT®. It is a colorless liquid with a sweet, sharp odor. 1,1,1-Trichloroethane dissolves slightly in water. The liquid evaporates quickly and becomes a vapor. Most people begin to smell 1,1,1-trichloroethane in the air when its levels reach 120–500 (ppm). If the chemical makes up 7.5–12.5% (7,000–125,000 ppm) of the air, it can burn easily when it contacts a spark or flame (NIOSH 2019). A poisonous gas known as phosgene can be produced when 1,1,1-trichloroethane is heated to decomposition or during welding if 1,1,1-trichloroethane is used to clean the metal (Reid and Muianga 2012). 1,1,1-Trichloroethane also can be found in soil and water, particularly at hazardous waste sites. Because of its tendency to evaporate easily, the vapor form is most commonly found in the environment.

1,1,1-Trichloroethane had many industrial and household uses. It was often used as a solvent to dissolve other substances, such as glues and paints. In industry, it was widely used to remove oil or grease from manufactured parts. In the home, it used to be an ingredient of products such as spot cleaners, glues, and aerosol sprays. The production of 1,1,1-trichloroethane was banned for domestic use in the United States after January 1, 2002 by the U.S. Environmental Protection Agency (EPA) because it affects the ozone layer. However, until 2005, limited amounts were still allowed to be produced for essential purposes, and until 2012, production of 1,1,1-trichloroethane was allowed for export. U.S. production of 1,1,1-trichloroethane was intended to be incrementally cut as per Section 604 of the Clean Air Act and Montreal Protocol (Kapp 2014). 1,1,1-Trichloroethane was slated to be phased out by January 2002 and production stopped by 2012 as a result of ozone depletion agreements from the Montreal Protocol (Kapp 2014). While the Montreal Protocol did not stop the production of 1,1,1-trichloroethane, it did reduce the production, thus resulting in a steady decline in ambient levels. Some production of 1,1,1-trichloroethane does continue (CDR 2020), and the waste management and/or disposal agencies continue processing and destroying 1,1,1-trichloroethane. Some U.S. facilities continue to report quantities of 1,1,1-trichloroethane to EPA databases such as the Toxics Release Inventory (TRI) and Chemical Data Reporting (CDR); most of these are predominantly hazardous waste management and/or disposal facilities that process and destroy large volumes of 1,1,1-trichloroethane.

Health effects are observed when there is an exposure to large amounts of 1,1,1-trichloroethane. 1,1,1-Trichloroethane is found in air samples taken from all over the world. In the United States, levels in outdoor air between 2003 and 2004 averaged around 0.2 µg/m^3 (0.04 ppb) of 1,1,1-trichloroethane, with a maximum concentration of around 0.9 µg/m^3 (0.2 ppb) (Brenner 2010). Levels in indoor air averaged around 0.2 µg/m^3 (0.04 ppb) of 1,1,1-trichloroethane, with a maximum concentration also around 0.2 µg/m^3 (0.04 ppb) (Brenner 2010). More recent ambient air measurements taken in 2020 are considerably lower, with a median concentration of 0 and a maximum concentration of around 0.3 µg/m^3 (0.06 ppb) (EPA 2022a). 1,1,1-Trichloroethane has also been found in water samples from wells near waste disposal sites.

Common consumer products that contained 1,1,1-trichloroethane included glues, household cleaners, and aerosol sprays. In the workplace, exposure to 1,1,1-trichloroethane could occur while using some metal degreasing agents, paints, glues, and cleaning products, especially from inhalation of vapors or dermal exposure to liquids containing 1,1,1-trichloroethane. High levels of exposure have occurred when 1,1,1-trichloroethane vapors were deliberately inhaled, as in glue-sniffing or solvent abuse. However, as 1,1,1-trichloroethane has been phased out of production in the United States, the current exposure risk from consumer products and in workplaces is likely minimal.

1.2 SUMMARY OF HEALTH EFFECTS

The health effects of 1,1,1-trichloroethane have been evaluated in epidemiological studies, controlled human trials, and experimental animal studies. Toxicity studies on 1,1,1-trichloroethane have evaluated a variety of endpoints, primarily neurological, hepatic, body weight, cardiovascular, and developmental. The genotoxicity of 1,1,1-trichloroethane has also been tested on a variety of species test systems.

As displayed in Figures 1-1, 1-2, and 1-3, the most sensitive endpoints for 1,1,1-trichloroethane toxicity appear to be neurological and hepatic. A systematic review was conducted on these endpoints. Weight-of-evidence conclusions are defined in Appendix C. The review resulted in the following hazard identification[1] conclusions:

- Neurological effects are a known health effect with inhalation exposure.
- Hepatic effects are a presumed health effect with inhalation exposure.

[1]For additional details on the definitions on the hazard identification categories, the reader is referred to Appendix C.

Figure 1-1. Health Effects Found in Humans Following Inhalation Exposure to 1,1,1-Trichloroethane

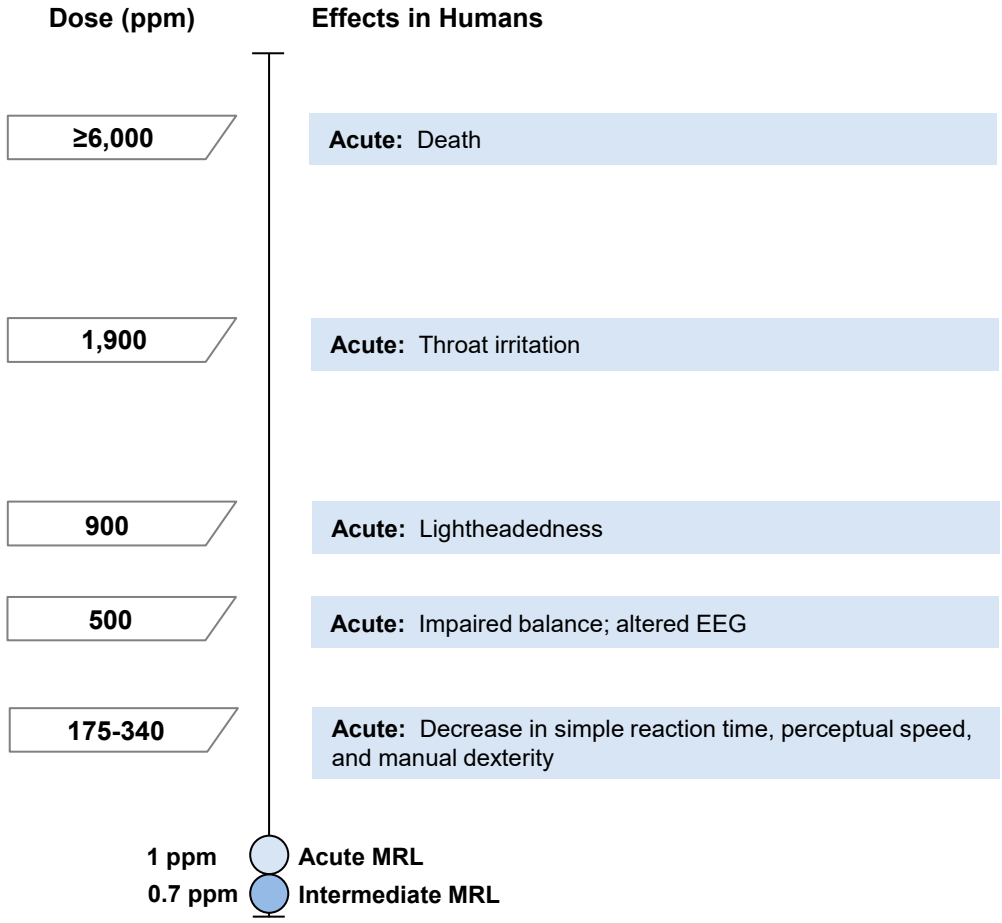


Figure 1-2. Health Effects Found in Animals Following Inhalation Exposure to 1,1,1-Trichloroethane

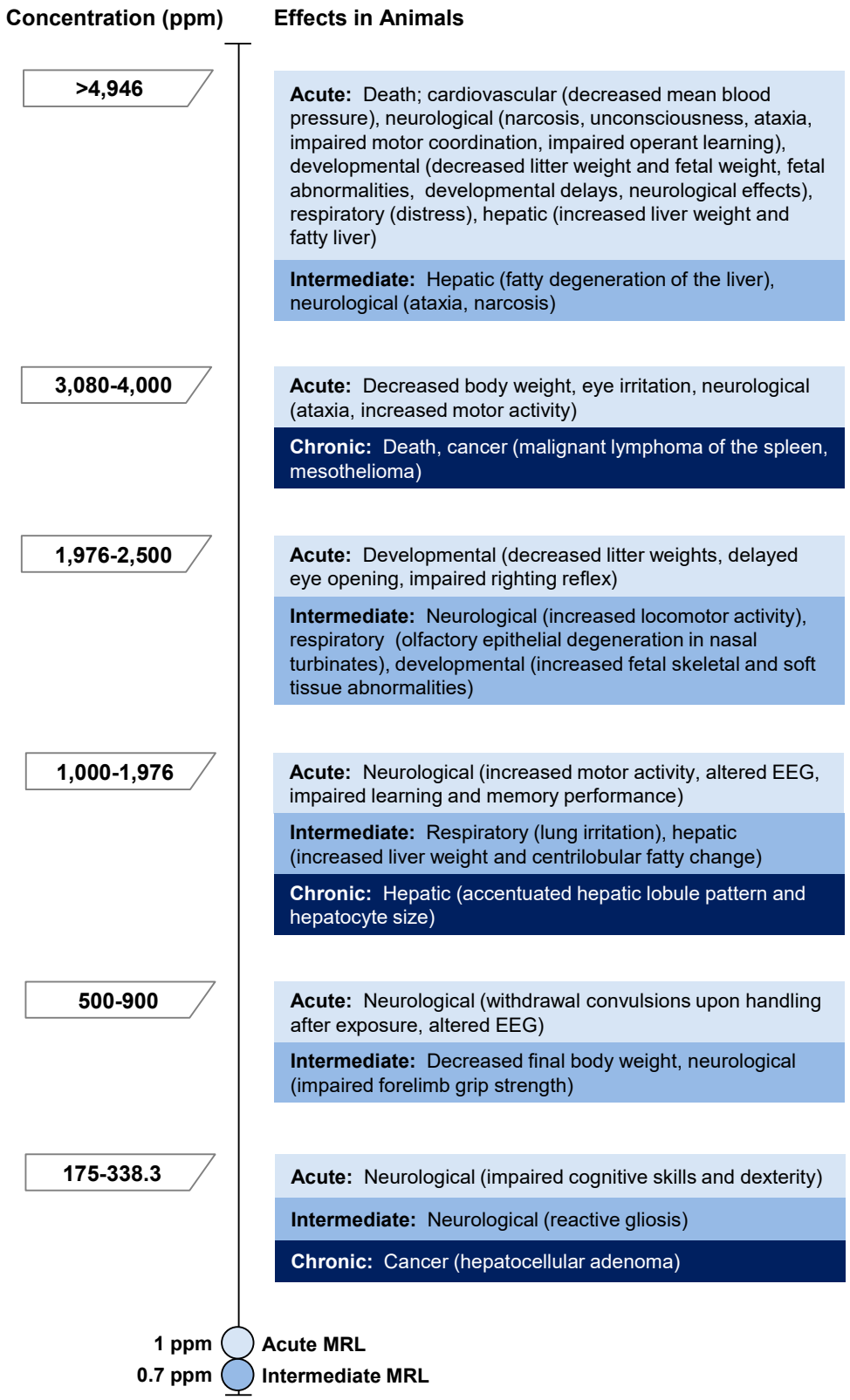
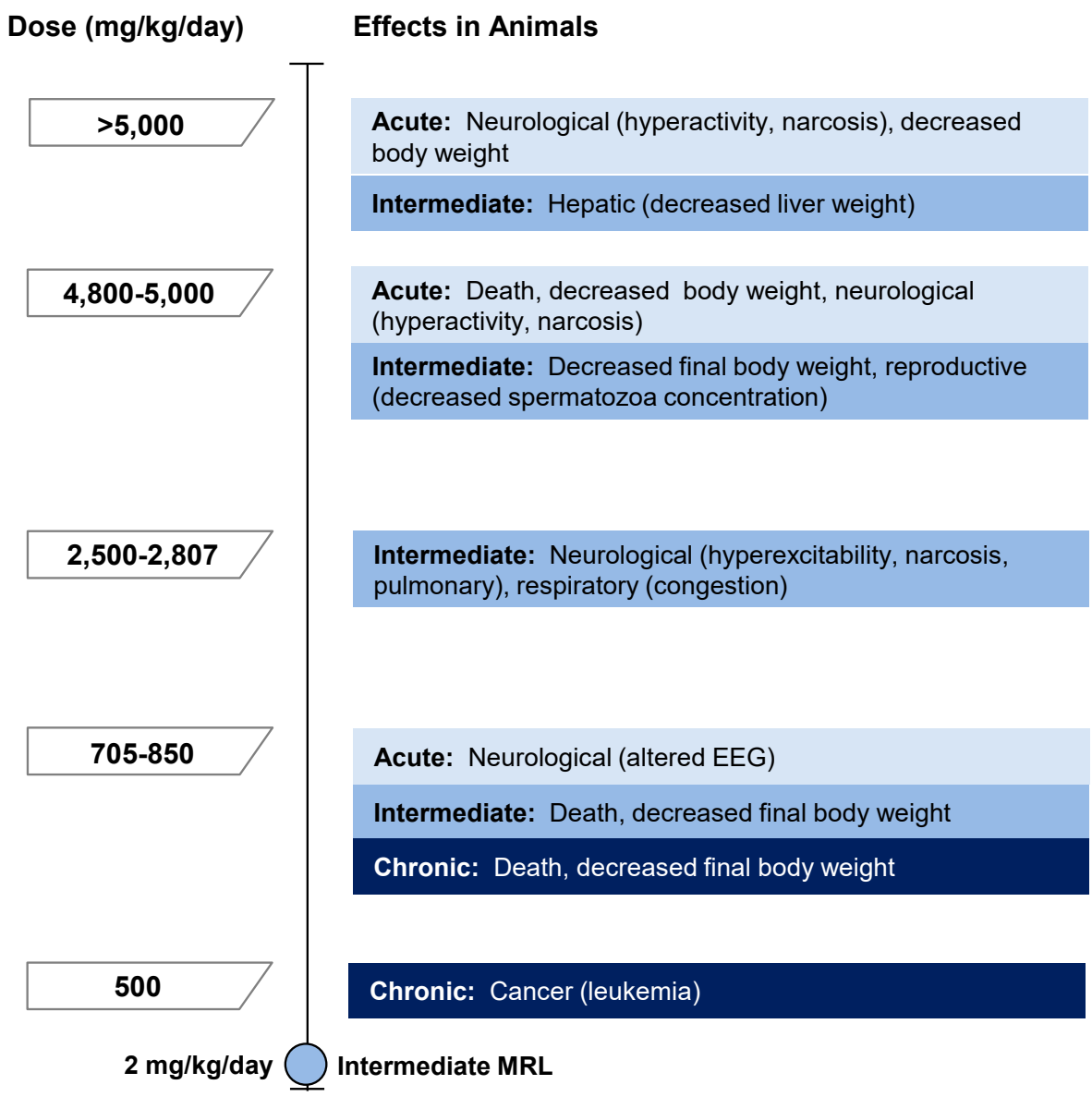


Figure 1-3. Health Effects Found in Animals Following Oral Exposure to 1,1,1-Trichloroethane



Neurological Effects. Inhalation studies in laboratory animals and humans strongly support neurological effects as one of two most sensitive endpoints following exposure to 1,1,1-trichloroethane. Observed health effects in controlled human exposure studies include impaired cognitive skills and manual dexterity, as well as disturbances of equilibrium and coordination (Gamberale and Hultengren 1973; Mackay et al. 1987; Muttray et al. 2000; Stewart et al. 1961). The principal neurological effects observed in animals exposed to 1,1,1-trichloroethane are signs of central nervous system depression, such as impaired performance in behavioral tests, ataxia, and unconsciousness, and are similar to those seen in

humans (Adams et al. 1950; Balster et al. 1982; Calhoun et al. 1981; Evans and Balster 1993; Geller et al. 1982; George et al. 1989; Jones et al. 1996; Mullin and Krivanek 1982; Torkelson et al. 1958). In addition, neurochemical (Hougaard et al. 1984; Rosengren et al. 1985; You and Dallas 2000), behavioral (Balster et al. 1982; Bowen and Balster 1996, 1998, 2006; Bowen et al. 1996a, 1996b; Kjellstrand et al. 1985b; Mullin and Krivanek 1982; Mattsson et al. 1993), and physiological (Evans and Balster 1993) changes have also been observed.

Hepatic Effects. Studies in laboratory animals support hepatic toxicity as another sensitive endpoint following inhalation exposure to 1,1,1-trichloroethane. Although no evidence of liver effects was noted in controlled exposure studies in humans, data from case reports of individuals exposed to high 1,1,1-trichloroethane concentrations suggest that the chemical may produce hepatic effects in humans, including changes in liver enzymes and progressive liver disease (Cohen and Frank 1994; Halevy et al. 1980; Hodgson et al. 1989). Consistent effects were observed in animal studies, which suggest 1,1,1-trichloroethane produces hepatic effects after inhalation exposure. The liver effects include increased liver weight, fatty changes in the liver, and swelling of hepatocytes (Adams et al. 1950; Fuller et al. 1970; Koizumi et al. 1983; MacEwen and Vernot 1974; McNutt et al. 1975; Quast et al. 1988; Toftgard et al. 1981; Torkelson et al. 1958).

1.3 MINIMAL RISK LEVELS (MRLS)

Minimal risk levels (MRLs) for inhalation and oral exposures to 1,1,1-trichloroethane were derived. Figures 1-4 and 1-5 summarize sensitive targets of 1,1,1-trichloroethane for inhalation and oral exposures, respectively. As shown in Table 1-1 and discussed in greater detail in Appendix A, the inhalation database was considered adequate for derivation of acute- and intermediate-duration MRLs for 1,1,1-trichloroethane. The oral database was considered adequate for derivation of an intermediate-duration MRL.

As illustrated in Figure 1-4, neurological and hepatic effects appear to be the most sensitive targets of inhaled 1,1,1-trichloroethane. As shown in Figure 1-5, the most sensitive targets for oral exposure are neurological for acute-duration exposure, body weight for intermediate-duration exposure, and body weight and cancer for chronic-duration exposure.

Figure 1-4. Summary of Sensitive Targets of 1,1,1-Trichloroethane – Inhalation

Available data indicate that the neurological and hepatic endpoints are the most sensitive targets of 1,1,1-trichloroethane following inhalation exposure.

Number in triangles and circles are the lowest LOAELs among health effects in humans and animals, respectively.

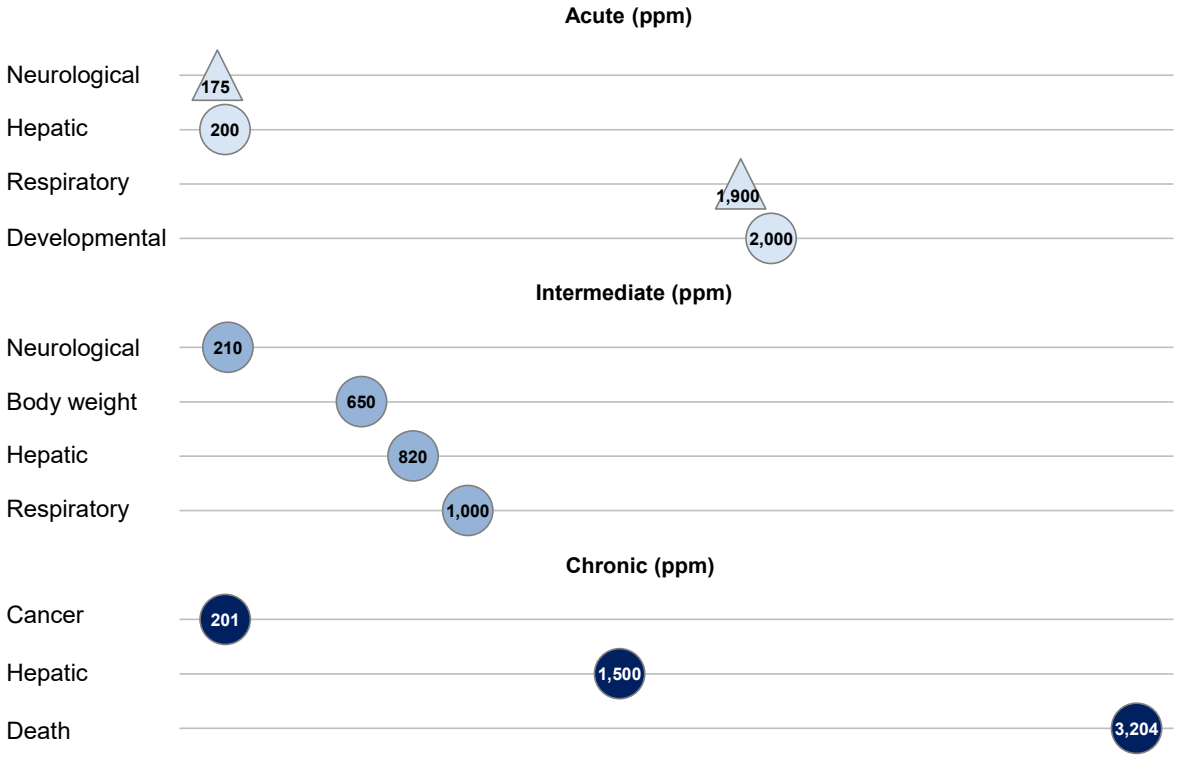


Figure 1-5. Summary of Sensitive Targets of 1,1,1-Trichloroethane – Oral

Available data indicate that the neurological and hepatic endpoints are the most sensitive targets of 1,1,1-trichloroethane following oral exposure.

Numbers in circles are the lowest LOAELs among health effects in animals.

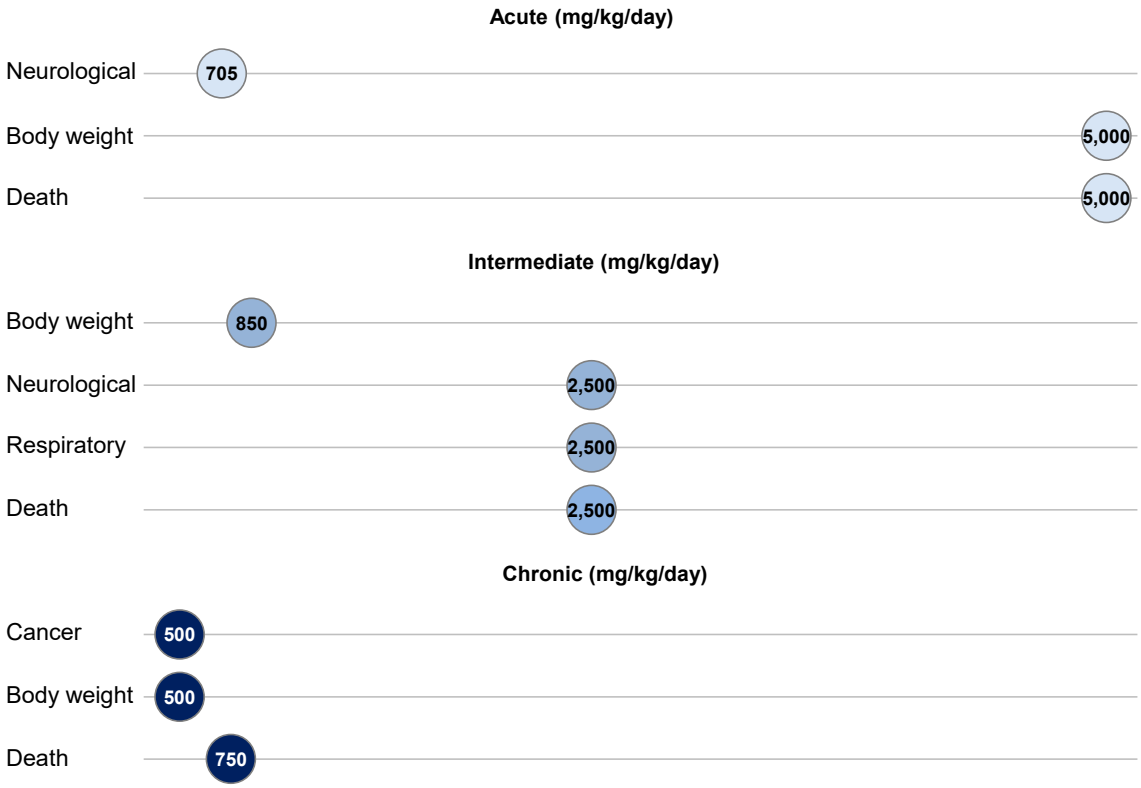


Table 1-1. Minimal Risk Levels (MRLs) for 1,1,1-Trichloroethane[a]

Exposure route	Exposure duration	MRL	Critical effect	POD type	POD value	Uncertainty/ modifying factor	Reference
Inhalation	Acute	**1 ppm** (6 mg/m^3)	Impaired performance in measures of cognitive skills in humans	$LOAEL_{ADJ}$	119 ppm	UF: 100	Mackay et al. 1987
	Intermediate	**0.7 ppm** (4 mg/m^3)	Reactive gliosis measured by increased GFAP in gerbils	NOAEL	70 ppm	UF: 100	Rosengren et al. 1985
	Chronic	None	–	–	–	–	–
Oral	Acute	None	–	–	–	–	–
	Intermediate	**2 mg/kg/day**	Decreased final body weight in mice	$BMDL_{10}$	208 mg/kg/day	UF: 100	NTP 2000
	Chronic	None	–	–	–	–	–

[a]See Appendix A for additional information.

ADJ = adjusted for intermittent exposure; $BMDL_{10}$ = benchmark dose lower confidence limit 10%; GFAP = glial fibrillary acid protein; LOAEL = lowest-observed-adverse-effect level; NOAEL = no-observed-adverse-effect level; UF = uncertainty factor