CHAPTER 1. RELEVANCE TO PUBLIC HEALTH

1.1 OVERVIEW AND U.S. EXPOSURES

1,2-Dichloroethene is a volatile, low molecular weight halogenated liquid that is used as a chemical intermediate or an industrial solvent. Although 1,2-dichloroethene is often referred to as a single chemical, it exists as two geometric isomers that have distinct properties.

When 1,2-dichloroethene is released to the environment, most will quickly end up as a gas in the atmosphere. Once in the atmosphere, it will break down by reactions with substances in the air. When released to lakes, rivers, and other bodies of water, most of it evaporates into the air. When released to soil, it also volatilizes to air but its high leachability indicates that it may migrate to groundwater.

Most studies indicate that both isomers of 1,2-dichloroethene are highly resistant to biodegradation in an aerobic environment but may biodegrade under anaerobic conditions. Biodegradation of 1,2-dichloroethene can produce vinyl chloride, which is a hazardous chemical substance. Based on the high measured vapor pressure and large estimated Henry's law constant, volatilization of 1,2-dichloroethene from water is expected to be an important fate process.

Exposure to 1,2-dichloroethene originates from primarily anthropogenic sources. Since 1,2-dichloroethene is a volatile liquid at room temperature, the most likely route of exposure would be from breathing air containing 1,2-dichloroethene. Occurrences of 1,2-dichloroethene in air can be attributed to releases from factories that manufacture or use 1,2-dichloroethene and/or evaporation from some landfills, solvents, and refrigerants.

Occupational exposure to trans- and cis-1,2-dichloroethene is most likely to occur through inhalation and dermal routes. The general population is most likely exposed by inhalation of contaminated air and ingestion of contaminated food and drinking water.

1.2 SUMMARY OF HEALTH EFFECTS

For this profile, toxicity studies for 1,2-dichloroethene are categorized by isomer composition: trans-1,2-dichloroethene; cis-1,2-dichloroethene; and mixtures of the cis- and trans- isomers. Only a few studies investigating health effects from exposure to 1,2-dichloroethene in humans were identified, with

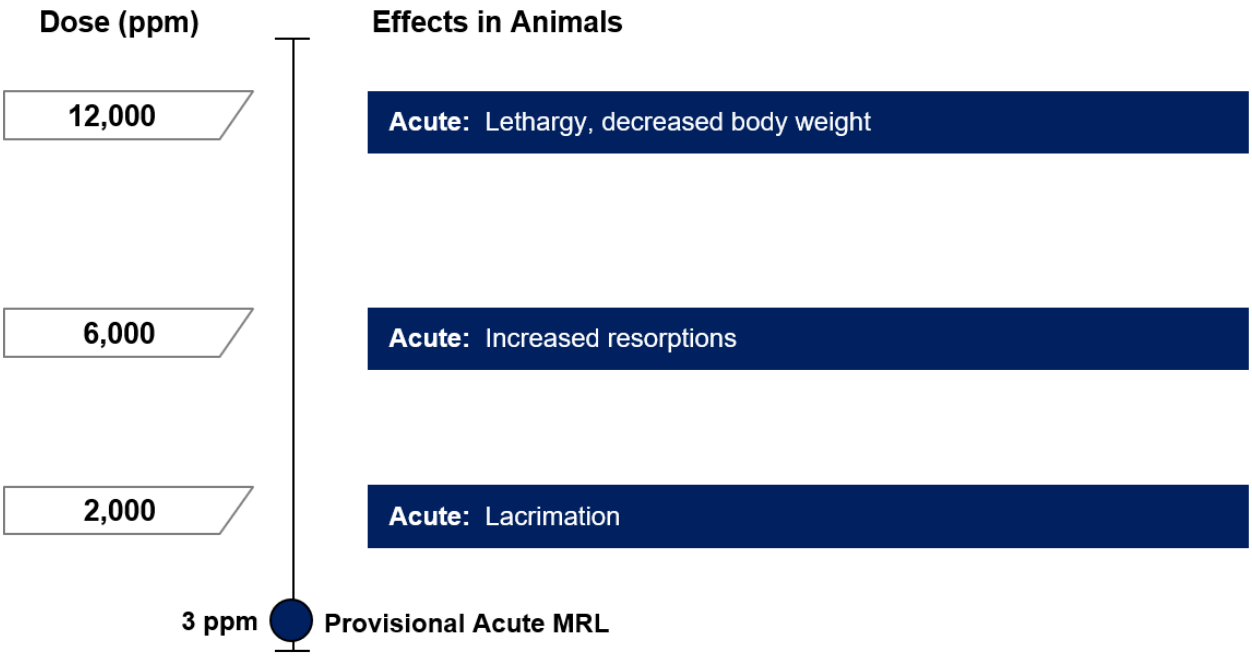
data limited to studies on trans-1,2-dichloroethene. Information on the health effects in experimental animals is available as follows:

- trans-1,2-dichloroethene: acute- and intermediate-duration oral and inhalation exposures and acute-duration dermal exposure;
- cis-1,2-dichloroethene: acute-duration inhalation exposure and acute- and intermediate-duration oral exposures; and
- mixtures of cis- and trans-1,2-dichloroethene: acute-duration inhalation exposure and acute- and intermediate-duration oral exposures.

No studies on chronic-duration exposure to trans-1,2-dichloroethene, cis-1,2-dichloroethene, or mixtures of cis- and trans- isomers were identified for any exposure route in animals.

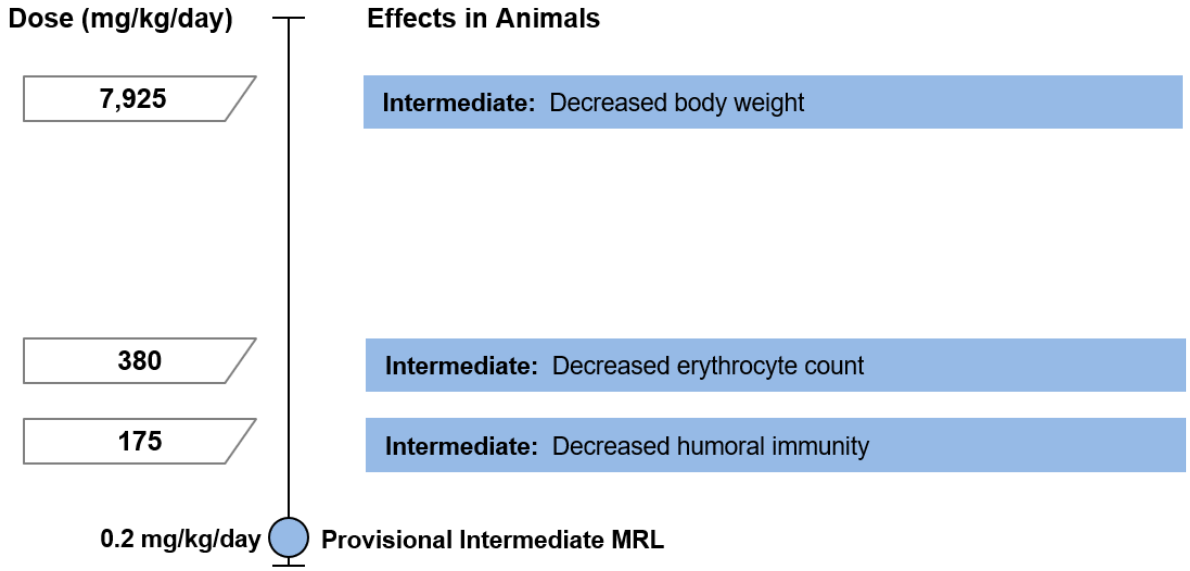
For trans-1,2-dichloroethene, the most sensitive effect of acute-duration inhalation exposure is contact irritation of the eye (lacrimation), and the most sensitive effect of intermediate-duration oral exposure is the immune system (decreased humoral immunity), as shown in Figures 1-1 and 1-2, respectively. Dermal exposure studies also indicate that trans-1,2-dichloroethene can damage the skin. ATSDR conducted a systematic review assessing ocular irritation and decreased immune function. Studies on cis-1,2-dichloroethene and mixtures of cis- and trans-1,2-dichlorothene did not identify toxicologically significant effects at sublethal levels.

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



*No intermediate- or chronic-duration MRLs were derived for trans-1,2-dichloroethene

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



*No acute- or chronic-duration MRLs were derived for trans-1,2-dichloroethene

Information on the most sensitive effects of trans-1,2-dichloroethene is summarized as follows.

Ocular Effects. Exposure to trans-1,2-dichloroethene in air and by instillation into the eye produces ocular irritation. In pregnant rats exposed by whole-body inhalation for 10 days, lacrimation was observed at concentrations of 2,000, 6,000, and 12,000 ppm (Hurtt et al. 1993). Brown, periocular staining, due to excessive lacrimation, was observed in the 6,000 ppm (18/24) and 12,000 ppm (22/24) exposure groups. Instillation of 0.01 trans-1,2-dichloroethene to the eyes of rabbits for 20 seconds resulted in transient severe corneal opacity, moderate iritis, and conjunctivitis (DuPont 1988c).

Immunological Effects. Immunological function has been assessed in acute- and intermediate-duration oral exposure studies (Munson et al. 1982; Shopp et al. 1985). Humoral immunity, as measured by the number of spleen IgM antibody-forming cells (AFCs) directed against sheep red blood cells (sRBCs), was decreased in mice following oral exposure to trans-1,2-dichloroethene at doses of 17, 175, and 387 mg/kg/day for 90 days (Shopp et al. 1985). Cellular immune function was not affected. No additional intermediate-duration oral exposure studies evaluating immune studies were identified. No effects on humoral or cellular immunity were observed in acute-duration oral studies in mice at doses up to 220 mg/kg/day for 14 days (Munson et al. 1982; Shopp et al. 1985).

Other effects observed in laboratory animals exposed to trans-1,2-dichloroethene are summarized below, although these effects do not appear to be sensitive targets.

Body Weight Effects. Conflicting results have been observed regarding decreased body weight and body weight gain. Maternal body weight gain was reduced in pregnant rats exposed via inhalation to 12,000 ppm trans-1,2-dichloroethene during gestation (Hurtt et al. 1993), although body weight was similar to controls at the end of pregnancy. In contrast, no effect on body weight was observed in male or female rats following inhalation of 4,000 ppm trans-1,2-dichloroethene for 90 days (DuPont 1998). Body weight was also decreased in female rats following dietary exposure to 7,928 mg/kg/day for 14 weeks. Other studies found no effects of oral acute-duration exposures to trans-1,2-dichloroethene in rats or mice at maximum oral doses tested of 210–220 mg/kg/day (Barnes et al. 1985; Munson et al. 1982) or 387–8,065 mg/kg/day (Barnes et al. 1985; Hayes et al. 1987; NTP 2002), respectively.

Hematological Effects. Results of studies of effects of trans-1,2-dichloroethene on hematological parameters are inconsistent. Small, dose-related decreases in erythrocyte counts were observed in male and female rats exposed to dietary trans-1,2-dichloroethene for 14 weeks at doses of 380, 770, 1,540, and 3,210 mg/kg/day (NTP 2002). In female rats, erythrocyte counts were decreased in the 1,580 and 3,245 mg/kg/day exposure groups. However, other oral exposure studies did not observe adverse hematological effects following acute-duration exposure of rats and mice to maximum doses of 210–8,065 mg/kg/day (Barnes et al. 1985; Hayes et al. 1987; NTP 2002) or in a 90-day drinking water study at doses up to 2,809 and 3,114 mg/kg/day in male and female rats, respectively (Hayes et al. 1987). In addition, no hematological effects were observed in rats exposed to 4,000 ppm for 90 days by inhalation (DuPont 1998).

Neurological Effects. Little information on neurological effects of trans-1,2-dichloroethene is available. At sublethal levels, narcosis (incidence data not reported) was observed in rats exposed by inhalation on gestation days (GDs) 7–16 at concentrations of 6,000 and 12,000 ppm, but not at 2,000 ppm (Hurtt et al. 1993). Lethargy was observed in rats exposed to 12,000 ppm, but not at lower exposure concentrations (Hurtt et al. 1993). In single-dose oral lethality studies in rats, clinical signs of neurotoxicity (central nervous system depression, decreased activity, ataxia, loss of righting reflex, and depressed respiration) have been observed (Barnes et al. 1985; Hayes et al. 1987); however, due to the lack of incidence data, reliable no-observed-adverse-effect level (NOAEL) and lowest-observed-adverse-effect level (LOAEL) values could not be identified. No neurotoxicity (assessed by functional observational batteries, cage-side evaluations for clinical signs, and histopathology of neurological tissues) was observed in male and female rats at maximum doses of 3,210 and 3,245 mg/kg/day, respectively, or in male and female mice at maximum doses of 8,065 and 7,925 mg/kg/day, respectively, in a 14-week dietary study.

Developmental Effects. An epidemiological study did not find associations between maternal exposure to trans-1,2-dichloroethene during pregnancy and birth defects (neural tube defect or oral cleft defects (Ruckart et al. 2013). A gestational exposure study in rats observed increased resorptions following inhalation exposure to 6,000 ppm trans-1,2-dichloroethene and decreased fetal weight in females at 12,000 ppm (Hurtt et al. 1993). No additional developmental studies were identified for trans-1,2-dichloroethene.

1,2-Dichloroethene is not listed by Department of Health and Human Services (HHS) National Toxicology Program (NTP) in the 15th Report on Carcinogens (NTP 2021). The U.S. Environmental Protection Agency (EPA) has not classified the carcinogenicity of 1,2-dichloroethene due to inadequate

information (IRIS 2010a, 2010b). The International Agency for Research on Cancer (IARC) has not evaluated the carcinogenicity of 1,2-dichloroethene (IARC 2022).

1.3 MINIMAL RISK LEVELS (MRLs)

Development of MRLs was considered for the individual cis- and trans- isomers, but not for mixtures of the isomers. The database for trans-1,2-dichloroethene was considered adequate to derive an acute-duration inhalation MRL and an intermediate-duration oral MRL. The MRL values for trans-1,2-dichloroethene are summarized in Table 1-1. Data were not considered adequate for derivation of intermediate- and chronic-duration inhalation MRLs or acute- and chronic-duration oral MRLs for trans-1,2-dichloroethene. As presented in Figures 1-3 and 1-4, available data for trans-1,2-dichloroethene show that contact irritation of the eye and the immune system function are the most sensitive effects. The database for cis-1,2-dichloroethene was not considered adequate for derivation of inhalation or oral MRLs for any exposure duration (Table 1-2).

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

The eye is the most sensitive target of trans-1,2-dichloroethene inhalation exposure.
Numbers in circles are the lowest LOAELs for all health effects in animals; exposure data for humans are uncertain.

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

The immune system is the most sensitive target of trans-1,2-dichloroethene inhalation exposure. Numbers in circles are the lowest LOAELs for all health effects in animals; exposure data for humans are uncertain.

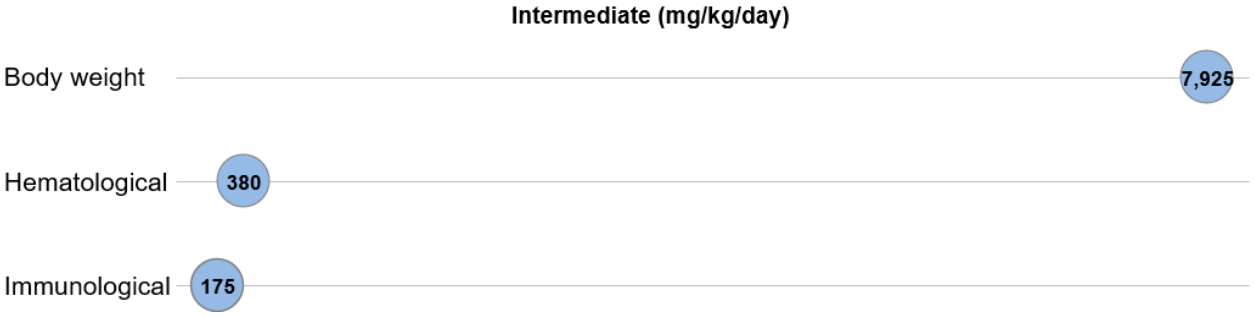


Table 1-1. Minimal Risk Levels (MRLs) for trans-1,2-Dichloroethene[a]

Exposure route	Exposure duration	Provisional MRL	Critical effect	POD type	POD value	Uncertainty/ modifying factor	Reference
Inhalation	Acute	**3 ppm** (12 mg/m^3)	Lacrimation	$BMCL_{10}$	256.47 ppm	UF: 100	Hurtt et al. 1993
	Intermediate	None	–	–	–	–	–
	Chronic	None	–	–	–	–	–
Oral	Acute	None	–	–	–	–	–
	Intermediate	**0.2 mg/kg/day**	Decreased humoral immunity	$BMDL_{1SD}$	16.75 mg/kg/day	UF: 100	Shopp et al. 1985
	Chronic	None	–	–	–	–	–

[a]See Appendix A for additional information.

$BMCL_{10}$ = 95% lower confidence limit on the benchmark concentration (subscripts denote benchmark response: i.e., 10 = dose associated with 10% extra risk); BMDL = 95% lower confidence limit on the benchmark dose; HEC = human equivalent concentration; LOAEL = lowest-observed-adverse-effect level; POD = point of departure; SD = standard deviation; UF = uncertainty factor

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

No MRLs were derived for any exposure route or duration for cis-1,2-dichloroethene.

[a]See Appendix A for additional information.