Health-Based Guidance for Water
Health Risk Assessment Unit, Environmental Health Division
651-201-4899

Adopted as Rule: November 2023

Toxicological Summary for: trans-1,2-Dichloroethene

CAS: **156-60-5**

Synonyms: 1,2-Dichloroethylene (trans); 1,2-trans-dichloroethylene; (E)-1,2-dichloroethene; (E)-1,2-Dichloroethylene; trans-1,2-Dichloroethene; trans-1,2-dichloroethylene; trans-1,2-dichloroethylene ; trans-1,2-DCE; trans-acetylene dichloride; trans-dichloroethylene

Acute Non-Cancer Health Risk Limit ($nHRL_{Acute}$) = Not Derived (Insufficient Data)

Short-term Non-Cancer Health Risk Limit ($nHRL_{Short\text{-}term}$) = Not Derived (Insufficient Data)

Subchronic Non-Cancer Health Risk Limit ($nHRL_{Subchronic}$) = 50 µg/L

$$\frac{\text{(Reference Dose, mg/kg-d) x (Relative Source Contribution) x (Conversion Factor)}}{\text{(Subchronic Intake Rate, L/kg-d)}}$$

$$= \frac{\text{(0.020 mg/kg-d) x (0.2)}^{*} \text{ x (1000 µg/mg)}}{\text{(0.074 L/kg-d)}^{**}}$$

= 54 rounded to **50 µg/L**

*Relative Source Contribution: MDH 2008, Section IV.E.1.
**Intake Rate: MDH 2008, Section IV.E.1. and US EPA 2019, Exposure Factors Handbook, Tables 3-1, 3-3 and 3-5

Reference Dose/Concentration:	HED/Total UF = 2.03/100 = 0.020 mg/kg-d (CD-1 mouse)
Source of toxicity value:	Determined by MDH in 2019
Point of Departure (POD):	14.5 mg/kg-d ($BMDL_{ADM\text{-}1SD}$ based on 2018 OEHHA modeling of immunotoxicity data from Shopp et al 1985)
Dose Adjustment Factor (DAF):	0.14, Body weight scaling, default (USEPA, 2011) (MDH, 2017)
Human Equivalent Dose (HED):	POD x DAF = 14.5 mg/kg-d x 0.14 = 2.03 mg/kg-d
Total uncertainty factor (UF):	100
Uncertainty factor allocation:	3 for interspecies differences (for toxicodynamics), 10 for intraspecies variability, and 3 for database uncertainty due to lack of a multigenerational study and supplementing database with inhalation studies
Critical effect(s):	Decreased ability to produce antibodies against sheep RBCs in male spleen cells

Co-critical effect(s):	Decreased thymus weight, clinical chemistry effects
Additivity endpoint(s):	Immune system

Chronic Non-Cancer Health Risk Limit ($nHRL_{Chronic}$) = 9 µg/L

$$\frac{\text{(Reference Dose, mg/kg-d) x (Relative Source Contribution) x (Conversion Factor)}}{\text{(Chronic Intake Rate, L/kg-d)}}$$

$$= \frac{\text{(0.0020 mg/kg-d) x (0.2)}^{*} \text{ x (1000 µg/mg)}}{\text{(0.045 L/kg-d)}^{**}}$$

= 8.8 rounded to **9 µg/L**

*Relative Source Contribution: MDH 2008, Section IV.E.1.
**Intake Rate: MDH 2008, Section IV.E.1. and US EPA 2019, Exposure Factors Handbook, Tables 3-1, 3-3 and 3-5

Reference Dose/Concentration:	HED/Total UF = 2.03/1000 = 0.0020 mg/kg-d (CD-1 mouse)
Source of toxicity value:	Determined by MDH in 2019
Point of Departure (POD):	14.5 mg/kg-d ($BMDL_{ADM\text{-}1SD}$ based on 2018 OEHHA modeling of immunotoxicity data from Shopp et al 1985, subchronic exposure)
Dose Adjustment Factor (DAF):	0.14, Body weight scaling, default (USEPA, 2011) (MDH, 2017)
Human Equivalent Dose (HED):	POD x DAF = 14.5 mg/kg-d x 0.14 = 2.03 mg/kg-d
Total uncertainty factor (UF):	1000
Uncertainty factor allocation:	3 for interspecies differences (for toxicodynamics), 10 for intraspecies variability, 10 for subchronic-to-chronic extrapolation due to clear and significant immunotoxicity in the subchronic study, and 3 for database uncertainty due to lack of a multigenerational study and supplementing database with inhalation studies
Critical effect(s):	Decreased ability to produce antibodies against sheep RBCs in male spleen cells
Co-critical effect(s):	Decreased thymus weight, clinical chemistry effects
Additivity endpoint(s):	Immune system

Cancer Health Risk Limit (cHRL) = Not Applicable

Cancer classification:	*"Inadequate information to assess the carcinogenic potential"* of trans-1,2-DCE
Slope factor (SF):	Not Applicable
Source of cancer slope factor (SF):	EPA IRIS 2010
Tumor site(s):	Not Applicable

Volatile: Yes (High)

Summary of Guidance Value History:

A chronic HRL of 100 µg/L was promulgated in 1993. In 2011, subchronic and chronic Health-Based Values (HBVs) of 600 and 100 µg/L, respectively, were derived. In 2012, MDH re-evaluated the HBVs to incorporate HED methodology, resulting in subchronic and chronic HBVs of 200 and 40 µg/L, respectively. The 2012 HBVs were adopted as HRLs in 2013 and the 1993 HRL was repealed. In 2020, MDH re-evaluated the 2013 HRLs and derived subchronic and chronic HBVs of 60 and 9 µg/L, respectively. The re-evaluation resulted in values that were 3 to 4-fold lower as the result of using the most recent risk assessment methodology (specifically, improvements in benchmark dose modeling for POD calculation). In 2020 MDH incorporated updated intake rates (US EPA 2019). Use of the updated intake rates resulted in a decrease in the Subchronic HBV from 60 µg/L to 50 µg/L. In November 2023, the guidance values were adopted into Minnesota Rules, 4717.7860, as Health Risk Limits (HRLs).

Summary of toxicity testing for health effects identified in the Health Standards Statute (144.0751):

Even if testing for a specific health effect was not conducted for this chemical, information about that effect might be available from studies conducted for other purposes. MDH has considered the following information in developing health protective guidance.

	Endocrine	Immunotoxicity	Development	Reproductive	Neurotoxicity
Tested for specific effect?	No	Yes	Yes	No	No
Effects observed?	No	Yes[1]	Yes[2]	No[3]	Secondary observations[4]

Comments on extent of testing or effects:

[1]Shopp et al. (1985) measured depression in humoral immune status following 90 days of exposure via drinking water. These effects form the basis of the subchronic and chronic HBVs.
[2]A single inhalation developmental study exists. Decreased fetal body weight was observed at doses estimated to be over 400-fold higher than the minimal short-term critical Human Equivalent Dose. A database uncertainty factor has been applied, in part, due to the lack of oral developmental/reproductive studies.
[3]Examination of the reproductive organs of animals in the 90-day study did not report any histological changes. A database uncertainty factor has been applied, in part, due to the absence of a multigenerational study.
[4]Neurological effects have not been adequately studied. Acute exposures (e.g., a single high dose) have reported effects.

Resources Consulted During Review:

Agency for Toxic Substances and Disease Registry (ATSDR). Minimal Risk Levels.
URL: https://www.atsdr.cdc.gov/mrls/index.html

Agency for Toxic Substances and Disease Registry (ATSDR). 1996. Toxicological Profile for 1,2 Dichloroethane.

Barnes DW, VM Sanders, KL White, GM Shopp, AL Munson. 1985. Toxicology of Trans-1,2-Dichloroethylene in the Mouse. Drug and Chem Tox 8(5)373-392.

California Environmental Protection Agency, OEHHA Toxicity Criteria Database. URL: http://www.oehha.ca.gov/risk/ChemicalDB/index.asp

California Environmental Protection Agency, OEHHA Public Health Goals for Chemicals in Drinking Water: *Cis*- and *Trans*-1,2-Dicholorethylene (2018). URL: http://www.oehha.ca.gov/water/phg/allphgs.html

Freundt KJ, GP Liebaldt and E Lieberwirth. 1977. Toxicity Studies on Trans-1,2-Dichloroethylene. Toxicology 7:141-153.

Minnesota Department of Health (MDH). (2008). Statement of Need and Reasonableness (SONAR), July 11, 2008. https://www.leg.state.mn.us/archive/sonar/SONAR-03733.pdf#page=2

Minnesota Department of Health (MDH). 2011. MDH Health Risk Assessment Methods to Incorporate Human Equivalent Dose Calculations into Derivation of Oral Reference Doses. Available: https://www.health.state.mn.us/communities/environment/risk/docs/guidance/hedrefguide.pdf

National Toxicology Program (NTP) 2002. NTP Technical Report on the Toxicity Studies of trans-1,2-Dichloroethylene Administered in Microcapsules in Feed to F344/N Rats and B6C3F$_1$ Mice.

Shopp GM, VM Sanders, KL White, and AE Munson. 1985. Humoral and Cell-Mediated Immune Status of Mice Exposed to trans-1,2-Dichloroethylene. Drug Chem. Tox., 8(5):393-407.

Syracuse Research PhysProp Database.

U.S. Environmental Protection Agency (EPA) - Health Effects Assessment Summary Tables (HEAST). July 1997.

U.S. Environmental Protection Agency (EPA), Integrated Risk Information System. Trans-1,2-Dichloroethylene. URL: https://cfpub.epa.gov/ncea/iris2/chemicalLanding.cfm?substance_nmbr=314

U.S. Environmental Protection Agency (EPA), Office of Drinking Water. Drinking Water Standards and Health Advisories (August, 2006).

U.S. Environmental Protection Agency - Office of Research and Development. (1988). Recommendations for and Documentation of Biological Values for Use in Risk Assessment. from http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=34855

U.S. Environmental Protection Agency - Office of the Science Advisor. (2011). Recommended Use of Body Weight¾ as the Default Method in Derivation of the Oral Reference Dose.

U.S. Environmental Protection Agency (EPA) - Toxicological Review of cis-1,2-dichloroethylene and trans-1,2-dichloroethylene. 2010. URL: https://cfpub.epa.gov/ncea/iris/iris_documents/documents/toxreviews/0418tr.pdf

U.S. Environmental Protection Agency (EPA). (2019). Exposure Factors Handbook Chapter 3 Update 2019. Retrieved from https://www.epa.gov/expobox/exposure-factors-handbook-chapter-3