Adopted as Rule: September 30, 2013

Toxicological Summary for 1,2-Dichloroethane: CAS: 107-06-2

Synonyms: ethylene dichloride, 1,2-DCA

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

Due to limited information, no acute guidance value is derived. Based on the available information, the short-term HRL for 1,2-DCA is also protective of developmental effects.

Short-term Non-Cancer Health Risk Limit ($nHRL_{short\text{-}term}$) = 200 µg/L

$$= \frac{\text{(Reference Dose, mg/kg/d) x (Relative Source Contribution) x (Conversion Factor)}}{\text{(Short-term intake rate, L/kg/d)}}$$

$$= \frac{\text{(0.23 mg/kg/d) x (0.2) x (1000 µg/mg)}}{\text{(0.289 L/kg-d)}}$$

= 159 rounded to **200 µg/L**

Reference Dose / Concentration:	0.23 mg/kg-d (rats)
Source of toxicity value:	MDH 2012
Point of Departure:	30 mg/kg-d (NOAEL based on Daniel et al., 1994)
Human Equivalent Dose Adjustment:	6.9 mg/kg-d [30 x 0.23] (MDH, 2011)
Total uncertainty factor:	30
UF allocation:	3 for interspecies extrapolation (toxicodynamics), 10 for intraspecies variability
Critical effect(s):	Increased liver weight accompanied by increased serum cholesterol levels.
Co-critical effect(s):	None
Additivity endpoint(s):	Hepatic (liver) system

Subchronic Non-Cancer Health Risk Limit ($nHRL_{ubchronic}$) = $HRL_{short\text{-}term}$ = 200 µg/L

$$= \frac{\text{(Reference Dose, mg/kg/d) x (Relative Source Contribution) x (Conversion Factor)}}{\text{(Subchronic intake rate, L/kg/d)}}$$

$$= \frac{\text{(0.12 mg/kg/d) x (0.2) x (1000 µg/mg)}}{\text{(0.077 L/kg-d)}}$$

= 311 rounded to 300 µg/L

Reference Dose / Concentration:	0.12 mg/kg-d (rats)
Source of toxicity value:	MDH 2012
Point of Departure:	58 mg/kg-d (LOAEL based on NTP, 1991)

Human Equivalent Dose Adjustment:	12.2 mg/kg-d [58 x 0.21] (MDH, 2011)
Total uncertainty factor:	100
UF allocation:	3 for interspecies extrapolation (toxicodynamics), 10 for intraspecies variability, 3 for use of a minimal LOAEL-to-NOAEL
Critical effect(s):	Increased kidney weights (supported as adverse by tubular regeneration lesions seen at higher doses in the same study)
Co-critical effect(s):	Increased liver weight with changes in liver enzymes at next dose level, decreased body weight
Additivity endpoint(s):	Renal (kidney) system, hepatic (liver) system

The subchronic HRL must be protective of the short-term exposures that occur within the subchronic period and therefore, the subchronic HRL is set equal to the Short-term HRL of 200 µg/L. Health Endpoint(s): Hepatic (liver) system.

Chronic Non-Cancer Health Risk Limit ($nHRL_{chronic}$) = 60 µg/L

$$= \frac{\text{(Reference Dose, mg/kg/d) x (Relative Source Contribution) x (Conversion Factor)}}{\text{(Chronic intake rate, L/kg/d)}}$$

$$= \frac{\text{(0.012 mg/kg/d) x (0.2) x (1000 µg/mg)}}{\text{(0.043 L/kg-d)}}$$

= 56 rounded to **60 µg/L**

Reference Dose / Concentration:	0.012 mg/kg-d (rats)
Source of toxicity value:	MDH 2012
Point of Departure:	58 mg/kg-d (LOAEL based on NTP, 1991)
Human Equivalent Dose Adjustment:	12.2 mg/kg-d [58 x 0.21] (MDH, 2011)
Total uncertainty factor:	1000
UF allocation:	3 for interspecies extrapolation (toxicodynamics), 10 for intraspecies variability, 3 for use of a minimal LOAEL-to-NOAEL, 10 applied for using a less than chronic study (evidence that a longer duration may cause more severe adverse effects)
Critical effect(s):	Increase kidney weights (supported as adverse by tubular regeneration lesions seen at higher doses in the same study)
Co-critical effect(s):	Increased liver weight with changes in liver enzymes at next highest dose level, decreased body weight
Additivity endpoint(s):	Renal (kidney) system, hepatic (liver) system

Cancer Health Risk Limit (cHRL) = 1 µg/L

$$= \frac{\text{(Additional Lifetime Cancer Risk) x (Conversion Factor)}}{[(SF \times ADAF_{<2\ yr} \times IR_{<2yr} \times 2) + (SF \times ADAF_{2\text{-}<16\ yr} \times IR_{2\text{-}<16yr} \times 14) + (SF \times ADAF_{16+\ yr} \times IR_{16+yr} \times 54)] / 70}$$

$$= \frac{(1E\text{-}5) \times (1000\ \mu g/mg)}{[(9.1E\text{-}2\ (mg/kg\text{-}d)^{-1})(10)(0.137\ L/kg\text{-}d)(2) + (9.1E\text{-}2\ (mg/kg\text{-}d)^{-1})(3)(0.047\ L/kg\text{-}d)(14) + (9.1E\text{-}2\ (mg/kg\text{-}d)^{-1})(1)(0.039\ L/kg\text{-}d)(54)]/70}$$

= 1.13 rounded to **1 µg/L**

Cancer classification:	B2 probable human carcinogen
Slope factor:	9.1E-2 (laboratory animal) (NCI, 1978)
Source of slope factor:	IRIS, 1991
Tumor site(s):	Hemangiosarcoma – basis of slope factor calculation (additional tumor types also observed include squamous-cell carcinomas, mammary adenocarcinoma alveolar/bronchiolar adenomas, endometrial stromal polyps and sarcomas, and hepatocellular carcinomas

Volatile: Yes, Highly

Summary of Guidance Value History:
A cancer HRL of 4 µg/L was promulgated in 1993. In 2011, MDH derived a cancer Health-Based Value (HBV) (1 µg/L) that was 4-fold lower than the 1993 HRL as the result of: 1) application of the early-life age-dependent default potency adjustment factors; 2) utilization of higher intake rates; and 3) rounding to one significant figure. In 2011, Short-term, Subchronic and Chronic HBVs of 200, 200, and 90 µg/L were derived. MDH reevaluated the non-cancer HBVs in 2012 to incorporate HED methodology. The resulting Short-term and Subchronic HBVs (200 µg/L) were unchanged. The updated Chronic HBV (60 µg/L) was 1.5-fold lower than the 2011 value. The HBVs were adopted as HRLs in 2013 and the 1993 HRL was repealed.

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

	Endocrine	Immunotoxicity	Development	Reproductive	Neurotoxicity
Tested?	No	Yes	Yes	Yes	Secondary Observation
Effects?	No	Yes[1]	Yes[2]	Yes[3]	Yes[4]

Note: 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. Most chemicals have been subject to multiple studies in which researchers identify a dose where no effects were observed, and the lowest dose that caused one or more effects. A toxicity value based on the effect observed at the lowest dose across all available studies is considered protective of all other effects that occur at higher doses.

Comments on extent of testing or effects:
[1] Conflicting data exists for 1,2-DCA regarding immunologic effects. In a 14-day gavage study in mice by Munson et al., a dose related reduction in IgM, and a significant but not dose related reduction in cell-mediated immunity were reported. In the high dose group (49 mg/kg-d administered dose, 6.9 mg/kg-d Human Equivalent Dose), a 30% decrease in total leukocyte number was observed. However, in a 90-day drinking water study in mice by the same authors, no immune related effects were reported. The authors commented that the conflicting data may be the result of differences in dosing protocol (gavage vs. drinking water) and duration of exposure. Similar effects were not reported in the 1991 NTP 90-day drinking water and gavage study in rats that included interim measurement of some immunological parameters (e.g. leukocyte numbers) on days 3, 7, 14, and 45.

[2] Developmental toxicity studies in animals have not shown 1,2-dichloroethane to be fetotoxic or teratogenic following oral exposure, although indications of embryolethality at maternally toxic doses have been reported by Payan et al., 1995 and are the basis of the acute HBV value described above.

[3] Studies in animals suggest that reproductive effects of 1,2-dichloroethane may be induced at oral doses that are maternally toxic. In a study using higher doses of 1,2-dichloroethane, rats that were treated with an administered dose 198 mg/kg-d (45.5 mg/kg-d Human Equivalent Dose) for 14 days during gestation showed 30% reduced body weight gain and dose-related increased percentages of non-surviving implants per litter (resorptions plus dead fetuses) and resorption sites per litter (Payan et al. 1995).

[4] In a 13 week gavage study in rats (NTP, 1991), clinical signs included tremors, salivation, ruffed fur, and dyspnea at administered doses 240 mg/kg-d (55.2 mg/kg-d Human Equivalent Dose) and higher. Mild necrotic lesions of the cerebellum were also observed at these doses which are several times higher than the critical Human Equivalent Dose (12.2 mg/kg-d) selected for the subchronic and chronic HBVs. Acute inhalation studies have shown that high concentration of 1,2,-DCA can cause central nervous system depression that included tremors, uncertain gait, and narcosis were seen in rats, guinea pigs, and rabbits.

References:

Agency for Toxic Substances and Disease Registry (ATSDR) - MRLs. (2009). Minimal Risk Levels for Hazardous Substances (MRLs). from http://www.atsdr.cdc.gov/mrls/mrls_list.html

Agency for Toxic Substances and Disease Registry (ATSDR) - Toxicological Profiles. Toxicological Profile Information Sheet. from http://www.atsdr.cdc.gov/toxpro2.html

Agency for Toxic Substances and Disease Registry (ATSDR). (2001). *Toxicological Profile for 1,2-Dichloroethane*.

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

California Environmental Protection Agency - OEHHA. (1999). *Publich Health Goald for 1,2,-Dichloroethane in Drinking Water*.

California Environmental Protection Agency - OEHHA Cancer Potency Values. (2005). OEHHA Toxicity Criteria Database. from http://www.oehha.ca.gov/risk/pdf/cancerpotalpha81005.pdf

California Water Resources Control Board. (2008). Water Quality Limits for Consituents and Parameters. from http://www.waterboards.ca.gov/water_issues/programs/water_quality_goals/docs/limit_tables_2008.pdf

Daniel, F. B., Robinson, M., Olson, G. R., York, R. G., & Condie, L. W. (1994). Ten and ninety-day toxicity studies of 1,2-dichloroethane in Sprague-Dawley rats. *Drug Chem Toxicol, 17*(4), 463-477.

European Union Pesticide Database. from http://ec.europa.eu/sanco_pesticides/public/index.cfm

Health Canada - Priority Substances Assessment Program and Screening Assessment Reports. from http://www.hc-sc.gc.ca/ewh-semt/pubs/contaminants/index-eng.php#existsub

HERA - Human Environmental Risk Assessment on Ingredients of household cleaning products. from http://www.heraproject.com/RiskAssessment.cfm

International Agency for Research on Cancer (IARC). Complete List of Agents evaluated and their classification. from http://monographs.iarc.fr/ENG/Classification/index.php

Kavlock, R., Chernoff, N., Carver, B., & Kopfler, F. (1979). Teratology studies in mice exposed to municipal drinking-water concentrates during organogenesis. *Food Cosmet Toxicol, 17*(4), 343-347.

Lane, R. W., Riddle, B. L., & Borzelleca, J. F. (1982). Effects of 1,2-dichloroethane and 1,1,1-thichloroethane in drinking water on reproduction and development in mice. *Toxicol Appl Pharmacol, 63*(3), 409-421.

Minnesota Department of Health (MDH). (2011). MDH Health Risk Assessment Methods to Incorporate Human Equivalent Dose Calculations into Derivation of Oral Reference Doses. from http://www.health.state.mn.us/divs/eh/risk/guidance/hedrefguide.pdf

Munson, A. E., Sanders, V. M., Douglas, K. A., Sain, L. E., Kauffmann, B. M., & White, K. L., Jr. (1982). In vivo assessment of immunotoxicity. *Environ Health Perspect, 43*, 41-52.

National Cancer Institute (NCI). (1978). Bioassay of 1,2-dichloroethane for possible carcinogenicity. *Natl Cancer Inst Carcinog Tech Rep Ser, 55*, 1-103.

National Toxicology Porgram (NTP). (1991). NTP technical report on the toxicity studies of 1,2-Dichloroethane (Ethylene Dichloride) in F344/N Rats, Sprague Dawley Rats, Osborne-Mendel Rats, and B6C3F1 Mice (Drinking Water and Gavage Studies) (CAS No. 107-06-2). *Toxic Rep Ser, 4*, 1-54.

National Toxicology Program. from http://ntp.niehs.nih.gov/?objectid=25BC6AF8-BDB7-CEBA-F18554656CC4FCD9

Payan, J. P., Saillenfait, A. M., Bonnet, P., Fabry, J. P., Langonne, I., & Sabate, J. P. (1995). Assessment of the developmental toxicity and placental transfer of 1,2-dichloroethane in rats. *Fundam Appl Toxicol, 28*(2), 187-198.

Syracuse Research PhysProp Database. from http://www.syrres.com/what-we-do/databaseforms.aspx?id=386

The International Programme on Chemical Safety. Chemicals Assessment. from http://www.who.int/ipcs/assessment/en/

Toxicology Excellence for Risk Assessment - ITER International Toxicity Estimates for Risk (ITER). from http://iter.ctcnet.net/publicurl/pub_search_list.cfm

U. S. Environmental Protection Agency - IRIS. Integrated Risk Information Systems (IRIS) A-Z List of Substances. from http://cfpub.epa.gov/ncea/iris/index.cfm?fuseaction=iris.showSubstanceList

U. S. Environmental Protection Agency - National Center for Environmental Assessment. from http://cfpub.epa.gov/ncea/cfm/archive_whatsnew.cfm

U. S. Environmental Protection Agency - Office of Drinking Water. 2006 Edition of the Drinking Water Standards and Health Advisories.
from http://www.epa.gov/waterscience/criteria/drinking/dwstandards.pdf

U. S. Environmental Protection Agency - Office of Pesticide Programs Reregistration Status. Pesticide Registration Status. from http://www.epa.gov/pesticides/reregistration/status.htm

U. S. Environmental Protection Agency - Voluntary Children's Chemical Evaluation Program (VCCEP). VCCEP Chemicals. from http://www.epa.gov/oppt/vccep/pubs/chemmain.html

U. S. Environmental Protection Agency -Toxicity and Exposure Assessment for Children's Health (TEACH).
from http://www.epa.gov/teach/

U. S. Geological Survey - Health-Based Screening Levels.
from http://infotrek.er.usgs.gov/apex/f?p=HBSL:HOME:0

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

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.
from http://www.epa.gov/raf/publications/pdfs/recommended-use-of-bw34.pdf

U.S. Environmental Protection Agency - Regional Screening Tables. Mid-Atlantic Risk Assessment - Regional Screening Table. from http://www.epa.gov/reg3hwmd/risk/human/rb-concentration_table/index.htm

U.S. Environmental Protection Agency (EPA) - IRIS. (1991). 1,2-Dichloroethane (CASRN 107-06-2).
from http://www.epa.gov/ncea/iris/subst/0149.htm

U.S. Environmental Protection Agency (EPA) - NCEA. (2008). *PPRTV for 1,2-Dichloroethane*.

World Health Organization - Guidelines for Drinking-Water Quality. (2008).
from http://www.who.int/water_sanitation_health/dwq/gdwq3rev/en/index.html