

Adopted as Rule: August 2018

Toxicological Summary for: Vinyl Chloride

CAS: 75-01-4

Synonyms: Chloroethene, chloroethylene, ethylene monochloride, Monochloroethene, Monochloroethylene

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

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

Subchronic Non-Cancer Health Risk Limit (nHRL_{Subchronic}) = 90 µg/L

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

$$= \frac{(0.033 \text{ mg/kg-d}) \times (0.2)^* \times (1000 \text{ µg/mg})}{(0.070 \text{ L/kg-d})^{**}}$$

$$= 94.3 \text{ rounded to } \mathbf{90 \text{ µg/L}}$$

*Relative Source Contribution: MDH 2008, Section IV.E.1.

**Intake Rate: MDH 2008, Section IV.E.1. and US EPA 2011, Exposure Factors Handbook, Tables 3-1 and 3-81

Reference Dose/Concentration:	HED/Total UF = 0.033 mg/kg-d (CD rat)
Source of toxicity value:	Determined by MDH in 2007
Point of Departure (POD):	10 ppm (NOAEL, CMA 1998 as cited by USEPA, 2000)
Dose Adjustment Factor (DAF):	Chemical-Specific PBPK model (USEPA, 2000)
Human Equivalent Dose (HED):	1 mg/kg-d (HED from chemical-specific PBPK model (USEPA, 2000))
Total uncertainty factor (UF):	30
Uncertainty factor allocation:	3 for interspecies differences (for toxicodynamics), 10 for intraspecies variability
Critical effect(s):	Increased liver weight, hypertrophy, and hepatocellular foci
Co-critical effect(s):	Increased liver weight
Additivity endpoint(s):	Hepatic (liver) system

Chronic Non-Cancer Health Risk Limit/Risk Assessment Advice (nHRL_{Chronic}) = 10 µg/L

$$\frac{(\text{Reference Dose, mg/kg-d}) \times (\text{Relative Source Contribution}) \times (\text{Conversion Factor})}{(\text{Chronic Intake Rate, L/kg-d})}$$
$$= \frac{(0.0030 \text{ mg/kg-d}) \times (0.2)^* \times (1000 \text{ µg/mg})}{(0.044 \text{ L/kg-d})^{**}}$$
$$= 13.6 \text{ rounded to } \mathbf{10 \text{ µg/L}}$$

*Relative Source Contribution: MDH 2008, Section IV.E.1.

**Intake Rate: MDH 2008, Section IV.E.1. and US EPA 2011, Exposure Factors Handbook, Tables 3-1 and 3-81

Reference Dose/Concentration:	HED/Total UF= 0.0030 mg/kg-d (Wistar rat)
Source of toxicity value:	Determined by MDH in 2007
Point of Departure (POD):	0.13 mg/kg-d (NOAEL, Til et al. 1991 as cited by USEPA, 2000)
Dose Adjustment Factor (DAF):	Chemical-Specific PBPK model (USEPA, 2000)
Human Equivalent Dose (HED):	0.09 mg/kg-d (HED from chemical-specific PBPK model (USEPA, 2000))
Total uncertainty factor (UF):	30
Uncertainty factor allocation:	3 for interspecies differences (for toxicodynamics), 10 for intraspecies variability
Critical effect(s):	Liver cell polymorphism, liver cyst formation
Co-critical effect(s):	Increased liver weight
Additivity endpoint(s):	Hepatic (liver) system

Cancer Health Risk Limit (cHRL) = 0.2 µg/L

$$\frac{(\text{Additional Lifetime Cancer Risk, } 1 \times 10^{-5}) \times (\text{Conversion Factor, } 1000 \text{ µg/mg})}{(\text{Slope Factor, (mg/kg-d)}^{-1}) \times (\text{Lifetime Adjustment Factor}) \times (\text{Lifetime Intake Rate, L/kg-d})}$$
$$= \frac{(1 \times 10^{-5}) \times 1,000}{[(1.4 \times 1^*) \times 0.044 \text{ L/kg-day}]^{**}}$$
$$= 0.162 \text{ rounded to } \mathbf{0.2 \text{ µg/L}}$$

*Lifetime Adjustment Factor: MDH 2008, Section IV.E.2.

**Intake Rate: MDH 2008, Section IV.E.2. and US EPA 2011, Exposure Factors Handbook, Tables 3-1 and 3-81

Cancer classification:	Known Human Carcinogen (USEPA, 2000) Group 1: Carcinogenic to Humans (IARC, 2012)
Slope factor (SF):	1.4 (mg/kg-d) ⁻¹ (total of liver angiosarcoma, hepatocellular carcinoma, and neoplastic nodules -

adjusted for continuous lifetime exposure from birth) (female Wistar rats, Feron et al. 1981)

Source of cancer slope factor (SF): USEPA, 2000
Tumor site(s): Hepatic (liver)

Volatile: Yes (high)

Summary of Guidance Value History:

A cancer Health Risk Limit (HRL) of 0.2 µg/L was promulgated in 1993. Sub-chronic and chronic non-cancer Health Based Values (HBVs) of 80 µg/L and 10 µg/L were derived in 2007. The HBVs were adopted as HRLs in 2009 along with a cancer value of 0.2 µg/L, which was the same as the previous HRL. In 2016, MDH re-evaluated the HRLs resulting in non-cancer subchronic and chronic HBVs of 90 µg/L and 10 µg/L and a cancer HBV of 0.2 µg/L. The 2016 non-cancer subchronic HBV was higher than the previous HRL as a result of 1) using MDH’s most recent risk assessment methodology and 2) rounding to one significant digit. The 2016 re-evaluation did not result in changes to the chronic non-cancer HBV or the cancer HBV. The 2018 guidance was adopted into rule as HRLs in 2018.

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	Yes	Yes
Effects observed?	No ¹	Yes ²	Yes ³	Yes ⁴	Yes ⁵

Comments on extent of testing or effects:

¹ Vinyl chloride has not been directly evaluated for endocrine effects. A study of workers exposed to vinyl chloride in PVC manufacturing plants reported that most workers who presented with scleroderma were shown to have thyroid insufficiency. No histopathology effects on the adrenals were reported in guinea pigs exposed to 400,000 ppm for 30 minutes. Rats were found to have colloid goiter and markedly increased numbers of perifollicular cells.

² Stimulation of spontaneous lymphocyte transformation was observed in mice following inhalation exposure. There is some evidence to suggest that an adaptive process may lead to a reduction or elimination of this effect over time. Also, it is not clear from the evidence that a clear adverse effect to the immune system is taking place.

- ³ Developmental toxicity occurred in inhalation experiments at doses that caused maternal toxicity. These effects occurred at exposure levels significantly higher than those producing liver toxicity (i.e., the basis of the RfD)
- ⁴ Testicular histopathological changes and decreased male fertility have been reported in inhalation studies. These effects occur at exposure levels significantly higher than those producing liver toxicity (i.e., the basis of the RfD).
- ⁵ Nervous system toxicity has been observed in inhalation studies at high exposure levels. Vinyl chloride was once considered for use as an inhalation anesthetic. Investigators studying the effects of vinyl chloride exposure frequently report central nervous system symptoms that are consistent with the anesthetic properties of vinyl chloride. The most commonly reported central nervous system effects are ataxia or dizziness, drowsiness or fatigue, loss of consciousness, and/or headache. Other central nervous system effects that have been reported by vinyl chloride workers include euphoria and irritability, visual and/or hearing disturbances, nausea, memory loss, and nervousness and sleep disturbances.

Resources Consulted During Review:

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