Toxicological Summary for: Tetrachloroethylene
CAS: 127-18-4
Synonyms: Perchloroethene; Perchloroethylene; PERC; PCE

Acute Non-Cancer Health Based Value (nHBV_{Acute}) = Not Derived (Insufficient Data)

Short-term Non-Cancer Health Based Value (nHBV_{Short-term}) = Not Derived (Insufficient Data)

Subchronic Non-Cancer Health Based Value (nHBV_{Subchronic}) = 7 µg/L

\[
\text{(Reference Dose, mg/kg/d)} \times \text{(Relative Source Contribution)} \times \text{(Conversion Factor)}
\]
\[
= (0.0026 \text{ mg/kg/d}) \times (0.2)^* \times (1000 \text{ µg/mg})
\]
\[
= (0.074 \text{ L/kg-d})^{**}
\]
\[
= 7.0 \text{ rounded to 7 µg/L}
\]

**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: 0.0026 mg/kg-d (human)
Source of toxicity value: MDH, 2014
Point of Departure (POD): 2.6 mg/kg-d (EPA calculated the LOAEL based on route-to-route extrapolation of Cavalleri et al. 1994)

Human Equivalent Dose (MDH, 2011): NA
Total uncertainty factor: 1000
Uncertainty factor allocation: 10 for intraspecies variability, 10 for LOAEL-to-NOAEL because results from residential studies suggest points of departure 3 to 15 times lower than the current LOAEL, and 10 for database uncertainty due to lack of data regarding immune, hematological, and developmental neurotoxicity

Critical effect(s): Impacts on visual color domain – dyschromatopsia
Co-critical effect(s): None
Additivity endpoint(s): Nervous system
Chronic Non-Cancer Health Based Value (nHBV\text{chronic}) = nHBV\text{subchronic} = 7 \, \mu g/L

\[
\text{(Reference Dose, mg/kg/d) \times (Relative Source Contribution) \times (Conversion Factor)} \\
\text{(Chronic intake rate, L/kg-d)}
\]

\[
= (0.0026 \, \text{mg/kg/d}) \times (0.2)^* \times (1000 \, \mu g/mg) \\
(0.045 \, \text{L/kg-d})^{**}
\]

\[= 11.5 \, \text{rounded to 10} \, \mu g/L\]


**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: 0.0026mg/kg-d (human)

Source of toxicity value: MDH, 2014

Point of Departure (POD): 2.6 mg/kg-d (EPA calculated the LOAEL based on route-to-route extrapolation of Cavalleri et al. 1994)

Human Equivalent Dose (MDH, 2011): NA

Total uncertainty factor: 1000

Uncertainty factor allocation: 10 for intraspecies variability, 10 for LOAEL-to-NOAEL because results from residential studies suggest points of departure 3 to 15 times lower than the current LOAEL, and 10 for database uncertainty due to lack of data regarding immune and hematological effects and concerns about early life sensitivity

Critical effect(s): Impacts on visual color domain – dyschromatopsia

Co-critical effect(s): None

Additivity endpoint(s): Nervous system

The Chronic nHBV must be protective of the shorter duration exposures that occur within the chronic period and therefore, the Chronic nHBV is set equal to the Subchronic nHBV of 7 µg/L. Additivity endpoint: Nervous system.

Cancer Health Based Value (cHBV) = 4 µg/L

\[
\text{(Additional Lifetime Cancer Risk) \times (Conversion Factor)} \\
\left[ (SF \times ADAF_{<2 \, \text{yr}} \times IR_{<2 \, \text{yr}} \times 2) + (SF \times ADAF_{2^-<16 \, \text{yr}} \times IR_{2^-<16 \, \text{yr}} \times 14) + (SF \times ADAF_{16+ \, \text{yr}} \times IR_{16+ \, \text{yr}} \times 54) \right] / 70
\]

\[
= \frac{(1E-5) \times (1000 \, \mu g/mg)}{(0.025 \times 10^* \times 0.155 \, L/kg-d^{**} \times 2) + (0.025 \times 3^* \times 0.040 \, L/kg-d^{**} \times 14) + (0.025 \times 1^* \times 0.042 \, L/kg-d^{**} \times 54)} / 70
\]

\[= 4 \, \mu g/L\]
Tetrachloroethylene - 3 of 7

*ADAF (Age-dependent adjustment factor) and Lifetime Adjustment Factor: MDH 2008, Section IV.E.2.
**Intake Rate: MDH 2008, Section IV.E.2. and US EPA 2019, Exposure Factors Handbook, Tables 3-1, 3-3, and 3-5.

Cancer classification: Likely to be carcinogenic in humans by all routes of exposure (EPA, 2012)
Slope factor: \(2.49 \times 10^{-2}\) (laboratory animal) (Japan Industrial Safety Association (JISA), 1993)
Source of slope factor: Massachusetts Department of Environmental Protection 2014
Tumor site(s): Leukemia

Volatile: Yes (high)

Summary of Guidance Value History:
The 2014 subchronic and chronic noncancer HBVs (7 µg/L) are new guidance. The 2014 cancer HBV (4 µg/L) is slightly lower than the 2009 Maximum Contaminant Level (MCL) based HRL of 5 µg/L due to: 1) new toxicity data, 2) application of age-dependent early life cancer sensitivity adjustment factors, 3) water intake rates that incorporate higher intakes during early life, and 4) rounding to one significant digit.

In 2021 MDH incorporated updated intake rates (US EPA 2019). Use of the updated intake rates did not result in any changes to the guidance values.

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

<table>
<thead>
<tr>
<th>Tested?</th>
<th>Endocrine</th>
<th>Immunotoxicity</th>
<th>Development</th>
<th>Reproductive</th>
<th>Neurotoxicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effects?</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

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 Few studies in humans or animals have examined altered hormones, and those that did generally found no adverse effects or were inconsistent.
2 There have been reports indicating potential associations between tetrachloroethylene exposure and immune suppression, allergy/hypersensitivity, and autoimmune disease in humans. Several occupational and environmental studies in humans have reported a statistically significant association with exposure to tetrachloroethylene and leukemia. The most sensitive target for tetrachloroethylene-induced cancer is an immune cell type, mononuclear cell leukemia. Other immune effects, such as increases in white blood cells, lymphocytes, and natural killer cells, have been reported in studies that evaluated dry cleaning worker exposures. Effects on T-cells, natural killer cells, IgE and interleukin-4 suggest a potential for hypersensitivity but limited studies in children do not support associations between tetrachloroethylene and allergy or asthma. However, there have been limited case reports of occupational hypersensitivity. One residential study reported increased incidence of kidney/urinary tract and respiratory infections associated with drinking well water containing tetrachloroethylene. There have been a few occupational case reports and a few case-control studies reporting non-significant associations with sclerosis, an autoimmune disease. There is some evidence suggesting the developing immune system could be susceptible from exposure to tetrachloroethylene. There are very limited data for the evaluation of immune effects in animal studies, but mice exposed via inhalation had
increased susceptibility to respiratory infections and greater mortality from infection. The noncancer immune effects generally occur at high doses greater than 200-fold above the RfD, while the cancer effect of induction of mononuclear cell leukemia is the basis of the cancer HBV.

3 There is not conclusive evidence from human studies that tetrachloroethylene exposure is linked to developmental effects. Many human studies that have evaluated the association between tetrachloroethylene and developmental effects have confounders and the evaluation of effects is complicated by exposures to solvent mixtures. Most animal studies that evaluated developmental effects did not show specific adverse effects on offspring. Developmental effects have been reported in animal inhalation toxicity studies at high levels of exposure (at 1500 mg/m³ or higher). The effects include impacts on the developing nervous system (impacts on behavior, impacts on motor activity, and developmental delays) as well as decreased fetal body weight at exposures greater than 4500 mg/m³ and increased malformations in pups at exposures greater than 1500 mg/m³.

4 The evidence of reproductive effects from exposure to tetrachloroethylene is limited from both human and animal studies. Human studies in dry cleaning and laundry workers evaluated reproductive outcomes and showed evidence of impacts on menstrual cycles, altered sperm quality, and longer time to pregnancy in workers exposed to tetrachloroethylene through inhalation. Decreased sperm quality and reduced fertilization of extracted oocytes was also reported in an animal inhalation study at high levels of exposure (12,000 mg/m³).

5 The nervous system is the most sensitive target following exposure to tetrachloroethylene. The visual and cognitive domains are the most sensitive neurological endpoints and impacts on vision and cognition have been reported in several human occupational and environmental studies. Subtle visual effects including impacts on visual color domain – dyschromatopsia; impacts on visual cognitive domain and reaction times - decrements in visual reproduction, pattern memory, and pattern recognition, were identified as critical endpoints and are the basis of the non-cancer reference dose (0.0026 mg/kg-d) derived in MDH’s evaluation of tetrachloroethylene. Acute CNS depression has been reported in children and adults following inhalation and ingestion of high levels of tetrachloroethylene.

References:


Tetrachloroethylene - 4 of 7


Tetrachloroethylene - 5 of 7


National Toxicology Program (NTP). (1986). *Toxicology and Carcinogenesis Studies of Tetrachloroethylene (Perchloroethylene) in F344/N Rats and B6C3F1 Mice (Inhalation Studies).*


U.S. Environmental Protection Agency - Regional Screening Tables. Mid-Atlantic Risk Assessment - Regional Screening Table. from https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

