Trichloroethylene (TCE) Health-Based Guidance for Drinking Water

The Minnesota Department of Health issued new health-based guidance for TCE in May 2013. The information in this document provides greater detail about the basis of the guidance. The information below is intended for toxicologists, engineers, risk managers, and others involved in answering questions about human health and exposure.

For more detail about the guidance derivation, please see the Toxicological Summary for TCE (https://www.health.state.mn.us/communities/environment/risk/docs/guidance/gw/tcesummary.pdf).

MDH TCE Health-Based Guidance Summary

The Minnesota Department of Health (MDH) has issued Health Based Values (HBVs) for Trichloroethylene (TCE) in drinking water. MDH developed an HBV of 0.4 micrograms per liter (µg/L) based on non-cancer immune effects and 2 µg/L based on cancer health effects.

MDH TCE Health-Based Values (HBVs)

- **0.4 µg/L** - protects all individuals exposed to TCE from drinking water, including those exposed at any point from conception through old age
- **2 µg/L** - protects against cancer for all individuals, even those exposed for an entire lifetime. Also protects:
  - Healthy adults who are only exposed to TCE after age 18
  - Pregnant women and the developing fetus against heart defects

Health Effects of TCE

Immune effects have been identified as the most sensitive non-cancer health effect caused by exposure to TCE. The immune effects that form the basis of MDH non-cancer HBVs were observed in animal toxicity studies and the effects are consistent with those observed in human studies. TCE is also associated with kidney, liver, neurological, and reproductive effects at higher doses of exposure than those that cause immune effects in early life. TCE causes cancer in animals, and human studies show a link between exposures and kidney cancer, liver cancer, and non-Hodgkin Lymphoma.

MDH non-cancer HBVs account for toxicological sensitivity in humans and exposure (how much an individual drinks). The MDH TCE drinking water guidance values were set at levels likely to pose little or no health risk to most people, including during sensitive and highly exposed life stages (including bottle fed infants) and for individuals who are immune compromised. The value of 0.4 µg/L for TCE is based on a dose to humans that is well below the levels shown to harm animals in toxicity studies. This means that HBVs are protective of health and unlikely to result in exposures that could cause an adverse effect.

History of TCE Review

MDH conducted the TCE assessment by carefully evaluating the 2011 U.S. Environmental Protection Agency (EPA) Integrated Risk Information System (IRIS) TCE Toxicological Review (EPA 2011a), reviewing

key scientific studies, deriving oral toxicity values and using the toxicity values along with MDH methods to derive HBVs (MDH 2008). The EPA review document provided a thorough evaluation of human epidemiology and animal toxicity studies that assessed the health impacts from inhalation and ingestion of TCE. After reviewing hundreds of scientific studies, the EPA developed three critical non-cancer oral toxicity values (reference doses or RfDs) and a cancer oral toxicity value (cancer slope factor or CSF). The basis of the RfDs and CSF derived by the EPA were reviewed as part of the MDH TCE assessment.

Cancer and non-cancer health effects were evaluated separately in the MDH assessment for TCE. Due to differences in MDH and EPA methods for deriving toxicity values, MDH derived different oral RfDs for the non-cancer assessment than what the EPA derived. The MDH RfDs were then applied to derive non-cancer HBVs. MDH used the EPA CSF for the cancer assessment and used MDH methodology to derive a cancer based HBV.

MDH Health-Based Guidance for TCE as Compared to the Maximum Contaminant Level (MCL) for TCE

The previous MDH TCE health-based water guidance value for drinking water (a Health Risk Limit or HRL established in 2007) was 5 µg/L, and was based on the EPA Maximum Contaminant Level (MCL) for TCE. MCLs are enforceable drinking water standards set by the EPA for public water supplies. The EPA MCL for TCE became effective in 1989. As TCE is considered a carcinogen, the EPA set the MCL as close as possible to zero while accounting for cost, benefits, and the ability of public water systems to detect and remove TCE at the time the regulatory guideline was established. It is unknown when the EPA will reevaluate the TCE MCL based on the recent IRIS assessment, but EPA is currently considering regulating carcinogenic volatile organic compounds (VOCs) as a group, and the result might include TCE.

The reasons that the new MDH HBVs for TCE are lower than the MCL of 5 µg/L are:

- Many new scientific toxicological and epidemiologic studies have published since the MCL was developed.
- Additional health effects (immune effects) were found in recent studies. Some of these effects occur at doses that are lower than doses that cause cancer effects.
- Use of updated risk assessment methods that account for sensitive populations and early life exposures (exposures that occur *in utero*, infancy, or early childhood).
- HBVs are based solely on health concerns and do not consider practical issues such as cost or the technical feasibility of measuring or removing TCE.

Risk Levels

HBVs are set at levels that are protective of health, even for sensitive individuals. The guidance values account for the different amounts of water people drink and the different sensitivities people have to a chemical following exposure and incorporate adjustment factors to account for uncertainties in our understanding of the health risks posed by a chemical.

The TCE HBV of 0.4 µg/L represents a level that is not expected to result in an increased risk of adverse health effects for any individual, including those that are considered most sensitive – the rapidly developing fetus, infants, children up to age 8, and immune compromised individuals. It is not expected that health effects would immediately be observed or diagnosable if TCE is present above an HBV. For the most sensitive individuals – infants, children, and immune compromised individuals - there is a possibility of a small increased risk for immune effects from exposures above 0.4 µg/L. It is difficult to

determine whether a slight increased risk would actually translate into an adverse health effect in any individual exposed above 0.4 µg/L.

Some immune effects in humans were associated with exposure to TCE in studies where TCE was present in drinking water. One study reported contact dermatitis or increased risk for bacterial infections. These effects were associated with drinking water levels over 100 µg/L. This value is 20-fold and 250-fold higher than guidance values of 5 µg/L and 0.4 µg/L, respectively. However, these studies did not evaluate TCE exposure during infancy or childhood or in those with immune conditions, so the level of exposure to TCE that results in an observable health effect could be lower for more highly exposed and sensitive individuals.

MDH Non-Cancer and Cancer Assessment

MDH derived short-term, subchronic, and chronic non-cancer HBVs as well as a cancer based HBV for TCE. An acute guidance value was not derived. MDH relied upon the cancer slope factor or CSF developed by the EPA to derive a cancer HBV.

MDH defines exposure as follows:

- **Acute** - One day or less
- **Short-term** - One day up to approximately 30 days
- **Subchronic** - Continuous exposure lasting 30 days up to 10 percent of a lifetime
- **Chronic** - Continuous exposure that lasts longer than 10 percent of a lifetime.

For the calculations used to derive the MDH TCE HBVs, please see: Toxicological Summary for TCE (PDF) (https://www.health.state.mn.us/communities/environment/risk/docs/guidance/gw/tcesummary.pdf).

Acute Duration Assessment

MDH considered but did not derive an acute RfD or HBV. An animal toxicity study in rats by Johnson and others, which reported fetal heart malformations in offspring exposed to *TCE in utero*, was carefully considered by MDH for selection as an acute critical study (Johnson et al. 2003). This study was one of three studies selected by EPA as the basis of the EPA non-cancer oral RfD of 0.0005 mg/kg-day. However, due to the available information for this study, MDH determined that it could not identify with confidence the dose at which the association exists for development of fetal heart malformations. Despite this uncertainty, MDH has determined that the non-cancer HBVs derived for TCE based on longer exposure durations, both 0.4 and 2 µg/L, are protective of the malformations reported in the Johnson study.

Short-Terms and Subchronic Duration Assessment

The HBV for the short-term and subchronic durations is 0.4 µg/L. The HBV is protective of exposures to TCE for all individuals, including those exposed during sensitive life stages. The RfDs developed for both durations are based on a developmental immunotoxicity study in mice (Peden-Adams et al. 2006). In this study mice were exposed through maternal dosing *in utero,* during lactation, and directly from drinking water post weaning. The immune effects that were found are indicative of hypersensitivity and autoimmunity, and immunosuppression at higher doses. Immunological function in offspring was evaluated at 3 and 8 weeks of age.

The MDH-derived a short-term RfD of 0.00052 mg/kg-day and applied an intake rate of 0.289 L/kg-d based on the 95th percentile water intake for infants 1-3 months of age to derive the short-term HBV of 0.4 µg/L. MDH derived a subchronic RfD of 0.00017 mg/kg-day and applied an intake rate of 0.077 L/kg-d based on the 95th percentile water intake from birth through age 8 to derive the subchronic HBV of 0.4 µg/L. The short-term and subchronic HBVs happen to be the same value.

Chronic Duration

The MDH chronic HBV is set to 0.4 µg/L in order to be protective of effects that could occur during sensitive life stages (pregnancy, infancy, and early childhood) within the chronic duration. The actual calculated chronic HBV is 0.8 µg/L, which combines effects reported in a subchronic study duration (and based on the subchronic RfD) with a long term drinking water intake rate of 0.043 L/kg-day based on a lifetime 95th percentile drinking water intake rate.

MDH also considers 2 µg/L protective of adult chronic exposure for healthy adults exposed after age 18. This is a chronic value based on immune effects in a study of adult mice and the 95th percentile water intake averaged over a lifetime (0.043 L/kg-day). This adult chronic HBV is based on a significant decrease in thymus weight in mice exposed only in adulthood (Keil et al. 2009).

Histological changes in the kidneys were reported in chronic toxicity studies in which adult animals were exposed at doses similar to those that resulted in immune and thymus system effects in adult animals. The values of 0.4 or 2 µg/L are considered protective of thymus and kidney effects that were reported in chronic toxicity studies.

Cancer Assessment

The MDH cancer-based HBV is 2 µg/L. TCE is classified by the EPA as: *"carcinogenic to humans by all routes of exposure based on convincing evidence of a causal association between TCE exposure in humans and kidney cancer and some human evidence of TCE carcinogenicity in the liver and lymphoid tissues. This conclusion is further supported by rodent bioassay data indicating carcinogenicity of TCE in rats and mice at tumor sites that include those identified in human epidemiologic studies."*

The cancer slope factor or CSF derived by EPA from human epidemiology studies is 0.05 (mg/kg-day)$^{-1}$ based on kidney tumors, liver tumors, and non-Hodgkin Lymphoma. MDH applied age adjustment factors (ADAFs) to account for early life sensitivity in the calculation used to derive the HBV of 2 µg/L.

Other Sources of Exposure

The HBVs developed by MDH account for exposure to TCE from other sources (soil, air, and household products) in addition to drinking water. A relative source contribution (RSC) factor is used to account for other potential exposures. MDH uses an RSC of 0.2 when calculating non-cancer guidance values for highly volatile chemicals. This means that exposure from drinking contaminated water will be no more than one-fifth of the RfD (the total dose or exposure that is considered safe).

- TCE is highly volatile, and inhalation can be a significant source of exposure.
- TCE can move from water into household air from activities such as bathing or cooking.
- TCE can also get into air from household products that contain TCE or from vapor intrusion.

References

Johnson, P. D., S. J. Goldberg, M. Z. Mays and B. V. Dawson (2003). Threshold of trichloroethylene contamination in maternal drinking waters affecting fetal heart development in the rat. *Environmental health perspectives* 111(3): 289-292.

Keil, D. E., M. M. Peden-Adams, S. Wallace, P. Ruiz and G. S. Gilkeson (2009). Assessment of trichloroethylene (TCE) exposure in murine strains genetically-prone and non-prone to develop autoimmune disease. *Journal of environmental science and health. Part A, Toxic/hazardous substances & environmental engineering* 44(5): 443-453.

Minnesota Department of Health (MDH). (2008). "Statement of Need and Reasonableness (SONAR), July 11, 2008. Support document relating to Health Risk Limits for Groundwater Rules.", from https://www.leg.mn.gov/archive/sonar/SONAR-03733.pdf#page=2.

Peden-Adams, M. M., J. G. Eudaly, L. M. Heesemann, J. Smythe, J. Miller, G. S. Gilkeson, et al. (2006). Developmental immunotoxicity of trichloroethylene (TCE): studies in B6C3F1 mice. *Journal of environmental science and health. Part A, Toxic/hazardous substances & environmental engineering* 41(3): 249-271.

U.S. Environmental Protection Agency (EPA). (2011a). "Toxicological Review of Trichloroethylene (CAS No. 79-01-6)." Retrieved December 21, 2011, from http://www.epa.gov/iris/toxreviews/0199tr/0199tr.pdf.

Minnesota Department of Health
Health Risk Assessment Unit
health.risk@state.mn.us
www.health.state.mn.us

OCTOBER 2020

To obtain this information in a different format, call: 651-201-4899.