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

Adopted As Rule: November 2023

Toxicological Summary for: Bromodichloromethane

CAS: **75-27-4**

Synonyms: Dichlorobromomethane, Monobromodichloromethane, BDCM

Acute Non-Cancer Health Risk Limit ($nHRL_{Acute}$) = 400 µg/L

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

$$= \frac{\text{(0.073 mg/kg-d) x (0.2)}^{*} \text{ x (1000 µg/mg)}}{\text{(0.038 L/kg-d)}^{**}}$$

= 384 rounded to **400 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. The RfD is based on full litter resorptions, which occurs in utero; therefore, the intake rate for a pregnant woman is used rather than the default infant intake rate as described in the 2008 SONAR (p. 46).

Reference Dose/Concentration:	HED/Total UF = 2.18/30 = 0.073 mg/kg-d (F344 rat)
Source of toxicity value:	Determined by MDH in 2018
Point of Departure (POD):	10.4 mg/kg-d (administered dose $BMDL_{05}$, Narotsky 1997 with support from Bielmeier 2001 as an acute effect)
Dose Adjustment Factor (DAF):	0.21, Body weight scaling, default (MDH 2017 and US EPA 2011)
Human Equivalent Dose (HED):	POD x DAF = 10.4 mg/kg-d x 0.21 = 2.18 mg/kg-d
Total uncertainty factor (UF):	30
Uncertainty factor allocation:	3 for interspecies differences (for toxicodynamics), 10 for intraspecies variability
Critical effect(s):	Full litter resorptions, associated with changes in female hormones that maintain pregnancy
Co-critical effect(s):	None
Additivity endpoint(s):	Female Reproductive system (E)

Short-term Non-Cancer Health Risk Limit ($nHRL_{Short\text{-}term}$) = 30 µg/L

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

$$= \frac{(0.039 \text{ mg/kg-d}) \times (0.2)^{*} \times (1000 \text{ µg/mg})}{(0.290 \text{ L/kg-d})^{**}}$$

= 26.8 rounded to **30 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 = 3.94/100 = 0.039 mg/kg-d (CD-1 mouse)
Source of toxicity value:	Determined by MDH in 2018
Point of Departure (POD):	30.3 mg/kg-d (administered dose $BMDL_{10}$, Munson 1982)
Dose Adjustment Factor (DAF):	0.13, Body weight scaling, default (US EPA 2011 and MDH 2017)
Human Equivalent Dose (HED):	POD x DAF = 30.3 mg/kg-d x 0.13 = 3.94 mg/kg-d
Total uncertainty factor (UF):	100
Uncertainty factor allocation:	e.g. 3 for interspecies differences (for toxicodynamics), 10 for intraspecies variability, and 3 for database uncertainty (due to outstanding concerns related to BDCM-induced hormonal changes in females and immunotoxicity changes in a 2-generation study that is not confounded by vehicle, BDCM volatilization, water palatability, or animal dehydration issues)
Critical effect(s):	Decreased spleen weight
Co-critical effect(s):	Full litter resorptions***
Additivity endpoint(s):	Immune system, Spleen

***Since an infant water ingestion rate exposure forms the basis of the Short-term HRL calculation, and full litter resorptions is relevant only to pregnant women and is based on a pregnant woman water ingestion rate exposure, an additivity endpoint for full litter resorptions is not necessary.

Subchronic Non-Cancer Health Risk Limit ($nHRL_{Subchronic}$) = $nHRL_{Short\text{-}term}$ = 30 µg/L

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

$$= \frac{(0.039 \text{ mg/kg-d})^{\#} \times (0.2)^{*} \times (1000 \text{ µg/mg})}{(0.074 \text{ L/kg-d})^{**}}$$

= 105 rounded to 100 µg/L

#No Subchronic RfD was calculated due to study limitations. Therefore, the Short-term RfD was applied to the subchronic duration.

*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

The Subchronic nHRL must be protective of the acute and short-term exposures that occur within the subchronic period and therefore, the Subchronic nHRL is set equal to the Short-term nHRL of 30 µg/L. Additivity endpoints: Immune system, Spleen

Chronic Non-Cancer Health Risk Limit ($nHRL_{Chronic}$) = 30 µg/L

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

$$= \frac{\text{(0.0075 mg/kg-d) x (0.2)}^{*} \text{ x (1000 µg/mg)}}{\text{(0.045 L/kg-d)}^{**}}$$

= 33 rounded to **30 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 = 0.225/30 = 0.0075 mg/kg-d (Wistar rat)
Source of toxicity value:	Determined by MDH in 2018
Point of Departure (POD):	0.776 mg/kg-d (administered dose $BMDL_{10}$, Aida 1992)
Dose Adjustment Factor (DAF):	0.29, Body weight scaling, default (US EPA 2011 and MDH 2017)
Human Equivalent Dose (HED):	POD x DAF = 0.776 mg/kg-d x 0.29 = 0.225 mg/kg-d
Total uncertainty factor (UF):	30
Uncertainty factor allocation:	3 for interspecies differences (for toxicodynamics), 10 for intraspecies variability
Critical effect(s):	Fatty degeneration of the liver
Co-critical effect(s):	None
Additivity endpoint(s):	Hepatic (liver) system

Cancer Health Risk Limit (cHRL) = 3 µg/L

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

$$= \frac{\text{(1E-5) x (1000 µg/mg)}}{[(0.035 \times 10^{*} \times 0.155\ \text{L/kg-d}^{**} \times 2) + (0.035 \times 3^{*} \times 0.040\ \text{L/kg-d}^{**} \times 14) + (0.035 \times 1^{*} \times 0.042\ \text{L/kg-d}^{**} \times 54)] / 70}$$

= 2.8 rounded to **3 µg/L**

*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 to humans

Slope factor (SF): 0.035 per mg/kg-d, renal tumors in male B6C3F1 mice (NTP 1987)
Source of cancer slope factor (SF): (US EPA 1998) as cited in US EPA 2005
Tumor site(s): Kidney, Large intestine, Liver, Lymphatic system

Volatile: Yes (high)

Summary of Guidance Value History: In 1993, MDH promulgated a cancer HRL of 6 µg/L. The new 2018 HBV for cancer (3 µg/L) is lower because of 1) the use of a more recent slope factor; 2) the use of MDH's most recent risk assessment methodology; and 3) rounding to one significant digit. In 2018 MDH also derived noncancer HBVs of 300 µg/L for Acute and 30 µg/L for Short-term, Subchronic, and Chronic durations. In 2020 MDH incorporated updated intake rates (US EPA 2019). Use of the updated intake rates resulted in an increase of the Acute duration HBV from 300 µg/L to 400 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?	Yes	Yes	Yes	Yes	Yes
Effects observed?	Yes[1]	Yes[2]	Yes[3]	Yes[4]	Yes[5]

Comments on extent of testing or effects:

[1]A hormone profile was conducted on pregnant rats exposed to BDCM during pregnancy that resulted in full litter resorptions (acute critical effect). Maternal hormone changes occurred at levels 200-300 times higher than the acute RfD and 400-500 times higher than the short-term RfD.

[2]The short-term RfD is based on reduced spleen weights in mice exposed to BDCM. Altered immune cell levels and function occurred at doses 300-400 times higher than the RfD. Other studies in rodents demonstrated changes in thymus weights at levels 100 times higher than the short-term RfD and lymphoid atrophy of the thymus, spleen, and lymph nodes at levels 1,000 times higher than the short-term RfD.

[3]The acute-duration RfD is based on maternally-mediated full litter resorptions in rats, which was noted in a reproductive and developmental study. At doses 300 times higher than the short-duration RfD, fetal skeletal anomalies were also reported in rats. However, there were no fetal or pup developmental effects noted in rabbits at doses between 50 to 900 times higher than the short-term RfD.

[4]The acute RfD is based on maternally-mediated full litter resorptions in rats, and this effect is also identified as a co-critical effect for the short-term duration, occurring at a dose approximately 200 times higher than the Short-term RfD. Ovarian abscesses were reported in mice at doses 200 times higher than the short-term RfD, and sperm velocity in rats was observed to decrease at BDCM doses 300 times higher than the short-term RfD, although with no supporting histology.

[5]Neurotoxic effects appear to be minimal after BDCM exposure. At levels 400 times higher than the short-term RfD, rats in one study had slightly altered behavior. At BDCM doses 3,000 times higher than the short-term RfD, another study reported hyperactivity in rats.

Resources Consulted During Review:

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