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

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Toxicological Summary for: 1,2-Dibromoethane

CAS: **106-93-4**
Synonyms: Ethylene dibromide; ethane, 1,2-dibromo-

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

Short-term Non-Cancer Health-Based Value ($nHBV_{Short\text{-}term}$) = 10 µg/L

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

$$= \frac{\text{(0.018 mg/kg-d) x (0.2)}^{*} \text{ x (1000 µg/mg)}}{\text{(0.290 L/kg-d)}^{**}}$$

= 12.4 rounded to **10 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 = 17.5/1000 = 0.018 mg/kg-d (female B6C3F1 mice)
Source of toxicity value:	Determined by MDH in 2022
Point of Departure (POD):	125 mg/kg-d (LOAEL, Ratajczak, 1994)
Dose Adjustment Factor (DAF):	0.14, Body weight scaling, default (US EPA 2011 and MDH 2017)
Human Equivalent Dose (HED):	POD x DAF = 125 mg/kg-d x 0.14 = 17.5 mg/kg-d
Total uncertainty factor (UF):	1000
Uncertainty factor allocation:	3 for interspecies differences (for toxicodynamics), 10 for intraspecies variability, 3 for using a LOAEL in place of a NOAEL, and 10 for database uncertainty due to the lack of two-generation reproductive, developmental, and developmental immunotoxicity studies
Critical effect(s):	Increased liver weight, increased cholesterol, and reduced T-cell response
Co-critical effect(s):	Increased kidney weight, increased neutrophils, decreased immune function in the lung, decreased viable cells in the spleen, increased estrus cycle length, increased percentage of abnormal sperm
Additivity endpoint(s):	Female reproductive system, Hepatic (liver) system, Immune system, Male reproductive system, Renal (kidney) system, Respiratory system, Spleen

Subchronic Non-Cancer Health-Based Value ($nHBV_{Subchronic}$) = $nHBV_{Short\text{-}term}$ = 10 µg/L

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

$$= \frac{\text{(0.021 mg/kg-d) x (0.2)}^{*} \text{ x (1000 µg/mg)}}{\text{(0.074 L/kg-d)}^{**}}$$

= 56.8 rounded to 60 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 = 6.24/300 = 0.021 mg/kg-d (female B6C3F1 mice)
Source of toxicity value:	Determined by MDH in 2022
Point of Departure (POD):	44.6 mg/kg-d (NOAEL, Ratajczak, 1995)
Dose Adjustment Factor (DAF):	0.14, Body weight scaling, default (US EPA 2011 and MDH 2017)
Human Equivalent Dose (HED):	POD x DAF = 44.6 mg/kg-d x 0.14 = 6.24 mg/kg-d
Total uncertainty factor (UF):	300
Uncertainty factor allocation:	3 for interspecies differences (for toxicodynamics), 10 for intraspecies variability, and 10 for database uncertainty for lack of two-generation reproductive, developmental and developmental immunotoxicity studies
Critical effect(s):	Decreased T- and B-cell responses, increased cholesterol and triglycerides
Co-critical effect(s):	Increased liver weight, increased cholesterol, decreased T-cell response, decreased immune function in the lung, increased estrus cycle length, and increased percentage of abnormal sperm
Additivity endpoint(s):	Female reproductive system, Hepatic (liver) system, Immune system, Male reproductive system, Respiratory system

The Subchronic nHBV must be protective of shorter duration exposures that occur within the subchronic period and therefore, the Subchronic nHBV is set equal to the Short-term nHBV of 10 µg/L. Additivity endpoints: Female reproductive system, Hepatic (liver) system, Immune system, Male reproductive system, Renal (kidney) system, Respiratory system, Spleen

Chronic Non-Cancer Health-Based Value ($nHBV_{Chronic}$) = 9 µg/L

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

$$= \frac{\text{(0.0021 mg/kg-d) x (0.2)}^{*} \text{ x (1000 µg/mg)}}{\text{(0.045 L/kg-d)}^{**}}$$

= 9.33 rounded to **9 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 = 6.24/3000 = 0.0021 mg/kg-d (female B6C3F1 mice)
Source of toxicity value:	Determined by MDH in 2022
Point of Departure (POD):	44.6 mg/kg-d (NOAEL, Ratajczak et al. 1995, subchronic exposure)
Dose Adjustment Factor (DAF):	0.14, Body weight scaling, default (US EPA 2011 and MDH 2017)
Human Equivalent Dose (HED):	POD x DAF = 44.6 mg/kg-d x 0.14 = 6.24 mg/kg-d
Total uncertainty factor (UF):	3000
Uncertainty factor allocation:	3 for interspecies differences (for toxicodynamics), 10 for intraspecies variability, 10 for extrapolation to a chronic duration from a subchronic study, and 10 for database uncertainty for lack of two-generation reproductive, developmental, and developmental immunotoxicity studies
Critical effect(s):	Decreased T- and B-cell responses, increased cholesterol and triglycerides
Co-critical effect(s):	Increased relative liver weight, increased cholesterol, decreased T-cell response, decreased immune function in the lung, increased estrus cycle length, increased percentage of abnormal sperm
Additivity endpoint(s):	Female reproductive system, Hepatic (liver) system, Immune system, Male reproductive system, Respiratory system

Cancer Health-Based Value (cHBV) = 0.03 µg/L

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

$$\frac{= (1E\text{-}5) \times (1000\ \mu g/mg)}{[(3.6 \times 10^{*} \times 0.155\ L/kg\text{-}d^{**} \times 2) + (3.6 \times 3^{*} \times 0.040\ L/kg\text{-}d^{**} \times 14) + (3.6 \times 1^{*} \times 0.042\ L/kg\text{-}d^{**} \times 54)] / 70}$$

= 0.028 rounded to **0.03 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:	2A- probably carcinogenic to humans (IARC, 1999); Likely to be carcinogenic to humans (EPA, 2004)
Slope factor (SF):	3.6 $(mg/kg\text{-}day)^{-1}$ based on forestomach tumors in male and female rats and mice (NCI, 1978)
Source of cancer slope factor (SF):	Cal EPA (2003)

Tumor site(s): Forestomach, esophagus, blood vessels, liver, lung, thyroid gland, and adrenal gland

Volatile: Yes (high)

Summary of Guidance Value History:

A cancer HRL of 0.004 µg/L was promulgated in 1993. The new cancer HBV of 0.03 µg/L is higher than the previous cancer HRL as the result of: 1) use of MDH's most recent risk assessment methodology; 2) the use of a new slope factor derived by Cal EPA 2003; and 3) rounding to one significant digit.

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	No	Yes	No
Effects observed?	Yes[1]	Yes[2]	- [3]	Yes [4]	Yes[5]

[1] Testicular atrophy and degenerative changes to the adrenal cortex were observed in rats and mice exposed chronically to oral doses more than 400 times higher than the short-term RfD. An increased estrus cycle length was observed in mice exposed to levels nearly 700 times higher than the short-term RfD and is included as a co-critical effect for all durations.
[2] The short-term, subchronic, and chronic critical effects are based on immunotoxicity in female mice (decreased T- and B-cell response). Dose levels 1,200 times higher than the short-term RfD are associated with increased neutrophils, decreased bactericidal response in the lung, and decreased viable cells in the spleen. Dose levels 1,600 times higher than the short-term RfD are associated with decreased relative thymus weight, increased spleen weight, and decreased natural killer cell function. Chronic exposure in mice at levels 300 times higher than the short-term RfD resulted in increased splenic hematopoiesis.
[3] Developmental effects have not been studied using oral ingestion as a route of exposure. A database uncertainty factor is included in the guidance to account for the lack of developmental studies in the oral database.
[4] An occupational study in men exposed to 1,2-dibromoethane via inhalation and dermally for an average of 5 years found reductions in sperm count, viability, and motility and increases in sperm abnormalities at dose levels 10-fold higher than the short-term RfD. A shorter-duration study in men exposed via inhalation and dermally for 6 weeks reported reductions in sperm velocity and semen volume at a time weighted dose approximately 8 times higher than the short-term RfD.
Testicular atrophy, the male reproductive system chronic co-critical effect, was observed in rats and mice at more than 400 times higher than the short-term RfD. However, a subchronic study evaluating male reproductive toxicity did not observed any changes to fertility and sex organs using doses almost 700 times higher than the short-term RfD. The subchronic and chronic co-critical effect of lengthened estrus cycles in female mice was observed at doses 700 times higher than the short-term RfD. A database uncertainty factor is included in the RfD to account for the lack of a multigeneration or two-generation reproductive toxicity study.

[5] Neurotoxicity has been observed in human case studies involving ingestion, and manifests as confusion, coma, and brain lesions. Oral animal studies did not observe specific indications of neurotoxicity.

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