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

Adopted as Rule: November 2023

Toxicological Summary for: Tris(2-butoxyethyl) Phosphate

CAS: **78-51-3**
Synonyms: TBEP, Tributoxyethyl phosphate

Acute Noncancer Health Risk Limit ($nHRL_{Acute}$) = Not Derived (Insufficient Data)

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

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

$$= \frac{\text{(0.043 mg/kg-d) x (0.2)}^{*} \text{ x (1000 µg/mg)}}{\text{(0.290 L/kg-d)}^{**}}$$

= 29.6 rounded to **30 µg/L**

*Relative Source Contribution: MDH 2008, Section IV.E.1. Based on the potential for infants to be exposed at levels equal to a significant fraction of the short-term MDH RfD value from house dust (Fromme, 2014), an RSC of 0.2 has been used.
**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 = 4.34 / 100 = 0.043 mg/kg-d (SD rats)
Source of toxicity value:	Determined by MDH in 2020
Point of Departure (POD):	18.08 mg/kg-d (administered dose $BMDL_{10}$, HRI, 1996)
Dose Adjustment Factor (DAF):	0.24 sex averaged body weight scaling, default (US EPA 2011 and MDH 2017)
Human Equivalent Dose (HED):	POD x DAF = 18.08 mg/kg-d x 0.24 = 4.34 mg/kg-d
Total uncertainty factor (UF):	100
Uncertainty factor allocation:	3 for interspecies differences (for toxicodynamics), 10 for intraspecies variability, and 3 for database uncertainty due to a lack of any 2-generational study and additional studies in a second test species
Critical effect(s):	Liver cell vacuolization
Co-critical effect(s):	None
Additivity endpoint(s):	Hepatic (liver) system

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

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

$$= \frac{\text{(0.022 mg/kg-d) x (0.2)}^{*} \text{ x (1000 µg/mg)}}{\text{(0.074 L/kg-d)}^{**}}$$

= 59.4 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 = 2.23 / 100 = 0.022 mg/kg-d (SD rats)
Source of toxicity value:	Determined by MDH in 2020
Point of Departure (POD):	8.92 mg/kg-d (administered dose $BMDL_{10}$, Reyna & Thake, 1987)
Dose Adjustment Factor (DAF):	Body weight scaling, default (US EPA 2011 and MDH 2017)
Human Equivalent Dose (HED):	POD x DAF = 8.92 mg/kg-d x 0.25 = 2.23 mg/kg-d
Total uncertainty factor (UF):	100
Uncertainty factor allocation:	3 for interspecies differences (for toxicodynamics), 10 for intraspecies variability, and 3 for database uncertainty due to a lack of any 2-generational study and additional studies in a second test species
Critical effect(s):	Liver cell vacuolization
Co-critical effect(s):	None
Additivity endpoint(s):	Hepatic (liver) system

The Subchronic nHRL must be protective of the 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: Hepatic (liver) system

Chronic Noncancer Health Risk Limit ($nHRL_{Chronic}$) = 30 µg/L

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

$$= \frac{\text{(0.0074 mg/kg-d) x (0.2)}^{*} \text{ x (1000 µg/mg)}}{\text{(0.045 L/kg-d)}^{**}}$$

= 32.8 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 = 2.23 / 300 = 0.0074 mg/kg-d (SD rats)
Source of toxicity value:	Determined by MDH in 2020

Point of Departure (POD):	8.92 mg/kg-d (administered dose $BMDL_{10}$, Reyna & Thake, 1987, subchronic exposure)
Dose Adjustment Factor (DAF):	Body weight scaling, default (US EPA 2011 and MDH 2017)
Human Equivalent Dose (HED):	POD x DAF = 8.92 mg/kg-d x 0.25 = 2.23 mg/kg-d
Total uncertainty factor (UF):	300
Uncertainty factor allocation:	3 for interspecies differences (for toxicodynamics), 10 for intraspecies variability, and 3 for database uncertainty due to a lack of any 2-generational study and additional studies in a second test species, and 3 for use of a subchronic study for chronic guidance
Critical effect(s):	Liver cell vacuolization
Co-critical effect(s):	None
Additivity endpoint(s):	Hepatic (liver) system

Cancer Health Risk Limit (cHRL) = Not Applicable

Cancer classification:	Not Classified
Slope factor (SF):	Not Applicable
Source of cancer slope factor (SF):	Not Applicable
Tumor site(s):	Not Applicable

Volatile: No

Summary of Guidance Value History:

In 2020 MDH derived guidance for TBEP. Previously no MDH guidance existed. Later in 2020 MDH incorporated updated intake rates (US EPA 2019). Use of the updated intake rates did not result in any changes to the guidance values. 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?	No	No	Yes	Yes	Yes
Effects observed?	-[1]	-[2]	No[3]	Yes[4]	Yes[5]

Comments on extent of testing or effects:

[1] No specific animal studies are available. A general toxicity study in rats noted a slight endocrine system organ weight change (thyroid) at a dose approximately 2,000 times higher than the subchronic

reference dose. In cell culture studies, a small number of tests have been positive for endocrine activity.

[2] No specific animal studies are available. A general toxicity study in rats noted a slight decrease in spleen weight after five weeks of exposure at a dose over 10,000 times higher than the short-term reference dose. A small reduction in white blood cells has also been reported in two studies at doses over 6,000 times higher than the subchronic reference dose.

[3] Two studies have examined developmental effects in rats, and neither reported developmental effects at doses 1,700 and 8,000 times higher than the short-term reference dose. However, due to the lack of specific developmental studies and the lack of a second test species, a database uncertainty factor was applied.

[4] Male reproductive toxicity in adult rats was reported at a dose 1,700 times higher than the short-term reference dose. A slight increase in testis weight and a slight decrease in ovary weight has been reported at doses over 10,000 times higher than the subchronic reference dose. A database uncertainty factor has been applied due to the overall lack of reproductive studies.

[5] Neurotoxicity has been examined in two dated studies where effects were not seen until approximately 5,000 – 10,000 times higher than the short-term reference dose. Serum cholinesterase decreases have also been observed at doses 1,000 – 10,000 times higher than the subchronic reference dose.

Resources Consulted During Review:

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