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

Web Publication Date: March 2025

Toxicological Summary for: Tributyl phosphate

CAS: 126-73-8
Synonyms: TBP; tri-n-butyl phosphate; TnBP

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

Short-term Non-Cancer Health-Based Value ($nHBV_{Short\text{-}term}$) = 4 µg/L

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

$$= \frac{\text{(0.0059 mg/kg-d) x (0.2)}^{*} \text{ x (1000 µg/mg)}}{\text{(0.290 L/kg-d)}^{**}}$$

= 4.07 rounded to **4 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 = 0.593/100 = 0.0059 mg/kg-d (Sprague-Dawley Rat)
Source of toxicity value:	Determined by MDH in 2024
Point of Departure (POD):	2.28 mg/kg-d (administered dose $BMDL_{0.5SD}$, Tyl 1997)
Dose Adjustment Factor (DAF):	Body weight scaling, default [US EPA 2011 and MDH 2017]
Human Equivalent Dose (HED):	POD x DAF = 2.28 mg/kg-d x 0.26 = 0.593 mg/kg-d
Total uncertainty factor (UF):	100
Uncertainty factor allocation:	3 for interspecies (toxicodynamic) differences, 10 for intraspecies variability, 3 for database uncertainty to account for the lack of adequate endocrine and developmental neurotoxicity studies
Critical effect(s):	Reduced pup body weight
Co-critical effect(s):	None
Additivity endpoint(s):	Developmental

Subchronic Non-Cancer Health-Based Value ($nHBV_{Subchronic}$) = 4 µg/L

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

$$= \frac{\text{(0.0059 mg/kg-d)}^{\#} \text{ x (0.2)}^{*} \text{ x (1000 µg/mg)}}{\text{(0.074 L/kg-d)}^{**}}$$

= 15.9 rounded to 20 µg/L

[#]The calculated subchronic RfD (0.022 mg/kg-day) is higher than the short-term RfD (0.0059 mg/kg-d), which is based on developmental effects. The subchronic RfD must be protective of all types of adverse effects that could occur from subchronic exposure, including short-term effects (MDH 2008, page 34). Therefore, the short-term RfD is used in place of the calculated subchronic RfD when deriving subchronic water guidance.
[*]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 nHBV must be protective of shorter duration exposures that occur within the subchronic duration and therefore, the Subchronic nHBV is set equal to the Short-term nHBV of 4 µg/L. Additivity endpoints: Developmental

Chronic Non-Cancer Health-Based Value ($nHBV_{Chronic}$) = 4 µg/L

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

$$= \frac{(0.0059 \text{ mg/kg-d})^{\#} \times (0.2)^{*} \times (1000 \text{ µg/mg})}{(0.045 \text{ L/kg-d})^{**}}$$

= 26.2 rounded to 30 µg/L

[#]The calculated chronic RfD (0.042 mg/kg-day) is higher than the short-term RfD (0.0059 mg/kg-d), which is based on developmental effects. The chronic RfD must be protective of all types of adverse effects that could occur from chronic exposure, including short-term effects (MDH 2008, page 34). Therefore, the short-term RfD is used in place of the calculated chronic RfD when deriving chronic water guidance.
[*]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 Chronic nHBV must be protective of shorter duration exposures that occur within the chronic duration and therefore, the Chronic nHBV is set equal to the Short-term nHBV of 4 µg/L. Additivity endpoints: Developmental

Cancer Health-Based Value (cHBV) = Not Applicable

Cancer classification: Likely to be Carcinogenic to Humans (EPA 2005)
Tumor site(s): Bladder, liver

Statement for non-linear carcinogens:

MDH has determined that tributyl phosphate is a nonlinear carcinogen. This is due to its lack of genotoxicity and because the noncancer bladder effects observed after shorter exposures can progress to tumors after longer exposures. The Short-term RfD and nHBV are based on noncancer bladder effects and considered to be protective against cancer.

Volatile: Yes (low)

Summary of Guidance Value History:
Tributyl phosphate has not previously been evaluated by MDH.

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?	No[1]	No[2]	Yes[3]	Yes[4]	Yes[5]

Comments on extent of testing or effects:
[1] No effects of tributyl phosphate exposure were observed on weights or histopathology of the adrenal glands or thyroid at doses up to 16,000- and 45,000-fold the short-term reference dose (RfD) in rats and mice, respectively. A database uncertainty factor of 3 has been applied, in part, to account for the lack of adequate endocrine toxicity studies.

[2] No effects of chronic tributyl phosphate exposure were observed on thymus weight and histopathology at doses up to 8,000- and 17,000-fold the short-term RfD in rats and mice, respectively.

[3] The short-term RfD is based on developmental toxicity in rats (decreased pup body weight). One study identified decreased rat fetal body weight at a dose 3,700-fold higher than the short-term RfD. Doses 7,300- to 19,000-fold higher than the short-term RfD induced skeletal abnormalities in rat pups.

[4] Multiple studies in rats, mice, and rabbits evaluated reproductive effects of tributyl phosphate. Reduced maternal body weight gain was observed at doses 7,300- and 31,000-fold higher than the short-term RfD for rats and rabbits, respectively. Maternal extrauterine body weight gain in rats was observed at doses 3,500- to 3,900-fold higher than the short-term RfD in two studies. One study reported increased deaths of pregnant rats at a dose 30000-fold higher than the short-term RfD.

[5] No treatment-related effects were observed in rats using the functional observational battery at doses up to 14,000-fold higher than the short-term RfD. Rat caudal nerve function effects were observed at doses 11,000- to 17,000-fold higher than the short-term RfD. Increased brain weight was reported in one study at a dose 17,000-fold higher than the short-term RfD. Reduced acetylcholinesterase expression was reported in red blood cells of female rats in one study at a dose 10,000-fold higher than the short-term RfD while increased cholinesterase activity was reported in brain homogenates of rats exposed to a dose 17,000-fold higher than the short-term RfD. A database uncertainty factor of 3 has been applied, in part, to account for the lack of adequate neurotoxicity studies, especially during the developmental window.

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