

Toxicological Summary for: 4-*tert*-Octylphenol

CAS: 140-66-9

Synonyms: 4-(1,1,3,3-Tetramethylbutyl)phenol, *p*-(1,1,3,3-Tetramethylbutyl)phenol, *p-tert*-Octylphenol, 4-(2,4,4-trimethylpentan-2-yl)phenol

Acute Non-Cancer Health Risk Limit (nHRL_{Acute}) = Not Derived (Insufficient Data)

Short-term Non-Cancer Health Risk Limit (nHRL_{Short-term}) = 100 µg/L

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

$$= \frac{(0.17 \text{ mg/kg-d}) \times (0.2^*) \times (1000 \text{ µg/mg})}{(0.290 \text{ L/kg-d})^{**}}$$

$$= 117 \text{ rounded to } 100 \text{ µg/L}$$

*The available data indicate that infant exposures, from sources such as breast milk and baby food, are not lower than adult exposures. As infant exposures are equal to or exceed adult exposures based on the available exposure data, a relative source contribution of 0.2 has been selected for all durations.

** 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 = 5.06/30 = 0.17 mg/kg-d (Sprague-Dawley rats)
Source of toxicity value:	Determined by MDH in 2015
Point of Departure (POD):	22 mg/kg-d (administered dose NOAEL, 2-generation reproductive study, Tyl <i>et al.</i> 1999)
Dose Adjustment Factor (DAF):	0.23, Body weight scaling, default (US EPA 2011, MDH 2017)
Human Equivalent Dose (HED):	POD X DAF = 22 mg/kg-d x 0.23 = 5.06 mg/kg-d
Total uncertainty factor (UF):	30
Uncertainty factor allocation:	3 for interspecies differences (for toxicodynamics) and 10 for intraspecies variability
Critical effect(s):	Decreased pup body weight and increased time to preputial separation
Co-critical effect(s):	Decreased adult body weight
Additivity endpoint(s):	Developmental

Subchronic Non-Cancer Health Risk Limit (nHRL_{Subchronic}) = nHRL_{Short-term} = 100 µg/L

(Reference Dose, mg/kg-d) x (Relative Source Contribution) x (Conversion Factor)
(Subchronic Intake Rate, L/kg-d)

$$= \frac{(0.17 \text{ mg/kg-d}) \times (0.2) \times (1000 \text{ µg/mg})}{(0.074 \text{ L/kg-d})^{**}}$$

$$= 459 \text{ rounded to } 500 \text{ µg/L}$$

** 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 = 5.06/30 = 0.17 mg/kg-d (Sprague-Dawley rats)
Source of toxicity value: Determined by MDH in 2015
Point of Departure (POD): 22 mg/kg-d (administered dose NOAEL, 2-generation reproductive study, Tyl *et al.* 1999)
Dose Adjustment Factor (DAF): 0.23, Body weight scaling, default (US EPA 2011, MDH 2017)
Human Equivalent Dose (HED): POD X DAF = 22 mg/kg-d x 0.23 = 5.06 mg/kg-d
Total uncertainty factor (UF): 30
Uncertainty factor allocation: 3 for interspecies differences (for toxicodynamics) and 10 for intraspecies variability
Critical effect(s): Decreased uterine weight
Co-critical effect(s): Decreased adult body weight
Additivity endpoint(s): Female Reproductive 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 100 µg/L. Additivity endpoints: Developmental

Chronic Non-Cancer Health Risk Limit (nHRL_{Chronic}) = nHRL_{Short-term} = 100 µg/L

(Reference Dose, mg/kg-d) x (Relative Source Contribution) x (Conversion Factor)
(Chronic Intake Rate, L/kg-d)

$$= \frac{(0.051 \text{ mg/kg-d}) \times (0.2) \times (1000 \text{ µg/mg})}{(0.045 \text{ L/kg-d})^{**}}$$

$$= 226 \text{ rounded to } 200 \text{ µg/L}$$

** 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: $\text{HED/Total UF} = 5.06/100 = 0.051 \text{ mg/kg-d}$ (Sprague-Dawley rats)

Source of toxicity value: Determined by MDH in 2015

Point of Departure (POD): 22 mg/kg-d (administered dose NOAEL, 2-generation reproductive study, Tyl *et al.* 1999, subchronic exposure)

Dose Adjustment Factor (DAF): 0.23, Body weight scaling, default (US EPA 2011, MDH 2017)

Human Equivalent Dose (HED): $\text{POD} \times \text{DAF} = 22 \text{ mg/kg-d} \times 0.23 = 5.06 \text{ mg/kg-d}$

Total uncertainty factor (UF): 100

Uncertainty factor allocation: 3 for interspecies differences (for toxicodynamics), 10 for intraspecies variability, and 3 for subchronic to chronic extrapolation

Critical effect(s): Decreased uterine weight

Co-critical effect(s): Decreased adult body weight

Additivity endpoint(s): Female Reproductive system

The Chronic nHRL must be protective of the short-term and subchronic exposures that occur within the chronic period and therefore, the Chronic nHRL is set equal to the Short-term nHRL of 100 µg/L.

Additivity endpoints: Developmental

Cancer Health Risk Limit (cHRL) = Not Applicable

Volatile: Yes (low)

Summary of Guidance Value History:

An HBV of 100 µg/L for all durations was developed in 2015. In 2020, MDH re-evaluated 4-tert-octylphenol resulting in no changes to the guidance value, however, the recent detections of 4-tert-octylphenol in Minnesota groundwater made it eligible for rule. Also 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?	Yes	No	Yes	Yes	Yes
Effects observed?	Yes ¹	-- ²	Yes ³	Yes ⁴	Yes ⁵

Comments on extent of testing or effects:

¹Endocrine effects such as increased uterine weights, increased vaginal and uterine thickness, and

changes in estrus cyclicity were reported in female rats receiving doses approximately 35-275 times higher than the short-term RfD. In addition, male animals receiving doses approximately 225 times higher than the short-term RfD had increased prolactin levels.

² No oral studies specifically evaluating immunotoxicity have been conducted. Studies examining other endpoints reported reduced thymus and spleen weights at approximately 300 times higher than the short-term RfD, and increased white blood cell/platelet counts around 650-700 times higher than the short-term RfD.

³ The short-term RfD is based on reduced pup body weights and delayed preputial separation after rats were exposed to 4-*tert*-Octylphenol through their diet. Precocious vaginal patency was observed at doses more than 250 times the short-term RfD.

⁴ The subchronic and chronic reference doses are based on reduced uterine weights of rats exposed to 4-*tert*-Octylphenol through their diet. In other studies, doses more than 650 times higher than the short-term RfD resulted in changes in epididymis and prostate weights. In addition, an increase in post-implantation loss and the reduction of number of live fetuses per litter were observed at doses 41-160 times higher than the short-term RfD.

⁵ Neurobehavioral effects, including effects on a variety of sexually dimorphic behaviors and water maze performance, were evaluated in a single oral study. The effects occurred at an estimated dose approximately 150 times higher than the short-term RfD.

Resources Consulted During Review:

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