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

Adopted as Rule: November 2023

Toxicological Summary for: *p*-Nonylphenol, branched isomers

CAS: **84852-15-3**

Synonyms: 4-Nonylphenol; Phenol, *p*-nonyl-; 4-*p*-Nonyl phenol; Phenol, 4-nonyl-; *para* Nonyl phenol, branched (mixed isomers)

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

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

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

$$= \frac{\text{(0.21 mg/kg-d) x (0.2)}^{*} \text{ x (1000 µg/mg)}}{\text{(0.290 L/kg-d)}^{**}}$$

= 144 rounded to **100 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 = 6.27/30 = 0.21 mg/kg-d (SD rats)
Source of toxicity value:	Determined by MDH in 2015
Point of Departure (POD):	33 mg/kg-d (administered dose NOAEL; NTP 1997/Chapin 1999)
Dose Adjustment Factor (DAF):	0.19, Body weight scaling, study-specific (US EPA 2011 and MDH 2017)
Human Equivalent Dose (HED):	POD x DAF = 33 mg/kg-d x 0.19 = 6.27 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):	Accelerated vaginal opening
Co-critical effect(s):	Decreased pup body weight and increased duration of estrous cycle
Additivity endpoint(s):	Developmental, Female Reproductive system

Subchronic Non-Cancer Health Risk Limit ($nHRL_{Subchronic}$) = 40 µg/L

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

$$= \frac{\text{(0.016 mg/kg-d) x (0.2)}^{*} \text{ x (1000 µg/mg)}}{}$$

(0.074 L/kg-d)**

= 43.2 rounded to **40 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 = 0.485/30 = 0.016 mg/kg-d (SD rats)
Source of toxicity value:	Determined by MDH in 2015
Point of Departure (POD):	1.94 mg/kg-d (administered dose $BMDL_{10}$, NTP 1997/Chapin 1999)
Dose Adjustment Factor (DAF):	0.25, Body weight scaling, default (US EPA 2011 and MDH 2017)
Human Equivalent Dose (HED):	POD x DAF = 1.94 mg/kg-d x 0.25 = 0.485 mg/kg-d
Total uncertainty factor (UF):	30
Uncertainty factor allocation:	3 for interspecies differences (for toxicodynamics), 10 for intraspecies variability
Critical effect(s):	Renal mineralization in male rats
Co-critical effect(s):	None
Additivity endpoint(s):	Renal (kidney) system

Chronic Non-Cancer Health Risk Limit ($nHRL_{Chronic}$) = 20 µg/L

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

$$= \frac{\text{(0.0049 mg/kg-d) x (0.2)* x (1000 µg/mg)}}{\text{(0.045 L/kg-d)**}}$$

= 21.7 rounded to **20 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 = 0.485/100 = 0.0049 mg/kg-d (SD rats)
Source of toxicity value:	Determined by MDH in 2015
Point of Departure (POD):	1.94 mg/kg-d (administered dose $BMDL_{10}$, NTP 1997/Chapin 1999, subchronic exposure)
Dose Adjustment Factor (DAF):	0.25, Body weight scaling, default (US EPA 2011 and MDH 2017)
Human Equivalent Dose (HED):	POD x DAF = 1.94 mg/kg-d x 0.25 = 0.485 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):	Renal mineralization in male rats

Co-critical effect(s): None
Additivity endpoint(s): Renal (kidney) system

Cancer Health-Based Value (cHRL) = Not Applicable

Volatile: Yes (low)

Summary of Guidance Value History:
MDH developed non-cancer Health-Based Values for Short-term, Subchronic and Chronic durations of 100, 40, and 20 ug/L, respectively, for p-nonylphenol in 2015. In 2020, MDH incorporated updated intake rates (US EPA 2019) and performed a re-evaluation of p-Nonylphenol. Use of the updated intake rates and results from the re-evaluation did not result in any changes to the 2015 guidance values. Recent detections of *p*-nonylphenol in Minnesota's groundwater make it eligible for promulgation as a Health Risk Limit. 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]The short-term reference dose (RfD) is based on a developmental and endocrine-mediated effect (accelerated vaginal opening). Endocrine effects have been well studied. Hormone level changes in adult rats have been observed at approximately 60 times higher than the current short-term reference dose. Endocrine-mediated alterations in development and reproduction were not observed, at doses up to 160 times the short-term reference dose, in three multiple generation studies.

[2]Immunotoxicity has been evaluated in two studies. Subtle alterations in immune cell populations were observed at a dose approximately 30 times higher than the current subchronic reference dose. More overt effects on immune system organ weights and immune cellular parameters were not observed until doses reached over 2000 times the current subchronic reference dose.

[3]Development effects have been well studied. The critical effect for the short-term duration is accelerated vaginal opening, a developmental effect. The only other consistent developmental effect seen was decreased pup body weight at weaning occurring at doses over 150 times higher than the current short-term reference dose.

[4]Reproductive effects have been well studied. Altered hormone levels in female rats, identified as a co-critical effect, was observed at 50 times higher than the short-term reference dose. Male

reproductive toxicity noted as altered sperm and decreased testes weight was observed at 800 times up to 3500 times the subchronic reference dose.

[5]Both neurotoxicity and developmental neurotoxicity have been studied. Small alterations in maze performance tests on rodents were noted at 800 times the subchronic reference dose. At doses 2000 times the subchronic reference dose, no effects were seen on neurobehavioral endpoints. Certain gender-specific behaviors may be altered by nonylphenol exposure, but not until doses reach over 900 times the subchronic reference dose.

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