



## 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-Based Value (nHBV<sub>Acute</sub>) = Not Derived (Insufficient Data)**

**Short-term Non-Cancer Health-Based Value (nHBV<sub>Short-term</sub>) = 100 µg/L**

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

$$= \frac{(0.21 \text{ mg/kg-d}) \times (0.2^*) \times (1000 \text{ µg/mg})}{(0.289 \text{ L/kg-d})}$$

$$= 145 \text{ rounded to } \mathbf{100 \text{ µg/L}}$$

\*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.

Reference Dose/Concentration:	0.21 mg/kg-d (SD rats)
Source of toxicity value:	MDH, 2015
Point of Departure (POD):	33 mg/kg-d (NOAEL; NTP, 1997/Chapin, 1999)
Human Equivalent Dose (MDH, 2011):	33 mg/kg-d x 0.19 = 6.3 mg/kg-d
Total uncertainty factor:	30
Uncertainty factor allocation:	3 for interspecies extrapolation (to address potential differences in 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-Based Value (nHBV<sub>Subchronic</sub>) = 40 µg/L**

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

(Subchronic Intake Rate, L/kg-d)

$$= \frac{(0.016 \text{ mg/kg-d}) \times (0.2) \times (1000 \text{ } \mu\text{g/mg})}{(0.077 \text{ L/kg-d})}$$

$$= 41.6 \text{ rounded to } \mathbf{40 \text{ } \mu\text{g/L}}$$

Reference Dose/Concentration: 0.016 mg/kg-d (SD rats)  
Source of toxicity value: MDH, 2015  
Point of Departure (POD): 1.94 mg/kg-d (MDH BMDL<sub>10</sub>; NTP, 1997/Chapin, 1999)  
Human Equivalent Dose (MDH, 2011): 1.94 mg/kg-d x 0.25 = 0.49 mg/kg-d  
Total uncertainty factor: 30  
Uncertainty factor allocation: 3 for interspecies extrapolation (to address potential differences in toxicodynamics) and 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-Based Value (nHBV<sub>Chronic</sub>) = 20  $\mu$ g/L**

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

$$= \frac{(0.0049 \text{ mg/kg-d}) \times (0.2) \times (1000 \text{ } \mu\text{g/mg})}{(0.043 \text{ L/kg-d})}$$

$$= 22.8 \text{ rounded to } \mathbf{20 \text{ } \mu\text{g/L}}$$

Reference Dose/Concentration: 0.0049 mg/kg-d (SD rats)  
Source of toxicity value: MDH, 2015  
Point of Departure (POD): 1.94 mg/kg-d (MDH BMDL<sub>10</sub>; NTP, 1997/Chapin, 1999, subchronic exposure duration)  
Human Equivalent Dose (MDH, 2011): 1.94 mg/kg-d x 0.25 = 0.49 mg/kg-d  
Total uncertainty factor: 100  
Uncertainty factor allocation: 3 for interspecies extrapolation (to address potential differences in toxicodynamics), 10 for intraspecies variability, and 3 for subchronic to chronic extrapolation.  
Critical effect(s): Renal Mineralization  
Co-critical effect(s): None  
Additivity endpoint(s): Renal (kidney) system

**Cancer Health Based Value (cHBV) = Not Applicable**

**Volatile: No**

**Summary of Guidance Value History:** No previous guidance from 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?	Yes <sup>1</sup>	Yes <sup>2</sup>	Yes <sup>3</sup>	Yes <sup>4</sup>	Yes <sup>5</sup>

**Comments on extent of testing or effects:**

<sup>1</sup> Endocrine effects have been well studied. The critical effect for the short-term duration is accelerated vaginal opening, an endocrine mediated effect. 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.

<sup>2</sup> 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.

<sup>3</sup> 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.

<sup>4</sup> Reproductive effects have been well studied. Altered hormone levels in female rats were 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.

<sup>5</sup> 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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