2013 Health Risk Limits for Groundwater
Health Risk Assessment Unit, Environmental Health Division
651-201-4899

Adopted as Rule: September 30, 2013

# Toxicological Summary for Naphthalene:

## CAS: 91-20-3

Synonyms: Camphor tar; mighty 150; mighty rd1; Mothballs; Moth Flakes; Naphthalene; Naphthalene, crude; Naphthalene; Naphthalene, molten; Naphthene; tar camphor; white tar

**Non-Cancer Acute Health Risk Limit ($nHRL_{acute}$) = 70 µg/L**

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

$$= \frac{\text{(0.038 mg/kg/d) x (0.5) x (1000 µg/mg)}}{\text{(0.289 L/kg-d)}}$$

= 66 rounded to **70 µg/L**

| | |
|---|---|
| Reference Dose / Concentration: | 0.038 mg/kg-day (Sprague Dawley rats) |
| Source of toxicity value: | MDH, 2011 |
| Point of Departure: | 50 mg/kg-day (LOAEL), (National Toxicology Program (NTP) 1991) developmental gavage study in SD rats (No NOAEL) |
| Human Equivalent Dose Adjustment: | 11.5 [50 mg/kg-d x 0.23] (MDH, 2011) |
| Total uncertainty factor: | 300 |
| UF allocation: | 3 interspecies extrapolation (toxicodynamics); 10 intraspecies variation; 3 database gaps – lack of 2-generation reproductive toxicity studies and lack of dose-response data for hemolytic anemia and cataract formation which have been observed in human epidemiological studies for naphthalene; 3 LOAEL-to-NOAEL – a default of 10 was not applied because the neurological effects observed did not persist at this dose for the entire length of the NTP study (however the neurological effects did persist at higher doses) |
| Critical effect(s): | Maternal nervous system effects which included lethargy, shallow breathing and impaired posture |
| Co-critical effect(s): | None |
| Additivity endpoint(s): | Nervous system |

**Non-Cancer Short-term Health Risk Limit ($nHRL_{short\text{-}term}$) = 70 µg/L**

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

$$= \frac{\text{(0.038 mg/kg/d) x (0.5) x (1000 µg/mg)}}{\text{(0.289 L/kg-d)}}$$

= 66 rounded to **70 µg/L**

| | |
|---|---|
| Reference Dose / Concentration: | 0.038 mg/kg-day (Sprague Dawley rats) |
| Source of toxicity value: | MDH, 2011 |
| Point of Departure: | 50 mg/kg-day (LOAEL), (National Toxicology Program (NTP) 1991) developmental gavage study in SD rats (No NOAEL) |
| Human Equivalent Dose Adjustment: | 11.5 [50 mg/kg-d x 0.23] (MDH, 2011) |
| Total uncertainty factor: | 300 |
| UF allocation: | 3 interspecies extrapolation (toxicodynamics); 10 intraspecies variation; 3 database gaps – lack of 2-generation reproductive toxicity studies and lack of dose-response data for hemolytic anemia and cataract formation which have been observed in human epidemiological studies for naphthalene; 3 LOAEL-to-NOAEL – a default of 10 was not applied because the neurological effects observed did not persist at this dose for the entire length of the NTP study (however the neurological effects did persist at higher doses) |
| Critical effect(s): | Maternal nervous system effects which included lethargy, shallow breathing and impaired posture |
| Co-critical effect(s): | None |
| Additivity endpoint(s): | Nervous system |

**Non-Cancer Subchronic Health Risk Limit ($nHRL_{subchronic}$) = $nHRL_{short\text{-}term}$ = 70 µg/L**

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

$$= \frac{\text{(0.052 mg/kg/d) x (0.2) x (1000 µg/mg)}}{\text{(0.077 L/kg-d)}}$$

= 135 rounded to 100 µg/L

| | |
|---|---|
| Reference Dose / Concentration: | 0.052 mg/kg-day (Fischer 344 rats) |
| Source of toxicity value: | MDH, 2011 |
| Point of Departure: | 71 mg/kg-day (NOAEL), (Battelle's Columbus Laboratories (BCL) 1980a) gavage study in F344 rats |
| Human Equivalent Dose Adjustment: | 15.6 [71 mg/kg-d x 0.22] (MDH, 2011) |
| Total uncertainty factor: | 300 |
| UF allocation: | 3 interspecies extrapolation (toxicodynamics); 10 intraspecies variation; 10 database gaps – lack of 2-generation reproductive toxicity studies, lack of dose-response data for hemolytic anemia and cataract formation which have been observed in human epidemiological studies for naphthalene, and a lack of neurotoxicity studies in the subchronic and chronic durations |
| Critical effect(s): | Decrease in terminal body weight |
| Co-critical effect(s): | Decreased spleen weight, lethargy, slow breathing, prone body posture, increased rooting behavior, decreased body weight associated with decreased food and water consumption |
| Additivity endpoint(s): | Nervous system; spleen |

**The subchronic nHRL must be protective of the short-term exposures that occur within the short-term period and therefore, the subchronic nHRL is set equal to the acute / short-term nHRL of 70 µg/L. Additivity endpoints: Nervous system**

**Non-Cancer Chronic Health Risk Limit ($nHRL_{chronic}$) = 70 µg/L**

$$= \frac{\text{(Reference Dose, mg/kg/d) x (Relative Source Contribution) x (Conversion Factor)}}{\text{(Chronic intake rate, L/kg/d)}}$$

$$= \frac{\text{(0.016 mg/kg/d) x (0.2) x (1000 µg/mg)}}{\text{(0.043 L/kg-d)}}$$

= 74 rounded to **70 µg/L**

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|---|---|
| Reference Dose / Concentration: | 0.016 mg/kg-day (Fischer 344 rats) |
| Source of toxicity value: | MDH 2011 |
| Point of Departure: | 71 mg/kg-day (NOAEL), (Battelle's Columbus Laboratories (BCL) 1980a) gavage study in F344 rats |
| Human Equivalent Dose Adjustment: | 15.6 [71 mg/kg-d x 0.22] (MDH, 2011) |
| Total uncertainty factor: | 1000 |
| UF allocation: | 3 interspecies extrapolation (toxicodynamics); 10 intraspecies variation; 10 database gaps – lack of 2-generation reproductive toxicity studies, lack of dose-response data for hemolytic anemia and cataract formation which have been observed in human epidemiological studies for naphthalene, and a lack of neurotoxicity studies in the subchronic and chronic durations; 3 subchronic-to-chronic extrapolation because effects did not increase in severity with increasing exposure duration and most effects were observed within a shorter duration |
| Critical effect(s): | Decrease in terminal body weight |
| Co-critical effect(s): | Decreased spleen weight, lethargy, slow breathing, prone body posture, increased rooting behavior, decreased body weight associated with decreased food and water consumption |
| Additivity endpoint(s): | Nervous system; spleen |

**Cancer Health Risk Limit (cHRL) = Not Applicable**

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|---|---|
| Cancer classification: | Group C – there is evidence of carcinogenicity following inhalation exposure |
| Slope factor: | NA |
| Source of slope factor: | NA |
| Tumor site(s): | NA |

**Volatile: Yes (moderate)**

**Summary of changes since 1993/1994 HRL promulgation:**
The acute, short-term, subchronic, and chronic HRLs (70 µg/L) are 4 times lower than the 1993/94 chronic HRL (300 µg/L) as the result of: 1) utilizating of more recent intake rate data that incorporates higher intakes early in life, 2) more recent lower RfD values, and 3) rounding to one significant digit.
The HRLs were adopted in 2013 and the 1993 HRL was repealed.

**Summary of toxicity testing for health effects identified in the Health Standards Statute:**

| | Endocrine | Immunotoxicity | Development | Reproductive | Neurotoxicity |
|---|---|---|---|---|---|
| Tested? | No | Yes | Yes | No | Yes |
| Effects? | - | Yes[1] | Yes[2] | Secondary Observation | Yes[3] |

Note: 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. Most chemicals have been subject to multiple studies in which researchers identify a dose where no effects were observed, and the lowest dose that caused one or more effects. A toxicity value based on the effect observed at the lowest dose across all available studies is considered protective of all other effects that occur at higher doses.

**Comments on extent of testing or effects:**
Note: individuals, particularly, infants, deficient in G6PDH are thought to be especially sensitive to naphthalene-induced hemolytic anemia.

[1]Decreased spleen weights seen in mice exposed to naphthalene for 14-days and 90-day by gavage (Shopp et al 1984) and it is listed as a co-critical effect for the subchronic and chronic durations. Lymphoid depletion of the thymus was seen in 2/10 female rats exposed to naphthalene by gavage for 13 weeks at 2 times the critical subchronic and chronic $LOAEL_{HED}$.

[2] Developmental studies were conducted in three species (rats, mice, and rabbits). A reduction in number of live pups per litter were observed at levels approximately 4 times critical acute and short-term $LOAEL_{HED}$ of 11.5 mg/kg-day. Malformations in offspring were observed at an HED of 104 mg/kg-day which is 3 times greater than the critical subchronic and chronic $LOAEL_{HED}$. No developmental effects were seen in the absence of significant maternal toxicity.

[3] Neurotoxicity (lethargy, slow breathing) was considered the critical acute and short-term effect. Tolerance to neurological effects developed in low dose groups but persisted at higher doses. Neurological effects are listed as co-critical effects for the subchronic and chronic durations.

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