Oregon Department of Environmental Quality
Toxic Air Contaminant Review and Update Rulemaking 2025

1-Methylnaphthalene ATSAC Feedback Organizer

The purpose of this document is to compile ATSAC member feedback during DEQ's TAC Review and Update Rulemaking.

Background

DEQ and OHA requested written responses from ATSAC members in response to a nationwide state risk assessor group email, received September 3, 2024, about the 2024 PPRTV 1-methylnaphthalene noncancer chronic reference concentration (RfC; see email below forwarded to ATSAC February 20, 2025). The 2024 PPRTV documentation for 1-methylnaphthalene can be found online here. In the ATSAC TRV review materials, 1-methylnaphthalene information is in ATSAC Workbook #2 on the ATSAC website (see row #416 on appendix tab #6). ATSAC members were asked to review the PPRTV documentation for 1-methylnaphthalene and answer the following question: **Do you support or have concerns about the 1-methylnaphthalene PPRTV noncancer chronic RfC?**

ATSAC members' written responses were submitted to OHA in March 2025 and compiled into this document.

Email from Nationwide Listserv Forwarded to ATSAC (February 20, 2025)

"The May RSL update included a PPRTV Reference Concentration (RfC) for 1-Methylnaphthalene (3E-06 mg/m3). At first, I just noted the change and updated our table of VISLs and RSL accordingly. However, as we have been addressing sites with 1-Methylnaphthalene (1-MN) we have noticed that it is suddenly a primary risk driver at many sites. Thus, I did some digging and wanted to see if any of my colleagues in other states have similar concerns about this PPRTV RfC.

The paper used to create the RfC is from a subchronic study that did not follow an established protocol (at least not completely), that had an Uncertainty Factor of 3000 and yielded a "low confidence" rating from PPRTV. Importantly, it was unclear if the response to nasopharyngeal tissues were adverse (toxic) or adaptive (reversible).

Furthermore, the other toxicity values for 1-MN (CSF & RfD) are very similar (within one order of magnitude) to the other two Naphthalenes (2-MN and Naph), and almost all of the chemical-specific parameters (HLC, VP, Solubility, Koc, etc.) are very similar (on the same order of magnitude). Thus, this RfC for 1-MN appears to be a significant departure from what was previously understood about the Naphthalenes in general, indicating either it is suspect or all of the other toxicity values are suspect, or both.

The programmatic implications of this new RfC value are considerable. 1-MN will now drive many of the risks at gasoline and diesel release sites much more than Benzene or Naphthalene. The Tapwater RSL is 0.0063 ug/L, which likely cannot even be detected. In fact, EPA updated the Industrial Groundwater VISL to 1.6 ug/L (based on HI=1.0) compared to a Benzene Industrial VISL of 118 ug/L (based on ELCR=1E-06). Meanwhile LUST sites rarely even sample for 1-MN or 2-MN and completely ignore their risks.

EPA Region 3 is planning on using this new RfC value, but I am having sincere doubts about the validity of this new RfC. Private-sector Toxicologists have contacted me to complain about this RfC (one asking us to reject it) and I was wondering if other states were having the same concerns or issues, and if so, how are you addressing them? Some options I have thought of:

1. Accept it and move on with significant alterations to our programs

2. Reject it and keep the status quo

3. Reject it and use route-to-route extrapolation to develop a RfC (0.28 mg/m3)

4. Reject it and use the Naphthalene RfC as a surrogate (I do not think 1-MN is appropriate for route-to-route extrapolation), which strikes a compromise by accounting for non-cancer inhalation risks but using a value with much higher confidence (albeit for a slightly different chemical)."

ATSAC Member Written Responses

John Budroe, PhD

The Oregon Department of Environmental Quality (DEQ) has proposed to establish a chronic Toxicity Reference Value (TRV) for 1-methylnaphthalene (1-MN) of 0.003 µg/m^3. This TRV is directly adopted from the chronic provisional Reference Concentration (p-RfC) of 0.003 µg/m^3 developed by the US EPA Provisional Peer-Reviewed Toxicity Value (PPRTV) program (US EPA, 2024).

The p-RfC is based on a 13-week inhalation study using 10 male and 10 female F344 rats, exposed 6 hours/day, 5 days/week (Kim et al., 2020). Nominal exposure concentrations were 0, 0.5, 4 and 30 ppm. US EPA identified increased incidence of mucous cell hyperplasia in nasopharyngeal tissues in males and females and increased incidence of transitional epithelial cell hyperplasia in nasopharyngeal tissues in males as the critical study effects.

The study effects data were modeled using the dichotomous models contained in US EPA's Benchmark Dose Software (BMDS, version 3.2). The dose metric employed was the Human Equivalent Concentration (HEC) based on extrathoracic effects (HEC_{ET}), and a benchmark response (BMR) of 10% extra risk for incidence data was used. The HEC_{ET} was calculated using study-specific time-weighted average body weights for each exposure group. US EPA chose the 10% benchmark concentration lower confidence limit ($BMCL_{10}$) on the HEC_{ET} of 0.009 mg/m^3 (0.0015 ppm, 1 ppm = 5.91 mg/m^3) for increased incidence of mucous cell hyperplasia in nasopharyngeal tissues in male F344 rats as the lowest point-of-departure (POD) for derivation of both a subchronic and chronic 1-MN p-RfC. The best fitting model for this endpoint was the multistage 1-degree.

The subchronic 1-MN p-RfC was derived by dividing the POD of 0.009 mg/m^3 by a composite uncertainty factor (UF_C) of 300 (UF_A = 3 (animal-human extrapolation, including HEC derivation) x UF_D = 10 (database uncertainty) x UF_H = 10 (interhuman variability) x UF_L = 1 (POD is a BMCL) x UF_S = 1 (subchronic data used)), resulting in a value of 3 x 10^{-5} mg/m^3 (0.03 µg/m^3, 5 x 10^{-4} ppb).

US EPA also developed a chronic 1-MN p-RfC from the same data set and methodology used to develop the subchronic 1-MN p-RfC, with the exception that a UF_S of 10 was used to account for subchronic to chronic extrapolation, resulting in a UF_C of 3000, and a chronic 1-MN p-RfC of 3 x 10^{-6} mg/m^3 (0.003 µg/m^3; 5 x 10^{-5} ppb).

The Agency for Toxic Substances and Disease Registry (ATSDR) released a Toxicological Profile (TP) for Naphthalene, 1-Methylnaphthalene and 2-Methylnaphthalene (Draft for Public Comment) in May 2024 (ATSDR, 2024). This document used the same data set and adverse effect endpoints (Kim et al., 2020) to develop an intermediate (15 – 364 days exposure) Minimal Risk Level (MRL) that US EPA used to develop subchronic and chronic 1-MN p-RfC values. The study effects data were modeled using BMDS version 3.2. The dose metric employed was exposure concentration.

ATSDR chose the $BMCL_{10}$ for increased incidence of mucous cell hyperplasia in male F344 rat nasopharyngeal tissues generated using a dichotomous Hill model as the lowest appropriate POD for deriving an intermediate 1-MN MRL. The $BMCL_{10}$ was adjusted for exposure duration and converted to a $BMCL_{10HEC}$ of 0.0027 ppm (0.016 mg/m^3). The $BMCL_{10HEC}$ was then divided by a composite uncertainty factor (UF_C) of 30 (UF_A = 3 (animal-human extrapolation, including HEC derivation) x UF_H = 10 (interhuman variability)), resulting in an intermediate 1-MN MRL of 0.00009 ppm (0.09 ppb; 0.05 µg/m^3).

There are some small methodological differences between the 1-MN intermediate MRL and subchronic/chronic p-RfC derivations. For the HEC calculations, ATSDR appeared to use default physiological parameters for the study animals, as compared to US EPA's use of study-specific time-weighted average body weights for each exposure group to develop an HEC. Additionally, ATSDR used a dichotomous Hill model to generate a POD for

male F344 rat 1-MN-induced nasopharyngeal tissue mucous cell hyperplasia, while US EPA used a multistage 1-degree model for the same purpose. However, the PODs differ by less than 2-fold (US EPA 0.009 mg/m^3; ATSDR 0.016 mg/m^3).

Also, ATSDR deciding not to use the Kim et al. (2020) 13-week exposure data to develop a chronic MRL is a policy choice. Both US EPA IRIS and the California Office of Environmental Health Hazard Assessment (OEHHA)(two of DEQ's authoritative sources) will develop RfCs and chronic RELs, respectively, from subchronic exposure data. Having both US EPA and ATSDR decide that the Kim et al. data (2020) are useful for developing subchronic health values and the similarity of the PODs that were calculated indicate that the use of the 1-MP chronic p-RfC to develop a chronic TRV is appropriate.

However, DEQ may wish to consider revising some of the UFs that US EPA used to generate the 1-MN chronic p-RfC from the POD. For example, US EPA used a UF_D of 10 (database uncertainty) and a UF_S of 10 (subchronic to chronic extrapolation). In this case, OEHHA would use a UF_D of 3 and a UF_S of 3 (OEHHA considers 13-week studies to be subchronic). This would reduce the UF_C to 300, and result in a 1-MN chronic TRV of 0.03 µg/m^3.

References

Kim YS, Lee MJ, Seo DS, et al. 2020. Thirteen-week inhalation toxicity study of 1-methylnaphthalene in F344 rats. Toxicol Res 36(1):13-20.

U.S. Environmental Protection Agency (US EPA). Provisional Peer-Reviewed Toxicity Values for 1-Methylnaphthalene (CASRN 90-12-0). Center for Public Health and Environmental Assessment, Office of Research and Development Cincinnati, OH 45268. EPA/690/R-24/001F. March 2024.

Agency for Toxic Substances and Disease Registry (ATSDR). Toxicological Profile for Naphthalene, 1-Methylnaphthalene and 2-Methylnaphthalene. Draft for Public Comment. Centers for Disease Control and Prevention, U.S. Department of Health and Human Services. May 2024.

Daisy Dong, PhD

I took a detailed look at the PPRTV document. I have to say it is too shady for them to run benchmark dose modeling on the histopathological data of the nasopharyngeal tissues. I also dig into the critical study (Kim et al, 2020) they used for POD derivation. I have to say that I agree with authors' conclusion that the NOAEL should be 4 ppm because 1) the HE readings are mostly minimal or mild in 4 ppm group; 2) most likely these are adaptive responses, and 3) negative findings in 4 ppm for all other parameters measured. This POD (NOAEL=4 ppm) is more solid than the BMCL10 from the PPRTV document. I did some calculations based on the NOAEL = 4 ppm and the derived chronic TRV would be 0.83 or 4.14 µg/m^3 depending on which RGDR default value to pick (see attached files).

Thus, I don't advise adopting the PPRTV chronic RfC. Rather, I think ATSAC members can help DEQ calculate a new TRV based on the PPRTV document.

Chronic TRV for 1-methylnaphthalene based on Kim 2020 study

Based on study author, **NOALE =4 ppm** (I agree with the study author given the overall assessments of all parameters and the minimal and mild effects noted in the histopathological finding of the nasopharyngeal tissues.

Exposure: F344 rat, 6 hours/d, 5 days/wk, 13 weeks total (a subchronic inhalation study-whole body)

Parameters	**Method 1**	**Method 2**
POD =NOAEL=4 ppm x 5.8*= 23.2 mg/m^3	23.2	23.2
POD_{ADJ} = POD x (6/24) x (5/7), mg/m^3	4.14	4.14
DAF (either use EPA 1994 or EPA 2012 default value for extrathoracic region, ET)	$RGDR_{ET}$=0.20 (EPA 1994)	$RGDR_{ET}$=1 (EPA 2012)
POD_{HEC} = POD_{ADJ} x DAF, mg/m^3	0.83	4.14
UF_A	3	3
UF_H	10	10
UF_{DB}	10	10
UF_{SUB}	3	3
UF_{TOTAL}	1000	1000
TRV= POE_{HEC}/UF_{TOTAL} x 1000, **µg/m^3**	**0.83**	**4.14**

*The conversion factor for 1-methylnaphthalene is 1 ppm=5.8 mg/m^3 (Formula=MW/24.45, MW=142.20 g/mol)

John Stanek, PhD

John Stanek recused himself from the email thread because he worked on the PPRTV chronic RfC in some capacity recently as part of his role at EPA.

Susan Tilton, PhD

The request for the committee is to consider the proposed TRV for chronic 1-MN adopted from the EPA PPRTV of 0.003 ug/m3 and the questions proposed by WVDEP about the relevance of the underlying study used to derive the POD (Kim et al 2020). Based on the prevalence of 1-MN in studies collected by our program, it is understandable that 1-MN could potentially drive risk due to abundance when measured. I agree with using the Kim et al study as the basis for deriving the POD for the EPA PPRTV. Mucous cell hyperplasia in the nasopharyngeal tissue was used as the critical effect and even though the authors recommended a NOAEL of 4ppm, effects were observed in tissues at this dose that were relevant to the critical effect in a 13-week inhalation study with male and female F344 rats based on dose and severity. Therefore, I would support the EPA's use of the data from Kim et al (2020) for determining a POD rather than using a NOAEL of 4ppm as recommended in Kim et al (2020). This would be consistent with (1) prior reports for evidence of respiratory irritation from 1-MN (Korsak et al 1998), (2) the recommendation by the American Conference on the Governmental Industrial Hygienists for a lower acute threshold limit value of 0.5ppm, (3) the observation in a prior study with 1-MN that adverse effects (pulmonary alveolar proteinosis in the lung) were related to duration of exposure and only observed after chronic exposure (Murata et al 1992), and (4) the expectation by the authors (Kim et al.) that chronic exposure to 1-MN by inhalation exposure may cause lesions in the lung based on the observed tissue effects.

I am not able to comment on the BMD approach used to calculating the BMDL10 (HECet) and so other's may be able to provide input here, but it was based on the BMDL10 for the most sensitive endpoint for deriving a subchronic and chronic provisional reference concentration. Based on default UFs reported by OEHHA, which have previously been adopted by Oregon DEQ for other TRVs, I support John's recommendation of reducing uncertainty for UFd and UFsub (based on the 13-week study) to 3 for consistency.

Kim YS, Lee MJ, Seo DS, et al. 2020. Thirteen-week inhalation toxicity study of 1-methylnaphthalene in F344 rats. Toxicol Res 36(1):13-20.

Murata Y, Denda A, Maruyama H, Konishi Y (1992) Chronic toxicity and carcinogenicity studies of 1-methylnaphthalene in B6C3F1 mice. Toxicol Sci 21:44–51.

American Conference of Governmental Hygienists Inc. (2017) 1-Methylnaphthalnee and 2-methylnaphthalene. Documentation of the threshold limit values and biological exposure indices, 7th edn.

Korsak Z, Majcherek W, Rydzynski K (1998) Toxic effects of acute inhalation exposure to 1-methylnaphthalene and 2-methylnaphthalene in experimental animals. Int J Occup Med Environ Health 11:335–342.

John Vandenberg, PhD

I reviewed the PPRTV document and the comments from Daisy and John Budroe were very useful.

I also considered the cancer and oral data provided in the PPRTV document to get a sense of the other studies available for this chemical. I found the cancer and oral study data to indicate effects of concern were observed from other study designs and via the oral route of exposure.

This is a case where the ATSAC may be helpful, but it is clear that within the group we may have different opinions as to the path forward.

In my opinion the data are suitable for benchmark dose modeling as done by EPA (and also ATSDR in their draft report). The key question then is the application of uncertainty factors to the BMCL10hec to derive a chronic Reference Concentration.

My preferred approach would be to follow the PPRTV application of uncertainty factors, i.e. apply 3-fold UFa for animal-human extrapolation, 10-fold UFh for human variability and susceptibility, and 10-fold UFs for subchronic to chronic extrapolation, a 1-fold UFl for use of BMCL as POD, and 10-fold UFd for database uncertainty, resulting in a total UF of 3000 (as described on page 39 of the PPRTV document). With PPRTV documents considered as an "authoritative source" I support the use of the EPA PPRTV evaluation for 1-methlynaphthalene.

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