Food and Chemical Toxicology 182 (2023) 114215

Contents lists available at ScienceDirect

Food and Chemical Toxicology

journal homepage: www.elsevier.com/locate/foodchemtox

Short Review

RIFM fragrance ingredient safety assessment, 1-methylnaphthalene, CAS Registry Number 90-12-0

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ARTICLE INFO

Handling Editor: Dr. Bryan Delaney

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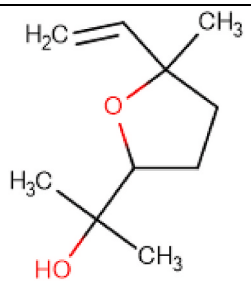
https://doi.org/10.1016/j.fct.2023.114215
Received 5 September 2023; Received in revised form 2 October 2023; Accepted 19 November 2023
Available online 25 November 2023

Version: 083123. Initial publication. All fragrance materials are evaluated on a five-year rotating basis. Revised safety assessments are published if new relevant data become available. Open access to all RIFM Fragrance Ingredient Safety Assessments is here: **fragrancematerialsafetyresource.elsevier.com**.



Name: 1-Methylnaphthalene CAS Registry Number: 90-12-0

Abbreviation/Definition List:

2-Box Model - A RIFM, Inc. proprietary *in silico* tool used to calculate fragrance air exposure concentration
AF - Assessment Factor
BCF - Bioconcentration Factor
CNIH – Confirmation of No Induction in Humans test. A human repeat insult patch test that is performed to confirm an already determined safe use level for fragrance ingredients (Na et al., 2021)
Creme RIFM Model - The Creme RIFM Model uses probabilistic (Monte Carlo) simulations to allow full distributions of data sets, providing a more realistic estimate of aggregate exposure to individuals across a population (Comiskey et al., 2015, 2017; Safford et al., 2015; Safford et al., 2017) compared to a deterministic aggregate approach
DEREK - Derek Nexus is an *in silico* tool used to identify structural alerts
DRF - Dose Range Finding
DST - Dermal Sensitization Threshold
ECHA - European Chemicals Agency
ECOSAR - Ecological Structure-Activity Relationships Predictive Model
EU - Europe/European Union
GLP - Good Laboratory Practice
IFRA - The International Fragrance Association
LOEL - Lowest Observed Effect Level
MOE - Margin of Exposure
MPPD - Multiple-Path Particle Dosimetry. An *in silico* model for inhaled vapors used to simulate fragrance lung deposition
NA - North America
NESIL - No Expected Sensitization Induction Level
NOAEC - No Observed Adverse Effect Concentration
NOAEL - No Observed Adverse Effect Level
NOEC - No Observed Effect Concentration
NOEL - No Observed Effect Level
OECD - Organisation for Economic Co-operation and Development
OECD TG - Organisation for Economic Co-operation and Development Testing Guidelines
PBT - Persistent, Bioaccumulative, and Toxic
PEC/PNEC - Predicted Environmental Concentration/Predicted No Effect Concentration
Perfumery - In this safety assessment, perfumery refers to fragrances made by a perfumer used in consumer products only. The exposures reported in the safety assessment include consumer product use but do not include occupational exposures.
QRA - Quantitative Risk Assessment
QSAR - Quantitative Structure-Activity Relationship
REACH - Registration, Evaluation, Authorisation, and Restriction of Chemicals
RfD - Reference Dose
RIFM - Research Institute for Fragrance Materials
RQ - Risk Quotient
Statistically Significant - Statistically significant difference in reported results as compared to controls with a $p < 0.05$ using appropriate statistical test
TTC - Threshold of Toxicological Concern
UV/Vis spectra - Ultraviolet/Visible spectra
VCF - Volatile Compounds in Food
VoU - Volume of Use
vPvB - (very) Persistent, (very) Bioaccumulative
WoE - Weight of Evidence

The Expert Panel for Fragrance Safety* concludes that this material is safe as described in this safety assessment.

(*continued on next column*)

(*continued*)

This safety assessment is based on the RIFM Criteria Document (Api, 2015), which should be referred to for clarifications.
Each endpoint discussed in this safety assessment includes the relevant data that were available at the time of writing (version number in the top box is indicative of the date of approval based on a 2-digit month/day/year), both in the RIFM Database (consisting of publicly available and proprietary data) and through publicly available information sources (e.g., SciFinder and PubMed). Studies selected for this safety assessment were based on appropriate test criteria, such as acceptable guidelines, sample size, study duration, route of exposure, relevant animal species, most relevant testing endpoints, etc. A key study for each endpoint was selected based on the most conservative endpoint value (e.g., PNEC, NOAEL, LOEL, and NESIL).
*The Expert Panel for Fragrance Safety is an independent body that selects its own members and establishes its own operating procedures. The Expert Panel is comprised of internationally known scientists that provide RIFM with guidance relevant to human health and environmental protection.

Summary: The existing information supports the use of this material as described in this safety assessment.
1-Methylnaphthalene was evaluated for genotoxicity, repeated dose toxicity, reproductive toxicity, local respiratory toxicity, photoirritation/photoallergenicity, skin sensitization, and environmental safety. Data show that 1-methylnaphthalene is not genotoxic. Data on 1-methylnaphthalene provide a calculated Margin of Exposure (MOE) > 100 for the repeated dose toxicity and reproductive toxicity endpoints. The skin sensitization endpoint was completed using the Dermal Sensitization Threshold (DST) for reactive materials (64 μg/cm^2); exposure is below the DST. The photoirritation/photoallergenicity endpoints were evaluated based on ultraviolet/visible (UV/Vis) spectra; 1-methylnaphthalene is not expected to be photoirritating/photoallergenic. The local respiratory toxicity endpoint was evaluated using the Threshold of Toxicological Concern (TTC) for a Cramer Class III material, and the exposure to 1-methylnaphthalene is below the TTC (0.47 mg/day). The environmental endpoints were evaluated; 1-methylnaphthalene was found not to be Persistent, Bioaccumulative, and Toxic (PBT) as per the International Fragrance Association (IFRA) Environmental Standards, and its risk quotients, based on its current volume of use (VoU) in Europe and North America (i.e., Predicted Environmental Concentration/Predicted No Effect Concentration [PEC/PNEC]), are <1.

Human Health Safety Assessment

Genotoxicity: Not genotoxic. (RIFM, 2021c; RIFM, 2021b)
Repeated Dose Toxicity: NOAEL = 83.3 mg/kg/day. MITI (2011)
Reproductive Toxicity: Developmental toxicity NOAEL = 250 mg/kg/day. Fertility NOAEL = 250 mg/kg/day. MITI (2011)
Skin Sensitization: Not a concern for skin sensitization under the declared use levels; exposure is below the DST.
Photoirritation/Photoallergenicity: Not expected to be photoirritating/photoallergenic. (UV/Vis Spectra; RIFM Database)
Local Respiratory Toxicity: No NOAEC available. Exposure is below the TTC.

Environmental Safety Assessment

Hazard Assessment:

Persistence:
Screening-level: 2.81 (BIOWIN 3) (EPI Suite v4.11; US EPA, 2012a)

Bioaccumulation:
Screening-level: 166.1 L/kg (EPI Suite v4.11; US EPA, 2012a)

Ecotoxicity:
Screening-level: Fish LC50: 9.50 mg/L (RIFM Framework; Salvito, 2002)

Conclusion: Not PBT or vPvB as per IFRA Environmental Standards

Risk Assessment:
Screening-level: PEC/PNEC (North America and Europe) < 1 (RIFM Framework; Salvito, 2002)
Critical Ecotoxicity Endpoint: Fish LC50: 9.50 mg/L (RIFM Framework; Salvito, 2002)
RIFM PNEC is: 0.00950 μg/L
- **Revised PEC/PNECs (2019 IFRA VoU):** North America and Europe: Not applicable; cleared at screening-level

1. Identification

1. **Chemical Name:** 1-Methylnaphthalene
2. **CAS Registry Number:** 90-12-0

3. **Synonyms:** α-Methylnaphthalene; Naphthalene, 1-methyl-; Meth naphthalene, 1; 1-Methylnaphthalene
4. **Molecular Formula:** $C_{11}H_{10}$
5. **Molecular Weight:** 142.2 g/mol
6. **RIFM Number:** 6892
7. **Stereochemistry:** No stereoisomer possible.

2. Physical data

1. **Boiling Point:** 249.6 °C (EPI Suite v4.11)
2. **Flash Point:** >200 °F; closed cup (Fragrance Materials Association [FMA]), >93 °C (Globally Harmonized System)
3. **Log K_{OW}:** LogK pdms/w = 3.512 (n = 12) (Xia et al., 2007), 3.72 (EPI Suite), Log Kow = 3.95 (Mackay et al., 1980)
4. **Melting Point**: 22.15 °C (EPI Suite v4.11), −22.0 C (Mackay et al., 1980)
5. **Water Solubility:** 40.62 mg/L (EPI Suite v4.11)
6. **Specific Gravity:** Not Available
7. **Vapor Pressure:** 0.0214 mm Hg at 20 °C (EPI Suite v4.0), 0.005 mm Hg at 20 °C (FMA), 0.0368 mm Hg at 25 °C (EPI Suite v4.11)
8. **UV Spectra:** Minor absorbance between 290 and 700 nm; molar absorption coefficients (118, 159, and 83 L mol^{-1} • cm^{-1} under neutral, acidic, and basic conditions, respectively) are below the benchmark (1000 L mol^{-1} • cm^{-1})
9. **Appearance/Organoleptic:** Not available

3. Volume of use (worldwide band)

1. <0.1 metric ton per year (IFRA, 2019)

4. Exposure to fragrance ingredient (Creme RIFM aggregate exposure model v3.0)

1. **95**th **Percentile Concentration in Fine Fragrance:** 0.000027% (RIFM, 2021a)
2. **Inhalation Exposure*: *:** 0.0000041 mg/kg/day or 0.00031 mg/day (RIFM, 2021a)
3. **Total Systemic Exposure**:** 0.000013 mg/kg/day (RIFM, 2021a)

*95th percentile calculated exposure derived from concentration survey data in the Creme RIFM Aggregate Exposure Model (Comiskey, 2015; Safford et al., 2015a; Safford et al., 2017; and Comiskey, 2017).

**95th percentile calculated exposure; assumes 100% absorption unless modified by dermal absorption data as reported in Section V. It is derived from concentration survey data in the Creme RIFM Aggregate Exposure Model and includes exposure via dermal, oral, and inhalation routes whenever the fragrance ingredient is used in products that include these routes of exposure (Comiskey, 2015; Safford et al., 2015a; Safford et al., 2017; and Comiskey, 2017).

5. Derivation of systemic absorption

1. **Dermal:** Assumed 100%
2. **Oral:** Assumed 100%
3. **Inhalation:** Assumed 100%

6. Computational toxicology evaluation

1. **Cramer Classification:** Class III, High

Expert Judgment	Toxtree v3.1	OECD QSAR Toolbox v4.5 (OECD, 2021)
III	III	III

2. **Analogs Selected**:

a. **Genotoxicity:** None
b. **Repeated Dose Toxicity:** None
c. **Reproductive Toxicity:** None
d. **Skin Sensitization:** None
e. **Phototirritation/Photoallergenicity:** None
f. **Local Respiratory Toxicity:** None
g. **Environmental Toxicity:** None

3. **Read-across Justification:** None

7. Metabolism

No relevant data available for inclusion in this safety assessment.
Additional References:
None.

8. Natural occurrence

1-Methylnaphthalene is reported to occur in the following foods by the VCF*.

Allium species	Lobster
Apple processed (*Malus* species)	Olive (*Olea europaea*)
Capsicum species	Passion fruit (*Passiflora* species)
Crab	Peach (*Prunus persica* L.)
Fish	Tea

*VCF (Volatile Compounds in Food): Database/Nijssen, L.M.; Ingen-Visscher, C.A. van; Donders, J.J.H. (eds). – Version 15.1 – Zeist (The Netherlands): TNO Triskelion, 1963–2014. A continually updated database containing information on published volatile compounds that have been found in natural (processed) food products. Includes FEMA GRAS and EU-Flavis data. This is a partial list.

9. REACH dossier

Available (ECHA, 2011); accessed on 03/15/23.

10. Conclusion

The existing information supports the use of this material as described in this safety assessment.

11. Summary

11.1. Human health endpoint summaries

11.1.1. Genotoxicity

Based on the current existing data, 1-methylnaphthalene does not present a concern for genotoxicity.

11.1.1.1. Risk assessment. The mutagenic activity of 1-methylnaphthalene has been evaluated in a bacterial reverse mutation assay conducted in compliance with GLP regulations and in accordance with OECD TG 471 using the standard plate incorporation method. *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537, and *Escherichia coli* strain WP2uvrA were treated with 1-methylnaphthalene in dimethyl sulfoxide (DMSO) at concentrations up to 5000 μg/plate. No increases in the mean number of revertant colonies were observed at any tested concentration in the presence or absence of S9 (RIFM, 2021c). Under the conditions of the study, 1-methylnaphthalene was not mutagenic in the Ames test.

The clastogenic activity of 1-methylnaphthalene was evaluated in an *in vitro* micronucleus test conducted in compliance with GLP regulations and in accordance with OECD TG 487. Human peripheral blood lymphocytes were treated with 1-methylnaphthalene in DMSO at concentrations up to 1420 μg/mL in the dose range finding (DRF) study; micronuclei analysis was conducted at concentrations up to 150 μg/mL in the presence and absence of metabolic activation. 1-methylnaphthalene did not induce binucleated cells with micronuclei when tested up to the cytotoxic level concentration in either the presence or absence of an S9 activation system (RIFM, 2021b). Under the conditions of the study, 1-methylnaphthalene was considered to be non-clastogenic in the *in vitro* micronucleus test.

Based on the data available, 1-methylnaphthalene does not present a concern for genotoxic potential.

Additional References: None.

Literature Search and Risk Assessment Completed On: 03/10/23.

11.1.2. Repeated dose toxicity

The MOE for 1-methylnaphthalene is adequate for the repeated dose toxicity endpoint at the current level of use.

11.1.2.1. Risk assessment. There are sufficient repeated dose toxicity data on 1-methylnaphthalene. In a GLP and OECD 422-compliant study, 12 Crl:CD (SD) rats/sex/dose were administered 1-methylnaphthalene via gavage at doses of 0, 10, 50, and 250 mg/kg/day. Males were treated for 42 days. Females were treated from 14 days before mating to day 4 of lactation. An additional 5 Crl:CD (SD) rats/sex/dose were maintained for 14 days after the treatment period as recovery groups. No mortality occurred throughout the study period. No treatment-related effects were seen on reflex/reaction, grip strength, locomotor activity, body weight changes, food consumption, urinalysis, hematology, blood biochemistry, gross pathology, or histopathology. Absolute and relative liver weights were increased in males at the high dose, but these effects were reversed after the recovery period. Relative liver weights were increased in females at the high dose and did not reverse after the recovery period. In the absence of correlated histopathological effects, the liver weight changes were not considered adverse. Based on no adverse treatment-related effects seen up to the highest dose, the NOAEL for this study was considered to be 250 mg/kg/day (MITI, 2011).

In a carcinogenicity study (compliance with GLP unclear), 50 B6C3F1 mice/sex/dose were administered 1-methylnaphthalene via diet at concentrations of 0, 0.075, and 0.15% (equivalent to 0, 112.5, and 225 mg/kg/day) for 81 weeks. The examined parameters included clinical signs, body weights, food consumption, hematology, gross pathology, organ weights, histopathology, and biochemistry. There was little mortality throughout the study; 1 control male and 1 high-dose female died of leukemia on weeks 60 and 68, respectively. There were no treatment-related effects on food consumption. Mean body weights were reduced in both sexes at the high dose after 10 weeks, but the difference disappeared after 80 and 72 weeks in males and females, respectively. Brain weight was significantly increased in males only at the low and high doses. Heart weight was significantly decreased in both sexes at the low and high doses. Salivary gland weight was significantly decreased in females only at the low and high doses. Overall, tumors occurred at the following rates: 17/49 control males (34.7%), 14/50 control females (28%), 20/50 low-dose males (40%), 7/50 low-dose females (14%), 18/50 high-dose males (36%), 13/49 high-dose females (26.5%). There were no significant differences in the incidences of these tumors between controls and treatments of either sex. The most frequent site of tumor formation was the lung (bronchiolar/alveolar adenomas and carcinomas). Histological sections revealed that the number of lung tumors counted per mouse was mostly one. The incidence of lung adenomas (but not adenocarcinomas) was significantly increased in males (but not females) at both treated doses. Lung adenoma incidences were: 2/49 control males (4.1%), 4/50 control females (8%), 13/50 low-dose males (26%), 2/50 low-dose females (4%), 12/50 high-dose males (24%), and 4/50 high-dose females (8%). After the lungs, the next most frequent site of tumor formation was the liver (adenomas, hepatocellular carcinomas, and hemangiomas), but the number of liver tumors was not significantly different between the control and treated groups. Monocytes were significantly increased in both sexes at the low and high doses. Hemoglobin (Hb), mean corpuscular hemoglobin (MCH), and MCH concentration (MCHC) were significantly increased in females at the low and high doses. Total lipid, phospholipid, and neutral fat were increased in both sexes at the low and high doses. Based on organ weight changes and hematological changes at the lowest dose, the LOAEL for this study was considered to be 112.5 mg/kg/day, but a NOAEL was not derived due to the use of only 2 treatment doses, and the narrow spacing of those doses in the carcinogenicity study (Murata et al., 1993).

Because the dose spacing of the 81-week study was too narrow to draw a robust NOAEL from, the NOAEL was obtained from the OECD 422-compliant study. A default safety factor of 3 was used when deriving a NOAEL from an OECD 422 study (ECHA, 2012). The safety factor has been approved by the Expert Panel for Fragrance Safety*. The derived NOAEL for the repeated dose toxicity data is 250/3 or 83.3 mg/kg/day.

The 1-methylnaphthalene MOE for the repeated dose toxicity endpoint can be calculated by dividing the 1-methylnaphthalene NOAEL in mg/kg/day by the total systemic exposure to 1-methylnaphthalene, 83.3/0.000013, or 6407692.

In addition, the total systemic exposure to 1-methylnaphthalene (0.013 μg/kg/day) is below the TTC (1.5 μg/kg/day; Kroes et al., 2007) for the repeated dose toxicity endpoint of a Cramer Class III material at the current level of use.

*The Expert Panel for Fragrance Safety is composed of scientific and technical experts in their respective fields. This group provides advice and guidance.

Additional References: None.

Literature Search and Risk Assessment Completed On: 02/22/23.

11.1.3. Reproductive toxicity

The MOE for 1-methylnaphthalene is adequate for the reproductive toxicity endpoint at the current level of use.

11.1.3.1. Risk assessment. There are sufficient reproductive toxicity data on 1-methylnaphthalene. An OECD 422/GLP combined repeated dose toxicity study with reproduction/developmental toxicity screening test was conducted in Crl:CD (SD) rats. Groups of 12 rats/sex/dose were exposed to the test material 1-methylnaphthalene at doses of 0, 10, 50, or 250 in olive oil via oral gavage. Rats were treated for 14 days pre-mating, during mating, and for females up to 4 days of lactation. An additional 5 Crl:CD (SD) rats/sex/dose were maintained for 14 days after the treatment period as recovery groups. No treatment-related mortality was observed. No treatment-related effects were observed in the estrous cycle, copulation index, fertility index, or pairing days until copulation. Histopathological examination at the end of the administration period showed no abnormalities due to the test material for males and females. No adverse effects were observed in any

developmental toxicity parameters at any dose groups. No external abnormality or macroscopic finding was detected in any pups at the necropsy. Thus, the NOAEL for developmental toxicity and fertility was considered to be 250 mg/kg/day, the highest dose tested (MITI, 2011).

The 1-methylnaphthalene MOE for the reproductive toxicity endpoint can be calculated by dividing the 1-methylnaphthalene NOAEL in mg/kg/day by the total systemic exposure to 1-methylnaphthalene, 250/0.000013, or 19230769.

In addition, the total systemic exposure to 1-methylnaphthalene (0.013 μg/kg/day) is below the TTC (1.5 μg/kg/day; Kroes et al., 2007; Laufersweiler et al., 2012) for the reproductive toxicity endpoint of a Cramer Class III material at the current level of use.

Additional References: None.

Literature Search and Risk Assessment Completed On: 02/28/23.

11.1.4. Skin sensitization

Based on the application of DST, 1-methylnaphthalene does not present a safety concern for skin sensitization under the current declared levels of use.

11.1.4.1. Risk assessment. No skin sensitization data are available for 1-methylnaphthalene (Table 1). 1-Methylnaphthalene is predicted *in silico* to be non-reactive with skin proteins directly (Roberts et al., 2007; Toxtree v3.1.0; OECD Toolbox v4.5); however, this material was determined to be reactive to skin proteins by expert judgment. Acting conservatively due to the absence of data, the reported exposure was benchmarked utilizing the reactive DST of 64 μg/cm^2 (Safford, 2008; Safford et al., 2011; Roberts et al., 2015; Safford et al., 2015b). The current exposure from the 95th percentile concentration is below the DST for reactive materials when evaluated in all QRA categories. Table 2 provides the supported concentrations for 1-methylnaphthalene that present no appreciable risk for skin sensitization based on the reactive DST. These levels represent supported concentrations based on the DST approach. However, additional studies may show it could be used at higher levels.

Additional References: None.

Literature Search and Risk Assessment Completed On: 03/02/23.

11.1.5. Photoirritation/photoallergenicity

Based on the available UV/Vis absorption spectra, 1-methylnaphthalene would not be expected to present a concern for photoirritation or photoallergenicity.

11.1.5.1. Risk assessment. There are no photoirritation studies available for 1-methylnaphthalene in experimental models. UV/Vis absorption spectra indicate minor absorption between 290 and 700 nm. The corresponding molar absorption coefficient is below the benchmark of concern for photoirritation and photoallergenicity (Henry et al., 2009). Based on the lack of absorbance, 1-methylnaphthalene does not present a concern for photoirritation or photoallergenicity.

11.1.6. UV spectra analysis

UV/Vis absorption spectra (OECD TG 101) were obtained. The spectra indicate no absorbance in the range of 290–700 nm. The molar absorption coefficients (118, 159, 83 L mol^{-1} • cm^{-1} under neutral, acidic, and basic conditions, respectively) are below the benchmark of concern for photoirritating and photoallergenic effects, 1000 L mol^{-1} • cm^{-1} (Henry et al., 2009).

Table 1
Summary of existing data on 1-methylnaphthalene.

WoE Skin Sensitization Potency Category[1]	Human Data				Animal Data		
	NOEL-CNIH (induction) μg/cm²	NOEL-HMT (induction) μg/cm²	LOEL (induction) μg/cm²	WoE NESIL μg/cm²	LLNA Weighted Mean EC3 Value μg/cm²	GPMT	Buehler
Human potency category unknown; Current exposure level below the DST for reactive materials.	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	In vitro Data				*In silico* protein binding alerts (OECD Toolbox v4.5)		
	KE 1	KE 2	KE 3		Target Material	Autoxidation simulator	Metabolism simulator
	N/A	N/A	N/A		No alert found	No alert found	No alert found

NOEL = No observed effect level; CNIH = Confirmation of No Induction in Humans; GPMT = Guinea Pig Maximization Test; HMT = Human Maximization Test; LOEL = lowest observed effect level; KE = Key Event; N/A = Not Available.

[1]WoE Skin Sensitization Potency Category is only applicable for identified sensitizers with sufficient data, based on collective consideration of all available data (Na et al., 2021).

Table 2
Supported concentrations for 1-methylnaphthalene that present no appreciable risk for skin sensitization based on reactive DST.

IFRA Category[a]	Description of Product Type	Supported Concentrations[b] (%) in Finished Products Based on Reactive DST	Reported 95th Percentile Use Concentrations in Finished Products
1	Products applied to the lips	0.0049	2.1×10^{-5}
2	Products applied to the axillae	0.0015	3.0×10^{-5}
3	Products applied to the face using fingertips	0.029	1.3×10^{-5}
4	Fine fragrance products	0.027	2.7×10^{-5}
5	Products applied to the face and body using the hands (palms), primarily leave-on	0.0070	3.1×10^{-5}
6	Products with oral and lip exposure	0.016	NRU[d]
7	Products applied to the hair with some hand contact	0.056	3.6×10^{-7}
8	Products with significant ano-genital exposure	0.0029	No Data[c]
9	Products with body and hand exposure, primarily rinse-off	0.054	8.7×10^{-6}
10	Household care products with mostly hand contact	0.19	7.5×10^{-5}
11	Products with intended skin contact but minimal transfer of fragrance to skin from inert substrate	0.11	No Data[c]
12	Products not intended for direct skin contact, minimal or insignificant transfer to skin	Not restricted	0.0068

[a] For a description of the categories, refer to the IFRA/RIFM Information Booklet.
[b] These levels represent maximum acceptable concentrations based on the DST. However, additional studies may show it could be used at higher levels.
[c] Fragrance exposure from these products is very low. These products are not currently in the Creme RIFM Aggregate Exposure Model.
[d] No reported use.

Additional References: None.

Literature Search and Risk Assessment Completed On: 02/21/23.

11.1.7. Local Respiratory Toxicity

The MOE could not be calculated due to a lack of appropriate data. The exposure level for 1-methylnaphthalene is below the Cramer Class III TTC value for inhalation exposure local effects.

11.1.7.1. Risk assessment. There are no inhalation data available on 1-methylnaphthalene. Based on the Creme RIFM Model, the inhalation exposure is 0.00031 mg/day. This exposure is 1516 times lower than the Cramer Class III TTC value of 0.47 mg/day (based on human lung weight of 650 g; Carthew et al., 2009); therefore, the exposure at the current level of use is deemed safe.

Additional References: Meng et al., 2011; Dodd et al., 2012.

Literature Search and Risk Assessment Completed On: 03/08/23.

11.2. Environmental endpoint summary

11.2.1. Screening-level assessment

A screening-level risk assessment of 1-methylnaphthalene was performed following the RIFM Environmental Framework (Salvito, 2002), which provides 3 tiered levels of screening for aquatic risk. In Tier 1, only the material's regional VoU, its log K_{OW}, and its molecular weight are needed to estimate a conservative risk quotient (RQ), expressed as the ratio of Predicted Environmental Concentration/Predicted No Effect Concentration (PEC/PNEC). A general QSAR with a high uncertainty factor applied is used to predict fish toxicity, as discussed in Salvito et al. (2002). In Tier 2, the RQ is refined by applying a lower uncertainty factor to the PNEC using the ECOSAR model (US EPA, 2012b), which provides chemical class-specific ecotoxicity estimates. Finally, if necessary, Tier 3 is conducted using measured biodegradation and ecotoxicity data to refine the RQ, thus allowing for lower PNEC uncertainty factors. The data for calculating the PEC and PNEC for this safety assessment are provided in the table below. For the PEC, the range from the most recent IFRA VoU Survey is reviewed. The PEC is then calculated using the actual regional tonnage, not the extremes of the range. Following the RIFM Environmental Framework, 1-methylnaphthalene was identified as a fragrance material with no potential to present a possible risk to the aquatic environment (i.e., its screening-level PEC/PNEC <1).

A screening-level hazard assessment using EPI Suite v4.11 (US EPA, 2012a) did not identify 1-methylnaphthalene as possibly being persistent or bioaccumulative based on its structure and physical–chemical properties. This screening-level hazard assessment considers the potential for a material to be persistent *and* bioaccumulative *and* toxic or very persistent *and* very bioaccumulative as defined in the Criteria Document (Api, 2015). As noted in the Criteria Document, the screening criteria applied are the same as those used in the EU for REACH (ECHA, 2017). For persistence, if the EPI Suite model BIOWIN 3 predicts a value < 2.2 and either BIOWIN 2 or BIOWIN 6 predicts a value < 0.5, then the material is considered potentially persistent. A material would be considered potentially bioaccumulative if the EPI Suite model BCFBAF predicts a fish BCF $\geq$2000 L/kg. Ecotoxicity is determined in the above screening-level risk assessment. If, based on these model outputs (Step 1), additional assessment is required, a WoE-based review is then performed (Step 2). This review considers available data on the material's physical–chemical properties, environmental fate (e.g., OECD Guideline biodegradation studies or die-away studies), fish bioaccumulation, and higher-tier model outputs (e.g., US EPA's BIOWIN and BCFBAF found in EPI Suite v4.11).

11.2.1.1. Risk assessment. Based on the current VoU (2019), 1-methylnaphthalene presents no risk to the aquatic compartment in the screening-level assessment.

11.2.1.2. Key studies. ***Biodegradation***:
No data available.
Ecotoxicity:
No data available.

11.2.1.3. Other available data. 1-Methylnaphthalene has been registered for REACH, with no additional information available at this time.

11.2.1.4. Risk assessment refinement. Ecotoxicological data and PNEC derivation (all endpoints reported in mg/L; PNECs in μg/L).

Endpoints used to calculate PNEC are underlined.

	LC50 (Fish) (mg/L)	EC50 (*Daphnia*) (mg/L)	EC50 (Algae) (mg/L)	AF	PNEC (μg/L)	Chemical Class
RIFM Framework Screening-level **(Tier 1)**	9.50			1000000	0.00950	

Exposure information and PEC calculation (following RIFM Environmental Framework: Salvito et al., 2002).

Exposure	Europe (EU)	North America (NA)
Log K_{OW} Used	3.50	3.50
Biodegradation Factor Used	0	0
Dilution Factor	3	3
Regional VoU Tonnage Band	<1	<1
Risk Characterization: PEC/PNEC	**<1**	**<1**

Based on available data, the RQ for this material is < 1. No further assessment is necessary.

The RIFM PNEC is 0.00950 μg/L. The revised PEC/PNECs for EU and NA are not applicable. The material was cleared at the screening-level; therefore, it does not present a risk to the aquatic environment at the current reported VoU.

Literature Search and Risk Assessment Completed On: 03/07/23.

12. Literature Search*

- **RIFM Database:** Target, Fragrance Structure-Activity Group materials, other references, JECFA, CIR, SIDS
- **ECHA:** https://echa.europa.eu/
- **NTP:** https://ntp.niehs.nih.gov/
- **OECD Toolbox:** https://www.oecd.org/chemicalsafety/risk-assessment/oecd-qsar-toolbox.htm
- **SciFinder:** https://scifinder.cas.org/scifinder/view/scifinder/scifinderExplore.jsf
- **PubChem:** https://pubchem.ncbi.nlm.nih.gov/
- **PubMed:** https://www.ncbi.nlm.nih.gov/pubmed
- **National Library of Medicine Technical Bulletin:** https://www.nlm.nih.gov/pubs/techbull/nd19/nd19_toxnet_new_locations.html
- **IARC:** https://monographs.iarc.fr
- **OECD SIDS:** https://hpvchemicals.oecd.org/ui/Default.aspx
- **EPA ACToR:** https://actor.epa.gov/actor/home.xhtml
- **US EPA ChemView:** https://chemview.epa.gov/chemview/
- **Japanese NITE:** https://www.nite.go.jp/en/chem/chrip/chrip_search/systemTop
- **Japan Existing Chemical Data Base (JECDB):** http://dra4.nihs.go.jp/mhlw_data/jsp/SearchPageENG.jsp
- **Google:** https://www.google.com
- **ChemIDplus:** https://pubchem.ncbi.nlm.nih.gov/source/ChemIDplus

Search keywords: CAS number and/or material names.

*Information sources outside of RIFM's database are noted as appropriate in the safety assessment. This is not an exhaustive list. The links listed above were active as of 08/31/23.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper. We wish to confirm that there are no known conflicts of interest associated with this publication and there has been no significant financial support for this work that could have influenced its outcome. RIFM staff are employees of the Research Institute for Fragrance Materials, Inc. (RIFM). The Expert Panel receives a small honorarium for time spent reviewing the subject work.

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