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# RIFM fragrance ingredient safety assessment, hexanoic acid, 6-(acetyloxy)-, ethyl ester, CAS Registry Number 104986-28-9

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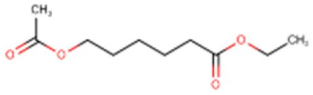
**Name**: Hexanoic acid, 6-(acetyloxy)-, ethyl ester
**CAS Registry Number**: 104986-28-9



**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
**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., 2015a; 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 Observable Effect Level

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**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.**
This safety assessment is based on the RIFM Criteria Document (Api et al., 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.**
Hexanoic acid, 6-(acetyloxy)-, ethyl ester was evaluated for genotoxicity, repeated dose toxicity, reproductive toxicity, local respiratory toxicity, phototoxicity/photoallergenicity, skin sensitization, and environmental safety. Data show that hexanoic acid, 6-(acetyloxy)-, ethyl ester is not genotoxic. Data on hexanoic acid, 6-(acetyloxy)-, ethyl ester provide a calculated MOE $> 100$ for the repeated dose toxicity endpoint. The reproductive and local respiratory toxicity endpoints were evaluated using the TTC for a Cramer Class I material, and the exposure to hexanoic acid, 6-(acetyloxy)-, ethyl ester is below the TTC (0.03 mg/kg/day, and 1.4 mg/day, respectively). Data show that there are no safety concerns for hexanoic acid, 6-(acetyloxy)-, ethyl ester for skin sensitization under the current declared levels of use. The phototoxicity/photoallergenicity endpoints were evaluated based on UV spectra; hexanoic acid, 6-(acetyloxy)-, ethyl ester is not expected to be phototoxic/photoallergenic. The environmental endpoints were evaluated; hexanoic acid, 6-(acetyloxy)-, ethyl ester was found not to be PBT as per the IFRA Environmental Standards, and its risk quotients, based on its current volume of use in Europe and North America (i.e., PEC/PNEC), are $< 1$.

**Human Health Safety Assessment**

| | |
|---|---|
| **Genotoxicity**: Not genotoxic. | (RIFM, 2018; RIFM, 1993b) |
| **Repeated Dose Toxicity:** NOAEL = 100 mg/kg/day. | RIFM (1993h) |
| **Reproductive Toxicity:** No NOAEL available. Exposure is below the TTC. | |
| **Skin Sensitization:** Not a concern for skin sensitization at the current, declared levels of use. | RIFM (1986b) |
| **Phototoxicity/Photoallergenicity:** Not expected to be phototoxic/photoallergenic. | (UV Spectra, RIFM Database) |
| **Local Respiratory Toxicity:** No NOAEC available. Exposure is below the TTC. | |

**Environmental Safety Assessment**

| | |
|---|---|
| **Hazard Assessment:** | |
| **Persistence:** Critical Measured Value: 100% (OECD 301C) | RIFM (1993e) |
| **Bioaccumulation:** Screening-level: 16.99 L/kg | (EPI Suite v4.11; US EPA, 2012a) |
| **Ecotoxicity:** Screening-level: Fish LC50: 272.8 mg/L | (RIFM Framework; Salvito et al., 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 et al., 2002) |
| **Critical Ecotoxicity Endpoint:** Fish LC50: 272.8 mg/L | (RIFM Framework; Salvito et al., 2002) |
| **RIFM PNEC is:** 0.2728 μg/L | |

- Revised PEC/PNECs (2015 IFRA VoU): North America and Europe: not applicable; cleared at screening-level

## 1. Identification

1. **Chemical Name:** Hexanoic acid, 6-(acetyloxy)-, ethyl ester
2. **CAS Registry Number:** 104986-28-9
3. **Synonyms:** Ethyl 6-acetoxyhexanoate; Berryflor; Hexanoic acid, 6-(acetyloxy)-, ethyl ester
4. **Molecular Formula:** $C_{10}H_{18}O_4$
5. **Molecular Weight:** 202.25
6. **RIFM Number:** 6323
7. **Stereochemistry:** Stereoisomer not specified. No stereocenter present and no stereoisomer possible.

## 2. Physical data

1. **Boiling Point:** 114 °C at 1000 Pa (RIFM, 1993a), 226.14 °C (EPI Suite)
2. **Flash Point:** > 93 °C (Globally Harmonized System)
3. **Log $K_{OW}$:** log $P_{ow}$ = 2.0 (RIFM, 1993a), 2.37 (EPI Suite), Log $P_{ow}$ = 1.82 (RIFM, 1989)
4. **Melting Point**: < 20 °C (RIFM, 1993a), −48.83 °C (EPI Suite)
5. **Water Solubility:** 403.8 mg/L (EPI Suite)
6. **Specific Gravity:** 1.008 g/mL at 20 °C (RIFM, 1993e), 1.008 g/L at 20 °C (RIFM, 1993a)
7. **Vapor Pressure:** 0.0955 mm Hg @ 25 °C (EPI Suite), 0.0624 mm Hg @ 20 °C (EPI Suite v4.0)
8. **UV Spectra:** No significant absorbance between 290 and 700 nm; molar absorption coefficient is below the benchmark (1000 L $mol^{-1} \cdot cm^{-1}$)
9. **Appearance/Organoleptic:** Not Available

## 3. Exposure

1. **Volume of Use (worldwide band):** 1–10 metric tons per year (IFRA, 2015)
2. **95**th **Percentile Concentration in Hydroalcoholics:** 0.26% (RIFM, 2017)
3. **Inhalation Exposure*:** 0.00048 mg/kg/day or 0.037 mg/day (RIFM, 2017)
4. **Total Systemic Exposure**:** 0.0053 mg/kg/day (RIFM, 2017)

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

**95th percentile calculated exposure; assumes 100% absorption unless modified by dermal absorption data as reported in Section IV. 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 et al., 2015; Safford et al., 2015; Safford et al., 2017; and Comiskey et al., 2017).

## 4. Derivation of systemic absorption

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

## 5. Computational toxicology evaluation

1. **Cramer Classification:** Class I, Low

| Expert Judgment | Toxtree v 2.6 | OECD QSAR Toolbox v 3.2 |
|---|---|---|
| I | I | I |

2. Analogs Selected:
   a. **Genotoxicity:** None
   b. **Repeated Dose Toxicity:** None
   c. **Reproductive Toxicity:** None
   d. **Skin Sensitization:** None
   e. **Phototoxicity/Photoallergenicity:** None
   f. **Local Respiratory Toxicity:** None
   g. **Environmental Toxicity:** None
3. **Read-across Justification:** None

## 6. Metabolism

Not considered for this risk assessment and therefore not reviewed except where it may pertain in specific endpoint sections as discussed below.

## 7. Natural occurrence (discrete chemical) or composition (NCS)

Hexanoic acid, 6-(acetyloxy)-, ethyl ester is not reported to occur in foods by the VCF*.

*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.

## 8. REACH dossier

Hexanoic acid, 6-(acetyloxy)-, ethyl ester has been pre-registered for 2018; no dossier available as of 04/16/20.

## 9. Conclusion

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

## 10. Summary

### *10.1. Human health endpoint summaries*

#### *10.1.1. Genotoxicity*

Based on the current existing data, hexanoic acid, 6-(acetyloxy)-, ethyl ester does not present a concern for genotoxicity.

*10.1.1.1. Risk assessment.* The mutagenic activity of hexanoic acid, 6-(acetyloxy)-, ethyl ester has been evaluated in a bacterial reverse mutation assay conducted in compliance with GLP regulations and in accordance with OECD TG 471 using the preincubation method. *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537, and *Escherichia coli* strain WP2uvrA were treated with hexanoic acid, 6-(acetyloxy)-, ethyl ester 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, 2018). Under the conditions of the study, hexanoic acid, 6-(acetyloxy)-, ethyl ester was not mutagenic in the Ames test.

The clastogenicity of hexanoic acid, 6-(acetyloxy)-, ethyl ester was assessed in an *in vitro* chromosome aberration study conducted in compliance with GLP regulations and equivalent to OECD TG 473. Chinese hamster ovary cells were treated with hexanoic acid, 6-(acetyloxy)-, ethyl ester in DMSO at concentrations up to 1600 μg/mL in the presence and absence of metabolic activation. No statistically significant increases in the frequency of cells with structural chromosomal aberrations or polyploid cells were observed with any concentration of the test material, either with or without S9 metabolic activation (RIFM, 1993b). Under the conditions of the study, hexanoic acid, 6-(acetyloxy)-, ethyl ester was considered to be non-clastogenic in the *in vitro* chromosome aberration assay.

Based on the data available, hexanoic acid, 6-(acetyloxy)-, ethyl ester does not present a concern for genotoxic potential.

**Additional References:** RIFM, 1987b.

**Literature Search and Risk Assessment Completed On:** 04/18/19.

*10.1.2. Repeated dose toxicity*

The MOE for hexanoic acid, 6-(acetyloxy)-, ethyl ester is adequate for the repeated dose toxicity endpoint at the current level of use.

*10.1.2.1. Risk assessment.* In a 28-day non-guideline and GLP-compliant oral toxicity study groups of 6 RORO SPF Albino rats/sex/group were administered hexanoic acid, 6-(acetyloxy)-, ethyl ester through gavage at doses of 0 (vehicle control: rape oil), 100, 300, and 900 mg/kg/day. A recovery group of 4 animals/sex was maintained for 11 days following 900 mg/kg/day treatment. No treatment-related mortalities were reported. In addition, no treatment-related changes were reported in urinalysis, hematology, histopathology, or bodyweight analysis. However, a 15% increase in average liver weight per 100 g body weight was reported in females receiving the highest dose. Since no histopathological alterations were reported in the liver, the increase in liver weight was attributed to increased metabolic load resulting from a high oral dose. Based on the alteration in female liver weight in the high-dose group, the NOAEL for repeated dose toxicity was considered to be 300 mg/kg/day (RIFM, 1993h).

In the absence of a chronic, 90-day study, a default safety factor of 3 was used when deriving a NOAEL from the 28-day 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 considered 300/3 or 100 mg/kg/day for the repeated dose toxicity endpoint.

Therefore, the MOE can be calculated by dividing the NOAEL for hexanoic acid, 6-(acetyloxy)-, ethyl ester by the total systemic exposure, 100/0.0053 or 18868.

In addition, the total systemic to hexanoic acid, 6-(acetyloxy)-, ethyl ester (5.3 μg/kg/day) is below the TTC (30 μg/kg/day; Kroes et al., 2007) for the repeated dose toxicity endpoint of a Cramer Class I 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:** 03/28/19.

*10.1.3. Reproductive toxicity*

There are insufficient reproductive toxicity data on hexanoic acid, 6-(acetyloxy)-, ethyl ester or on any read-across materials. The total systemic exposure to hexanoic acid, 6-(acetyloxy)-, ethyl ester is below the TTC for the reproductive toxicity endpoint of a Cramer Class I material at the current level of use.

*10.1.3.1. Risk assessment.* There are insufficient reproductive toxicity data on hexanoic acid, 6-(acetyloxy)-, ethyl ester or on any read-across materials that can be used to support the reproductive toxicity endpoint. The total systemic exposure to hexanoic acid, 6-(acetyloxy)-, ethyl ester (5.3 μg/kg/day) is below the TTC (30 μg/kg/day; Kroes et al., 2007; Laufersweiler et al., 2012) for the reproductive toxicity endpoint of a Cramer Class I material at the current level of use.

**Additional References:** RIFM, 1993h.bib_RIFM_1993h

**Literature Search and Risk Assessment Completed On:** 03/27/19.

*10.1.4. Skin sensitization*

Based on the existing data, hexanoic acid, 6-(acetyloxy)-, ethyl ester does not present a concern for skin sensitization under the current, declared levels of use.

*10.1.4.1. Risk assessment.* Based on the existing data, hexanoic acid, 6-(acetyloxy)-, ethyl ester is not considered a skin sensitizer. The chemical structure of this material indicates that it would not be expected to react with skin proteins (Roberts et al., 2007; Toxtree 3.1.0; OECD Toolbox v4.2). In Freund's Complete Adjuvant Test (FCAT), hexanoic acid, 6-(acetyloxy)-, ethyl ester did not present reactions indicative of sensitization up to 100% (RIFM, 1986a). In a guinea pig open epicutaneous test (OET), hexanoic acid, 6-(acetyloxy)-, ethyl ester did not present reactions indicative of sensitization up to 100% (RIFM, 1986b). In a confirmatory human repeat insult patch test (HRIPT) with 10% (5000 μg/cm$^2$) of hexanoic acid, 6-(acetyloxy)-, ethyl ester in an unspecified vehicle, no reactions indicative of sensitization were observed in any of the 59 volunteers (RIFM, 1987a).

Based on the WoE from structural analysis and animal and human studies, hexanoic acid, 6-(acetyloxy)-, ethyl ester does not present a concern for skin sensitization under the current, declared levels of use.

**Additional References:** None.

**Literature Search and Risk Assessment Completed On:** 03/05/19.

*10.1.5. Phototoxicity/photoallergenicity*

Based on the available UV/Vis spectra, hexanoic acid, 6-(acetyloxy)-, ethyl ester would not be expected to present a concern for phototoxicity or photoallergenicity.

*10.1.5.1. Risk assessment.* There are no phototoxicity studies available for hexanoic acid, 6-(acetyloxy)-, ethyl ester in experimental models. UV/Vis absorption spectra indicate no significant absorption between 290 and 700 nm. The corresponding molar absorption coefficient is well below the benchmark of concern for phototoxicity and photoallergenicity (Henry et al., 2009). Based on the lack of absorbance, hexanoic acid, 6-(acetyloxy)-, ethyl ester does not present a concern for phototoxicity or photoallergenicity.

*10.1.5.2. UV spectra analysis.* UV/Vis absorption spectra (OECD TG 101) were obtained. The spectra indicate no significant absorbance in the range of 290–700 nm. The molar absorption coefficient is below the benchmark of concern for phototoxic effects, 1000 L mol$^{-1}$ · cm$^{-1}$ (Henry et al., 2009).

**Additional References:** None.

**Literature Search and Risk Assessment Completed On:** 04/03/19.

*10.1.6. Local Respiratory Toxicity*

The MOE could not be calculated due to a lack of appropriate data. The exposure level for hexanoic acid, 6-(acetyloxy)-, ethyl ester is below the Cramer Class I TTC value for inhalation exposure local effects.

*10.1.6.1. Risk assessment.* There are insufficient inhalation data available on hexanoic acid, 6-(acetyloxy)-, ethyl ester. Based on the Creme RIFM Model, the inhalation exposure is 0.037 mg/day. This exposure is 37.8 times lower than the Cramer Class I TTC value of 1.4 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:** None.

**Literature Search and Risk Assessment Completed On:** 04/04/19.

*10.2. Environmental endpoint summary*

*10.2.1. Screening-level assessment*

A screening-level risk assessment of hexanoic acid, 6-(acetyloxy)-, ethyl ester was performed following the RIFM Environmental Framework (Salvito et al., 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 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 Volume of Use Survey is reviewed. The PEC is then calculated using the actual regional tonnage, not the extremes of the range. Following the RIFM Environmental Framework, hexanoic acid, 6-(acetyloxy)-, ethyl ester 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 hexanoic acid, 6-(acetyloxy)-, ethyl ester as possibly 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 et al., 2015). As noted in the Criteria Document, the screening criteria applied are the same as those used in the EU for REACH (ECHA, 2012). 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 ≥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). Data on persistence and bioaccumulation are reported below and summarized in the Environmental Safety Assessment section prior to Section 1.

*10.2.2. Risk assessment*

Based on current VoU (IFRA, 2015), hexanoic acid, 6-(acetyloxy)-, ethyl ester presents no risk to the aquatic compartment in the screening-level assessment.

*10.2.3. Key studies*

*10.2.3.1. Biodegradation.* RIFM, 1993e: The ready biodegradability of the test material was evaluated using the respirometric method (modified MITI Test I) according to the OECD guideline 301C. Biodegradation of 100% was observed after 28 days.

*10.2.3.2. Ecotoxicity.* RIFM, 1993c: A 96-h fish (*Oncorhynchus mykiss*) acute toxicity test was conducted according to the OECD 203 method under continuous flow conditions. Based on the mean measured concentration, the LC50 value was reported to be 15.1 mg/L.

RIFM, 1993d: The activated sludge respiration inhibition test was performed on the test material according to the OECD 209 method. The EC50 value was reported to be 2000–3000 mg/L.

RIFM, 1993f: A *Daphnia magna* acute immobilization test was conducted according to the OECD TG 202 method under static conditions. Based on the mean measured concentration, the 48-h EC50 value was reported to be 33.5 mg/L.

RIFM, 1993g: An algae growth inhibition test was conducted according to the OECD 201 method. The 72-h EC50 based growth rate was reported to be 166 mg/L (95% CI: 125–224 mg/L).

*10.2.4. Other available data*

Hexanoic acid, 6-(acetyloxy)-, ethyl ester has been pre-registered for REACH with no additional data at this time.

*10.2.5. Risk assessment refinement*

Since hexanoic acid, 6-(acetyloxy)-, ethyl ester has passed the screening criteria, measured data is included for completeness only and has not been used in PNEC derivation.

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)** | 272.8 | | | 1000000 | 0.2728 | |

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

| Exposure | Europe (EU) | North America (NA) |
|---|---|---|
| Log $K_{ow}$ Used | 2.0 | 2.0 |
| Biodegradation Factor Used | 0 | 0 |
| Dilution Factor | 3 | 3 |
| Regional Volume of Use Tonnage Band | < 1 | < 1 |
| **Risk Characterization: PEC/PNEC** | **< 1** | **< 1** |

The RIFM PNEC is 0.2728 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 volumes of use.

**Literature Search and Risk Assessment Completed On:** 03/07/19.

## 11. 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**
- **SciFinder:** https://scifinder.cas.org/scifinder/view/scifinder/scifinderExplore.jsf
- **PubMed:** https://www.ncbi.nlm.nih.gov/pubmed
- **National Library of Medicine's Toxicology Information Services:**

https://toxnet.nlm.nih.gov/
- **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 HPVIS:** https://ofmpub.epa.gov/oppthpv/public_search.publicdetails?submission_id=24959241&ShowComments=Yes&sqlstr=null&recordcount=0&User_title=DetailQuery%20Results&EndPointRpt=Y#submission
- **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://chem.nlm.nih.gov/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 04/16/20.

## 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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