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# RIFM fragrance ingredient safety assessment, pinocarvyl acetate, CAS Registry Number 1078-95-1

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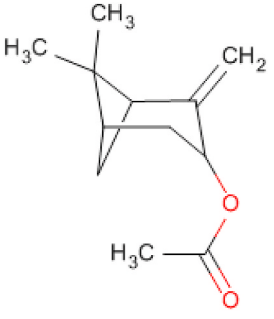
**Name**: Pinocarvyl acetate
**CAS Registry Number**: 1078-95-1

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**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., 2020)
**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.,

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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
**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.**

Pinocarvyl acetate was evaluated for genotoxicity, repeated dose toxicity, reproductive toxicity, local respiratory toxicity, phototoxicity/photoallergenicity, skin sensitization, and environmental safety. Data show that pinocarvyl acetate is not genotoxic. The repeated dose, reproductive, and local respiratory toxicity endpoints were evaluated using the Threshold of Toxicological Concern (TTC) for a Cramer Class I material, and the exposure to pinocarvyl acetate is below the TTC (0.03 mg/kg/day, 0.03 mg/kg/day, and 1.4 mg/day, respectively). Data provided pinocarvyl acetate a No Expected Sensitization Induction Level (NESIL) of 550 μg/cm$^2$ for the skin sensitization endpoint. The phototoxicity/photoallergenicity endpoints were evaluated based on UV/Vis spectra; pinocarvyl acetate is not expected to be phototoxic/photoallergenic. The environmental endpoints were evaluated; pinocarvyl acetate 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 in Europe and North America (i.e., Predicted Environmental Concentration/Predicted No Effect Concentration [PEC/PNEC]), are <1.

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**Human Health Safety Assessment**

| | |
|---|---|
| **Genotoxicity:** Not genotoxic. | (RIFM, 2018; RIFM, 2019) |
| **Repeated Dose Toxicity:** No NOAEL available. Exposure is below TTC. | |
| **Reproductive Toxicity:** No NOAEL available. Exposure is below the TTC. | |
| **Skin Sensitization:** NESIL = 550 μg/cm$^2$. | RIFM (2013a) |
| **Phototoxicity/Photoallergenicity:** Not expected to be phototoxic/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: 2.7 (BIOWIN 3) | (EPI Suite v4.11; US EPA, 2012a) |
| **Bioaccumulation**: Screening-level: 152.6 L/kg | (EPI Suite v4.11; US EPA, 2012a) |
| **Ecotoxicity:** Screening-level: Fish LC50: 6.98 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: 6.98 mg/L | (RIFM Framework; Salvito et al., 2002) |

**RIFM PNEC is:** 0.00698 μg/L

- **Revised PEC/PNECs (2015 IFRA VoU):** North America and Europe: Not Applicable; Cleared at screening-level

## 1. Identification

1. **Chemical Name:** Pinocarvyl acetate
2. **CAS Registry Number:** 1078-95-1
3. **Synonyms:** Bicyclo[3.1.1]heptan-3-ol, 6,6-dimethyl-2-methylene-, acetate; Sylvestryl acetate; 6,6-Dimethyl-2-methylenebicyclo[3.1.1]hept-3-yl acetate; Pinocarvyl acetate
4. **Molecular Formula:** $C_{12}H_{18}O_2$
5. **Molecular Weight:** 194.27
6. **RIFM Number:** 1205
7. **Stereochemistry:** Isomer not specified. Three stereocenters present and 2 stereoisomers possible.

## 2. Physical data

1. **Boiling Point:** >204 °C (Fragrance Materials Association [FMA]), 231.06 °C (EPI Suite)
2. **Flash Point:** 183 °F; CC (FMA)
3. **Log $K_{OW}$:** 3.81 (EPI Suite)
4. **Melting Point**: 38.44 °C (EPI Suite)
5. **Water Solubility:** 25.86 mg/L (EPI Suite)
6. **Specific Gravity:** 1.00 (FMA)
7. **Vapor Pressure:** 0.03 mm Hg at 20 °C (FMA), 0.031 mm Hg at 20 °C (EPI Suite v4.0), 0.0528 mm Hg at 25 °C (EPI Suite)
8. **UV Spectra:** No absorbance between 290 and 700 nm; molar absorption coefficient (0 L mol$^{-1}$ • cm$^{-1}$) is 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, 2015)

## 4. Exposure to fragrance ingredient (Creme RIFM Aggregate Exposure Model v1.0)

1. **95**th **Percentile Concentration in Fine Fragrance:** 0.00017% (RIFM, 2017)
2. **Inhalation Exposure*:** 0.0000004 mg/kg/day or 0.000028 mg/day (RIFM, 2017)
3. **Total Systemic Exposure**:** 0.000013 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 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 et al., 2015; Safford et al., 2015; Safford et al., 2017; and Comiskey et al., 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 I, Low

| Expert Judgment | Toxtree v3.1 | OECD QSAR Toolbox v4.2 |
|---|---|---|
| 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

## 7. Metabolism

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

## 8. Natural occurrence

Pinocarvyl acetate is reported to occur in the following foods by the VCF*:

Asafoetida oil.
Celery (*Apium graveolens* L.)
Citrus fruits.

*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.

## 9. Reach dossier

Pre-registered for 2010; no dossier available as of 03/11/21.

## 10. Conclusion

The maximum acceptable concentrations[a] in finished products for pinocarvyl acetate are detailed below.

| IFRA Category[b] | Description of Product Type | Maximum Acceptable Concentrations[a] in Finished Products (%)[c] |
|---|---|---|
| 1 | Products applied to the lips (lipstick) | 0.042 |
| 2 | Products applied to the axillae | 0.013 |
| 3 | Products applied to the face/body using fingertips | 0.25 |
| 4 | Products related to fine fragrances | 0.24 |
| 5A | Body lotion products applied to the face and body using the hands (palms), primarily leave-on | 0.060 |
| 5B | Face moisturizer products applied to the face and body using the hands (palms), primarily leave-on | 0.060 |
| 5C | Hand cream products applied to the face and body using the hands (palms), primarily leave-on | 0.060 |
| 5D | Baby cream, oil, talc | 0.060 |
| 6 | Products with oral and lip exposure | 0.14 |
| 7 | Products applied to the hair with some hand contact | 0.48 |
| 8 | Products with significant ano-genital exposure (tampon) | 0.025 |
| 9 | Products with body and hand exposure, primarily rinse-off (bar soap) | 0.46 |
| 10A | Household care products with mostly hand contact (hand dishwashing detergent) | 1.7 |
| 10B | Aerosol air freshener | 1.7 |
| 11 | Products with intended skin contact but minimal transfer of fragrance to skin from inert substrate (feminine hygiene pad) | 0.92 |
| 12 | Other air care products not intended for direct skin contact, minimal or insignificant transfer to skin | No Restriction |

Note: [a]Maximum acceptable concentrations for each product category are based on the lowest maximum acceptable concentrations (based on systemic toxicity, skin sensitization, or any other endpoint evaluated in this safety assessment). For pinocarvyl acetate, the basis was a predicted skin absorption value of 40% and a skin sensitization NESIL of 550 μg/cm$^2$.
[b]For a description of the categories, refer to the IFRA RIFM Information Booklet (https://www.rifm.org/downloads/RIFM-IFRA%20Guidance-for-the-use-of-IFRA-Standards.pdf).
[c]Calculations by Creme RIFM Aggregate Exposure Model v3.0.5.

## 11. Summary

### *11.1. Human health endpoint summaries*

#### *11.1.1. Genotoxicity*

Based on the current existing data and use levels, pinocarvyl acetate does not present a concern for genetic toxicity.

*11.1.1.1. Risk assessment.* Pinocarvyl acetate was assessed in the BlueScreen assay and found negative for both cytotoxicity (positive: <80% relative cell density) and genotoxicity, with and without metabolic activation (RIFM, 2013b). BlueScreen is a human cell-based assay for measuring the genotoxicity and cytotoxicity of chemical compounds and mixtures. Additional assays were considered to fully assess the potential mutagenic or clastogenic effects of the target material.

The mutagenic activity of pinocarvyl acetate 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 pinocarvyl acetate 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, pinocarvyl acetate was not mutagenic in the Ames test.

The clastogenic activity of pinocarvyl acetate 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 pinocarvyl acetate in DMSO at concentrations up to 1940 μg/mL in the DRF study. Micronuclei analysis was conducted at concentrations up to 325 μg/mL in the presence and absence of S9 for 4 h and in the absence of metabolic activation for 24 h. Pinocarvyl acetate did not induce binucleated cells with micronuclei when tested up to cytotoxic levels in either the presence or absence of an S9 activation system (RIFM, 2019). Under the conditions of the study, pinocarvyl acetate was considered to be non-clastogenic in the *in vitro* micronucleus test.

Based on the data available, pinocarvyl acetate does not present a concern for genotoxic potential.

**Additional References:** None.

**Literature Search and Risk Assessment Completed On:** 12/17/20.

*11.1.2. Repeated dose toxicity*

There are no repeated dose toxicity data on pinocarvyl acetate or any read-across materials. The total systemic exposure to pinocarvyl acetate is below the TTC for the repeated dose toxicity endpoint of a Cramer Class I material at the current level of use.

*11.1.2.1. Risk assessment.* There are no repeated dose toxicity data on pinocarvyl acetate or any read-across materials that can be used to support the repeated dose toxicity endpoint. The total systemic exposure to pinocarvyl acetate (0.013 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.

**Additional References:** None.

**Literature Search and Risk Assessment Completed On:** 12/15/20.

*11.1.3. Reproductive toxicity*

There are no reproductive toxicity data on pinocarvyl acetate or on any read-across materials. The total systemic exposure to pinocarvyl acetate is below the TTC for the reproductive toxicity endpoint of a Cramer Class I material at the current level of use.

*11.1.3.1. Risk assessment.* There are no reproductive toxicity data on pinocarvyl acetate or on any read-across materials that can be used to support the reproductive toxicity endpoint. The total systemic exposure to pinocarvyl acetate (0.013 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:** None.

**Literature Search and Risk Assessment Completed On:** 12/15/20.

*11.1.4. Skin sensitization*

Based on the available data, pinocarvyl acetate is considered to be a weak skin sensitizer with a defined NESIL of 550 μg/cm$^2$.

*11.1.4.1. Risk assessment.* Based on the existing data, pinocarvyl acetate is considered a skin sensitizer. The chemical structure of this material indicates that it would be expected to react with skin proteins (Roberts et al., 2007; Toxtree v3.1.0; OECD Toolbox v4.2). In a guinea pig maximization study, no reactions indicative of skin sensitization were observed in response to pinocarvyl acetate (RIFM, 1976). In a human maximization test, no skin sensitization reactions were observed (RIFM, 1982). Additionally, in a Confirmation of No Induction in Humans test (CNIH) with 4264 μg/cm$^2$ of pinocarvyl acetate in alcohol SDA39C, 1/41 volunteer subjects exhibited a reaction indicative of skin sensitization (RIFM, 1971). In another CNIH with 551 μg/cm$^2$ pinocarvyl acetate in 1:3 ethanol:diethyl phthalate (EtOH:DEP), no skin sensitization reactions were observed in any of the 106 volunteer subjects (RIFM, 2013a).

Based on WoE from structural analysis and animal and human studies, pinocarvyl acetate is a sensitizer with a WoE NESIL of 550 μg/cm$^2$ (Table 1). Section X provides the maximum acceptable concentrations in finished products, which take into account skin sensitization and application of the Quantitative Risk Assessment (QRA2) described by Api et al. (RIFM, 2020).

**Additional References:** None.

**Literature Search and Risk Assessment Completed On:** 12/18/20.

*11.1.5. Phototoxicity/photoallergenicity*

Based on UV/Vis absorption spectra, pinocarvyl acetate would not be expected to present a concern for phototoxicity or photoallergenicity.

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

*11.1.5.2. 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 coefficient (0 L mol$^{-1}$ • cm$^{-1}$) 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:** 12/11/20.

*111.1.6. Local Respiratory Toxicity*

The MOE could not be calculated due to a lack of appropriate data.

**Table 1**
Data Summary for pinocarvyl acetate.

| LLNA weighted mean EC3 value μg/cm$^2$ [No. Studies] | Potency Classification | Human Data | | | |
|---|---|---|---|---|---|
| | | NOEL-CNIH (induction)μg/cm$^2$ | NOEL-HMT (induction)μg/cm$^2$ | LOEL[a] (induction)μg/cm$^2$ | WoE NESIL[b] μg/cm$^2$ |
| NA | NA | 551 | 6897 | 4264 | 550 |

NOEL = No observed effect level; CNIH = Human Repeat Insult Patch test; HMT = Human Maximization Test; LOEL = lowest observed effect level; NA = Not Available.
[3] WoE NESIL limited to 2 significant figures.
[a] Based on animal data using classification defined in ECETOC, Technical Report No. 87, 2003.
[b] Data derived from CNIH or HMT.

The exposure level for pinocarvyl acetate is below the Cramer Class I TTC value for inhalation exposure local effects.

*11.1.6.1. Risk assessment.* There are insufficient inhalation data available on pinocarvyl acetate. Based on the Creme RIFM Model, the inhalation exposure is 0.000028 mg/day. This exposure is 50000 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:** Buchbauer et al., 1993; Matsubara et al., 2011.

**Literature Search and Risk Assessment Completed On:** 12/16/20.

### *11.2. Environmental endpoint summary*

#### *11.2.1. Screening-level assessment*

A screening-level risk assessment of pinocarvyl acetate 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, pinocarvyl acetate 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 pinocarvyl acetate 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 $\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).

#### *11.2.2. Risk assessment*

Based on current VoU (2015), pinocarvyl acetate does not present a risk to the aquatic compartment in the screening-level assessment.

*11.2.2.1. Key studies.* ***Biodegradation:*** No data available.

***Ecotoxicity:*** No data available.

***Other available data***

Pinocarvyl acetate has been pre-registered for REACH with no additional data at this time.

#### *11.2.3. 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)** | 6.98 | | | 1000000 | 0.00698 | |

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

| Exposure | Europe (EU) | North America (NA) |
|---|---|---|
| Log $K_{ow}$ Used | 3.81 | 3.81 |
| Biodegradation Factor Used | 0 | 0 |
| Dilution Factor | 3 | 3 |
| Regional Volume of Use Tonnage Band | <1 | <1 |
| **Risk Characterization: PEC/PNEC** | **<1** | **<1** |

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

The RIFM PNEC is 0.00698 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:** 12/16/20.

## 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
- **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 03/11/21.

## 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.

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