



RIFM fragrance ingredient safety assessment, 2-cyclopentene-1-acetic acid, ethyl ester, CAS Registry Number 15848-49-4

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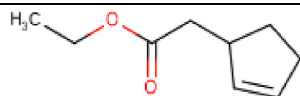
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Name: 2-Cyclopentene-1-acetic acid, ethyl ester
CAS Registry Number: 15848-49-4

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

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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., 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 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.

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.

2-Cyclopentene-1-acetic acid, ethyl ester was evaluated for genotoxicity, repeated dose toxicity, reproductive toxicity, local respiratory toxicity, photoirritation/photoallergenicity, skin sensitization, and environmental safety. Data show that 2-cyclopentene-1-acetic acid, ethyl ester 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

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exposure to 2-cyclopentene-1-acetic acid, ethyl ester is below the TTC (0.03 mg/kg/day, 0.03 mg/kg/day, and 1.4 mg/day, respectively). Data show that there are no safety concerns for 2-cyclopentene-1-acetic acid, ethyl ester for skin sensitization under the current declared levels of use. The photoirritation/photoallergenicity endpoints were evaluated based on ultraviolet/visible (UV/Vis) spectra; 2-cyclopentene-1-acetic acid, ethyl ester is not expected to be photoirritating/photoallergenic. The environmental endpoints were evaluated; 2-cyclopentene-1-acetic acid, ethyl ester 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, 2011; RIFM, 2012i)

Repeated Dose Toxicity: No NOAEL is available. Exposure is below TTC.

Reproductive Toxicity: Developmental toxicity and Fertility: No NOAEL available. Exposure is below the TTC.

Skin Sensitization: No concern for skin sensitization. RIFM (2012a)

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: Critical Measured Value: 82.8% (OECD 310) RIFM (2012d)

Bioaccumulation: Screening-level: 39.16 L/kg (EPI Suite v4.11; US EPA, 2012a)

Ecotoxicity: Screening-level: Fish LC50: 36.37 mg/L (RIFM Framework; Salvitto 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; Salvitto et al., 2002)

Critical Ecotoxicity Endpoint: Fish LC50: 36.37 mg/L (RIFM Framework; Salvitto et al., 2002)

RIFM PNEC is: 0.03637 $\mu\text{g/L}$ $\mu\text{g/L}$

• **Revised PEC/PNECs (2019 IFRA VoU):** North America and Europe; not applicable; cleared at screening-level

1. Identification

- Chemical Name:** 2-Cyclopentene-1-acetic acid, ethyl ester
- CAS Registry Number:** 15848-49-4
- Synonyms:** Sultanene; 2-Cyclopentene-1-acetic acid, ethyl ester
- Molecular Formula:** $\text{C}_9\text{H}_{14}\text{O}_2$
- Molecular Weight:** 154.2 g/mol
- RIFM Number:** 1234
- Stereochemistry:** One stereocenter and 2 possible stereoisomers.

2. Physical data

- Boiling Point:** 196.6 °C (RIFM, 2012g)
- Flash Point:** 67 °C (RIFM, 2012g)
- Log K_{ow}:** 2.92 (EPI Suite), 2.89 at 25 °C (RIFM, 2012h)
- Melting Point:** Not Available
- Water Solubility:** Not Available
- Specific Gravity:** Not Available
- Vapor Pressure:** Not Available
- UV Spectra:** No absorbance between 290 and 700 nm; molar absorption coefficient is below the benchmark (1000 L mol⁻¹ • cm⁻¹)
- Appearance/Organoleptic:** Not Available

3. Volume of use (Worldwide band)

- < 0.1 metric ton per year (IFRA, 2019)

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4. Exposure to fragrance ingredient (Creme RIFM aggregate exposure model v3.2.6)

1. **95th Percentile Concentration in Fine Fragrance:** 0.003% (RIFM, 2022)
2. **Inhalation Exposure*:** 0.000021 mg/kg/day or 0.0017 mg/day (RIFM, 2022)
3. **Total Systemic Exposure**:** 0.00015 mg/kg/day (RIFM, 2022)

*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; 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; 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. **Photoirritation/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

2-Cyclopentene-1-acetic acid, 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.

9. REACH dossier

Available; accessed 01/28/22 (ECHA, 2013).

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, 2-cyclopentene-1-acetic acid, ethyl ester does not present a concern for genotoxicity.

11.1.1.1. Risk assessment. The mutagenic activity of 2-cyclopentene-1-acetic acid, 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 standard plate incorporation and preincubation method. *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537, and *Escherichia coli* strain WP2uvrA were treated with 2-cyclopentene-1-acetic acid, 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, 2011). Under the conditions of the study, 2-cyclopentene-1-acetic acid, ethyl ester was not mutagenic in the Ames test.

The clastogenic activity of 2-cyclopentene-1-acetic acid, ethyl ester 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 2-cyclopentene-1-acetic acid, ethyl ester in DMSO. Micronuclei analysis was conducted at concentrations up to 1542 µg/mL in the presence and absence of metabolic activation. 2-Cyclopentene-1-acetic acid, ethyl ester did not induce binucleated cells with micronuclei when tested in either the presence or absence of an S9 activation system (RIFM, 2012i). Under the conditions of the study, 2-cyclopentene-1-acetic acid, ethyl ester was considered to be non-clastogenic in the *in vitro* micronucleus test.

Based on the data available, 2-cyclopentene-1-acetic acid, ethyl ester does not present a concern for genotoxic potential.

Additional References: None.

Literature Search and Risk Assessment Completed On: 01/21/22.

11.1.2. Repeated dose toxicity

There are insufficient repeated dose toxicity data on 2-cyclopentene-1-acetic acid, ethyl ester or any read-across materials. The total systemic exposure to 2-cyclopentene-1-acetic acid, ethyl ester 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 2-cyclopentene-1-acetic acid, ethyl ester or any read-across materials that can be used to support the repeated dose toxicity endpoint. The total systemic exposure to 2-cyclopentene-1-acetic acid, ethyl ester (0.15 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: 01/13/22.

11.1.3. Reproductive toxicity

There are insufficient reproductive toxicity data on 2-cyclopentene-1-acetic acid, ethyl ester or any read-across materials. The total systemic exposure to 2-cyclopentene-1-acetic acid, ethyl ester 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 2-cyclopentene-1-acetic acid, ethyl ester or on any read-across materials that can be used to support the reproductive toxicity endpoint. The total systemic exposure to 2-cyclopentene-1-acetic acid, ethyl ester (0.15 µg/kg/day) is below the TTC (30 µg/kg/day; Kroes et al., 2007; Lauferweiler 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: 01/13/22.

11.1.4. Skin sensitization

Based on the existing data, 2-cyclopentene-1-acetic acid, ethyl ester presents no concern for skin sensitization.

11.1.4.1. Risk assessment. Based on the existing data, 2-cyclopentene-1-acetic acid, ethyl ester is not considered a skin sensitizer. The data are summarized in Table 1. The chemical structure of this material indicates that it would not be expected to react with skin proteins directly (Roberts et al., 2007; Toxtree v3.1.0; OECD Toolbox v4.2). In a guinea pig maximization test, 2-cyclopentene-1-acetic acid, ethyl ester did not lead to skin sensitization reactions (RIFM, 2012a).

Based on the weight of evidence (WoE) from structural analysis and animal study, 2-cyclopentene-1-acetic acid, ethyl ester does not present a concern for skin sensitization.

Additional References: None.

Literature Search and Risk Assessment Completed On: 01/20/22.

11.1.5. Photoirritation/photoallergenicity

Based on the available UV/Vis absorption spectra, 2-cyclopentene-1-acetic acid, ethyl ester 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 2-cyclopentene-1-acetic acid, ethyl ester 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 photoirritation and photoallergenicity (Henry et al., 2009). Based on the lack of absorbance, 2-cyclopentene-1-acetic acid, ethyl ester does not present a concern for photoirritation or photoallergenicity.

Table 1

Summary of existing data on 2-cyclopentene-1-acetic acid, ethyl ester.

WoE Skin Sensitization Potency Category ^a	Human Data				Animal Data		
	NOEL-CNIH (induction) µg/cm ²	NOEL-HMT (induction) µg/cm ²	LOEL ^b (induction) µg/cm ²	WoE NESIL ^c µg/cm ²	LLNA Weighted Mean EC3 Value µg/cm ²	GPMT ^d	Buehler ^d
No evidence of sensitization ^f	NA	NA	NA	NA	NA	Negative	NA
	In vitro Data^e				In silico protein binding alerts (OECD Toolbox v4.2)		
	KE 1	KE 2	KE 3		Target Material	Autoxidation simulator	Metabolism simulator
	NA	NA	NA		No alert found	Radical reactions	No alert found

NOEL = No observed effect level; CNIH = Confirmation of No Induction in Humans test; HMT = Human Maximization Test; LOEL = lowest observed effect level; KE = Key Event; NA = Not Available.

^a 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).

^b Data derived from CNIH or HMT.

^c WoE NESIL limited to 2 significant figures.

^d Studies conducted according to the OECD TG 406 are included in the table.

^e Studies conducted according to the OECD TG 442, Cottrez et al. (2016), or Forreryd et al. (2016) are included in the table.

^f Determined based on Criteria for the Research Institute for Fragrance Materials, Inc. (RIFM) safety evaluation process for fragrance ingredients (Api et al., 2015).

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 is below the benchmark of concern for photoirritating effects, 1000 L mol⁻¹ • cm⁻¹ (Henry et al., 2009).

Additional References: None.

Literature Search and Risk Assessment Completed On: 01/11/22.

11.1.6. Local Respiratory Toxicity

The margin of exposure could not be calculated due to a lack of appropriate data. The exposure level for 2-cyclopentene-1-acetic acid, ethyl ester is below the Cramer Class I TTC value for inhalation exposure local effects.

11.1.6.1. Risk assessment. There are no inhalation data available on 2-cyclopentene-1-acetic acid, ethyl ester. Based on the Creme RIFM Model, the inhalation exposure is 0.0017 mg/day. This exposure is 823.5 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: 01/19/22.

11.2. Environmental endpoint summary

11.2.1. Screening-level assessment

A screening-level risk assessment of 2-cyclopentene-1-acetic acid, 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 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, 2-cyclopentene-1-acetic acid, 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 2-cyclopentene-1-acetic acid, ethyl ester 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 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, 2017). For persistence, if the EPI Suite

Based on the mean measured concentration, the 48-h EC50 value was reported to be 34.2 mg/L (95% CI: 30.9–42.4 mg/L).

11.2.1.4. Other available data. 2-Cyclopentene-1-acetic acid, ethyl ester has been registered under REACH with no additional data at this time.

11.2.1.5. Risk assessment refinement. Since 2-cyclopentene-1-acetic acid, ethyl ester has passed the screening criteria, measured data are included for completeness only and have 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)	EC50 (Algae)	AF	PNEC (µg/L)	Chemical Class
RIFM Framework Screening-level (Tier 1)	<u>36.37</u>			1000000	0.03637	

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.

11.2.1.1. Risk assessment. Based on the current VoU (2019), 2-cyclopentene-1-acetic acid, ethyl ester does not present a risk to the aquatic compartment in the screening-level assessment.

11.2.1.2. Key studies

11.2.1.2.1. Biodegradation. RIFM, 2012d: The biodegradability of the test material was evaluated according to the OECD 310 method. Under the conditions of this study, biodegradation of 82.8% was observed after 28 days.

11.2.1.2.3. Ecotoxicity. RIFM, 2012b: A fish (*Brachydanio rerio*) acute toxicity test was conducted according to the OECD 203 guidelines under static conditions. Under the conditions of this study, the 96-h LC50 was 8.67 mg/L with confidence intervals of 6.24 and 12.94 mg/L.

RIFM, 2012f: The acute toxicity of the test material to Fathead minnow (*Pimephales promelas*) was evaluated according to the OPPTS draft 850.1075 (1996) and OPPTS 850.1000 (1996) under flow-through conditions. Under the conditions of this study, the 96-h LC50 was 4.75 mg/L with confidence intervals of 3.28 and 6.40 mg/L.

RIFM, 2012c: An algae growth inhibition test was conducted according to OECD 201 method under static conditions. The 72-h EC50 and NOEC values for cell growth inhibition were reported to be 12.7 mg/L (95% CI: 11.6–13.7 mg/L) and 8.21 mg/L, respectively.

RIFM, 2012e: A *Daphnia magna* acute immobilization test was conducted according to the OECD 202 method under semi-static conditions.

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

Exposure	Europe (EU)	North America (NA)
Log K _{ow} Used	2.92	2.92
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 0.03294 µg/L. The revised PEC/PNECs for the EU and North America 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: 05/24/22.

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'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 ChemView:** <https://chemview.epa.gov/chemview/>
 - **Japanese NITE:** https://www.nite.go.jp/en/chem/chrip/chr_ip_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 06/20/22.

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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