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Short Review

RIFM fragrance ingredient safety assessment, 2-(1-methylpropyl)-1-vinylcyclohexyl acetate, CAS Registry Number 37172-02-4

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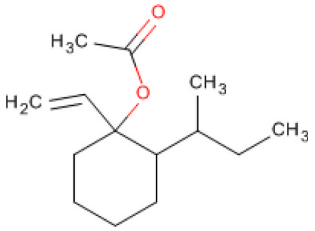

Abbreviation/Definition List:

2-Box Model - A RIFM, Inc. proprietary *in silico* tool used to calculate fragrance air exposure concentration
AF - Assessment Factor
BCF - Bioconcentration Factor
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, 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, 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).

(*continued on next column*)

(*continued*)

*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-(1-Methylpropyl)-1-vinylcyclohexyl acetate was evaluated for genotoxicity, repeated dose toxicity, reproductive toxicity, local respiratory toxicity, phototoxicity/photoallergenicity, skin sensitization, and environmental safety. Data show that 2-(1-methylpropyl)-1-vinylcyclohexyl 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 2-(1-methylpropyl)-1-vinylcyclohexyl acetate 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-(1-methylpropyl)-1-vinylcyclohexyl acetate for skin sensitization under the current declared levels of use. The phototoxicity/photoallergenicity endpoints were evaluated based on data and ultraviolet (UV) spectra; 2-(1-methylpropyl)-1-vinylcyclohexyl acetate is not expected to be phototoxic/photoallergenic. The environmental endpoints were evaluated; 2-(1-methylpropyl)-1-vinylcyclohexyl 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.

Human Health Safety Assessment

Genotoxicity: Not genotoxic. (RIFM, 2003; RIFM, 2015)
Repeated Dose Toxicity: No NOAEL available. Exposure is below the TTC.
Reproductive Toxicity: No NOAEL available. Exposure is below the TTC.
Skin Sensitization: Not a concern for skin sensitization at the current, declared use levels. (RIFM, 1976; RIFM, 1977a; RIFM, 1977b; RIFM, 1977c)
Phototoxicity/Photoallergenicity: Not phototoxic/photoallergenic (UV Spectra, RIFM Database; RIFM, 1979; RIFM, 1980)
Local Respiratory Toxicity: No NOAEC available. Exposure is below the TTC.

Environmental Safety Assessment

Hazard Assessment:
Persistence: Critical Measured Value: 9% (OECD 301F) RIFM (1999)
Bioaccumulation: Screening-level: 1390 L/kg (EPI Suite v4.11; US EPA, 2012a)
Ecotoxicity: Screening-level: 96-h Algae EC50: 0.137 mg/L (ECOSAR; US EPA, 2012b)
Conclusion: Not PBT or vPvB as per IFRA Environmental Standard

Risk Assessment:
Screening-level: PEC/PNEC (North America and Europe) > 1 (RIFM Framework; Salvito, 2002)
Critical Ecotoxicity Endpoint: 96-h Algae EC50: 0.137 mg/L (ECOSAR; US EPA, 2012b)
RIFM PNEC is: 0.0137 μg/L
•Revised PEC/PNECs (2015 IFRA VoU): North America and Europe <1

1. Identification

1. **Chemical Name:** 2-(1-Methylpropyl)-1-vinylcyclohexyl acetate
2. **CAS Registry Number:** 37172-02-4
3. **Synonyms:** Cyclohexanol, 1-ethenyl-2-(1-methylpropyl)-, acetate; Dihydro Ambrate; 2-sec-Butyl-1-vinylcyclohexyl acetate; 2-(1-Methylpropyl)-1-vinylcyclohexyl acetate
4. **Molecular Formula:** $C_{14}H_{24}O_2$
5. **Molecular Weight:** 224.44
6. **RIFM Number:** 5681
7. **Stereochemistry:** No isomer specified. Three stereocenters and 8 total stereoisomers possible.

2. Physical data

1. **Boiling Point:** 264.06 °C (EPI Suite)
2. **Flash Point:** > 212.00 °F TCC (>100.00 °C)*
3. **Log K_{OW}:** log Kow = 5.3 (RIFM, 2001), 5.27 (EPI Suite)
4. **Melting Point**: 33.76 °C (EPI Suite)

5. **Water Solubility:** 1.034 mg/L (EPI Suite)
6. **Specific Gravity:** Not Available
7. **Vapor Pressure:** 0.00609 mm Hg @ 20 °C (EPI Suite v4.0), 0.0107 mm Hg @ 25 °C (EPI Suite)
8. **UV Spectra:** Minor absorbance between 290 and 700 nm; the molar absorption coefficient is below the benchmark (1000 L mol^{-1} cm^{-1})
9. **Appearance/Organoleptic:** Colorless to pale yellow clear liquid with a medium woody and amber-like odor*

*http://www.thegoodscentscompany.com/data/rw1052371.html, retrieved 02/14/20.

3. Exposure

1. **Volume of Use (worldwide band):** 1–10 metric tons per year (IFRA, 2015)

4. Exposure to fragrance ingredient (Creme RIFM aggregate exposure model v2.0)

1. 95th Percentile Concentration in Hydroalcoholics: 0.3% (RIFM, 2019)
2. Inhalation Exposure*: 0.00059 mg/kg/day or 0.041 mg/day (RIFM, 2019)
3. Total Systemic Exposure**: 0.0046 mg/kg/day (RIFM, 2019)

*95th percentile calculated exposure derived from concentration survey data in the Creme RIFM Aggregate Exposure Model (Comiskey, 2015, 2017; Safford, 2015, 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, 2017; Safford, 2015, 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 v2.6	OECD QSAR Toolbox v3.2
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

7. Metabolism

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

8. Natural occurrence (discrete chemical) or composition (NCS)

2-(1-Methylpropyl)-1-vinylcyclohexyl acetate is not reported to occur in food 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

Pre-registered for 2010; No dossier available as of 07/12/19.

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 and use levels, 2-(1-methylpropyl)-1-vinylcyclohexyl acetate does not present a concern for genotoxic potential.

11.1.1.1. Risk assessment. 2-(1-Methylpropyl)-1-vinylcyclohexyl acetate was assessed in the BlueScreen assay and found negative for cytotoxicity with metabolic activation, and positive for cytotoxicity without metabolic activation (positive: <80% relative cell density); and negative for genotoxicity, with and without metabolic activation (RIFM, 2013). The mutagenic activity of 2-(1-methylpropyl)-1-vinylcyclohexyl 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 and preincubation methods. *Salmonella typhimurium* strains TA1535, TA1537, TA98, TA100, and TA102 were treated with 2-(1-methylpropyl)-1-vinylcyclohexyl 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, 2003). Under the conditions of the study, 2-(1-methylpropyl)-1-vinylcyclohexyl acetate was not mutagenic in the Ames test.

The clastogenic activity of 2-(1-methylpropyl)-1-vinylcyclohexyl 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 2-(1-methylpropyl)-1-vinylcyclohexyl acetate in DMSO at concentrations up to 2240 μg/mL in the dose range finding (DRF) study; micronuclei analysis was conducted at concentrations up to 100 μg/mL in the presence and absence of metabolic activation. 2-(1-Methylpropyl)-1-vinylcyclohexyl 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, 2015). Under the conditions of the study, 2-(1-methylpropyl)-1-vinylcyclohexyl acetate was considered to be non-clastogenic in the *in vitro* micronucleus test.

Based on the available data, 2-(1-methylpropyl)-1-vinylcyclohexyl acetate does not present a concern for genotoxic potential.

Additional References: None.

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

11.1.2. Repeated dose toxicity

There are no repeated dose toxicity data on 2-(1-methylpropyl)-1-vinylcyclohexyl acetate or any read-across materials. The total systemic exposure to 2-(1-methylpropyl)-1-vinylcyclohexyl 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 2-(1-methylpropyl)-1-vinylcyclohexyl acetate or any read-across materials that can be used to support the repeated dose toxicity endpoint. The total systemic exposure to 2-(1-methylpropyl)-1-vinylcyclohexyl acetate (4.6 μg/kg/day) is below the TTC (30 μg/kg/day; Kroes, 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: 08/21/19.

11.1.3. Reproductive toxicity

There are no reproductive toxicity data on 2-(1-methylpropyl)-1-vinylcyclohexyl acetate or on any read-across materials. The total systemic exposure to 2-(1-methylpropyl)-1-vinylcyclohexyl 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 2-(1-methylpropyl)-1-vinylcyclohexyl acetate or on any read-across materials that can be used to support the reproductive toxicity endpoint. The total systemic exposure to 2-(1-methylpropyl)-1-vinylcyclohexyl acetate (4.6 μg/kg/day) is below the TTC (30 μg/kg/day; Kroes, 2007; Laufersweiler, 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: 08/07/19.

11.1.4. Skin sensitization

Based on the existing data, 2-(1-methylpropyl)-1-vinylcyclohexyl acetate has no concern for skin sensitization under the current, declared levels of use.

11.1.4.1. Risk assessment. Based on the existing data, 2-(1-methylpropyl)-1-vinylcyclohexyl acetate 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, 2007; Toxtree v3.1.0). In a guinea pig Buehler test, no reactions indicative of sensitization were observed at 10% 2-(1-methylpropyl)-1-vinylcyclohexyl acetate in neantine (diethyl phthalate) (RIFM, 1976). Similarly, in an open epicutaneous test (OET) and a Freund's complete adjuvant test (FCAT) with 2-(1-methylpropyl)-1-vinylcyclohexyl acetate, no reactions indicative of sensitization were observed (RIFM, 1977b; RIFM, 1977a). Additionally, in a confirmatory human repeat insult patch test (HRIPT) with 2% 2-(1-methylpropyl)-1-vinylcyclohexyl acetate in dimethyl phthalate, no reactions indicative of sensitization were observed in any of the 54 volunteers (RIFM, 1977c). The dose per unit area for this HRIPT could not be calculated as the patch size was not specified in the report.

Based on the weight of evidence (WoE) from structural analysis and animal and human studies, 2-(1-methylpropyl)-1-vinylcyclohexyl acetate 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: 07/26/19.

11.1.5. Phototoxicity/photoallergenicity

Based on UV/Vis absorption and existing data, 2-(1-methylpropyl)-1-vinylcyclohexyl acetate does not present a concern for phototoxicity or photoallergenicity.

11.1.5.1. Risk assessment. UV/Vis absorption spectra indicate minor absorption between 290 and 700 nm. The corresponding molar absorption coefficient is well below the benchmark of concern for phototoxicity and photoallergenicity (Henry, 2009). In guinea pig phototoxicity and phototallergenicity studies, there were no reactions observed (RIFM, 1979; RIFM, 1980). Based on the lack of absorbance and the existing *in vivo* study data, 2-(1-methylpropyl)-1-vinylcyclohexyl acetate does not present a concern for phototoxicity or photoallergenicity.

11.1.5.2. UV spectra analysis. UV/Vis absorption spectra (OECD TG 101) for 2-(1-methylpropyl)-1-vinylcyclohexyl acetate were obtained. The spectra indicate minor absorbance in the range of 290–700 nm. The molar absorption coefficient is below the benchmark of concern for phototoxic effects, 1000 L $mol^{-1} \cdot cm^{-1}$ (Henry, 2009).

Additional References: None.

Literature Search and Risk Assessment Completed On: 07/22/19.

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-(1-methylpropyl)-1-vinylcyclohexyl 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 2-(1-methylpropyl)-1-vinylcyclohexyl acetate. Based on the Creme RIFM Model, the inhalation exposure is 0.041 mg/day. This exposure is 34.15 times lower than the Cramer Class I TTC value of 1.4 mg/day (based on human lung weight of 650 g; Carthew, 2009); therefore, the exposure at the current level of use is deemed safe.

Additional References: Belsito (2008).

Literature Search and Risk Assessment Completed On: 08/07/19.

11.2. Environmental endpoint summary

11.2.1. Screening-level assessment

A screening-level risk assessment of 2-(1-methylpropyl)-1-vinylcyclohexyl acetate 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 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 2-(1-methylpropyl)-1-vinylcyclohexyl acetate was identified as a fragrance material with the potential to present 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) identified 2-(1-methylpropyl)-1-vinylcyclohexyl acetate as possibly persistent and not 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, 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.

11.2.2. Risk assessment

Based on current VoU (2015), 2-(1-methylpropyl)-1-vinylcyclohexyl acetate presents a risk to the aquatic compartment in the screening-level assessment.

11.2.2.1. Key studies

11.2.2.1.1. Biodegradation. RIFM, 2001: The inherent biodegradability of the test material was evaluated by using the manometric respirometry test according to the OECD 302C guideline. At a concentration of 30 mg/L, no biodegradation was observed after the 31-day study.

RIFM, 1999: The ready biodegradability of the test material was evaluated by using the manometric respirometry test according to the OECD 301F guideline. The test material underwent 9% biodegradation after 28 days.

Ecotoxicity: No data available.

11.2.2.1.2. Other available data. 2-(1-Methylpropyl)-1-vinylcyclohexyl acetate has been pre-registered for REACH with no additional data available 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 highlighted.

Exposure information and PEC calculation (following RIFM

	LC50 (Fish) (mg/L)	EC50 (*Daphnia*) (mg/L)	EC50 (Algae) (mg/L)	AF	PNEC (μg/L)	Chemical Class
RIFM Framework Screening-level **(Tier 1)**	0.41			1000000	0.00041	
ECOSAR Acute Endpoints **(Tier 2)** ***Ver 1.11***	0.370	0.542	0.137	10000	0.0137	Esters
ECOSAR Acute Endpoints **(Tier 2)** ***Ver 1.11***	0.464	1.154	0.234			Vinyl/Allyl Esters
ECOSAR Acute Endpoints **(Tier 2)** ***Ver 1.11***	0.214	0.164	0.426			Neutral Organic SAR (Baseline Toxicity)

Framework: Salvito, 2002).

Exposure	Europe (EU)	North America (NA)
Log K_{ow} Used	5.27	5.27
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 0.0137 μg/L. The revised PEC/PNECs for EU and NA <1; therefore, the material does not present a risk to the aquatic environment at the current reported volumes of use.

Literature Search and Risk Assessment Completed On: 07/25/19.

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**
- **SciFinder:** https://scifinder.cas.org/scifinder/view/scifinder/scifinderExplore.jsf
- **PubMed:** https://www.ncbi.nlm.nih.gov/pubmed
- **TOXNET:** 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 01/31/20.

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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