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Short Review

RIFM fragrance ingredient safety assessment, 1-(2-methylprop-2-enoloxy)-2,2,4-trimethylpentan-3-ol, CAS Registry Number 526218-21-3

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ABSTRACT

Summary: The existing information supports the use of this material as described in this safety assessment. 1-(2-Methylprop-2-enoloxy)-2,2,4-trimethylpentan-3-ol was evaluated for genotoxicity, repeated dose toxicity, reproductive toxicity, local respiratory toxicity, phototoxicity/photoallergenicity, skin sensitization, and environmental safety. Data show that 1-(2-methylprop-2-enoloxy)-2,2,4-trimethylpentan-3-ol is not genotoxic. Data on 1-(2-methylprop-2-enoloxy)-2,2,4-trimethylpentan-3-ol provide a calculated margin of exposure (MOE) > 100 for the repeated dose toxicity endpoint. The reproductive and local respiratory toxicity endpoints were evaluated using the threshold of toxicological concern (TTC) for a Cramer Class III material, and the exposure to 1-(2-methylprop-2-enoloxy)-2,2,4-trimethylpentan-3-ol is below the TTC (0.0015 mg/kg/day and 0.47 mg/day, respectively). Data show that there are no safety concerns for 1-(2-methylprop-2-enoloxy)-2,2,4-trimethylpentan-3-ol for skin sensitization under the current declared levels of use. The phototoxicity/photoallergenicity endpoints were evaluated based on ultraviolet (UV) spectra; 1-(2-methylprop-2-enoloxy)-2,2,4-trimethylpentan-3-ol is not expected to be phototoxic/photoallergenic. The environmental endpoints were evaluated; for the hazard assessment based on the screening data, 1-(2-methylprop-2-enoloxy)-2,2,4-trimethylpentan-3-ol is not persistent, bioaccumulative, and toxic (PBT) as per the International Fragrance Association (IFRA) Environmental Standards. For the risk assessment, 1-(2-methylprop-2-enoloxy)-2,2,4-trimethylpentan-3-ol was not able to be risk screened as there were no reported volumes of use for either North America or Europe in the 2015 IFRA Survey.

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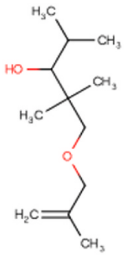

Abbreviation/Definition List:

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., 2015a, 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).

*The Expert Panel for Fragrance Safety is an independent body that selects its own members and establishes its own operating procedures. The Expert Panel is comprised of internationally known scientists that provide RIFM with guidance relevant to human health and environmental protection.

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

1-(2-Methylprop-2-enoloxy)-2,2,4-trimethylpentan-3-ol was evaluated for genotoxicity, repeated dose toxicity, reproductive toxicity, local respiratory toxicity, phototoxicity/photoallergenicity, skin sensitization, and environmental safety. Data show that 1-(2-methylprop-2-enoloxy)-2,2,4-trimethylpentan-3-ol is not genotoxic. Data on 1-(2-methylprop-2-enoloxy)-2,2,4-trimethylpentan-3-ol provide a calculated margin of exposure (MOE) > 100 for the repeated dose toxicity endpoint. The reproductive and local respiratory toxicity endpoints were evaluated using the threshold of toxicological concern (TTC) for a Cramer Class III material, and the exposure to 1-(2-methylprop-2-enoloxy)-2,2,4-trimethylpentan-3-ol is below the TTC (0.0015 mg/kg/day and 0.47 mg/day, respectively). Data show that there are no safety concerns for 1-(2-methylprop-2-enoloxy)-2,2,4-trimethylpentan-3-ol for skin sensitization under the current declared levels of use. The phototoxicity/photoallergenicity endpoints were evaluated based on ultraviolet (UV) spectra; 1-(2-methylprop-2-enoloxy)-2,2,4-trimethylpentan-3-ol is not expected to be phototoxic/photoallergenic. The environmental endpoints were evaluated; for the hazard assessment based on the screening data, 1-(2-methylprop-2-enoloxy)-2,2,4-trimethylpentan-3-ol is not persistent, bioaccumulative, and toxic (PBT) as per the International Fragrance Association (IFRA) Environmental Standards. For the risk assessment, 1-(2-methylprop-2-enoloxy)-2,2,4-trimethylpentan-3-ol was not able to be risk screened as there were no reported volumes of use for either North America or Europe in the 2015 IFRA Survey.

Human Health Safety Assessment

Genotoxicity: Not genotoxic. (RIFM, 2003c; RIFM, 2004a; RIFM, 2005a)
Repeated Dose Toxicity: NOAEL = 167 mg/kg/day. RIFM (2004b)

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 (2003a)
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: 15% (OECD 301B) RIFM (2003b)
Bioaccumulation:
Screening-level: 57.78 L/kg (EPI Suite v4.11; US EPA, 2012a)
Ecotoxicity:
Screening-level: Not applicable
Conclusion: Not PBT or vPvB as per IFRA Environmental Standards
Risk Assessment:
- **Revised PEC/PNECs (**2015 IFRA **VoU):** North America and Europe: Not applicable; no Volume of Use in 2015 reported for Europe and North America

1. Identification

1. **Chemical Name:** 1-(2-methylprop-2-enoloxy)-2,2,4-trimethylpentan-3-ol
2. **CAS Registry Number:** 526218-21-3
3. **Synonyms:** 3-Pentanol, 2,2,4-trimethyl-1-[(2-methyl-2-propenyl) oxy]-; Polymeflor; 1-(2-menthyl-2-propenyl-oxy)-2,2,4-trimethylpentan-3-ol; 1-(2-Methylprop-2-enoloxy)-2,2,4-trimethylpentan-3-ol
4. **Molecular Formula:** Not Available
5. **Molecular Weight:** 200.32
6. **RIFM Number:** 9445
7. **Stereochemistry:** No isomer specified. One stereocenter and 2 total stereoisomers possible.

2. Physical data

1. **Boiling Point:** Not Available
2. **Flash Point:** Not Available
3. **Log K_{OW}:** Not Available
4. **Melting Point**: Not Available
5. **Water Solubility:** Not Available
6. **Specific Gravity:** Not Available
7. **Vapor Pressure:** Not Available
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. Volume of use (worldwide band)

1. 0.1–1 metric ton per year (IFRA, 2015)

4. Exposure to fragrance ingredient (Creme RIFM aggregate exposure model v1.0)

1. **95**th **Percentile Concentration in Hydroalcoholics:** 0.003% (RIFM, 2017)
2. **Inhalation Exposure*:** 0.0000002 mg/kg/day or 0.000012 mg/day (RIFM, 2017)
3. **Total Systemic Exposure**:** 0.000035 mg/kg/day (RIFM, 2017)

*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 III, High

Expert Judgment	Toxtree v2.6	OECD QSAR Toolbox v3.2
III	III	III

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

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

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

1-(2-Methylprop-2-enoloxy)-2,2,4-trimethylpentan-3-ol 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

Not pre-registered; no dossier available as of 06/28/19.

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, 1-(2-methylprop-2-enoloxy)-2,2,4-trimethylpentan-3-ol does not present a concern for genotoxic potential.

11.1.1.1. Risk assessment. The mutagenic activity of 1-(2-methylprop-2-enoloxy)-2,2,4-trimethylpentan-3-ol has been evaluated in a bacterial reverse mutation assay conducted in compliance with GLP regulations and in accordance with OECD TG 471 using the standard plate incorporation method. *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537, and *Escherichia coli* strain WP2uvrA were treated with 1-(2-methylprop-2-enoloxy)-2,2,4-trimethylpentan-3-ol 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, 2003c). Under the conditions of the study, 1-(2-methylprop-2-enoloxy)-2,2,4-trimethylpentan-3-ol was not mutagenic in the Ames test.

The clastogenicity of 1-(2-methylprop-2-enoloxy)-2,2,4-trimethylpentan-3-ol was assessed in an *in vitro* chromosome aberration study conducted in compliance with GLP regulations and similar to OECD TG 473. Chinese hamster lung cells were treated with 1-(2-methylprop-2-enoloxy)-2,2,4-trimethylpentan-3-ol in DMSO at concentrations up to 2000 μg/mL in the presence and absence of S9. A statistically significant and dose-related increase in the frequency of cells with structural chromosomal aberrations was observed in the presence of S9 at 93.75 μg/mL, the maximum concentration selected for metaphase analysis. The test material did not induce any statistically significant increases in the number of polyploid cells at any concentration in either the presence and absence of S9 metabolic activation (RIFM, 2004a). Under the conditions of the study, 1-(2-methylprop-2-enoloxy)-2,2,4-trimethylpentan-3-ol was considered to be clastogenic to in the *in vitro* chromosome aberration assay. A follow-up *in vivo* micronucleus study was conducted in mice.

The clastogenic activity of 1-(2-methylprop-2-enoloxy)-2,2,4-trimethylpentan-3-ol was evaluated in an *in vivo* micronucleus test conducted in compliance with GLP regulations and in accordance with OECD TG 474. The test material was administered in Arachis oil via the intraperitoneal route of administration to groups of male and female albino Crl:CD-1 (ICR)BR mice. Doses of 150, 300, or 600 mg/kg were administered in male albino mice. Mice from each dose level were euthanized at 24 or 48 h, and the bone marrow was extracted and examined for polychromatic erythrocytes. The test material did not induce a statistically significant increase in the incidence of micronucleated polychromatic erythrocytes in the bone marrow (RIFM, 2005a). Under the conditions of the study, 1-(2-methylprop-2-enoloxy)-2,2,4-trimethylpentan-3-ol was considered to be not clastogenic in the *in vivo* micronucleus test.

Based on the data available from the Ames and micronucleus tests, 1-(2-methylprop-2-enoloxy)-2,2,4-trimethylpentan-3-ol does not present a concern for genotoxic potential.

Additional References: None.

Literature Search and Risk Assessment Completed On: 08/06/19.

11.1.2. Repeated dose toxicity

The MOE for 1-(2-methylprop-2-enoloxy)-2,2,4-trimethylpentan-3-ol is adequate for the repeated dose toxicity endpoint at the current level of use.

11.1.2.1. Risk assessment. There are sufficient repeated dose toxicity data on 1-(2-methylprop-2-enoloxy)-2,2,4-trimethylpentan-3-ol. In an OECD 407 and GLP-compliant study, 5 Sprague Dawley CrI:CD (SD) IGS BR rats/sex/dose were orally administered the test material through gavage at doses of 0 (Arachis oil), 15, 150, and 500 mg/kg/day for 28 days. Recovery groups of 5 animals/sex/dose were maintained for an additional 14 days for the 0 and 500 mg/kg/day groups. No treatment-related adverse effects were reported for any of the tested parameters in any treatment group. Thus, the NOAEL for repeated dose toxicity was considered to be 500 mg/kg/day (RIFM, 2004b).

A default safety factor of 3 was used when deriving a NOAEL from the 28-day OECD 407 study (ECHA, 2012a). The safety factor has been approved by the Expert Panel for Fragrance Safety*.

Thus, the derived NOEL for the repeated dose toxicity data is 500/3 or 167 mg/kg/day.

Therefore, the MOE can be calculated by dividing the NOAEL for 1-(2-methylprop-2-enoloxy)-2,2,4-trimethylpentan-3-ol by the total systemic exposure, 167/0.000035 or 4771429.

In addition, the total systemic exposure to 1-(2-methylprop-2-enoloxy)-2,2,4-trimethylpentan-3-ol (0.035 μg/kg/day) is below the TTC (1.5 μg/kg/day; Kroes, 2007) for the repeated dose toxicity endpoint of a Cramer Class III material at the current level of use.

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

Additional References: none.

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

11.1.3. Reproductive toxicity

There are insufficient reproductive toxicity data on 1-(2-methylprop-2-enoloxy)-2,2,4-trimethylpentan-3-ol or on any read-across materials. The total systemic exposure to 1-(2-methylprop-2-enoloxy)-2,2,4-trimethylpentan-3-ol is below the TTC for the reproductive toxicity endpoint of a Cramer Class III material at the current level of use.

11.1.3.1. Risk assessment. There are insufficient reproductive toxicity data on 1-(2-methylprop-2-enoloxy)-2,2,4-trimethylpentan-3-ol or on any read-across materials that can be used to support the reproductive toxicity endpoint. The total systemic exposure to 1-(2-methylprop-2-enoloxy)-2,2,4-trimethylpentan-3-ol (0.035 μg/kg/day) is below the TTC (1.5 μg/kg/day; Kroes, 2007; Laufersweiler, 2012) for the reproductive toxicity endpoint of a Cramer Class III material at the current level of use.

Additional References: RIFM, 2004b.

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

11.1.4. Skin sensitization

Based on the existing data, 1-(2-methylprop-2-enoloxy)-2,2,4-trimethylpentan-3-ol does not present a concern for skin sensitization under the current, declared levels of use.

11.1.4.1. Risk assessment. Based on the existing data, 1-(2-methylprop-2-enoloxy)-2,2,4-trimethylpentan-3-ol 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 3.1.0; OECD Toolbox v4.2). In a murine local lymph node assay (LLNA), 1-(2-methylprop-2-enoloxy)-2,2,4-trimethylpentan-3-ol was found to be non-sensitizing up to 100% (RIFM, 2003a).

Based on weight of evidence (WoE) from structural analysis and animal studies, 1-(2-methylprop-2-enoloxy)-2,2,4-trimethylpentan-3-ol

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: 06/12/19.

11.1.5. Phototoxicity/photoallergenicity

Based on the available UV/Vis spectra, 1-(2-methylprop-2-enoloxy)-2,2,4-trimethylpentan-3-ol 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 1-(2-methylprop-2-enoloxy)-2,2,4-trimethylpentan-3-ol 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, 2009). Based on the lack of absorbance, 1-(2-methylprop-2-enoloxy)-2,2,4-trimethylpentan-3-ol 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 significant absorbance in the range of 290–700 nm. The molar absorption coefficient is below the benchmark of concern for phototoxic effects, 1000 L $mol^{-1} \cdot cm^{-1}$ (Henry, 2009).

Additional References: None.

Literature Search and Risk Assessment Completed On: 08/05/19.

11.1.6. Local respiratory toxicity

The MOE could not be calculated due to a lack of appropriate data. The exposure level for 1-(2-methylprop-2-enoloxy)-2,2,4-trimethylpentan-3-ol is below the Cramer Class III TTC value for inhalation exposure local effects.

11.1.6.1. Risk assessment. There are no inhalation data available on 1-(2-methylprop-2-enoloxy)-2,2,4-trimethylpentan-3-ol. Based on the Creme RIFM Model, the inhalation exposure is 0.000012 mg/day. This exposure is 39167 times lower than the Cramer Class III TTC value of 0.47 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: None.

Literature Search and Risk Assessment Completed On: 08/05/19.

11.2. Environmental endpoint summary

11.2.1. Screening-level assessment

A screening-level risk assessment of 1-(2-methylprop-2-enoloxy)-2,2,4-trimethylpentan-3-ol 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. 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, 1-(2-methylprop-2-enoloxy)-2,2,4-trimethylpentan-3-ol was not able to be risk screened as there were no reported volumes of use for either North America or Europe in the 2015 IFRA Survey.

A screening-level hazard assessment using EPI Suite v4.11 (US EPA, 2012a) identified 1-(2-methylprop-2-enoloxy)-2,2,4-trimethylpentan-3-ol 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, 2012b). 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

Not applicable.

11.2.2.1. Key studies

11.2.2.1.1. Biodegradation. RIFM, 2003b: The ready biodegradability of the test material was evaluated using the CO_2 evolution test according to the OECD 301B guideline. Biodegradation of 15% was observed after 28 days.

11.2.2.1.2. Ecotoxicity. RIFM, 2004d: The acute toxicity of the test material to fish (rainbow trout) was assessed according to the OECD 203 guidelines under semi-static conditions. The 96-h LC50 based on nominal test concentrations was reported to be 24 mg/L (95% CI: 18–32 mg/L).

RIFM, 2004c: The *Daphnia magna* acute immobilization test was conducted according to the OECD 202 guidelines under static conditions. The 48-h EC50 value based on nominal test concentrations was reported to be 16 mg/L (95% CI: 14–17 mg/L).

RIFM, 2005b: The algae growth inhibition test was conducted according to the OECD 201 guideline. The 72-h EbC50 (biomass) value was reported to be 33 mg/L (95% CI: 30–35 mg/L) and ErC50 (growth rate) value was reported to be 63 mg/L (95% CI: 53–76 mg/L).

11.2.2.1.3. Other available data. 1-(2-methylprop-2-enoloxy)-2,2,4-trimethylpentan-3-ol has not been registered under REACH at this time.

11.2.3. Risk assessment refinement

Not applicable.

Literature Search and Risk Assessment Completed On: 07/24/19.

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
- **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 01/30/20.

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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