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Short Review

RIFM fragrance ingredient safety assessment, lauryl alcohol, CAS Registry Number 112-53-8

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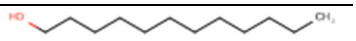

Name: Lauryl alcohol CAS Registry Number: 112-53-8

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
CAESAR - Computer-Assisted Evaluation of industrial chemical Substances According to Regulations
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., 2015, 2017, 2024) 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; please note that the citation dates used for studies sourced from the ECHA website are the dates the dossiers were first published, not the dates that the studies were conducted
ECOSAR - Ecological Structure-Activity Relationships Predictive Model
EU - Europe/European Union
GLP - Good Laboratory Practice
HESS - Hazard Evaluation Support System; a repeated dose profiler that is used to identify the toxicological profiler of chemicals
IFRA - The International Fragrance Association
IRB - Institutional Review Board
ISS - Istituto Superiore di Sanità (Italian National Institute of Health)
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
OASIS - OASIS Laboratory of Mathematical Chemistry (LMC)
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
Toxtree - an *in silico* tool that can estimate toxic hazard by applying a decision tree approach
TTC - Threshold of Toxicological Concern

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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.

Lauryl alcohol was evaluated for genotoxicity, repeated dose toxicity, reproductive toxicity, local respiratory toxicity, photoirritation/photoallergenicity, skin sensitization, and environmental safety. Data from read-across analog heptyl alcohol (CAS # 111-70-6) show that lauryl alcohol is not expected to be genotoxic. Data on lauryl alcohol provide a calculated Margin of Exposure (MOE) > 100 for the repeated dose toxicity and reproductive toxicity endpoints. Data from read-across analog 1-decanol (CAS # 112-30-1) provided lauryl alcohol a No Expected Sensitization Induction Level (NESIL) of 10000 μg/cm^2 for the skin sensitization endpoint. The photoirritation/photoallergenicity endpoints were evaluated based on ultraviolet/visible (UV/Vis) spectra; lauryl alcohol is not expected to be photoirritating/photoallergenic. The local respiratory toxicity endpoint was evaluated using the Threshold of Toxicological Concern (TTC) for a Cramer Class I material, and the exposure to lauryl alcohol is below the TTC (1.4 mg/day). The environmental endpoints were evaluated; lauryl alcohol 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 expected to be genotoxic.	ECHA (2012b)
Repeated Dose Toxicity: NOAEL = 682 mg/kg/day.	ECHA (2011b)
Reproductive Toxicity: NOAEL = 2046 mg/kg/day.	ECHA (2011b)
Skin Sensitization: NESIL = 10000 μg/cm^2.	RIFM (2023a)
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:	
Screening-level: 3.24 (BIOWIN 3)	(EPI Suite v4.11; US EPA, 2012a)
Bioaccumulation:	
Screening-level: 47.59 L/kg	(EPI Suite v4.11; US EPA, 2012a)
Ecotoxicity:	
Screening-level: 48-h *Daphnia magna* LC50: 0.365 mg/L	(ECOSAR v2.0; US EPA, 2012b)

Conclusion: Not PBT or vPvB as per IFRA Environmental Standards

Risk Assessment:

Screening-level: PEC/PNEC (North America and Europe) > 1	(Salvito et al., 2002)
Critical Ecotoxicity Endpoint: 48-h *Daphnia magna* LC50: 0.365 mg/L	(ECOSAR v2.0; US EPA, 2012b)

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RIFM PNEC is: 0.0365 μg/L
- **Revised PEC/PNECs (2019 IFRA VoU):** North America and Europe: <1

1. Identification

1. **Chemical Name:** Lauryl alcohol
2. **CAS Registry Number:** 112-53-8
3. **Synonyms:** Alcohol C-12; Alfol-12; 1-Dodecanol; n-Dodecyl alcohol; Lauric alcohol; Undecyl carbinol; Laurex 12; Cachalot L-90; CO-1214; Laurex NC; Laurex L1; Nacol 12–99; Alfol 1216 CO Alcohol; 1-Hydroxydodecane; Didecyl alcohol; アルカノール(C = 5–38); Dodecan-1-ol; Lauryl alcohol
4. **Molecular Formula:** $C_{12}H_{26}O$
5. **Molecular Weight:** 186.33 g/mol
6. **RIFM Number:** 277
7. **Stereochemistry:** No stereocenter present and no stereoisomer possible.

2. Physical data

1. **Boiling Point:** 260 °C (Fragrance Materials Association [FMA]), 272.96 °C (EPI Suite v4.11)
2. **Flash Point:** 135 °C (Globally Harmonized System), >200 °F; closed cup (FMA)
3. **Log K_{OW}:** 5.13 (Abraham and Rafols, 1995), 4.77 (EPI Suite v4.11)
4. **Melting Point**: 29.19 °C (EPI Suite v4.11)
5. **Water Solubility:** 6.898 mg/L at 25 °C (EPI Suite v4.11)
6. **Specific Gravity:** 0.832 at 20 °C (FMA), 0.830 at 25 °C (FMA)
7. **Vapor Pressure:** <0.001 mm Hg at 20 °C, 0.00181 mm Hg (EPI Suite v4.11)
8. **UV Spectra:** No absorbance between 290 and 700 nm; molar absorption coefficient is below the benchmark (1000 L mol^{-1} • cm^{-1})
9. **Appearance/Organoleptic:** Colorless to very pale-yellow liquid above 20 °C with a fatty odor

3. Volume of use (worldwide band)

1. 10–100 metric tons per year (IFRA, 2019)

4. Exposure to fragrance ingredient (Creme RIFM aggregate exposure model v3.3.0)

1. **95**th **Percentile Concentration in Fine Fragrance:** 0.0052 % (RIFM, 2023b)
2. **Inhalation Exposure*:** 0.00012 mg/kg/day or 0.0084 mg/day (RIFM, 2023b)
3. **Total Systemic Exposure**:** 0.0012 mg/kg/day (RIFM, 2023b)

*95th percentile calculated exposure derived from concentration survey data in the Creme RIFM Aggregate Exposure Model (Comiskey et al., 2015, 2017; Safford et al., 2015, 2017, 2024).

**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, 2017; Safford et al., 2015, 2017, 2024).

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 v4.6 (OECD, 2023)
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2. Analogs Selected:
   a **Genotoxicity:** Heptyl alcohol (CAS # 111-70-6)
   b **Repeated Dose Toxicity:** None
   c **Reproductive Toxicity:** None
   d **Skin Sensitization:** 1-Decanol (CAS # 112-30-1)
   e **Photoirritation/Photoallergenicity:** None
   f **Local Respiratory Toxicity:** None
   g **Environmental Toxicity:** None
3. Read-across Justification: See Appendix below

7. Metabolism

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

8. Natural occurrence

Lauryl alcohol is reported to occur in the following foods by the VCF*:

Allium species	Mangifera species
Apple brandy (non-categorized)	Mastic (*Pistacia lentiscus*)
Cheese, various types	Milk and milk products
Clam	Thyme (*Thymus* species)
Honey	Whisky

*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. This is a partial list.

9. REACH dossier

Available (ECHA, 2011b); accessed on 02/21/24.

10. Conclusion

The maximum acceptable concentrations[a] in finished products for lauryl alcohol 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)	0.30
2	Products applied to the axillae	0.23
3	Products applied to the face/body using fingertips	4.6
4	Products related to fine fragrances	4.3
5A	Body lotion products applied to the face and body using the hands (palms), primarily leave-on	1.1
5B	Face moisturizer products applied to the face and body using the hands (palms), primarily leave-on	1.1

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IFRA Category[b]	Description of Product Type	Maximum Acceptable Concentrations[a] in Finished Products (%)[c]
5C	Hand cream products applied to the face and body using the hands (palms), primarily leave-on	1.1
5D	Baby cream, oil, talc	0.37
6	Products with oral and lip exposure	2.5
7	Products applied to the hair with some hand contact	8.8
8	Products with significant ano-genital exposure (tampon)	0.37
9	Products with body and hand exposure, primarily rinse-off (bar soap)	8.4
10A	Household care products with mostly hand contact (hand dishwashing detergent)	30
10B	Aerosol air freshener	24
11	Products with intended skin contact but minimal transfer of fragrance to skin from inert substrate (feminine hygiene pad)	0.37
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 lauryl alcohol, the basis was the subchronic reference dose of 6.82 mg/kg/day, a predicted skin absorption value of 40 %, and a skin sensitization NESIL of 10000 μg/cm^2. As a conservative approach, we assumed that 100 % of the material exposed via the skin is bioavailable, thereby deriving the most stringent MOE (see Section V). Since the MOE is > 100 (see the repeated dose and reproductive toxicity sections), we then refined the exposure to 40 % using an *in silico* Skin Absorption Model (SAM) to determine the Maximum Allowable Concentrations for each category listed in Section X.

[b] For a description of the categories, refer to the IFRA/RIFM Information Booklet (https://ifrafragrance.org/docs/default-source/51st-amendment/ifra-51st-amendment—guidance-for-the-use-of-ifra-standards.pdf?sfvrsn=79750005_2; June 2023).

[c] Calculations by Creme RIFM Aggregate Exposure Model v3.4.4.

11. Summary

11.1. Human Health Endpoint Summaries

11.1.1. Genotoxicity

Based on the current existing data, lauryl alcohol does not present a concern for genotoxicity.

11.1.1.1. Risk Assessment. There are no studies assessing the mutagenic or clastogenic activity of lauryl alcohol; however, read-across can be made to heptyl alcohol (CAS # 111-70-6; see Section VI).

The mutagenic activity of heptyl alcohol 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 TA98, TA100, TA1535, TA1537, and TA102 were treated with heptyl alcohol 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 (ECHA, 2012b). Under the conditions of the study, heptyl alcohol was not mutagenic in the Ames test, and this can be extended to lauryl alcohol.

The clastogenicity of heptyl alcohol was assessed in an *in vitro* chromosome aberration study conducted in compliance with GLP regulations and in accordance with OECD TG 473. Human peripheral blood lymphocytes were treated with heptyl alcohol in DMSO at concentrations up to 5000 μg/mL in the dose range finding study; the main study was conducted at concentrations up to 468.75 μg/mL in the presence or absence of S9. No statistically significant increases in the frequency of cells with structural chromosomal aberrations or polyploid cells were observed with any concentration of the test material, either in the presence or absence of S9 (ECHA, 2012b). Under the conditions of the study, heptyl alcohol was considered to be non-clastogenic in the *in vitro* chromosome aberration assay, and this can be extended to lauryl alcohol.

Based on the data available, heptyl alcohol does not present a concern for genotoxic potential, and this can be extended to lauryl alcohol.

Additional References: None

Literature Search and Risk Assessment Completed On: 04/26/24

11.1.2. Repeated Dose Toxicity

The MOE for lauryl alcohol 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 lauryl alcohol. In a GLP- and OECD 422-compliant study, groups of 12 Wistar rats/sex/dose were administered lauryl alcohol via the diet at doses of 0, 1500, 7500, or 30000 ppm for 41−45 in males and 54 days in females. The actual doses received by both sexes are as follows: males - 102, 531, and 2046 mg/kg/day; females - 131, 658, and 2871 mg/kg/day. There was no treatment-related mortality throughout the study period. There were no changes to body weight, food consumption, or organ weights in both sexes. Hematology was only performed for male rats and revealed a dose-dependent reduction in total white blood cells, reaching statistical significance at the mid and high doses. However, there were no differences in differential white cell count to explain this observation. Clinical chemistry was also only performed in males, showing a significant decrease in plasma triglycerides at the high dose. There were no microscopic findings. Thus, based on no adverse effects seen up to the highest dose, the repeated dose toxicity NOAEL for this study was determined to be 2046 mg/kg/day (ECHA, 2011b).

A default safety factor of 3 was used when deriving a NOAEL from OECD 422 studies (ECHA, 2012a). The safety factor has been approved by the Expert Panel for Fragrance Safety*.

The derived NOAEL for the repeated dose toxicity endpoint is 2046/3 or 682 mg/kg/day.

Therefore, the lauryl alcohol MOE for the repeated dose toxicity endpoint can be calculated by dividing the lauryl alcohol NOAEL in mg/kg/day by the total systemic exposure to lauryl alcohol, 682/0.0012 or 568333.

Additionally, the total systemic exposure to lauryl alcohol (1.2 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.

11.1.2.1.1. Derivation of Subchronic Reference Dose (RfD). 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. (2020) and a subchronic RfD of 6.82 mg/kg/day.

The RIFM Criteria Document (Api et al., 2015) calls for a default MOE of 100 (10 × 10), based on uncertainty factors applied for inter-species (10 ×) and intraspecies (10 ×) differences. The subchronic RfD for lauryl alcohol was calculated by dividing the lowest NOAEL (from the Repeated Dose or Reproductive Toxicity sections) of 682 mg/kg/day by the uncertainty factor, 100 = 6.82 mg/kg/day.

Additional References: None

Literature Search and Risk Assessment Completed On: 04/25/24

11.1.3. Reproductive Toxicity

The MOE for lauryl alcohol is adequate for the reproductive toxicity endpoint at the current level of use.

11.1.3.1. Risk Assessment. There are sufficient reproductive toxicity data on lauryl alcohol. In a GLP- and OECD 422-compliant study, groups of 12 Wistar rats/sex/dose were administered lauryl alcohol via the diet at doses of 0, 1500, 7500, or 30000 ppm for 41−45 in males and 54 days in females. The actual doses received by both sexes are as follows: males 102, 531, and 2046 mg/kg/day; females 131, 658, and 2871 mg/kg/day. There was no treatment-related mortality throughout the study period. There were no changes to body weight or food consumption. There were no reproductive organ weight changes nor microscopic findings in parental animals. There were no changes to pregnancy rates, uterine parameters, time to pregnancy, gestation length, pup viability, or body weight. Finally, there were no changes to the number of corpora lutea, implantations, or resorptions. Thus, based on no adverse effects seen up to the highest dose, the reproductive toxicity NOAEL for this study was determined to be 2046 mg/kg/day (ECHA, 2011b).

Therefore, the lauryl alcohol MOE for the reproductive toxicity endpoint can be calculated by dividing the lauryl alcohol NOAEL in mg/kg/day by the total systemic exposure to lauryl alcohol, 2046/0.0012 or 1705000.

Additionally, the total systemic exposure to lauryl alcohol (1.2 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: 04/25/24

11.1.4. Skin Sensitization

Based on the existing data on the target material and the read-across material 1-decanol, lauryl alcohol was assigned a NESIL of 10000 μg/cm^2, and the maximum acceptable concentrations in finished products are provided in Section X.

11.1.4.1. Risk Assessment. Limited data are available on the skin sensitization potential of lauryl alcohol. Therefore, a structurally related

Table 1
Summary of existing data on 1-decanol as a read-across for lauryl alcohol.

WoE Skin Sensitization Potency Category[1]	Human Data				Animal Data		
	NOEL-CNIH (induction) μg/cm^2	NOEL-HMT (induction) μg/cm^2	LOEL (induction) μg/cm^2	WoE NESIL[2] μg/cm^2	LLNA Weighted Mean EC3 Value μg/cm^2	GPMT[3]	Buehler[3]
Weak	10038	2070	N/A	10000	N/A	Positive	Negative
	In vitro Data[4]				*In silico* protein binding alerts (OECD Toolbox v4.6)		
	KE 1	KE 2	KE 3		Target Material	Autoxidation simulator	Metabolism simulator
	Negative	Negative	Borderline		No alert found	No alert found	Schiff base formation

NOEL = No observed effect level; CNIH = Confirmation of No Induction in Humans; HMT = Human Maximization Test; LOEL = lowest observed effect level; EC3 = concentration of test chemical required to induce a 3-fold increase in lymph node cell proliferation; GPMT = Guinea Pig Maximization Test; KE = Key Event; N/A = Not Available.

[1]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).

[2]WoE NESIL limited to 2 significant figures.

[3]Studies conducted according to the OECD TG 406 are included in the table.

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

material, 1-decanol (CAS # 112-30-1; see Section VI), was used for the risk assessment of lauryl alcohol. The data on the read-across material are summarized in Table 1. Lauryl alcohol and read-across material are predicted *in silico* to be non-reactive with skin proteins directly (Roberts et al., 2007; Toxtree v3.1.0; OECD Toolbox v4.6). Read-across material 1-decanol was found to be negative in an *in vitro* direct peptide reactivity assay (DPRA) and KeratinoSens and borderline in a human cell line activation test (h-CLAT) (RIFM, 2020; RIFM, 2022b; RIFM, 2022a). The results were evaluated following the OECD Guideline No. 497: Defined Approaches on Skin Sensitization (OECD, 2021), and based on the 2 out of 3 Defined Approach, read-across material 1-decanol is considered a non-sensitizer. In a guinea pig maximization test (intradermal injection: 3 % in liquid paraffin; topical induction: 50 % in liquid paraffin; topical challenge: 3 % and 10 % in liquid paraffin), lauryl alcohol did not lead to skin sensitization reactions (ECHA, 2011b). In a guinea pig maximization test (intradermal injection: 4 % in dodecylbenzene sulfonate/saline; topical induction: 50 % in acetone/polyethylene glycol [PEG]; topical challenge: 10 % in acetone/PEG), read-across material 1-decanol led to skin sensitization reactions (RIFM, 1982b). In a guinea pig Buehler test (topical induction: 100 %; topical challenge: 25 % w/w in mineral oil), read-across material 1-decanol did not present reactions indicative of sensitization (ECHA, 2011a). In 2 separate human maximization tests, no skin sensitization reactions were observed when lauryl alcohol and read-across material 1-decanol were tested at 2760 μg/cm^2 and 2070 μg/cm^2, respectively (RIFM, 1972). Additionally, in a Confirmation of No Induction in Humans (CNIH) test with 10038 μg/cm^2 of read-across material 1-decanol in 1:3 ethanol:diethyl phthalate, no reactions indicative of sensitization were observed in any of the 105 volunteers (RIFM, 2023a).

Based on the weight of evidence (WoE) from structural analysis, *in vitro* studies, animal studies, and human studies on the read-across material and the target material, lauryl alcohol was assigned a WoE NESIL of 10000 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. (2020) and a subchronic RfD of 6.82 mg/kg/day.

Additional References: Sharp (1978); RIFM, 1962; Klecak (1979); RIFM, 1969; Klecak (1985); RIFM, 1982a.

Literature Search and Risk Assessment Completed On: 04/15/24

11.1.5. Photoirritation/Photoallergenicity

Based on the available UV/Vis absorption spectra, lauryl alcohol would not be expected to present a concern for photoirritation or photoallergenicity.

11.1.5.1. Risk Assessment. There are no photosafety studies available for lauryl alcohol in experimental models. UV/Vis absorption spectra indicate no absorption between 290 and 700 nm. Thus, it does not present a concern for photoirritant or photoallergenic effects (Henry et al., 2009). Based on the lack of absorbance, lauryl alcohol does not present a concern for photoirritation 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. Thus, it does not present a concern for photoirritant or photoallergenic effects (Henry et al., 2009).

Additional References: None

Literature Search and Risk Assessment Completed On: 04/23/24

11.1.6. Local Respiratory Toxicity

The MOE could not be calculated due to a lack of appropriate data. The exposure level for lauryl alcohol 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 lauryl alcohol. Based on the Creme RIFM Model, the inhalation exposure is 0.0084 mg/day. This exposure is 166.7 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: Gerarde and Ahlstrom, 1966; Ulrich and Marold, 1979

Literature Search and Risk Assessment Completed On: 04/16/24

11.2. Environmental endpoint Summary

11.2.1. Screening-level Assessment

A screening-level risk assessment of lauryl alcohol 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, lauryl alcohol was identified as a fragrance material with the 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 lauryl alcohol 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, 2017a). 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).

11.2.1.1. Risk Assessment. Based on the current VoU (IFRA, 2019), lauryl alcohol presents a risk to the aquatic compartment in the screening-level assessment.

11.2.1.2. Key Studies. Biodegradation:

No data available.

Ecotoxicity:

No data available.

11.2.1.2.1. Other available data. Lauryl alcohol has been registered under REACH, and the following additional data are available (ECHA, 2011b):

A 96-h fish (fathead minnow) acute toxicity study was conducted according to the US EPA 1975 method, and the LC50 was reported to be 1.01 mg/L.

A *Daphnia magna* immobilization study has been conducted according to the OECD 202 method, and the 48-h EC50 was reported to be 0.765 mg/L.

A *Daphnia magna* reproduction study was conducted according to the OECD 211 method under semi static conditions. The 21-day NOEC has been reported to be 12 µg/L.

An algae growth inhibition study was conducted according to the OECD 201 method, and the 72-h EC50 was reported to be 0.62 mg/L and 2.6 mg/L based on biomass and growth rate, respectively.

11.2.2. Risk Assessment Refinement

Since lauryl alcohol has passed the screening criteria (Tier 2), 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*) (mg/L)	EC50 (Algae) (mg/L)	AF	PNEC (µg/L)	Chemical Class
RIFM Framework Screening-level **(Tier 1)**	<u>1.125</u>			1000000	0.001125	
ECOSAR Acute Endpoints **(Tier 2)** ***v2.0***	0.498	<u>0.365</u>	0.783	10000	0.0365	Neutral Organic

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

Exposure	Europe (EU)	North America (NA)
Log K_{ow} Used	4.7	4.7
Biodegradation Factor Used	1	1
Dilution Factor	3	3
Regional VoU Tonnage Band	10–100	1–10
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 0.0365 µg/L. The revised PEC/PNECs for EU and NA are <1; therefore, the material does not present a risk to the aquatic environment at the current reported VoU.

Literature Search and Risk Assessment Completed On: 04/09/24

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 Technical Bulletin:** https://www.nlm.nih.gov/pubs/techbull/nd19/nd19_toxnet_new_locations.html
- **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/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://pubchem.ncbi.nlm.nih.gov/source/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 02/03/25.

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.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.fct.2025.115426.

Appendix

Read-across Justification:

Methods

The read-across analogs were identified using RIFM fragrance chemicals inventory clustering and read-across search criteria (Date et al., 2020). These criteria are in compliance with the strategy for structuring and reporting a read-across prediction of toxicity as described in Schultz et al. (2015) and are consistent with the guidance provided by OECD within Integrated Approaches for Testing and Assessment (OECD, 2015) and the European Chemicals Agency read-across assessment framework (ECHA, 2017b).

- First, materials were clustered based on their structural similarity. Second, data availability and data quality on the selected cluster were examined. Third, appropriate read-across analogs from the cluster were confirmed by expert judgment.
- Tanimoto structure similarity scores were calculated using FCFC4 fingerprints (Rogers and Hahn, 2010).
- The physical–chemical properties of the target material and the read-across analogs were calculated using EPI Suite (US EPA, 2012a).
- J_{max} values were calculated using RIFM's skin absorption model (SAM). The parameters were calculated using the consensus model (Shen et al., 2014).
- DNA binding, mutagenicity, genotoxicity alerts, and oncologic classification predictions were generated using OECD QSAR Toolbox v4.6 (OECD, 2023).
- ER binding and repeat dose categorization were generated using OECD QSAR Toolbox v4.6 (OECD, 2023).
- Developmental toxicity was predicted using CAESAR v2.1.7 (Cassano et al., 2010), and skin sensitization was predicted using Toxtree v2.6.13.
- Protein binding was predicted using OECD QSAR Toolbox v4.6 (OECD, 2023).
- The major metabolites for the target material and read-across analogs were determined and evaluated using OECD QSAR Toolbox v4.6 (OECD, 2023).
- To keep continuity and compatibility with *in silico* alerts, OECD QSAR Toolbox v4.6 was selected as the alert system.

	Target Material	Read-across Material	Read-across Material
Principal Name	Lauryl alcohol	Heptyl alcohol	1-Decanol
CAS No.	112-53-8	111-70-6	112-30-1
Structure			
Similarity (Tanimoto Score)		0.94	1.00
SMILES	CCCCCCCCCCCCO	CCCCCCCO	CCCCCCCCCCO
Endpoint		Genotoxicity	Skin sensitization
Molecular Formula	$C_{12}H_{26}O$	$C_7H_{16}O$	$C_{10}H_{22}O$
Molecular Weight (g/mol)	186.339	116.204	158.285
Melting Point (°C, EPI Suite)	24.00	−34.00	6.90
Boiling Point (°C, EPI Suite)	259.00	176.40	231.10
Vapor Pressure (Pa @ 25°C, EPI Suite)	1.13E-01	3.12E+01	1.13E+00
Water Solubility (mg/L, @ 25°C, WSKOW v1.42 in EPI Suite)	4.00E+00	1.80E+03	3.70E+01
Log K_{OW}	5.13	2.62	4.57

(*continued on next page*)

(*continued*)

	Target Material	Read-across Material	Read-across Material
J_{max} (µg/c m^2/h, SAM)	0.70	187.03	6.84
Henry's Law (Pa·m^3/mol, Bond Method, EPI Suite)	2.25E+00	1.90E+00	3.24E+00
Genotoxicity			
DNA Binding (OASIS v1.4, QSAR Toolbox v4.6)	No alert found	No alert found	
DNA Binding (OECD QSAR Toolbox v4.6)	No alert found	No alert found	
Carcinogenicity (ISS)	No alert found	No alert found	
DNA Binding (Ames, MN, CA, OASIS v1.1)	No alert found	No alert found	
***In Vitro* Mutagenicity (Ames, ISS)**	No alert found	No alert found	
***In Vivo* Mutagenicity (Micronucleus, ISS)**	No alert found	No alert found	
Oncologic Classification	Not classified	Not classified	
Skin Sensitization			
Protein Binding (OASIS v1.1)	No alert found		No alert found
Protein Binding (OECD)	No alert found		No alert found
Protein Binding Potency	Not possible to classify according to these rules (GSH)		Not possible to classify according to these rules (GSH)
Protein Binding Alerts for Skin Sensitization (OASIS v1.1)	No alert found		No alert found
Skin Sensitization Reactivity Domains (Toxtree v2.6.13)	No skin sensitization reactivity domain alerts identified		No skin sensitization reactivity domain alerts identified
Metabolism			
Rat Liver S9 Metabolism Simulator and Structural Alerts for Metabolites (OECD QSAR Toolbox v4.6)	See Supplemental Data 1	See Supplemental Data 2	See Supplemental Data 3

Summary

There are insufficient toxicity data on lauryl alcohol (CAS # 112-53-8). Hence, *in silico* evaluation was conducted to determine read-across analogs for this material. Based on structural similarity, reactivity, physical–chemical properties, and expert judgment, heptyl alcohol (CAS # 111-70-6) and 1-decanol (CAS # 112-30-1) were identified as read-across analogs with sufficient data for toxicological evaluation.

Conclusions

- Heptyl alcohol (CAS # 111-70-6) was used as a read-across analog for the target material, lauryl alcohol (CAS # 112-53-8), for the genotoxicity endpoint.
  - o The target material and the read-across analog are structurally similar and belong to the group of saturated aliphatic alcohols.
  - o The key difference between the target material and the read-across analog is that the read-across analog contains a shorter carbon chain. This structural difference is toxicologically insignificant.
  - o The similarity between the target material and the read-across analog is indicated by the Tanimoto score. Differences between the structures that affect the Tanimoto score are toxicologically insignificant.
  - o The physical–chemical properties of the target material and the read-across analog are sufficiently similar to enable a comparison of their toxicological properties.
  - o Differences are predicted for J_{max}, which estimates skin absorption. J_{max} for the target material corresponds to skin absorption $\leq$40 %, and J_{max} for the read-across analog corresponds to skin absorption $\leq$80 %. While the percentage of skin absorption estimated from J_{max} indicates exposure to the substance, it does not represent hazard or toxicity. This parameter provides context to assess the impact of bioavailability on toxicity comparisons between the materials evaluated.
  - o According to the OECD QSAR Toolbox v4.6, structural alerts for toxicological endpoints are consistent between the target material and the read-across analog.
  - o Neither the target material nor read-across analog contains *in silico* alerts for genotoxicity. The data from the genotoxicity section confirms that the read-across analog is not genotoxic. Therefore, based on the structural similarity between the target material and the read-across analog and the data on the read-across analog, the *in silico* alerts are consistent with the data.
  - o The target material and the read-across analog are expected to be metabolized similarly, as shown by the metabolism simulator.
  - o The structural alerts for the endpoints evaluated are consistent between the metabolites of the read-across analog and the target material.
- 1-Decanol (CAS # 112-30-1) was used as a read-across analog for the target material, lauryl alcohol (CAS # 112-53-8), for the skin sensitization endpoint.
  - o The target material and the read-across analog are structurally similar and belong to the group of saturated aliphatic alcohols.
  - o The key difference between the target material and the read-across analog is that the read-across analog contains a shorter carbon chain. This structural difference is toxicologically insignificant.
  - o The similarity between the target material and the read-across analog is indicated by the Tanimoto score. Differences between the structures that affect the Tanimoto score are toxicologically insignificant.
  - o The physical–chemical properties of the target material and the read-across analog are sufficiently similar to enable a comparison of their toxicological properties.
  - o According to the OECD QSAR Toolbox v4.6, structural alerts for toxicological endpoints are consistent between the target material and the read-across analog.
  - o Neither the target material nor read-across analog contains *in silico* alerts for skin sensitization. The data from the skin sensitization section indicates that the read-across analog is a very weak sensitizer. Therefore, based on the structural similarity between the target material and the read-across analog and the data on the read-across analog, the predictions are superseded by the data.
  - o The target material and the read-across analog are expected to be metabolized similarly, as shown by the metabolism simulator.
  - o The structural alerts for the endpoints evaluated are consistent between the metabolites of the read-across analog and the target material.

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