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Short review

RIFM fragrance ingredient safety assessment, dodecanal dimethyl acetal, CAS Registry Number 14620-52-1

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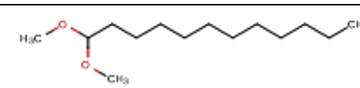
Version: 100417. This version replaces any previous versions.



Name: Dodecanal dimethyl acetal

CAS Registry Number: 14620-52-1

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; Safford et al., 2015; Safford et al., 2017; Comiskey et al., 2017) compared to a deterministic aggregate approach
DEREK - Derek Nexus is an *in silico* tool used to identify structural alerts
DST - Dermal Sensitization Threshold
ECHA - European Chemicals Agency
EU - Europe/European Union
GLP - Good Laboratory Practice
IFRA - The International Fragrance Association

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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
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
QRA - Quantitative Risk Assessment
REACH - Registration, Evaluation, Authorisation, and Restriction of Chemicals
RIFM - Research Institute for Fragrance Materials
RQ - Risk Quotient
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 under the limits 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 two-digit month/day/year), both in the RIFM database (consisting of publicly available and proprietary data) and through publicly available information sources (i.e., 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 guidance relevant to human health and environmental protection.

Summary: The use of this material under current conditions is supported by existing information.

Dodecanal dimethyl acetal was evaluated for genotoxicity, repeated dose toxicity, developmental and reproductive toxicity, local respiratory toxicity, phototoxicity/photoallergenicity, skin sensitization, and environmental safety. Data from read across analog octanal dimethyl acetal (CAS # 10022-28-3) show that dodecanal dimethyl acetal is not expected to be genotoxic. The skin sensitization endpoint was completed using DST for non-reactive materials (900 μg/cm^2/day); exposure is below the DST. The repeated dose, developmental and reproductive, and local respiratory toxicity endpoints were completed using the TTC for a Cramer Class I material and the exposure to dodecanal dimethyl acetal is below the TTC (0.03, 0.03 mg/kg/day and 1.4 mg/day, respectively). The phototoxicity/photoallergenicity endpoint was completed based on UV spectra; dodecanal dimethyl acetal is not expected to be phototoxic/photoallergenic. The environmental endpoints were evaluated, dodecanal dimethyl acetal was found not to be PBT as per the IFRA Environmental Standards, and its risk quotients, based on its current volume of use in Europe and North America (i.e., PEC/PNEC) are < 1.

Human Health Safety Assessment

Genotoxicity: Not genotoxic. (RIFM, 2014a; RIFM, 2014b)
Repeated Dose Toxicity: No NOAEL available. Exposure is below the TTC.
Developmental and Reproductive Toxicity: No NOAEL available. Exposure is below the TTC.
Skin Sensitization: No safety concerns at current, declared use levels. Exposure is below the DST.
Phototoxicity/Photoallergenicity: Not phototoxic/photoallergenic. (UV Spectra, RIFM DB)
Local Respiratory Toxicity: No NOAEC available. Exposure is below the TTC.

Environmental Safety Assessment

Hazard Assessment:

Persistence: Screening-Level: 2.9 (Biowin 3) (US EPA, 2012a)
Bioaccumulation: Screening-Level: 47.8 L/kg (US EPA, 2012a)
Ecotoxicity: Screening-Level: Fish LC50: 0.626 mg/L (RIFM Framework; Salvito et al., 2002)
Conclusion: Not PBT or vPvB as per IFRA Environmental Standards

Risk Assessment:

Screening-Level: PEC/PNEC (North America and Europe) < 1 (RIFM Framework; Salvito et al., 2002)
Critical Ecotoxicity Endpoint: Fish LC50: 0.626 mg/L (RIFM Framework; Salvito et al., 2002)
RIFM PNEC is: 0.000626 μg/L

- **Revised PEC/PNECs (2011 IFRA Volume of Use):** North America and Europe: Not applicable; cleared at screening-level

1. Identification

1. **Chemical Name:** Dodecanal dimethyl acetal
2. **CAS Registry Number:** 14620-52-1
3. **Synonyms:** 1,1-Dimethoxydodecane; Dodecane, 1,1-dimethoxy-; Lauraldehyde, dimethyl acetal; 1,1′-Bis(methoxy)dodecane; Lauryl aldehyde dimethyl acetal; Dodecanal dimethyl acetal
4. **Molecular Formula:** $C_{14}H_{30}O_2$
5. **Molecular Weight:** 230.92
6. **RIFM Number:** 5417

2. Physical data

1. **Boiling Point:** 268.53 °C [US EPA, 2012a]
2. **Flash Point:** >93 °C [GHS Database]
3. **Log K_{ow}:** 5.13 [US EPA, 2012a]
4. **Melting Point**: 23.49 °C [US EPA, 2012a]
5. **Water Solubility:** 1.25 mg/L [US EPA, 2012a]
6. **Specific Gravity:** 0.85000 @ 25.00 °C*
7. **Vapor Pressure:** 0.0107 mmHg @ 20 °C [US EPA, 2012a], 0.017 mm Hg @ 25 °C [US EPA, 2012a]
8. **UV Spectra:** No significant absorbance between 290 and 700 nm; molar absorption coefficient is below the benchmark (1000 L·mol^{-1}·cm^{-1})
9. **Appearance/Organoleptic:** A colorless liquid which has a very faint, fresh-green and slightly oily odor with a fruity-waxy undertone.

*http://www.thegoodscentscompany.com/data/rw1001691.html#tophyp, retrieved 10/21/2015.

3. Exposure

1. **Volume of Use (Worldwide Band):** < 0.1 metric tons per year	(IFRA , 2011)
2. **95th Percentile Concentration in Hydroalcoholics:** 0.018%	(RIFM, 2015)
3. **Inhalation Exposure***: 0.00041 mg/kg/day or 0.027 mg/day	(RIFM, 2015)
4. **Total Systemic Exposure****: 0.00095 mg/kg/day	(RIFM, 2015)

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

**95th percentile calculated exposure; assumes 100% absorption unless modified by dermal absorption data as reported in Section 4. It is derived from concentration survey data in the Creme RIFM aggregate exposure model and includes exposure via dermal, oral and inhalation routes whenever the fragrance ingredient is used in products that include these routes of exposure (Comiskey et al., 2015; Safford et al., 2015, 2017; Comiskey et al., 2017).

4. Derivation of systemic absorption

1. **Dermal:** Assumed 100%
2. **Oral:** Assumed 100%
3. **Inhalation:** Assumed 100%

5. Computational toxicology evaluation

1. **Cramer Classification:** Class I, Low

Expert Judgment	Toxtree v 2.6	OECD QSAR Toolbox v 3.2
I	I	I

2. **Analogs Selected:**
   a. **Genotoxicity:** Octanal dimethyl acetal (CAS # 10022-28-3)
   b. **Repeated Dose Toxicity:** None
   c. **Developmental and Reproductive Toxicity:** None
   d. **Skin Sensitization:** None
   e. **Phototoxicity/Photoallergenicity:** None
   f. **Local Respiratory Toxicity:** None
   g. **Environmental Toxicity:** None
3. **Read across Justification:** See Appendix below

6. Metabolism

No relevant data available for inclusion in this safety assessment.

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

Dodecanal dimethyl acetal 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 that contains information on published volatile compounds which have been found in natural (processed) food products. Includes FEMA GRAS and EU-Flavis data.

8. IFRA standard

None.

9. REACH dossier

Pre-registered for 11/30/2010, no dossier available as of 10/05/2017.

10. Summary

10.1. Human health endpoint summaries

10.1.1. Genotoxicity

Based on the current existing data, dodecanal dimethyl acetal does not present a concern for genotoxicity.

10.1.1.1. Risk assessment. Dodecanal dimethyl acetal was assessed in the BlueScreen assay and found to be negative for genotoxicity, with and without metabolic activation (RIFM, 2014c). There are no data assessing the mutagenic activity of dodecanal dimethyl acetal. However, read-across can be made to octanal dimethyl acetal (CAS # 10022-28-3; see Section 5). The mutagenic activity of octanal dimethyl acetal 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, and TA1537 and *Escherichia coli* strain WP2uvrA were treated with octanal dimethyl acetal in DMSO (dimethyl sulfoxide) at concentrations up to 5000 μg/plate. No increases in the mean number of revertant colonies were observed at any tested dose in the presence or absence of S9 (RIFM, 2014a). Under the conditions of the study, octanal dimethyl acetal was not mutagenic in the Ames test.

There are no studies assessing the clastogenic activity of dodecanal dimethyl acetal. However, read-across can be made to octanal dimethyl acetal of read-across (CAS # 10022-28-3; see Section 5). The clastogenic activity of octanal dimethyl acetal 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 octanal dimethyl acetal in DMSO (dimethyl sulfoxide) at concentrations up to 1744 μg/mL in the presence and absence of metabolic activation (S9) at the 3-h and 24-h timepoints. Octanal dimethyl acetal did not induce binucleated cells with micronuclei when tested up to cytotoxic levels in either non-activated or S9-activated test systems (RIFM, 2014b). Under the conditions of the study, octanal dimethyl acetal was considered to be non-clastogenic in the *in vitro* micronucleus test.

Based on the data available, octanal dimethyl acetal does not present a concern for genotoxic potential, and this can be extended to dodecanal dimethyl acetal.

Additional References: None.

Literature Search and Risk Assessment Completed On: 10/25/2016.

10.1.2. Repeated dose toxicity

There are insufficient repeated dose toxicity data on dodecanal dimethyl acetal or any read-across materials. The total systemic exposure to dodecanal dimethyl acetal is below the TTC for the repeated dose toxicity endpoint of a Cramer Class I material at the current level of use.

10.1.2.1. Risk assessment. There are no repeated dose toxicity data on dodecanal dimethyl acetal or any read-across materials that can be used to support the repeated dose toxicity endpoint. The total systemic exposure to dodecanal dimethyl acetal (0.95 μg/kg/day) is below the TTC (30 μg/kg bw/day; Kroes et al., 2007) for the repeated dose toxicity endpoint of a Cramer Class I material at the current level of use.

Additional References: None.

Literature Search and Risk Assessment Completed On: 03/10/2017.

10.1.3. Developmental and reproductive toxicity

There are insufficient developmental and reproductive toxicity data on dodecanal dimethyl acetal or any read-across materials. The total systemic exposure to dodecanal dimethyl acetal is below the TTC for the developmental and reproductive toxicity endpoints of a Cramer Class I material at the current level of use.

10.1.3.1. Risk assessment. There are no developmental toxicity data on dodecanal dimethyl acetal or any read-across materials that can be used to support the developmental toxicity endpoint. The total systemic exposure to dodecanal dimethyl acetal (0.95 μg/kg/day) is below the TTC (30 μg/kg bw/day; Kroes et al., 2007; Laufersweiler et al., 2012) for the developmental toxicity endpoint of a Cramer Class I material at the current level of use.

There are no reproductive toxicity data on dodecanal dimethyl acetal or any read-across materials that can be used to support the reproductive toxicity endpoint. The total systemic exposure to dodecanal dimethyl acetal (0.95 μg/kg/day) is below the TTC (30 μg/kg bw/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: 03/10/2017.

10.1.4. Skin sensitization

Based on application of DST, dodecanal dimethyl acetal does not present a safety concern for skin sensitization under the current, declared levels of use.

10.1.4.1. Risk assessment. The chemical structure of this material indicates that it would not be expected to react with skin proteins (Roberts et al., 2007; Toxtree 2.6.13; OECD toolbox v3.4). No predictive or human confirmatory skin sensitization studies are available for dodecanal dimethyl acetal. Acting conservatively, due to the insufficient data, the reported exposure was benchmarked utilizing the non-reactive Dermal Sensitization Threshold (DST) of 900 μg/cm^2. The current 95th percentile concentration is below the DST for non-reactive materials when evaluated in all QRA categories. Table 1 provides the acceptable concentration for dodecanal dimethyl acetal, which presents no appreciable risk for skin sensitization based on the non-reactive DST.

Additional References: None.

Literature Search and Risk Assessment Completed On: 03/20/17.

10.1.5. Phototoxicity/photoallergenicity

Based on the available UV/Vis spectra along with existing data, dodecanal dimethyl acetal would not be expected to present a concern for phototoxicity or photoallergenicity.

10.1.5.1. Risk assessment. There are no phototoxicity studies available for dodecanal dimethyl acetal in experimental models. UV/Vis absorption spectra indicate no significant absorption between 290 and 700 nm. Corresponding molar absorption coefficient is well below the benchmark of concern for phototoxicity and photoallergenicity, 1000 L·mol^{-1}·cm^{-1} (Henry et al., 2009). Based on lack of absorbance, dodecanal dimethyl acetal does not present a concern for phototoxicity or photoallergenicity.

Additional References: None.

Literature Search and Risk Assessment Completed On: 02/28/17.

10.1.6. Local Respiratory Toxicity

The margin of exposure could not be calculated due to lack of appropriate data. The material, dodecanal dimethyl acetal, exposure level is below the Cramer Class I TTC value for inhalation exposure local effects.

10.1.6.1. Risk assessment. There are no inhalation data available on dodecanal dimethyl acetal. Based on the Creme RIFM model, the inhalation exposure is 0.027 mg/day. This exposure is 51.9 times lower than the Cramer Class I TTC value of 1.4 mg/day (based on human lung weight of 650 g; Carthew et al., 2009); therefore, the exposure at the current level of use is deemed safe.

Additional References: None.

Literature Search and Risk Assessment Completed On: 3/17/2017.

10.2. Environmental endpoint summary

10.2.1. Screening-level assessment

A screening-level risk assessment of dodecanal dimethyl acetal was performed following the RIFM Environmental Framework (Salvito et al., 2002) which provides for 3 levels of screening for aquatic risk. In Tier 1, only the material's volume of use in a region, its log K_{ow} and molecular weight are needed to estimate a conservative risk quotient (RQ; Predicted Environmental Concentration/Predicted No Effect Concentration or PEC/PNEC). In Tier 1, a general QSAR for fish toxicity is used with a high uncertainty factor as discussed in Salvito et al. (2002). At Tier 2, the model ECOSAR (US EPA, 2012b; providing

Table 1
Acceptable concentrations for dodecanal dimethyl acetal based on non-reactive DST–.

IFRA Category[a]	Description of product type	Acceptable concentrations in finished products	95th percentile concentration
1	Products applied to the lips	0.069%	0.00%
2	Products applied to the axillae	0.021%	0.02%
3	Products applied to the face using fingertips	0.41%	0.00%
4	Fine fragrance products	0.39%	0.00%
5	Products applied to the face and body using the hands (palms), primarily leave-on	0.10%	0.01%
6	Products with oral and lip exposure	0.23%	0.00%
7	Products applied to the hair with some hand contact	0.79%	0.00%[b]
8	Products with significant ano-genital exposure	0.04%	0.000%
9	Products with body and hand exposure, primarily rinse off	0.75%	0.00% [b]
10	Household care products with mostly hand contact	2.70%	0.094%
11	Products with intended skin contact but minimal transfer of fragrance to skin from inert substrate	1.50%	0.000%
12	Products not intended for direct skin contact, minimal or insignificant transfer to skin	Not Restricted	0.558%

Note: [a]For a description of the categories, refer to the IFRA/RIFM Information Booklet.
[b]Negligible exposure (< 0.01%).

chemical class specific ecotoxicity estimates) is used, and a lower uncertainty factor is applied. Finally, if needed, at Tier 3, measured biodegradation and ecotoxicity data are used to refine the RQ (again, with lower uncertainty factors applied to calculate the PNEC). Provided in the table below are the data necessary to calculate both the PEC and the PNEC determined within this safety assessment. For the PEC, while the actual regional tonnage, which is considered proprietary information, is not provided, the range from the most recent IFRA Volume of Use Survey is reported. The PEC is calculated based on the actual tonnage and not the extremes noted for the range. Following the RIFM Environmental Framework, dodecanal dimethyl acetal was identified as a fragrance material with no potential to present a possible risk to the aquatic environment (i.e., its screening-level PEC/PNEC < 1).

A screening-level hazard assessment using EPI Suite v4.11 (US EPA, 2012a) did not identify dodecanal dimethyl acetal as possibly persistent or bioaccumulative based on its structure and physical-chemical properties. This screening-level hazard assessment is a weight of evidence review of a material's physical-chemical properties, available data on environmental fate (e.g., OECD Guideline biodegradation studies or die-away studies) and fish bioaccumulation, and review of model outputs (e.g., USEPA's BIOWIN and BCFBAF found in EPI Suite v4.11).

10.2.2. Risk assessment

Based on current Volume of Use (2011), dodecanal dimethyl acetal does not present a risk to the aquatic compartment in the screening-level assessment.

10.2.2.1. Biodegradation. No data available.

10.2.2.2. Ecotoxicity. No data available.

10.2.2.3. Other available data. Dodecanal dimethyl acetal has been pre-registered for REACH with no additional data at this time.

11. Risk assessment refinement

Ecotoxicological data and PNEC derivation (all endpoints reported in mg/L; PNECs in µg/L).

Endpoints used to calculate PNEC are underlined.

	LC50 (Fish)	EC50 (*Daphnia*)	EC50 (Algae)	AF	PNEC	Chemical Class
RIFM Framework Screening-Level **(Tier 1)**	<u>0.626 mg/L</u>	X	X	1,000,000	0.000626 µg/L	X

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

Exposure	Europe (EU)	North America (NA)
Log K_{ow} Used	5.13	5.13
Biodegradation Factor Used	0	0
Dilution Factor	3	3
Regional Volume of Use Tonnage Band	< 1	Not reported
Risk Characterization: PEC/PNEC	**< 1**	**N/A**

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

The RIFM PNEC is 0.000626 µg/L. The revised PEC/PNECs for EU and NA (not reported): Not applicable; cleared at the screening-level and therefore, does not present a risk to the aquatic environment at the current reported volumes of use.

Literature Search and Risk Assessment Completed On: 03/09/17.

12. Literature Search*

- **RIFM database:** target, Fragrance Structure Activity Group materials, other references, JECFA, CIR, SIDS
- **ECHA:** http://echa.europa.eu/

- **NTP:** http://tools.niehs.nih.gov/ntp_tox/index.cfm
- **OECD Toolbox**
- **SciFinder:** https://scifinder.cas.org/scifinder/view/scifinder/scifinderExplore.jsf
- **PUBMED:** http://www.ncbi.nlm.nih.gov/pubmed
- **TOXNET:** http://toxnet.nlm.nih.gov/
- **IARC:** (http://monographs.iarc.fr):
- **OECD SIDS:** http://www.chem.unep.ch/irptc/sids/oecdsids/sidspub.html
- **EPA Actor:** http://actor.epa.gov/actor/faces/ACToRHome.jsp;jsessionid=0EF5C212B7906229F477472A9A4D05B7
- **US EPA HPVIS:** http://www.epa.gov/hpv/hpvis/index.html
- **US EPA Robust Summary:** http://cfpub.epa.gov/hpv-s/
- **Japanese NITE:** http://www.safe.nite.go.jp/english/db.html
- **Japan Existing Chemical Data Base:** http://dra4.nihs.go.jp/mhlw_data/jsp/SearchPageENG.jsp
- **Google:** https://www.google.com/webhp?tab=ww&ei=KMSoUpiQK-arsQS324GwBg&ved=0CBQQ1S4

*Information sources outside of RIFM's database are noted as appropriate in the safety assessment. This is not an exhaustive list.

Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.fct.2017.11.033.

Transparency document

Transparency document related to this article can be found online at http://dx.doi.org/10.1016/j.fct.2017.11.033.

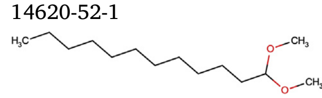
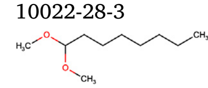
Appendix

Read-across justification

Methods

The read-across analogs were identified following the strategy for structuring and reporting a read-across prediction of toxicity described in Schultz et al. (2015). The strategy is also consistent with the guidance provided by OECD within Integrated Approaches for Testing and Assessment (OECD, 2015) and the European Chemical Agency read-across assessment framework (ECHA, 2016).

- First, materials were clustered based on their structural similarity. Second, data availability and data quality on the selected cluster was 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 substance and the read-across analogs were calculated using EPI Suite™ v4.11 (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 v3.4 (OECD, 2012).
- ER binding and repeat dose categorization were generated using OECD QSAR Toolbox v3.4 (OECD, 2012).
- Developmental toxicity was predicted using CAESAR v2.1.7 (Cassano et al., 2010) and skin sensitization was predicted using Toxtree 2.6.13.
- Protein binding was predicted using OECD QSAR Toolbox v3.4 (OECD, 2012).
- The major metabolites for the target and read-across analogs were determined and evaluated using OECD QSAR Toolbox v3.4 (OECD, 2012).

	Target material	Read across material
Principal Name	Dodecanal dimethyl acetal	Octanal dimethyl acetal
CAS No.	14620-52-1	10022-28-3
Structure		
Similarity (Tanimoto score)		0.95
Read-across endpoint		• Genotoxicity
Molecular Formula	$C_9H_{20}O_2$	C10H22O2
Molecular Weight	230.39	174.29
Melting Point (°C, EPISUITE)	23.49	−20.44
Boiling Point (°C, EPISUITE)	268.53	195.26
Vapor Pressure (Pa @ 25 °C, EPISUITE)	2.27	86.4
Log Kow (KOWWIN v1.68 in EPISUITE)	5.13	3.17
Water Solubility (mg/L, @ 25 °C, WSKOW v1.42 in EPISUITE)	1.25	115.3
J_{max} (mg/cm^2/h, SAM)	2.370	45.652
Henry's Law (Pa·m^3/mol, Bond Method, EPISUITE)	1.16 + 002	3.72E+001
Genotoxicity		
DNA binding (OASIS v 1.4 QSAR Toolbox 3.4)	• No alert found • No alert found	• No alert found • No alert found

DNA binding by OECD QSAR Toolbox (3.4)		
Carcinogenicity (genotoxicity and non-genotoxicity) alerts (ISS)	• Non-carcinogen (low reliability)	• Non-carcinogen (low reliability)
DNA alerts for Ames, MN, CA by OASIS v 1.1	• No alert found	• No alert found
In vitro Mutagenicity (Ames test) alerts by ISS	• No alert found	• No alert found
In vivo mutagenicity (Micronucleus) alerts by ISS	• No alert found	• No alert found
Oncologic Classification	• Not classified	• Not classified
Metabolism		
OECD QSAR Toolbox (3.4) Rat liver S9 metabolism simulator and structural alerts for metabolites	See supplemental data 1	See supplemental data 2

Summary

There are insufficient toxicity data on the target material dodecanal dimethyl acetal (CAS # 14620-52-1). Hence, *in silico* evaluation was conducted to determine a read-across analog for this material. Based on structural similarity, reactivity, metabolism data, physical-chemical properties and expert judgment, octanal dimethyl acetal (CAS # 10022-28-3) was identified as a read across material with data for the relevant endpoint.

Conclusion/Rationale

- Octanal dimethyl acetal (CAS # 10022-28-3) was used as a read-across analog for target material dodecanal dimethyl acetal (CAS # 14620-52-1) for the genotoxicity endpoint.
- The target substance and the read-across analog are structurally similar and belong to the structural class of saturated aliphatic acetals.
- The target substance and the read-across analog share an alkyl dimethyl acetal substructure.
- The key difference between the target substance and the read-across analog is that the target substance has 4 more carbons on the aliphatic chain on the aldehyde portion than the target. This structural difference between the target substance and the read across analog does not affect consideration of the toxicological endpoint.
- Similarity between the target substance and the read-across analog is indicated by the Tanimoto score in the above table. Differences between the structures that affect the Tanimoto score do not affect consideration of the toxicological endpoint.
- The physical-chemical properties of the target substance and the read-across analog are sufficiently similar to enable comparison of their toxicological properties. Differences are predicted for J_{max}, which estimates skin absorption. The J_{max} values translate to ≤80% skin absorption for the read-across analog, ≤ 40% absorption for the target substance. While percentage skin absorption estimated from J_{max} values indicate exposure of the substance, they do not represent hazard or toxicity parameters. Therefore, the J_{max} of the target substance and the appropriate read-across analog material are not used directly in comparing substance hazard or toxicity. However, these parameters provide context to assess the impact of bioavailability on toxicity comparisons between the individual materials.
- According to the QSAR OECD Toolbox (v3.4), structural alerts for toxicological endpoints are consistent between the target substance and the read-across analog.
- The target substance and the read-across analog are expected to be metabolized similarly, as shown by the metabolism simulator.

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