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Short review

RIFM fragrance ingredient safety assessment, heptanal dimethyl acetal, CAS Registry Number 10032-05-0

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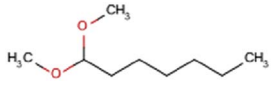
Version: 100417. This version replaces any previous versions.

Name: Heptanal dimethyl acetal

CAS Registry Number: 10032-05-0



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

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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
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 - Ultra Violet/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.

Heptanal 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 heptanal 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 exposure to heptanal 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; heptanal dimethyl acetal is not expected to be phototoxic/photoallergenic. The environmental endpoints were evaluated, heptanal 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: 3.12 (Biowin 3) (US EPA, 2012a)

Bioaccumulation: Screening-Level: 3.12 L/kg (US EPA, 2012a)

Ecotoxicity: Screening-Level: Fish LC50: 55.36 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: 1001 mg/L (RIFM Framework; Salvito et al., 2002)

RIFM PNEC is: 1.001 μg/L

- **Revised PEC/PNECs (2011 IFRA VoU):** North America and Europe: not Applicable; cleared at screening level

1. Identification

1. **Chemical Name:** Heptanal dimethyl acetal
2. **CAS Registry Number:** 10032-05-0
3. **Synonyms:** Aldehyde C-7 dimethyl acetal; 1,1-Dimethoxyheptane; Enanthal dimethyl acetal; Heptaldehyde dimethyl acetal; Oenanthal dimethyl acetal; Heptane, 1,1-dimethoxy-; Heptanal dimethyl acetal
4. **Molecular Formula:** $C_9H_{20}O_2$
5. **Molecular Weight:** 160.26
6. **RIFM Number:** 654

2. Physical data

1. **Boiling Point:** 60 °C @ 1 mm Hg [FMA Database], 174.69 °C [US EPA, 2012a]
2. **Flash Point:** 59 °C [GHS Database], 138 °F; CC [FMA Database]
3. **Log K_{ow}:** 2.68 [US EPA, 2012a]
4. **Melting Point:** −32.09 °C [US EPA, 2012a]
5. **Water Solubility:** 352.3 mg/L [US EPA, 2012a]
6. **Specific Gravity:** 0.85 [FMA Database]
7. **Vapor Pressure:** 1.2 mm Hg @ 20 °C [US EPA, 2012a], 0.6 mm Hg 20 °C [FMA Database], 1.69 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 $mol^{-1} \cdot cm^{-1}$)
9. **Appearance/Organoleptic:** Arctander Volume I 1969: Colorless liquid. Green-herbaceous, vegetable-like odor, reminiscent of green beans, almost cabbage-leafy, with sweet-oily, somewhat coconut-like undertones. Peculiar green-vegetable taste with a nuance of fungus-like taste.

3. Exposure

1. **Volume of Use (Worldwide Band):** 0.1–1 metric tons per year (IFRA , 2011)
2. **95th Percentile Concentration in Body lotion:** 0.010% (RIFM, 2015) (No reported use in Hydroalcoholics)
3. **Inhalation Exposure*:** 0.00011 mg/kg/day or 0.0078 mg/day (RIFM, 2015)
4. **Total Systemic Exposure**:** 0.00037 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 IV. 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)

Heptanal 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 10/04/2017.

10. Summary

10.1. Human health endpoint summaries

10.1.1. Genotoxicity

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

10.1.1.1. Risk assessment. Heptanal dimethyl acetal was assessed in the BlueScreen assay and found to be negative for both cytotoxicity and genotoxicity, with and without metabolic activation (RIFM, 2013). There are no data assessing the mutagenic activity of heptanal dimethyl

Table 1
Acceptable concentrations for heptanal 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%	0.00%
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%
8	Products with significant ano-genital exposure	0.04%	0.00%
9	Products with body and hand exposure, primarily rinse off	0.75%	0.01%
10	Household care products with mostly hand contact	2.70%	0.00%
11	Products with intended skin contact but minimal transfer of fragrance to skin from inert substrate	1.50%	0.00%
12	Products not intended for direct skin contact, minimal or insignificant transfer to skin	Not Restricted	0.071%

Note: [a]For a description of the categories, refer to the QRA Informational Booklet (www.rifm.org/doc/QRAInfoJuly2011.pdf).

acetal. However, read-across can be made to octanal dimethyl acetal (CAS # 10022-28-3; see Section V). 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 heptanal dimethyl acetal. However, read-across can be made to octanal dimethyl acetal (CAS # 10022-28-3). 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 heptanal dimethyl acetal.

Additional References: None.

Literature Search and Risk Assessment Completed On: 10/19/2016.

10.1.2. Repeated dose toxicity

There are insufficient repeated dose toxicity data on heptanal dimethyl acetal or any read-across materials. The total systemic exposure to heptanal 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 heptanal dimethyl acetal or any read-across materials that can be used to support the repeated dose toxicity endpoint. The total systemic exposure to heptanal dimethyl acetal (0.37 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 heptanal dimethyl acetal or any read-across materials. The total systemic exposure to heptanal 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 heptanal dimethyl acetal or any read-across materials that can be used to support the developmental toxicity endpoint. The total systemic exposure to heptanal dimethyl acetal (0.37 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 heptanal dimethyl acetal or any read-across materials that can be used to support the reproductive toxicity endpoint. The total systemic exposure to heptanal dimethyl acetal (0.37 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, heptanal 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 skin sensitization studies are available for heptanal dimethyl acetal. However, in a human maximization test, no skin sensitization reactions were observed when 8% or 5520 μg/cm^2 heptanal dimethyl acetal in petrolatum was used for induction and challenge (RIFM, 1975). Similarly, in a human repeat insult patch test (HRIPT), no reactions were observed when 0.5% or 388 μg/cm^2 heptanal dimethyl acetal in 95% ethanol was used for induction and challenge (RIFM, 1965). Due to the limited data, the reported exposure was benchmarked utilizing the non-reactive Dermal Sensitization Threshold (DST) of 900 μg/cm^2 (see Table 1). The current 95th

percentile concentration is below the DST for non-reactive materials when evaluated in all QRA categories. Heptanal dimethyl acetal does not present a concern for skin sensitization.

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, heptanal 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 heptanal 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 $mol^{-1} \cdot cm^{-1}$ (Henry et al., 2009). Based on lack of absorbance, heptanal 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, heptanal 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 heptanal dimethyl acetal. Based on the Creme RIFM model, the inhalation exposure is 0.0078 mg/day. This exposure is 179 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 heptanal 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 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, heptanal 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 heptanal 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).

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

10.2.1.2. Biodegradation. No data available.

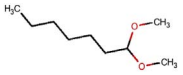
10.2.1.3. Ecotoxicity. Data available.

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

10.2.2. 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.



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

Exposure	Europe (EU)	North America (NA)
Log K_{ow} Used	2.68	2.68
Biodegradation Factor Used	0	0
Dilution Factor	3	3
Regional Volume of Use Tonnage Band	< 1	< 1
Risk Characterization: PEC/PNEC	**< 1**	**< 1**

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

The RIFM PNEC is 0.05536 µg/L. The revised PEC/PNECs for EU and NA: Not applicable; cleared at screening-level.

Literature Search and Risk Assessment Completed On: 3/9/17.

11. 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.2017.11.043.

Transparency document

Transparency document related to this article can be found online at http://dx.doi.org/10.1016/j.fct.2017.11.043.

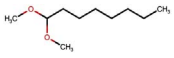
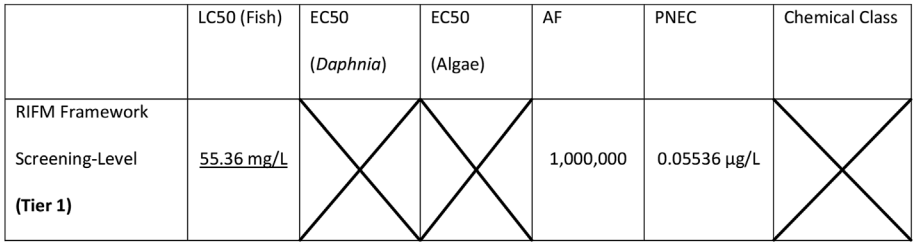
Appendix

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	Heptanal dimethyl acetal	Octanal dimethyl acetal
CAS No.	10032-05-0	10022-28-3
Structure		
Similarity (Tanimoto score)		0.95
Read-across endpoint		• Genotoxicity
Molecular Formula	$C_9H_{20}O_2$	C10H22O2
Molecular Weight	160.26	174.29
Melting Point (°C, EPISUITE)	−32.09	−20.44
Boiling Point (°C, EPISUITE)	174.69	195.26
Vapor Pressure (Pa @ 25 °C, EPISUITE)	225	86.4
Log Kow (KOWWIN v1.68 in EPISUITE)	2.68	3.17

Water Solubility (mg/L, @ 25 °C, WSKOW v1.42 in EPISUITE)	352.3	115.3
J_{max} (mg/cm^2/h, SAM)	82.13	7.570
Henry's Law (Pa·m^3/mol, Bond Method, EPISUITE)	2.81E + 001	3.72E + 001
Genotoxicity		
DNA binding (OASIS v 1.4 QSAR Toolbox 3.4)	• No alert found	• No alert found
DNA binding by OECD QSAR Toolbox (3.4)	• No alert found	• No alert found
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 heptanal dimethyl acetal (CAS # 10032-05-0). 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.

Conclusion/Rationale:

- Octanal dimethyl acetal (CAS # 10022-28-3) was used as a read-across analog for the target material heptanal dimethyl acetal (CAS # 10032-05-0) for the genotoxicity endpoint.
  - o The target substance and the read-across analog are structurally similar and belong to the structural class of saturated aliphatic acetals.
  - o The target substance and the read-across analog share an alkyl dimethyl acetal substructure.
  - o The key difference between the target substance and the read-across analog is that the read-across analog has 2 more carbons on the aliphatic chain than the target. This structural difference between the target substance and the read-across analog does not affect consideration of the toxicological endpoint.
  - o 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.
  - o 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 target substance, ≤ 40% absorption for the read-across analog. 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 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.
  - o According to the QSAR OECD Toolbox (v3.4), structural alerts for toxicity endpoints are consistent between the target substance and the read-across analog.
  - o The target substance and the read-across analog are expected to be metabolized similarly, as shown by the metabolism simulator.

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