Food and Chemical Toxicology xxx (xxxx) xxx–xxx

Contents lists available at ScienceDirect

Food and Chemical Toxicology

journal homepage: www.elsevier.com/locate/foodchemtox

RIFM fragrance ingredient safety assessment, 2,6-nonadien-1-ol, CAS Registry Number 7786-44-9

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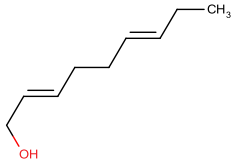
Version: 050218. This version replaces any previous versions.
Name: 2,6-Nonadien-1-ol
CAS Registry Number: 7786-44-9
Additional CAS Numbers*:
28069-72-9 (2E,6Z)-Nona-2,6-dien-1-ol
*This material was included because the materials are isomers.



Abbreviation/Definition List:

2-Box Model - A RIFM, Inc. proprietary *in silico* tool used to calculate fragrance air exposure concentration
AF - Assessment Factor
BCF - Bioconcentration Factor
Creme RIFM Model - The Creme RIFM Model uses probabilistic (Monte Carlo) simulations to allow full distributions of data sets, providing a more realistic estimate of aggregate exposure to individuals across a population (Comiskey et al., 2015, 2017; Safford et al., 2015, 2017) compared to a deterministic aggregate approach

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https://doi.org/10.1016/j.fct.2018.10.016
Received 2 May 2018; Received in revised form 6 September 2018; Accepted 3 October 2018

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
LOEL - Lowest Observable Effect Level
MOE - Margin of Exposure
MPPD - Multiple-Path Particle Dosimetry. An *in silico* model for inhaled vapors used to simulate fragrance lung deposition
NA - North America
NESIL - No Expected Sensitization Induction Level
NOAEC - No Observed Adverse Effect Concentration
NOAEL - No Observed Adverse Effect Level
NOEC - No Observed Effect Concentration
NOEL - No Observed Effect Level
OECD - Organisation for Economic Co-operation and Development
OECD TG - Organisation for Economic Co-operation and Development Testing Guidelines
PBT - Persistent, Bioaccumulative, and Toxic
PEC/PNEC - Predicted Environmental Concentration/Predicted No Effect Concentration
QRA - Quantitative Risk Assessment
REACH - Registration, Evaluation, Authorisation, and Restriction of Chemicals
RfD - Reference Dose
RIFM - Research Institute for Fragrance Materials
RQ - Risk Quotient
Statistically Significant - Statistically significant difference in reported results as compared to controls with a $p < 0.05$ using appropriate statistical test
TTC - Threshold of Toxicological Concern
UV/Vis spectra - Ultraviolet/Visible spectra
VCF - Volatile Compounds in Food
VoU - Volume of Use vPvB - (very) Persistent, (very) Bioaccumulative
WoE - Weight of Evidence

The Expert Panel for Fragrance Safety* concludes that this material is safe 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 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 use of this material under current conditions is supported by existing information.

2,6-Nonadien-1-ol was evaluated for genotoxicity, repeated dose toxicity, reproductive toxicity, local respiratory toxicity, phototoxicity/photoallergenicity, skin sensitization, and environmental safety. Data from read-across analog *trans*-2-hexenol (CAS# 928-95-0) show that this material is not expected to be genotoxic. The skin sensitization endpoint was completed using the DST for non-reactive materials. The repeated dose, developmental and reproductive, and local respiratory toxicity endpoints were completed using the TTC (Threshold of Toxicological Concern) for a Cramer Class I material (0.03 mg/kg/day, 0.03 mg/kg/day, and 1.4 mg/day, respectively). The phototoxicity/photoallergenicity endpoint was completed based on UV spectra. The environmental endpoint was completed as described in the RIFM Framework.

Human Health Safety Assessment

Genotoxicity: Not genotoxic. (RIFM, 2012b; 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: Not a sensitization concern. 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: Critical Measured Value: 79% (OECD 301F) (RIFM, 2012a)
Bioaccumulation: Screening-level: 36.17 L/kg (EPI Suite v4.1; US EPA, 2012a)
Ecotoxicity: Screening-level: Fish LC50: 33.1 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: 33.1 mg/L (RIFM Framework; Salvito et al., 2002)
RIFM PNEC is: 0.03310 μg/L
- **Revised PEC/PNECs (2011 IFRA VoU):** North America and Europe: Not Applicable; cleared at screening-level

1. Identification

Chemical Name: 2,6-Nonadien-1-ol	**Chemical Name:** (2E,6Z)-Nona-2,6-dien-1-ol
CAS Registry Number: 7786-44-9	**CAS Registry Number:** 28069-72-9
Synonyms: Cucumber alcohol; 2,6-Nonadienol; Violet leaf alcohol; Nona-2,6-dien-1-ol; Base XXI; 2,6-Nonadien-1-ol	**Synonyms:** 2,6-Nonadien-1-ol, (E,Z)-; Nona-2,6-dien-1-ol; 2-*trans*-6-*cis*-Nonadien-1-ol; 脂肪族不飽和アルコール（C = 9 ~ 24）
Molecular Formula: $C_9H_{16}O$	**Molecular Formula:** $C_9H_{16}O$
Molecular Weight: 140.23	**Molecular Weight:** 140.26
RIFM Number: 28	**RIFM Number:** 5639

2. Physical data*

1. **Boiling Point:** 100 °C @ 11 mm Hg (FMA), 231.61 °C (EPI Suite)
2. **Flash Point:** 200°F; CC (FMA)
3. **Log K_{OW}:** 2.87 (EPI Suite)
4. **Melting Point**: -4.87 °C (EPI Suite)
5. **Water Solubility:** 963.8 mg/L (EPI Suite)
6. **Specific Gravity:** 0.86 (FMA)
7. **Vapor Pressure:** 0.00623 mm Hg @ 20 °C (EPI Suite v4.0), 0.1 mm Hg 20 °C (FMA), 0.0105 mm Hg @ 25 °C (EPI Suite)
8. **UV Spectra:** No significant absorbance between 290 and 700 nm; molar absorption coefficient below the benchmark (1000 L mol^{-1} · cm^{-1})
9. **Appearance/Organoleptic:** A colorless liquid with oily, green, herbaceous odor.

*Physical data is identical for both materials included in this assessment (see Table 1).

3. Exposure

1. **Volume of Use (worldwide band):** 1–10 metric tons per year (IFRA, 2011)
2. **95th Percentile Concentration in Hydroalcoholics:** 0.0027% (RIFM, 2014a)
3. **Inhalation Exposure*:** 0.000014 mg/kg/day or 0.00098 mg/day (RIFM, 2014a)
4. **Total Systemic Exposure**:** 0.00012 mg/kg/day (RIFM, 2014a)

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

***When a safety assessment includes multiple materials, the highest exposure out of all included materials will be recorded here for the 95th Percentile Concentration in Hydroalcoholics, inhalation exposure and total exposure.

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:** *trans*-2-hexenol (CAS # 928-95-0)
   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

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

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

2,6-Nonadien-1-ol is reported to occur in the following foods by the VCF*:
Malt
Mentha oils
Prickly pear (*Opunita ficus indica*)
(2E,6Z)-Nona-2,6-dien-1-ol is reported to occur in the following foods by the VCF*:
Brown algae
Cucumber (*Cucumis sativus* L.)
Fish
Malt
Melon
Prickly pear (*Opuntia ficus indica*)
*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.

Table 1
Acceptable exposure limits for 2,6-nonadien-1-ol based on DST non-reactive.

IFRA Category[a]	Examples of Product Type	Calculated QRA
1	Lip Products	0.026%
2	Deodorant/Antiperspirant	0.033%
3	Hydroalc., Shaved Skin	0.136%
4	Hydroalc., Unshaved Skin	0.407%
5	Women Facial Cream	0.214%
6	Mouthwash	0.652%
7	Intimate Wipes	0.068%
8	Hair Styling Aids Non-Spray	0.91%
9	Conditioners, Rinse-off	4.50%
10	Hard Surface Cleaners	2.5%
11	Candle (Non-Skin/Incidental Skin)	Not Restricted

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

8. IFRA standard

None.

9. REACH dossier

2,6-Nonadien-1-ol and (2E,6Z)-nona-2,6-dien-1-ol are pre-registered for 2010; no dossier available as of 02/24/2017.

10. Summary

10.1. Human health endpoint summaries

10.1.1. Genotoxicity

Based on the current existing data and use levels, 2,6-nonadien-1-ol does not present a concern for genetic toxicity.

10.1.1.1. Risk assessment. The genotoxic potential of 2,6-nonadien-1-ol was evaluated in the Bluescreen assay and was reported as not genotoxic in the presence and absence of S9 metabolic activation (RIFM, 2014c). The mutagenic activity of 2,6-nonadien-1-ol was assessed in a *Salmonella* (Ames) mutagenicity assay conducted with OECD TG 471/GLP using the plate incorporation method. *Salmonella typhimurium* strains TA98, TA100, TA102, TA1535, and TA1537 were treated with 2,6-nonadien-1-ol in ethanol at concentrations of 3–1000 μg/plate in the presence and absence of S9 metabolic activation. No increases in the mean number of revertant colonies were observed at any tested dose in the presence or absence of S9 metabolic activation (RIFM, 2012b). Under the conditions of this study 2,6-nonadien-1-ol was considered not mutagenic.

There are no data assessing the clastogenic activity of 2,6-nonadien-1-ol however, read-across can be made to *trans*-2-hexenol (CAS # 928-95-0; see Section V). The clastogenic potential of *trans*-2-hexenol was evaluated in an *in vitro* micronucleus test in compliance with GLP regulations and in accordance with OECD TG 487. Human peripheral blood lymphocytes were treated with *trans*-2-hexenol in DMSO (dimethyl sulfoxide) at concentrations of 0.1–1000 μg/mL in the presence and absence of metabolic activation (S9) at 4 h and 24 h timepoints. *trans*-2-Hexenol 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, *trans*-2-hexenol was considered to be non-clastogenic in the *in vitro* micronucleus test, and this can be extended to 2-6-nonadien-1-ol.

Based on the available data, 2-6-nonadien-1-ol does not present a concern for genotoxic potential.

Additional References: RIFM, 2013a.

Literature Search and Risk Assessment Completed On: 05/27/15.

10.1.2. Repeated dose toxicity

There are insufficient repeated dose toxicity data on 2,6-nonadien-1-ol or any read-across materials. The total systemic exposure to 2,6-nonadien-1-ol 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 2,6-nonadien-1-ol or any read-across materials that can be used to support the repeated dose toxicity endpoint. The total systemic exposure to 2,6-nonadien-1-ol (0.12 μg/kg/day) is below the TTC (30 μg/kg bw/day) for the repeated dose toxicity endpoint of a Cramer Class I material at the current level of use.

Additional References: None.

Literature Search and Risk Assessment Completed On: 08/10/2015.

10.1.3. Developmental and reproductive toxicity

There are insufficient developmental and reproductive toxicity data on 2,6-nonadien-1-ol or any read-across materials. The total systemic exposure to 2,6-nonadien-1-ol is below the TTC for the developmental or 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 or reproductive toxicity data on 2,6-nonadien-1-ol or any read-across materials that can be used to support the developmental or reproductive toxicity endpoints. The total systemic exposure to 2,6-nonadien-1-ol (0.12 μg/kg/day) is below the TTC (30 μg/kg bw/day) for the developmental or reproductive toxicity endpoints of a Cramer Class I material at the current level of use.

Additional References: None

Literature Search and Risk Assessment Completed On: 08/10/2015

10.1.4. Skin sensitization

Based on the existing data and application of DST, 2,6-nonadien-1-ol may present a concern for skin sensitization.

10.1.4.1. Risk assessment. Based on the limited data and application of DST, 2,6-nonadien-1-ol does not present a concern for skin sensitization. The chemical structure of this material indicates that it would not be expected to react with skin proteins (Roberts et al., 2007; Toxtree 2.6.6; OECD toolbox v3.3). No predictive animal test exists to determine sensitization potential of this chemical. However, in a human maximization test with 1% or 690 μg/cm^2 2,6-nonadien-1-ol, no reaction indicative of sensitization were observed (RIFM, 1972). Due to limited data, current exposure was benchmark analyzed using DST of 900 μg/cm^2 for non-reactive chemicals. The current 95th percentile dermal exposure is below the DST for non-reactive materials when evaluated in all QRA categories. 2,6-nonadien-1-ol does not present a concern for skin sensitization.

Additional References: None

Literature Search and Risk Assessment Completed On: 09/23/16

10.1.5. Phototoxicity/photoallergenicity

Based on available UV/Vis spectra, 2,6-nonadien-1-ol would not be expected to present a concern for phototoxicity or photoallergenicity.

10.1.5.1. Risk assessment. There are no predictive studies available on 2,6-nonadien-1-ol in experimental models. The available UV/Vis spectra for 2,6-nonadien-1-ol indicate no significant absorbance between 290 and 700 nm. The corresponding molar absorption coefficient is below the benchmark of concern for phototoxic effects. Based on the lack of absorbance in the critical range, and benchmark evaluation, 2,6-nonadien-1-ol does not present a concern for

phototoxicity or photoallergenicity.

10.1.5.2. UV spectra analysis. UV/Vis absorption spectra (OECD TG 101) were obtained. The spectra indicate no significant absorbance in the range of 290–700 nm. The molar absorption coefficient is below the benchmark of concern for phototoxic effects, 1000 L mol^{-1} · cm^{-1} (Henry et al., 2009).

Additional References: None.

Literature Search and Risk Assessment Completed On: 09/07/16.

10.1.6. Local respiratory toxicity

The margin of exposure could not be calculated due to lack of appropriate data. The material, 2,6-nonadien-1-ol, 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 2,6-nonadien-1-ol. Based on the Creme RIFM Model, the inhalation exposure is 0.00098 mg/day. This exposure is 1429 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: 9/2016.

10.2. Environmental endpoint summary

10.2.1. Screening-level assessment

A screening-level risk assessment of 2,6-nonadien-1-ol 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 Volume of Use Survey is reviewed. The PEC is then calculated using the actual regional tonnage, not the extremes of the range. Following the RIFM Environmental Framework, 2,6-nonadien-1-ol 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 v4.1 did not identify 2,6-nonadien-1-ol as either being possibly persistent nor 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, 2012). For persistence, if the EPI Suite model BIOWIN 3 predicts a value < 2.2 and either BIOWIN 2 or BIOWIN 6 predicts a value < 0.5, then the material is considered potentially persistent. A material would be considered potentially bioaccumulative if the EPI Suite model BCFBAF predicts a fish BCF ≥2000 L/kg. Ecotoxicity is determined in the above screening-level risk assessment. If, based on these model outputs (Step 1), additional assessment is required, a WoE-based review is then performed (Step 2). This review considers available data on the material's physical–chemical properties, environmental fate (e.g., OECD Guideline biodegradation studies or die-away studies), fish bioaccumulation, and higher-tier model outputs (e.g., US EPA's BIOWIN and BCFBAF found in EPI Suite v4.1). Data on persistence and bioaccumulation are reported below and summarized in the Environmental Safety Assessment section prior to Section 1.

10.2.2. Risk assessment

Based on the current Volume of Use (2011), 2,6-nonadien-1-ol does not present a risk to the aquatic compartment in the screening-level assessment.

10.2.2.1. Biodegradation. RIFM, 2012a: The ready biodegradability of the test material using the manometric respirometry test according to the OECD 301F method. Under the conditions of the study, biodegradation of 79% was observed after 28 days.

10.2.2.2. Ecotoxicity. None.

10.2.2.3. Other available data. 2,6-Nonadien-1-ol has been pre-registered for REACH with no additional data available at this time.

10.2.3. Risk assessment refinement

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

Endpoints used to calculate PNEC are 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)**	33.10			1,000,000	0.0331	

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

Exposure	Europe (EU)	North America (NA)
Log K_{ow} used	2.87	2.87
Biodegradation Factor Used	0	0
Dilution Factor	3	3
Regional Volume of Use Tonnage Band	< 1*	< 1*
Risk Characterization: PEC/PNEC	**< 1**	**< 1**

*Combined volumes for both CAS numbers

The RIFM PNEC is 0.03310 µg/L. The revised PEC/PNECs for EU and NA are: not applicable. The material was 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: 6/2/15.

11. Literature search*

- **RIFM Database:** Target, Fragrance Structure Activity Group materials, other references, JECFA, CIR, SIDS
- **ECHA:** http://echa.europa.eu/
- **NTP:** https://ntp.niehs.nih.gov/
- 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://webnet.oecd.org/hpv/ui/Default.aspx
- **EPA ACToR:** https://actor.epa.gov/actor/home.xhtml
- **US EPA HPVIS:** https://ofmpub.epa.gov/oppthpv/public_search.publicdetails?submission_id=24959241&ShowComments=Yes&sqlstr=null&recordcount=0&User_title=DetailQuery%20Results&EndPointRpt=Y#submission
- **Japanese NITE:** http://www.safe.nite.go.jp/english/db.html
- **Japan Existing Chemical Data Base (JECDB):** http://dra4.nihs.go.jp/mhlw_data/jsp/SearchPageENG.jsp
- **Google:** https://www.google.com
- **ChemIDplus:** https://chem.nlm.nih.gov/chemidplus/

Search keywords: CAS number and/or material names

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

Conflicts of interest

The authors declare that they have no conflicts of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.fct.2018.10.016.

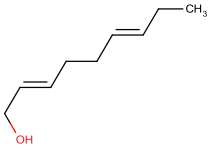
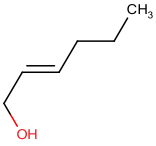
Appendix

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, 2015a,b) 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 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 substance 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 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	2,6-Nonadien-1-ol	trans-2-Hexenol
CAS No.	7786-44-9	928-95-0
Structure		
Similarity (Tanimoto score)		0.743
Read-across endpoint		• Genotoxicity
Molecular Formula	$C_9H_{16}O$	$C_6H_{12}O$
Molecular Weight	140.23	100.16
Melting Point (°C, EPI Suite)	−4.87	−38.47
Boiling Point (°C, EPI Suite)	231.63	165.73
Vapor Pressure (Pa @ 25°C, EPI Suite)	1.4	121
Log Kow (KOWWIN v1.68 in EPI Suite)	2.87	1.6[1]
Water Solubility (mg/L, @ 25°C, WSKOW v1.42 in EPI Suite)	963.8	16000
J_{max} (mg/cm^2/h, SAM)	76.12	527.97
Henry's Law (Pa·m^3/mol, Bond Method, EPI Suite)	3.19E-005	1.55E-005
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 (genotox and non-genotox) alerts (ISS)	• Non-carcinogen (moderate 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)	Supplemental Data 1	Supplemental Data 2
Rat liver S9 metabolism simulator		

1. RIFM, 2013b.

Summary

There are insufficient toxicity data on 2,6-nonadien-1-ol (CAS # 7786-44-9). Hence, *in silico* evaluation was conducted by determining read-across analogs for this material. Based on structural similarity, reactivity, metabolism data, physical–chemical properties, and expert judgment, *trans*-2-hexenol (CAS # 928-95-0) was identified as a read-across analog with sufficient data for toxicological evaluation.

Conclusions

- trans-2-Hexenol (CAS # 928-95-0) was used as a structurally similar read-across analog for the target material 2,6-nonadien-1-ol (CAS # 7786-44-9) for the genotoxicity endpoint.
  - ○ The target substance and the read-across analog are structurally similar and belong to the structural class of unsaturated alcohols.
  - ○ The target substance and the read-across analog have the 2-hexanol fragment common among them.
  - ○ The key difference between the target substance and the read-across analog is that the target has a higher degree of unsaturation and a 3 carbon longer aliphatic chain compared to the read-across material. This structural difference between the target substance and the read-across analog do not raise additional structural alerts, so the structural differences are not relevant from a toxicological endpoint perspective.
  - ○ The target substance and the read-across analog have a Tanimoto score as mentioned in the above table. The Tanimoto score is mainly driven by the hexanol fragment. The differences in the structure that are responsible for Tanimoto score < 1 are not relevent from a toxicological endpoint perspective.
  - ○ The target substance and the read-across analog have similar physical–chemical properties. Any differences in some of the physical–chemical properties of the target substance and the read-across analog are estimated to be toxicologically insignificant for the genotoxicity endpoint.
  - ○ According to the QSAR OECD Toolbox (v3.4), structural alerts for genotoxicity endpoint 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 metabolism simulator.
  - ○ The structural alerts for the genotoxicity endpoint are consistent between the metabolites of the read-across analog and the target substance.
  - ○ The structural differences between the target substance and the read-across analog are deemed to be toxicologically insignificant.

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