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Short review

RIFM fragrance ingredient safety assessment, Isopropylphenylbutanal, CAS Registry Number 125109-85-5

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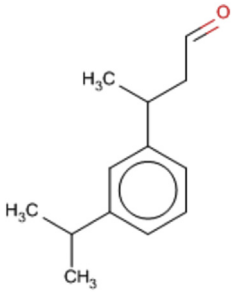

(*continued*)

Abbreviation 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) 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
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

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(*continued*)

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
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

RIFM's Expert Panel* 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 reviews the relevant data that were available at the time of writing (six digit version number in the top box is indicative of the date of approval based on two digits each for month, day, and year), both in the RIFM database (consisting of publicly available and proprietary data) and through publicly available information sources (see reference section). 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 end-point value (e.g., PNEC, NOAEL, LOEL, and DST).

*RIFM's Expert Panel 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.

This material was evaluated for genotoxicity, repeated dose toxicity, developmental and reproductive toxicity, local respiratory toxicity, phototoxicity/photoallergenicity, skin sensitization, as well as environmental safety. Data show that this material is not genotoxic, provided a MOE >100 for the repeated dose toxicity endpoint and it does not have skin sensitization potential. The 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 and 1.4 mg/day, respectively). The phototoxicity/photoallergenicity endpoint was completed based on suitable UV spectra along with data on the target material. The environmental endpoint was completed as described in the RIFM Framework.

Human Health Safety Assessment

Genotoxicity: Not genotoxic. (RIFM, 1989a; RIFM, 2006; RIFM, 1991a)
Repeated Dose Toxicity: NOEL = 20 mg/kg/day (RIFM, 1991b)
Developmental and Reproductive Toxicity: No NOAEL available. Exposure is below the TTC.
Skin Sensitization: Not sensitizing (RIFM, 1988c; ECHA Dossier 1 Accessed 2/25/16)
Phototoxicity/Photoallergenicity: Not phototoxic/photoallergenic (UV Spectra, RIFM DB; RIFM, 1988a; RIFM, 1988b)
Local Respiratory Toxicity: No NOAEC available. Exposure is below the TTC.

Environmental Safety Assessment

Hazard Assessment:
Persistence: Critical Measured Value: 104% (OECD 302C) (RIFM, 1993a)
Bioaccumulation: Screening Level: 175.6 l/kg (Epi Suite ver 4.1)
Ecotoxicity: Critical Ecotoxicity Endpoint: *Daphnia magna* OECD 211: NOEC: 0.71 mg/l (RIFM, 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: *Daphnia magna* OECD 211: NOEC: 0.71 mg/l (RIFM, 2002)
RIFM PNEC is: 14.2 μg/L
•Revised PEC/PNECs (2011 IFRA VoU): North America and Europe <1

1. Identification

1. **Chemical Name:** Isopropylphenylbutanal
2. **CAS Registry Number:** 125109-85-5
3. **Synonyms:** Benzenepropanal, .β.-methyl-3-(1-methylethyl)-; 3-(3-Isopropylphenyl)butanal; .β.-Methyl-3-(1-methylethyl)benzenepropanal; β-Methyl-3-(1-methylethyl)benzenepropanal; Benzenepropanal, β-methyl-3-(1-methylethyl)-; Isopropylphenylbutanal; Florhydral
4. **Molecular Formula:** $C_{13}H_{18}O$
5. **Molecular Weight:** 190.29
6. **RIFM Number:** 6334

2. Physical data

1. **Boiling Point:** 115 °C at 1000 Pa [RIFM, 1993b], 115 °C at 1000 Pa [RIFM, 1993c], 115 °C at 1000 Pa [RIFM, 1993a], 270.29 °C [EPI Suite]
2. **Flash Point:** 154.00 °F TCC (67.78 °C)*
3. **Log KOW:** log Pow = 3.8 [RIFM, 1993c], 3.91 [EPI Suite], log Pow = 3.1 [RIFM, 2012]
4. **Melting Point:** <20 °C [RIFM, 1993c], <20 °C [RIFM, 1993a], <20 °C [RIFM, 1993b], 29.1 °C [EPI Suite]
5. **Water Solubility:** 22.59 mg/L [EPI Suite]
6. **Specific Gravity:** 0.952 g/l at 20 °C [RIFM, 1993a], 0.952 g/l at 20 °C [RIFM, 1993c], 0.952 g/l at 20 °C [RIFM, 1993b]
7. **Vapor Pressure:** 0.00856 mm Hg @ 25 °C [EPI Suite], 0.00483 mm Hg @ 20 °C [EPI Suite 4.0], 0.65 Pa at 20 °C [RIFM, 2012]
8. **UV Spectra:** No absorbance between 290 and 400 nm; molar absorption coefficient below the benchmark (1000 L mol-1 cm-1).
9. **Appearance/Organoleptic:** Colorless to pale yellow clear liquid with a medium floral, green, muguet, linden, flower, lily of the valley, and fresh odor.*
   * http://www.thegoodscentscompany.com/data/rw1131041.html, retrieved 8/15/2016

3. Exposure

1. **Volume of Use (worldwide band):** 10–100 metric tons per year (IFRA, 2011)
2. **95**th **Percentile Concentration in Hydroalcoholics:** 0.052% (RIFM, 2015)
3. **Inhalation Exposure*:** 0.00026 mg/kg/day or 0.019 mg/day (RIFM, 2015)
4. **Total Systemic Exposure**:** 0.0018 mg/kg/day (RIFM, 2015)
   * 95th percentile calculated exposure derived from concentration survey data in the Creme RIFM exposure model (Comiskeyet al., 2015 and Safford et al., 2015).
   * *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 and Safford et al., 2015).

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. Analogues Selected:
   a. **Genotoxicity:** None
   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 justifications:** None

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)

Isopropylphenylbutanal 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, 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

Available; accessed on 04/23/14.

10. Summary

10.1. Human health endpoint summaries

10.1.1. Genotoxicity

Based on the current existing data and use levels, isopropylphenylbutanal does not present a concern for genetic toxicity.

10.1.2. Risk assessment

Isopropylphenylbutanal was tested by the BlueScreen assay and found negative for both cytotoxicity and genotoxicity indicating a lack for genotoxic concern (RIFM, 2013b). The mutagenic activity of isopropylphenylbutanal was assessed in an Ames assay conducted in compliance with GLP regulations and in accordance with OECD TG 471 using the standard plate incorporation method. *Salmonella typhimurium* strains TA1535, TA1537, TA1538, TA98 and TA100 were treated with isopropylphenylbutanal at the following concentrations: 0.0005, 0.01, 0.010, 0.025, 0.050, 0.100, 0.250 μl/plate without exogenous metabolically active microsomal mix (S9 mix) and 0.001, 0.010, 0.025, 0.05, 0.10, 0.25, 0.50 μl/plate with S9 mix in DMSO (dimethyl sulfoxide). In *E. coli* WP2uvrA strain the concentrations used were: 3, 10, 33, 100, 333, 1000, 2500 and 5000 μg/plate with and without S9 mix in ethanol. There was no increase in revertant colonies in any of the strains at the concentrations tested (RIFM, 1989a; RIFM, 2006). Under the conditions of the studies, isopropylphenylbutanal was considered not mutagenic.

The clastogenic activity of isopropylphenylbutanal was tested in an *in vivo* micronucleus assay conducted in compliance with GLP regulations and in accordance with OECD TG 474. Groups of male and female Fullinsdorf Moro Albino outbred strain mice were treated with isopropylphenylbutanal in 10 ml of Standard Suspension Vehicle (SSV) via a single oral dose at concentrations of 1000 and 2000 mg/kg b.w. Twenty four hours after dose administration animals were euthanized, femurs were dissected and bone marrow was prepared. No significant increase in the frequency of micronucleated polychromatic erythrocytes was observed (RIFM, 1991a). Under the conditions of the study, isopropylphenylbutanal was considered not clastogenic.

Based on the available data, isopropylphenylbutanal does not present a concern for genotoxic potential.

Additional References: None.

Literature Search and Risk Assessment Completed on: 08/15/2016.

10.1.3. Repeated dose toxicity

The margin of exposure for isopropylphenylbutanal is adequate for the repeated dose toxicity endpoint at the current level of use.

10.1.4. Risk assessment

The repeated dose toxicity data on isopropylphenylbutanal are sufficient for the repeated dose toxicity endpoint. An OECD 407 gavage 28-day subchronic toxicity study conducted in rats determined the NOEL to be 60 mg/kg/day, based on a transient sedative effect and increased liver weights (RIFM, 1991b).

A default safety factor of 3 was used when deriving a NOEL from the 28 day or OECD 422/421/407 studies. The safety factor has been approved by RIFM's Independent Expert Panel*.

Thus the derived NOEL for the repeated dose toxicity data is 60/3 or 20 mg/kg/day.

Therefore, the MOE is equal to the NOEL in mg/kg/day divided by the total systemic exposure, 20/0.0018 or 11111.

In addition, the total systemic exposure for isopropylphenylbutanal (1.8 μg/kg/day) is below the TTC (30 μg/kg bw/day) for the repeated dose toxicity endpoint at the current level of use.

*RIFM's Expert Panel is composed of scientific and technical experts in their respective fields. This group provides advice and guidance.

Additional References: RIFM, 2012; RIFM, 2013a; Pelling et al., 1976; Robinson et al., 1954; Meyer, 1965; Meyer and Meyer, 1959; Ishida et al., 1989; RIFM, 2014.

Literature Search and Risk Assessment Completed on: 08/15/2016.

10.1.5. Developmental and reproductive toxicity

There are insufficient developmental or reproductive toxicity data on isopropylphenylbutanal or any read across materials. The exposure is below the Threshold of Toxicological Concern (TTC).

10.1.6. Risk assessment

There are no developmental toxicity data on isopropylphenylbutanal. A gavage 14-day repeated dose reproduction screening study conducted in male rats determined the NOAEL for male reproductive toxicity to be 250 mg/kg/day, the highest dosage tested (RIFM, 2010). While the reproductive toxicity screening study is not sufficient to identify a reproductive NOAEL, it indicates no specific concern for male reproductive toxicity. There are no reproductive toxicity data for females with isopropylphenylbutanal or developmental or reproductive data on any read across materials that can be used to support the developmental or reproductive toxicity endpoints. The total systemic exposure (1.8 μg/kg/day) is below the TTC for isopropylphenylbutanal (30 μg/kg bw/day).

Additional References: RIFM, 2012; RIFM, 2013a; Pelling et al., 1976; Robinson et al., 1954; Meyer, 1965; Meyer and Meyer, 1959; Ishida et al., 1989; Posternak et al., 1969; RIFM, 2009a; RIFM, 2011c; RIFM, 2009b; RIFM, 2011a; RIFM, 2011b; RIFM, 2000; RIFM, 2014.

Literature Search and Risk Assessment Completed on: 08/15/2016.

10.1.7. Skin sensitization

Based on the available data, isopropylphenylbutanal does not present a concern for skin sensitization.

10.1.8. Risk assessment

Based on the available data, isopropylphenylbutanal does not present a concern for skin sensitization. The chemical structure indicates that this material would be expected to react directly with skin proteins (Roberts et al., 2007; Toxtree 2.5.0; OECD toolbox v3.1). However, in the guinea pig maximization test, isopropylphenylbutanal was considered to be non-sensitizing (RIFM, 1988c, ECHA REACH: β-methyl-3-(1-methylethyl)benzenepropanal Dossier 1 Accessed 5/23/14; ECHA REACH: β-methyl-3-(1-methylethyl)benzenepropanal Dossier 2 Accessed 5/23/14). In a human confirmatory study no sensitization reactions were observed to isopropylphenylbutanal (RIFM, 1989b).

Additional References: RIFM, 1988a and RIFM, 1988d.

Literature Search and Risk Assessment Completed on: 08/15/2016.

10.1.9. Phototoxicity/photoallergenicity

Based on the available *in vivo* data and UV absorption spectra, isopropylphenylbutanal does not present a concern for phototoxicity or photoallergenicity.

10.1.10. Risk assessment

The available UV absorption spectrum for isopropylphenylbutanal demonstrates no absorption in the region of 290–400 nm, with a corresponding molar absorption coefficient below the benchmark of concern for phototoxic effects, 1000 L mol^{-1} cm^{-1} (Henry et al., 2009). Additionally, in guinea pig phototoxicity and photoallergenicity studies no reactions indicative of phototoxicity or photoallergy were observed (RIFM, 1988a; RIFM, 1988b). Based on the *in vivo* data and lack of absorbance in the UV range, isopropylphenylbutanal does not present a concern for phototoxicity or photoallergenicity.

Additional References: None.

Literature Search and Risk Assessment Completed on: 07/18/16.

10.1.11. Local respiratory toxicity

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

10.1.12. Risk assessment

There are no inhalation data available on isopropylphenylbutanal. Based on the Creme RIFM model, the inhalation exposure is 0.019 mg/day. This exposure is 73.7 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: None.

Literature Search and Risk Assessment Completed on: 7/20/2016.

10.2. Environmental endpoint summary

10.2.1. Screening-level assessment

A screening level risk assessment of isopropylphenylbutanal 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 (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 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, isopropylphenylbutanal 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 EPISUITE ver 4.1 did identify isopropylphenylbutanal as possibly persistent but not 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 EPISUITE ver.4.1). Specific key data on biodegradation and fate and bioaccumulation are reported below and summarized in the Environmental Safety Assessment section prior to Section 1.

10.2.2. Risk assessment

Based on current Volume of Use (2011), isopropylphenylbutanal presents a risk to the aquatic compartment in the screening level assessment.

10.2.3. Key studies

10.2.3.1. Biodegradation

10.2.3.1.1. RIFM, 1993a. The inherent biodegradability of the test article was evaluated by the modified MITI Test II according to the OECD 302C method. Flasks were partly filled with 7.5 mg of the test material (final concentration of 30 mg/l) as the nominal sole source of organic carbon. Flask contents were continually stirred and kept at a constant temperature for 28 days. Biodegradation of 104% was

observed.

10.2.3.1.2. RIFM, 1993b. The ready biodegradability of the test article was evaluated by the modified MITI Test I according to the OECD 301C method. Flasks were partly filled with 25 mg of the test material (final concentration of 100 mg/l). Flask contents were continually stirred and kept at a constant temperature for 28 days. Under the conditions of this study, the test article was regarded as not readily biodegradable. In addition, the test material at 100 mg/l was slightly inhibitory to the microorganisms during the first 14 days.

test material in Daphnia magna was 1.7 mg/l. The NOEC and LOEC (measured concentrations) were determined to be 0.71 mg/l and 2.6 mg/l, respectively. The 21-day EC50 for the reproduction rate of *Daphnia magna* was determined to be 1.7 mg/l.

10.2.4.5. Other available data. Isopropylphenylbutanal has been registered under REACH; however no additional data is available.

10.2.5. 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)**	6.973 mg/l			1,000,000	0.006973 μg/l	
ECOSAR Acute Endpoints **(Tier 2)** ***Ver 1.11***	1.092 mg/l	0.681 mg/l	1.6 mg/l	10,000	0.0681 μg/l	Aldehydes (mono)
ECOSAR Acute Endpoints **(Tier 2)** ***Ver 1.11***	3.032 mg/l	2.053 mg/l	3.166 mg/l			Neutral organics
Tier 3: Measured Data						
	LC50	EC50	NOEC	AF	PNEC	Comments
Fish	1.082 mg/l					
Daphnia		7.7 mg/l	0.71 mg/l	50	14.2 μg/l	
Algae		0.74 mg/l	3.2 mg/l			

10.2.3.1.3. RIFM, 2011d. The ready biodegradability of the test material was determined by the manomentric respirometry test following the OECD 301F method. After 28 days isopropylphenylbutanal underwent 74% biodegradation under the conditions of the study.

10.2.4. Ecotoxicity

10.2.4.1. RIFM, 1991c. A 96 h fish (*Salmo gairdneri*) acute toxicity test was conducted according to the OECD 203 method. The LC50 was reported to be 1.082 mg/l.

10.2.4.2. RIFM, 1991d. The 48 h *Daphnia magna* acute toxicity test was conducted following the OECD 202 method. The EC50 was determined to be 7.70 mg/l (Logit-model) at 48 h with a 95% confidence interval of 6.27–10.21 mg/l. The EC0 and EC100 were reported to be 2.5 and > 10 mg/l, respectively.

10.2.4.3. RIFM, 1999. An algae inhibition test was conducted according to OECD 201 guideline. Isopropylphenylbutanal was evaluated for its ability to inhibit the growth of *Scenedesmus subspicatus* at nominal concentrations of 0.46, 1, 2.2, 4.6, 10 or 22 mg/l. The LOEC was reported to be 7.2 mg/l and the NOEC was reported to be 3.2 mg/l. The EC50 for growth rate was 11 mg/l (95% CI 7.4–20); the EC50 was not determined for biomass. The 72 h NOEC was reported to be 3.2 mg/l for biomass and growth rate.

10.2.4.4. RIFM, 2002. A 21 day *Daphnia magna* chronic study was conducted according to the OECD 211 method under semi-static conditions. Under conditions of the study, the 21 day EC50 for the

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

Exposure	Europe (EU)	North America (NA)
Log K_{ow} used	3.8	3.8
Biodegradation Factor Used	1	1
Dilution Factor	3	3
Regional Volume of Use Tonnage Band	10–100	10–100
Risk Characterization: PEC/PNEC	**<1**	**<1**

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

The RIFM PNEC is 14.2 μg/L. The revised PEC/PNECs for EU and NA are < 1 and therefore, do not present a risk to the aquatic environment at the current reported volumes of use.

Literature Search and Risk Assessment Completed on: 08/15/2016.

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.

Transparency document

Transparency document related to this article can be found online at http://dx.doi.org/10.1016/j.fct.2016.10.018.

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