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Short Review

RIFM FRAGRANCE INGREDIENT SAFETY ASSESSMENT, [2-Isopropoxyethyl]benzene, CAS Registry Number 68039-47-4

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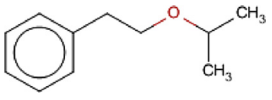
Version: 051618. This version replaces any previous versions.
Name: [2-Isopropoxyethyl]benzene
CAS Registry Number: 68039-47-4



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
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

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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-Isopropoxyethyl]benzene was evaluated for genotoxicity, repeated dose toxicity, reproductive toxicity, local respiratory toxicity, phototoxicity/photoallergenicity, skin sensitization, and environmental safety. Data from read-across analog phenylethyl isoamyl ether (CAS# 56011-02-0) show that [2-isopropoxyethyl]benzene is not expected to be genotoxic. The skin sensitization endpoint was completed using the DST for non-reactive materials (900 μg/cm^2/day); exposure is below the DST. The repeated dose, reproductive, and local respiratory toxicity endpoints were completed using the TTC for a Cramer Class III material, and the exposure to [2-isopropoxyethyl]benzene is below the TTC (0.0015 mg/kg/day, 0.0015 mg/kg/day, and 0.47 mg/day, respectively). The phototoxicity/photoallergenicity endpoint was completed based on UV spectra and data; [2-isopropoxyethyl]benzene is not phototoxic/photoallergenic. The environmental endpoints were evaluated; [2-isopropoxyethyl]benzene 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.
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; RIFM, 1981)
Local Respiratory Toxicity: No NOAEC available. Exposure is below the TTC.

Environmental Safety Assessment

Hazard Assessment:
Persistence: Screening-level: 2.7 (BIOWIN 3) (EPI Suite v4.1; US EPA, 2012a)
Bioaccumulation: Screening-level: 57.7 L/kg (EPI Suite v4.1; US EPA, 2012a)
Ecotoxicity: Screening-level: Fish LC50: 24.49 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: 24.49 mg/L (RIFM Framework; Salvito et al., 2002)
RIFM PNEC is: 0.02449 μg/L
- **Revised PEC/PNECs (2011 IFRA VoU):** North America and Europe: Not applicable; cleared at screening-level

1. Identification

1. **Chemical Name:** [2-Isopropoxyethyl]benzene
2. CAS Registry Number: 68039-47-4
3. Synonyms: Benzene, [2-(1-methylethoxy)ethyl]-; [2-(1-Methylethoxy)ethyl]benzene; 1-Phenyl-4-methyl-3-oxapentane; Petiole; (2-Isopropoxyethyl)benzene; [2-Isopropoxyethyl]benzene
4. Molecular Formula: $C_{11}H_{16}O$
5. Molecular Weight: 164.48
6. RIFM Number: 5880

2. Physical data

1. **Boiling Point:** 219.02 °C (EPI Suite)
2. **Flash Point:** 79 °C (GHS)
3. **Log K_{ow}:** 3.1 (RIFM, 2013b), 3.17 (EPI Suite)
4. **Melting Point**: −5.78 °C (EPI Suite)
5. **Water Solubility:** 127.3 mg/L (EPI Suite)
6. **Specific Gravity:** Not Available
7. **Vapor Pressure:** 0.091 mm Hg @ 20 °C (EPI Suite v4.0), 0.138 mm Hg @ 25 °C (EPI Suite)
8. **UV Spectra:** No absorbance between 290 and 450 nm; molar absorption coefficient is below the benchmark (1000 L mol^{-1} · cm^{-1})
9. **Appearance/Organoleptic:** A colorless clear liquid with a medium green, rose, plastic, metallic, spicy, foliage odor*

*http://www.thegoodscentscompany.com/data/rw1020111.html#toorgano retrieved 3/22/2017.

3. Exposure

1. **Volume of Use (worldwide band):** 1–10 metric tons per year (IFRA, 2011)
2. **95th Percentile Concentration in Hydroalcoholics:** 0.029% (RIFM, 2016)
3. **Inhalation Exposure*:** 0.00011 mg/kg/day or 0.0081 mg/day (RIFM, 2016)
4. **Total Systemic Exposure**:** 0.00093 mg/kg/day (RIFM, 2016)