



Short review

RIFM fragrance ingredient safety assessment, benzyl isobutyrate, CAS Registry Number 103-28-6



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Genotoxicity

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Skin sensitization

Phototoxicity/photoallergenicity

Local respiratory toxicity

Environmental safety

3. **Synonyms:** Benzyl isobutyrate, Benzyl 2-methylpropanoate, Propanoic acid, 2-methyl-, phenylmethyl ester, アルカン酸(C = 1 ~ 6) ヘンシル, アルキル (C = 1 ~ 5) カルボン酸7エニルアルキル (C = 1 ~ 6)
4. **Molecular Formula:** C₁₁H₁₄O₂
5. **Molecular Weight:** 178.23
6. **RIFM Number:** 227

2. Physical data

1. **Boiling Point:** 229 °C [FMA database], 241.5 °C [EPI Suite]
2. **Flash Point:** >200 °F;CC [FMA database]
3. **Log K_{ow}:** 2.99 [EPI Suite]
4. **Melting Point:** 10.84 °C [EPI Suite]
5. **Water Solubility:** 157.2 mg/L [EPI Suite]
6. **Specific Gravity:** 1.000–1.005 [FMA], 1.002–1.007 [FMA database]
7. **Vapor Pressure:** 0.0274 mm Hg @ 20 °C [EPI Suite 4.0], 0.04 mm Hg @ 20 °C [FMA database], 0.0428 mm Hg @ 25 °C [EPI Suite]
8. **UV Spectra:** No absorption between 290 and 400 nm; molar absorption coefficient is below the benchmark (1000 L mol⁻¹ cm⁻¹).
9. **Appearance/Organoleptic:** A colorless to pale yellow liquid having a fruity and jasmine-like odor.

1. Identification

1. **Chemical Name:** Benzyl isobutyrate
2. **CAS Registry Number:** 103-28-6

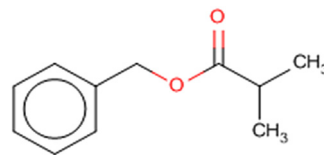
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Version: 030816. This version replaces any previous versions.

Name: Benzyl isobutyrate

CAS Registry Number: 103-28-6



Abbreviation list:

2-Box Model – a RIFM, Inc. proprietary *in silico* tool used to calculate fragrance air exposure concentration

97.5th percentile – The concentration of the fragrance ingredient is obtained from examination of several thousand commercial fine fragrance formulations. The upper 97.5th percentile concentration is calculated from these data and is then used to estimate the dermal systemic exposure in ten types of the most frequently used personal care and cosmetic products. The dermal route is the major route in assessing the safety of fragrance ingredients. Further explanation of how the data were obtained and of how exposures were determined has been previously reported by Cadby et al. (2002) and Ford et al. (2000).

AF – Assessment Factor

BCF – Bioconcentration Factor

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

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

3. Exposure

- Volume of Use (worldwide band):** 1–10 metric tons per year (IFRA, 2011)
- Average Maximum Concentration in Hydroalcohols:** 0.16% (IFRA, 2008)
- 97.5th Percentile:** 0.71% (IFRA, 2008)
- Dermal Exposure*:** 0.0180 mg/kg/day (IFRA, 2008)
- Oral Exposure:** Not applicable
- Inhalation Exposures*:** 0.0011 mg/kg/day (IFRA, 2008)
- Total Systemic Exposure (Dermal + Inhalation):** (0.018 mg/kg/day x 78.7% absorption) + 0.0011 mg/kg/day = 0.015 mg/kg/day

*Calculated using the reported 97.5th percentile concentration based on the levels of the same fragrance ingredient in ten of the most frequently used personal care and cosmetic products (i.e., anti-perspirant, bath products, body lotion, eau de toilette, face cream, fragrance cream, hair spray, shampoo, shower gel, and toilet soap) (Cadby et al., 2002; Ford et al., 2000).

**Combined (fine fragrances, hair sprays, antiperspirants/deodorants, candles, aerosol air fresheners, and reed diffusers/heated oil plug-ins) result calculated using RIFM's 2-Box/MPPD *in silico* models, based on the IFRA survey results for the 97.5th percentile use in hydroalcohols for a 60 kg individual.

4. Derivation of systemic absorption

- Dermal:** 78.7%

Bronaugh et al., 1990: The skin absorption of read across material [^{14}C] benzyl acetate (CAS # 104-11-1; see Section 5) was measured in 4 female rhesus monkeys. The test material in acetone was applied at a concentration of 4 $\mu\text{g}/\text{cm}^2$ to a 1 cm^2 area of abdominal skin for 24 h. Urine was collected for an additional 4 days. The extent of dermal absorption was estimated from the amount of ^{14}C -equivalents excreted in the urine over the 5 day collection period. When the application site was occluded with either plastic wrap or a glass chamber, the absorption of benzyl acetate was $17.3 \pm 2.7\%$ and $78.7 \pm 7.5\%$, respectively. When the site was not occluded, the absorption was $34.6 \pm 9.4\%$.

- Oral:** Data not available – not considered.
- Inhalation:** Assumed 100%
- Total:** Dermal (78.7%) + Inhalation (assume 100%) absorbed = (0.018 mg/kg/day x 78.7%) + 0.0011 mg/kg/day = 0.015 mg/kg/day

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