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Short review

RIFM fragrance ingredient safety assessment, acetic acid, C7-9-branched alkyl esters, C8-rich, CAS Registry Number 108419-32-5

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ABSTRACT

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. Data from the suitable read across analog isoamyl acetate (CAS# 123-92-2) show that this material does not have skin sensitization potential. The 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 repeated dose and developmental endpoint was completed using data on the target material, which provided a MOE > 100. The phototoxicity/photoallergenicity endpoint was completed based on suitable UV spectra. The environmental endpoint was completed as described in the RIFM Framework

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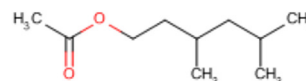
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Name: Acetic acid, C7-9-branched alkyl esters, C8-rich

CAS Registry Number: 108419-32-5



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

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 (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 end-point value (e.g., PNEC, NOAEL, LOEL, and NESIL).

*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. Data from the suitable read across analogue isoamyl acetate (CAS# 123-92-2) show that this material does not have skin sensitization potential. The 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 repeated dose and developmental endpoint was completed using data on the target material, which provided a MOE >100. The phototoxicity/photoallergenicity endpoint was completed based on suitable UV spectra. The environmental endpoint was completed as described in the RIFM Framework.

Human Health Safety Assessment

Genotoxicity: Not genotoxic.

Repeated Dose Toxicity: NOAEL = 1000 mg/kg/day.

Developmental and Reproductive Toxicity: Developmental toxicity NOAEL = 500 mg/kg/day. No reproductive toxicity data available, exposure is below the TTC.

Skin Sensitization: Not a sensitization concern.

Phototoxicity/Photoallergenicity: Not phototoxic/photoallergenic.

Local Respiratory Toxicity: No NOAEC available. Exposure is below the TTC.

(EPA HPVIS, 1994)

(EPA HPV Test Plan – Alkyl Acetate C6-C13 Category, 2000)

(EPA HPV Test Plan – Alkyl Acetate C6-C13 Category, 2000)

(RIFM, 1987)

(UV Spectra, RIFM DB)

Environmental Safety Assessment

Hazard Assessment:

Persistence: Screening Level: 2.95 (Biowin 3)

(EpiSuite ver 4.1)

Bioaccumulation: Screening Level: 121 L/kg

(EpiSuite ver 4.1)

Ecotoxicity: Screening Level: Fish LC50: 8.356 mg/L

(RIFM Framework; Salvito et al., 2002)

Conclusion: Not PBT or vPvB as per IFRA Environmental Standards

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