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Short Review

RIFM fragrance ingredient safety assessment, benzyl acetone, CAS Registry Number 2550-26-7

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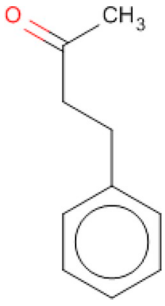
Version: 091818. This version replaces any previous versions.
Name: Benzyl acetone
CAS Registry Number: 2550-26-7



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

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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
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 as 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 existing information supports the use of this material as described in this safety assessment.

Benzyl acetone was evaluated for genotoxicity, repeated dose toxicity, developmental and reproductive toxicity, local respiratory toxicity, phototoxicity, skin sensitization potential, and environmental safety. Data show that benzyl acetone is not expected to be genotoxic and that there are no safety concerns for skin sensitization under the current, declared levels of use. Data on benzyl acetone provide a calculated MOE > 100 for the repeated dose and reproductive toxicity endpoints. The developmental and local respiratory toxicity endpoints were evaluated using the TTC for a Cramer Class I material, and the exposure to benzyl acetone is below the TTC (0.03 mg/kg/day and 1.4 mg/day, respectively). The phototoxicity/photoallergenicity endpoints were evaluated based on UV spectra; benzyl acetone is not expected to be phototoxic/photoallergenic. The environmental endpoints were evaluated; benzyl acetone 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 expected to be genotoxic.	(RIFM, 1999a: RIFM, 2013a)
Repeated Dose Toxicity: NOAEL = 500 mg/kg/day.	RIFM (2012a)
Developmental toxicity: No NOAEL available. Exposure is below the TTC. **Reproductive Toxicity:** NOAEL = 165 mg/kg/day	RIFM (2012a)
Skin Sensitization: No safety concerns at current, declared use levels.	RIFM (2012d)
Phototoxicity/Photoallergenicity: Not expected to be phototoxic/photoallergenic.	(UV Spectra, RIFM DB)
Local Respiratory Toxicity: No NOAEC available. Exposure is below the TTC.	Zissu (1995)

Environmental Safety Assessment

Hazard Assessment:

Persistence: Critical Measured Value: 78% (OECD 301F)	RIFM (1997b)
Bioaccumulation: Screening-level: 9.179 L/kg	(EPI Suite v4.11; US EPA, 2012a)
Ecotoxicity: Screening-level: 96-h Algae EC50: 54.5 mg/L	(ECOSAR; US EPA, 2012b)
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: 96-h Algae EC50: 54.5 mg/L	(ECOSAR; US EPA, 2012b)
RIFM PNEC is: 5.454 μg/L	
• **Revised PEC/PNECs (2015 IFRA VoU):** North America and Europe < 1	

1. Identification

1. **Chemical Name:** Benzyl acetone
2. **CAS Registry Number:** 2550-26-7
3. **Synonyms:** 2-Butanone, 4-phenyl-; Methyl phenylethyl ketone; 4-Phenylbutan-2-one; β-Phenylethyl methyl ketone; 4-ﾌｪﾆﾙﾌﾞﾀﾝ-2-ｵﾝ; Benzyl acetone
4. **Molecular Formula:** $C_{10}H_{12}O$
5. **Molecular Weight:** 148.21
6. **RIFM Number:** 1071

2. Physical data

1. **Boiling Point:** 239.6 °C (RIFM, 2012c), 235 °C (FMA Database), 228.74 °C (calculated; EPI Suite)
2. **Flash Point:** 101 °C (RIFM, 2012b), > 200 °F; CC (FMA Database)
3. **Log K_{OW}:** 2.0 (RIFM, 1997a), 1.96 (EPI Suite)
4. **Melting Point**: 12.78 °C (EPI Suite)
5. **Water Solubility:** 1625 mg/L (EPI Suite)
6. **Specific Gravity:** 0.988 (FMA Database)
7. **Vapor Pressure:** 0.0421 mm Hg @ 20 °C (EPI Suite v4.0), 0.1 mm Hg 20 °C (FMA Database), 0.0651 mm Hg @ 25 °C (EPI Suite)
8. **UV Spectra:** Minor absorption in the region 290–700 nm; molar absorption coefficient is below the benchmark (1000 $L\,mol^{-1} \cdot cm^{-1}$).
9. **Appearance/Organoleptic:** A colorless to yellow clear liquid to solid with a medium floral and balsam odor and a strawberry like taste*

*http://www.thegoodscentscompany.com/data/rw1024231.html, retrieved 05/16/14.

3. Exposure

1. **Volume of Use (worldwide band):** 100–1000 metric tons per year (IFRA, 2015)
2. **95**th **Percentile Concentration in Hydroalcoholics:** 0.18% (RIFM, 2017)
3. **Inhalation Exposure*:** 0.00082 mg/kg/day or 0.062 mg/day (RIFM, 2017)
4. **Total Systemic Exposure**:** 0.0046 mg/kg/day (RIFM, 2017)

*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).

4. Derivation of systemic absorption

1. **Dermal:** 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:** 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 Justification**: 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)

Benzyl acetone is reported to occur in the following foods by the VCF*:

Alpina species.
Beef.
Cocoa category.
Egg.
Raspberry, blackberry, and boysenberry.
Water yam (*Dioscorea alata*).

*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.

8. IFRA standard

None.

9. Reach dossier

Available; assessed on 02/10/14.

10. Summary

10.1. Human health endpoint summaries

10.1.1. Genotoxicity

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

10.1.1.1. Risk assessment. Benzyl acetone was assessed in the BlueScreen assay and found negative for both cytotoxicity (positive: < 80% relative cell density) and genotoxicity, with and without metabolic activation (RIFM, 2013c). BlueScreen is a screening assay that assesses genotoxic stress through alterations in gene expressions in a human cell line. Additional assays were considered to fully assess the potential mutagenic or clastogenic effects on the target material.

The mutagenic activity of benzyl acetone was assessed in an Ames study conducted in compliance with GLP regulations and in accordance with OECD TG 471 using the standard plate incorporation method. *Salmonella typhimurium* strains TA1535, TA1537, TA98, TA100, and TA102 were treated with benzyl acetone in dimethyl sulfoxide (DMSO) at concentrations up to 5000 μg/plate. No increases in the mean number of revertant colonies were observed at any tested dose in the presence or absence of S9 (RIFM, 1999a). Under the conditions of the study, benzyl acetone was considered not mutagenic in the Ames assay.

The clastogenic potential of benzyl acetone was assessed in an *in vitro* micronucleus assay conducted in compliance with GLP regulations in accordance with OECD TG 487. Human peripheral blood lymphocytes were treated with benzyl acetone in DMSO at concentrations up to 1482.0 μg/plate in the presence and absence of metabolic activation. No induction of micronuclei was detected in any of the test concentrations (RIFM, 2013a). Under the conditions of the study, benzyl acetone was considered not clastogenic in the *in vitro* micronucleus test.

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

Additional References: RIFM, 2013b.

Literature Search and Risk Assessment Completed On: 12/29/17.

10.1.2. Reapeated dose toxicity

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

10.1.2.1. Risk assessment. There are sufficient repeated dose toxicity data on benzyl acetone. In a GLP (OECD 408) subchronic toxicity study, 10 Sprague Dawley rats/sex/group were administered daily orally via gavage with benzyl acetone at dose levels of 0 (vehicle control, corn oil), 55, 165, 250, and 500 mg/kg/day for a period of 13 weeks. High-dose recovery and control group animals (5/sex/group) were included in the study. Mortality was reported among all treatment groups. One female treated with 55 mg/kg/day was found dead on day 11 (before the administration on this day). Clinical signs reported for this female included decreased activity, hunched posture, abnormal gait, and tachypnea on day 10. It could be not excluded that this was test material-related because the reason of the death could not be established. One male treated with 165 mg/kg/day was found dead on treatment day 21. The reason for these 2 deaths could not be established. One male treated with 250 mg/kg/day was found dead on day 27 due to a misgavage. One female treated with 500 mg/kg/day was terminated in extremis on day 45 due to a misgavage because perforation of the esophagus was noted. Another female of this group was found dead on day 83. The reason for the death was not clear. At 500 mg/kg/day, salivation was reported in both sexes (few animals) during the treatment period. No treatment-related findings were reported in clinical sings (during recovery period), functional observational battery (grip strength and locomotor activity), ophthalmoscopy, body weights, or food consumption. Statistically significant reductions in mean value of methaemoglobin of males and females in all groups were reported in week 14. These changes were considered to be treatment-related. No treatment-related changes were reported on clinical chemistry and urinalysis. Statistically significant increases in kidney weights (absolute and relative) and kidney-to-brain weight ratios were reported in males treated with 500 mg/kg/day. Statistically significant increases in relative liver weights in both sexes treated with ≥165 mg/kg/day as well as liver-to-brain weight ratios in males treated with 165 and 250 mg/kg/day and in females treated with 250 and 500 mg/kg/day were reported. These changes in organ weights were reversed during the recovery period. In liver, minimal to slight centrilobular hepatocellular hypertrophy was reported at 250 mg/kg/day (7/10 males) and 500 mg/kg/day (10/10 males and 7/10 females). Incidences of minimal bile duct hyperplasia (age-related) was increased in females treated with 500 mg/kg/day. The minimal histologic changes reported in the liver (hepatocellular hypertrophy) were considered to be an adaptive response to treatment since this reversed during the recovery period. In the thyroid, minimal to slight diffuse follicular cell hypertrophy was reported at 500 mg/kg/day (3/10 males), which enhanced liver cell metabolism with accelerated thyroid hormone breakdown in liver cells. In kidneys, minimal to moderate tubular degeneration/regeneration in the cortex (outer and inner) at 250 mg/kg/day (3/10 males) and at 500 mg/kg/day (10/10 males) were reported. These changes were also reported during the recovery period at 500 mg/kg/day (5/5 males). These kidney changes in males were associated with an increase in hyaline droplets (α-2u-globulin protein, confirmed with Mallory Heidenhain stain) in proximal tubules and consistent with documented changes of α-2u-globulin nephropathy, which is species-specific to male rats in response to treatment with some hydrocarbons. This effect is not considered a hazard to human health (Lehman-McKeeman and Caudill, 1992 and Lehman-McKeeman et al., 1990). Based on the results, the NOAEL was considered to be 500 mg/kg/day, the highest dose tested, as histopathological changes reported in the liver and thyroid were adaptive responses to treatment. (RIFM, 2012a).

Therefore, MOE for the repeated dose toxicity endpoint can be calculated by dividing the benzyl acetone NOAEL by the total systemic exposure to benzyl acetone, 500/0.0046 or 108696.

In addition, the total systemic exposure to benzyl acetone (4.6 μg/kg bw/day) is below the TTC (30 μg/kg bw/day Kroes et al., 2007; Laufersweiler et al., 2012) of a Cramer Class I material for the repeated dose toxicity endpoint at the current level of use.

Additional References: None.

Literature Search and Risk Assessment Completed On: 01/10/18.

10.1.3. Developmental and Reproductive Toxicity

There are no developmental toxicity data on benzyl acetone or any read-across materials evaluated. The total systemic exposure to benzyl acetone is below the TTC for the developmental toxicity endpoint of a Cramer Class I material at the current level of use.

The margin of exposure for benzyl acetone is adequate for the reproductive toxicity endpoint at the current level of use.

10.1.3.1. Risk assessment. There are no developmental toxicity data on benzyl acetone or any of the read-across materials to support the developmental toxicity endpoint. The total systemic exposure to benzyl acetone (4.6 μg/kg bw/day) is below the TTC (30 μg/kg bw/day; Kroes et al., 2007; Laufersweiler et al., 2012 of a Cramer Class I material) for the developmental toxicity endpoint at the current level of use.

There are sufficient reproductive toxicity data on benzyl acetone. In a GLP (OECD 408) subchronic toxicity study, 10 Sprague Dawley rats/sex/group were administered daily orally via gavage with benzyl acetone at dose levels of 0 (vehicle control, corn oil), 55, 165, 250, and 500 mg/kg/day for a period of 13 weeks. High-dose recovery and control group animals (5/sex/group) were maintained for 4 weeks after the end of dosing. In females, a vaginal smear was taken, and the stage of estrus was evaluated during weeks 6 and 12. At the end of the treatment period, animals were necropsied, and organ weights (ovaries, uterus with cervix, testes, epididymis, prostate gland, seminal vesicles including coagulating glands) and histological examinations were performed. At necropsy, sperm parameters (sperm motility, morphology, count) was performed. No treatment-related changes were reported in the estrus cycle of treated females or sperm parameters (motility, morphology, sperm count) in males. At 500 mg/kg/day, the mean absolute testes weights were slightly decreased at terminal and reversal phase. This was considered to be due to a slightly increased mean body weight and not considered treatment-related. No treatment-related changes were reported on organ weights. At 250 and 500 mg/kg/day, incidences of reduced corpora lutea (size/number) with increased cystic tertiary follicles were increased when compared with controls. These changes in ovaries were reversible. No treatment-related histopathology changes on other reproductive organs were reported. A conservative NOAEL of 165 mg/kg/day was considered for the reproductive toxicity endpoint, based on increased incidences of reduced corpora lutea (size/number) and cystic tertiary follicles among higher dose females (RIFM, 2012a).

Therefore, the benzyl acetone MOE for the reproductive toxicity endpoint can be calculated by dividing the benzyl acetone NOAEL by the total systemic exposure to benzyl acetone, 165/0.0046 or 35870.

In addition, the total systemic exposure to benzyl acetone (4.6 μg/kg bw/day) is below the TTC (30 μg/kg bw/day; Kroes et al., 2007; Laufersweiler et al., 2012 of a Cramer Class I material) for the reproductive toxicity endpoint at the current level of use.

Additional References: None.

Literature Search and Risk Assessment Completed On: 01/11/18.

10.1.4. Skin sensitization

Based on the existing data, benzyl acetone does not present a safety concern for skin sensitization under the current, declared levels of use.

10.1.4.1. Risk assessment. Based on the existing data, benzyl acetone does not present a safety concern for skin sensitization under the current, declared levels of use. The chemical structure of this material indicates that it would not be expected to react with skin proteins (Toxtree 2.6.13; OECD toolbox v4.1). In a murine local lymph node assay (LLNA), benzyl acetone was found to be negative up to maximum tested concentration of 100%, which resulted in a Stimulation Index (SI) of 1.6 (RIFM, 2012d). In a human maximization test, no skin sensitization reactions were observed (RIFM, 1980). Additionally, in a confirmatory human repeat insult patch test (HRIPT) with 1550 μg/cm^2 of benzyl acetone in alcohol SDA 39C, no reactions indicative of sensitization were observed in any of the 39 volunteers (RIFM, 1975a). In another confirmatory HRIPT with 930 μg/cm^2 of benzyl acetone in petrolatum, no reactions indicative of sensitization were observed in any of the 41 volunteers (RIFM, 1975b).

Based on weight of evidence from structural analysis and animal and human studies, benzyl acetone does not present a concern for skin sensitization.

Additional References: None.

Literature Search and Risk Assessment Completed On: 12/21/17.

10.1.5. Phototoxicity/photoallergenicity

Based on the available UV spectra, benzyl acetone does not present a concern for phototoxicity or photoallergenicity.

10.1.5.1. Risk assessment. There are no phototoxicity studies available for benzyl acetone in experimental models. UV/Vis absorption spectra indicate minor absorbance between 290 and 700 nm. The corresponding molar absorption coefficient is below the benchmark of concern for phototoxicity and photoallergenicity (Henry et al., 2009). Based on lack of significant absorbance in the critical range, benzyl acetone does not present a concern for phototoxicity or photoallergenicity.

10.1.5.2. UV spectra analysis. UV/Vis absorption spectra (OECD TG 101) for benzyl acetone were obtained. The spectra indicate minor 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: 09/20/17.

10.1.6. Local Respiratory Toxicity

The margin of exposure could not be calculated due to lack of appropriate data. The exposure level for benzyl acetone 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 benzyl acetone. Based on the Creme RIFM Model, the inhalation exposure is 0.062 mg/day. This exposure is 22.5 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: 01/05/17.

10.2. Environmental endpoint summary

10.2.1. Screening-level assessment

A screening-level risk assessment of benzyl acetone 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, benzyl acetone 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 EPI Suite v4.1 (US EPA, 2012a) did not identify benzyl acetone as persistent or 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 current VoU (2015), benzyl acetone presents a risk to the aquatic compartment in the screening-level assessment.

10.2.3. Key studies

10.2.3.1. Biodegradation. RIFM, 1997b: The ready biodegradability of the test material was determined by the Manometric Respirometry Test according to the OECD 301F method. Benzyl acetone at 100 mg/L underwent 78% biodegradation after 28 days under the test conditions.

10.2.3.2. Ecotoxicity. RIFM, 1999b: An acute toxicity study with benzyl acetone was conducted over a period of 48 h in a static system as a limit test in accordance with OECD 202 guidelines. The EC50 based on immobilization of test animals by the test material (arithmetic mean of analytical values) after 48 h was ≥95.4 mg/L.

10.2.3.3. Other available data. Benzyl acetone has been registered under REACH and full dossier is available, however the additional data is for the read –across material and not the benzyl acetone.

10.2.3.4. Risk assessment refinement. Since benzyl acetone has passed the 2 Screening criteria, measured data is included in the document for completeness only and has not been used in PNEC derivation.

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)**	199.9			1000000	0.1999	
ECOSAR Acute Endpoints **(Tier 2)** ***Ver 1.11***	131.1	74.24	54.54	10000	5.454	Neutral Organics

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

Exposure	Europe (EU)	North America (NA)
Log K_{ow} used	2.0	2.0
Biodegradation Factor Used	1	1
Dilution Factor	3	3
Regional Volume of Use Tonnage Band	100–1000	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 5.454 μg/L. The revised PEC/PNECs for EU and NA are < 1; therefore, the material does not present a risk to the aquatic environment at the current reported volumes of use.

Literature Search and Risk Assessment Completed On: 01/02/18.

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. The links listed above were active as of 09/06/2018.

Conflicts of interest

The authors declare that they have no conflicts of interest.

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