CLH report

Proposal for Harmonised Classification and Labelling

Based on Regulation (EC) No 1272/2008 (CLP Regulation),
Annex VI, Part 2

International Chemical Identification:

benzyl alcohol

EC Number: **202-859-9**

CAS Number: **100-51-6**

Index Number: **603-057-00-5**

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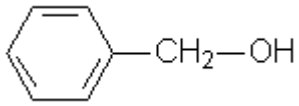
CONTENTS

1 IDENTITY OF THE SUBSTANCE

1.1 Name and other identifiers of the substance

Table 1: Substance identity and information related to molecular and structural formula of the substance

Name(s) in the IUPAC nomenclature or other international chemical name(s)	Phenylmethanol
Other names (usual name, trade name, abbreviation)	alpha-Hydroxytoluene Benzenemethanol
ISO common name (if available and appropriate)	
EC number (if available and appropriate)	202-859-9
EC name (if available and appropriate)	benzyl alcohol
CAS number (if available)	100-51-6
Other identity code (if available)	
Molecular formula	C_7H_8O
Structural formula	
SMILES notation (if available)	OCc1ccccc1
Molecular weight or molecular weight range	108.1378
Degree of purity (%) (if relevant for the entry in Annex VI)	100 %

1.2 Composition of the substance

Table 2: Constituents (non-confidential information)

Constituent (Name and numerical identifier)	Concentration range (% w/w minimum and maximum in multi-constituent substances)	Current CLH in Annex VI Table 3.1 (CLP)	Current self-classification and labelling (CLP)
benzyl alcohol CAS-No: 100-51-6	100 %		

Table 3: Impurities (non-confidential information) if relevant for the classification of the substance

Impurity (Name and numerical identifier)	Concentration range (% w/w minimum and maximum)	Current CLH in Annex VI Table 3.1 (CLP)	Current self-classification and labelling (CLP)	The impurity contributes to the classification and labelling
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Table 4: Additives (non-confidential information) if relevant for the classification of the substance

Additive (Name and numerical identifier)	Function	Concentration range (% w/w minimum and maximum)	Current CLH in Annex VI Table 3.1 (CLP)	Current self-classification and labelling (CLP)	The additive contributes to the classification and labelling
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Table 5: Test substances (non-confidential information) (this table is optional)

Identification of test substance	Purity	Impurities and additives (identity, %, classification if available)	Other information	The study(ies) in which the test substance is used
-				

2 PROPOSED HARMONISED CLASSIFICATION AND LABELLING

2.1 Proposed harmonised classification and labelling according to the CLP criteria

Table 6: Proposed harmonised classification and labelling according to the CLP criteria

	Index No	Chemical name	EC No	CAS No	Classification		Labelling			Specific Conc. Limits, M-factors and ATEs	Notes
					Hazard Class and Category Code(s)	Hazard statement Code(s)	Pictogram, Signal Word Code(s)	Hazard statement Code(s)	Suppl. Hazard statement Code(s)		
Current Annex VI entry	603-057-00-5	benzyl alcohol	202-859-9	100-51-6	Acute Tox. 4* Acute Tox. 4*	H302 H332	GHS07 Wng	H302 H332			
Dossier submitter's proposal					**Modify:** Acute Tox. 4 **Remove:** Acute Tox. 4 **Add:** Eye Irrit. 2 Skin Sens. 1B	 H302 H332 H319 H317	GHS07 Wng	H302 H319 H317		Oral: ATE=1570 mg/kg bw	
Resulting entry in Annex VI if adopted by RAC and agreed by Commission					Acute Tox. 4 Eye Irrit. 2 Skin Sens. 1B	H302 H319 H317	GHS07 Wng	H302 H319 H317		Oral: ATE=1570 mg/kg bw	

Table 7: Reason for not proposing harmonised classification and status under public consultation

Hazard class	Reason for no classification	Within the scope of public consultation
Explosives	*Hazard class not assessed in this dossier*	No
Flammable gases (including chemically unstable gases)		
Oxidising gases		
Gases under pressure		
Flammable liquids		
Flammable solids		
Self-reactive substances		
Pyrophoric liquids		
Pyrophoric solids		
Self-heating substances		
Substances which in contact with water emit flammable gases		
Oxidising liquids		
Oxidising solids		
Organic peroxides		
Corrosive to metals		
Acute toxicity via oral route		**Yes**
Acute toxicity via dermal route	**No classification proposed**	**Yes**
Acute toxicity via inhalation route	**No classification proposed**	**Yes**
Skin corrosion/irritation	*Hazard class not assessed in this dossier*	No
Serious eye damage/eye irritation		**Yes**
Respiratory sensitisation	*Hazard class not assessed in this dossier*	No
Skin sensitisation		**Yes**
Germ cell mutagenicity	*Hazard class not assessed in this dossier*	No
Carcinogenicity		
Reproductive toxicity		
Specific target organ toxicity-single exposure		
Specific target organ toxicity-repeated exposure		
Aspiration hazard		
Hazardous to the aquatic environment		
Hazardous to the ozone layer		

3 HISTORY OF THE PREVIOUS CLASSIFICATION AND LABELLING

The current acute toxicity classification for benzyl alcohol is based on Directive 67/548/EEC and translates into a minimum classification of:

Acute Tox. 4* (oral) H302: "Harmful if swallowed." and

Acute Tox. 4* (inhalation) H332: "Harmful if inhaled."

Minimum classification for category is indicated by an asterisk.

4 JUSTIFICATION THAT ACTION IS NEEDED AT COMMUNITY LEVEL

- Change in existing entry due to changes in the criteria
- Differences in self-classification
- Disagreement by DS with current self-classification

Further detail on need of action at Community level

The current acute toxicity classification of benzyl alcohol is a minimum classification according to Directive 67/548/EEC. For certain hazard classes, including acute toxicity, the classification according to the criteria in Directive 67/548/EEC does not correspond directly to the classification in a hazard class and category under the CLP Regulation.

For benzyl alcohol in total 2414 notifications to the C&L inventory are reported on the ECHA website (last accessed 2019-02-13), but there are differences in the self-classification of a substantial number of C&L notifiers. Only one notifier has self-classified benzyl alcohol as Skin Sens. 1. However, reliable studies were identified during substance evaluation showing that benzyl alcohol may act as a moderate skin sensitizer. Around half of the notifiers self-classified benzyl alcohol as Eye Irrit. 2, 126 notifiers self-classified benzyl alcohol as Eye Dam. 1. Reliable studies were identified during substance evaluation which justify the classification of benzyl alcohol as irritating to the eye.

Based on the information given on ECHA's dissemination website significant exposure is to be expected as the substance is used as a solvent, in coating materials and paint strippers. Consumers are exposed to benzyl alcohol through various uses (wide-dispersive use). Benzyl alcohol was detected in cosmetic products and articles, air care products, washing and cleaning products, textile processing aids, and modelling clay. Harmonised classification proposal was considered as a follow-up measure to substance evaluation (CoRAP 2016).

5 IDENTIFIED USES

Benzyl alcohol is a colourless liquid with a faint, nondescript odour, which is used as a solvent, preservative, and fragrance ingredient. Benzyl alcohol is manufactured and/or imported in the European Economic Area in a volume of 10 000 – 100 000 tons per year with widespread uses by consumers and professional workers, in formulation or re-packing, at industrial sites, and in manufacturing (ECHA dissemination website):

- Professional workers:
  - Adhesives, sealants
  - Air care products
  - Biocidal products (e.g. disinfectants, pest control)
  - Coatings, paints, thinners, paint removers

- Fillers, putties, plasters, modelling clay
- Metal surface treatment products
- Non-metal-surface treatment products
- Ink and toners
- Products such as pH-regulators, flocculants, precipitants, neutralisation agents
- Laboratory chemicals
- Leather treatment products
- Lubricant, greases, release products
- Paper and board treatment products
- Plant protection products
- Perfumes, fragrances
- Pharmaceuticals
- Photo-chemicals
- Polishes and wax blends
- Polymer preparations and compounds
- Textile dyes and impregnating products
- Washing and cleaning products
- Cosmetics, personal care products

▪ Consumers:
- Adhesives, sealants
- Air care products
- Coatings, paints, thinners, paint removers
- Fillers, putties, plasters, modelling clay
- Ink and toners
- Leather treatment products
- Perfumes and fragrances
- Polishes and wax blends
- Textile dyes and impregnating products
- Washing and cleaning products
- Cosmetics and personal care products

Benzyl alcohol is largely available to consumers for day-by-day use. When used in cosmetic products it may be percutaneously absorbed over more or less the entire body and/or on smaller localised skin areas. Exposure could also occur through eye contact.

5.1 Data SOURCES

In addition to the information that is available on the website of ECHA, in the IUCLID registration dossier and in the dossier submitted for the assessment as biocidal active substance, an extensive literature search was conducted in several relevant online resources (e.g. PubMed, SCOPUS, Web of Science, Wiley, Toxnet, Science Direct).

Furthermore, evaluations by EFSA and EMA were reviewed. The European Medicines Agency (EMA) summarised the data for "benzyl alcohol and benzoic acid group as excipients"[1] with the main focus on benzyl alcohol used as solubilising agent and/or preservative in medicinal products. The EFSA published a report "Re-evaluation of benzyl alcohol (E1519) as food additive"[2] which includes data on acute toxicity and a short summary on hypersensitivity. However, no relevant additional data was identified in these reports.

6 PHYSICOCHEMICAL PROPERTIES

Table 8: Summary of physicochemical properties

Property	Value	Reference	Comment (e.g. measured or estimated)
Physical state at 20°C and 101.3 kPa	Benzyl alcohol is a colourless liquid with a slightly aromatic odour	(Lide, 2006)	experimental
Melting/freezing point	-15.4 °C at 1013 hPa	(Lide, 2006)	experimental
Boiling point	205.31 °C	(Lide, 2006)	experimental
Relative density	1.045 g/cm^3 at 20°C	(Brühne and Wright, 2005)	experimental
Vapour pressure	7 Pa at 20 °C 12 Pa at 25 °C	(Apelblat et al., 1984)	experimentally measured based on an (isoteniscope) established and documented method in the temperature range of 20 - 45 °C.
Surface tension	39 mN/m at 20 °C 33 mN/m at 80 °C	(Mookherjee and Wilson, 1992)	experimental
Water solubility	40 g/L at 25 °C	(Mookherjee and Wilson, 1992)	experimental
Partition coefficient n-octanol/water	1.05 at 20 °C	(Sangster, 1989)	Shake-flask method, two values are determined with the HPLC method.
Flash point			not assessed in this dossier
Flammability			
Explosive properties			
Self-ignition temperature			
Oxidising properties			
Granulometry			A test on particle size distribution does not need to be conducted since benzyl alcohol is a liquid substance under normal conditions.

[1] https://www.ema.europa.eu/en/documents/report/benzyl-alcohol-benzoic-acid-group-used-excipients-report-published-support-questions-answers-benzyl/chmp/508188/2013-t_en.pdf

[2] https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2019.5876

Property	Value	Reference	Comment (e.g. measured or estimated)
Stability in organic solvents and identity of relevant degradation products			In accordance with column 2 of REACH Annex IX, the test on stability in organic solvents and identity of relevant degradation products does not need to be conducted as the stability of benzyl alcohol is not considered to be critical.
Dissociation constant	15.4 at 25 °C Benzyl alcohol does not tend to dissociate in water under normal environmental conditions.	(Serjeant and Dempsey, 1979)	kinetic measurement
Viscosity	5.84 mPa· s at 20 °C	(Brühne and Wright, 2005)	experimental

7 EVALUATION OF PHYSICAL HAZARDS

Not assessed in this dossier.

8 TOXICOKINETICS (ABSORPTION, METABOLISM, DISTRIBUTION AND ELIMINATION)

Benzyl alcohol is rapidly absorbed from the gastro-intestinal tract after oral exposure in humans and animals (Chidgey and Caldwell, 1986; EMEA, 1997). In humans 75-85 % of the applied substance is excreted within 6 h (EMEA, 1997). Dermal absorption ranged from 56 to 80 % in rhesus monkeys under occluded conditions (Bronaugh et al., 1990; EMEA, 1997). Evaporative loss contributes to a lower skin penetration (approx. 30%) under unoccluded conditions in vitro and in vivo (EMEA, 1997; Miller et al., 2006). Benzyl alcohol is an intermediate in the metabolism of Benzyl acetate and is further metabolised to benzaldehyde and finally to benzoic acid (JECFA, 1997; OECD, 2001). It is rapidly excreted as hippuric acid mainly via urine and there is no indication of a bioaccumulating potential of benzyl alcohol (Bronaugh et al., 1990; Chidgey and Caldwell, 1986; EMEA, 1997; JECFA, 1997; Miller et al., 2006; OECD, 2001).

9 EVALUATION OF HEALTH HAZARDS

9.1 Acute toxicity - oral route

Table 9: Summary table of animal studies on acute oral toxicity

Method, guideline, deviations if any	Species, strain, sex, no/group	Value LD_{50}	Reference
Acute Oral Toxicity Similar to OECD TG 401, GLP compliance not specified - No information available on purity of the substance - Only male rats were tested Reliable with restrictions as only a summary of the study was available	**Rat,** Wistar 10 male rats/dose	1 620 mg/kg bw for males	Unpublished study report (Bayer AG, 1978)
Procter and Gamble standard procedure No. 1 for toxicological evaluation (1977-11-04) Similar to OECD TG 401, GLP compliance not specified - No information available on purity of the substance - Observation period not stated Reliable with restrictions as only a summary of the study was available	**Rat,** Sprague-Dawley 5/sex/dose	1 570 mg/kg bw	Unpublished study report (Proctor & Gamble, 1980) (RIFM, 1992)
Acute Oral Toxicity Study details not available, no GLP compliance Reliability not assignable	**Rat,** Osborne-Mendel 5/sex/dose	1 230 mg/kg bw	(Jenner et al., 1964)
Acute Oral Toxicity Study details not available, no GLP compliance Reliability not assignable	**Rat,** Strain, sex and no. of animals not reported	3 100 mg/kg bw	(Smyth et al., 1951)
Acute Oral Toxicity Study details not available, no GLP compliance Reliability not assignable	**Rat,** Strain and sex not reported 5/dose group	2 080 mg/kg bw	(Graham and Kuizenga, 1945)
Acute Oral Toxicity Study details not available, no GLP compliance	**Rat,** Strain, sex and no. of animals not reported	1 400 < LD_{50} < 3 120 mg/kg bw	(Macht, 1918)

Method, guideline, deviations if any	Species, strain, sex, no/group	Value LD_{50}	Reference
Reliability not assignable			
Acute Oral Toxicity Study details not available, no GLP compliance Reliability not assignable	**Mouse,** Strain not reported 5/sex/dose	1 580 mg/kg bw	(Jenner et al., 1964)
Acute Oral Toxicity Study details not available, no GLP compliance Reliability not assignable	**Mouse,** Strain and sex not reported No. of animals/ group not specified	1 150 mg/kg bw	(Carter et al., 1958)
Acute Oral Toxicity Study details not available, no GLP compliance Reliability not assignable	**Mouse,** Strain, sex and no. of animals not reported	1 040 mg/kg bw	(Macht, 1918)
Acute Oral Toxicity Study details not available, no GLP compliance Reliability not assignable	**Rabbit,** Strain and sex not reported 9 in total	1 040 mg/kg bw	(Graham and Kuizenga, 1945)
Acute Oral Toxicity Study details not available, no GLP compliance Reliability not assignable	**Guinea pig,** Strain, sex and no. of animals not reported	1 040 < LD_{50} < 2 600 mg/kg bw	(Macht, 1918)

9.1.1 Short summary and overall relevance of the provided information on acute oral toxicity

Various studies are available in rats or mice, as well as one each in rabbits and guinea pigs. Two studies (Bayer AG, 1978; Proctor & Gamble, 1980), which were performed similar to OECD guideline 401, state comparable LD_{50} values for rats of 1 620 and 1 570 mg/kg bw.

Further studies are less reliable as essential study details are missing. The study by (Jenner et al., 1964) obtained similar LD_{50} of 1 230 mg/ kg bw and 1 580 mg/kg bw values for rats and mice. In other studies the reported LD_{50} values range from 1 040 up to 3 120 mg/kg bw. However, most LD_{50} values described are between 1 000 and 2 000 mg/kg bw. It is not clear why some values reported are > 2 000 mg/kg bw as details of these studies are limited.

9.1.2 Comparison with the CLP criteria

As described above, the lowest available LD_{50} value, taken from the studies performed similar to OECD TG 401, is 1570 mg/kg bw for rats.

According to the criteria shown in the Table 3.1.1 of Annex I, Part 3 of CLP, substances can be allocated to one of four toxicity categories based on acute toxicity by the oral route. In general, classification is based on the lowest ATE value available i.e. the lowest ATE in the most sensitive appropriate species tested. Acute toxicity values are expressed as approximate LD_{50} values (oral) or as acute toxicity estimates (ATE):

Acute oral toxicity - Category 4: 300 < ATE ≤ 2 000 mg/kg bw

9.1.3 Conclusion on classification and labelling for acute oral toxicity

Based on the results shown above, it is proposed to classify benzyl alcohol as:

Acute Tox. 4 after oral exposure (H302 – Harmful if swallowed).

An ATE value of 1570 mg/kg bw is proposed based on the most sensitive value from the two studies performed similar to OECD TG 401.

9.2 Acute toxicity - dermal route

Table 10: Summary table of animal studies on acute dermal toxicity

Method, guideline, deviations if any	Species, strain, sex, no/group	Value LD_{50}	Reference
Acute Dermal Toxicity Study details not available, no GLP compliance Reliability not assignable	**Rabbit,** Strain not reported 4 male/female	> 2 000 mg/kg bw	(National Printing Ink Research Institute [Corporate Author], 1974)
	Guinea pig, Strain, sex and no. of animals not reported	< 5 000 mg/kg bw	(Opdyke, 1973)
	Cat, Strain, sex not reported 2 animals	2 930 mg/kg bw	(Graham and Kuizenga, 1945)

9.2.1 Short summary and overall relevance of the provided information on acute dermal toxicity

There is limited data on acute toxicity after dermal administration with very little details concerning study design. However, the LD_{50} values reported are all above 2000 mg/kg bw.

9.2.2 Comparison with the CLP criteria

The lowest of the available LD_{50} value was > 2 000 mg/kg bw.

Substances can be allocated to one of four toxicity categories based on acute toxicity by the dermal route according to the criteria shown in the Table 3.1.1 of Annex I, Part 3 of CLP. Acute toxicity values are expressed as approximate LD_{50} values (dermal) or as acute toxicity estimates (ATE):

'Acute dermal toxicity - Category 4: 1 000 < ATE ≤ 2 000 mg/kg bw.'

9.2.3 Conclusion on classification and labelling for acute dermal toxicity

There is no need to classify benzyl alcohol as acutely toxic after dermal application.

9.3 Acute toxicity - inhalation route

Table 11: Summary table of animal studies on acute inhalation toxicity

Method, guideline, deviations if any	Species, strain, sex, no/group	Value LC_{50}	Reference
Acute Inhalation Toxicity According to OECD TG 403 (version 1981) and GLP compliant Reliable with restrictions as only a summary of the study was available	**Rat**, Wistar **Aerosol**, nose/head only 5/sex/dose	> 4 178 mg/m^3 (> 4.18 mg/L) Maximum technically achievable concentration	Unpublished study report (Bayer AG, 1990b)
Acute Inhalation Toxicity According to OECD TG 403 (version 1981) and GLP compliant Reliable with restrictions as only a summary of the study was available	**Rat,** albino rat of the CD strain **Aerosol**, snout only 5/sex/dose	> 5 400 mg/m^3 (> 5.4 mg/L) limit concentration	Unpublished study report (Elf-Atochem, 1993)
Acute Inhalation Toxicity Study details not available, no GLP compliance Reliability not assignable	**Rat,** Exposure to saturated **vapour** Strain, sex and no. of animals not reported	200 ppm (> 0.9 mg/L air)	(Clayton, 1982) Book chapter citing (Smyth et al., 1951) (see below) and personal communication with the author
Acute Inhalation Toxicity Non-guideline study, no GLP compliance Reliability not assignable	**Rat,** **Vapour**, 8 h exposure Strain, sex, no. of animals not reported	1 000 ppm (4.4 mg/L) for 8 h exposure Equivalent to **5.5 mg/L** for 4 h exposure Based on mortality of 3/6 rats within 14 days	(Smyth et al., 1951)
Acute Inhalation Toxicity Non-guideline study, no GLP compliance - No analytical checks on the concentration of prepared vapour Reliable with restrictions	**Rat,** Sherman **Vapour,** 4 h exposure 6/sex/dose	2 000 ppm (**8.8 mg/L**)	(Carpenter et al., 1949)

9.3.1 Short summary and overall relevance of the provided information on acute inhalation toxicity

There are two studies available performed in rats according to OECD TG 403 and in compliance with GLP. The first study reports an LC_{50} value > 4.18 mg/L air (aerosol), which was the maximum technically achievable concentration in this study (Bayer AG, 1990b). There were no mortalities and only minor transient symptoms observed at this concentration. The second study reports an LC_{50} value > 5.4 mg/l (aerosol) (Elf-Atochem, 1993). Neither mortality nor clinical signs related to the exposure of benzyl alcohol were observed at this limit concentration.

Three other LC_{50} values have been reported for vapour application (Carpenter et al., 1949; Clayton, 1982; Smyth et al., 1951). The study by Smyth et al. showed an LC_{50} value of 5.5 mg/L (vapour) when extrapolated to a 4-hour exposure, whereas in the study by Carpenter et al., the LC_{50} value was 8.8 mg/L (vapour) for a 4-hour exposure. It should be noted that according to the author: "*No analytical checks were made on the concentration of the prepared vapour. The concentration is based upon empirical calculation. Experience indicates that the calculated concentrations are slightly higher than would actually be found if it were practical to determine them analytically on the exposure air.*" The third LC_{50} value described by Clayton et al. seems questionable. The value given refers to the study performed by Smyth et al. and personal communication with the author. It is unknown why the LC_{50} value in this book differs from the value reported in the original publication.

9.3.2 Comparison with the CLP criteria

There appears to be a difference between the application of aerosol and vapour. Benzyl alcohol is a low-volatile liquid. Therefore, newer studies performed according to OECD TG 403 and GLP used aerosol, whereas older studies used vapour.

For aerosols an LC_{50} value of > 5.0 mg/L seems reasonable as there are only minor transient symptoms found at 4.178 mg/L (the maximum technically achievable concentration in the other guideline-conform study).

Substances (as aerosols) can be allocated to one of four toxicity categories based on acute toxicity by the inhalation route according to the criteria shown in the Table 3.1.1 of Annex I, Part 3 of CLP. Acute toxicity values are expressed as approximate LC_{50} values (inhalation) or as acute toxicity estimates (ATE):

'Acute inhalation toxicity - Category 4 (dusts and mists): $1.0 < ATE \leq 5.0$ mg/L'.

The values for administration as vapour are somewhat different to exposure to aerosol. The described LC_{50} values are 8.8 mg/L and 5.5 mg/L (estimated value from an 8-hour exposure). The third value reported by (Clayton, 1982) seems to be questionable as described above. However, the accuracy of the given exposure values is uncertain as concentrations were not checked analytically. Moreover, MAK (Hartwig, 2017) calculated a saturation concentration of 567 mg/m^3 (≈ 0.57 mg/L and 126 ml/m^3) for benzyl alcohol at 25 °C on basis of its vapour pressure of 0.12 hPa at this temperature. Based on this data it is assumed that there is an equilibrium of benzyl alcohol aerosol and vapour above a concentration of 500-600 mg/m^3 (≈ 0.5 – 0.6 mg/L and 111-133 ml/m^3).

As vapours, substances can be allocated to one of four toxicity categories based on acute toxicity by the inhalation route according to the criteria shown in the Table 3.1.1 of Annex I, Part 3 of CLP. Acute toxicity values are expressed as approximate LC_{50} values (inhalation) or as acute toxicity estimates (ATE):

'Acute inhalation toxicity - Category 3 (vapours): $2.0 < ATE \leq 10.0$ mg/l.'

9.3.3 Conclusion on classification and labelling for acute inhalation toxicity

The estimated LC_{50} values for aerosol indicate that benzyl alcohol does not need to be classified. Taking the uncertainty of exposure concentrations of the data for vapour application into account, a classification of benzyl alcohol vapour as acutely toxic after inhalation is considered unnecessary.

There is no need to classify benzyl alcohol as acutely toxic after inhalation.

9.4 Skin corrosion/irritation

Not assessed in this dossier.

9.5 Serious eye damage/eye irritation

Table 12: Summary table of animal studies on eye irritation

Method, guideline, deviations if any*	**Species, strain, sex, no/group**	**Test substance, dose levels duration of exposure**	**Results**	**Reference**
Acute Eye Irritation according to OECD TG 405 and GLP Observation for 21 days Reliable with restrictions as only a summary of the study was available	**Rabbit,** New Zealand White N= 3	Benzyl alcohol: purity 99.99% 100 µl (104.5 µg); substance washed out after 24 hours Second eye served as control **Corneal opacity score: 1** 1 of max. 4; animals no. 1-3; fully reversible within 21 days **Iris score: 0.1** 0 of max. 2; animals no. 1+3 ≥0 ≤1 of max. 2; animal no. 2; fully reversible within 48 hours (mean score: 0.3) **Conjunctivae score: 2** 2 of max. 3; animals no. 1-3; fully reversible within 21 days **Chemosis score: 0.8** 1 of max. 4; animal no. 1; fully reversible within 7 days ≥0 ≤1 of max. 4; animals no. 2+3; fully reversible within 7 days (mean score: 0.7)	Irritating to the eyes of rabbits, but fully reversible within 21 days	Unpublished study report (Bayer AG, 1990a)
Acute Eye Irritation according to OECD TG 405 and GLP Observation for 18 days Reliable with restrictions as only a summary of the study was available	**Rabbit,** New Zealand White N= 3	Benzyl alcohol: purity 99.98% 100 µl applied Second eye server as control **Animal no. 3 was killed on day 10 for ethical reasons (not-substance related)** **Corneal opacity score: 2** 2 of max. 4; animals no. 1-3; fully reversible within 18 days **Iris score: 1** 1 of max. 2**;** animals no. 1-3; fully reversible within 11 days **Conjunctivae score: 2.4** 2 of max. 3; animal no. 1; fully reversible within 11 days 3 of max. 3; animal no. 2; fully reversible within 11 days ≥2 ≤3 of max. 3; animal no.3 (mean score: 2.3) **Chemosis score: 2.2** ≥1 ≤2 of max. 4; animal no. 1; fully	Slightly irritating to the eyes of rabbits, but fully reversible within 18 days	Unpublished study report (Elf-Atochem, 1998)

Method, guideline, deviations if any*	Species, strain, sex, no/group	Test substance, dose levels duration of exposure	Results	Reference
		reversible within 11 days (mean score: 1.7) 3 of max. 4; animal no.2; fully reversible within 11 days 2 of max. 4; animal no. 3		
Acute Eye Irritation similar to OECD TG 405 and GLP Observation for 7 days	**Rabbit,** New Zealand White N= 2	Benzyl alcohol, no data on purity 100 µl applied Second eye server as control **Corneal opacity score:** 1 of max. 4; animals no. 1+2; not fully reversible within 7 days **Iris score:** ≥0 ≤1 of max. 2; animals no. 1+2; fully reversible within 7 hours **Conjunctivae score:** ≥0 ≤2 of max. 3; animals no. 1+2; fully reversible within 7 days **Chemosis score**: ≥0 ≤1 of max. 4; animal no. 1; fully reversible within 7 days ≥0 ≤2 of max. 4; animal no. 2; fully reversible within 7 days	Moderately irritating to the eyes of rabbits, but varying results between the two animals	Unpublished study report (Bayer AG, 1979)
Acute Eye Irritation	**Rabbit,** New Zealand White N= 3	No details reported	Highly irritating	(Smyth et al., 1951)
Acute Eye Irritation	**Rabbit** N= 3	0.08% aqueous solution, 2 drops; applications on 4 successive days	Not irritating	(Carter et al., 1958)
Acute Eye Irritation	**Rabbit**	4% solution	Not irritating	(Macht and Shohl, 1920)

9.5.1 Short summary and overall relevance of the provided information on serious eye damage

There are two studies available in rabbits which were performed according to OECD TG 405 and GLP (Bayer AG, 1990a; Elf-Atochem, 1998). Both studies show that benzyl alcohol is irritating to the eyes of rabbits but effects were fully reversible within 21 days. The study performed by (Elf-Atochem, 1998) generally showed higher scores and it should be noted that one animal had to be killed on day 10 due to ethical reasons (but not substance related). One more study was performed similar to OECD TG 405 (Bayer AG, 1979) which also showed moderate eye irritation in rabbits. However, only two animals were used in this study, the observation period was only 7 days after exposure and not all effects were reversible within that period.

Further studies (Carter et al., 1958; Macht and Shohl, 1920; Smyth et al., 1951) are of limited relevance as study details are missing. The results from these studies range from not irritating to highly irritating.

9.5.2 Comparison with the CLP criteria

The two studies performed according to OECD TG 405 and GLP (Bayer AG, 1990a; Elf-Atochem, 1998) both showed eye irritation of benzyl alcohol with values for corneal opacity ≥1 and for conjunctival redness ≥2 for all three animals in each study. The values for iritis and chemosis are ≤1 and ≤2, respectively in the study by (Bayer AG, 1990a) and ≥1 and ≥2, respectively, in the study by (Elf-Atochem, 1998) and the effects vary between the animals used. All effects were reversible within 21 days.

According to the Table 3.3.2 of Annex I, Part 3 of CLP a substance should be classified as category 2, if

"Substances that produce in at least in 2 of 3 tested animals, a positive response of:
(a) corneal opacity ≥1 and/or
(b) iritis ≥ 1, and/or
(c) conjunctival redness ≥ 2 and/or
(d) conjunctival oedema (chemosis) ≥ 2
calculated as the mean scores following grading at 24, 48 and 72 hours after installation of the test material, and which fully reverses within an observation period of 21 days"

9.5.3 Conclusion on classification and labelling for serious eye damage

Based on the results shown above, it is proposed to classify benzyl alcohol as

Eye Irrit. Cat. 2 (H319 – Causes serious eye irritation).

This conclusion is also in line with the current self-classification.

9.6 Respiratory sensitisation

Not assessed in this dossier

9.7 Skin sensitisation

Benzyl alcohol is used as a solvent, preservative, and fragrance ingredient with a widespread use in cosmetic products, toiletries, perfumes, inks and paints, household cleaners and detergents. According to the Cosmetics Regulation (EC) No 1223/2009 Annex III, benzyl alcohol has to be labelled as an ingredient when its concentration exceeds 0.001 % in leave-on products and 0.01 % in rinse-off products, respectively. As a preservative, benzyl alcohol shall not exceed 1 % in a ready-for-use preparation.

This CLH report summarises relevant animal, human and other data on skin sensitisation. Detailed summaries can be found in Annex I of this CLH report.

9.7.1 Animal data

Animal studies on benzyl alcohol are summarised in the review publication by (Scognamiglio et al., 2012). The studies include a local lymph node assay (LLNA) in mice as well as various tests in guinea pig (Table 13).

Table 13: Summary table of animal studies as summarised by (Scognamiglio et al., 2012)

Method, guideline, deviations if any*	Species, strain, sex, no/group	Test substance, dose levels duration of exposure	Results	Reference
LLNA According to OECD TG 429, GLP compliance not specified - Higher doses should have been tested according to OECD TG 429 Reliable with restrictions as only a summary of the study was available	**Mouse**, CBA, female 8-12 weeks N = 4/group	Benzyl alcohol: purity 99.8 % Vehicle: diethyl phthalate:EtOH (3:1) 0, 2.5, 5, 10, 25, 50 % w/v Stimulation index: 1, 0.9, 0.5, 0.6, 1.2 EC_3 > 50 % corresponds to > 12 500 µg/cm^2 M = > 4.62	No skin sensitisation at the doses applied	(RIFM, 2005a)
Modified Freund's Complete Adjuvant (FCA) test Study details not available, no GLP compliance Reliability not assignable	**Guinea pig,** 10 per dose No further details reported	Benzyl alcohol Purity not specified Challenge dose 3 % in acetone	Weak sensitiser	(Hausen et al., 1992)
Guinea Pig Maximisation Test (GPMT) Study details not available, no GLP compliance Reliability not assignable	**Guinea pig,** No further details reported	Benzyl alcohol Purity, vehicle and test concentrations not specified No further details provided	Negative	(Ishihara et al., 1981) Article in Japanese
Freunds Complete Adjuvant (FCA) test Study details not available, no GLP compliance Reliability not assignable	**Guinea pig,** No further details reported	Benzyl alcohol Purity, vehicle and test concentrations not specified No further details provided	Positive	
Draize guinea pig sensitization test Study details not available, no GLP compliance Reliability not assignable	**Guinea pig,** No further details reported	Benzyl alcohol Purity, vehicle and test concentrations not specified No further details provided	Negative	
Open epicutaneous test Study details not available, no GLP compliance Reliability not assignable	**Guinea pig,** No further details reported	Benzyl alcohol Purity, vehicle and test concentrations not specified No further details provided	Positive	
Open epicutaneous test	**Guinea pig,**	10 % benzyl alcohol	Negative	(Klecak, 1979;

Method, guideline, deviations if any*	Species, strain, sex, no/group	Test substance, dose levels duration of exposure	Results	Reference
Study details not available, no GLP compliance Reliability not assignable	No further details reported	Purity and vehicle not specified		Klecak, 1985)
Guinea Pig Maximisation Test (GPMT) Similar to OECD Guideline 406, no GLP compliance Reliable with restrictions	**Guinea pig**, Himalayan 10 per dose Sex not reported	Benzyl alcohol Purity and vehicle not specified 5 % intradermal induction 25 % epicutaneous induction Challenge: subirritant concentration (value not shown)	Negative	(Klecak et al., 1977)
Freund's Complete Adjuvant (FCA) test Similar to OECD Guideline 406, no GLP compliance Reliable with restrictions	**Guinea pig**, Himalayan Sex and no. of animals not reported	Benzyl alcohol Purity not specified Induction: Undiluted test substance mixed with Freund's Complete Adjuvant (FCA) Challenge: subirritant concentration in petrolatum	Positive	
Draize guinea pig sensitisation test Similar to OECD Guideline 406, no GLP compliance Reliable with restrictions	**Guinea pig**, Himalayan Sex and no. of animals not reported	Benzyl alcohol Purity and vehicle not specified Induction: 0.05 ml of a 0.1 % solution, 10 intradermal injections on alternate days Challenge: 0.05 ml of a 0.1 % solution	Negative	
Open epicutaneous test Similar to OECD Guideline 406, no GLP compliance Reliable with restrictions	**Guinea pig**, Himalayan 6-8 per dose Sex not reported	Benzyl alcohol Purity and vehicle not specified Induction: 0.1 ml undiluted test substance, up to several diluted concentrations, challenge with lowest irritant and non-irritant concentration	Positive	
Guinea Pig Maximisation Test (GPMT) Study details not available, no GLP compliance Reliability not assignable	**Guinea pig,** No further details reported	Benzyl alcohol Purity and vehicle not specified 10 % for induction and challenge	Positive	(Ishihara et al., 1986)
Closed epicutaneous Test Study details not available, no GLP compliance	**Guinea pig,** 10 per test Sex and strain	Benzyl alcohol Purity and vehicle not specified 30 % for induction and 1 % for	Negative	

Method, guideline, deviations if any*	Species, strain, sex, no/group	Test substance, dose levels duration of exposure	Results	Reference
Reliability not assignable	not reported	challenge		
Freund's Complete Adjuvant (FCA) test Study details not available, no GLP compliance Reliability not assignable	**Guinea pig,** No further details reported	Benzyl alcohol Purity and vehicle not specified 10 % challenge concentration	Moderate sensitiser	(Hausen et al., 1992)
Modified Draize guinea pig sensitisation test Non-guideline study, induction and challenge protocol differ from OECD TG 406, no GLP compliance Reliable with restrictions	**Guinea pig,** Hartley, male and female N = 10	Benzyl alcohol Purity and vehicle not specified 0.25 % injection challenge concentration 10 % application challenge concentration	Negative	(Sharp, 1978)
Delayed contact hypersensitivity test (modified cumulative contact enhancement test) Non-guideline study, no GLP compliance Reliable with restrictions	**Guinea pig,** female Strain not reported N = 5	Benzyl alcohol Purity and vehicle not specified 30 % induction concentration, 10 % benzyl alcohol in ethanol challenge concentration	Weak sensitiser	(Kashima et al., 1993)

* Information on studies is available as short summaries of unpublished studies or studies are not available in English only.

An LLNA test according to OECD TG 429 was negative up to 50 % benzyl alcohol (RIFM, 2005a). No higher doses were tested, therefore possible sensitisation at doses > 12 500 µg/cm^2 cannot be ruled out. It is unclear why higher doses were not tested. In a study on Acute Dermal Irritation according to OECD TG 404 using albino rabbits, benzyl alcohol was evaluated as not irritating to the skin (unpublished study report, (Bayer AG, 1990b)).

The available guinea pig tests show equivocal results: Only one out of the three Guinea Pig Maximisation Tests (GPMT) described caused a positive skin reaction. Further tests on guinea pigs showed that benzyl alcohol is a weak sensitiser in Freund's Complete Adjuvant (FCA) test but non-sensitising in the Draize guinea pig sensitisation test. The open epicutaneous tests described show ambiguous results (2/3 positive).

Nevertheless (Scognamiglio et al., 2012) list benzyl alcohol as a weak sensitiser in a potency classification based on animal data.

9.7.2 Human data

A substantial human database is available for benzyl alcohol. The available studies include human repeated insult patch tests (HRIPT) and a human maximisation test (HMT) in presumably healthy human volunteers, patch test results in consecutive dermatitis patients as well as a number of case studies. There are no details regarding the selection process for the volunteer studies, therefore it is assumed that the volunteers are healthy individuals rather than dermatitis patients.

Table 14: Human volunteer studies on the potential of benzyl alcohol to induce sensitisation in either a maximisation test or repeated insult patch tests (HRIPT); data taken from (Scognamiglio et al., 2012)

Relevant information about the study	Test substance, concentration	Number of volunteers	Results	Reference*
Human repeat insult patch test (HRIPT) Induction with 0.3 ml benzyl alcohol onto an occlusive patch applied to the upper arm or back for 24 h 9 induction applications on alternate days during a 3 week period 10-14 day rest period Challenge patch applied on previously unexposed site for 24 h Reactions scored at 24, 48, 72 and/or 96 h after application Information available as short summaries of unpublished studies No information available on - composition of the study populations, (only "human volunteers" mentioned) - purity of the substance Reliable with restrictions as only a summary of the study was available	20 % benzyl alcohol Diethyl phthalate:EtOH (3:1) 23 622 µg/cm²	56	5 subjects with oedematous reactions during induction, patching was continued for 1 subject with transient reactions Challenge: 2 with '2+' oedema (3.6 %) 3 with '1+' oedema (5.4 %) Other subjects exhibited transient (±/1) reactions Re-challenge: 1 with '2+' oedema (1.8 %) 1 with '1+' oedema (1.8 %) 1 with low level (+/-) reaction at both occlusive and semi-occlusive test sites (1.8 %) 1 with low level (+/-) reaction at occlusive test site (1.8 %) No reactions under „normal use" conditions	(RIFM, 2002)
	15 % benzyl alcohol Diethyl phthalate:EtOH (3:1) 17 717 µg/cm²	46	5 subjects with oedematous reactions during induction, patching was continued for 1 subject with transient reactions Challenge: 4 subjects with '2+' oedema (8.7 %) 1 with '1+' oedema (2.2 %) 1 with transient (±/1) reactions (2.2 %) The level 2+ and 1+ reactions indicative for skin sensitisation according to the author.	(RIFM, 2003)
	7.5 % benzyl alcohol Diethyl phthalate:EtOH (3:1) LOEL (induction): 8 858 µg/cm²	110	1 subject with severe irritation during patching (induction) Challenge: 1 with (2+) oedema, still existent 96 h after challenge (0.9 %) 2/110 with reaction upon challenge (1.8 %) Re-challenge indicated sensitisation in 1/ 3 (positive with occlusive, semi-occlusive and antecubital fossa sites) but not in the others (only minimal erythema)	(RIFM, 2004b)
	5 % benzyl alcohol in Diethyl phthalate:EtOH	101	2 subjects with oedematous reactions during induction, patching was discontinued for both subjects	(RIFM, 2005b)

Relevant information about the study	Test substance, concentration	Number of volunteers	Results	Reference*
	(3:1) NOEL (induction): 5 906 µg/cm^2		one with low level reaction Challenge: 1 with '3+' oedema (1 %) 1 with '1+' oedema (1 %) **indicative of pre-sensitisation for 2 subjects according to the authors**	
	3 % benzyl alcohol in Diethyl phthalate:EtOH (3:1) 3 543 µg/cm^2	107	Negative, no skin reactions	(RIFM, 2004a)
Human maximisation test (HMT) according to (Kligman, 1966) Patches on volar forearms under occlusion 5 alternate-day 48 h periods Patch sites pre-treated for 24 h with 5% aqueous sodium lauryl sulphate (SLS) under occlusion, 10-14 day rest period Challenge for 48 h – reactions read upon removal and again at 48 and 72 h Reliable with restrictions as only a summary of the study was available	10 % benzyl alcohol in petrolatum NOEL (induction): 6 900 µg/cm^2	25	Negative	(RIFM, 1970)

* Full references can be accessed from the original publication

The results of human repeated insult patch tests with doses ranging from 3 543 µg/cm^2 to 23 622 µg/cm^2 (3 to 20% benzyl alcohol for induction and challenge) show that increasing doses of benzyl alcohol (above 8 858 µg/cm^2 or 7.5% benzyl alcohol) led to increasing numbers of sensitised subjects (0 – 11%). Since results stem from separate studies, reproducibility of a skin sensitising effect can be inferred. Some volunteers reacted with oedematous reactions during the induction phase. As benzyl alcohol is considered to be non-irritating, it could be speculated that these volunteers are already sensitised to benzyl alcohol due to its ubiquitous presence in a large number of cosmetic products.

A human maximisation test (HMT) on 25 volunteers was negative for 10% benzyl alcohol. However, it should be noted that according to (Kligman, 1966): "*There is a greater variability in the borderline group especially with substances which are recognized as occasional sensitisers.*" This means that for occasional sensitisers more accurate and reproducible results can be obtained by using larger numbers of test subjects and in this specific case a higher concentration of the test substance would be needed to produce a positive result.

In addition to the studies in human volunteers, there are various retrospective analyses of hospital statistics regarding the number of dermatitis patients reacting to benzyl alcohol in all tested patients over a certain period of time.

Table 15: Human patch test studies performed with benzyl alcohol on dermatitis patients

Relevant information about the study	Test substance, concentration	Number of patients	Results	Reference
Human patch test Retrospective study on data from all eczema patients routinely tested with the fragrance series and the European baseline series (2011-2012) retrieved from the database at St John's Institute of Dermatology at St Thomas' Hospital, London. Patch test reactions to the fragrance series include concentrations of allergens in the fragrance series and fragrance mixes, and data on co-reactions between fragrance series allergens and fragrance markers, fragrance mix I (FM I), or fragrance mix II (FM II).	**10 %** benzyl alcohol in petrolatum Purity not specified	1 951	4 subjects with positive reactions **(0.21 %)** Co-reactions with any fragrance marker (% of reactions to fragrance series substance) 3/4 (75 %) Co-reactions with FM I (% of reactions to ingredient): 1/4 (25) Co-reactions with FM II (% of positive reactions to ingredient): 2/4 (50)	(Mann et al., 2014)
Human patch test Prospective study of 93 consecutive patients suspected of having allergic contact dermatitis tested with the European standard series and cosmetic series at the Dermatology Department, Baskent University Faculty of Medicine, Ankara, Turkey (2005-2006).	**10%** benzyl alcohol Purity and vehicle not specified	93	1 subject with positive reaction **(1.1 %)**	(Ada and Seckin, 2010)
Human patch test Retrospective analysis of data on patch testing of preservatives contained in the standard series and special series collected by the IVDK (1996–2009).	**1 %** benzyl alcohol in petrolatum Purity not specified	79 770	258 subjects with positive reactions (**0.28 %)** **(64 men (0.18 %), 194 women (0.34 %))** Association with leg dermatitis reported	(Schnuch et al., 2011a)
Human patch test Data on all patients patch tested in the departments of the Information Network of Departments of Dermatology between 2005 and 2008. Diagnostic procedure follows international guidelines.	**1 %** benzyl alcohol Purity and vehicle not specified	23 257	51 subjects with positive reactions **(0.22 %)**	(Uter et al., 2010)
Human patch test Retrospective study on patients with suspected allergic contact dermatitis tested with a preservative series, data collected from 24 departments participating in the German Information Network of Departments of Dermatology (IVDK, 1990-1994).	**1 %** benzyl alcohol in petrolatum Purity not specified	11 373	46 subjects with positive reactions **(0.4 %)**	(Schnuch et al., 1998)

Relevant information about the study	Test substance, concentration	Number of patients	Results	Reference
Human patch test Analysis of data on the frequency of sensitisation to selected antimicrobials in all patients with current or previous atopic eczema compared with patients without past or current atopic eczema, patch test data collected by Departments of Dermatology participating in the IVDK (1995-1999).	**1%** benzyl alcohol in petrolatum Purity not specified	5 183 (atopic) 14 722 (non-atopic)	15 atopic patients with positive reactions **(0.28 %)** 44 non-atopic patients with positive reactions (**0.3 %)** (standardised for age and sex, patients with current leg ulcer/stasis dermatitis were excluded)	(Jappe et al., 2003)
Human patch test First retrospective study of patch testing results, aggregated from four patch test clinics in three centres in Melbourne and Sydney (1993–2006). Data were collected for a minimum of five years from each centre.	**1 %** benzyl alcohol Purity not specified	4 552	18 subjects with positive reactions **(0.4 %)**	(Chow et al., 2013)
Human patch test Study on the frequency of sensitisation to fragrances to be labelled according to current European regulation. During 4 periods of 6 months, from 1 January 2003 to 31 December 2004, 25 fragrances were successively patch-tested additionally to the standard series in a total of 21 325 unselected patients; the number of patients tested with each of the fragrances ranged from 1658 to 4238.	**1 %** benzyl alcohol Purity and vehicle not specified	2 166	7 subjects with positive reactions **(0.3 %):** 3 subjects +, 3 subjects + +, 1 subject + + +) 12 irritant or doubtful reactions Sensitisation to Benzyl alcohol associated with leg dermatitis (29 %). Low frequency, but some strong allergenic reactions are indicative of Benzyl alcohol to be an – albeit rare – sensitiser	(Schnuch et al., 2007)
Human patch test Retrospective study based on data from the Department of Dermato-Allergology, Copenhagen University Hospital Gentofte. Eczema patients were patch tested (2008-2010) with the 26 fragrance ingredients, including Benzyl alcohol. All eczema patients suspected of having contact allergy were tested consecutively according to international guidelines. Responses were categorised in terms of the following categories: Positive (++/++/+), doubtful (+?) or irritant reactions (IR).	**1 %** benzyl alcohol Purity and vehicle not specified	1 508	2 subjects with positive reaction **(0.1 %)** In addition: - 3 subjects with doubtful reaction - 1 subject with irritant reaction	(Heisterberg et al., 2011)

Relevant information about the study	Test substance, concentration	Number of patients	Results	Reference
Human patch test 4-year retrospective study of patients tested with the Spanish baseline and/or fragrance series (2004-2008). A fragrance series has been tested in a selected group of 86 patients. Patients selected were either positive to baseline series (54 patients) or there was clinical suspicion (32 patients).	**1 %** benzyl alcohol in petrolatum Purity not specified	86	2 subjects with positive reactions **(2.3 %)**	(Cuesta et al., 2010)
Human patch test Frequency of sensitisation to preservatives analysed on the basis of data from the IVDK (2006–2009).	Benzyl alcohol Purity, vehicle and test concentrations not specified	17 740	31 subjects with positive reactions (**0.17 %)**	(Schnuch et al., 2011b)
Human patch test Retrospective multicentre survey of patch test reactions to standard, cosmetic and hairdressing series collected by 7 Finnish dermatological clinics representing the Finnish Contact Dermatitis Group (comparing results from 1995-1996 and 2000-2002).	Benzyl alcohol Purity, vehicle and test concentrations not specified	4 922 (1995-1996) 6 125 (2000-2002)	1995-1996: 1 subject with positive reaction **(0.02 %)** 2000-2002: **No** allergic reactions	(Hasan et al., 2005)
Human patch test Study on patients tested with Belgian Contact Patch-test series.	Benzyl alcohol Purity, vehicle and test concentrations not specified	5 202 (with known contact dermatitis)	48 subjects with positive reactions **(0.9 %)**	(Broeckx et al., 1987)
Human patch test Risk of sensitisation to fragrances estimated on the basis of patch test data and exposure according to use volumes. Patients were tested for their reaction to three different fragrance mixes (FM I, FM II, and "further fragrances"). Patients tested positive to a mix were tested with the individual components. The frequency of sensitisation in the study population was extrapolated from the frequency of reactions to the single compound.	Fragrances mix and benzyl alcohol Composition of fragrances mix, purity of test substance(s), vehicle and test concentrations not specified	1 870	**0.7 %** of the patients sensitised to the fragrances mix tested positive for Benzyl alcohol. This corresponded with a frequency of **0.16 %** when extrapolated to all 1 870 patients.	(Schnuch et al., 2015)
Human patch test Prospective study of cosmetic adverse reactions by eleven dermatologists (1977-1980) using standard screening, perfume or vehicle-preservative series of the North American Contact Dermatitis Group	Benzyl alcohol Purity, vehicle and test concentrations not specified	487	2 subjects with positive reactions **(0.4 %)**	(Eiermann et al., 1982)

Relevant information about the study	Test substance, concentration	Number of patients	Results	Reference
Human patch test (short report) Patients with clinical suspicion of cosmetic contact dermatitis patch tested at Contact Dermatitis Clinic of Rabin Medical Center in Israel from 1997-2000. European standard series and cosmetic series used.	Benzyl alcohol Purity, vehicle and test concentrations not specified	244	5 subjects with positive reactions **(2.0 %)**	(Trattner et al., 2002)
Human patch test Frequency of cosmetics as causal factors of allergic contact dermatitis are reported and the cosmetic allergens identified during the previous six years are discussed (2010–2015). The data were retrieved from and evaluated with a patient database developed in-house.	Benzyl alcohol Purity, vehicle and test concentrations not specified	147	1 subject with positive reaction **(0.68 %)**	(Goossens, 2016)
Human patch test Study on 35 consecutive patients tested with chemical compounds recommended by North American Contact Dermatitis Group. In cases with positive reactions chemical compounds were re-applied at day 7 and read again at day 9.	Benzyl alcohol Purity, vehicle and test concentrations not specified	35	2 subjects with positive reactions on day 2 and at re-testing **(6 %)**	(Mitchell, 1977)

The data from collectives of consecutive dermatitis patients tested with a concentration of 1% benzyl alcohol show sensitisation rates ranging from 0.1 % to 2.3 %, two studies performed with 10% benzyl alcohol show rates of 0.21 % and 1.1 %. The studies, in which the concentration of benzyl alcohol used is not specified, lie within the same range (up to 2% positives). Out of these 18 studies there is only one study (Mitchell, 1977) reporting a higher incidence of sensitisation (6 %) and one study with no positive or 0.02 % positive reactions during the two time periods reported (Hasan et al., 2005). The largest collective of patients (79 770 patients in total) was evaluated by (Schnuch et al., 2011a) who performed a retrospective analysis on consecutive dermatitis patients from 1996 to 2009. The authors list benzyl alcohol as rare contact allergen with an association to leg dermatitis and report a higher incidence in women (0.34 %) compared to men (0.18 %). Overall studies with > 100 patients show sensitisation rates > 0.1 and < 1 %.

Further human patch test studies, mainly studies in consecutive dermatitis patients in clinical departments of dermatology, have been summarised in the review by (Scognamiglio et al., 2012).

Table 16: Summary of human diagnostic patch test studies performed with benzyl alcohol as reported by (Scognamiglio et al., 2012). The purity of benzyl alcohol was not reported for these studies.

No.	Concentration	Incidence	References
1	20 % in petrolatum	**5 %** from 1971-74; **4 %** from 1975-77, **1 %** from 1978-80 in cosmetic dermatitis patients Number of patients not reported	(Nakayama et al., 1984)
2	10 % in petrolatum	0/501	(De Groot et al., 1986)
3	10 % (vehicle not reported)	3/182 **(1.6 %)**	(Malten et al., 1984)
4	10 % in petrolatum	2/394 **(0.5 %)**	(Mid-Japan Contact Dermatitis Research Group, 1984) (Ueda, 1994)
	5 % in petrolatum	1/394 **(0.3 %)**	
	1 % in petrolatum	0/394	
5	5 % in petrolatum or 10% in alcohol	19/95 **(20 %)**	(Hjorth, 1961)
6	5 % in petrolatum	1/2261 **(0.04 %)** from 1978-79 0/1934 from 1979-80	(Mitchell et al., 1982)
7	5 % in petrolatum	3/991 **(0.3 %)**	(Dickel et al., 2001)
8	5 % in petrolatum	3/669 **(0.4 %)**	(Katoh et al., 1995)
9	5 % in petrolatum	0/667	(van Joost et al., 1984)
10	5 % in petrolatum	6/661 **(0.9 %)**	(Itoh et al., 1988)
11	5 % in petrolatum	9/585 **(1.5 %)**	(Itoh et al., 1986)
12	5 % in petrolatum	1/479 **(0.2 %)**	(Nagareda, 1996)
13	5 % in petrolatum	3/425 **(0.71 %)**	(Nagareda et al., 1992)
14	5 % in petrolatum	1/398 **(0.3 %)**	(Sugai, 1996)
15	5 % in petrolatum	0/241	(Ferguson and Sharma, 1984)
16	5 % in petrolatum	2/200 **(1 %)**	(Nethercott, 1982)
17	5 % in petrolatum	8/102 **(7.8 %)**	(Hausen, 2001)
18	5 % (vehicle not reported)	0/3037	(Angelini et al., 1985)
19	5 % (vehicle not reported)	13/1206 **(1.1 %)**	(Sugai, 1982)
20	5 % (vehicle not reported)	0/574	(Hirose et al., 1987)
21	5 % (vehicle not reported)	8/427 **(1.9 %)**	(Nishimura et al., 1984)
22	5 % (vehicle not reported)	1/457 **(0.2 %)**	(Addo et al., 1982)
23	5 % (vehicle not reported)	2/242 **(1.7 %)**	(Van Joost et al., 1985)
24	5 % (vehicle not reported)	6/220 **(2.7 %)**	(Ishihara et al., 1979)
25	5 % (vehicle not reported)	0/178	(Hirano and Yoshikawa, 1982)
26	5 % (vehicle not reported)	3/167 **(1.8 %)**	(Larsen et al., 1996)
27	5 % (vehicle not reported)	0/145	(Suzuki et al., 1997)

No.	Concentration	Incidence	References
28	5 % (vehicle not reported)	1/84 **(1.1 %)**	(Takase et al., 1984)
29	5 % (vehicle not reported)	1/81 **(1.2 %)**	(Haba et al., 1993)
30	5 % (vehicle not reported)	3/78 **(3.8 %)**	(Ishihara et al., 1979)
	2 % (vehicle not reported)	2/78 **(2.6 %)**	
	1 % (vehicle not reported)	2/78 **(2.6 %)**	
31	1 % in petrolatum	7/2166 **(0.3 %)** Association with leg dermatitis	(Schnuch et al., 2007)
32	1 % in petrolatum	1/1082 **(0.1 %)**	(Geier et al., 2003)
33	1 % in petrolatum	1/320 **(0.3 %)**	(van Oosten et al., 2009)
34	1 % (vehicle not reported)	0/3115	(Cooper and Shaw, 2000)
35	1 % (vehicle not reported)	0/436	(Penchalaiah et al., 2000)
36	1 % (vehicle not reported)	0/422	(An et al., 2005)
37	1 % (vehicle not reported)	1/390 **(0.3 %)**	(Torgerson et al., 2007)
38	0.2 % (vehicle not reported)	18/614 **(2.9 %)**	(Fuji et al., 1972)

The studies described were performed with concentrations ranging from 0.2 to 20 % benzyl alcohol. The observed frequency of skin reactions ranged from 0 to 20 %. Considering studies with > 100 patients only, the sensitisation rates range from 0 up to 7.8 % (14 studies < 1 % and 9 studies > 1 %), whereas 12 of the studies did not show any positive reactions.

In addition to the patch test studies on consecutive dermatitis patients a number of case reports of patients, reacting to benzyl alcohol can be found.

Table 17: Case reports of patients reacting to benzyl alcohol.

Relevant information about the study (as applicable)	Observations	References
30 year-old facial dermatitis patient	Patch testing with benzyl alcohol (no test concentration reported) produced macular erythema	Case reports cited by (Johnson et al., 2017)
38 year-old eczema patient	1 % aqueous benzyl alcohol: Negative prick test results and positive (++) intradermal injection test results. (Negative injection test results in 10 healthy controls)	
39 year-old female with pruritic erythema of foot	5 % benzyl alcohol in petrolatum: Weak (+) reaction in patch test and strong positive reaction in repeated open application test	
67 year-old male with leg dermatitis	1 % benzyl alcohol in petrolatum: + + occlusive patch test reaction. 0.9 % benzyl alcohol in saline: Negative prick test reaction at 0.5 hours reading, but marked induration and proximal spread over arm at days 3 to 8	
53 year-old with stasis dermatitis	1 % benzyl alcohol in petrolatum: Redness and swelling at 1 hour after patch application, wheal 1 day later, and mild urticaria at day 5	
16 year-old female with possible anaphylactic reactions after IM	Benzyl alcohol preparation (concentration not reported):	

Relevant information about the study (as applicable)	Observations	References
injection with B12 preparation containing 0.9 % benzyl alcohol	Negative in prick tests, but positive in intradermal tests	
57 year-old female with pruritic dermatitis	Allergic contact dermatitis after patch testing with benzyl alcohol (concentration not reported)	
40 year-old female with dermatitis	9.5 % benzyl alcohol in petrolatum: Positive patch test reaction (+++)	
65 year-old female with eyelid dermatitis	Macular erythema after patch testing with benzyl alcohol (concentration not stated)	
30 year-old female with eyelid dermatitis	Positive (+) patch test reaction to benzyl alcohol (concentration not stated)	
46 year-old man with atopic excema	Patch testing with 5 % benzyl alcohol in petrolatum: Positive (+ +) reaction at day 2 and day 3	(Corazza et al., 1996)
43 year-old patient with recurrent right leg ulceration	Patch testing with 0.1 % benzyl alcohol in aqueous solution: Strong positive (+ + +) reaction at day 1 and day 3	(Jager et al., 1995)
63 year-old woman	Patch testing with 5 % benzyl alcohol (vehicle not reported): positive (+ +) reaction	(Li and Gow, 1995)
37 year-old woman with acute excema	Patch testing with 1 % benzyl alcohol in petrolatum: Strong positive (+ + +) reaction at day 2 and 4	(Aguirre et al., 1994)
50 year-old man	Patch testing with 5 % benzyl alcohol in petrolatum: Strong positive (+ + +) reaction after 48 and 96 hours	(Wurbach et al., 1993)
28 year-old metal grinder with patchy rash	Patch testing with 1 % benzyl alcohol in petrolatum: Positive (+ +) reaction at day 2 and 3	(Mitchell and Beck, 1988)
41 year-old Japanese women	Patch testing with 5 % benzyl alcohol (vehicle not reported): Positive reaction (+ +) after 48 and 72 hours Negative in open patch test	(Shoji, 1983)
80 year-old man	Patch testing with 5 % benzyl alcohol in petrolatum: Positive reaction at days 2 (+) and 4 (++)	(Kleyn et al., 2004)
36 year-old female and 43-year old male with contact dermatitis	Patch testing with 1 % benzyl alcohol in petrolatum: Strong positive reaction in patch test. Scratch, intradermal and subcutaneous injections of 1 % benzyl alcohol in saline solution: negative	(Fisher, 1975)

Available case reports describe positive reactions to benzyl alcohol to a varying degree.

Overall, the results on human volunteers or consecutive dermatitis patients show that benzyl alcohol has the potential to cause skin sensitisation in humans with a relatively low frequency of occurrence as described in the studies. However, the experimental and clinical studies described above do not allow for a reliable estimate of the level of exposure to benzyl alcohol. Given the ubiquitous presence of benzyl alcohol in a broad range of cosmetic products, exposure can be assumed to be relatively high according to section 3.4.2.2.3.1 of the Guidance on the application of the CLP criteria (ECHA, 2017). Johnson et al., 2017 supported this view in the publication: *"Products containing these ingredients may be applied as frequently as several times per day and may come in contact with the skin, nails, or hair for variable periods following application. Daily or occasional use may extend over many years*". This means with respect to Table 3.3 of the Guidance on the Application of the CLP Criteria (ECHA, 2017), frequency of exposure can be assumed to be ≥ once/daily (score 2) and the total number of exposures can be estimated to exceed 100 (score 2),

whereas the range of concentrations in those products is largely unknown (leading to an intermediate score of 1). This results in an overall score of 5 reflecting high exposure (ECHA, 2017).

9.7.3 Other data relevant for skin sensitisation

Traditionally the skin sensitising potential of a substance has been evaluated using animal testing. However, recently a battery of in vitro, in chemico, and in silico tests for evaluation of skin sensitisation have been developed. A number of methods have been validated and are described in OECD guidelines 442C, 442D and 442E (updated in June 2018). As each of the current test methods address only one specific key event involved in the adverse outcome pathway (AOP) leading to skin sensitisation, they cannot be used as stand-alone methods but have to be used in combination.

Table 18: Summary table of other studies relevant for skin sensitisation

	Type of test	Test substance	Result	Reference
Key event 1 Peptide/ protein binding	DPRA (in chemico) Direct peptide reactivity assay	Benzyl alcohol Purity and test concentrations not reported as detailed study reports are unpublished)	Negative	(Urbisch et al., 2015)
Key event 2 Keratinocyte response	KeratinoSens™ (in vitro) ARE-Nrf2 luciferase assay		Negative	
	LuSens (in vitro) ARE-Nrf2 luciferase assay		Positive	
Key event 3 Monocytic/ Dendritic cell response	h-CLAT (in vitro) Human cell line activation test		Positive	

The assays shown in Table 18 address three different key events of the skin sensitisation AOP as indicated in row 1. Detailed summaries of these studies can be found in Annex I to this dossier.

The DPRA assay addressing key event 1 shows a negative result whereas the h-CLAT assay addressing key event 3 shows a positive result. Metabolic activation of benzyl alcohol to benzaldehyde is possible (Urbisch et al., 2015), however, some of the assays such as the DRPA assay lack the required metabolic competence and therefore might lead to false negative results. It is not entirely clear why the KeratinoSens™ and the LuSens™, which are both ARE-Nrf2 luciferase assays, show differing results. The most likely explanation for this phenomenon might be that benzyl alcohol elicits a rather low sensitisation potency and is, thus, a borderline skin sensitiser based on in-vitro testing. Having in mind that the two assays exhibit different sensitivities, the differing results, hence, might be attributable to the low sensitising potency of the test chemical. Nevertheless, overall data point towards a sensitising potential of benzyl alcohol.

Currently, the CLP regulation does not yet include criteria for how to use these data in the context of classification and labelling for skin sensitisation or for sub-categorisation. Therefore, the available publications on in vitro and in silico data were reviewed, but were only considered as supportive evidence in the overall assessment.

9.7.4 Short summary and overall relevance of the provided information on skin sensitisation

A large number of human studies was identified which consist of reports on HRIPT and HMT data in human volunteers, patch tests of consecutive dermatitis patients in dermatological hospitals as well as a number of case reports. The results of HRIPT tests in presumably healthy volunteers show that increasing doses of benzyl alcohol (3 – 20 %) led to increasing numbers of sensitised subjects (0 – 11 %). According to section 3.4.2.2.3.1 of the Guidance on the Application of the CLP Criteria (ECHA, 2017) positive responses at > 500 µg/cm^2 for HRIPT studies should be considered for classification in category 1B.

In contrast to these results, a human maximisation test in 25 healthy volunteers was negative for 10 % benzyl alcohol, but given the absence of details regarding experimental conditions, the small number of volunteers, as well as the fact that only one dose was tested, it is difficult to judge the reliability of this result.

The retrospective analyses from multicentre studies support the conclusion from the HRIPT studies as they show sensitisation rates ranging from 0.1 to 2.3 % in collectives of consecutive dermatitis patients reacting to 1 or 10 % benzyl alcohol. Additional data from human patch test studies performed with 0.2 – 20 % benzyl alcohol show frequencies of skin reactions ranging from 0 (in 1/18 studies) up to 20 %. In general, most studies on collectives > 100 patients show a frequency of sensitisation of < 1 %. According to section 3.4.2.2.3.1 of the Guidance on the Application of the CLP Criteria (ECHA, 2017), positive responses from diagnostic patch test data where there is a relatively low but substantial incidence of reactions in a defined population in relation to relatively high exposure should be considered for classification. A percentage of < 0.2 % of skin sensitising incidences in general population studies and a percentage of < 1 % in consecutive, unselected dermatitis patients is considered to reflect a low to moderate frequency of occurrence of skin sensitisation. Given the ubiquitous presence of benzyl alcohol in cosmetic products, a relatively high frequency of exposure can be assumed as described in section 9.7.4.

There is no clear outcome from the available animal data. The available studies in guinea pigs investigating the skin sensitisation potential of benzyl alcohol show equivocal results: 1 out of 3 positive in the Guinea Pig Maximisation Test, 2 out of 3 in the Open Epicutaneous Test, a weak sensitiser in Freund's Complete Adjuvant Test and non-sensitising in the Draize Guinea Pig Sensitisation Test.

A guideline compliant LLNA showed no sensitisation up to 50 % benzyl alcohol. No higher doses were included in the test, although the substance should have been tested at higher concentrations as well according to OECD TG 429. Therefore, a possible sensitisation at doses > 12 500 µg/cm^2 cannot be ruled out. It should be noted that a retrospective analysis of LLNA data in comparison to human and/or guinea pig data performed by ICCVAM (2011) revealed that of 27 strong sensitising substances analysed, approximately half were underclassified in the LLNA based on an EC3 cut-off value of < 2 % (ECHA, 2017).

Some of the studies found in the literature also assess the skin sensitising potential of benzyl alcohol. The publication on benzyl alcohol by (Api et al., 2015) states: "Based on the available data, summarised in the current IFRA (International Fragrance Association) Standard, benzyl alcohol is considered to be a weak skin sensitizer". The Scientific Committee on Consumer Safety (SCCS) lists benzyl alcohol as "established contact allergen in humans" (SCCS, 2012). Furthermore, the International Fragrance Association (IFRA) recommends limiting the use of benzyl alcohol depending on the product (leave-on or rinse-off products) (IFRA, 2007).

In contrast earlier publications conclude that benzyl alcohol is an insignificant or questionable contact allergen based on clinical human data, negative human experimental data and positive as well as negative animal data (Schlede et al., 2003). However, it remains unclear which data was used for the evaluation, thus, possibly only the HMT and not the HRIPT data was considered. In a classification based solely on LLNA data and including reaction mechanistic domains (Safford et al., 2011) benzyl alcohol was classified in the non-reactive domain. According to the author, "*some chemicals classified into the non-reactive domain have been shown to be skin sensitisers in the LLNA. This sensitisation potential may be attributed to the presence of contaminants in the samples tested, formation of oxidation products or some other biological processes although this has not been categorically proven*". However, it is not clear how the authors concludes that contaminants or oxidation products could be the cause of the sensitisation potential of these chemicals or why the data based on the mechanistic domain of the substances should be given preference over the experimental LLNA data. Relating the relative frequency of sensitisation and the relative frequency of use, benzyl alcohol is included in the group of less important or even unimportant allergens (Schnuch et al., 2011b).

However, according to the Guidance on the Application of the CLP Criteria (ECHA, 2017), all data sources have to be considered in a weight-of-evidence approach when assessing the skin sensitising potential of a chemical: *"Since the data used in hazard or risk assessment should be relevant, reliable and sufficient for the regulatory purpose, it is necessary to base the assessment on the totality of available information, i.e. to apply Weight of Evidence (WoE) considerations"* (ECHA, 2017).

Overall, the data from HRIPT studies on benzyl alcohol, data from dermatitis patients, as well as diverse animal data clearly point to a weak to moderate skin sensitising potential of benzyl alcohol. Thus, although data of a recently conducted LLNA performed according to OECD TG 429 indicated no sensitizing potential of benzyl alcohol up to 50 %, the other available animal studies (even if documentation is sometimes limited) and especially data regarding the sensitising potential of benzyl alcohol in humans cannot be overruled by the LLNA test result only, especially since it is not clear why higher concentrations were omitted in the LLNA test design.

9.7.5 Comparison with the CLP criteria

The Guidance on the Application of the CLP Criteria (ECHA, 2017) states that *"positive effects seen in either humans or animals for skin sensitisation will normally justify classification. Evidence from animal studies on skin sensitisation is usually more reliable than evidence from human exposure, although adequate reliable and representative human data are usually more relevant. In cases where evidence is available from both sources, and there is conflict between the results, the quality and reliability of the evidence from both sources must be assessed in order to decide on the classification on a case-by-case basis".* Therefore, all data sources are compared to the criteria of the CLP regulation, which is summarised in Table 19.

Table 19: Comparison of experimental results confirming the skin sensitisation potential with benzyl alcohol in humans with the respective criteria of the CLP regulation

Reference(s)	Criteria acc. to CLP regulation, as laid out in detail in (ECHA, 2017)	Relevant result	Resulting Classification
Human data			
HRIPT	Annex I: 3.4.2.2.2.1. **Human evidence for sub-category 1A can include**: (a) positive responses at ≤ 500 µg/cm² (HRIPT, HMT–induction threshold); (b) diagnostic patch test data where there is a relatively high and substantial incidence of reactions in a defined population in relation to relatively low exposure; (c) other epidemiological evidence where there is a relatively high and substantial incidence of allergic contact dermatitis in relation to relatively low exposure. Annex I: 3.4.2.2.2.2. **Human evidence for sub-category 1B can include:** (a) positive responses at > 500 µg/cm² (HRIPT, HMT–induction threshold); (b) diagnostic patch test data where there is a relatively low but substantial incidence of reactions in a defined population in relation to relatively high exposure; (c) other epidemiological evidence where there is a relatively low but substantial incidence of allergic contact dermatitis in relation to relatively high exposure.	NOAEL: 5 906 µg/cm² LOAEL : 8 858 µg/cm²	**Skin Sens. 1B**
HMT	Criteria as above	Negative	**No classification**
Consecutive dermatitis patients	**Skin Sens. 1:** relatively high frequency **(**≥ 1.0 %) and "relatively high exposure" or relatively low/moderate frequency (< 1.0 %) and "relatively low exposure" **Skin Sens. 1A:** relatively high frequency (≥ 1.0 %) and "relatively low exposure"	Low/moderate frequency, presumed relatively high exposure	**Skin Sens. 1B**

Reference(s)	Criteria acc. to CLP regulation, as laid out in detail in (ECHA, 2017)	Relevant result	Resulting Classification
	Skin Sens. 1B: relatively low/moderate Frequency (< 1.0 %) and "relatively high exposure"		
Case reports	**Skin Sens. 1:** relatively high frequency **(**Number of published cases ≥ 100) and "relatively high exposure" or relatively low frequency **(**number of published cases < 100) and "relatively low exposure" **Skin Sens. 1A:** relatively high frequency **(**Number of published cases ≥ 100) and "relatively low exposure" **Skin Sens. 1B:** relatively low frequency **(**Number of published cases < 100) and "relatively high exposure"	< 100 cases and presumed relatively high exposure	**Skin Sens. 1B**
Animal data			
LLNA test	**Skin Sens. 1A:** EC3 ≤ 2 % **Skin Sens. 1B:** EC3 > 2 %	EC3 > 50 % corresponds to > 12 500 µg/cm^2	**No classification**
Guinea Pig Maximisation Test		1 out of 3 tests positive	**No classification**
Freund's Complete Adjuvant Test		Positive	**Sensitiser**
Draize Guinea Pig Sensitisation Test		Negative	**No Classification**
Open Epicutaneous Test		2 out of 3 tests positive	**Sensitiser**

The evidence for classification of benzyl alcohol can be summarised as follows. Human evidence for classification into sub-category 1B include positive responses at > 500 µg/cm^2 (induction threshold) in several HRIPT studies, multiple diagnostic patch test data where there is a relatively low but substantial incidence of reactions in a defined population (< 1 %) in relation to a relatively high exposure, as well as various case reports showing positive reactions to benzyl alcohol. It is not possible to identify individual exposures to benzyl alcohol but given the ubiquitous presence of benzyl alcohol in cosmetic products a high exposure can be assumed as discussed above. The animal data described including LLNA test and guinea pig assays, on the other hand, do not allow for classification and sub-categorisation, as reported data is sometimes limited and the results are overall ambiguous.

Similarly the available in chemico and in vitro data are ambiguous, but collectively point towards a skin sensitising potential of benzyl alcohol. In weight of evidence of all available data, benzyl alcohol has to be considered a weak skin sensitiser.

With regard to classification and sub-categorisation according to the Guidance on the Application of the CLP Criteria, table 3.4.3 (ECHA, 2017):"Substances showing a low to moderate frequency of occurrence in humans and/or a low to moderate potency in animals can be presumed to have the potential to produce sensitisation in humans" and should therefore be considered for classification into sub-category 1B.

9.7.6 Conclusion on classification and labelling for skin sensitisation

Based on the results shown above, it is proposed to classify benzyl alcohol as skin sensitiser, subcategory 1B (Skin Sens. Category 1B, H317 - May cause an allergic skin reaction). In line with (ECHA, 2017) table 3.9 no Specific Concentration Limit (SCL) is proposed as classification for benzyl alcohol is largely based on human data.

9.8 Germ cell mutagenicity

Not assessed in this dossier.

9.9 Carcinogenicity

Not assessed in this dossier.

9.10 Reproductive toxicity

Not assessed in this dossier.

9.11 Specific target organ toxicity-single exposure

Not assessed in this dossier.

9.12 Specific target organ toxicity-repeated exposure

Not assessed in this dossier.

10 EVALUATION OF ENVIRONMENTAL HAZARDS

Not assessed in this dossier.

11 EVALUATION OF ADDITIONAL HAZARDS

Not assessed in this dossier.

12 ADDITIONAL LABELLING

Not applicable.

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14 ANNEXES

Detailed summaries of all studies can be found in Annex I.