Committee for Risk Assessment

RAC

Annex 2

Response to comments document (RCOM)

to the Opinion proposing harmonised classification and labelling at EU level of

Benzyl alcohol

EC Number: 202-859-9
CAS Number: 100-51-6

CLH-O-0000007024-83-01/F

Adopted

16 September 2021

COMMENTS AND RESPONSE TO COMMENTS ON CLH: PROPOSAL AND JUSTIFICATION

Comments provided during consultation are made available in the table below as submitted through the web form. Any attachments received are referred to in this table and listed underneath, or have been copied directly into the table.

All comments and attachments including confidential information received during the consultation have been provided in full to the dossier submitter (Member State Competent Authority), the Committees and to the European Commission. Non-confidential attachments that have not been copied into the table directly are published after the consultation and are also published together with the opinion (after adoption) on ECHA's website. Dossier submitters who are manufacturers, importers or downstream users, will only receive the comments and non-confidential attachments, and not the confidential information received from other parties. Journal articles are not confidential; however they are not published on the website due to Intellectual Property Rights.

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Substance name: Benzyl alcohol
EC number: 202-859-9
CAS number: 100-51-6
Dossier submitter: Germany

GENERAL COMMENTS

Date	Country	Organisation	Type of Organisation	Comment number
15.12.2020	France		MemberState	1
Comment received				
The minimum purity of test item used to perform physicochemical properties tests should have been reported. A typo error has occurred in the SMILES notation of the substance (OCc1ccccc1)				
Dossier Submitter's Response				
The DS appreciates the comments on errors in the dossier. The errors have been corrected.				

Date	Country	Organisation	Type of Organisation	Comment number
17.12.2020	Germany	Lanxess Deutschland GmbH	Company-Manufacturer	2
Comment received				
Please refer to the attachment for further information ECHA note – An attachment was submitted with the comment above. Refer to public attachment LetterBzOH_ECHA_HarmonisedClassification_final 171220_Redacted.pdf ECHA note – An attachment was submitted with the comment above. Refer to confidential attachment Benzylalkohol_Med_Stellungnahme_08092019.pdf				

Dossier Submitter's Response
The DS appreciates the comments submitted. The comment asks to "*reassess the justification for a classification of skin sensitisation of benzyl alcohol…a sensitisation rate of up to 0.3% in very large collectives of dermatitis patients over decades seems not to meet the criteria of Reg. (EU)1272/2008 of a substantial number of persons. This conclusion is in line with current scientific evaluations (MAK, 2017).*" Furthermore, an expert statement, mentioned in the comments, reviewed the available animal and in vitro data. However, it does not consider the human data. A further letter refers to the occupational medical surveillance of "ca. 25 employees" (between 2006 and 2016) which did not reveal any health effects in regards to benzyl alcohol exposure. Overall, the DS described all available data in the dossier. The dataset might be inconsistent in regards to in vitro, in vivo experimental studies and human data. With regard to human data, however, it is clearly stated in tables 3.2, 3.3 and 3.4 of the 'Guidance on the Application of the CLP Criteria' (2017), which frequency of occurrence of skin sensitisation and which exposure data are required for triggering classification of a substance as skin sensitiser. Moreover, all available data should be considered for classification in a weight of evidence approach. In regards to the CLP criteria, the available data clearly point towards a weak sensitising potential of benzyl alcohol.
RAC's response
RAC concurs that the human data fulfil the critera aided by the guidance on the application of the CLP criteria on exposure and frequency. RAC notes the comments on the non-human data, and agrees on their ambiguity. However, all data should be included in a weight of evidence approach to conclude on classification.

Date	Country	Organisation	Type of Organisation	Comment number
18.12.2020	United States	Household & Commercial Products Association	Industry or trade association	3
Comment received				
HCPA appreciates the opportunity to offer these comments. Accurate and scientifically supported classifications are necessary to avoid unintended consequences on manufacturers and marketers of formulated products that utilize benzyl alcohol as a component and their ability to innovate new products with this substance. ECHA note – An attachment was submitted with the comment above. Refer to public attachment HCPA Comments on Proposal for Harmonized Classification and Labelling on Benzyl Alcohol NC.pdf ECHA note – An attachment was submitted with the comment above. Refer to confidential attachment HCPA Comments on Proposal for Harmonized Classification and Labelling on Benzyl Alcohol.pdf				
Dossier Submitter's Response				
The DS appreciates the comments submitted. The attached letter states that *"severity of reaction may also be considered and should be utilised when substances show a low frequency of occurrence in humans and animals.*				

Further, the data is inconsistent and the conclusions are not aligned with the reports from the RIFM".

The DS described all available data in the dossier, which overall point towards a weak sensitising potential of benzyl alcohol within the CLP criteria for classification based on hazard considerations.
Severity of reactions are not always reported in human studies. Furthermore, the IFRA agreed that benzyl alcohol is a weak sensitiser and recommends concentration limits for benzyl alcohol in different product categories based on an exposure based quantitative risk assessment for fragrance materials and a No Expected Sensitization Induction Level (NESIL) established by the RIFM Expert Panel.

RAC's response

RAC concurs with the response from the DS.

Date	Country	Organisation	Type of Organisation	Comment number
08.12.2020	Germany	IVDK - Information Network of Departments of Dermatology, Institute at the University Medical Center Göttingen	Academic institution	4

Comment received

We do not agree to the "Conclusion on classification and labelling for skin sensitisation" (section 9.7.6, page 33 of the CLH report). Considering the fact that benzyl alcohol is an extremely rare contact sensitizer, despite its very widespread use, categorizing benzyl alcohol as skin sensitizer 1B and labelling it with H 317 is not justified from the dermato-allergological point of view.

ECHA note – An attachment was submitted with the comment above. Refer to public attachment IVDK Comment on Benzyl alcohol.zip

Dossier Submitter's Response

The DS appreciates the comments submitted.

IVDK attached a letter including a review of the data from 2010-2019 from IVDK clinics including severity of reactions, reproducibility and population characteristics of groups of patients.

The DS described the available data in the dossier submitted and overall, based on a weight of evidence approach, the available data point towards a weak sensitising potential of benzyl alcohol within the CLP criteria for classification.

With regard to human data, it is clearly stated in tables 3.2, 3.3 and 3.4 of the 'Guidance on the Application of the CLP Criteria' (2017), which frequencies of occurrence of skin sensitisation (in the general population and dermatitis patients, respectively) and which exposure data trigger classification of a substance as skin sensitiser. In closer inspection of the data you presented and taking into consideration the information presented in the Guidance document, the DS comes to the conclusion that the data presented by you do not contradict, but rather support classification of benzyl alcohol as Skin Sens. 1B.

You state that no lower threshold values for "low/moderate frequency of sensitisation" is defined, and that hence, every substance eliciting a contact allergy reaction in only 1 individual must be categorized as Skin Sens. 1B, which you consider a general problem of the category definition. Although the DS considers that there may be some truth to that statement (evaluation of this hazard class is currently under discussion at OECD level), in the case at hand, positive diagnostic patch test reactions to benzyl alcohol of ≥0.2% are reported reaching a sensitisation frequency > 1% in individual studies. The upper threshold for "low/moderate frequency of sensitisation" is <1% in dermatitis patients, a high frequency is defined when a frequency ≥ 1% is reached. Thus, in weight of evidence the patch test results clearly fall into the "low/moderate frequency of occurrence" category justifying classification. Moreover, data from Human Repeated Insult Patch Tests (HRIPT) testing benzyl alcohol in healthy volunteers show that increasing doses of benzyl alcohol (3 – 20%) lead to increasing numbers of sensitised subjects (up to 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.

You further state you consider that it is very probable that the correct proportion of truly sensitised patients in the diagnostic patch tests is even lower than 0.2%, due to the low diagnostic performance of the test preparation benzyl alcohol in 1% pet. The DS considers this statement as speculation which in retrospect cannot be supported by data. Thus, this assumption cannot be considered in the weight of evidence.

RAC's response

RAC notes the additional information on patch tests studies including large number of patients, and the IVDKs interpretation of these data. However, RAC concurs with the DS that the proportion of "true" positive reactions are in the same range as the data already included in the classification report. RAC notes the IVDKs comments on the category definition open endedness. However, applying the guidance on patch tests results – including the new information point to classification in category 1B, which also is the conclusion from the HRIPT studies and the result of the weight of evidence evaluation.

OTHER HAZARDS AND ENDPOINTS – Acute Toxicity

Date	Country	Organisation	Type of Organisation	Comment number
15.12.2020	France		MemberState	5

Comment received

Acute Toxicity by oral route:
FR agrees with the proposal as Acute Tox 4 based on the available dataset. However, it has to be noted that the level of details prevents clear assessment of the data (only summary available or reliability not assignable). In this context, the generic ATE of 500 mg/kg bw can be more appropriate considering the uncertainties of the results instead of the proposed ATE of 1570 mg/kg bw/day.

Acute Toxicity by dermal route:
FR agrees that benzyl alcohol should not be classified based on the data available.

Acute toxicity by inhalation:
According to CLP guidance : "Differentiation between vapour and mist will be made on the basis of the saturated vapour concentration (SVC) for a volatile substance, which can be estimated as follows:
SVC [mg/l] = 0.0412 x MW x vapour pressure (vapour pressure in hPa at 20°C).

An LC50 well below the SVC will be considered for classification according to the criteria for vapours; whereas an LC50 close to or above the SVC will be considered for classification according to the criteria for mists”

According to the calculation based on the equation above, the LC50 > 3 mg/L should be compared to the classification thresholds for mist in the case of benzyl alcohol. In this context, since nearly all the LC50 are about 5 mg/L, the substance should not be classified for acute toxicity by inhalation. However, it has to be noted that the quality of the overall dataset is quite limited (old studies, only summary available or reliability not assignable) that may raise a doubt when deleting a current classification.

Dossier Submitter’s Response

The DS appreciates the comments.

Acute toxicity oral route: Although there are only study summaries available, two of the more reliable studies show similar LD50 values for the rat (1620 and 1570 mg/kg bw). However, a discussion in RAC is welcomed regarding the use of the generic ATE of 500 mg/kg bw.

Acute toxicity dermal route: The DS appreciates the support.

Acute toxicity by inhalation: The available studies and their uncertainties especially regarding the form of benzyl alcohol are described in the dossier. A discussion in the RAC is welcomed regarding classification for acute toxicity via the inhalation route.

RAC’s response

RAC response:
Acute oral toxicity: RAC considers that is possible and relevant to use a specific ATE rather than the lower default ATE of 500 mg/kg bw. Altough some of the data are only available as summaries, details appear sufficiently robust in a study form Jenner et al., 1964 to be used for ATE setting, which RAC therefore proposes to set at 1230 mg/kg bw.

Acute dermal toxicity: RAC also appreciates the support for no classification.

Acute inhalation toxicity: The comments on the guidance for the distinction whether vapour or aerosol studies are helpful. RAC considers the aerosol studies to be more relevant, leading to not classifying for this end-point. even if the background for the existing classification is unknown.

Date	Country	Organisation	Type of Organisation	Comment number
18.12.2020	United States	Household & Commercial Products Association	Industry or trade association	6

Comment received

N/A

ECHA note – An attachment was submitted with the comment above. Refer to public attachment HCPA Comments on Proposal for Harmonized Classification and Labelling on Benzyl Alcohol NC.pdf
ECHA note – An attachment was submitted with the comment above. Refer to confidential attachment HCPA Comments on Proposal for Harmonized Classification and Labelling on Benzyl Alcohol.pdf

Dossier Submitter's Response
The attachment is the same as comment number 3. The DS appreciates the comments submitted and refers to the response to comment number 3.
RAC's response
For RAC response see coment number 3.

Date	Country	Organisation	Type of Organisation	Comment number
18.12.2020	Belgium		MemberState	7
Comment received				
ORAL BECA supports the DS proposal for classification as Acute tox. 4; H302. Indeed, the most reliable and recent studies (1978 and 1980) based on similar guidelines to OECD TG 401 both concluded on comparable LD50 of 1620 and 1570 mg/kg bw for the rat. Less reliable studies (poorly reported) mentioned LD50 < 2000 mg/kg bw in the rat and the mouse, which is consistent with the above mentioned LD50 and are therefore considered as supportive information. In the guinea pig, the LD50 was determined to be between 1040 and 2600 mg/kg bw. Therefore, a LD50 < 2000 mg/kg bw warranting a classification as Acute Tox. 4 is supported by BECA. Furthermore, an ATE of 1570 mg/kg bw (the most sensitive LD50, from one the most reliable studies, probably combined for both sexes) is supported. However, it should be stressed that no purity was stated and the reliability of this study is considered to bare several restrictions. DERMAL Three poorly reported studies are available for the following species: Guinea pig, cat and rabbit. All the mentioned LD50 are above 2000 mg/kg bw, not warranting a classification according to the CLP guidance for criteria. However, no data on either the rat, nor the mouse are available. Furthermore, the LD50 for the guinea pig is mentioned to be lower than 5000 mg/kg bw. It is not excluded that this LD50 could be under 2000 mg/kg bw. In conclusion, BECA is of the opinion that there is not enough data to correctly assess this endpoint and therefore considers that there is not enough data to conclude. However, BE CA notes that benzyl alcohol is currently classified Acute Tox 4* (H332, dermal) according to the former Directive on chemicals. BE CA would therefore kindly ask the Dossier Submitter to detail the grounds of the actual Acute Tox 4* (H332) classification and to ensure that all available information is detailed in the CLH dossier, including the studies used to justify this classification according to the former Directive. INHALATION Five studies are available for this endpoint. Two studies, with more reliable data (test design similar to OECD 403 and GLP-compliance), exposed rats to an aerosol of benzyl alcohol. They concluded on a LC50 > 4.18 and LC50 > 5.4 mg/L for Bayer 1990 and Elf-Atochem 1993, respectively. BECA agrees that the studies conducted with aerosol do not seem to warrant any classification for benzyl alcohol since the LC50 of 4.18 induced only transient effects (no more details) and it could be expected that death would have occurred at a much higher concentration.				

However, other studies conducted with vapours of benzyl alcohol concluded on a LC50 that could warrant a classification as acute tox. 4 (Smyth 1951 and Carpenter 1949). These findings are very poorly reported and analytical concentrations were not monitored. Concerning the remaining study, the DS highlighted that the LC50 value proposed by Clayton (1982) was questionable.

The relevant guidance values for classification as Acute Tox. are:
- For aerosol: 1.0 < ATE < 5.0 (Acute Tox. cat.4)
- For vapours: 2.0 < ATE < 10.0 mg/L (Acute Tox. cat.3) and 10.0 < ATE < 20.0 mg/L (cat. 4)

All in all, it looks like benzyl alcohol behaves differently depending of its form and may induce toxic effects when the animals are exposed to vapours of the test substance, but not to aerosol.

Since the reliability of the studies is quite low considering the poor amount of available information, and the previous owned classification of benzyl alcohol as Acute Tox. 4; H332, BECA is of the opinion to consider the available data as inconclusive.

Dossier Submitter's Response

The DS appreciates the comments and the support regarding acute oral toxicity.

For acute toxicity dermal, all available studies were reported in the dossier. It is not clear which studies were used to justify classification according to the former Directive. The DS considers that based on the available and reported data no classification can be proposed.

For acute toxicity inhalation, the available studies and their uncertainties especially regarding the different behaviour of different forms (vapour, aerosol) are described in detail in the dossier. A discussion in RAC regarding classification for inhalation is welcomed.

RAC's response

Acute oral toxicity: RAC agrees that there are uncertainties with all available studies, due to summarised reporting. However, RAC considers that is possible and relevant to use the study from Jenner et al., 1964 to set the ATE. Altough this study was performed prior to OECD test guidelines and only available as a summary, details appear sufficiently robust in to be used for ATE setting, which would be lower than the one from the recent study, and RAC therefore proposes to set at 1230 mg/kg bw.

Acute dermal toxicity: RAC notes that the substance is currently classified for acute dermal toxicity, H332* is a classification for acute inhalation toxicity. The available data support not to classify, as proposed by the DS.
Acute inhalation toxicity: The comments on the guidance for the distinction whether vapour or aerosol studies are helpful. RAC recognises that the whole database carries uncertainties but considers the aerosol studies being more relevant, and thus support the DS conclusion of deleting the current classification.

OTHER HAZARDS AND ENDPOINTS – Eye Hazard

Date	Country	Organisation	Type of Organisation	Comment number
15.12.2020	France		MemberState	8
Comment received				
Eye irritation: FR agrees with the classification as Eye Irrit 2 based on the in vivo data on rabbit.				
Dossier Submitter's Response				
The DS appreciates the support.				
RAC's response				
RAC notes the support.				

Date	Country	Organisation	Type of Organisation	Comment number
18.12.2020	United States	Household & Commercial Products Association	Industry or trade association	9
Comment received				
N/A ECHA note – An attachment was submitted with the comment above. Refer to public attachment HCPA Comments on Proposal for Harmonized Classification and Labelling on Benzyl Alcohol NC.pdf ECHA note – An attachment was submitted with the comment above. Refer to confidential attachment HCPA Comments on Proposal for Harmonized Classification and Labelling on Benzyl Alcohol.pdf				
Dossier Submitter's Response				
The attachment is the same as comment number 3. The DS appreciates the comments submitted and refers to the response to comment number 3.				
RAC's response				
RAC refers to comment 3 above.				

Date	Country	Organisation	Type of Organisation	Comment number
18.12.2020	Belgium		MemberState	10
Comment received				
In line with the current classification, BECA supports the classification proposed for benzyl alcohol as Eye Irrit. Cat. 2 (H319 – causes serious eye irritation), based on two different studies showing consistent results, including corneal opacity ≥1 and for conjunctival redness ≥2 for all three animals in each study. The effects were however fully reversible within 21 days.				
Dossier Submitter's Response				
The DS appreciates the support.				
RAC's response				
RAC notes the support.				

OTHER HAZARDS AND ENDPOINTS – Skin Sensitisation Hazard

Date	Country	Organisation	Type of Organisation	Comment number
18.12.2020	France	Johnson & Johnson Santé Beauté France	Company-Downstream user	11

Comment received

Johnson & Johnson Consumer Health welcomes the opportunity to provide its views on the proposed classification of Benzyl Alcohol (CAS: 100-51-6, EC: 202-859-9) under Regulation (EC) n°1272/2008 on classification, labelling and packaging of substances and mixtures.
While Johnson & Johnson Consumer Health supports efforts to harmonize classification and ensure high protection of workers, consumers and environment, Johnson & Johnson Consumer Health believes the proposed classification of benzyl alcohol as Skin Sens. 1B appears to be overly conservative given the extensive safety data, both from external professional dermatology literature as well as our pre-market safety evaluations.

ECHA note – An attachment was submitted with the comment above. Refer to public attachment Benzyl Alcohol public consultation JJ non confidential.pdf
ECHA note – An attachment was submitted with the comment above. Refer to confidential attachment Benzyl Alcohol public consultation JJ confidential.pdf

Dossier Submitter's Response

The DS appreciates the comments.

The attached letter states that "*the proposed classification of benzyl alcolhol as Skin Sens. 1B appears overly conservative*" as benzyl alcohol should be considered as "*rare sensitiser*". Furthermore, it is stated that "*classification of benzyl alcohol as Skin Sens. 1B will likely contribute to the overall decrease of preservatives available to preserve efficiently cosmetic products*" and it is suggested to await the generation of new data before a decision on classification should be made.

The DS prepared the dossier based on the available data. In weight of evidence and considering the data summaries submitted by you, the data overall points towards a weak sensitising potential of benzyl alcohol within the CLP criteria for classification warranting classification as Skin Sens 1B.
It is highlighted that only the data that is available and presented in the dossier, as well as additional data submitted during Public Consultation can be used during this CLH process.

RAC's response

RAC concurs with the response from the DS

Date	Country	Organisation	Type of Organisation	Comment number
18.12.2020	United States	Household & Commercial Products Association	Industry or trade association	12

Comment received

HCPA does not believe the data supports the proposed classification as it is inconsistent and the conclusions presented are not aligned with the reports from RIFM (pages 1-2).

ECHA note – An attachment was submitted with the comment above. Refer to public attachment HCPA Comments on Proposal for Harmonized Classification and Labelling on Benzyl Alcohol NC.pdf ECHA note – An attachment was submitted with the comment above. Refer to confidential attachment HCPA Comments on Proposal for Harmonized Classification and Labelling on Benzyl Alcohol.pdf
Dossier Submitter's Response
The attachment is the same as comment number 3. The DS appreciates the comments submitted and refers to the response to comment number 3.
RAC's response
RAC refers to response to comment 3.

Date	Country	Organisation	Type of Organisation	Comment number
10.12.2020	United Kingdom		Individual	13
Comment received				
Please see attachment ECHA note – An attachment was submitted with the comment above. Refer to confidential attachment Benzyl Alcohol. Animal and in vitro data. 10th December 2020.pdf				
Dossier Submitter's Response				
The DS appreciates the comments which include a review of the available animal in vivo, and in vitro data. However, no new data was presented by you. Overall it is concluded in the review that "animal and in vitro test data do not provide evidence that benzyl alcohol has the potential to cause skin sensitisation". It is agreed that only based on animal and in vitro data, no final conclusion on the skin sensitising potential of benzyl alcohol can be drawn, as data are rather conflicting (several positive and negative results, respectively). However, it should be noted that the review presented by you does not include any human data which certainly have to be considered for classification as well. Hence, the DS performed a weight-of-evidence approach, in which the synergy of conflicting animal and in vitro data showing positive and negative results together with the vast amount of human data demonstrating a weak sensitising potential of benzyl alcohol led to the conclusion that classification of benzyl alcohol as Skin Sens. 1B is warranted.				
RAC's response				
RAC also agrees that the animal data quality is variable, and that neither they nor the in vitro/in chemico data can lead to decision. However, classification decision must be based on a weight of evidence approach as laid down in the CLP criteria, which for benzyl alcohol also includes human data from volunteer studies, patch testing studies and cases and overall leads to the conclusion that a skin sens 1B classification is warranted.				

Date	Country	Organisation	Type of Organisation	Comment number
16.12.2020	Netherlands	Valtris AO Maastricht BV	Company-Manufacturer	14

Comment received

As a manufacturer of benzyl alcohol for multiple decades, Valtris AO Maastricht BV is highly committed to the safety of the products we manufacture. The well-being and health of our employees and customers is one of our top priorities.

During all these years of manufacturing benzyl alcohol by Valtris and its predecessors, no cases of skin sensitization due to the aforementioned product were reported by our employees. This is confirmed by the attached statement issued by our health and safety provider DPSO Arbozorg. Moreover, whilst supplying this product to a multitude of different markets, including to the personal care industry, no issues about skin sensitization by benzyl alcohol have been notified to us by our customers.

We understand that the above-mentioned examples have limited scientific value. However, for the scientific arguments with regard to our position, we refer to the comments submitted by Lanxess Germany GmbH on behalf of the consortium for the registrants of benzyl alcohol under REACH. Valtris fully supports the points raised by Lanxess and believes these comments clearly indicate that the currently available human and animal data are inconsistent and do not clearly demonstrate that benzyl alcohol can be classified as a skin sensitizer.

We therefore strongly recommend the Committee to take into account the arguments submitted on behalf of the consortium in order to avoid an overly conservative classification of benzyl alcohol as skin sensitizer.

ECHA note – An attachment was submitted with the comment above. Refer to public attachment Public attachments Valtris AO Maastricht BV on skin sensitization proposal benzyl alcohol.zip
ECHA note – An attachment was submitted with the comment above. Refer to confidential attachment Confidential attachments Valtris AO Maastricht BV on skin sensitization proposal benzyl alcohol.zip

Dossier Submitter's Response

The DS appreciates the comments submitted.

The attached letter refers to the medical examinations of employees and states that the current control measures are adequate regarding exposure of benzyl alcohol. Furthermore, it is stated that "*the available data are inconsistent and do not clearly demonstrate that benzyl alcohol can be classified as a skin sensitiser.*"

The DS described all available data in the dossier and in weight of evidence, the available data point towards a weak sensitising potential of benzyl alcohol within the CLP criteria for classification as Skin Sens 1B.

RAC's response

RAC concurs with the DS that the weight of evidence evaluation including all available data as ruled in the criteria for classification lead to the conclusion that benzyl alcohol should be classified as Skin Sens 1B.

Date	Country	Organisation	Type of Organisation	Comment number
09.12.2020	Germany	Working Group Epoxy Resins	National NGO	15

Comment received

Benzyl alcohol is a common ingredient of epoxy resin products. Due to the extremely low sensitisation reaction and taking into account the very wide distribution of benzyl alcohol in different products, the working group does not consider this substance to be an allergen.

For substances whose sensitising property is not clear, chapter 3.4.2.2. of Regulation (EC) No 1272/2008 must be applied. According to this regulation, small numbers of cases may lead to classification. However, an evaluation of over 70,000 cases, carried out by the IVDK shows very few and then only weak, often ambiguous reactions to benzyl alcohol (personal communication from Prof. Geier, IVDK, publication in preparation). According to chapter 3.4.2.2. of Regulation (EC) No 1272/2008, these aspects must be considered.

The consequences of labelling benzyl alcohol with H317 would have a serious impact on the necessary substitution check for users of products containing benzyl alcohol, which is required according to the risk assessment. The procedure is described in the TRGS 600.

The substitution check stipulates that benzyl alcohol, as a substance classified as skin-sensitising (high risk), must be replaced by corrosive or eye-damaging substances (medium risk). In this specific case, this leads to an increase of risk.

Products that are already labeled with H317 and contain very potent allergens can thus be used because they are equivalent. This applies e.g. for epoxy resins, which have excellent technical properties, but can lead to severe and recurring allergic skin diseases after just a few contacts.

ECHA note – An attachment was submitted with the comment above. Refer to public attachment Statement_WG_ER_benzyl_alcohol_2020_Redacted.pdf

Dossier Submitter's Response

The DS appreciates the comments.

Overall, the DS submitted all available data in the dossier. The dataset might be inconsistent in regards to in vitro, in vivo experimental studies and human data. With regard to human data, however, it is clearly stated in tables 3.2, 3.3 and 3.4 of the 'Guidance on the Application of the CLP Criteria' (2017), which frequency of occurrence of skin sensitisation and which exposure data are required for triggering classification of a substance as skin sensitiser. Moreover, all available data should be considered for classification in a weight of evidence approach.
In regards to the CLP criteria, the available data clearly point towards a weak sensitising potential of benzyl alcohol.

RAC's response

RAC concurs with the response from the DS that the classification is the result of a weight of evidence evaluation and application of the CLP criteria leading to its classification as Skin Sens. 1B.

Date	Country	Organisation	Type of Organisation	Comment number
17.12.2020	Germany	Lanxess Deutschland GmbH	Company-Manufacturer	16

Comment received

Please refer to the attachment for further information

ECHA note – An attachment was submitted with the comment above. Refer to public attachment LetterBzOH_ECHA_HarmonisedClassification_final 171220_Redacted.pdf
ECHA note – An attachment was submitted with the comment above. Refer to confidential attachment Benzylalkohol_Med_Stellungnahme_08092019.pdf

Dossier Submitter's Response

The attachement is the same as comment number 2.

The DS appreciates the comments submitted and refers to the response to comment number 2.

RAC's response

RAC refers to response to comment 2.

Date	Country	Organisation	Type of Organisation	Comment number
18.12.2020	Belgium		MemberState	17

Comment received

Available animal dataset indicates heterogenous results for benzyl alcohol skin sensitisation potential : one LLNA (RFIM, 2005a), two GPMT (Ishihara, 1981; Klecak, 1977), three Draize test (Ishihara, 1981; Klecak, 1977; Sharp, 1978) and two epicutaneous test (Klecak, 1979; Ishihara, 1986) were concluded negative ; benzyl alcohol was concluded as a weak sensitizer in one FCA test (Hausen, 1991) and one delayed contact hypersensitivity test (Kashima, 1993) and showed clear positive results in three FCA test (Ishihara, 1981; Klecak, 1977, Hausen, 1992), two epicutaneous test (Ishihara, 1981; Klecak, 1977) and one GPMT (Ishihara, 1986). All studies are considered of limited reliability.

Furthermore, there are several evidences of skin sensitisation in human exposed to benzyl alcohol. A human repeated insult patch tests with doses ranging from 3 543 µg/cm² to 23 622 µg/cm² showed dose-dependent increase in numbers of sensitised subjects (0 – 11%) above 7.5% benzyl alcohol (RIFM). Due to the large presence of this compound in cosmetic products, it could not be excluded that the volunteers were already sensitised to benzyl alcohol. In contrast, a HMT on 25 volunteers showed negative results for 10% benzyl alcohol (RFIM). We however note that this study is older that the RIFM and of limited reliability. BE CA is of the view that the HMT study is not sufficient to discard positive results in other studies.

In addition, several human patch tests are described in the CLH proposal. Sensitisation rates ranged 0.1-2.3 % with a concentration of 1% benzyl alcohol and were comprised between 0.21-1.1 % with a concentration of 10% benzyl alcohol. The studies in which the concentration of benzyl alcohol used is not specified were up to 2% positives. Further human patch studies were also described in a review from 2012 (Scognamiglio). 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.

Finally, various case reports were also available in the CLH proposal, showing evidences of skin sensitisation after exposure to 0.1-9.5 % benzyl alcohol, indicating that benzyl alcohol has the potential to cause skin sensitisation in humans with a relatively low frequency of occurrence.

Dossier Submitter's Response
The DS appreciates the support.
RAC's response
RAC notes the valuable observations on the data.

Date	Country	Organisation	Type of Organisation	Comment number
15.12.2020	France		MemberState	18
Comment received				
Skin sensitisation: No classification can be reached based on the experimental studies: contradictory results were obtained from under-reported studies that prevent independent interpretation. Positive results from HRIPT and Maximisation assays seem questionable since dermal reactions are already observed during the induction phase. No additional reactions are observed after challenge (and sometimes less reactions after rechallenge). Thus, discrimination of sensitizing versus irritation effects should be further discussed for adequate interpretation of these studies. Regarding patch test diagnostic studies in table 15, it is not clear in most of the described studies if the patients included are selected or unselected. From these studies, sensitisation rates > 1% were reported in 3 studies but only consist in 1 to 5 positive cases among the patients tested. This suggests a very low frequency of dermal sensitisation. From table 16, studies report sensitisation rates: from 0% to 20% (19/95 cases), however, it is difficult to explain these different values by the vehicle and the concentrations used. Overall, the dataset is not very consistent with a wide range of responses based on in vitro assays, in vivo experimental studies and human data. However, considering the low frequency of reactions associated with a high exposure in humans in regards to CLP criteria, FR agrees with the proposal Skin Sens. 1B.				
Dossier Submitter's Response				
The DS appreciates the support.				
RAC's response				
RAC notes the observations on some of the data.				

Date	Country	Organisation	Type of Organisation	Comment number
08.12.2020	Germany	IVDK - Information Network of Departments of Dermatology, Institute at the University Medical Center Göttingen	Academic institution	19

Comment received

Section 9.7 "Skin sensitisation" (p. 16-33), in particular sections 9.7.2 and 9.7.6.

ECHA note – An attachment was submitted with the comment above. Refer to public attachment IVDK Comment on Benzyl alcohol.zip

Dossier Submitter's Response

The attachement is the same as comment number 4.

The DS appreciates the comments submitted and refers to the response to comment number 4.

RAC's response

RAC refers to its reponse to comment 4

Date	Country	Organisation	Type of Organisation	Comment number
17.12.2020	United States	Emerald Kalama Chemical B.V.	Company-Manufacturer	20

Comment received

Emerald Kalama Chemical B.V. disagrees with the proposed classification of benzyl alcohol as Skin Sens. 1B. We base our conclusion on the same data set referenced in the CLH report, and have provided detailed comments on key elements. We would specifically like to direct attention to the 2018 MAK Value Review for benzyl alcohol. As a general point, Emerald feels that both the animal and human data on skin sensitisation potentially caused by benzyl alcohol are inconsistent, and do not support the proposed classification. Please see our detailed comments attached.

ECHA note – An attachment was submitted with the comment above. Refer to public attachment Benzyl Alcohol CLH Consultation - EKC BV Comments - 16 Dec 2020_Redacted.pdf

Dossier Submitter's Response

The DS appreciates the comments submitted.

The comments state that there is "*an inconsistency in regards to in vitro, in vivo experimental studies and human data"*. Furthermore, "*severity of reactions in human studies should be considered and there is potentially a misinterpretation of the in vitro data and it is suggested to await the generation of new data before a decision on classification should be made.*"

Overall, the DS described all available data in the dossier. The dataset might be inconsistent in regards to in vitro, in vivo experimental studies and human data. However, all data should be considered for classification in a weight of evidence approach.

With regards to the CLP criteria, the data point to a weak sensitising potential of benzyl alcohol warranting classification as Skin Sens 1B. It is highlighted that only the data that is available and presented in the dossier, as well as additional data submitted during Public Consultation can be used in this CLH process.
RAC's response
RAC has noted the comments on the interpretation of data, on the database inconsistency and the proposal to provide further documentation. RAC however concurs with the DS on the weight of evidence conducted regarding all human, animal and in vitro data, having regard to their reliability in comparison with to the CLP criteria, leading to classification as Skin sens 1B of benzyl alcohol.

PUBLIC ATTACHMENTS
1. Benzyl Alcohol public consultation JJ non confidential.pdf [Please refer to comment No. 11]
2. HCPA Comments on Proposal for Harmonized Classification and Labelling on Benzyl Alcohol NC.pdf [Please refer to comment No. 3, 6, 9, 12]
3. LetterBzOH_ECHA_HarmonisedClassification_final 171220_Redacted.pdf [Please refer to comment No. 2, 16]
4. Benzyl Alcohol CLH Consultation - EKC BV Comments - 16 Dec 2020_Redacted.pdf [Please refer to comment No. 20]
5. Public attachments Valtris AO Maastricht BV on skin sensitization proposal benzyl alcohol.zip [Please refer to comment No. 14]
6. Statement_WG_ER_benzyl_alcohol_2020_Redacted.pdf [Please refer to comment No. 15]
7. IVDK Comment on Benzyl alcohol.zip [Please refer to comment No. 4, 19]

CONFIDENTIAL ATTACHMENTS
1. Benzyl Alcohol public consultation JJ confidential.pdf [Please refer to comment No. 11]
2. HCPA Comments on Proposal for Harmonized Classification and Labelling on Benzyl Alcohol.pdf [Please refer to comment No. 3, 6, 9, 12]
3. Benzylalkohol_Med_Stellungnahme_08092019.pdf [Please refer to comment No. 2, 16]
4. Confidential attachments Valtris AO Maastricht BV on skin sensitization proposal benzyl alcohol.zip [Please refer to comment No. 14]
5. Benzyl Alcohol. Animal and in vitro data. 10th December 2020.pdf [Please refer to comment No. 13]