baua:
Bundesanstalt für Arbeitsschutz
und Arbeitsmedizin
Federal Institute for Occupational
Safety and Health

SUBSTANCE EVALUATION CONCLUSION

as required by REACH Article 48

and

EVALUATION REPORT

for

Benzyl alcohol

EC No 202-859-9

CAS No 100-51-6

Evaluating Member State(s): Germany

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Evaluating Member State Competent Authority

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Year of evaluation in CoRAP: 2016

Before concluding the substance evaluation a Decision to request further information was issued on: 18 April 2018

Further information on registered substances here:

http://echa.europa.eu/web/guest/information-on-chemicals/registered-substances

DISCLAIMER

This document has been prepared by the evaluating Member State as a part of the substance evaluation process under the REACH Regulation (EC) No 1907/2006. The information and views set out in this document are those of the author and do not necessarily reflect the position or opinion of the European Chemicals Agency or other Member States. The Agency does not guarantee the accuracy of the information included in the document. Neither the Agency nor the evaluating Member State nor any person acting on either of their behalves may be held liable for the use which may be made of the information contained therein. Statements made or information contained in the document are without prejudice to any further regulatory work that the Agency or Member States may initiate at a later stage.

Foreword

Substance evaluation is an evaluation process under REACH Regulation (EC) No. 1907/2006. Under this process the Member States perform the evaluation and ECHA secretariat coordinates the work. The Community rolling action plan (CoRAP) of substances subject to evaluation, is updated and published annually on the ECHA web site (ECHA, 2016c)[1].

Substance evaluation is a concern driven process, which aims to clarify whether a substance constitutes a risk to human health or the environment. Member States evaluate assigned substances in the CoRAP with the objective to clarify the potential concern and, if necessary, to request further information from the registrants concerning the substance. If the evaluating Member State concludes that no further information needs to be requested, the substance evaluation is completed. If additional information is required, this is sought by the evaluating Member State. The evaluating Member State then draws conclusions on how to use the existing and obtained information for the safe use of the substance.

This Conclusion document, as required by Article 48 of the REACH Regulation, provides the outcome of the Substance Evaluation carried out by the evaluating Member State. The document consists of two parts i.e. A) the conclusion and B) the evaluation report. In the conclusion part A, the evaluating Member State considers how the information on the substance can be used for the purposes of regulatory risk management such as identification of substances of very high concern (SVHC), restriction and/or classification and labelling. In the evaluation report part B the document provides explanation how the evaluating Member State assessed and drew the conclusions from the information available.

With this Conclusion document the substance evaluation process is finished and the Commission, the registrants of the substance and the Competent Authorities of the other Member States are informed of the considerations of the evaluating Member State. In case the evaluating Member State proposes further regulatory risk management measures (RMMs), this document shall not be considered initiating those other measures or processes. Further analyses may need to be performed which may change the proposed regulatory measures in this document. Since this document only reflects the views of the evaluating Member State, it does not preclude other Member States or the European Commission from initiating regulatory RMMs which they deem appropriate.

[1] http://echa.europa.eu/regulations/reach/evaluation/substance-evaluation/community-rolling-action-plan

Contents

Part A. Conclusion

1. CONCERN(S) SUBJECT TO EVALUATION

Benzyl alcohol was originally selected for substance evaluation in order to clarify concerns about:

- Wide dispersive use
- Suspected sensitiser
- Exposure of workers
- High Risk Characterisation Ratios (RCRs)

During the evaluation, consumer exposure was identified as an additional concern.

2. OVERVIEW OF OTHER PROCESSES / EU LEGISLATION

According to the Cosmetic Products Regulation (EC) No 1223/2009 (EU, 2009b), the presence of benzyl alcohol must be indicated in the list of ingredients when it is used as a fragrance or in aromatic compositions or their raw materials and its concentration exceeds 0.001% in leave-on products and 0.01% in rinse-off products, respectively. As a preservative, the maximum allowed concentration of benzyl alcohol is 1% in ready-for-use preparations.

Allergenic substances such as benzyl alcohol must be labelled on the packaging of detergents if added at concentrations exceeding 0.01% (EU Regulation No 648/2004 on detergents (EC, 2004; EMA, 2017; EFSA, 2019).

Directive 2009/48/EC states that toys shall not contain benzyl alcohol because it is considered to be an allergenic fragrance (EU, 2009a). Exceptions are made for olfactory board games, cosmetic kits and gustative games under certain conditions.

Benzyl alcohol is regulated under the biocides product regulation (BPR, Regulation (EU) 528/2012). It is listed in Annex I of Regulation (EU) 1451/2007 (EU, 2007) as an existing biocidal active substance. Currently, benzyl alcohol is in the biocidal active substance approval process for product type (PT) 6 (preservatives for products during storage).

Benzyl alcohol is classified by EFSA's Scientific Committee for Food (SCF-L) as a substance that is approved for the use of materials and articles intended to come into contact with food (List 1). The acceptable or tolerable daily intake (ADI/TDI) as set by this committee is 5 mg/kg bw (Council of Europe, 2002).

The addition of benzyl alcohol to some food items is further regulated in Regulation (EC) 1333/2008). The EFSA Panel on Contaminants in the Food Chain (CONTAM) recently re-evaluated the use of benzyl alcohol (E 1519) when used as food additive (EC, 2004; EMA, 2017; EFSA, 2019) and established an ADI of 4 mg/kg bw per day. Overall it was concluded *"that the exposure to benzyl alcohol (E 1519) does not raise a safety concern at the reported uses and use levels"*.

According to Regulation (EU) 10/2011 on Plastic Materials and Articles Intended to Come into Contact with Food (EU, 2011), the use as additive or polymer production aid is not allowed.

In 2017, the European Medicines Agency (EMA) concluded that benzyl alcohol must not be used as excipient in the medicinal products intended for pre-term and full-term neonates (EC, 2004; EMA, 2017; EFSA, 2019). EMA accordingly recommended revising and implementing information on this exemption in the package leaflet of medicinal products. The conclusion was based on data showing that *"benzyl alcohol administered intravenously has led to 'gasping syndrome' in several pre-term neonates with metabolic acidosis*

involving deterioration of the neurological state, cardio-vascular failure and haematological anomalies. The majority of poisonings were fatal. This syndrome was associated with the accumulation of benzyl alcohol and its metabolite, benzoic acid."

Currently, benzyl alcohol has a harmonised classification (CLH) for acute toxicity only, which was set under 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" according to the criteria of Regulation (EC) 1272/2008 (CLP Regulation).

Minimum classification for a category is indicated by an asterisk. A proposal for harmonised classification and labelling of benzyl alcohol (according to CLP art. 37(2)) was prepared by the evaluating member state competent authority (eMSCA) with regard to the endpoints acute toxicity, eye irritation and skin sensitisation. The proposal was submitted to ECHA in October 2019. For details see section 4.1.1.

3. CONCLUSION OF SUBSTANCE EVALUATION

The evaluation of the available information on the substance has led the evaluating Member State (eMSCA) to the conclusions summarised in the table below.

Table 1

CONCLUSION OF SUBSTANCE EVALUATION	
Conclusions	**Tick box**
Need for follow-up regulatory action at EU level	x
Harmonised Classification and Labelling	x
Identification as SVHC (authorisation)	
Restrictions	
Other EU-wide measures (enforcement/use advice against)	x
No need for regulatory follow-up action at EU level	

4. FOLLOW-UP AT EU LEVEL

RMOA

A Regulatory Management Option Analysis (RMOA) for benzyl alcohol is currently under preparation by the eMSCA and was initiated in 2020[2]. The EU-wide consultation aims at obtaining a better understanding of the variety of consumer products with solvents on the market including benzyl alcohol to enable more realistic exposure estimation and risk assessment. Currently, solvent-related risks cannot be ruled out for consumers. The assessments made by the eMSCA are based on general information on typical product characteristics. Detailed information about the products and their applications is usually missing. The eMSCA is particularly interested in an exchange with companies and stakeholders who are familiar with solvent-based consumer products. These include, in particular, formulators, product developers and end users, as well as fabric manufacturers, importers, distributors/dealers, associations, NGOs and interested third parties.
In addition, market inquiries at the national level are ongoing for paint removers and adhesives and sealants. These inquiries complement the consultation and provide

[2] https://echa.europa.eu/de/rmoa/-/dislist/details/0b0236e184ff4aa4

exposure-relevant data. In addition, consumer surveys are ongoing or initiated to generate data that can be used to evaluate and possibly substantiate the exposure estimation, in particular for the consumer use of adhesives and paint removers. The RMOA will be used to determine whether benzyl alcohol poses a health risk to consumers, whether further risk management measures are necessary for the use of consumer products and which measure(s) can be considered best suited in order to minimise the potential risk for the consumer.

4.1. Need for follow-up regulatory action at EU level

4.1.1. Harmonised Classification and Labelling

The eMSCA has evaluated hazard data on benzyl alcohol and considers that the following classification is appropriate:

Table 2

CLASSIFICATION AND LABELLING FOR BENZYL ALCOHOL AS CONSIDERED APPROPRIATE BY THE EVALUATING MEMBER STATE COMPETENT AUTHORITY			
Hazard Class and Category Code(s)	**Hazard Statement Code(s)**	**Pictograms, Signal Word**	**Specific Concentration limits**
Acute Tox. 4	H302: Harmful if swallowed	GHS07: Exclamation mark; Warning	ATE: 1570 mg/kg bw
Eye Irrit. 2	H319: Causes serious eye irritation	GHS07: Exclamation mark; Warning	No SCL proposed
Skin Sens. 1B	H317: May cause an allergic skin reaction	GHS08: Health Hazard; Danger	No SCL proposed

Therefore, the eMSCA has recently prepared a CLH proposal[3] for benzyl alcohol according to Art. 37(2) CLP (cf. Table 10) which was submitted to ECHA in October 2019.

The current harmonised classification for acute toxicity 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. Based on the available data, the eMSCA agrees with the registrants to classify benzyl alcohol as Acute Tox. 4 after oral exposure according to the CLP Regulation.

The eMSCA further considers that based on the available data and according to criteria of CLP Regulation , Annex I (EC, 2015), the aerosol of benzyl alcohol does not need to be classified for acute inhalation toxicity. Moreover, results from two OECD Guideline 405 studies support classification of benzyl alcohol as "Eye Irrit. 2, H319" according to the criteria of CLP Regulation, Annex I (EC, 2015). In addition, evidence that benzyl alcohol may act as a moderate/weak skin sensitiser justifies a proposal for harmonised classification with regard to this endpoint. The eMSCA considers an updated CLP entry for benzyl alcohol as appropriate to warrant the safe use of the substance. In summary, the eMSCA considers that available data warrant a harmonisation of the classification for benzyl alcohol as Acute Tox. 4 (H302), Eye Irrit. 2 (H319), and Skin Sens. 1B (H317).

[3] https://echa.europa.eu/de/registry-of-clh-intentions-until-outcome/-/dislist/details/0b0236e1837d7a72

4.1.2. Identification as a substance of very high concern, SVHC (first step towards authorisation)

Not applicable.

4.1.3. Restriction

Not applicable.

4.1.4. Other EU-wide regulatory risk management measures

Enforcement and "use advice against"

Benzyl alcohol is registered for the use in finger paints. Finger paints are toys according to Directive 2009/48/EC which shall not contain benzyl alcohol because the substance is assumed to be an allergenic fragrance. Therefore, intensified measures should be considered by enforcement and "use advice against" statements should be considered by the registrants.

5. CURRENTLY NO FOLLOW-UP FORESEEN AT EU LEVEL

Not applicable.

6. TENTATIVE PLAN FOR FOLLOW-UP ACTIONS (IF NECESSARY)

Table 3

FOLLOW-UP		
Follow-up action	**Date for intention**	**Actor**
Proposal for harmonised classification with regard to acute toxicity, eye irritation and skin sensitisation according to CLP	Submitted to ECHA in October 2019	eMSCA
RMOA	2020/2021	eMSCA

Part B. Substance evaluation

7. EVALUATION REPORT

7.1. Overview of the substance evaluation performed

Benzyl alcohol was originally selected for substance evaluation in order to clarify concerns about:

- Wide dispersive use
- Suspected sensitiser
- Exposure of workers
- High Risk Characterisation Ratios (RCRs)

During the evaluation, consumer exposure was identified as an additional concern.

Table 4

EVALUATED ENDPOINTS	
Endpoint evaluated	**Outcome/conclusion**
Acute Toxicity and Irritation	No additional concern identified. CLH proposal for acute oral toxicity and eye irritation submitted to ECHA.
Skin sensitisation	Weak to moderate skin sensitising potential confirmed. Classification as skin sensitiser Cat. 1B justified based on positive reactions above 500 µg/cm^2 in Human Repeated Insult Patch Tests (HRIPTs) and a low, but substantial incidence of up to 0.3% in large study populations with consecutive patients in clinical departments of dermatology. CLH proposal for skin sensitisation submitted to ECHA.
Repeated dose toxicity	Although oral repeated dose toxicity studies are available, the eMSCA considers the oral route less relevant and risk assessment is therefore focused on exposure via inhalation. In a subacute inhalation toxicity study, no adverse effects were observed up to the highest tested dose of 1 072 mg/m³. However, it should be noted that the highest dose tested was not the maximum tolerated dose. The most relevant dose descriptors are used for DNEL derivation.
Carcinogenicity	No concern identified.
Mutagenicity	No concern identified.
Toxicity to reproduction: fertility	No concern identified.
Toxicity to reproduction: developmental toxicity	No concern identified.
Exposure of professionals/workers	Concern needed to be clarified. Safe use for ES 15 (WCS 7, 8, 9, 10 and 11) by exposure assessment not demonstrated, body exposure has not been taken into account and ECETOC TRA v3 has been used outside its scope of application. Therefore, revision of exposure assessment and risk characterisation for the inhalation and dermal routes or representative workplace measurement data taken under operational conditions and risk management measures as specified by the registrants were requested.

	The registrants have submitted an updated CSR on 25 April 2019 according to the requirements specified in the substance evaluation decision (ECHA, 18 April 2018). An examination of the CSR showed that the registrants have essentially complied with the requirements regarding worker request A and B. Therefore, exposure concern is clarified.
Exposure of consumers	Based on the available data on products available for consumer use it cannot be concluded that the concentrations used for exposure assessment in the CSRs cover the situation on the market. There is a need for better understanding of the consumer market with its diversity of applications to finally assess exposure to benzyl alcohol. The eMSCA will clarify this in the RMOA.

7.2. Procedure

In August 2014 benzyl alcohol was proposed for substance evaluation according to Article 44(1) of the REACH Regulation (EC) No 1907/2006 (EC, 2016). The use of benzyl alcohol is widespread, e.g. in consumer, professional and industrial settings. In October 2014 ECHA published the draft CoRAP. A substance evaluation for benzyl alcohol was initiated in March 2016. During the process of substance evaluation all data available until the end of March 2017 were considered. A substance evaluation decision was issued on 18 April 2018 containing requests with regard to the exposure of workers. The registrants provided data within the given time frame on 25 April 2019 and the concern could be clarified. No further information from the registrants is considered necessary to conclude the substance evaluation of benzyl alcohol. The evaluation did not encompass environmental endpoints.

With respect to human health, the evaluation was comprehensive, addressing the following human health endpoints as required according to REACH Regulation, Annex VII-X: acute toxicity and corrosion/irritation, skin sensitisation, repeated dose toxicity, carcinogenicity, mutagenicity, toxicity to reproduction (fertility and developmental toxicity).

This substance evaluation referred to the Chemical Safety Report (CSR) and the IUCLID endpoint records from the registration data for benzyl alcohol. In addition, it also considered other relevant information, i.e. a number of reference assessments and reports available up to March 2017.

Exposure and risk assessment - workers:

The following sources were checked as a matter of routine to access information on benzyl alcohol:

- GESTIS database (IFA, 2016a);
- Kirk Othmer, Encyclopedia of Chemical Technology, fourth edition (1998) (Kirk et al., 1998)
- ECHA homepage (information on chemicals) (ECHA, 2016b);
- IFA publications
- GISBAU publications

The exposure scenarios (ESs) for workers as provided by the registrants in the CSR were checked whether they are exhaustive, plausible and well-documented with regard to operational conditions (OCs) and information about RMMs.

The eMSCA considered the following aspects of particular importance for ESs for workers:

- Sufficient description of OCs and RMMs including personal protective equipment (PPE).
- The priority of implementation for protective and prevention measures shall comply with the order laid down in Directive 98/24/EC Art.6(2) (EU, 1998).

For risk characterisation, the long-term systemic derived no-effect levels (DNELs) for the inhalation and dermal pathways of exposure were checked for compliance to the REACH requirements and compared with the respective exposure estimates derived by the eMSCA. Subsequently, the combined RCRs for both exposure routes were calculated in order to conclude on the safe use of the substance.

Exposure and risk assessment – consumers:

In order to identify possible risks, the CSRs were checked with regard to whether the ESs and risk characterisation ratios for consumers are exhaustive, plausible and well-documented regarding relevant uses, exposure routes and targeted population groups. Furthermore, CSRs were checked for missing data and default values used as well as justifications for deviations were reviewed.

An internet search was conducted to cross-check uses and, as far as possible, OCs for the use of consumer products containing benzyl alcohol. This included safety data sheets (SDS). In addition, information from various product databases was used.

The eMSCA established own consumer exposure estimates using ConsExpo according to ECHA Guidance on Information Requirements and Chemical Safety Assessment R.15 (ECHA R.15, 2016) on the basis of the OCs default assumptions in ConsExpo (valid in 2019) and concentrations given in the CSRs. For scenarios with RCR > 1, the eMSCA carried out sensitivity analyses to identify concentrations that would not result in RCRs above 1. Uses with high concentration of benzyl alcohol and frequent uses were in the focus of the evaluation.

Questions regarding consumer exposure (clarification of identified uses, providing ESs for all identified uses, information on consumer products with focus on concentrations, technical functions [solvent, odour agent]) had been addressed in a direct communication with the lead registrant (14 July 2016) that resulted in an update of the CSR (30 September 2016) by one registrant (update of some uses and providing additional ESs). Further questions had been raised with the lead registrant (25 October 2016) regarding concentrations in and composition of paint removers as well as assumptions made in two ESs that could not be clarified sufficiently.

To assess if risks are adequately controlled, the RCRs were recalculated on the basis of the exposure estimations carried out by eMSCA and DNELs derived by the eMSCA.

Conclusions

Human health risks – workers:

Based on data from the repeated dose toxicity studies, a long-term systemic DNEL (inhalation) for workers of 22 mg/m^3 and a long-term systemic DNEL (dermal) for workers of 8 mg/kg bw/day were derived. These values are identical with those calculated in the registration. In addition, a DNEL for induction of skin sensitisation of 66 µg/cm^2 was calculated by the eMSCA. Due to the inherent uncertainties associated with data derived from non-standardised human tests (HRIPT), this DNEL was only used as a means to judge on the remaining/residual likelihood of risks after implementation of all appropriate risk management measures and operational conditions ascertained on the basis of the qualitative risk assessment (IR&CSA Guidance R.8).

Comparing the long-term systemic DNELs with workplace exposure estimates involving both dermal and inhalation pathways revealed combined RCR > 1 indicating that for several ESs (i.e., WCS 7, 8 9, 10, 11 except for WCS 10, PROC 10) risks may not be sufficiently controlled.

Upon request the registrants have submitted an updated CSR on 25 April 2019 according to the requirements specified in the substance evaluation decision (ECHA, 18 April 2018). A subsequent examination of the CSR showed that the registrants have essentially complied with the requirements of the ECHA decision regarding worker exposure.

Human health risks – consumers:

Based on data from the repeated dose toxicity studies (oral and inhalation), a long-term systemic DNEL (inhalation) of 4 mg/m³ and a long-term systemic DNEL (dermal and oral) of 3 mg/kg bw/day were derived for consumers. These values are in the same range as those calculated by the registrants (i.e. 5.4 mg/m³ and 4 mg/kg bw/d, respectively). In addition, in the recent re-evaluation of benzyl alcohol as food additive, EFSA concluded on a very similar threshold level, i.e. an ADI of 4 mg/kg bw/d (EC, 2004; EMA, 2017; EFSA, 2019). Furthermore, infrequent DNELs for systemic effects for consumers were derived by the eMSCA for the inhalation route (8 mg/m³) and a DNEL for induction of skin sensitisation of 33 µg/cm² for consumers was calculated.

With regard to consumers, a comparison of the respective DNELs with the exposure value revealed numerous dermal and inhalation ESs for which RCRs are well above 1.

An RMOA for benzyl alcohol and other solvents is currently under preparation by the eMSCA and was initiated in 2020, focussing on product features in combination with information on the concentrations of the respective substances in consumer products. After the conclusion of the RMOA it should be possible to evaluate whether benzyl alcohol poses a realistic health risk to consumers and whether and which further risk management measures are necessary for the use of consumer products.

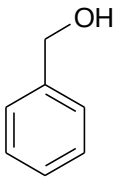
7.3. Identity of the substance

Table 5

SUBSTANCE IDENTITY	
Public name:	Benzyl alcohol
EC number:	202-859-9
CAS number:	100-51-6
Index number in Annex VI of the CLP Regulation:	603-057-00-5
Molecular formula:	C_7H_8O
Molecular weight range:	-
Synonyms:	(Hydroxymethyl)benzene Benzenecarbinol

Type of substance ☒ Mono-constituent ☐ Multi-constituent ☐ UVCB

Structural formula:



7.4. Physico-chemical properties

Table 6

OVERVIEW OF PHYSICOCHEMICAL PROPERTIES		
Property	**Value**	**Remarks**
Physical state at 20 °C and 101.3 kPa	liquid	

Melting/freezing point	-15.4 °C	Lide, 2006 [p. 3-42]
Boiling point	205.3 °C	Lide, 2006 [p. 3-12]
Density	1.045 g/cm^3 @ 20 °C	Lide, 2006 [p. 3-42]
Vapour pressure	7 Pa @ 20 °C, 12 Pa @ 25 °C	Apelblat 1984
Water solubility	40 g/L @ 25 °C	Mookherjee and Wilson, 1992 [p. 2]
Partition coefficient n-octanol/water (Log Kow)	1.05 @ 20 °C	Shake-flask and HPLC method
Granulometry	Data waiving	In accordance with Column 2 of REACH, Annex VII, Section 7.14, the study does not need to be conducted if the substance is marketed or used in a non-solid or granular form.
Stability in organic solvents and identity of relevant degradation products	Data waiving	In accordance with column 2 of REACH Annex IX, the test on stability in organic solvents and identity of relevant degradation products (required in section 7.15) does not need to be conducted as the stability of benzyl alcohol is not considered to be critical.
Dissociation constant	15.4 @ 25 °C	Serjeant and Dempsey, 1979 [p. 272]

7.5. Manufacture and uses

7.5.1. Quantities

Table 7

AGGREGATED TONNAGE (PER YEAR)				
☐ 1 – 10 t	☐ 10 – 100 t	☐ 100 – 1000 t	☐ 1000- 10,000 t	☒ 10,000-50,000 t
☒ 50,000 – 100,000 t	☐ 100,000 – 500,000 t	☐ 500,000 – 1000,000 t	☐ > 1000,000 t	☐ Confidential

7.5.2. Overview of uses

Due to its favourable properties, benzyl alcohol is an important solvent for surface-coating materials and resins. It dissolves cellulose esters and ethers, alkyd resins, acrylic resins, and fats; it is also used as an ingredient in inks for ball-point pens. It is added in small amounts to surface-coating materials to improve their flow and gloss. In the textile industry, it is used as an auxiliary in the dyeing of wool, polyamides, and polyesters. Because it has only a relatively faint odour, it is used as a solvent and diluting agent in the manufacture of perfumes and flavours. However, some publications (including those from the International Fragrance Association - IFRA) and information on the technical function in some CSRs substantiate the use of benzyl alcohol as an odour agent in consumer products (see below). Benzyl alcohol is used in a wide range of applications both in the industrial sector and in professional settings, typically in coatings, cleaning agents, binders, adhesives, paint strippers, fragrances, laboratory agents etc.. One of the major uses for benzyl alcohol is as a curing agent in epoxy coatings, where it becomes chemically bound after reaction (Kirk et al., 1998).

Benzyl alcohol is also a starting material (intermediate) for the preparation of numerous benzyl esters that are used as odorants, flavours, stabilisers for volatile perfumes, and plasticisers. Table 8 lists the uses and the corresponding PROCs for benzyl alcohol according to the ECHA dissemination site (January 2020).

Consumers are exposed to benzyl alcohol through various uses (wide-dispersive use). Information provided on the dissemination website within "Chemical Substance Search" (on 29 November 2016, last updated: 21 January 2020) are listed in Table 8. These uses are in line with the findings from secondary sources: product databases of Germany, Slovenia, Nordic countries, and Switzerland, as well as Mintel GNPD (Global New Products Database)[4] and safety data sheets. Some uses are already covered by various regulations (see section 2). Benzyl alcohol is also a natural ingredient of some food items (EFSA, 2011). Furthermore, consumers can be exposed to benzyl alcohol by pharmaceutical products, which are outside the scope of REACH. The use of benzyl alcohol in cosmetics should be taken into account in the risk management.

Directive 2009/48/EC states that toys shall not contain benzyl alcohol because it is considered to be an allergenic fragrance. The eMSCA considers PC9c (finger paints) to be a toy product according to the directive. Consequently, the registered use "finger paints" is not allowed and will therefore not be considered in the substance evaluation as it is already regulated. A German product database (national monitoring program) indicated that benzyl alcohol is still present in some toy products.

Information from databases presented below does not cover exposure to benzyl alcohol by consumer products entirely, but provides some insight in the range of products on the market available to consumers and possible concentrations of benzyl alcohol.

Information on concentrations (and subcategories) is confidential.

The German Federal Office of Consumer Protection and Food Safety analysed benzyl alcohol in 4213 consumer products as part of the screening programs[5] between 2000 and 2016. Consumer products in these screening programs belong to consumer goods with body contact and personal care products, household chemicals, cosmetics, packing materials and toys (incl. modelling clay). Benzyl alcohol was detected in cosmetic products and articles, air care products, washing and cleaning products, textile processing aids, and modelling clay. Highest concentrations were detected in cosmetic products. The maximum value measured in other typical consumer products is 0.305% (in an all-purpose cleaner), whereas modelling clay contains 0.717% benzyl alcohol at maximum. These concentrations are covered by the ESs in the CSRs. Modelling clay has also to be considered as a toy product. The database does not cover consumer products entirely and products with higher concentrations are considered possible.

GIFAS (Giftinformations- und Archivierungssystem) provides data on 1536 consumer products belonging to product categories 1, 3, 9a, 34, and 35. Maximum concentration of benzyl alcohol are 55% (PC 1), 27.5% (PC 3), 70% (PC 9a; 100% in paint remover), and up to 100% (PC 34/35; 20% in all-purpose cleaner). These concentrations are not covered by the CSRs. They were not considered in the exposure assessment of the eMSCA but will be deliberated in the subsequent RMOA.

An annex to a report by Zarogiannis et al. provides information on the composition of paint strippers and indicates products on the European market with concentrations above the concentrations assumed in the CSRs (Zarogiannis et al., 2007). However, it is not known if these products are in fact available for consumers.

Overall, based on available data on products available for consumer use, it cannot be concluded whether concentrations used for exposure assessment in the CSRs cover the situation on the market.

[4] https://www.mintel.com/global-new-products-database

[5] based on the national monitoring program "Bundesweiter Überwachungsplan – BÜP" and "Monitoring Programme" (an independent legal task in the framework of official control on the basis of §§ 50 – 52 of the German Food and Feed Code).

Even though benzyl alcohol as an odour agent seems to be insignificant with respect to tonnage and number of preparations on the market in comparison to other uses such as 'paints, lacquers and vanishes', 'process regulators', 'construction materials', and 'cleaning/washing agents' (SPIN), it is identified in several scientific publications as a fragrance used in consumer products (e.g. air fresheners, electrical room perfumes, candles, printings [post cards, Christmas cards, calendar sheets], writing paper, erasers, internals of speed markers, and other products) in which benzyl alcohol is detected frequently (Bartsch et al., 2016; BEUC, 2005; Ezendam et al., 2009; Glensvig and Ports, 2006; ter Burg et al., 2014).

New consumer product placements on the European market with benzyl alcohol as an ingredient can be observed for products on which benzyl alcohol has to be labelled (cosmetic products, household washing and cleaning products, air care). Throughout the last 10 years such new product placements have increased continuously (Mintel GNPD). Within the product categories mentioned, cosmetic products dominate with 96%.

Benzyl alcohol is used for several technical functions. However, in the scientific literature it is mostly regarded as a fragrance in consumer products (e.g. air fresheners, electrical room perfumes, candles, cleaning products, and other products) (Ezendam et al., 2009; Nørgaard Andersen et al., 2015; Wijnhoven et al., 2008). The technical function as odour agent is considered by some, but not all registrants.

In paint strippers, benzyl alcohol is one of several substitutes for dichloromethane (Zarogiannis et al., 2007).

Table 8

USES OF BENZYL ALCOHOL	
	Use(s)
Manufacture	Manufacture of benzyl alcohol (PROC 1, 2, 3, 4, 5, 6, 8a, 8b, 9)
Formulation	Formulation (PROC 1, 2, 3, 4, 5, 8a, 8b, 9, 19) Formulation (PROC 1, 2, 3, 4, 5, 8a, 8b, 9, 13, 15, 19) Formulation in materials – industrial (PROC 1, 2, 3, 4, 5, 8a, 8b, 9, 13) Formulation of preparations – industrial (PROC 1, 2, 3, 4, 5, 8a, 8b, 9, 13) Formulation of preparations – professional (PROC 1, 2, 3, 4, 5, 8a, 8b, 9, 13, 19)
Uses at industrial sites	Paper/board dye, finishing/impregnation (PROC 5, 6, 7, 8b, 10, 13, 14) Building & construction/distributors (PROC 5, 7, 8a, 8b, 9, 10, 13, 14, 15, 19) Building & construction/distributors (PROC 5, 8a, 8b, 9, 10, 13, 14) Polymer preparations - industrial use (PROC 13) Non-metal surface treatment products - industrial use (PROC 5, 8a, 8b, 9, 15) Photo-chemicals (PROC 8a, 8b, 13) Photo-chemicals (PROC 8a, 8b) Coatings, paints, fillers, putties thinners - industrial use (PROC 5, 7, 8a, 8b, 9, 10, 13) Metal surface treatment products (PROC 5, 8a, 8b, 9, 15, 23, 24, 25) Washing & cleaning products - industrial use (PROC 7, 8a, 8b, 9, 10, 13) Intermediates (PROC 1, 2, 3) Intermediates (PROC 1, 2, 3, 8b, 9) Adhesives & sealants - industrial use (PROC 5, 7, 8a, 8b, 9, 10, 12, 13, 14) Cosmetics & personal care products (PROC 13) Adhesives & sealants, coatings and paints, thinners, paint removers, fillers, putties , plasters, modelling clay, finger paints, metal surface and non-metal surface treatment products, ink and toners (PROC 5, 7, 8a, 8b, 9, 10, 12, 13, 14, 23, 24, 25) Adhesives & sealants (PROC 5, 7, 8a, 8b, 9, 10, 12, 13, 14) Ink & toners (PROC 7, 8a, 8b, 9, 10, 13) Textile dyes, finishing/impregnation products (PROC 5, 6, 7, 8a, 8b, 9, 10, 13, 14) Laboratory reagent (PROC 15) Lubricants, greases, release products (PROC 18) Building and construction/distributors (PROC 5, 7, 8a, 8b, 14, 15, 19

Uses by professional workers	Building & construction/distributors (PROC 5, 8a, 8b, 9, 10, 11, 13, 19) Non-metal surface treatment products (PROC 8a, 8b, 9, 10, 11, 13, 19) Metal surface treatment products (PROC 8a, 8b, 9, 10, 11, 13, 19, 23, 24, 25) Photo-chemicals (PROC 8a, 8b) Coatings, paints, fillers, putties thinners (PROC 5, 8a, 8b, 9, 10, 11, 13, 19) Polymer preparations (PROC 8a, 8b, 9, 10, 11) Ink & toners (PROC 5, 8a, 8b, 10, 11, 13, 19) Adhesives & sealants (PROC 5, 8a, 8b, 9, 10, 11, 13, 19) Paper/board, dye finishing/impregnation (PROC 5, 6, 8a, 8b, 11, 13, 14, 19, 21) Cosmetics & personal care products (PROC 13) Laboratory reagent (PROC 15) Laboratory agent (PROC 8a, 8b, 15) Polishes & wax blends (PROC 8b, 10, 11) Professional Use - indoors - all uses (PROC 5, 6, 8a, 8b, 9, 10, 11, 13, 14, 19, 21, 23, 24, 25) Professional Use - outdoor - all uses (PROC 5, 6, 8a, 8b, 9, 10, 11, 13, 14, 19, 21, 23, 24, 25) Washing & cleaning products (PROC 8a, 8b, 9, 10, 11, 13, 19)
Consumer Uses	PC 1: Adhesives, sealants PC 3: Air care products PC 9a: Coatings and paints, thinners, paint removes PC 9b: Fillers, putties, plasters, modelling clay PC 9c: Finger paints PC 12: Fertilisers PC 14: Metal surface treatment products PC 18: Ink and toners PC 19: Intermediate (e.g. Use in cosmetics and personal care products) PC 20: Products such as pH-regulators, flocculants, precipitants, neutralisation agents PC 21: Laboratory chemicals PC 23: Leather tanning, dye, finishing, impregnation and care products PC 24: Lubricants, greases, release products PC 28: Perfumes, fragrances PC 31: Polishes and wax blends PC 32: Polymer preparations and compounds PC 34: Textile dyes, finishing and impregnating products; including bleaches and other processing aids PC 35: Washing and cleaning products (including solvent based products) PC 39: Cosmetics, personal care products PC 0: Other: Building & construction PC 0: Other: Tobacco products PC 0: Other: Tobacco Products and Liquids for Electronic Cigarettes PC 0: Other: Electronic cigarette PC 0: Other: Buildings & construction; distributors PC 0: Other: Building & construction
Article service life	AC 8: Paper articles (consumers) AC 13: Plastic articles AC 5: Fabrics, textiles and apparel (workers) AC 6: Leather articles (workers)

7.6. Classification and Labelling

7.6.1. Harmonised Classification (Annex VI of CLP)

Table 9

HARMONISED CLASSIFICATION ACCORDING TO ANNEX VI OF CLP REGULATION (REGULATION (EC) 1272/2008)			
Index No	**EC No**	**Classification**	**Notes**

	International Chemical Identification		CAS No	Hazard Class and Category Code(s)	Hazard statement code(s)	Spec. Conc. Limits, M-factors	
603-057-00-5	benzyl alcohol	202-859-9	100-51-6	Acute Tox. 4 * Acute Tox. 4 *	H302 H332		

Benzyl alcohol currently has a harmonised classification (CLH) for acute toxicity only which was set under 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 a category is indicated by an asterisk. A proposal for harmonised classification and labelling of benzyl alcohol (according to CLP art. 37(2)) was prepared by the eMSCA with regard to the endpoints acute toxicity, eye irritation and skin sensitisation. The proposal was submitted to ECHA in October 2019. For details see section 4.1.1.

7.6.2. Self-classification

- Proposed classification by the lead registrant (April 2019):

  Acute Tox. 4 H302 Harmful if swallowed.

  Acute Tox. 4 H332 Harmful if inhaled.

- Additional classification in the registrations:

  Eye Irrit. 2 H319 Causes serious eye irritation.

- The following hazard classes are in addition notified among the aggregated self-classifications in the C&L Inventory (December 2019):

  Acute Tox. 4 H312 Harmful in contact with skin.

  Eye Dam. 1 H318 Causes serious eye damage.

  Skin Irrit. 2 H315 Causes skin irritation.

  Skin Sens. 1 H317 May cause an allergic skin reaction.

  Not Classified

7.7. Environmental fate properties

Not assessed in this substance evaluation.

7.8. Environmental hazard assessment

Not assessed in this substance evaluation.

7.9. Human Health hazard assessment

7.9.1. Toxicokinetics

Benzyl alcohol is rapidly absorbed from the gastro-intestinal (GI) tract after oral exposure in humans and animals (Bronaugh et al., 1990; Chidgey and Caldwell, 1986; EMEA, 1997; JECFA, 1997; Miller et al., 2006; OECD, 2001). In humans, 75-85% of substance is excreted within 6 h after oral administration (Bronaugh et al., 1990; Chidgey and Caldwell, 1986; EMEA, 1997; JECFA, 1997; Miller et al., 2006; OECD, 2001). Dermal absorption ranged from 56 to 80% in rhesus monkeys under occluded conditions (Bronaugh et al.,

1990; Chidgey and Caldwell, 1986; EMEA, 1997; JECFA, 1997; Miller et al., 2006; OECD, 2001). Evaporative loss contributes to a lower skin penetration (approx. 30%) under unoccluded conditions *in vitro* and *in vivo* (Bronaugh et al., 1990; Chidgey and Caldwell, 1986; EMEA, 1997; JECFA, 1997; Miller et al., 2006; OECD, 2001). Benzyl alcohol is an intermediate in the metabolism of benzyl acetate and is further metabolised to benzaldehyde and, ultimately, benzoic acid (Bronaugh et al., 1990; Chidgey and Caldwell, 1986; EMEA, 1997; JECFA, 1997; Miller et al., 2006; OECD, 2001). It is rapidly excreted as hippuric acid mainly via urine (Bronaugh et al., 1990; Chidgey and Caldwell, 1986; EMEA, 1997; JECFA, 1997; Miller et al., 2006; OECD, 2001). 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).

7.9.2. Acute toxicity and Corrosion/Irritation

The registrants concluded that benzyl alcohol is acutely toxic (Cat. 4) after oral administration (Acute Tox. 4, H302: harmful if swallowed) and, based on the available information, the eMSCA agrees with this conclusion.

There is limited data on acute toxicity after dermal administration with very little details regarding the study design(s). However, the LD_{50} values reported are all above 2 000 mg/kg bw, indicating that benzyl alcohol does not warrant classification according to Regulation (EC) 1272/2008 (EC, 2015).

The registrants concluded that based on the available data and according to the criteria of Regulation (EC) 1272/2008, Annex I (EC, 2015), the aerosol of benzyl alcohol does not need to be classified for acute inhalation toxicity. The eMSCA agrees with this conclusion. Nevertheless, the registrants decided to apply the legal classification ('Acute inhalation toxicity - Category 4 (dusts and mists): 1.0 < ATE ≤ 5.0 mg/L').

Available data with benzyl alcohol vapours (Carpenter et al., 1949; Clayton, 1982; Smyth et al., 1951) indicate that the substance as vapour might require classification. The accuracy of the exposure values reported in the respective studies, however, is uncertain as concentrations were not checked analytically. Moreover, the German Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area ("MAK-Commission", MAK) calculated a saturation concentration of 0.57 mg/L for benzyl alcohol at 25 °C on the basis of its vapour pressure of 0.12 hPa at this temperature (Hartwig, 2017). Based on this data it is assumed that there is an equilibrium of benzyl alcohol aerosol and vapour above a concentration of 0.5 – 0.6 mg/L. Therefore, a separate classification of benzyl alcohol vapours is considered unnecessary. Nevertheless, the eMSCA included the respective data set in the submitted CLH proposal for transparent documentation.

Data regarding skin irritation/corrosion is controversial, as acute dermal irritation tests according to OECD TG 404 showed that benzyl alcohol was not irritating to the skin, whereas in older literature studies (Klecak et al., 1977 ; Smyth et al., 1951) benzyl alcohol was evaluated as slightly irritating to the skin. In weight of evidence, however, available data on skin irritation indicates that benzyl alcohol does not warrant classification with respect to this endpoint according to the criteria of Regulation (EC) 1272/2008 (EC, 2015).

Irritation to the eyes was observed in two studies with rabbits carried out in accordance with OECD TG 405. Results from these studies support classification of benzyl alcohol as Eye Irrit. 2 (H319) according to the criteria of Regulation (EC) 1272/2008 (EC, 2015). The registrants proposed a corresponding self-classification of the substance in their dossier. The eMSCA included this endpoint in the CLH proposal submitted to ECHA.

7.9.3. Sensitisation

For benzyl alcohol, numerous studies regarding its skin sensitising potential are available.

A guideline-compliant local lymph node assay (LLNA) was negative up to 50% of benzyl alcohol. No higher doses than this were included in the test. Therefore, possible sensitisation at doses of >12 500 µg/cm^2 in this test cannot be ruled out.

The available studies in guinea pigs investigating the skin sensitisation potential of benzyl alcohol show equivocal results.

A large number of human studies describe a sensitising potential of benzyl alcohol. Results of human repeated insult patch tests (HRIPT) with doses of 3 543 µg/cm^2 to 23 622 µg/cm^2 (3 to 20% for induction and challenge) point towards a weak to moderate skin sensitising potential of benzyl alcohol. Increasing doses of benzyl alcohol from 8 858 µg/cm^2 (7.5%) to 23 622 µg/cm^2 (20%) led to increasing numbers of sensitised subjects (Scognamiglio et al., 2012). The study authors concluded that the results were indicative of skin sensitisation. Since the single doses were tested in separate studies, reproducibility of the skin sensitising effect can be inferred.

The HRIPT results are supported by the outcomes of numerous human diagnostic patch tests. In these studies sensitisation rates of up to 0.3% in large collectives of consecutive patients in clinical departments of dermatology were identified (e.g. Chow et al. (2013); Heisterberg et al. (2011); Schnuch et al. (2015); Uter et al. (2010)). According to CLP, incidence rates of <0.2% in the general population and <1% in consecutive, unselected dermatitis patients are considered to reflect a low to moderate frequency of skin sensitisation.

In addition to the patch test studies, a number of case reports of patients reacting to benzyl alcohol can be found, which report positive reactions to benzyl alcohol to a varying degree (e.g. Hayakawa et al. (1988); Itoh et al. (1988); Itoh et al. (1986); Johnson et al. (2017); van Oosten et al. (2009)).

Furthermore, a number of *in chemico* and *in vitro* studies were performed with benzyl alcohol addressing several different key events of the OECD adverse outcome pathway (AOP) for skin sensitisation by covalent binding to skin proteins (Kleinstreuer et al., 2018; Urbisch et al., 2015). Results of these studies were contradictory, but all in all point towards a low sensitisation potency of benzyl alcohol. Currently, the CLP regulation does not 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 were reviewed and used as supportive evidence only.

According to REACH Guidance R.7a, all data sources have to be considered in a weight-of-evidence approach when assessing the skin sensitising potency of a chemical. When reliable and relevant human data are available, they can be useful for hazard identification and even preferable over animal data. Thus, although animal data of a recently conducted LLNA indicated no sensitising potential of benzyl alcohol, other available animal studies (even if documentation is sometimes limited), and in particular data regarding the sensitising potential of benzyl alcohol in humans cannot be overruled by that newer LLNA test result.

Overall, benzyl alcohol is considered a weak to moderate skin sensitiser and the available data justify classification of benzyl alcohol as skin sensitiser Cat. 1B based on positive reactions above 500 µg/cm^2 in HRIPT tests and a low, but substantial incidence of up to 0.3 % in large study populations with consecutive patients in clinical departments of dermatology. The eMSCA submitted a respective proposal for harmonised classification to ECHA in October 2019.

This conclusion is in line with the findings of the Scientific Committee on Consumer Safety which recognised benzyl alcohol as "established contact allergen in humans" (SCCS, 2012). Furthermore, the conclusion that benzyl alcohol is a weak sensitiser is also consistent with the outcomes reported in the recent Scientific Opinion by EFSA, in which the risks

associated with the use of benzyl alcohol as a food additive were re-evaluated (EFSA, 2019).

7.9.4. Repeated dose toxicity

Repeated dose toxicity studies for benzyl alcohol are available for the oral and inhalation route of exposure. No studies with repeated dermal administration were identified in the registration dossiers or the published literature. In subacute and subchronic oral studies signs of staggering, laboured breathing, and lethargy as well as decreased body weight gain were observed in rats and mice at ≤ 1000 mg/kg bw/day (NTP, 1989). These effects, however, were observed at dose levels outside the criteria for classification as STOT RE (after repeated oral administration) as specified in Regulation (EC) 1272/2008 (EC, 2015). Moreover, under the scope of this substance evaluation, the eMSCA considers the oral route less relevant and risk assessment is therefore focused on exposure via inhalation. In a subacute inhalation toxicity study, no adverse effects were observed in rats up to the highest tested dose of 1072 mg/m³ (Unpublished study report, 2010), indicating that benzyl alcohol does not warrant classification as STOT RE (after repeated inhalation) according to the criteria of Regulation (EC) 1272/2008 (EC, 2015). It is noted that in male rats exposed to the highest test concentration, minimal mononuclear cell infiltration was observed in lungs. This effect was only observed in one sex and was further not accompanied by respective histopathological alterations. These finding were considered not substance-related by the study authors. Nevertheless, it should be noted that the highest dose tested was not the maximum tolerated dose and that no histopathological exanimations were performed in the lower-dose treatment groups.

The most relevant dose descriptors were taken forward as points of departure (PODs) for DNEL derivation and are listed in Table 10 in section 7.9.9.2.

7.9.5. Mutagenicity

The registrants concluded that the substance is not genotoxic, and based on the available information on genotoxicity and carcinogenicity, the eMSCA agrees with this conclusion.

7.9.6. Carcinogenicity

The registrants concluded the substance is not carcinogenic, and based on the available information, the eMSCA agrees with this conclusion.

7.9.7. Toxicity to reproduction (effects on fertility and developmental toxicity)

7.9.7.1. **Fertility**

In the registration dossier, no study record of an extended one-generation reproductive toxicity study (EOGRTS) or a two-generation reproductive toxicity study on the substance is available which would meet the information requirement of Annex X, Section 8.7.3. The registrants sought to adapt the information requirement using data collected on benzoic acid, benzaldehyde and benzyl acetate.

For the endpoint reproductive toxicity, a non-GLP, non-guideline four-generation study with benzoic acid in rats was submitted as key information (Kieckebusch and Lang, 1960).

The eMSCA notes that the available information on reproductive toxicity (fertility) for benzyl alcohol cannot be regarded as comparable to a nowadays conducted EOGRTS. However, updated and consolidated information on the pre-GLP, pre-guideline 4-generation study from 1960 with the read-across substance benzoic acid (category approach accepted by ECHA and the eMSCA) was made available by the registrants during

the evaluation process. Taking into account this data and other information on the test substance (e.g. from repeated dose tests) and the substances belonging to the read-across category, the eMSCA concludes that the weight of evidence proposed by the registrants can be accepted.

Overall, based on the available database the eMSCA agrees with the registrants' conclusion that there is no concern regarding reproductive toxicity (fertility) of benzyl alcohol and that classification of benzyl alcohol for reproductive toxicity (fertility) is currently not warranted.

7.9.7.2. **Developmental toxicity**

Based on the results of the available studies, the eMSCA concludes that there is no concern regarding developmental toxicity of benzyl alcohol. Hence, the eMSCA considers classification of benzyl alcohol for reproductive toxicity (developmental toxicity) not warranted.

7.9.8. Hazard assessment of physico-chemical properties

Not evaluated in the present substance evaluation.

7.9.9. Selection of the critical DNEL(s)/DMEL(s) and/or qualitative/semi-quantitative descriptors for critical health effects

The risk characterisation is based on adverse effects, which were observed after repeated oral exposure as well as after dermal exposure with regard to skin sensitisation. For inhalation, no adverse effects were evident after repeated exposure in a subacute study up to a concentration of 1072 mg/m^3 air. It should be noted that the highest dose tested was not the maximum tolerated dose.

Table 10

OVERVIEW OF TYPICAL DOSE DESCRIPTORS FOR EVALUATED ENDPOINTS				
Endpoint	**Route**	**Dose descriptor or qualitative effect characterisation; test type**	**Relevant study**	**Justification/ Remarks**
Skin sensitisation	Dermal	Weakly sensitising NOAEL (induction) in a human repeated insult patch test: 5 906 µg/cm^2 based on oedematous skin reactions at higher tested doses upon challenge	(Scognamiglio et al., 2012)	Information available as summaries of unpublished studies No information on the composition of the study populations
Repeated dose toxicity (subchronic, 13-wk; rat)	Oral (systemic effects)	NOAEL: 400 mg/kg bw per day based on staggering, laboured breathing and lethargy, slightly reduced final mean body weight, necrosis of dentate gyrus (male and female), skeletal muscle necrosis, thymic congestion, haemor-rhage, atrophy, nephrosis (males) at the next higher dose	(NTP, 1989)	

Repeated dose toxicity (chronic, 2-yr; rat)	Oral (systemic effects)	NOAEL: 400 mg/kg bw per day	(NTP, 1989)	Only two doses tested. The authors concluded that no substance-related effects were observed up to the highest dose.
Repeated dose toxicity (sub-acute, 4-wk, rat)	Inhalation	NOAEC: 1 072 mg/m^3 (subacute 4-wk, highest tested dose) No compound-related adverse effect observed	(Unpublished study report, 2010)	Highest dose was not the maximum tolerated dose

7.9.9.1. **Workers**

Section R.8.4 of the REACH Guidance on information requirements and chemical safety assessment, Chapter R.8 (ECHA, 2012) specifies that a DNEL for the leading health effect needs to be derived for every relevant human population and every relevant route, duration and frequency of exposure, if feasible. For workers, the most relevant ESs are the long-term inhalation exposure and long-term dermal exposure. Based on the studies present in the dossier, the acute inhalation toxicity of benzyl alcohol is relatively low as evident from short-term tests with rats, where only transient effects related to sensory irritation were observed at the highest dose of 4 178 mg/m^3 (4 hour-exposure to aerosol) (Unpublished study report, 1990). Acute oral application of benzyl alcohol produced unspecific clinical signs such as sedation, side- and prone-position, bloody eyes and reduction of general condition with an LD_{50} of 1 610 mg/kg (Unpublished study report, 1978). Since benzyl alcohol has a harmonised classification for both acute inhalation and oral toxicity (Acute Tox. 4*), acute DNEL values are provided for the assessment of peak inhalation and dermal exposures at the workplace.

Quantitative dose-response data on inhalation toxicity of benzyl alcohol are available from a sub-acute inhalation toxicity study with male and female rats where no adverse effects were reported up to the highest test concentration (details in section 7.9.4; Unpublished study report (2010)). Thus, a no-observed adverse effect concentration (NOAEC) of 1 072 mg/m³ can be set as the point of departure (POD) for derivation of a long-term systemic DNEL for the assessment of inhalation exposures to benzyl alcohol at the workplace.

With respect to long-term systemic toxicity after oral application, sub-chronic and chronic studies in rats and mice are available from the US National Toxicology Programme (NTP, 1989). Considering the results from both the 2-year carcinogenicity and the 13-weeks studies, an overall NOAEL of 400 mg/kg bw/day for systemic toxicity in rats can be established. At the lowest observed adverse effect level (LOAEL) of 800 mg/kg bw/day (from the 13-week study) signs of neurotoxicity (staggering, laboured breathing and lethargy), reduced body weight, and histopathological effects in the brain, thymus, and skeletal muscle were reported. In mice, the respective carcinogenicity and 13-weeks studies revealed an overall no-observed adverse effect level (NOAEL) of 200 mg/kg bw/day. At the LOAEL of 400 mg/kg bw/day (13-week study), only a slight decrease in body weight gain was reported (ca. 5%), and at 800 mg/kg bw/day staggering after dosing during the first and second weeks of the studies was observed. In both mice studies, no compound-related histopathological effects were reported. Therefore, the NOAEL of 400 mg/kg bw/day obtained from the rat studies was considered as another relevant starting point for long-term systemic DNEL calculation for the oral/dermal pathways of exposure.

Benzyl alcohol is considered a moderate to weak skin sensitiser (Chapter 7.9.3). Based on the data from several HRIPT of benzyl alcohol in ethanol containing vehicle reviewed in Scognamiglio et al. (2012), a NOAEL of 5 906 µg/cm^2 was identified. These data allow for

calculation of a DNEL for skin sensitisation as a measure for comparison of dermal exposure at the workplace with the skin sensitising potential of benzyl alcohol. It is noted that this DNEL is based on data from non-standardised human tests and therefore associated with considerable uncertainties. In line with the REACH guidance, this DNEL was not further used for quantitative risk characterisation but only as a tool to judge on the remaining risks after implementation of all appropriate risk management measures.

The selected NOAEC and NOAEL values need to be adjusted for relevant occupational ESs. The standard assessment factors (AF) applied to adjust for the respiratory conditions during the test and for duration of exposure are outlined in Chapter R.8 of the REACH Guidance (ECHA, 2012). For the inhalation DNEL, the default AF of 6 for differences in duration of exposure (sub-acute to chronic) was replaced with a factor of 2 since both the sub-chronic and chronic studies in rats and mice showed similar dose-response and effect levels indicating that severity of systemic toxicity does not increase with exposure duration. In addition, the selected POD can be considered rather conservative due to the fact that the NOAEC from the inhalation study is the highest dose tested, i.e. an effect level (LOAEC) could not be established. Alternative inhalation DNEL calculations using a POD from the oral toxicity studies or an established acceptable daily intake (ADI) limit value as the starting point result in similar DNELs, indicating that the use of an AF of 2 for duration of exposure is justified (discussed above). The outlined approach to DNEL derivation, including POD selection and AFs application, has been used by the registrants to calculate DNEL values that are identical with those reported here.

Table 11

DETAILED OVERVIEW OF THE DERIVATION OF THE DNEL (WORKER, INHALATION, LONG-TERM, SYSTEMIC) FOR BENZYL ALCOHOL (BASED ON 28-DAY SUB-ACUTE INHALATION TOXICITY STUDY; UNPUBLISHED STUDY REPORT (2010)).		
Descriptor	**Value**	**Remarks**
Relevant dose descriptor	NOAEC: 1072 mg/m^3	Based on a 28-day inhalation study in rats with benzyl alcohol
Modification of the relevant dose descriptor	6 h/d → 8 h/d 6.7 m^3 → 10 m^3	Inhalation study in rats vs. workers exposure Respiratory volume (8 h) normal (6.7 m^3) to light activity (10 m^3)
Corrected dose descriptor	NOAEC(corr.) = 1072 mg/m^3 x 6/8 x 6.7/10 = 539 mg/m^3	
Assessment factor (AF)	**AF Value**	**Remarks**
Interspecies (allometric scaling)	1	As DNEL derivation is based on inhalation data, no AF for allometric scaling is applied here, according to REACH Guidance R.8.
Interspecies (remaining differences)	2.5	The default factor for remaining differences (2.5) is applied according to the REACH guidance R.8.
Intraspecies	5	Workers
Exposure duration	2	Default is 6, however toxicity does not seem to depend on exposure duration.
Dose-response	1	Selection of conservative POD, no LOAEC established.
Quality of whole database	1	
DNEL	539 mg/m^3 / (1 x 2.5 x 5 x 2 x 1 x 1) = **22 mg/m^3**	

The value of **22 mg/m³** is supported by the DNEL of 28 mg/m³ that can be calculated alternatively using a NOAEL of 400 mg/kg bw/day as a starting point obtained from the chronic toxicity studies in rats via the oral route (Table 12). Here, only standard assessment factors are applied as specified in the REACH Guidance R.8 (ECHA, 2012).

Table 12

DETAILED OVERVIEW OF THE DERIVATION OF AN ALTERNATIVE DNEL (WORKER, INHALATION, LONG-TERM, SYSTEMIC) FOR BENZYL ALCOHOL (BASED ON A 104 WEEK CHRONIC TOXICITY STUDY BY NTP TR 343, 1989 (NTP, 1989)		
Descriptor	**Value**	**Remarks**
Relevant dose descriptor	NOAEL: 400 mg/kg bw/day	Based on 104 weeks oral chronic study in rats
Modification of the relevant dose descriptor	0.38 m³/kg bw 0.5 6.7 m³ → 10 m³	Standard respiratory volume in rats for 8 h Oral absorption rat vs. inhalation absorption human Respiratory volume (8h) normal (6.7 m³) to light activity (10 m³)
Corrected dose descriptor	NOAEC(corr.) = 400 mg/kg bw/day / 0.38 m³/kg x 6.7/10 x 0.5 = 353 mg/m³	
Assessment factor (AF)	**AF Value**	**Remarks**
Interspecies (allometric scaling)	1	Allometric scaling already included in route-to-route extrapolation according to REACH Guidance R.8 (Appendix R.8-2).
Interspecies (remaining differences)	2.5	The default factor for remaining differences (2.5) is applied according to the REACH guidance R.8.
Intraspecies	5	Workers
Exposure duration	1	Chronic study
Dose-response	1	NOAEL is the highest dose tested; no LOAEL (systemic) recorded
Quality of whole database	1	
DNEL	353 mg/m³ / (1 x 2.5 x 5 x 1 x 1 x 1) = 28 mg/m³	

Furthermore, the inhalation DNEL of **22 mg/m³** is consistent with (and more conservative than) the current ADI value of (up to) 5 mg/kg bw/day developed by EFSA for exposure of general population to the chemical group of benzoates as residues in treated foods. Using the ADI as a starting point, a DNEL of 35 mg/m³ can be derived for a worker with standardised average body weight of 70 kg and a respiratory volume of 10 m³ per shift, default oral/inhalation absorption ratio of 0.5, and a factor of 10/5 to account for differences in interspecies variability in general population vs. workers.

DNEL: 5 mg/kg bw/day x (70 kg/10 m³ per shift) x 0.5 x 10/5 = 35 mg/m³ (inhalation, long-term, systemic)

According to Guidance R.8, Appendix R. 8-8 (ECHA, 2012), an acute DNEL can be set by multiplying the long-term inhalation DNEL with a factor of 1-5. Since the acute inhalation studies revealed only effects related to sensory irritation, a factor of 5 was chosen here.

DNEL: 22 x 5 = 110 mg/m³ (inhalation, acute, systemic)

Recently, the MAK established an occupational exposure limit (OEL; "MAK value") of 22 mg/m³ (5 ml/m³). The OEL calculation was based on the same 4-week inhalation study in rats described earlier (see 7.9.4; (Unpublished study report, 2010)), where microscopic lesions in the airways at 1072 mg/m³ were considered adverse (LOAEC) and were used as a POD. The NAEC was estimated to be 300 mg/m³, and a MAK value of 5 ml/m³ (22 mg/m³) has been derived using the Preferred Value Approach. As local effects are considered

critical, benzyl alcohol was classified in Peak Limitation Category I with an excursion factor of 2 (Hartwig, 2017).

The long-term systemic DNEL for dermal exposure can be calculated using a starting point of 400 mg/kg bw/day (NOAEL) obtained from the chronic and sub-chronic toxicity studies with rats exposed to benzyl alcohol via the oral route (NTP, 1989). Here, standard assessment factors are applied as specified in the REACH Guidance R.8 (ECHA, 2012), and equal rates of oral and dermal absorption in rats and humans are assumed (Table 13). This approach is consistent with the Guidance Document R.8. (ECHA, 2012) specifying that in general dermal absorption is not expected to be higher than the oral absorption and, thus, no specific default factor is needed when performing oral-to-dermal extrapolation.

Table 13

DETAILED OVERVIEW OF THE DERIVATION OF THE DNEL (WORKER, DERMAL, LONG-TERM, SYSTEMIC) FOR BENZYL ALCOHOL (BASED ON A 104-WEEK CHRONIC TOXICITY STUDY BY NTP TR 343, 1989 (NTP, 1989))		
Descriptor	**Value**	**Remarks**
Relevant dose descriptor	NOAEL: 400 mg/kg bw/day	Based on 104-week oral chronic study in rats
Modification of the relevant dose descriptor	1	Oral absorption rat vs. dermal absorption human
Corrected dose descriptor	NOAEL(dermal) = 400 mg/kg bw/day	
Assessment factor (AF)	**AF Value**	**Remarks**
Interspecies (allometric scaling)	4	A default AF of 4 is applied for allometric scaling (rat to human) according to REACH Guidance R.8.
Interspecies (remaining differences)	2.5	The default factor for remaining differences (2.5) is applied according to the REACH guidance R.8.
Intraspecies	5	Workers
Exposure duration	1	Chronic study
Dose-response	1	NOAEL is the highest dose tested; no LOAEL (systemic) recorded
Quality of whole database	1	
DNEL	400 mg/kg/day / (4 x 2.5 x 5 x 1 x 1 x 1) = **8 mg/kg bw/day**	

As demonstrated for inhalation exposures, an acute systemic DNEL of 40 mg/kg bw/day for systemic hazards via the dermal route of exposure can be calculated by multiplying the long-term dermal value with a factor of 5.

DNEL: 8 x 5 = 40 mg/kg bw/day (dermal, acute, systemic)

Using a NOAEL of 5 906 µg/cm^2 identified in several human repeat insult patch tests, a dermal DNEL value of 66 µg/cm^2 can be calculated for induction of skin sensitisation (Table 14Table 14). This DNEL was not used for quantitative risk characterisation, but only as a means to judge on the remaining likelihood of risks after implementation of appropriate RMMs and OCs ascertained on the basis of the qualitative risk assessment (IR&CSA Guidance R.8: Characterisation of dose [concentration]-response for human health, Appendix R 8-10).

Table 14

DETAILED OVERVIEW OF THE DERIVATION OF THE DNEL (WORKER, DERMAL, SKIN SENSITISATION) FOR BENZYL ALCOHOL		
Descriptor	**Value**	**Remarks**
Relevant dose descriptor	NOAEL: 5906 µg/cm^2	Based on data from human repeat insult patch tests (HRIPT)
Modification of the relevant dose descriptor	1	occlusive laboratory patch test at high doses versus workplace exposure
Corrected dose descriptor	NOAEL(dermal) = 5906 µg/cm^2	
Assessment factor (AF)	**AF Value**	**Remarks**
Interspecies scaling	1	Human data used.
Intraspecies	5	Default for workers
Exposure duration	1	Short-term exposure can induce dermal sensitisation
Dose-response	1	NOAEL used as a starting point
Quality of whole database	2	Summarised dose-response data originating from several studies with incomplete description
Skin sens. specific AF: Vehicle or matrix effect	3	Simultaneous exposure to penetration enhancers or irritants cannot be excluded. Thus, an AF of 3 is considered appropriate (1-10 according to REACH-Guidance R.8)
Exposure duration and different exposure conditions (*skin sens. specific*)	3	Repeated dermal exposure for long periods can be expected for some of the ESs, thus an AF of 3 is considered appropriate (1-10 according to REACH-Guidance R.8)
DNEL	5906 µg/cm^2 / (1 x 5 x 1 x 1 x 2 x 3 x 3) = **66 µg/cm^2**	

Table 15

OVERVIEW OF THE CALCULATED DNELS FOR WORKERS - CRITICAL DNELS/DMELS					
Endpoint of concern	**Type of effect**	**Critical study(ies)**	**Corrected dose descriptor(s) (e.g. NOAEL, NOAEC)**	**DNEL/ DMEL**	**Justification /Remarks**
Repeated dose toxicity, Inhalation	Systemic toxicity	(Unpublished study report, 2010)	NOAEC = 539 mg/m^3	22 mg/m^3	
Acute toxicity, Inhalation	Systemic toxicity	(Unpublished study report, 2010)		110 mg/m^3	long-term DNEL x 5
Repeated dose toxicity, Dermal	Systemic toxicity	(NTP, 1989)	NOAEL = 400 mg/kg bw/day	8 mg/kg bw/day	
Acute toxicity, Dermal	Systemic toxicity	(NTP, 1989)		40 mg/kg bw/day	long-term DNEL x 5
Skin sensitisation, induction	Dermal toxicity	(Scognamiglio et al., 2012)	NOAEL = 5906 µg/cm^2	66 µg/cm^2	

7.9.9.2. **Consumers**

For consumers, the most relevant exposure routes are via inhalation and dermal exposure.

As with the dose descriptors used for DNEL derivation for workers, quantitative dose-response data on the inhalation toxicity of benzyl alcohol from a subacute inhalation toxicity study with male and female rats was used as the POD for consumer DNEL derivation. No adverse effects were reported up to the highest test concentration of 1 072 mg/m³ (NOAEC) (Unpublished study report, 2010). For comparison, data from a chronic oral study in rats were used for the derivation of the long-term inhalation DNEL for local and systemic effects. In this study, a NOAEL of 400 mg/kg bw/d was reported (NTP, 1989).

With respect to derivation of long-term systemic DNELs after (oral and) dermal application, results of oral sub-chronic and chronic studies in rats were used as PODs (NTP, 1989). Overall, a NOAEL of 400 mg/kg bw/day for systemic toxicity in rats after both, subchronic and chronic oral administration was determined and used subsequently. This NOAEL was also used as POD by EFSA when calculating the ADI in its recent re-evaluation of benzyl alcohol as food additive (EC, 2004; EMA, 2017; EFSA, 2019).

As there are inhalation exposure scenarios with exposure frequencies > 15/year and < 15/year, long-term and infrequent DNELs were calculated according to REACH Guidance R.15 (Table R.15-1).

A NOAEL for induction of skin sensitisation in ethanol-containing vehicles of 5 906 µg/cm^2 was identified in human studies. This value was used as POD for derivation of the dermal DNEL for sensitising effects, although it is noted that this value is associated with uncertainties due to poor documentation of study methods and results. For the derivation of the induction-specific DNEL for skin sensitisation, skin sensitisation-specific AFs were used according to REACH Guidance R.8 (Appendix R.8-10).

Table 16

LONG-TERM DNEL, INHALATION, LOCAL AND SYSTEMIC EFFECTS (24 H/D) BASED ON A SUBACUTE INHALATION STUDY IN RATS		
Descriptor	**Value**	**Remarks**
Relevant dose descriptor	NOAEC = 1 072 mg/m^3	Based on the NOAEC from a 4 week subacute inhalation study in rats (6 h/d, 5 d/w) (Unpublished study report, 2010)
Modification of the relevant dose descriptor	1072 mg/m^3 * (6 h/24 h) * (5 d/7 d) = NOEC$_{corr.}$	According to REACH Guidance R.8, by default, DNEL for the general population shall be derived for 24 h exposure/d and 7 d/w using Haber's law.
Corrected dose descriptor	**NOAEC$_{corr.}$ = 191 mg/m^3** (24 h/d, 7 d/w)	
Assessment factor (AF)	**AF Value**	**Remarks**
Interspecies differences (allometric scaling)	1	As DNEL derivation is based on inhalation data, no AF for allometric scaling is applied here, according to REACH Guidance R.8.
Interspecies differences (remaining differences)	2.5	The default factor for remaining differences (2.5) is applied according to the REACH guidance R.8.
Intraspecies differences	10	The default factor is applied according to the REACH guidance R.8 because no substance-specific information is available for an adjustment.
Exposure duration	2	An AF of 2 was used, although the default AF for extrapolation of subacute to chronic study duration is 6 (REACH Guidance

		R.8 and R.15), because results of the various available repeated does studies indicate that study duration (≥28 days) does not affect toxicity.
Dose-response	1	NOAEC was used as point of departure, no additional AF necessary.
Quality of whole database	1	
Overall AF	**50**	
$DNEL_{long-term, inhalation, systemic, general population (24 h/d)}$	**4 mg/m³**	

Table 17

LONG-TERM DNEL, INHALATION, LOCAL AND SYSTEMIC EFFECTS (24 H/D) BASED ON A CHRONIC ORAL STUDY IN RATS		
Descriptor	**Value**	**Remarks**
Relevant dose descriptor	NOAEL = 400 mg/kg bw/d	Based on the NOAEL from a chronic (104 weeks) oral study in rats (5 d/w) (NTP, 1989)
Modification of the relevant dose descriptor	400 mg/m³ * (5 d/7 d) = 286 mg/kg bw/d	According to REACH Guidance R.8, by default, a DNEL for the general population shall be derived for 7 d/w using Haber's law.
Modification of the relevant dose descriptor (route-to-route extrapolation)	286 mg/kg bw/d / 1.15 m³/kg bw/1.3 = $NOAEC_{corr.}$	Route-to-route extrapolation is needed from the oral to the inhalation route. For this purpose, the NOAEL (oral) has to be divided by the respiratory volume accounting for 24 hours (1.15 m³/kg body weight) according to the REACH guidance R.8. In the absence of route-specific information an additional assessment factor of 2 shall be used to consider the different absorption properties of the respiratory tract (assumed to be 100%) and after oral intake (assumed to be 50%) according to ECHA guidance R.8. As for benzyl alcohol, absorption in the GI tract of humans was shown to be ≥ 75% (EMEA, 1997), an AF of 1.3 was applied for oral-to-inhalation extrapolation.
Corrected dose descriptor	**$NOAEC_{corr.}$ = 191 mg/m³** (24 h/d, 7 d/w)	
Assessment factor (AF)	**AF Value**	**Remarks**
Interspecies differences (allometric scaling)	1	Allometric scaling already included in route-to-route extrapolation according to REACH Guidance R.8 (Appendix R.8-2).
Interspecies differences (remaining differences)	2.5	The default factor for remaining differences (2.5) is applied according to the REACH guidance R.8.
Intraspecies differences	10	The default factor is applied according to the REACH guidance R.8 because no substance-specific information is available for an adjustment.
Exposure duration	-	No AF was used, as the study used as point of departure is a chronic study (REACH Guidance R.8 and R.15).
Dose-response	1	NOAEL was used as point of departure, no additional AF necessary.

Quality of whole database	1	Guideline-conform in vivo study.
Overall AF	**25**	
$DNEL_{long-term, inhalation, systemic, general population (24 h/d)}$	**8 mg/m³**	

The robustness of the long-term DNEL value of 4 mg/m³ (24 h/d) based on the NOAEC resulting from a subacute inhalation study (28 days) is supported by the long-term DNEL of 8 mg/m³ that can be calculated alternatively using the NOAEL of 400 mg/kg bw/day from the chronic toxicity study in rats via the oral route as a point of departure and applying route-to-route extrapolation. This DNEL is in the same range as the respective DNEL derived by the registrants (i.e. 5.4 mg/m³).

As for various exposure scenarios, daily exposure durations <<24 h/d are expected (see respective RIVM Fact Sheets), ECHA Guidance R.15 states that for exposure durations up to 8 h/day, the DNEL can be adjusted for shorter daily exposure durations using Haber's law and the default factors in Table R.15-1, respectively. An overview of the adjusted DNELs can be found in Table 18 below.

Table 18

ADJUSTMENT OF THE LONG-TERM DNEL (INHALATION, LOCAL AND SYSTEMIC EFFECTS, 24 H/D) OF 4 MG/M³ TO SHORTER DAILY EXPOSURE DURATIONS USING HABER'S LAW ACCORDING TO ECHA GUIDANCE R.15	
Daily exposure duration	**Long-term DNEL (inhalation) corrected for shorter daily exposure durations using Haber's law**
Up to 24 h	4 mg/m³
Up to 8 h	6 mg/m³
Up to 3 h	8 mg/m³
Up to 1 h	12 mg/m³
Up to 15 min	18 mg/m³

Table 19

INFREQUENT DNEL, INHALATION, LOCAL AND SYSTEMIC EFFECTS (24 H/D) BASED ON A SUBACUTE INHALATION STUDY		
Descriptor	**Value**	**Remarks**
Relevant dose descriptor	NOEC = 1 072 mg/m³	Based on the NOAEC from a 4 week subacute inhalation study in rats (6 h/d, 5 d/w) (Unpublished study report, 2010)
Modification of the relevant dose descriptor	1 072 mg/m³ * (6 h/24 h) * (5 d/7 d) = $NOEC_{corr.}$	According to REACH Guidance R.8, by default, DNEL for the general population shall be derived for 24 h exposure/d and 7 d/w using Haber's law.
Corrected dose descriptor	**$NOEC_{corr.}$ = 191 mg/m³** (24 h/d, 7 d/w)	
Assessment factor (AF)	**AF Value**	**Remarks**
Interspecies differences (allometric scaling)	1	As DNEL derivation is based on inhalation data, no AF for allometric scaling is applied here according to REACH Guidance R.8.

Interspecies differences (remaining differences)	2.5	The default factor for remaining differences (2.5) is applied according to the REACH guidance R.8.
Intraspecies differences	10	The default factor is applied according to the REACH guidance R.8 because no substance-specific information is available for an adjustment.
Exposure duration	-	No AF was used, as for infrequent DNELs an alternative point of departure using the results of an appropriate short-term study (e.g. 28 days) is considered appropriate (ECHA Guidance R.15, Table R.15-1).
Dose-response	1	NOEC was used as point of departure, no additional AF necessary.
Quality of whole database	1	Guideline-conform in vivo study.
Overall AF	**25**	
$DNEL_{infrequent,\ inhalation,\ general\ population\ (24\ h/d)}$	**8 mg/m³**	

The infrequent inhalation DNEL of 8 mg/m³ (24 h/d) was derived based on the NOAEC of a subacute inhalation study (28 days). As for various infrequent exposure scenarios, daily exposure durations <<24 h/d are expected (see respective RIVM Fact Sheets), the DNEL can be adjusted for shorter daily exposure durations using Haber's law (Table R.15-1). An overview of the adjusted DNELs can be found in Table 20 below.

Table 20

ADJUSTMENT OF THE INFREQUENT DNEL (INHALATION, LOCAL AND SYSTEMIC EFFECTS, 24 H/D) OF 8 MG/M³ TO SHORTER DAILY EXPOSURE DURATIONS USING HABER'S LAW ACCORDING TO ECHA GUIDANCE R.15	
Daily exposure duration	**Infrequent DNEL (inhalation) corrected for shorter daily exposure durations using Haber's law**
Up to 24 h	8 mg/m³
Up to 8 h	12 mg/m³
Up to 3 h	16 mg/m³
Up to 1 h	24 mg/m³
Up to 15 min	36 mg/m³

Table 21

LONG-TERM DNEL, DERMAL, SYSTEMIC EFFECTS (24 H/D) BASED ON A CHRONIC ORAL STUDY		
Descriptor	**Value**	**Remarks**
Relevant dose descriptor	NOAEL = 400 mg/kg bw/d	Based on the NOAEL from a chronic (104 weeks) oral study in rats (5 d/w) (NTP, 1989)
Modification of the relevant dose descriptor	400 mg/m³ * (5 d/7 d) = 286 mg/kg bw/d	According to REACH Guidance R.8, by default, DNEL for the general population shall be derived for 7 d/w using Haber's law.
Modification of the relevant dose descriptor (route-to-route extrapolation)	1	Route-to-route extrapolation is needed from the oral to the dermal route. Benzyl alcohol is rapidly absorbed from the GI tract after oral exposure in humans and animals (>85%), as well as after dermal

		administration in rhesus monkeys under occluded conditions (56 to 80%). Thus, it is assumed that absorption of benzyl alcohol is similar after oral and dermal administration, wherefore no additional modification of the point of departure was performed (REACH Guidance R.18, Appendix R.8-2).
Corrected dose descriptor	**$NOEC_{corr.}$ = 286 mg/kg bw/d** (7 d/w)	
Assessment factor (AF)	**AF Value**	**Remarks**
Interspecies differences (allometric scaling)	4	A default AF of 4 is applied for allometric scaling (rat to human) according to REACH Guidance R.8.
Interspecies differences (remaining differences)	2.5	The default factor for remaining differences (2.5) is applied according to the REACH guidance R.8.
Intraspecies differences	10	The default factor is applied according to the REACH guidance R.8 because no substance-specific information is available for an adjustment.
Exposure duration	-	No AF was used, as the study used as point of departure is a chronic study (REACH Guidance R.8 and R.15).
Dose-response	1	NOAEL was used as point of departure, no additional AF necessary.
Quality of whole database	1	Guideline-conform in vivo study.
Overall AF	**100**	
$DNEL_{long-term,\ dermal,\ systemic,\ general\ population\ (24\ h/d)}$	**3 mg/kg bw/d**	

The long-term DNEL value of 3 mg/kg bw/d (24 h/d) based on the NOAEL of a chronic oral study (104 weeks) is in the same range as the respective dermal DNEL derived by the registrants (4 mg/kg bw/d). As absorption of benzyl alcohol is similar after oral and dermal administration and no modification of the point of departure with regard to route-to-route extrapolation was conducted, the respective dermal DNEL for long-term systemic effects can be considered identical to the long-term oral DNEL for systemic effects. As reported in the recent Scientific Opinion by EFSA, a very similar threshold value (i.e. acceptable daily intake or ADI) of 4 mg/kg bw/d was determined for benzyl alcohol as food additive (EC, 2004; EMA, 2017; EFSA, 2019).

Table 22

LONG-TERM DNEL[6], SKIN SENSITISATION (24 H/D)		
Descriptor	**Value**	**Remarks**
Relevant dose descriptor	NOAEL = 5906 µg/cm^2	Based on oedematous skin reactions in humans in human repeated insult patch tests at higher doses (human volunteers; results justify classification in Cat. 1B as weak to moderate skin sensitiser). Exposure in general 9 times during the course of 3 weeks, after 2 further weeks challenge with a non-irritant concentration (Scognamiglio et al., 2012). According to REACH-Guidance R.8, a NOAEL

[6] According to ECHA Guidance on IR-CSA R.15, Version 3.0 (2016)

		from a well conducted HRIPT has precedence over the LLNA EC3 value or a NOAEL from HMT.
Assessment factor (AF)	**AF Value**	**Remarks**
Interspecies (allometric scaling)	1	Human study is basis for DNEL derivation.
Interspecies (remaining differences)	1	Human study is basis for DNEL derivation.
Intraspecies	10	The default factor is applied according to the REACH guidance R.8 because no substance-specific information is available for an adjustment.
Quality of whole database	2	Summarized data and rather poor documentation; purity not reported; only general methodological details reported
Skin sens. specific AF: Vehicle or matrix effect	3	There is no specific indication that human exposure to benzyl alcohol occurs in a matrix with penetration enhancers or irritants. However, simultaneous exposure to benzyl alcohol and penetration enhancers or irritants cannot be entirely excluded. Thus, an AF of 3 is considered appropriate according to REACH-Guidance R.8 ("AF of 1-10-fold should be considered).
Exposure duration and different exposure conditions (*skin sens. specific*)	3	As exposure in general was conducted 9 times during the course of 3 weeks (3/w) in the HRIPTs but (repeated) daily dermal exposure can be expected according to some of the exposure scenarios, an AF of 3 is considered appropriate according to REACH-Guidance R.8 ("an additional AF (1 – 10-fold) should be considered to account for specific exposure condition considerations", such as differences in exposure frequency). Short-term exposure can induce dermal sensitisation.
Overall AF	**180**	
DNEL	**33 µg/cm²**	

A DNEL for induction of skin sensitisation for consumers of 33 µg/cm^2 was calculated by the eMSCA. This dermal DNEL for skin sensitising effects considers the (additional) sensitisation-specific assessment factors (AFs) as laid down in REACH Guidance R.8., i.e. AFs for vehicle or matrix effects, differences in exposure conditions and the impact of repeated exposure (DNEL without skin sensitisation-specific AFs: 295.3 µg/cm²). The results on which the dermal DNEL for skin sensitisation is based on, i.e. the data from human repeated insult patch tests (HRIPT), are in most cases poorly documented, and therefore results are rather unreliable and, thus, unsuitable for a robust quantitative risk assessment. Accordingly, the ECHA Guidance R.8 (section R.8.6) states: "In terms of quantification however, there often are considerable uncertainties related to the underlying data to be used, as well as in determining the appropriate assessment factors." It further states, that in case of skin sensitisation, the first step should always be a qualitative approach to assessing and controlling the risks, whereas setting a DNEL (if possible) could be used to judge the remaining/residual likelihood of risks (IR&CSA Guidance R.8: Characterisation of dose [concentration]-response for human health, Appendix R 8-10). In particular with respect to these uncertainties it needs to be underscored that benzyl alcohol is considered a moderate to weak skin sensitiser and that the DNEL for skin sensitising effects may be seen as an upper bound "best case" DNEL-estimate only. This value does not represent an exposure level at which it can be assured that no sensitisation will occur in the exposed population. However, the eMSCA finds that any exposure exceeding this value indicates a significant risk of dermal allergy.

Table 23

OVERVIEW OF THE CALCULATED DNELS FOR CONSUMERS – CRITICAL DNELS					
Endpoint of concern	**Type of effect**	**Critical study (ies)**	**Corrected dose descriptor(s) (e.g. NOAEL, NOAEC)**	**DNEL**	**Remarks**
Dermal DNEL (local effects)					
Skin sensitisation in humans	Long term, dermal, local effects Oedematous skin reactions in humans in a human repeated insult patch test justify classification as weak skin sensitiser (Cat. 1B)	(Scognamiglio et al., 2012)	5906 µg/cm^2	33 µg/cm^2	DNEL shall be seen as upper bound "best case" DNEL-estimate only due to high uncertainties. It does not represent an exposure level at which no sensitisation will occur in the exposed population. However, any exposure exceeding this value clearly indicates a risk of dermal allergy.
Long-term dermal DNEL (systemic effects)					
Chronic oral toxicity study, rats	No effects observed up to the highest tested dose	(NTP, 1989)	400 mg/kg bw/day	3 mg/kg bw/d	Due to dermal exposure route, no adjustment for shorter daily exposure durations was applied This value is considered also applicable for oral administration and is similar to the recently derived ADI of 4 mg/kg bw/d for benzyl alcohol as food additive by EFSA (2019).
Long-term inhalation DNEL (local and systemic effects)					
Repeated dose toxicity, inhalation, rats	No effects observed up to the highest tested dose	(Unpublished study report, 2010)	1072 mg/m^3	4 mg/m^3 (24 h/d) 6 mg/m³ (≤8 h/d) 8 mg/m³ (≤3 h/d) 12 mg/m³ (≤1 h/d)	Adjustment for shorter daily exposure duration possible (using Haber's law acc. to ECHA Guidance R.15)

OVERVIEW OF THE CALCULATED DNELS FOR CONSUMERS – CRITICAL DNELS					
Endpoint of concern	**Type of effect**	**Critical study (ies)**	**Corrected dose descriptor(s) (e.g. NOAEL, NOAEC)**	**DNEL**	**Remarks**
				18 mg/m³ (≤0.25 h/d)	
Infrequent inhalation DNEL (local and systemic effects)					
Repeated dose toxicity, inhalation, rats	No effects observed up to the highest tested dose	(Unpublished study report, 2010)	1072 mg/m³	8 mg/m³ (24 h/d) 12 mg/m³ (≤8 h/d) 16 mg/m³ (≤3 h/d) 24 mg/m³ (≤1 h/d) 36 mg/m³ (≤0.25 h/d)	Adjustment for shorter daily exposure duration possible (using Haber's law acc. to ECHA Guidance R.15)

7.9.10. Conclusions of the human health hazard assessment and related classification and labelling

The current acute toxicity classification for benzyl alcohol is based on Directive 67/548/EEC and translates into a minimum classification (indicated by asterisk) of Acute Tox. 4* (oral) H302: "Harmful if swallowed", which was confirmed during the SEv process. However, as the current acute toxicity classification of benzyl alcohol is a minimum classification according to Directive 67/548/EEC a respective proposal for harmonised classification was prepared by the eMSCA.

Based on the available data and according to criteria of Regulation (EC) 1272/2008, Annex I, (EC, 2015) the aerosol of benzyl alcohol does not need to be classified for acute inhalation toxicity.

Further, results from two OECD Guideline 405 studies support classification of benzyl alcohol as "Eye Irrit. 2, H319" according to the criteria of Regulation (EC) 1272/2008, Annex I (EC, 2015). This endpoint was, thus, included in the CLH proposal by the eMSCA.

The data from the human repeated insult patch test data on benzyl alcohol clearly point to the skin sensitizing potential of benzyl alcohol. The data justify classification of benzyl alcohol as Skin Sensitiser Cat. 1B based on positive reactions above 500 µg/cm² and a comparatively low, but substantial incidence of up to 0.3% in large study populations with consecutive patients in clinical departments of dermatology. This conclusion is in line with the Scientific Committee on Consumer Safety which recognised benzyl alcohol as "established contact allergen in humans" (SCCS, 2012), as well as with the outcome of the recent re-evaluation of benzyl alcohol as food additive by EFSA (EC, 2004; EMA, 2017; EFSA, 2019)). A respective proposal for harmonised classification including this endpoint was submitted to ECHA for accordance check in October 2019. The public consultation on the dossier was conducted starting in October 2020.

7.10. Assessment of endocrine disrupting (ED) properties

Not assessed during this substance evaluation.

7.11. PBT and VPVB assessment

Not assessed during this substance evaluation.

7.12. Exposure assessment

7.12.1. Human health

7.12.1.1. **Workers**

As pointed out under 7.5.2 benzyl alcohol is used in a wide range of applications both in the industrial sector and in professional settings. According to the CSR, inhalation and dermal exposure of workers is anticipated for all situations where benzyl alcohol is used. In order to quantify the exposure levels (inhalation, dermal) the registrants have used the generic worker exposure model ECETOC TRA v3 in the first tier.

A cross-check carried out by the eMSCA proved the model calculations in the first tier to be formally correct and in most cases within the applicability domain of ECETOC TRA v3. In the opinion of the eMSCA, these ESs basically comply with the ECHA guidance on information requirements and chemical safety assessment Chapter R.14: Occupational exposure estimation (ECHA, 2016a) and are therefore considered acceptable. However, for some worker contributing scenarios the registrants diverge from the tool defaults. This applies in particular to the modification of initial exposure estimates due to the concentration of the substance in preparation. Instead of the ECETOC TRA default factors the registrants use a linear concentration reduction approach.

In this context it is important to note that all tools incorporate variability and uncertainties (Lamb et al., 2015). For instance, generic models like ECETOC TRA v3 do not take into account the molecular interactions of the constituents in mixtures which may lead to significant deviations from ideal (linear) behaviour (Gmehling and Kolbe, 1988). According to R.14 (ECHA, 2016a), it is therefore generally not admissible to further refine these outputs through, for example, applying linear reductions for elements such as concentration in mixtures or duration of exposure unless robust scientific justification is provided.

The eMSCA has therefore recalculated the corresponding scenarios using the default ECETOC TRA v3 modifying factors for the concentration in mixtures. As can be seen from Table 24, the recalculated exposure estimates for inhalation and dermal exposure deviate significantly from the values assessed with a linear modification approach. Since the reported assessment is outside the applicability domain of the model, the registrant was requested to provide a robust justification why this linear exposure modification is appropriate for this specific assessment case or should use an appropriate higher tier model.

Table 24

COMPARISON OF EXPOSURE ESTIMATES – ECETOC TRA DEFAULT MODIFYING FACTORS VS. LINEAR CONCENTRATION REDUCTION APPROACH

Exposure scenario	Contributing scenario	Process category	Long-term modelled exposure estimates (ECETOC TRA default modifying factors for concentration)		Long-term modelled exposure estimates (linear concentration reduction approach)	
			Inhalation [mg/m³]	Dermal [mg/kg·bw/day]	Inhalation [mg/m³]	Dermal [mg/kg·bw/day]

ES 4	WCS 11	PROC 19	13.5	8.49	4.5	2.82
ES 7	WCS 3	PROC 7	22.5	2.14	13.5	1.28
ES 9	WCS 4	PROC 7	22.5	2.14	13.5	1.28
ES 12	WCS 4	PROC 7	22.5	2.14	13.5	1.28
ES 13	WCS 2	PROC 7	22.5	2.14	13.5	1.28

The registrants also performed higher tier assessments for some non-dispersive use scenarios (e.g. mixing or blending, calendering operations, charging and discharging) where safe use was not demonstrated in the first tier. In these cases, the registrants used the Advanced REACH Tool v.1.5 (ART) to estimate inhalation exposure and ECETOC TRA v3 to estimate dermal exposure. The corresponding higher tier assessments were also cross-checked by the eMSCA and proved to be formally correct and plausible in terms of the criteria laid down in R.14.

In addition, the registrants also carried out some higher tier assessments for the following wide dispersive use scenarios (ES 15 - indoors) in professional settings using the ART v1.5 for inhalation exposure and in most cases RiskofDerm v2.0 for dermal exposure estimation:

- ES 15: Worker contributing scenario (WCS) 7: Roller application or brushing (PROC 10)
- ES 15: WCS 8: Non industrial spraying conc. 50% (Level) (PROC 11)
- ES 15: WCS 9: Non industrial spraying conc. 80% (Level) (PROC 11)
- ES 15: WCS 10: Non industrial spraying conc. 50% (overhead) (PROC 11)
- ES 15: WCS 11: Non industrial spraying conc. 80% (overhead) (PROC 11)

Only in the case of WCS 7, dermal exposure to hands was estimated using ECETOC TRA v3, which however, does not predict body exposure.

A cross-check of the corresponding assessments by the eMSCA revealed that the registrants did not take into account body exposure as suggested by RiskofDerm (Hughson and Aitken, 2004). In this context it is important to note that according to RiskofDerm, contact with contaminated surfaces during spraying and roller application/brushing respectively can result in considerable exposure of both hands and the body. The eMSCA has therefore recalculated these scenarios taking into account the exposure to the body as well (Table 25). The recalculation was based on the same input parameters and RMMs as proposed by the registrants. A protection factor of 90% was used for protective clothing. In order to allow comparison with the DNEL for the endpoint skin sensitisation, Table 25 also lists dermal exposure in terms of surface dose (expressed in µg/cm^2) for hands and body, respectively. For the calculation of the surface dose on the hands and the body (excluding hands), the surface areas used were 820 cm^2 and 18 720 cm^2, respectively (Hughson et al. 2004)).

With respect to PROC 11 in exposure scenario 15 the CSR lists limiting the task duration as a RMM: the task duration is limited for WCS 8 (conc. 50%) to 70 min, for WCS 9 (conc. 80%) to < 60 min, for WCS 10 (conc. 50%) to 25 min and for WCS 11 (conc. 80%) to < 20 min. The dermal and inhalation exposure estimates have been generated assuming these exposure durations. The eMSCA noted that if longer task durations were assumed, the exposure estimate was significantly increased. As these generic worker contributing scenarios according to BG BAU (BG BAU, 2015; GISBAU, 2011) may cover different tasks (e.g. paint stripping, wall paper removal) with possibly different use pattern, the eMSCA considered that further information was required on the tasks in order to conclude on the practicality of limiting task duration as a RMM. In this context, the eMSCA noted that according to data published by the German Social Accident Insurance (IFA, 2016b), exposure durations are often ≥ 6 h per shift for wide-dispersive surface treatments using benzyl alcohol.

Table 25

RECALCULATED HIGHER TIER EXPOSURE ESTIMATES FOR WIDE DISPERSIVE USE WCS. THE SURFACE DOSE EXPRESSED IN µG/CM2 IS GIVEN IN BRACKETS							
Exposure scenario	**Contributing scenario**	**Process category**	**Long-term modelled exposure estimates (90th percentile)**				
			Inhalation (ART v1.5) [mg/m³]		Dermal (RiskofDerm v2.0) [mg/kg bw/day] ([µg/cm²])		
			With RPE[7]	Without RPE	hands	body	total
ES 15 (prof)	WCS 7	PROC 10	-	6.6	5.5[8] (469.5)	-	5.5
ES 15 (prof)	WCS 8	PROC 11 50% BA (level)	0.48	4.8	7.6 (648.8)	29.3 (109.6)	36.9
ES 15 (prof)	WCS 9	PROC 11 80% BA (level)	0.8	8	7.7 (657.3)	34.0 (127.1)	41.7
ES 15 (prof)	WCS 10	PROC 11 50% BA (overhead)	0.51	5.1	7.6 (648.8)	29.3 (109.6)	36.9
ES 15 (prof)	WCS 11	PROC 11 80% BA (overhead)	0.66	6.6	7.2 (614.6)	31.7 (118.5)	38.9

Monitoring data on inhalation exposure for the use of benzyl alcohol in professional settings are available from two institutions. The German Social Accident Insurance (IFA, 2016b) has published exposure data for a number of sectors where benzyl alcohol is used. The data revealed that inhalation exposure at workplaces is in general quite low or even below the limit of quantification if the underlying uses are non-dispersive in character (transfer, filling etc.). However, exposure can be rather high if benzyl alcohol is used in wide dispersive applications. For instance, Table 26 indicates that the 90th percentile of 25 data points measured during surface treatments is about 25.5 mg/m³ (exposure duration ≥ 6 h). There is also monitoring data from hazardous substance information system (GISBAU) of the German legal accident insurance for the construction industry (BG BAU), that show high exposure levels for the surface application of paint strippers and cleaning agents (BG BAU, 2015; GISBAU, 2011) (Table 26).

Table 26

MEASURED DATA ON INHALATION EXPOSURE IN PROFESSIONAL SETTINGS FROM GISBAU AND BG BAU					
Use (Reference No.)	**Duration of exposure (h)**	**Number of data points**	**Number of facilities**	**Air concentration without RPE [mg/m³]**	
				90th Percentile	95th Percentile
Surface treatment (IFA, 2016)	≥ 6	25	20	25.5	36.25
Use of paint stripper (GISBAU, 2016)	-	16	-	31	39
Widespread stripping of wall paper (BG BAU, 2015)	-	14	-	-	38.7

[7] RPE: respiratory protective equipment
[8] Model estimate of ECETOC TRA v3.

The eMSCA had no further information on the background of the measured data as disclosed in the publications of IFA, BG BAU, and GISBAU. The corresponding contextual information on for example room sizes, ventilation efficacy, used amount and concentration of benzyl alcohol is either not or only fragmentarily documented. Therefore, a more specific allocation to the described WCSs by the registrants was not possible. However, the measured data reflect real situations and can be clearly allocated to ES 15 (widespread use by professional workers – professional use – indoor) which allowed to draw meaningful analogies regarding the pattern of use between measured and modelled scenarios. Since the data is also specific for benzyl alcohol, there is no uncertainty regarding volatility as this is the case with models,e.g. ART (Advanced REACH Tool), which are based on exposure data from a variety of substances and exposure situations. Such an analogy approach is also advocated in guidance R.14 (R.14.6.3.2) where the use measurement data from analogous situations is described.

Since the ART model is fitted to a set of measured exposure values, the result will not reflect all possible workplaces within one scenario equally well. Even within one scenario (e.g. painting operations in professional settings) there is still a range of possible exposure values reflecting differences that are not captured by the respective model parameters.

Thus, the result of an ART exposure estimation for a specific workplace will have a component of uncertainty that is caused by the variability of the underlying measurements on which it is based. In addition, ART has never been validated on the basis of independent measurement data from wide spread use scenarios in professional settings.

Taking this into account the eMSCA concluded that the substance specific measured data for ES 15 made the ART estimates at least questionable at that stage. Finally a comparison of the ART estimates (without RPE) with the monitoring data indicated that ART may significantly underestimate inhalation exposure for such wide dispersive use scenarios making the rather low exposure estimates provided by the registrants questionable.

Since the modelled and measured inhalation exposure, in particular in combination with dermal exposure estimates of RiskofDerm (body + hands), clearly exceeded the DNEL, the eMSCA was of the opinion that safe use had not been demonstrated in the CSR for the wide spread use of benzyl alcohol by professional workers. The eMSCA noted that inhalation exposure did not contribute to the major part of total exposure. The DNEL was exceeded in almost all cases by dermal exposure (body+hand) alone.

The registrants were therefore required to revise and provide further information for the professional wide spread use exposure scenario ES 15 (including WCS 7, 8, 9, 10 and 11) which have been identified as critical by the eMSCA. This included an improved task description for PROC 10 and 11 to determine if an RCR>1 is to be expected. In addition, for the listed PROCs, the registrants were required to provide all assumptions and model input parameters used to derive the exposure estimates, including the direction of application assumed, whether a correction factor for concentration was applied, the use rate assumed, whether a modification factor for local exhaust ventilation (LEV) was applied to the exposure estimate either within or outside the model and how a glove and protective clothing modification factor was applied to the exposure estimate where both hand and body dermal exposure estimates were generated. For dermal exposure estimates generated using RiskofDerm, the dermal exposure operator (DEO) unit selected had to be provided. With respect to WCS 8, 9, 10, 11 in exposure scenarios 15, the registrants were required to provide further justification for the task duration, taking into account the task description and the practicality of limiting task duration as a RMM in these scenarios.

The exposure assessment using model estimates and measured data for inhalation and dermal exposure should be performed in accordance with the procedure laid down in the 'REACH Guidance on Information Requirements and Chemical Safety Assessment', Chapter R.14; the risk assessment shall follow the procedure laid down in Part E.

In some contributing scenarios the registrants described durations of tasks > 4 h (input parameter of the used model for exposure assessment). This indicated an up to 8 h use of PPE such as gloves whenever such PPE is recommended (wearing of PPE, including gloves is also used as an input parameter for the model). In this context it was important to note

that extended use of gloves under occlusive conditions is considered as "wet work" since the hands become moist due to sweat (accumulation of heat and moisture). It has been demonstrated, e.g. by Behroozy and Keegel, that "wet work" conditions caused by a prolonged wearing time of gloves present a burden to workers and increases risk (Behroozy and Keegel, 2014).

Hence, when liquid-tight gloves are worn, the aim should be to have an appropriate alternation of activities because the extended wearing of liquid-tight gloves may lead to the formation of perspiration and skin damage (wet work). The frequency with which gloves are changed should be laid down in the risk assessment. According to the German Technical Rule for Hazardous Substances 401 (AGS, 2011), the eMSCA recommended that gloves be changed at least every hour or that cotton glove liners are worn. The requisite number of protective gloves and the times for a change of gloves should be considered in the work organisation and should be laid down in the ES and in the extended safety data sheet.

The registrants have submitted an updated CSR on 25 of April 2019 according to the requirements specified in ECHA's Decision (ECHA, 18 April 2018). An examination of the CSR showed that the registrants have essentially complied with the requirements of the eMSCA regarding worker request A in the substance evaluation decision:

The exposure estimates for the WCS 7, 8, 9, 10 and 11 in ES 15 (widespread use by professional workers) were plausibly changed taking into account new measurement data from BG Bau (BG Bau, 2019) as well as modified model estimates (Tier 2 with ART, partly with respiratory protection 90% effectiveness). The body exposure and the effectiveness of the protective suit (90%) were taken into account in the estimation of dermal exposure with RiskofDerm. In addition, the documentation of the measurement data also contains the required information on the quantities handled and the exposure duration regarding WCS 8, 9, 10, 11 in ES 15. For these scenarios the inhalation exposure (8 h TWA) is estimated (based on measured data, 90th percentile) to be 3.22 mg/m^3, taking into account respiratory protection (90% efficacy). The RiskofDerm estimates for dermal exposure are in the range between 2.743 – 6.77 mg/kg bw/day, taking into account hand and body exposure (efficacy of dermal protection 90%). Overall, the combined RCRs (inhalation+dermal) are almost always below 1.

However, there is one scenario where the combined RCR is (slightly) above 1: The exposure scenario 4 (WCS 11 (handmixing with intimate contact and only PPE available PROC 19) appears problematic, as a glove effectiveness of 95% is chosen for the professional sector. This contradicts the requirements of ECETOC TRAv3TRA v3 (technical report No. 114) where such high protection factors are only permitted for industrial applications with specific activity training. Although the RCR is with 1.1 only slightly above 1 (if a glove efficacy of 90% is assumed) the registrants should be aware of that issue. One option to solve this issue would be to allow ES 4 WCS 11 only for industrial sites. Another option would be to reduce the concentration of benzyl alcohol in the mixture to <5%.

Regarding worker request B in the substance evaluation decision, the registrants have not provided the requested justification for the use of linear reduction factors in ECETOC TRA estimates for inhalation and skin exposure. Instead, dermal exposure was recalculated for scenarios ES 7 (WCS 3), ES 9 (WCS 4), ES 12 (WCS 4) and ES 13 (WCS 2) using standard reduction factors. For inhalation exposure the registrants used a higher tier model (ART). Using this approach, overall the combined RCRs are below 1. Although the registrants have not fulfilled the request the eMSCA can accept this higher tier approach, because the registrants plausibly demonstrated the safe use of the substance for the scenarios in question.

7.12.1.2. **Consumers**

Comparison of registered uses and exposure scenarios with information from product databases raised questions with respect to whether consumer uses are covered sufficiently by exposure scenarios in the CSRs. In the course of the substance evaluation, exposure scenarios were added in the dossier of the lead registrant. However, it is still uncertain whether consumer uses are adequately covered by the present exposure scenarios, for

example for products such as panty liners, dry toilet tissue, ironing water, and dish washer freshener (Mintel GNPD).

Exposure parameters were not always sufficiently justified (for example in exposure scenarios for the use of paint remover). Assumptions of risk reduction measures, such as the use of protection gloves, had been observed in some exposure scenarios. This measure belongs to the "communicated risk reduction measures" which are not sufficiently effective in controlling the risks for consumers (ECHA R.15, 2016). Moreover, inadequate models were used in part (e.g. for spray applications).

The eMSCA derived own consumer exposure estimates using ConsExpo according to ECHA Guidance on Information Requirements and Chemical Safety Assessment R.15 (ECHA R.15, 2016) on the basis of the default assumptions in ConsExpo (valid in 2019) and concentrations given in the CSR for PC 1, PC 3, PC 9a, PC 9b, PC 18, PC 23, PC 31, PC 34, PC 35. An uncertainty assessment focussing on the impact of the applied model on the outcome for dermal exposure (local and systemic) was performed for joint sealants as an example. For scenarios with RCR > 1, the eMSCA carried out additional analyses to identify concentrations that would not result in RCRs above 1. Paint removers are in the focus of the exposure assessment because of the likelihood of very high concentrations in the products. In addition, PC 1 was selected for subsequent measures due to the high RCR values in this product category.

Some registrants used exposure parameters deviating from standard defaults without sufficient justification. Deviations between CSRs have been observed regarding the OCs. However, the eMSCA cannot conclude whether this is based on product specific differences in the supply chain of each registrant. The eMSCA recalculated exposure based on the concentrations given in the CSRs and assumption on defaults in accordance with ECHA Guidance R.15 and actual RIVM Fact Sheets. Available information does not allow a refinement at the moment.

Benzyl alcohol is used as a substitute for dichloromethane in paint removers (Zarogiannis et al., 2007). According to this report, acidic (pH of 2.5) formulations contain approximately 25 to 35% benzyl alcohol and basic formulations (pH of 11) contain approximately 30 to 50% benzyl alcohol. Neutral strippers with benzyl alcohol may also be used. The report also states that paint strippers with benzyl alcohol show some limitations: very slow reaction below 18 °C, additional time required to strip very thick coatings (over 0.02 cm), water-borne applied primers as opposed to solvent primers, and additional time required to strip coatings with a very aggressive conversion coating below the primer. Therefore it has been estimated that products with benzyl alcohol require increased time (approximately 25% more) to strip equipment and that this is more labour intensive compared to dichloromethane (Zarogiannis et al., 2007). As no time frame is given in the report, the eMSCA cannot conclude at the moment whether or not this additional time required is covered by the default assumptions in ConsExpo.

Overall, there is a need for better understanding of the consumer market with its diversity of applications to finally assess exposure to benzyl alcohol. In this regard, the intended RMOA is considered essential to obtain a better understanding of the variety of consumer products on the market using solvents such as benzyl alcohol and to enable more realistic exposure estimation and risk assessment.

7.12.2. Combined exposure assessment

7.12.2.1. **Workers**

Not evaluated.

7.12.2.2. **Consumers**

Benzyl alcohol is present in various consumer products and consumers are likely exposed to benzyl alcohol by different products at the same time (aggregated exposure as defined in R.15, see also 7.5.2). However, this combined exposure cannot be quantified based on

available data, therefore the eMSCA focussed on the evaluation and assessment of the specific single uses of Benzyl alcohol.

In addition, exposure to benzyl alcohol can occur via different routes (combination as defined in R.15). In this evaluation, the eMSCA focussed on the inhalation and dermal exposure. For most of the exposure scenarios, both routes contribute to the exposure. The predominant route and the extent of contribution depend on the respective scenario.

7.13. Risk characterisation

7.13.1. Workers

In view of the physicochemical properties of benzyl alcohol and its applications, workplace exposure occurs mainly via inhalation and dermal contact. For quantitative risk characterisation, modelled inhalation and dermal exposure data are compared to the long-term systemic DNEL (inhalation) of 22 mg/m^3 and to the long-term systemic DNEL (dermal) of 8 mg/kg bw/day, respectively. The RCRs per each route of exposure are then added to calculate the combined RCR for each ES. In addition to the modelled exposure estimates, air monitoring data from GISBAU and IFA were considered in this assessment.

As discussed in 7.12.1.1, the eMSCA has recalculated several worker contributing scenarios where the registrants diverged from the tool defaults using the default ECETOC TRA v3 modifying factors for the concentration of benzyl alcohol in mixtures. As a result, the recalculated estimates for inhalation and dermal exposure exceed significantly the values originally calculated by the registrants. The dermal exposure still appears to be controlled and remains below the long-term dermal DNEL of 8 mg/kg bw/day (except for ES 4). However, for the inhalation exposure the modelled exposure estimates, considering ECETOC TRA v3 default modifying factors for concentration, are as high as or above the long-term inhalation DNEL of 22 mg/m^3 (except for ES 4). Thus, the combined exposures via both the dermal and the inhalation pathway lead to RCR > 1 (Table 27). In order to allow comparison with the DNEL for the endpoint skin sensitisation, Table 27 also lists dermal exposure estimates expressed in terms of surface area dose for hands.

Table 27

OVERVIEW OF THE RCRS FOR MODELLED EXPOSURE ESTIMATES OF BENZYL ALCOHOL CONSIDERING ECETOC TRA DEFAULT MODIFYING FACTORS (TABLE 24 IN 6.12.1.1)*

Exposure scenario	Contributing scenario	Process category	Long-term modelled exposure estimates (ECETOC TRA default modifying factors for concentration)		RCR per route		RCR combined
			Inhalation [mg/m³]	Dermal [mg/kg·bw/day] ([µg/cm²])	Inhalation	Dermal	
ES 4	WCS 11	PROC 19	13.5	8.49 (306.3)	0.6	1	1.6
ES 7	WCS 3	PROC 7	22.5	2.14 (99.9)	1	0.2	1.2
ES 9	WCS 4	PROC 7	22.5	2.14 (99.9)	1	0.2	1.2
ES 12	WCS 4	PROC 7	22.5	2.14 (99.9)	1	0.2	1.2
ES 13	WCS 2	PROC 7	22.5	2.14 (99.9)	1	0.2	1.2

* Calculated exposure levels are compared to DNEL (worker, inhalation, systemic) of 22 mg/m3 for the inhalation route and DNEL (worker, dermal, systemic) of 8 mg/kg bw/day for the dermal route. The surface dose expressed in µg/cm2 is given in brackets.

Furthermore, the registrants also carried out some higher tier assessments for wide dispersive use scenarios (ES 15 – indoors) in professional settings using the ART v1.5 for inhalation exposure and in most cases RiskofDerm v2.0 for dermal exposure estimation (discussed in 7.12.1.1). Since the registrants did not consider the body exposure as suggested by RiskofDerm, the eMSCA has recalculated these scenarios (Table 25 in 7.12.1.1) taking into account both hand exposure and body exposure. With regard to WCS 7, it has to be noted that the dermal exposure estimate is based on ECETOC TRA v3 which

does not take into account body exposure. Inhalation exposure was calculated with ART without RPE since the registrants did not prescribe RPE for that scenario. The corresponding RCRs are well above 1 in most cases indicating that risks may not be sufficiently controlled (Table 28). This assessment was also supported by measured inhalation data from GISBAU and IFA (Table 26 in 7.12.1.1) indicating that ART may significantly underestimate inhalation exposure for such wide-dispersive use scenarios.

In addition, surface dose estimates for the exposure of the hands clearly exceed the DNEL of 66 µg/cm^2 indicating that the risks for induction of skin sensitisation to benzyl alcohol are not adequately controlled.

Table 28:

OVERVIEW OVERVIEW OF THE RCRS FOR MODELLED EXPOSURE DATA OF BENZYL ALCOHOL.*

Exposure scenario	Contributing scenario	Process category	Long-term modelled exposure estimates (90th percentile)				RCR per route		RCR combined
			Inhalation [mg/m^3]	Dermal [mg/kg bw/day] ([µg/cm^2])			Inhalation	Dermal	
				hands	body	total			
ES 15 (prof)	WCS 7	PROC 10	6.6*	5.5** (469.5)		5.5***	0.3	0.7	1.0
ES 15 (prof)	WCS 8	PROC 11 50% BA (level)	0.48	7.6 (648.8)	29.3 (109.6)	36.9	0.02	4.6	4.6
ES 15 (prof)	WCS 9	PROC 11 80% BA (level)	0.8	7.7 (657.3)	34.0 (127.1)	41.7	0.04	5.2	5.2
ES 15 (prof)	WCS 10	PROC 11 50% BA (overhead)	0.51	7.6 (648.8)	29.3 (109.6)	36.9	0.02	4.6	4.6
ES 15 (prof)	WCS 11	PROC 11 80% BA (overhead)	0.66	7.2 (614.6)	31.7 (118.5)	38.9	0.03	4.9	4.9

* The predicted exposure levels (estimated with ART v1.5 and RiskofDerm v2.0) are compared to the DNEL (worker, inhalation, systemic) of 22 mg/m^3 for the inhalation route and the DNEL(worker, dermal, systemic) of 8 mg/kg bw/day for the dermal route. The surface dose expressed in µg/cm^2 is given in brackets.
** Calculated without the application of RPE
*** Calculated with ECETOC TRA without considering whole body exposure

Since the measured inhalation exposure in particular in combination with dermal exposure estimates of RiskofDerm indicated clear exceedance of the DNEL, the eMSCA was of the opinion that safe use has not been demonstrated in the CSR for the widespread use of benzyl alcohol by professional workers. Therefore, the registrants were requested to provide an exposure assessment and risk characterisation (Annex I, Sections 5 and 6) for inhalation and dermal exposure: revise exposure estimates for worker contributing scenarios (WCS) 7, 8, 9, 10 and 11 in exposure scenario 15, using existing measured exposure data and/or higher tier models within their domain of applicability and revise the risk characterisation accordingly.

Since the modelled or measured exposure estimates indicated that risks are not adequately controlled, the registrants were requested to provide representative workplace measurement data taken under OCs and RMMs as specified in the corresponding worker contributing scenarios, in order to perform a higher tier exposure assessment for inhalation and dermal exposure in accordance with the procedure laid down in the 'REACH Guidance on Information Requirements and Chemical Safety Assessment', Chapter R.14 and a risk

assessment in accordance with the procedure laid down in Part E for particular exposure scenarios (ESs) with RCR > 1. With respect to worker contributing scenario 8, 9 10, 11 the registrants were also required to provide further justification for the task duration, taking into account the practicality of limiting task duration as a RMM in these scenarios.

A substance evaluation decision was issued on 18 April 2018 containing requests with regard to exposure of workers as outlined above. The registrants provided an updated CSR within the given time frame on 25 April 2019 and the concern could be clarified. An examination of the CSR showed that the registrants have essentially complied with the requirements of the eMSCA regarding worker request A: Based on measured data for WCS 7, 8, 9, 10 and 11 in ES 15 the inhalation exposure (8 h TWA) is estimated to be 3.22 mg/m^3, taking into account respiratory protection (90% efficacy). The RiskofDerm estimates for dermal exposure are in the range between 2.743 – 6.77 mg/kg bw/day. Overall, the combined RCRs (inhalation+dermal) are almost always below 1.

However, for exposure scenario 4 (WCS 11 (handmixing with intimate contact and only PPE available PROC 19) the registrants have estimated the dermal exposure by assuming a glove efficacy of 95% for the professional sector. This contradicts the requirements of ECETOC TRAv3 (technical report No. 114) where such high protection factors are only permitted for industrial applications with specific activity training. For the professional sector the technical report No. 114 only allows glove efficacies of 90% leading to a dermal estimate of 8.49 mg/kg bw/day. Since the RCR is (slightly) above 1, if a glove efficacy of 90% is assumed, the registrants should be informed about that issue.

Regarding worker request B, the registrants have not provided the requested justification but used a higher tier model to demonstrate that RCRs are below 1. Although the registrants have not fulfilled the request, the eMSCA can accept this higher tier approach, because the registrants plausibly demonstrated the safe use of the substance for the scenarios in question.

7.13.2. Consumers

Oral exposure of consumers to benzyl alcohol was not considered by the eMSCA. It is noted that EFSA recently re-evaluated the use of benzyl alcohol as food additive (EC, 2004; EMA, 2017; EFSA, 2019).

Benzyl alcohol proved to be a weak to moderate skin sensitiser showing weak but substantial effects in human repeated insult patch tests as well in human diagnostic patch tests in large collectives of consecutive patients in clinical departments of dermatology justifying classification in Cat. 1B according to the CLP regulation (Regulation (EC) No 1272/2008 (EC, 2015)), section 3.4.2.2. The eMSCA's conclusion to consider benzyl alcohol a weak to moderate skin sensitiser is in line with the "Panel on Food Additives and Flavourings (FAF)" (EC, 2004; EMA, 2017; EFSA, 2019), as well as with the Scientific Committee on Consumer Safety which recognised benzyl alcohol as "established contact allergen in humans" (SCCS, 2012). This conclusion further differs from the registrants' conclusion to consider benzyl alcohol a non-sensitiser. Benzyl alcohol is ubiquitously used in consumer products, i.e. cosmetics, medicines, biocides, foodstuffs and products regulated under REACH. In particular, the skin sensitising properties are not yet regulated for a large proportion of the products covered by REACH. A CLH proposal prepared by the eMSCA addressing the skin sensitising potential of benzyl alcohol was submitted to ECHA in October 2019.

RCRs calculated based on eMSCA exposure assessments and using the dermal DNEL for sensitising effects are well above 1 (max. value: 5 758) for numerous exposure scenarios (PC 1, PC 9 a, PC 9b, PC 18, PC 23, PC 31, PC 35) indicating that dermal exposure poses a risk for skin sensitisation/allergic reactions for consumers. Particularly, exposure estimates in PC 1 resulted in high RCRs. Uncertainty regarding the exposure model for dermal exposure only affects the level of the estimated risk, thus, those uncertainties do not affect the conclusion.

In addition, the DNEL for skin sensitising effects may only be seen as an upper bound DNEL estimate, not representing an exposure level at which no sensitisation will occur in the

exposed population. Any exposure exceeding this value indicates a significant risk of dermal allergy. As RCRs < 1 were calculated for several scenarios, it remains questionable whether the derivation of the DNEL for sensitising effects was sufficiently conservative. Accordingly, if a reliable DNEL could be derived, further scenarios could have resulted in RCR values above 1.

In comparison, the dermal DNEL for systemic effects was used for calculating RCRs for all dermal exposure scenarios. Using this DNEL, only four of the various dermal exposure scenarios resulted in RCRs above 1 (max. value of 3.33 for PC1, 9a and PC9b). It is noted that all RCR values were significantly lower when using this DNEL compared to the DNEL for skin sensitisation. Thus, for risk characterisation it seems more conservative to focus on controlling sensitisation risk.

Based on the findings above, the eMSCA concludes that health risks for consumers due to exposure to benzyl alcohol via the dermal route are not sufficiently controlled. Nevertheless, it is noted again that considerable uncertainty is associated with the derived dermal DNEL for skin sensitising effects, as well as regarding the calculation of the dermal exposure scenarios (e.g. actual and realistic concentrations of benzyl alcohol in the respective products).

The CLH proposal for benzyl alcohol submitted to ECHA proposes classification as Skin Sens. 1B according to the CLP Regulation. In light of the weak to moderate skin sensitisation potential of this compound (obviating the need for setting a specific concentration limit), a respective harmonised classification of benzyl alcohol would imply classification and labelling of mixtures containing benzyl alcohol at concentrations ≥ 1.0% (Table 3.4.5 of CLP Regulation). As substances classified as sensitisers may elicit a response in already sensitised individuals, when present in the mixture in quantities below the concentrations established in Table 3.4.5, further requirements are set in the CLP Regulation. I.e. section 2.8 of Annex II of the CLP Regulation states:

"The label on the packaging of mixtures not classified as sensitising but containing at least one substance classified as sensitising and present in a concentration equal to or greater than that specified in Table 3.4.6 of Annex I shall bear the statement:

EUH208 — 'Contains (name of sensitising substance). May produce an allergic reaction'."

For benzyl alcohol this would mean that a mixture containing this substance at or above concentrations of 0.1% has to be labelled with the statement 'Contains benzyl alcohol. May produce an allergic reaction', when the substance is eventually classified in a revised harmonised entry.

Labelling will provide guidance to informed and interested consumers (e.g. persons who have already been sensitised). However, this communicated risk reduction measure alone is considered not adequate and sufficient to protect consumers from health risks.

RCRs for exposure scenarios via the inhalation route were calculated using the systemic long-term DNEL and the DNEL for infrequent use, respectively, derived by the eMSCA.

It is concluded that health risks due to consumer exposure to benzyl alcohol via the inhalation route are not sufficiently controlled at the moment, as RCR values > 1 (up to 28 in PC 1) were derived for numerous exposure scenarios.

Summing up RCRs for systemic health effects (dermal and inhalation) within a contributing scenario resulted in four additional exposure scenarios with RCRs slightly above 1 (PC 9a, PC 23, PC 31). In all other exposure scenarios where combined risk assessment resulted in RCRs above 1, already one route alone resulted in a potential risk.

It is noted again that considerable uncertainties arise specifically when calculating the exposure scenarios (e.g. actual and realistic concentrations of benzyl alcohol in the respective products). These uncertainties will be addressed in the subsequent RMOA, which will be initiated by the eMSCA in 2020 and in which information on consumer products will be obtained via various sources to improve estimates on consumer exposure and to allow a sound deliberation on the most appropriate regulatory measure. After the conclusion of the RMOA it will be possible to evaluate whether and for which product categories benzyl

alcohol poses a realistic human health risk and whether further risk management measures are necessary for the use of consumer products, and if so, which measure(s) will be considered best suited in order to minimise this risk for the consumer.

7.14. References

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7.15. Abbreviations

ADI	acceptable daily intake
AOP	adverse outcome pathway
AF	assessment factor
AGS	Committee on Hazardous Substances ("Ausschuss für Gefahrstoffe")
ART	Advanced REACH Tool
ATE	acute toxicity estimates
BG Bau	professional association for construction sector ("Berufsgenossenschauft Bau")
CLH	harmonised classification and labelling as per Annex VI to Regulation (EC) 1272/2008
CLP	classification labelling packaging
CONTAM	Contaminants in the Food Chain
CoRAP	continuous rolling action plan
CSR	chemical safety report
DEO	dermal exposure operation
DNEL	derived no effect level
DMEL	derived minimum effect level
ECHA	European Chemical Agency
EFSA	European Food Safety Authority
EMA	European Medicines Agency
eMSCA	evaluating member state competent authority
EOGRTS	Extended one generation repeated dose toxicity study
ES	exposure scenario
FAF	Panel on Food Additives and Flavourings
GESTIS	Substance Database of hazardous substance information system (Gefahrstoffinformationssystem der des IFA)
GI	gastrointestinal
GIFAS	poison information and archiving systen ("Giftinformations- und

	Archivierungssystem")
GISBAU	hazardous substance information system ("Gefahrstoff-Informationssystem der BG BAU")
GLP	good laboratory practice
GNPD	Global New Products Database
HRIPT	human repeat insult patch tests
IFA	German social accident insurance
JEFCA	Joint FAO/WHO Expert Committee on Food Additives
LD_{50}	lethal dose 50
LEV	local exhaust ventilation
LLNA	local lymph node assay
LOAEL/C	lowest observed adverse effect level/concentration
MAK	German maximum workplace concentration ("Maximale Arbeitsplatzkonzentration")
NGO	non-governmental organisation
NOAEC	no observed adverse effect concentration
NOAEL	no observed adverse effect level
NTP	national toxicology program
OC	operational condition
OECD	organization for economic co-operation and development
OEL	occupational exposure limit
PC	product category
POD	point of departure
PPE	personal protective equipment
PT	product type
PROC	process category
RCR	risk characterisation ratio
RIVM	Dutch National Institute for Public Health and the Environment
RMM	risk management measure
RMOA	Regulatory Management Option Analysis
RPA	risk and policy analysts
RPE	respiratory protective equipment
SCCS	Scientific Committee on Consumer Safety
SCF-L	EFSA's Scientific Committee for Food
SCL	specific concentration limit
SDS	safety data sheet
SEv	substance evaluation
SPIN	substances in preparations in Nordic countries
SVHC	substances of very high concern
TDI	tolerable daily intake
TSH	thyroid stimulating hormone
WCS	worker contributing scenario