CORRIGENDUM

to the Part B of the

SUBSTANCE EVALUATION CONCLUSION

as required by REACH Article 48 and EVALUATION REPORT

for

4,4'-Isopropylidenediphenol

EC No 201-245-8

CAS No 80-05-7

Evaluating Member State(s): Germany

Dated: 02 October 2018

Evaluating Member State Competent Authority

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Year of evaluation in CoRAP: 2012

Before concluding the substance evaluation a Decision to request further information was issued on: 20 December 2013
Based on the registration updates provided by the registrants and further information supplied during the follow-up phase, the evaluating Member State concluded the evaluation without the need for further information requirements according to Article 46(1).

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.

Background

This document constitutes an erratum to Part B (Evaluation report) of the Substance Evaluation Conclusion as required by REACH and Evaluation report, prepared by the evaluating Member State Competent Authority of Germany. It addresses discrepancies occurring on the chapters on DNEL derivation and risk characterisation. In this regard, the Corrigendum supersedes the previously published Evaluation report.

A. Corrigendum for Section 7.9.9.

This section supersedes the section 7.9.9. (p. 36-40) of the original Substance Evaluation Report.

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

Oral DNEL, systemic, general population

A BMDL(10) of 8960 µg/kg/day was calculated by EFSA (2015) for changes in the mean relative kidney weight in a two generation toxicity study in mice (Tyl et al., 2008). This value has been taken by EFSA as a starting point for their TDI calculation and by ECHA (2015) as starting point for the DNEL derivation. The value is also used by the eMSCA for DNEL derivation for systemic effects.

ECHA (2015) has also agreed to use the Human Equivalent Dose (HED) approach as used by EFSA (2015) instead of a (default) assessment factor for toxicokinetics. The HED represents the multiples of the external dose (D) in an animal species by a specified route and life-stage that a human would require to obtain an equivalent Area under the Curve (AUC) from a specific route of administration. Based on a human equivalent dose factor (HEDF) of 0.068 (derived by comparison of an oral mouse AUC with an oral human AUC (derived by PBPK modelling), replacing the default adjustment factor of 0.14 (= reciprocal of the default assessment factor of 7) for toxicokinetic differences (allometric scaling) between mice and humans, an HED of 609 µg/kg bw/d was obtained from the BMDL(10) of 8960 µg/kg/day.

Using an assessment factor of 2.5 for toxicodynamics and an assessment factor of 10 for interindividual differences in the general population yields a DNEL of 24 µg/kg bw/d (609 µg/kg bw/d divided by 10 x 2.5). Based on a WoE analysis performed by EFSA (2015), ECHA (2015) concluded that the available data indicate that kidney effects are not the most critical effects of BPA. Whereas the data on other adverse effects do not allow to identify a sufficiently robust starting point, the WoE analysis by EFSA (2015) indicates that they could occur starting from a HED of 100 µg/kg bw/day, i.e. at a 6-fold lower level than the HED for kidney effects. Consequently, a DNEL (and also the temporary TDI as derived by EFSA) accounting for these effects would be 6-fold lower than a DNEL based on kidney effects alone. Thus, an additional assessment factor of 6 was used for DNEL and t-TDI-derivation. This results in an **oral DNEL** of **4 µg/kg bw/day** for the general population.

It should be kept in mind, that based on a recent report by RIVM, EFSA has been mandated to examine the results of the RIVM report and specificall review the toxicity of BPA on the immune system in light of two 2014 publications by Ménard et al. on immunotoxicity of BPA. In addition, it has to be kept in mind that EFSA committed to the re-evaluation of BPA when a two-year study by the U.S. National Toxicology Program becomes available in 2017. Thus, DNEL-derivations in this sections based on kidney effects detected in the study by Tyl et al., 2008 have a provisional nature and might be subject for revision in the near future.

Dermal DNEL, systemic, general population

A new in-vitro dermal penetration study has been provided in the context of this SEv. As discussed in section 7.9.1 (toxicokinetics), a dermal absorption percentage of 30 % was derived based on the results of this study.

In order to derive AUC estimates for humans after dermal exposure, ECHA (2015) utilized information from two PBPK studies (Mielke et al., 2011 and Yang et al., 2013) in order to calculate dermal AUCs for a dermally absorbed dose of 100 µg/kg bw.

It was calculated by ECHA (2015) that an oral dose of 100 µg/kg/d corresponds to an oral AUC of 29.2 nMol × h according to the Mielke model. In mice, an oral dose of 100 µg/kg bw/d yields an AUC of 0.244 nMol × h. By using an external dermal dose of 0.542

µg/kg bw per day (finger contact to thermal paper once a day) and a dermal absorption figure of 10 % (leading to a dermally absorbed dose of 0.0542 µg/kg bw per day), a dermal AUC of 0.19 nMol × h is obtained. By scaling to a dermally absorbed dose of 100 µg/kg/d, human dermal AUCs of 350.6 and 329.5 nMol × h were obtained from the Mielke and Fisher/Yang models, respectively, assuming linear kinetics.

Taking the dermal absorption figure of 30 % as obtained from the study described in section 7.9.1 instead of 10 % dermal absorption, the human dermal AUCs would be the same. This is because the changes in the dermally absorbed dose and human dermal AUC would cancel out.

According to ECHA (2015) the DNEL for the dermally absorbed dose is calculated as follows:

$$\text{DNEL dermally abs.} = \left(\frac{\text{BMDL}_{10/\text{Mouse / Tyl}}}{\left(\frac{\text{AUC dermal abs. Human}}{\text{AUC Oral abs. Mouse}} \right)} \right) \Big/ \text{AF (2.5 x 10 x 6)}$$

The dermal human AUC of 350.6 nMol × h is divided by the mouse oral AUC of 0.244 nMol × h yields a conversion factor of 1436.9.

The BMDL(10) of 8960 µg/kg/day as point of departure for DNEL derivation is converted to a human equivalent dermal dose (HED_{dermal}) by using this conversion factor (8960 µg/kg/day / 1436.9) resulting in a HED_{dermal} of 6.24 µg/kg bw/d.

The total assessment factor applied to HED_{dermal} is 150 for the general population (2.5 for toxicodynamic interspecies differences, 10 for interindividual (human) variability and 6 as the already discussed additional factor). The resulting DNEL for the dermally absorbed dose in the general population is **0.042** µg/kg bw/d.

ECHA (2015) suggested that the DNEL (for the dermally absorbed dose) of roughly 0.05 µg/kg bw/d (based on the calculated value of 0.04 µg/kg bw/d) should be rounded to 0.1 µg/kg bw/d, because a dermal biotransformation (i.e. inactivation) of 50 % due to skin metabolism was assumed (however, there was a lack of reliable data on the extent of BPA metabolism in skin at that time).

The new in vitro dermal absorption study described in section 7.9.1 of this document, however, indicated that metabolism takes place in human skin samples, but that the extent of metabolism is around 10 %. Therefore, the eMSCA suggests to keep the **DNEL for the dermally absorbed dose** for the general population at 0.042 µg/kg bw/d (rounded: **0.05 µg/kg bw/d**).

In the 2015 update of the CSR the lead registrant used an alternative approach based on pharmacokinetic principles and allometric scaling to calculate the dermal systemic DNEL. The registrant used this alternative approach because the data (from Doerge et al., 2011) used by EFSA (2015) to calculate the AUC for adult mice orally dosed with 100 µg/kg were associated with a high degree of uncertainty due to analytical difficulties in measuring very low serum concentrations. EFSA (2015) had used three approaches handling serum concentrations below the limit of detection and had derived an AUC value of 0.244 nM×h and an uncertainty range of 0.108–1.257 nM×h.

Based on the relationship between systemic clearance (CL), dose and AUC (AUC = dose/CL) and on the allometric scaling of clearance with body weight (BW, kg) ($CL = a \times BW^b$), the lead registrant performed a regression analysis using data from several toxicokinetic studies with oral dosing over a wide dose range in different species to derive estimates for the scaling parameters a and b. By using this method, the registrant determined parameter a as 36.5 L/h and the exponent b as 0.92. The latter parameter was close to unity, indicating that the predicted clearance scales almost linearly with body weight (Poet and Hays, 2017).

The predicted oral AUC for mice dosed with 100 µg/kg bw was 2.9 nM×h, which is roughly by a factor of 10 higher compared to the EFSA/ECHA (2015) value described above.

Based on the Mielke et al. (2011) study, a dermal AUC of 697 pg/ml × h was calculated for an external dermal dose of 0.97 µg/kg/d assuming 100 % dermal absorption. Scaling to an external dose of 100 µg/kg bw yields a dermal AUC of 314 nM×h. This is divided by 3 to cover 30 % dermal absorption leading to a dermal AUC of 94.2 nM×h.

From the oral BMDL of 8960 µg/kg bw/d the corrected starting point was calculated by the following equation:

8960 µg/kg bw/d × 2.9/94.2 = 275.8 µg/kg/d

The corrected starting point was then divided by an overall assessment factor of 150 (essentially the same as used in the EFSA/ECHA (2015) evaluations) yielding **an external dermal DNEL** of **1.84** µg/kg bw/d. This yields a **DNEL for the dermally absorbed dose** of 0.55 µg/kg bw/d when assuming a dermal absorption of 30 %.

Due to the approximately 10-fold higher oral AUC for mice that was used in the industry approach, a 10-fold higher **DNEL for the dermally absorbed dose** was calculated. It is noted that the oral AUC for mice as predicted from pharmacokinetic principles and allometric scaling is also associated with a great uncertainty due to the scattering of the experimental data points around the predicted relationship (cf. page 130 of the leaddossier). The scattered data show a lab-specific bias in the mouse and monkey data due to differences in the administration procedures (gavage *vs.* oral bolus) and vehicles (ethanolic solution vs. corn oil) (see Figure 2 and Table 1 of Poet and Hays, 2017). Moreover, some mouse data should additionally be excluded because of a unrealistically large elimination half life or a too high dose (EFSA, 2015). Finally, the obvious difference in the clearance of monkeys and humans is not well reflected by the predicted allometric relationship. Overall, the eMSCA concludes that the dermal DNEL derived by the industry approach is associated with a significant uncertainty as well.

Inhalation DNEL, systemic, general population

Starting point: a NOAEC of 10 mg/m^3 air was derived from a subchronic (13 week) inhalation study performed in the rat based on (Testing Laboratory, 1988) based on decreased body weights in males and females and decreased absolute liver weights in males, increased alkaline phosphatase in females and increased urea nitrogen in males at 10 mg/m^3 BPA) (Testing Laboratory, 1988).

100 % inhalation absorption is assumed for animals and humans. The first pass effect is not of relevance here. As animals were exposed 6 hrs/5d/week over 13 weeks and for human population, 24 h exposure is assumed, the corrected starting point according to the REACH guidance (Figure R. 8-2) is 1.79 mg/m^3 (10 mg/m^3 x 0.25 (6h/d/24h/d) x 0.71 (5days/7days) = 1.79 mg/m^3).

The exceptions are the scenarios PVC articles and thermal paper for consumers. The exposure time is 8 h (10 mg/m³ x 0.75 (6h/d/8h/d) x 0.71 (5 days/7 days)) yielding an inhalation DNEL of 5.36 mg/m^3.

Assessment factors:

- Interspecies differences: 2.5

- Intraspecies differences for Consumers/man exposed via environment (MvE): 10

- differences in duration of exposure: 2 (extrapolation from subchronic to lifetime)

- dose-response and endpoint specific/severity issues: 1

- quality of the database: 1

Overall Assessment factor: 50

Long-term inhalation DNEL for chronic-systemic effects: 1.79 mg/m^3/ 50 = 0.036 mg/m^3 (rounded value)

Exception PVC articles and thermal paper: 5.36 mg/m^3/ 50 = 0.11 mg/m^3

Inhalation DNEL, local, general population

Starting point: a NOAEC of 10 mg/m^3 air was derived from a subchronic (13 week) inhalation study performed in the rat based on reversible epithelial hyperplasia and chronic inflammation in the nasal cavity in males and females at 50 mg/m^3 (Testing Laboratory, 1988). As animals were exposed 6 hrs/5d/week over 13 weeks and for human population, 24 h exposure is assumed, the corrected starting point according to the REACH guidance (Figure R. 8-2) is 1.79 mg/m^3.

100 % inhalation absorption is assumed for animals and humans. The first pass effect is not of relevance here. As animals were exposed 6 hrs/5d/week over 13 weeks and for human population, 24 h exposure is assumed, the corrected starting point according to the REACH guidance (Figure R. 8-2) is 1.79 mg/m^3 (10 mg/m^3 x 0.25 (6h/d/24h/d) x 0.71 (5days/7days) = 1.79 mg/m^3 (10 mg/m^3 x 0.25 (6h/d/24h/d) x 0.71 (5days/7days) = 1.79 mg/m^3).

The exception are the scenarios PVC articles and thermal paper for consumers. The exposure time is 8 h (10 mg/m3 x 0.75 (6h/d/8h/d) x 0.71 (5days/7days))yielding an inhalation DNEL of 5.36 mg/m^3.

Assessment factors:

- Interspecies differences: 2.5

- Intraspecies differences for Consumers/man exposed via environment (MvE): 10

- differences in duration of exposure: 2 (extrapolation from subchronic to lifetime)

- dose-response and endpoint specific/severity issues: 1

- quality of the database: 1

Overall Assessment factor: 50

Long-term inhalation DNEL for chronic-systemic effects: 1.79 mg/m^3/ 50 = 0.036 mg/m^3 (rounded value)

Exception PVC articles and thermal paper: 5.36 mg/m^3/ 50 = 0.11 mg/m^3

Table 1

CRITICAL DNELS/DMELS FOR THE GENERAL POPULATION					
Endpoint of concern	**Type of effect**	**Critical study(ies)**	**Corrected dose descriptor(s) (e.g. NOAEL, NOAEC)**	**DNEL/ DMEL**	**Justification/ Remarks**
Oral: Repeat dose systemic effects [1)]	Effects on mammary gland, reproductive, neurobehavioural, immune and metabolic systems	See ECHA 2015	609 µg/kg bw/d	4 µg/kg bw/d	See ECHA 2015
Dermal: Repeat dose systemic effects [1)]	Effects on mammary gland, reproductive, neurobehavioural, immune and metabolic systems	See ECHA 2015	609 µg/kg bw/d	0.05 µg/kg bw/d	See ECHA 2015
Inhalation: Repeat dose systemic effects	decreased body weights in males and females; decreased absolute liver weights in males, increased alkaline phosphatase in females and increased urea nitrogen in males	Testing Laboratory, 1988	NOAEC of 10 mg/m^3 air;	0.036 mg/m^3 Exception: PVC articles **and** thermal paper: = 0.11 mg/m^3	
Inhalation: repeat dose local effects	reversible epithelial hyperplasia and chronic inflammation in the nasal cavity	Testing Laboratory, 1988	NOAEC of 10 mg/m^3 air;	0.036 mg/m^3 Exception: PVC articles and thermal paper: = 0.11 mg/m^3	

1) In accordance with the lead registrant's suggestion, oral and dermal systemic values for short-term and long-term exposure should be the same.

B. Corrigendum for Section 7.12.

This section supersedes the section 7.12.1. (p. 43-48) of the original Substance Evaluation Report.

7.12. Exposure assessment7.12.1. Human health

Consumer

During the SEv procedure four relevant consumer exposure scenarios were identified,discussed and assessed:

- Consumer use of thermal paper
- Consumer use of articles made of PVC
- Consumer use of articles made of polycarbonate
- Consumer use of articles of epoxy resins

Preface
The exposure estimations were carried out in accordance with the ECHA guidance on Information Requirements and Chemical Safety Assessment, Chapter R.15: Consumer exposure estimation, Version 2 (ECHA, April 2010). Assessments of exposure levels for the consumers were performed during the evaluation period of SEv-procedure (that means in 2012) with the tool ECETOC Targeted Risk Assessment Programme, Version 2.0 (ECETOC, 2009). Deviations from these estimates were justified by appropriate studies. The values used are based on an intense discussion with the lead registrant, who in consequence updated his chemical safety report (October 2012). Due to this process and the resulting documents the following assessment was conducted.

Consumer use of thermal paper

EC (2008a, p. 23 HS) has concluded that the use of thermal paper is considered to result in negligible potential for consumer exposure in comparison with other sources.

For this use AC 8 (Paper articles), especially the subcategory "Printed paper" covering papers, magazines and books, is relevant.

Oral exposure
The oral route is not relevant.

Dermal exposure
The consumer use of thermal paper has been evaluated in two important publications, done by Biedermann (2010) and Lassen (2011).
Lassen (2011) expects that consumers handle thermal paper up to 4.6 times per day using 8 fingers. Biedermann (2010) has shown that typically 1.13 µg of BPA are present on the skin of each finger (if thermal paper is touched with dry fingers). In comparison results of Lassen (2011) shows an average of 1.38 µg of BPA present on the skin of each finger(if thermal paper is touched with dry fingers).
In the publication of Biedermann (2010) additionally data on a specific quality of thermal paper were included. In this case Biedermann (2010) has demonstrated that 3 µg of BPA being present on the skin of each dry finger. Based on the assumptions of Lassen (2011) and the results of Biedermann (2010) the daily uptake can be calculated as follows:

4.6 (times per day) x 8 (fingers) x 3 µg (BPA concentration on the skin of each finger) = 110 µg.

Based on a body weight of 60 kg (110 µg:60 kg) a systemic exposure of **1.84×10^{-3} mg/kg bw day** can be calculated.

This assessment is based on the relevant literature (Biedermann 2010 and Lassen 2011) and uses the conservative assessments of these authors for the estimates of consumer exposure.The calculation is based on 3µg BPA per fingertip as highest value of Biedermann (2010) and not on an average of 1,13 µg per fingertip. Additionally 8 fingertips (not only 2) and 4,6 contacts per day from Lassen (2011) were used for the calculation.
Based on data of Liao (2011) an average systemic exposure of 1.08×10^{-6} mg/kg bw day can be calculated for a body weight of 60 kg . Using the data for the 95% percentile a systemic exposure of 3.35×10^{-5} mg/kg bw day is obtained. This value is by a factor of 50 below the systemic exposure of 1.84×10^{-3} mg/kg bw day as based on Biedermann (2010) and Lassen (2011).

Based on the data in Geens (2012a) an average systemic exposure of 2.75×10^{-5} mg/kg bw day can be calculated for a body weight of 60 kg.This value which is by a factor of 70 below the systemic exposure of 1.84×10^{-3} mg/kg bw day as based on Biedermann (2010) and Lassen (2011).

Inhalative exposure

Operational conditions:
Duration**-**time: 8h/day
Frequency of use: 365 days per year
Concentration: < 3 %
risk management measures related to consumers: no
This consumer use is an indoor use.

Model settings:
Molecular weight :228.29 g/mol
Vapour pressure: 4.12×10^{-9} hPa
Amount of product used per application: < 50 g
Product ingredient fraction by weight : 0.03

The inhalative exposure was calculated by ECETOC TRA : 4.57×10^{-3} (mg/kg bw day) equivalent to 2.50×10^{-2} mg/m3.

Total Exposure of consumers in AC 8
Member State concludes that the total exposure of consumers in AC 8 due to thermal paper was **6.41×10^{-3} mg/kg bw day.**

Consumer use of articles made of PVC

EC (2008a, p. 23 HS) concluded that the use of articles made of PVC is considered to result in negligible potential for consumers exposure.
For this use the catagories AC 2 (Machinery, mechanical appliances, electrical/electronic articles) and AC 13 (Plastic articles) are relevant.
It is not possible to calculate exposure by use of electrical/electronic articles (AC 2) with ECETOC TRA.
ECETOC (2009, p. 80) explain as follows: "Consumer use may not be totally ruled out for the category but there is a lack of adequate information for estimating a relevant value of consumer exposure at the present time."

In AC 13 it is necessary to differentiate 3 subcategories:
- Plastics –larger articles, covering a plastic chair, PVC-flooring or a lawn mover
- Plastics – small articles, covering a ball pen or a mobile phone.
- Toys

Operational conditions:
Duration**-**time: 8h/day for larger and small plastic articles and
24h/day for toys (as a worst case scenario for children)

Frequency of use: 365 days per year
Concentration: < 0.2 %
amount of product: < 1 KG
risk management measures related to consumers: no

Model settings:
Molecular weight :228.29 g/mol
Vapour pressure: 4.12 x 10^{-9} hPa
Amount of product used per application:1000 g
Product ingredient fraction by weight : 0.002

AC 13 (Plastic, larger articles)
Oral exposure: route not relevant – reasoning: Oral exposure does not occur as part of the intended product use (ECETOC,2009, p.87)
Dermal systemic exposure (mg/kg bw day): 2.92 x 10^{-1}
Inhalative exposure (mg/m3): 1.00 x 10^{-1}
Inhalative exposure (mg/kg bw day):1.83 x 10^{-2}

AC 13 (Plastic, small articles)
Oral exposure (mg/kg bw day): 2.00 x 10^{-3}
Dermal systemic exposure (mg/kg bw day):1.19 x 10^{-3}
Inhalative exposure (mg/m3): 1.00 x 10^{-1}
Inhalative exposure (mg/kg bw day):1.83 x 10^{-2}

AC 13 (Toys)
Oral exposure (mg/kg bw day):2.00 x 10^{-3}
Dermal systemic exposure (mg/kg bw day): 1.11 x 10^{-1}
Inhalative exposure:ECETOC TRA gives no data - reasoning: Formulations contain negligible amounts of volatiles or particulate matter- no inhalation exposure, (ECETOC,2009, p.87)

Total exposure of consumers in AC 13 (concentrations in mg/kg bw day)

AC 13 (Plastic, larger articles)	**3.10 x 10^{-1}**
AC 13 (Plastic, small articles)	**2,15 x 10^{-2}**
AC 13 (Toys)	**1.13 x 10^{-1}**

Consumer Use of Articles made of Polycarbonate

For this use the categories AC 1 (Vehicles), AC 2 (Machinery, mechanical appliances, electrical/electronic articles) and AC 13 (Plastic articles) are relevant.

Operational conditions:
Duration-time: <24h/day (as a worst case scenario)
Frequency of use: 365 days per year
Concentration of substance < 100 ppm (maximum); the typical concentration is < 10 ppm
Risk management measures related to consumers: no

Model settings:
Molecular weight: 228.29 g/mol
Vapour pressure: 4.12 x 10^{-9} hPa
Product ingredient: 100 ppm
Fraction by weight : 1.00 x 10^{-4}

Long-term exposure
It is not possible to calculate exposure by use of vehicles (AC 1) and use of machinery and mechanical appliances and electrical/electronic articles (AC 2) with ECETOC TRA. ECETOC (2009, p. 80) explain as follows: "Consumer use may not be totally ruled out for the category but there is a lack of adequate information for estimating a relevant value of consumer exposure at the present time."

AC 13 (Plastic, larger articles)
Oral exposure: route not relevant (ECETOC, 2009, p.87)
Dermal systemic exposure (mg/kg bw day): 1.46 x 10^{-2}
Inhalative exposure (mg/m^3): 3.86 x 10^{-5}
Inhalative exposure (mg/kg bw day*):* 7.06 x 10^{-6}

AC 13 (Plastic, small articles)
Oral exposure (mg/kg bw day): 1.67 x 10^{-4}
Dermal systemic exposure (mg/kg bw day): 5.95 x 10^{-5}
Inhalative exposure (mg/m^3): 3.86 x 10^{-5}
Inhalative exposure (mg/kg bw day): 7.06 x 10^{-6}

Total exposure of consumers in AC 13 (concentrations in mg/kg bw day)
AC 13 (Plastic, larger articles) : **1.47 x** 10^{-2}
AC 13 (Plastic, small articles) : **2.34 x 10^{-4}**

Refinement of dermal exposure estimation
The study of Mercea (2009)shows that the he release of BPA from polycarbonate does not correlate with the content of free Bisphenol A . The release of BPA is inhibited due to incorporation in the polymer matrix. Mercea (2009) reported that BPA only occurs if polycarbonate is subject to significant thermal, chemical or mechanical stress .For most articles made of polycarbonate any consumer contact is rather short and limited to skin contact**.** Typical examples for articles made of polycarbonate are casings of mobile phones and keypads.

The refinement done by the lead-registrant was based on a worst case scenario:
As an example for AC 13 (Plastic, larger articles) a chair made of polycarbonate was used. An adult consumer would have permanent dermal contact to the polycarbonate chair for 24 hours/day at a surrounding temperature of 40 °C. This temperature was selected to cover the same conditions as in a study with sweat simulant. In this study polycarbonate films were exposed to sweat simulant for 24 hours at 40 °C. The refinement was done with the highest release (business confidential data) of BPA from the films in this study. The relevant skin contact area in accordance with ECETOC (2012) is half of the default whole body skin surface area: 17.500 cm^2:2 = 8.750 cm^2. Considering a conservative default body weight of 60 kg the worst case dermal exposure of consumers from a polycarbonate chair was **0.57 µg/kg bw/day equivalent to 0.00057 mg/kg bw/day.**

Consumer Use of Articles made of Epoxy Resins

For this use the categories AC 1 (Vehicles), AC 2 (Machinery, mechanical appliances, electrical/electronic articles) and AC 13 (Plastic articles) are relevant.
Epoxy resins are produced by mixing BPA and epichlorohydrin. The reaction product is a basic monomer unit of epoxy resin called BADGE (or DGEBA), CAS No 25068-38-6. BADGE has been subject to a substance evaluation by Denmark in 2015. The evaluation is currently still ongoing.

The Epoxy Resin Committee states that epoxy resins in liquid form can contain a maximum of 10 ppm of residual unreacted BPA. For solid epoxy resins the maximum amount is 65 ppm of BPA.[1]

Notwithstandig the above, consumer use of articles made of epoxy resins was evaluated as decribed in the preface.

Operational conditions:
Duration-time: <24h/day (as a worst case scenario)
Frequency of use: 365 days per year

[1] http://www.epoxy-europe.eu/uploads/Modules/Resources/epoxy_erc_bpa_whitepapers_summarypaper.pdf

Concentration of substance :< 10 ppm
Risk management measures related to consumers: no

Model settings:
Molecular weight: 228.29 g/mol
Vapour pressure: 4.12 x 10^{-9} hPa
Product ingredient: 10 ppm
Fraction by weight : 1.00 x 10^{-5}

Long-term exposure
It is not possible to calculate exposure by use of vehicles (AC 1) and use of machinery and mechanical appliances and electrical/electronic articles (AC 2) with ECETOC TRA. ECETOC (2009, p. 80) explain as follows: "Consumer use may not be totally ruled out for the category but there is a lack of adequate information for estimating a relevant value of consumer exposure at the present time."

AC 13 (Plastic, larger articles)
Oral exposure: route not relevant (ECETOC,2009, p.87)
Dermal systemic exposure (mg/kg bw day): 1.46 x 10^{-3}
Inhalative exposure (mg/m^3): 3.86 x 10^{-5}
Inhalative exposure (mg/kg bw day): 7.06 x 10^{-6}

AC 13 (Plastic, small articles)
Oral exposure (mg/kg bw day): 1.67 x 10^{-5}
Dermal systemic exposure (mg/kg bw day): 5.95 x 10^{-6}
Inhalative exposure (mg/m^3): 6.47 x 10^{-6}
Inhalative exposure (mg/kg bw day): 1.18 x 10^{-6}

Total exposure of consumers (mg/kg bw day):
AC 13 (Plastic, larger articles) **1.47 x 10^{-3}**
AC 13 (Plastic, small articles) **2.38 x 10^{-5}**

Independent of these current uses EC (2003) has identified the following consumer uses for epoxy resin hardeners:

- Marine antifouling paints (content of epoxy resin in paint: 40%, content of residual BPA in epoxy resin: 10 ppm)
- wood varnish (content of epoxy resin in paint: 40%, content of residual BPA in epoxy resin: 10 ppm)
- wood fillers (content of epoxy resin: 20%, content of residual BPA in epoxy resin: 10 ppm)
- adhesives (content of residual BPA in epoxy resin: 10 ppm)

Based on data from EC (2003) the dermal exposure (mg/kg bw day) can be calculted as follows:

- Marine antifouling paints: 4.83 x 10^{-4}
- Wood varnish: 6.00 x 10^{-5}
- Wood fillers: 1.50 x 10-4
- Adhesives:1.67 x 10^{-5}

C. Corrigendum for Section 7.13.

This section supersedes the section 7.13. (p. 51-56) of the original Substance Evaluation Report).

7.13.Risk characterisation

The eMSCA presents the calculations of exposure and DNEL derivation in the sections above. In the following section these values are used by the eMSCA for the calculation of risk characterization ratios.

Risk characterisation for consumers

The following four relevant consumer exposure scenarios were identified,discussed and assessed previously in section 7.12.1.2:

- Consumer use of thermal paper
- Consumer use of articles made of PVC
- Consumer use of articles made of polycarbonate
- Consumer use of articles of epoxy resins

Consumer use of thermal paper

Table 2

RCR FOR DERMAL EXPOSURE OF CONSUMERS FOR USE OF THERMAL PAPER			
Operation	**Systemic Dermal exposure (mg/kg bw/day)**	**DNEL for dermal exposure (mg/kg bw/day)**	**Risk characterisation ratio for dermal exposure**
AC 8	1.84×10^{-3} Assuming 100 % absorption	5.0×10^{-5}	37
	5.52×10^{-4} Adaption to 30% absorption	5.0×10^{-5}	11

An adaption was performed for exposure calculation to reflect the 30% absorption rate of human skin.
The eMSCA used a very conservative exposure assessment in combination with a conservative DNEL derivation. Furthermore, eMSCA acknowledges the evaluation of RAC (ECHA 2015) on the restriction proposal of BPA in thermal paper which concluded with elevated RCR-values for workers only. Therefore and since the use of BPA in thermal paper will be restricted from 2020, the eMSCA concludes on no further action in the field of consumer of thermal paper.

Table 3

RCR FOR INHALATIVE EXPOSURE OF CONSUMERS FOR USE OF THERMAL PAPER			
Operation	**Inhalative exposure (mg/m^3)**	**DNEL for inhalative exposure (mg/m^3)**	**Risk characterisation ratio for inhalative exposure**
AC 8	2.5×10^{-2}	1.1×10^{-1}	0.227

The eMSCA concludes that the RCR for thermal paper and inhalative exposure is 0.227.

Table 4

RCR FOR TOTAL EXPOSURE OF CONSUMERS FOR USE OF THERMAL PAPER			
Operation	**Total exposure (mg/kg bw/day)**	**DNEL for total exposure (mg/kg bw/day)**	**Risk characterisation ratio for total exposure**
AC 8	6.41×10^{-3} assuming 100 % dermal absorption	4.0×10^{-3}	1.60
	5.12×10^{-3} adaption to 30% dermal absorption	4.0×10^{-3}	1.28

The eMSCA concludes that the RCR for the consumer use of thermal paper is above 1. However, since the use of BPA in thermal paper will be restricted from 2020, the eMSCA concludes on no further action in the field of consumer of thermal paper.

Consumer use of articles made of PVC

The registrants have divided the article category 13 in three subcategories:
- Plastics – larger articles,
- Plastics – small articles and
- Toys.

Table 5

RCR FOR ORAL EXPOSURE OF CONSUMERS FOR ARTICLES MADE OF PVC			
Operation	**Oral exposure (mg/kg bw/day)**	**DNEL for oral exposure (mg/kg bw/day)**	**Risk characterisation ratio for oral exposure**
AC 13 larger article	Not applicable	4.0×10^{-3}	Not derived
AC 13 small article	2.0×10^{-3}	4.0×10^{-3}	0.5
AC 13 toys	2.0×10^{-3}	4.0×10^{-3}	0.5

The eMSCA concludes that the RCR for PVC articles and oral exposure is 0.5.

Table 6

RCR FOR DERMAL EXPOSURE OF CONSUMERS FOR ARTICLES MADE OF PVC			
Operation	**Systemic Dermal exposure (mg/kg bw/day)**	**DNEL for dermal exposure (mg/kg bw/day)**	**Risk characterisation ratio for dermal exposure**
AC 13 larger article	2.92×10^{-1} Assuming 100 % absorption	5.0×10^{-5}	5840
	8.76×10^{-2}	5.0×10^{-5}	1752

	Adaption to 30 % absorption		
AC 13 small article	1.19×10^{-3} Assuming 100 % absorption	5.0×10^{-5}	24
	3.57×10^{-4} Adaption to 30% absorption	5.0×10^{-5}	7
AC 13 toys	1.11×10^{-1} Assuming 100 % absorption	5.0×10^{-5}	2220
	3.33×10^{-2} Adaption to 30 % absorption	5.0×10^{-5}	666

An adaption was performed for exposure calculation to reflect the 30% absorption rate of human skin as determined in the dermal absorption study requested during SEV.

The eMSCA concludes that the RCR for all PVC articles and dermal exposure is clearly above 1.[2]

Table 7

RCR FOR INHALATIVE EXPOSURE OF CONSUMERS FOR ARTICLES MADE OF PVC			
Operation	**Inhalative exposure (mg/ m³)**	**DNEL for inhalative exposure (mg/ m³)**	**Risk characterisation ratio for inhalative exposure**
AC 13 larger article	1.0×10^{-1}	1.1×10^{-1}	0.909
AC 13 small article	1.0×10^{-1}	1.1×10^{-1}	0.909
AC 13 toys	No data		Not derived

The eMSCA concludes that the RCR for PVC articles and inhalative exposure is 0.909.

Table 8

RCR FOR TOTAL EXPOSURE OF CONSUMERS FOR ARTICLES MADE OF PVC			
Operation	**Total exposure (mg/kg bw/day)**	**DNEL for total exposure (mg/kg bw/day)**	**Risk characterisation ratio for total exposure**
AC 13 larger article	3.1×10^{-1} assuming 100 % dermal absorption	4.0×10^{-3}	78
	1.06×10^{-1} adaption to 30% dermal absorption	4.0×10^{-3}	27

[2] In 2018, most of the registrants had the usage of BPA withdrawn in PVC articles for consumer use (including toys). Therefor, the eMSCA concludes on no further action in the field of consumer articles made of PVC.

AC 13 small article	2.15×10^{-2} assuming 100 % dermal absorption	4.0×10^{-3}	5.38
	2.07×10^{-2} adaption to 30% dermal absorption	4.0×10^{-3}	5.18
AC 13 toys	1.13×10^{-1}	4.0×10^{-3}	28
	$3,53 \times 10^{-2}$ adaption to 30% dermal absorption	4.0×10^{-3}	8.83

The eMSCA concludes that the RCR for consumer use of all PVC articles is clearly above 1. [3]

Consumer use of articles made of polycarbonate

The registrants have divided the article category 13 in two subcategories:
- Plastics – larger articles and
- Plastics – small articles.

Table 9

RCR FOR ORAL EXPOSURE OF CONSUMERS FOR ARTICLES MADE OF PC			
Operation	**Oral exposure (mg/kg bw/day)**	**DNEL for oral exposure (mg/kg bw/day)**	**Risk characterisation ratio for oral exposure**
AC 13 larger article	Not applicable	4.0×10^{-3}	Not derived
AC 13 small article	1.67×10^{-4}	4.0×10^{-3}	0.042

The eMSCA concludes that the RCR for small polycarbonate articles and oral exposure is below 1.

The dermal exposure for larger articles made of polycarbonate was refined by the lead registrant based on a worst case scenario.

Table 10

RCR FOR DERMAL EXPOSURE OF CONSUMERS FOR ARTICLES MADE OF PC			
Operation	**Dermal exposure (mg/kg bw/day)**	**DNEL for dermal exposure (mg/kg bw/day)**	**Risk characterisation ratio for dermal exposure**
AC 13 larger article	1.46×10^{-2} Assuming 100 % absorption	5.0×10^{-5}	292
	4.38×10^{-3} Adaption to 30 % absorption	5.0×10^{-5}	88

[3] See Footnote 5 on page 54.

AC 13 larger articles, refinement	5.7×10^{-4} Assuming 100 % absorption	5.0×10^{-5}	11.4
	1.71×10^{-4} Adaption to 30 % absorption	5.0×10^{-5}	3.4
AC 13 small article	5.95×10^{-5} Assuming 100 % absorption	5.0×10^{-5}	1.19
	1.785×10^{-5} Adaption to 30 % absorption	5.0×10^{-5}	0.36

An adaption was performed for exposure calculation to reflect the 30% absorption rate of human skin.

The eMSCA concludes that the RCR for all polycarbonate articles and dermal exposure is above 1. After adaption to 30 % absorption rate, the RCR values of the worst case scenario for larger articles amounts to 3.4 and the RCR for small articles is below 1.

Table 11

RCR FOR INHALATIVE EXPOSURE OF CONSUMERS FOR ARTICLES MADE OF PC			
Operation	**Inhalative exposure (mg/ m³)**	**DNEL for inhalative exposure (mg/ m³)**	**Risk characterisation ratio for inhalative exposure**
AC 13 larger article	3.86×10^{-5}	3.6×10^{-2}	0.0011
AC 13 small article	3.86×10^{-5}	3.6×10^{-2}	0.0011

The eMSCA concludes that the RCR for all polycarbonate articles and inhalative exposure is below 1.

Table 12

RCR FOR TOTAL EXPOSURE OF CONSUMERS FOR ARTICLES MADE OF PC			
Operation	**Total exposure (mg/kg bw/day)**	**DNEL for total exposure (mg/kg bw/day)**	**Risk characterisation ratio for total exposure**
AC 13 larger article	1.47×10^{-2} assuming 100 % absorption	4.0×10^{-3}	3.68
	$4{,}39 \times 10^{-3}$ adaption to 30% dermal absorption	4.0×10^{-3}	1.10
AC 13 larger articles, refinement	$1{,}78 \times 10^{-4}$ adaption to 30% dermal absorption	4.0×10^{-3}	0.0445
AC 13 small article	2.34×10^{-4} assuming 100 % dermal absorption	4.0×10^{-3}	0.0585

	1,92 x 10^{-4} adaption to 30% dermal absorption	4.0 x 10^{-3}	0.048

The eMSCA concludes that the RCR for consumer use of small polycarbonate articles is below 1 and the RCR for consumer use of larger articles is above 1.

Consumer use of articles made of expoxy resins

The registrants have divided the article category 13 in two subcategories:

- Plastics – larger articles and
- Plastics – small articles.

Table 13

RCR FOR ORAL EXPOSURE OF CONSUMERS FOR ARTICLES MADE OF EPOXY RESINS			
Operation	**Oral exposure (mg/kg bw/day)**	**DNEL for oral exposure (mg/kg bw/day)**	**Risk characterisation ratio for oral exposure**
AC 13 larger article	Not applicable	4.0 x 10^{-3}	Not derived
AC 13 small article	1.67 x 10^{-5}	4.0 x 10^{-3}	0.0042

The eMSCA concludes that the RCR for small epoxy resin articles and oral exposure is below 1.

Table 14

RCR FOR DERMAL EXPOSURE OF CONSUMERS FOR ARTICLES MADE OF EPOXY RESINS			
Operation	**Systemic Dermal exposure (mg/kg bw/day)**	**DNEL for dermal exposure (mg/kg bw/day)**	**Risk characterisation ratio for dermal exposure**
AC 13 larger article	1.46 x 10^{-3} Assuming 100 % absorption	5.0 x 10^{-5}	29.2
	4.38 x 10^{-4} Adaption to 30 % absorption	5.0 x 10^{-5}	8.8
AC 13 small article	5.95 x 10^{-6} Assuming 100 % absorption	5.0 x 10^{-5}	0.119
	1.785 x 10^{-6} Adaption to 30 % absorption	5.0 x 10^{-5}	0.036

An adaption was performed for exposure calculation to reflect the 30 % absorption rate of human skin.

The eMSCA concludes that the RCR for larger articles made of expoxy resins and dermal exposure is clearly above 1. Furthermore, eMSCA concludes that the RCR for small articles made of expoxy resins and dermal exposure is below 1.

Table 15

RCR FOR INHALATIVE EXPOSURE OF CONSUMERS FOR ARTICLES MADE OF EPOXY RESINS			
Operation	**Inhalative exposure (mg/m³)**	**DNEL for inhalative exposure (mg/m³)**	**Risk characterisation ratio for inhalative exposure**
AC 13 larger article	3.86×10^{-5}	3.6×10^{-2}	0.0011
AC 13 small article	6.47×10^{-6}	3.6×10^{-2}	0.00018

The eMSCA concludes that the RCR for all epoxy resin articles and inhalative exposure is below 1.

Table 16

RCR FOR TOTAL EXPOSURE OF CONSUMERS FOR ARTICLES MADE OF EPOXY RESINS			
Operation	**Total exposure (mg/kg bw/day)**	**DNEL for total exposure (mg/kg bw/day)**	**Risk characterisation ratio for total exposure**
AC 13 larger article	1.47×10^{-3} assuming 100 % dermal absorption	4.0×10^{-3}	0.368
	$4{,}45 \times 10^{-4}$ adaption to 30% dermal absorption	4.0×10^{-3}	0.111
AC 13 small article	2.38×10^{-5} assuming 100 % dermal absorption	4.0×10^{-3}	0.00595
	$1{,}97 \times 10^{-5}$ adaption to 30% dermal absorption	4.0×10^{-3}	0.00493

The eMSCA concludes that the RCR for consumer use of articles made of expoxy resins is below 1.

References

Committee for Risk Assessment (RAC) Committee for Socio-economic Analysis (SEAC) (2015) Opinion on an Annex XV dossier proposing restrictions on Bisphenol A. Available at: http://echa.europa.eu/documents/10162/9ce0977b-3540-4de0-af6d-16ad6e78ff20.

EFSA (2015): Scientific opinion on the risks to public health related to the presence of BPA (BPA) in foodstuffs. EFSA Journal, 13(1):3978.

Poet T. and Hays S. (2017): Extrapolation of plasma clearance to understand species differences in toxicokinetics of bisphenol A. Xenobiotica. doi: 10.1080/00498254.2017.1379626. [Epub ahead of print]