The SCCS Response to the comments received during Public Consultation on Preliminary Opinion on BPA in clothing (SCCS/1620/20)

#	Organisation/ person	Comment	Section	The SCCS Response	Change(s) made in the Opinion
1	EPA (DK)	The Danish EPA holds the opinion that BPA should not be found in textiles. Even though the concentrations measured in textiles displays a relatively low exposure, it contributes to an exposure from a variety of sources. DK EPA holds the opinion that effects (e.g. endocrine disruption) of BPA observed at low doses, raises health concerns for consumers such as infants and young children or pregnant women. The majority of textiles does not contain BPA and it is highly questionable if added values are essential enough to justify the presence of a substance of very high concern in textiles.	4. CONCLUSION	The SCCS is providing EU Commission with safety assessment upon specific mandate. EU Commission is responsible for the follow-up of the risk management measures as well as for implementation in the EU legislation. This comment should therefore be sent directly to the mandating DG unit and concern, i.e. DG JUST E4: JUST-E4@ec.europa.eu	No change.
2	German Federal Institute for Risk Assessment (BfR)	P4 line 16-17 (and P32 line 13-14) It should be emphasized that the limit value derived by ECHA is based on default assumptions instead of BPA-specific migration rates and elicitation thresholds.	1. ABSTRACT	The SCCS agrees with the comment made and will adjust the opinion accordingly.	Change introduced under 3.3.2. migration experiments and 3.6.3 Risk assessment by SCCS.
3		P7 line 19-20 The ECHA support document for SVHC classification (2017) also discusses neurodevelopmental effects as a consequence of endocrine disruption. Thus, brain development should be added to the list of effects in addition to	2. MANDATE FROM THE EUROPEAN COMMISSION	Regarding the comments made around the section mandate from the European commission, no changes will be introduced in the opinion. The SCCS provides the EU Commission with scientific opinions on the safety of ingredients in specific consumer goods. Details of the assessment, such as the health effects under investigation, are stipulated in the EU commission	No change.

		those on the mammary gland, reproductive function and metabolism.		mandate provided to the SCCS and cannot be altered.	
4		The SCCS is referring to Xue et al. (2017) for the use of BPA derivatives in the production of polyester fabrics. Xue et al. (2017) mainly refer to a blog ("oecotextiles") which again cites a site to buy products. We do not think that this is a reliable source.	3.2 Function and uses	The evidence that Xue et al. (2017) presents goes back to a dissertation (Mousavi, 2004) where an antioxidant provided by industry was investigated, which has BPA as a precursor. This reference is considered reliable. The paragraph was changed to include the original references for BPA use in the production of textiles, instead of Xue et al. (2017).	Section 3.2 function and uses was re-written so that the original references were cited.
5		<u>P11 line 34</u> The BfR default migration rate of 0.5% was derived for dyes, while for hydrophobic and hydrophilic textile auxiliaries migration rates were set to 0.1 and 2%, respectively. Thus, for BPA with a logP of 3.3 to 3.5, a migration rate of 0.1% would be more appropriate. One should also note that these migration values were experimentally derived from studies conducted using artificial sweat solution which is a hydrophilic matrix (see also Krätke and Platzeck 2004). Thus, using those migration rates determined using artificial sweat for the 'dry exposure' scenario comes with some uncertainties. <u>P14 line 1</u> It is rather 'surface weight' than 'surface density'. In addition, it is possible to calculate the surface weights from the Wang et al. (2019) paper by using the tables in the Supplemental Information. This results in approximately 130 g/m2 for two of the textiles investigated and 330 g/m2 for the third one. <u>P14 line 53</u> Consider to replace 'more highly' with 'higher'	3.3 Exposure to BPA from clothing articles	<u>P11 line 34</u> The SCCS is thanking the BfR for pointing out the important information that the default migration values have been derived from experimental studies with artificial sweat solution. This is not completely clear in BfR (2012) and Kraetke & Platzek (2004) and probably has led to the use of this default value for dry clothes in Wang et al. (2019), whereupon the original SCCS approach was based. The calculations and the respective explanatory paragraph were revised. For adults, exposure to dry clothes was considered negligible in comparison to exposure to sweaty clothes for which now the specific migration rate into sweat derived by Wang et al. was used. The same approach was used for toddlers. <u>P14 line 1</u> Parameter D in the opinion will now be called 'surface weight'. The surface weights determined for three selected textiles, each representing either median or P95 of the concentration distribution of BPA in the used clothing samples from Wang et al. (2019), will be used in the exposure calculations. <u>P14 line 53</u> The opinion will be altered accordingly.	Changes were made to the opinion under section 3.3 Exposure to BPA from clothing articles. Changes were made to the opinion under 3.3.3.2 Parameterization and exposure estimates. The text was changed section 3.3

		P16 Table 3 This table is difficult to understand. The calculations mix up values derived by Wang et al. (2019) and own approaches. For example, Wang et al. use an absorption rate of 1% for the dry scenario citing amongst others BfR (2012). In that publication an absorption rate of 1% is recommended for dyes while for hydrophobic auxiliaries, a default migration rate of 50% is suggested. Since experimental data for BPA are available, we would recommend recalculating the data for the dry scenario using the same absorption rate as for the sweaty scenario.		P16 Table 3 The dry scenario is no longer used (see above). The exposure values based on migration into sweat were recalculated with default values for European consumers and the dermal absorption fraction of 0.3. We understand that BfR (2012) recommends a default penetration rate of 50% and a default migration rate of 0.1% for hydrophobic auxiliaries.	Dry scenario was taken out of Table 3 section 3.3.4.
6		P23 line 31-32 Sasso et al. (2020) reported that 71–99% of the applied BPA remained unabsorbed. Excluding the implausible value of 99% unabsorbed BPA of one participant reduces this range to 71–88%. Consequently, this would mean that 29–12% of BPA had been absorbed, but in the paper, they hypothesize that this "is likely an over-estimate due to the experimental variations in rinsate recovery as well as unaccounted amounts lost to the environment." Furthermore, they mention the possibility of BPA remaining in the dermis and epidermis without becoming systemically available. Actually, an absorption rate of 30% for the dermal route turned out to be physiologically implausible based on considerations regarding blood clearance and hepatic blood flow. So, for their experimental setting, the authors conclude: "This strongly suggests that the 12–29%,	3.4.2 Toxicokinetics and metabolism after dermal uptake	The SCCS considered all available information from different study types (i.e. *in vitro*, *in vivo* rodents and human) to select the dermal absorption value of 30%. In brief, dermal absorption can vary between 1.7 to 46 % *in vitro* using human skin, depending on the length of exposure. Whilst in many *in vitro* experiments the dermal absorption was determined to be lower than 30%, a skin reservoir effect could result in an underestimation of the daily exposure to BPA (ANSES, 2014). Studies in human volunteers are highly variable with absorption of BPA as high as 95-100% (Biedermann, 2010), suggesting that certain solvents may act as a penetration enhancer of BPA. An *in vivo* dermal rat study, demonstrated that 26% of the applied dose was absorbed (Marquet et al., 2011). Moreover, recent *in vitro* dermal penetration data for BPA, generated as part of the community rolling action plan (CoRAP) by ECHA, determined a dermal absorption of 16-20% (Toner et al. 2018). However, also in the latter study high variability was observed so that according to the SCCS Notes of Guidance, the mean + 2 SD should be used. This would result in a rounded value of 30% dermal absorption. This is similar to a value suggested in a previous assessment by SCENHIR (2015), where it	No change.

		being the complement of the portion recovered from the application site, was mostly lost to the environment rather than absorbed."		was determined that a worst-case estimate could be in the range of 25-30% dermal absorption. Altogether, the SCCS believes that a value of 30% dermal absorption can be justified for BPA.	
7		General comment The risk assessment approach used by SCCS is based on exposure data using experimentally determined migration rates, skin penetration rates as well as default assumptions. For derivation of the internal human equivalent dose (HEDi), an oral mouse study was used to derive a POD, and a HED was calculated based on experimental area-under-the-curve (AUC) values from a mouse study and PBPK model-based human AUC for free serum BPA in analogy to EFSA and ECHA assessments from 2015. To determine the HEDi, the fraction of free BPA/total BPA (i.e., 1%) in serum was taken into account. This HEDi was then compared to the systemic dose after dermal contact with textiles, taking skin penetration rates experimentally derived from in vitro studies into account. A very recent study (Sasso et al., 2020) experimentally determined free BPA serum AUCs after dermal application in human subjects. Since both mouse oral and human dermal studies were conducted using the same external dose, a HEDi could be derived by comparing the AUC mouse oral with the AUC human dermal. This direct approach, which is described below, eliminates the uncertainties concerning dermal penetration rates and dermal metabolism of BPA. The direct approach follows the approach	3.6.3 Risk assessment by SCCS	The fraction of free BPA cited as 7.35 nM x h will be corrected into 7.51 nM x h, as this value was incorrectly taken over from the paper by Sasso et al. (2020). The SCCS furthermore welcomes the critical reflection on the risk assessment approach taken in the present opinion of BPA in clothing. As with many substances, several possible approaches to the risk assessment are possible for BPA. It is reassuring to know that the outcome would not change depending on the risk assessment approach taken. The HEDi approach was previously selected by SCENHIR (2015). Since changing the approach would not change the outcome of the risk assessment, the SCCS will not pursue the suggested change in risk assessment approach.	Value of 7.35 nM x h was changed into 7.51 nM x h in the text and Table 9 in section 3.4.2.1.

		for the derivation of the (internal) DNEL for the dermally absorbed dose used in the RAC/SEAC opinion on the restriction of BPA in thermal paper (see chapter 1.1.8.6 of that opinion). The human TK study with application of a dermal dose of 100 µg d6-BPA / kgBW (Sasso et al., 2020) determined an AUC of 7.51 nM×h for free d6-BPA in serum (in the SCCS opinion Sasso et al. is cited with an AUC of 7.35). Taking 2.2% percutaneous absorption as the physiologically plausible percentage becoming systemically available in this specific experimental setting into account, leads to an AUC of 341 nM×h which corresponds to a dermally absorbed dose of 100 µg/kg BW (341 = 7.51/(0.022*100)*100). This AUC is virtually identical to the AUC values predicted by the PBPK models of Mielke (350.5 nM×h) and Fisher/Yang (329.5 nM×h), used by the RAC/SEAC opinion to derive the (internal) DNEL for the general population of ~0.05 µg/kg BW/day after dermal application. Thus, the experimental data of Sasso et al. (2020) confirmed the DNEL derived by using PBPK modelling data. As a side note, dividing the HED of 609 µg/kg BW/day by 100 (to account for the assumption that 1% of the BPA taken up by the oral route becomes systemically available as free BPA) and considering the specific uncertainty factor of 150 for the general population (see RAC/SEAC opinion), leads to a value of 0.04 µg/kg BW/day, which is virtually identical to the DNEL above. Given that, the question arises whether the internal HED			

		(HEDi) needs to be introduced at all. <u>P31 Table 11</u> The MoS value of 11617 is actually 6,090/0.524=11622 if it is calculated using the rounded values from the table itself. In order to be consistent, we would suggest consistently using either the non-rounded or the rounded values for all MoS. <u>P32 line 2</u> The total BPA exposure derived from the HEDi and a MoS of 100 would be 60.9 ng/kg bw/d. <u>P32 line 2</u> Wouldn't it be justified to add an additional factor of 6 for uncertainties regarding possible endocrine effects (such as those on breast development) to the MoS in analogy to EFSA's derivation of the t-TDI? However, since interspecies differences in BPA metabolism were already taken into account by calculating the HED based on the serum AUCs, the uncertainty factor for interspecies differences could be reduced from 10 to 2.5. Thus, using an analogous approach, a MoS of 150 instead of 100 would be justified for calculating limit values.		<u>Page 31 Table 11</u> The MoS values in the table were recalculated. <u>Page 32 line 2</u> Thank you for pointing out that a mistake in unit was made. The opinion will be altered accordingly. <u>Page 32 line 2</u> The SCCS will follow EFSA's and ECHA's assessment factor of 150 to establish the limit values for BPA in textiles and recalculate the limit values accordingly.	New MoS were calculated and added to Table 11. Mistake in unit section 3.6.3 was changed from µg/kg bw/d into ng/kg bw/d. Limit values for BPA in textiles were recalculated using the assessment factor of 150 instead of 100.
8		<u>P32 Table 12</u> It is not clear which values were used to derive the limit concentration of BPA in textiles. The SCCS opinion refers to equation (3) which calculates the dermal	3.6.3 Risk assessment by SCCS	<u>Page 32 Table 12</u> The exposure estimation was changed to a more consistent approach. Using the same parameters, also the limit values were recalculated. In response to another comment, the uncertainties around the	Limit values were recalculated and added to Table 12.

		exposure as sum of exposures from dry and sweaty scenarios. However, the sweaty scenario was based on experimentally derived (total) migration rates. Thus, it is difficult to conclude on limit values with this approach, since the percentage of migrated BPA has not been calculated. In our calculation considering data from the Wang et al. (2019) study and taking into account the corresponding surface weights (which can be calculated with tables from the Wang study, see our previous comment), the percentage of migrated BPA is between 5.5 and 7.7%. It is also to note that with this high migration rates BPA content will decrease after some few uses of the textile which contrasts the data shown by Wang et al. (2019) showing no difference between the BPA contents of new and used textiles. However, according to Wang et al. (2019) a transfer of BPA from new to used clothes when washed together is described. For the sweaty (dry) scenario, assumption of a surface weight of 0.02 g/cm2, a BW of 60 kg (60.5 kg), a migration rate of 7.7% (1%), a dermal absorption rate of 30% (0.5%), and a contact surface area of 6,370 cm2 (16,335 cm2), results in a limit value of 3.68 mg BPA/kg textile, in order to reach a systemic exposure dose of 0.0609 µg/kg bw/d resulting from dermal contact (or 2.45 mg BPA/kg textile when using a MoS of 150). The calculation for toddlers is even harder to comprehend. It is		migration rates determined by Wang et al.(2019) (including the large migration fractions) have now been qualitatively described.	

		counterintuitive that for toddlers a lower limit value was set compared to textiles for adults, although the MoS was much higher (>21 fold). Using the parameters listed in Table 4 and the equation on p 14, and assuming a migration rate of 7.7% in the mouthing scenario and a surface weight of 0.02 g/cm2, the limit value for toddlers would be 123 mg BPA/kg textile (or 82 mg BPA/kg textile when using a MoS of 150).			
9	RIVM, National Institute for Public Health and the Environment	Dear SCCS, It is with interest that we read your opinion on bisphenol A (BPA) in textile articles. In our opinion, it is a clear and well written document. A few general comments, submitted on behalf of RIVM, are listed further for specific sections.	ACKNOWLEDGMENTS	The SCCS is thanking RIVM for their comments.	See below.
10		<u>Page 3, line 11:</u> We note that ECHA (2017) is the Background Document for identifying BPA as Substance of Very High Concern (SVHC) by the Member State Committee (MSC). This document is purely hazard based, and therefore is no risk assessment. Is the SCCS referring to ECHA (2015) here, the restriction proposal for BPA in thermal paper?	1. ABSTRACT	The SCCS agrees with the comment made, and will refer to ECHA (2015) instead of ECHA (2017) where mention is made of previous assessments throughout the opinion.	Changes were made under 3.5.1 Summary of existing assessments on BPA and in conclusion.
11		<u>Page 7, section on previous scientific opinions:</u> We note that the MSC agreed on identification of BPA as SVHC under Article 57 c) and f) of REACH based on its reproductive and endocrine properties. Especially the scientific opinion of MSC on 'identification of BPA as SVHC because of its endocrine properties which cause probable serious effects to human health which give rise	2. MANDATE FROM THE EUROPEAN COMMISSION	The SCCS appreciates the comments received and acknowledges that the MSC support document for identification of BPA as a substance of very high concern is an important review of the adverse health effects of BPA. Regarding the comments made around the section mandate from the European commission, no changes will be introduced in the opinion. The SCCS is providing EU Commission with safety assessment upon specific mandate. This mandate cannot be altered by the SCCS. EU Commission is responsible for the follow-up of the risk management measures as well as for	No change.

		to an equivalent level of concern to those of CMR and PBT/vPvB substances' is relevant to mention in the list of previous scientific opinions (see https://echa.europa.eu/documents/10162/908badc9-e65d-3bae-933a-3512a9262e59).		implementation in the EU legislation. This comment should therefore be sent directly to the mandating DG unit and concern, i.e. DG JUST E4: JUST-E4@ec.europa.eu	
		Page 8, lines 5-9 Although there are no restrictions on the use of BPA in textile, the inclusion of BPA on the Candidate List for Authorisation due to its SVHC properties does bring the legal obligation for importers and producers of articles to notify ECHA and Member State competent authorities when an article is produced containing BPA above the concentration of 0.1% (w/w), conform Article 7(2) of REACH. This is not required in case the producer or importer of an article can exclude the exposure of humans and the environment to BPA during normal or reasonably foreseeable conditions of use of the article, including its disposal. Or if BPA has already been registered by a manufacturer or importer in the EU for that use. However, both these exemptions do not seem to apply for BPA in clothing articles. Could you please elaborate on how this has been taken care of?		Page 8, lines 5-9 The EU commission mandate cannot be altered by the SCCS. Elaborating on the legal obligations of manufacturers or importers of products containing BPA is outside of the scope of the terms of reference for this opinion of the SCCS.	No change.
		Page 8, line 26 Besides the comment on the presence of parabens in clothing articles, we believe that it is also important to mention the presence of bisphenol analogues such as bisphenol S (BPS) and several other bisphenols in clothing articles. Xue et al.		Page 8, line 26 No change can be made in the opinion to the section mandate from the European commission. The SCCS acknowledges that there is data from several authors (Xue et al. 2017, Li and Kannan 2018 and Wang et al. 2019) to show that BPA analogues, such as BPS, are increasingly being used in textiles. However, the EC	No change was introduced to the section 2. Mandate from the European commission. A

		2017, Li and Kannan 2018 and Wang et al. 2019 all describe the detection of BPS in clothing. Xue et al. 2017 and Li and Kannan 2018 also give information on other bisphenols. Although this opinion is focused on BPA and a risk assessment on other bisphenols may not be in order, we feel that it is nevertheless important to mention that also BPA substitutes are being used that may have a similar toxicological profile compared to BPA.		mandate defines the subjects within scope of this opinion. Since BPA analogues are not within this remit, it is currently not deemed appropriate to elaborate on this subject. This will be clarified in the conclusion section.	comment was added to the conclusion section to stress that the present opinion only applies to BPA, and not its analogues.
12		Page 11, line 20 It is notable that only four experimental studies are available on the presence of BPA in clothing, and only one experimental study is available on the migration rate into artificial sweat. It is clear that this is an emerging topic of concern, and consequently a topic of investigation in scientific peer-reviewed literature. Considering the importance of their respective datasets for the risk assessment by SCCS, it may be of added value to add a few sentences on the quality of these four studies. Furthermore, it would be helpful to put into perspective how much confidence the SCCS has in the robustness of the exposure calculations based on the evidence from the article by Wang et al.	3.3.1 Occurrence and concentrations	Page 11 line 20 New paragraphs were added with a more in depth appraisal of the analytical studies and a qualitative evaluation of the migration study, respectively.	Opinion was changed section 3.3.1.

		(2019).			
13		Page 11, Table 1 We suggest to be more explicit in stating that the median concentration used in the exposure calculations is derived from Wang et al. (2019) specifically (34.2 ng/g) and is different from the median value reported in Table 1 (26.9 ng/g). Furthermore, it would be helpful to discuss how the values of 34.2 ng/g and 199 ng/g used in the calculations relate to the concentration ranges found in the four studies. We suggest that section 3.3.1 is the appropriate section to do so. Page 11, Table 1 As the detection rates mentioned in the research articles seem to apply to the number of samples rather than the number of products, it might be appropriate to change column 3 from 'No of samples' to 'No of products/No of samples. This would be 77/77 (Xue), 36/73 (Li and Kannan), 32/96 (Freire) and 93/93 (Wang).	3.3.2 Migration experiments	Page 11 Table 1 The whole approach to estimate exposure was changed and described in more detail. It is described now under Table 2 that the median of 34.2 relates to used clothes. Page 11 Table 1 The SCCS agrees with the comment that the number of products was listed, and not the number of samples. Table 1 in the opinion was changed as suggested.	Table 1 of the opinion was changed. Table 1 was changed to include the total number of samples.
14		*Section 3.3.3.2 Parameterization and exposure estimates* Page 14, lines 1-4 SCCS mentions that Ederm-dry was not recalculated with European reference values because 1) the density of clothes D was not given by Wang et al. 2019 and 2) Ederm-dry is very small compared to Ederm-sweaty. However, the latter argument does not hold for toddlers, since Ederm-sweaty is not considered relevant for this group. As toddlers are a vulnerable population with respect to risks arising from BPA	3.3.3 Dermal exposure calculation	Page 14, lines 1-4 The dry scenario is no longer used. Exposure values were recalculated using the European standard body weight for toddlers (EFSA, 2012) and the dermal absorption fraction of 0.3.	Section 3.3.3.2. parameterisation and exposure estimates was changed, so that all values used in the exposure assessment are clearly

		exposure, a recalculation would be of added value. We suggest to recalculate the Ederm-dry provide by Wang et al. (2019) only for the European standard BWs (for toddlers, 12 kg vs 16.3 kg) and for the fuptake selected by SCCS (0.3 vs 0.01). For toddlers, this would result in Ederm-dry values of 0.367 (median) and 5.583 (high) ng/kg bw/day instead of 0.009 (median) and 0.137 (high) ng/kg bw/day now presented in Table 2. The same conversion calculation, especially regarding fuptake, could be performed for Ederm-dry for adults. <u>Page 14, lines 14-16</u>: It is stated that toddlers sweat only marginally, and therefore exposure is only calculated using Ederm-dry. Since this has a substantial effect on the calculation of exposure for toddlers, it would be of added value to add a reference or substantiation to this statement.		<u>Page 14, lines 14-16:</u> The dry scenario is now no longer used. Children are, however, recognised to have an overall lower sweating rate compared to adults (Falk, 1998). However, because of the many additional factors influencing this sweat rate, the same migration fractions (based on an experimental sweat rate of 1.5 L/h) by Wang et al. (2019) will be used for children as for adults to allow a conservative estimation. The assumption of 2-hours of daily sweating over the trunk surface area only will also be applied to the exposure scenario for toddlers. The exposure values based on migration into sweat were recalculated with default body weight values for European consumers and the dermal absorption fraction of 0.3.	indicated. Changes introduced to Section 3.3.3.2 Parameterization and exposure estimates.
15		<u>Page 14, lines 32-34</u> SCCS states here that, in order to account for the uncertainty of the analogy between saliva and sweat, only the high migration rate of 0.308 ng/cm2/d is used for the oral exposure calculations. However, in later calculations (notably Table 4, Table 5 and Table 11), both average and high migration rates are used for the	3.3.4 Oral exposure calculation	The comparison for high and low migration will still be made in Table 4 of the opinion. However, only the high migration estimate, resulting in an oral exposure of 0.016 ng/kg bw/d, was used for the aggregate exposure calculation for toddlers. This is now clearly shown in Table 5.	Table 5 was adjusted so that only the high migration oral exposure for toddlers was used for further calculations of the aggregate

		calculations of oral exposure. There seems to be a discrepancy here between the text and the final calculations.			exposure.
16		Page 31, lines 24-25 It is noted here that, similar to the calculation of the internal HED (HEDi), 1% free BPA after uptake via the oral route is assumed to derive the SEDoral for free BPA. However, in Table 11, the MoS is calculated with an unadjusted SEDoral. No further comments on the SEDoral for free BPA are found, there seems to be a conflict between the description of the calculations of SEDoral for free BPA and the final calculations. Page 31, lines 41-43 SCCS concludes from the calculations that there is no health concern arising from BPA exposure levels due to the use of clothing articles. However, as BPA is a broadly applied chemical which is present in various consumer articles, the sum of exposure is of interest. Other uses are for example summarized in the reports published by ECHA and EFSA. We understand that the opinion is focused on BPA in textile only, and that other sources of exposure are out of the scope. However, we suggest to add a comment to this important topic to 1) stress the importance of exposure from multiple sources which add up and 2) to put the results on exposure via textile into context compared to other sources of exposure. The latter point is already illustrated in tables 3 and 4. But it would be relevant to add a conclusion or comment on these comparisons, especially since aggregate exposure would change the estimation of a limit	3.6.3 Risk assessment by SCCS	Page 31 line 24-25 In the calculations of the MoS, the Point of Departure (PoD) was adjusted according to the percentage of free BPA (1%). Practically this means that a HEDi of 6.09 µg/kg bw/d was used for risk assessment. Page 31, lines 41-43 A comment around the exposure level resulting from textile compared to the total exposure to BPA from different sources estimated by EFSA (2015) will be added to the section conclusion in the opinion.	No change. A comment comparing the contribution of BPA in clothing to dietary BPA exposure (EFSA, 2015) was added to the conclusion section. Additionally, a comparison of the estimated exposure resulting from clothing was made with the dermal DNEL by ECHA (2015) in section 3.6.1.

		concentration for BPA in clothing articles significantly. <u>Page 32, lines 12-14</u> Elaborating upon the latter point, SCCS uses the internal exposure of 60.9 ug/kg bw/d to back calculate Ederm-dry, to subsequently determine a limit value for BPA in clothing, assuming that clothing is the only source contributing to the internal exposure. We wonder whether SCCS could consider to introduce an allocation factor here, to correct for potential exposure resulting from other sources. This approach has been applied in setting drinking water limit values (https://apps.who.int/iris/rest/bitstreams/1080654/retrieve) and for lead in children's toys (https://ec.europa.eu/transparency/regexpert/index.cfm?do=groupDetail.groupDetailDoc&id=17381&no=1). This would correct for potential exposure from other sources. <u>In addition we noted a few minor editorials:</u> • Page 30, line 36: It is suggested to introduce the use of the abbreviation		<u>Page 32, lines 12-14</u> Exposure to BPA may occur from sources other than clothing. Since exposure calculations were not performed for sources other than clothing, it is not deemed appropriate to provide guidance around the portion of the limit value that should be dedicated to the different sources of exposure. EFSA (2015) previously assessed exposure to BPA resulting from dietary and non-dietary sources such as thermal paper, indoor/outdoor air (including air-borne dust), dust, toys, articles which may be mouthed, and cosmetics. It is worth noting that EFSA is currently re-evaluating the huge amount of data on BPA toxicity that came available since December 2012 to advise on the safety of BPA resulting from several different sources. <u>Page 30 line 36</u> On page 30, line 36 the abbreviation HED is used. This abbreviation was first introduced on under section 3.6.1 determination of the Human Equivalent Dose by EFSA. Introducing the abbreviation once more in a new section is therefore not deemed necessary.	A sentence was added to the conclusion, recognising that BPA exposure may result from different sources. No change.
17		<u>We noted a few minor editorials:</u> • Page 12, Table 2: The right three columns on EXPdaily do not contain high/low values, and we therefore propose to remove high/low;	3.3.2 Migration experiments	<u>Page 12 Table 2</u> With respect to Table 2, the mention of high/low and other information was removed from the final table to match the data discussed in the opinion.	Table 2 was adjusted so that the headings for each of the columns

		• Page 12, Table 2: It would be helpful to use the same term for Ederm-dry clothes consistently throughout the document. This would apply to the terms EXPdaily (Table 2), Ederm-dry clothes (Eq. 1) and Ederm dry (Table 3)		Page 12 Table 2 The opinion will be checked so that consistent terminology is used throughout.	accurately describe the information.
18	Plastics Europe	The PC/BPA Group of PlasticsEurope, representing the European producers of Bisphenol A, welcomes the opportunity to comment on the preliminary opinion on safety of presence of Bisphenol A (BPA) in clothing articles published in October 2020 by the Scientific Committee on Consumer Safety (SCCS). In general, the PC/BPA Group agrees with the outcome of this assessment that "[…] there is no risk for adverse effects of the estimated exposure levels of BPA resulting from the use of clothes, independent of the age group of the consumer." However, we would like to draw the attention of the SCCS to several specific aspects which we hope can be considered by the SCCS and included in the final report to be shared with the European Commission's Directorate General for Justice and Consumers. The PC/BPA group remains available for any further requests or clarifications needed.	1. ABSTRACT	The SCCS is thanking Plastics Europe for their comments.	See below.
19		In its toxicological evaluation the SCCS discussed existing assessments on BPA in chapter 3.5.1. In particular, the SCCS refers to a recently published study investigating non-monotonic effects of BPA in the developing rat mammary gland and stated that, "[…] using a combined morphometric and statistical	3.5.1 Summary of existing assessments on BPA	It is important to note that the SCCS by no means intends to conclude on the (non-)monotonicity of the substance under investigation, nor its relevance for the risk assessment of BPA. This subject is currently being evaluated by EFSA (2021; draft EFSA Scientific Committee Opinion on biological plausibility of non-monotonic dose responses and their impact on the risk assessment). The paragraph will be amended to reflect	The paragraph around carcinogenicity under 3.5.1. was amended. This includes the reference of Badding

		approach, non-monotonic effects of BPA on the developing rat mammary gland that differed from those of ethinyl estradiol have been reported (Montévil et al., 2020)." Within the study by Montévil et al., 2020, the description of the presented novel, exploratory measuring techniques is extremely limited, and moreover, no historical data are available that would allow one to put the findings into a broader context. The method to fit data points apparently applies curve fitting mathematics without explaining respective biological plausibility or relevance. On the contrary, using validated and toxicologically established methods of respective tissues received from the CLARITY Core study, the authors did not observe effects on the animals' mammary glands at the investigated points in time and dose levels (Montévil et al., 2020). This is consistent with the respective conclusions drawn by the US National Toxicology Program (NTP) in the report of CLARITY-BPA Core study for neoplastic lesions in the mammary gland (NTP, 2018). A profound evaluation of the totality of evidence revealed that "it [is] unlikely that this is a plausible BPA-treatment-related lesion." In line with this, the absence of evidence for NMDRs within the CLARITY-BPA Core study is also shown in an analysis of the CLARITY-BPA Core study data by applying systematic criteria for identification (Badding et al., 2019). The conclusion of positive evidence for NMDR		the state-of-the-art around the NMDR effects of BPA, including the references to the most recent publications and opinions on the subject. The SCCS furthermore agrees with the comment that results obtained using methods without explaining respective biological plausibility or relevance to study the effect should be interpreted carefully.	(2019) and others.

		effects on mammary glands from BPA exposure within the Montevil et al., 2020 study therefore appears highly questionable.			
20		Substance Evaluation (SEv) Conclusion prepared by the Federal Institute for Occupational Safety and Health (BAuA) is mentioned. In the course of the illustration how the DNEL dermally absorbed was derived the SCCS described that, "Using the PBPK model of Mielke et al. (2011), a dermal absorption percentage of 30% instead of 10% results in the same human dermal AUC value and, consequently, in the same value for the DNEL dermally absorbed." This conclusion drawn by the SCCS, which can also be found in a similar manner in the SEv Conclusion (BAuA, 2017) and in the Corrigendum to the SEv Conclusion (BAuA, 2018), is scientifically incorrect as further explained below. A scientifically robust instruction to derive an AUC human, dermal according to the physiologically based pharmacokinetic-(PBPK) model of Mielke et al., 2011, which takes into account dermal absorption, is described in the Chemical Safety Report of BPA in section 5.11.2. For the following calculation the assumed dermal dose is shown in brackets, whereas in square brackets the dermal absorption figure is presented. In brief, according to the PBPK model of Mielke et al., 2011, an external dose of 0.97 µg/kg/d would lead to an AUC human, dermal of 697 pg x h/mL =	3.6.2 Determination of the oral and dermal derived no effect level by ECHA	The SCCS agrees with the remark made and acknowledges that a mistake was taken over from the BAuA. This will be rectified in the opinion.	An SCCS comment was added to the opinion section 3.6.2. pointing to the mistake in the BAuA report.

		3,053 nmol x h/L (taking into account 100% dermal absorption through the skin = internal dose). Scaling this AUC human, dermal (0.97 µg/kg [100%]) to a dose of 100 µg/kg results in an AUC human, dermal (100 µg/kg [100%])= 314 nmol x h/L . Taking into account a dermal absorption figure of 30% results in an AUC human, dermal (100 µg/kg [30%]) = 0.3 x 314 nmol x h/L= 94.2 nmol x h/L . Assuming 10% dermal absorption instead of 30% absorption would result in an AUC human, dermal(100 µg/kg [10%]) = 0.1 x 314 nmol x h/L = 31.4 nmol x h/L . In conclusion, according to the PBPK-model in Mielke et al., 2011 and assuming an external dermal dose of 100 µg/kg, a dermal absorption rate of 10% does not lead to the same AUC human, dermal value as using a dermal absorption rate of 30%. Based on this incorrect assumption the AUC human, dermal would be too high and consequently, the DNEL dermal too low. <u>*References:*</u> *Mielke, H., Partosch, F. & Gundert-Remy, U. The contribution of dermal exposure to the internal exposure of bisphenol A in man. Toxicol Lett 204, 190-198, doi:10.1016/j.toxlet.2011.04.032 (2011).* *BAuA. Federal Institute for Occupational Safety and Health; Evaluating Member State(s): Germany; 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. (2017). *BAuA. Federal Institute for Occupational Safety and Health Evaluating Member State(s): Germany; 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. (2018).*			
21		In chapter 3.4.2.1, in SCCS's overall conclusion on dermal absorption, Toner et al., 2018 and Sasso et al., 2020 are designated as key studies for the derivation of the dermal absorption figure of BPA. The SCCS concludes that "From both studies, it can be concluded that a rounded value of 30% dermal absorption has to be considered." The PC/BPA group agrees that according to Toner et al., 2018 and by applying the SCCS Basic Criteria for the in vitro assessment of dermal absorption ingredients (SCCS, 2010), it can be concluded that the potentially bioavailable portion of BPA is 30%. However, the published primary human data in Sasso et al., 2020 do not support 30% dermal absorption of BPA. A Plausibility check of the dermal absorption rate, in terms of serum clearance (CL) of unconjugated BPA, indicated that a 30% dermal absorption rate will be too conservative. The value of 12–29% for the fraction dermally absorbed (Fabs), based on the recovery of unabsorbed BPA, translated to a	3.4.2 Toxicokinetics and metabolism after dermal uptake	Please refer to question 6 for an answer around the dermal absorption value selected in the opinion for BPA.	No change.

		serum clearance of 545–1318 L/h, "which is physiologically implausible as it grossly exceeds not only the values predicted by allometric scaling but also the hepatic blood flow (Collet et al., 2015)" according to the study authors (Sasso et al., 2020). The Fabs value of 2.2%, which was derived from the serum AUCs of total BPA after oral and dermal administration, yields into a serum clearance, "which is physiologically plausible as it is consistent with allometric scaling estimates." Moreover, the exposure durations in Toner et al., 2018 and Sasso et al., 2020 of 24 h and 12 h, respectively, are much longer than the exposure scenario with sweaty clothes included in SCCS's risk assessment. With longer exposure time, the depot of BPA in the skin would have continuously diffused into the blood and a higher dermal absorption rate will be derived. <u>*References:*</u> *Toner, F. et al. In vitro percutaneous absorption and metabolism of Bisphenol A (BPA) through fresh human skin, Toxicology in Vitro, Volume 47, https://doi.org/10.1016/j.tiv.2017.11.002. (2018),* *SCCS. The Scientific Committee on Consumer Safety: Basic criteria for the in vitro assessment of dermal absorption of cosmetic ingredients. (2010).* *Sasso, A. F. et al. Pharmacokinetics of bisphenol A in humans following dermal*			

		administration. Environment international 144, 106031, doi:10.1016/j.envint.2020.106031 (2020). *Collet, S. H. et al. Allometric scaling for predicting human clearance of bisphenol A. Toxicology and applied pharmacology 284, 323-329, doi:10.1016/j.taap.2015.02.024 (2015).*			
22		The assumption of 30% dermal absorption is an important factor leading to an overestimate of human exposure to BPA from clothing. In section 3.4.2.1, SCCS stated that this value is based on data from a 24-hour in vitro human skin exposure study (Toner et al., 2018) and a 12-hour human skin exposure study (Sasso et al., 2020), both of which used BPA in solvent solutions applied to the skin. Therefore, the assumption that 30% dermal absorption of BPA would occur via dry clothing for 16 of the 24 hours in a day is highly unlikely. Further, as discussed in our preceding comment submitted for chapter 3.4.2.1, the assumption of 30% uptake of BPA through the skin is likely too high, as the data from the Sasso et al., 2020 supports the use of a dermal absorption factor that is much lower than 30%. R*eference:* *Sasso, A. F. et al. Pharmacokinetics of bisphenol A in humans following dermal administration. Environment international 144, 106031, doi:10.1016/j.envint.2020.106031 (2020).*	3.4.2 Toxicokinetics and metabolism after dermal uptake	Please refer to question 6 for an answer around the dermal absorption value selected in the opinion for BPA.	No change.
23		The assumptions used by SCCS in estimating exposures to BPA through	3.3.3 Dermal exposure	The calculation was revisited and in the new approach the migration rates were used directly. This corresponds	Section 3.3.3. has been

		contact with clothing are very conservative and likely overestimate the actual human health risks from exposure by wearing clothing containing BPA. In section 3.3.3, the "high" migration rate scenario from the Wang et al., 2019 study relied on by SCCS in the exposure estimate calculations represents a beyond worst-case scenario for BPA release from fabric. The BPA concentration used in this scenario (199 ng/g) is the 95th percentile measurement of BPA content from clothing pieces subjected to 30 minutes of ultrasonic extraction in an ethyl acetate solution. The geometric mean concentration of BPA from this extraction experiment was approximately three-fold higher for non-cotton/artificial materials compared to cotton and cotton-blend materials, and the highest concentrations of BPA were obtained from the synthetic materials tested (Wang et al., 2019). Therefore, the 95th percentile BPA concentration used in SCCS's exposure calculations to estimate a high-end daily dermal exposure to BPA from clothes is assumed to be from synthetic materials. While it is certainly plausible for individuals to regularly wear clothing made from synthetic materials, it seems overly conservative to assume that only non-cotton/artificial materials are worn on a daily basis in the high migration scenario risk assessment. Additionally, the migration rates on a per day basis are derived from an experiment in which cloth pieces were soaked in artificial sweat solution and	calculation	to an assumption of 2 hours skin exposure to clothes soaked in sweat. This assumption is disputable, but no data are available from controlled studies e.g. investigating the actual uptake of substances released from clothes that could provide a benchmark for the exposure estimates. Therefore, there are also no scientific grounds to claim that the upper bound approach chosen by SCCS is "beyond worst case". Specifically, the choice of concentration is conservative, but uses the common approach of selecting P95 as a parameter value for a high scenario. The selected P95 concentration, called Textile 2 throughout the opinion, stems from the data set of the most comprehensive study with most variable clothing items (Wang et al. 2019), and the concentration range observed in this study is comparable to that of the other occurrence studies. Additionally, not all the parameter values in the study are high percentiles, e.g. the body weight is a default based on an average. In the new calculations, since the highest concentration yielded the lowest migration fraction in the experiments of Wang et al. 2019 and vice versa, this association was maintained by providing textile-specific calculations. Further, since the migration fractions determined in the study seem high compared to earlier studies on substance release from textiles (BfR 2012), and since the assumption of 2h wearing clothes fully soaked in sweat with close contact to the skin is based on a number of upper bound scenario decisions, the mid-range exposure estimate of the three textiles (*i.e.* textile 2) was chosen for the calculation of the MoS. It has to be noted that the largest uncertainties do not reside in the concentrations, but in the migration scenario, since it is currently largely unclear how much substance will be transferred by sweat with subsequent uptake, and how this depends on sweating, hence physical activity. Wang et al. 2019 attempt to provide an upper bound in their migration test, but it is currently	changed accordingly, parts of the response have been added to section 3.6.3. risk assessment by SCCS.

		were in direct contact with the receiving phase for only 2 hours (Wang et al., 2019). Therefore, it is unknown whether the amount of BPA released during the first 2 hours in contact with a solvent such as sweat would be consistent over several hours. Further, the assumption that an adult is in contact with wet, sweaty clothes for 8 hours every day (as specified in section 3.3.3) also very likely overestimates exposure to BPA. SCCS's calculation of internal BPA exposure assumes the rate of BPA release from the clothing is consistently at a high migration rate for those 8 hours, every day. <u>*Reference:*</u> *Wang, L. et al. Widespread Occurrence of Bisphenol A in Daily Clothes and Its High Exposure Risk in Humans. Environ. Sci. Technol. 53, 7095−7102 (2019).*		not possible to judge how far this scenario is away from a realistic scenario. Therefore, the SCCS adopted the described conservative approach, and advocates scientific research on migration rates in general, and in particular for BPA in different types of clothing fabrics.	
24	French Ministry in charge of Ecology	I have the feeling that our children are endangered by BPA presence in clothes. Please take the right decision for human preservation.	4. CONCLUSION	The SCCS is thanking French Ministry in charge of Ecology for their remark. The SCCS is providing EU Commission with safety assessment upon specific mandate. EU Commission is responsible for the follow-up of the risk management measures as well as for implementation in the EU legislation. This comment should therefore be sent directly to the mandating DG unit and concern, i.e. DG JUST E4: JUST-E4@ec.europa.eu	No change.
25	Stephanie Thunissen (Belgium)	line 49 - The study seems to focus on the daily exposure without considering the metabolism thus the effect of BPA accumulation in the human body. Is this not an incomplete review of the issue related to the impact of BPA on human's health?	1. ABSTRACT	In the case of BPA, metabolism results in detoxification (see section 3.4 of the opinion). BPA is readily excreted and there is no bioaccumulation of BPA in the human body. Therefore, the assumption of no metabolism is a worst case assumption. The assessment is based only on one source of BPA	No change.

		Do the exposure scenarios discuss the impact of BPA exposure from clothing on individuals who already present levels of BPA in their body? It is assumed that human bodies accumulate a certain amount of BPA from different sources from their exposure to food, the environment, cosmetics and chemicals. Do we have an estimation of the average BPA content of the human body? Has this been taken into account? Do the defined acceptable limit of exposure for BPA from clothing still guarantee the security of Europeans over time?		(clothing) and does not take into account the contribution of other sources. BPA is not accumulated in the human body. However, due to the steady exposure to BPA from various sources including food, most persons have BPA in their bodies. This can be measured by biomonitoring. Since this was not the focus of this opinion, for a review of biomonitoring studies on BPA please refer to EFSA, 2015. With the data available, the acceptable limits of exposure ensure the safety of BPA from clothing with respect to systemic toxicity.	