Outcome of a public consultation on the draft risk assessment of chlorinated paraffins in feed and food

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Outcome of a public consultation on the draft risk assessment of chlorinated paraffins in feed and food

European Food Safety Authority (EFSA)

Abstract

The European Food Safety Authority (EFSA) carried out a public consultation to receive input from interested parties on the draft scientific opinion on the risk assessment of chlorinated paraffins in feed and food. This draft scientific opinion was prepared by the EFSA Panel on Contaminants in the Food Chain (CONTAM Panel), supported by the Working Group on Chlorinated Paraffins in food and feed. The draft opinion was endorsed by the CONTAM Panel for public consultation by written procedure on 31 July 2019. The written public consultation was open from 6 August until 17 September 2019. EFSA received comments from 11 different interested parties. EFSA and its CONTAM Panel wish to thank all stakeholders for their contributions. The present report contains the comments received and explains the way they have been considered for finalisation of the opinion. The opinion was adopted at the CONTAM Plenary meeting on 17 December 2019 and published in the EFSA Journal.

Key words: chlorinated paraffins, SCCP, MCCP, LCCP, food, feed, public consultation

Requestor: European Commission

Question number: EFSA-Q-2019-00164

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Table of contents

1. Introduction

1.1. Background and Terms of Reference as provided by the requestor of the opinion

1.1.1. Background

Chlorinated paraffins (CPs) are complex mixtures of polychlorinated n-alkanes. The chlorination degree of CPs can vary between 30 and 70 weight percent (wt%). CPs are typically subdivided according to their carbon chain length into short chain CPs (SCCPs, C_{10-13}), medium chain CPs (MCCPs, C_{14-17}) and long chain CPs (LCCPs, $C_{>17}$).

CPs may be released into the environment during product use and though improper disposal. There is also potential for contamination of the feed and food chain. CPs, in particular SCCPs and to a lesser extent MCCPs, bioconcentrate in fish and molluscs. Food is considered the main source of human exposure to CPs.

SCCPs are considered to be persistent toxic substances. CPs with an average carbon-chain length C_{12} and an average degree of chlorination of approximately 60% are classified by the International Agency for Research on Cancer (IARC) as possibly carcinogenic to humans (Group 2B).

1.1.2. Terms of Reference

In accordance with Art. 29 (1) of Regulation (EC) No 178/2002, the European Commission asks the European Food Safety Authority for a scientific opinion on the risks for animal and human health related to the presence of chlorinated paraffins in feed and food.

1.2. Rationale for the public consultation and brief summary of its outcome

In line with EFSA's policy on openness and transparency, and in order for EFSA to receive comments on its work from the scientific community and stakeholders, EFSA engages in public consultations on key issues. Accordingly, the draft opinion together with its annex was released for public consultation from 6 August 2019 to 17 September 2019 by means of an electronical comment submission tool together with explanatory text on the EFSA website (See Appendix 1). Comments were received from 11 interested parties from seven countries. **Table 1** provides an overview on the interested parties that have submitted comments through the electronic submission. No comments were submitted by email.

Table 1: Overview on stakeholder comments received

Stakeholder	Category [a]	Country
Marina Ricci	Private capacity	BE
Jacob de Boer	Private capacity	NL
Per Ola Darnerud	Private capacity	SE
Adrian Covaci	Private capacity	BE
Federal Office of Consumer Protection and Food Safety	National Authority	DE
UK Committee on the Toxicity of Chemicals in Food, Consumer Products and the Environment (UK-COT)	National Authority [1]	UK
German Federal Institute for Risk Assessment (BfR)	National Authority	DE
Institute of Food Safety, Animal Health and Environment "BIOR"	University/Public Research Institute	LV

[1] Submitted by the UK-FSA on behalf of the UK-COT.

National Institute for Public Health and the Environment (RIVM)	University/Public Research Institute	NL
Euro Chlor (Cefic) Chloro Alkanes Product Group	Private section (e.g. industry, consultancy, etc)	BE
European Union Reference Laboratory for Halogenated POPs in Feed and Food	Other	DE

(a): As specified by the commenter.

2. Assessment of comments and use for finalisation of the opinion

The comments received were duly evaluated by the EFSA WG on Chlorinated Paraffins in food and feed and wherever appropriate taken into account for finalisation of the draft opinion. **Table 2** provides a detailed list with all comments received from interested parties together with EFSA responses and explanations how the comments were considered for finalisation of the draft opinion.

Table 2: Stakeholder comments and EFSA responses

Stakeholder	Comment number	Chapter	Comment	EFSA response
Marina Ricci, private capacity	1	1.3.4. Sampling and methods of analysis	- Table 3, last line: the carbon skeleton method has been used with the FID in the past but the most recent results are obtained coupling the GC with the MS. Please add this. - I disagree with the definition of the selectivity as "low" for the carbon skeleton method: as a matter of fact, it is highly selective because of the dechlorination process. The alkanes signals derivating from the CPs could be possibly interfered only by alkenes or alkanes already present in the sample, which can be eliminated before the instrumental analysis by an appropriate sample clean-up. - Line 903: "*In general, the techniques are not able to completely separate and detect isomeric groups, and individual congeners can not reported.*" The sentence should be changed (my suggestions in red), otherwise it conveys the wrong message, see indeed figure 4: are CPs groups separated? - Line 944-947: "*An alternative method is the GC carbon skeleton method coupled with flame ionisation detector (FID) (Cooke et al.1980) and more recently with MS detector (Pellizzato et al., 2009). This method dechlorinates the CPs to alkanes and quantification is performed with n-alkanes. This reduces the calibration problems found with ECNI as the FID detector response is independent of the chlorine content (see below).*" The last sentence misses a bit the point: because of the dechlorination process, FID or MS are detecting alkanes, thus of course their response is independent of the original CP chlorine content. - Line 974: "*it is challenging to find commercial technical CPs that are suitable for the quantification of CPs in environmental and food samples*" For a reliable quantification, SI-traceable standards (or mixture of) should be provided rather than technical CPs mixtures; and indeed, the match of the CPs calibrant to the CPs profile in the sample seems to be of importance to avoid gross quantification errors.	The CONTAM Panel has revised the text in the Opinion to take these comments into account.

Stakeholder	Comment number	Chapter	Comment	EFSA response
			- Line 977-978: "*Several inter-laboratory studies have been carried out using samples of different complexity (analytical standards, sample extracts and real samples) (van Mourik et al., 2015).*" Given that before the Quasimeme series of interlaboratory comparisons, only two other examples of comparisons on CPs were carried out, I would suggest mentioning also those for sake of completeness: Tomy et al. Anal Chem. 71 (1999) 4465, Pellizzato et al. Trends of Anal. Chem. 28 (2009) 1029.	
Jacob de Boer, private capacity	2	General comments	At the recent Dioxin symposium, one paper of Wang (2018) was mentioned by Per Ola Darnerud on the synergistic effect of chlorinated paraffins and PAHs. Attention should be paid to this as PAHs are abundant as are CPs. The draft EFSA safety limit of 36 mg/kg bw per day for MCCPs should preferably not be mentioned as it is based on rather old data. I suggest to mention a lack of data and request new tox studies.	The CONTAM Panel thanks the stakeholder for this information. For the risk assessment of CPs in food and feed, studies reporting on the effects of CPs only have been considered as to assess the hazard. Combined exposure/effects with other contaminants was out of the scope of the mandate. The CONTAM Panel considered that the study was suitable to use for the risk assessment. Under Recommendations, the CONTAM Panel highlighted the need for chronic toxicity studies for relevant CP mixtures.
Per Ola Darnerud, private capacity	3	Summary	In Summary, some data are mentioned that I would like to comment. They are dealing with target organs for toxicity, the MBDL for MCCPs, the summary of toxicokinetic data, and the exposure assessment. I believe all these points will be taken up in the different chapters and paragraphs below.	The replies to the comments made are given below.
	4	3.1.1.1. Toxicokinetics - Laboratory animals	The toxicokinetic part is written in a complicated way, and I lack clear conclusions. Also, the degradation of CPs to carbon dioxide in vivo (which in our experiments will mean a metabolic dechlorination of the CP) remains unclear to the reader. For example,the following concluding sentences could be added: "*In mice, highly chlorinated CPs are metabolised and excreted via faeces, whereas for lower chlorinated CPs the faecal excretion is modest. Instead, a significant part of the molecule will be degraded in vivo and exhaled as carbon dioxide and this degradation is shown to be inverse to the degree of chlorination in C12 and C16 chloroalkanes (Darnerud et al., 1982).*"	The CONTAM Panel decided to present the detailed study descriptions for laboratory animals in Appendix A and only the summaries of the studies in the body text. The CONTAM Panel is of the opinion that clear conclusions on toxicokinetics for CPs in general for laboratory animals cannot be drawn based on the available data. The Darnerud et al. (1982) study on SCCPs and the Darnerud and Brandt (1982) study on MCCPs are both described in the main body text

Stakeholder	Comment number	Chapter	Comment	EFSA response
				of the Opinion (see Section 3.1.1.1.2). Both studies were considered by the CONTAM Panel as being crucial for the conclusion that results from one CP are valid only for the CP studied and should not be taken as general for all CPs. However, the CONTAM Panel is of the opinion that a clear conclusion on metabolism and excretion for CPs in general in laboratory animals cannot be drawn based on only these two studies. To reflect the findings regarding carbon dioxide exhalation in relation to metabolism, the text in Section 3.1.1.4 of the Opinion on Summary on toxicokinetics has now been amended.
	5	3.1.2.2. Repeated dose toxicity studies	The relatively high BMDL for MCCPs is a bit suprising, as the NOAEL/LOAEL values are considerably lower in several toxicity studies. As I understand it, a LOAEL value of about 4-5 mg/kg bw/day could be derived in rats exposed to MCCPs, based on changes in thyroid structure and serum cholesterol levels (Poon et al., 1995), and a LOAEL of about 6 mg/kg bw/day was observed in MCCP-exposed rats, with effects on pup mean weights (Serrone et al., 1987). Apart from this, it could be discussed whether the liver effects seen in many toxicity studies could be disregarded as only an adaptive response and therefore not used in the risk assessment. As histological changes occur, and at high doses liver tumours will appear, I question the neglection of the liver effects.	The limitations of the Poon et al. (1995) study are described in the Opinion, as well as the reasons for why the CONTAM Panel could not identify a no-observed-adverse-effect level (NOAEL) from this study (see Section 3.1.2.2.2 of the Opinion): "*It was not possible for the CONTAM Panel to obtain the scorings for individual animals from the study authors. Therefore, the Panel was not able to interpret the histopathological findings in the liver, kidney and thyroid, and thus not able to identify a NOAEL from this study.*" Based on the original study report (IRDC, 1985) for the study described in Serrone et al. (1987), the CONTAM Panel evaluated that the lowest dose in the study corresponding to 9 mg/kg bw per day is a NOAEL for developmental toxicity, as described in Section 3.1.2.3.2 of the Opinion. The liver effects have not been neglected. The text in the Section on mode of action makes it clear that these effects were considered adverse

Stakeholder	Comment number	Chapter	Comment	EFSA response
			Regarding combination toxicity: Interesting results was shown in a study exposing rats for combinations of CPs and PBDE. Dose-dependent interactions were suggested regarding liver-somatic index, microsomal enzyme activities, and thyroid hormone plasma levels (Lundstedt-Enkel et al., J. Chemometrics (2010) 24: 710-718). This study is not mentioned in the EFSA document.	for the rat and what the relevance is to humans is explained. The CONTAM Panel thanks the stakeholder for this information. For the risk assessment of CPs in food and feed, studies reporting on the effects of CPs only have been considered as to assess the hazard identification and characterisation. Combined exposure/effects with other contaminants was out of the scope of the mandate.
	6	3.1.2.4. Neurotoxicity studies	In citing the study of Eriksson and Nordberg (1986), I believe there has been a mistake that could also have risk assessment implications. The EFSA document states that the dose in this study is 200 mg/kg bw, but according to the article the dose should instead read 1 mg/kg bw (!). Even if this 16C-chloroalkane is not a technical CPs by definition, I think that this study should be taken into consideration when discussing critical effects of CP toxicity	The CONTAM Panel noted that the dose is not clear as: (i) the dose of 1.4 µmol/kg bw corresponds to 1 mg according to the Abstract of the study, and to 1 mg/kg bw according to Methods section of the study, and (ii) there is no information on the identity / structure / composition of the test compound and thus, no information on the molecular weight to be applied for conversion of the dose in µmol/kg bw. This is now reflected in Section 3.1.2.4.2 of the Opinion. No signs of neurotoxicity have been reported in other studies in rodents than the Eriksson and Nordberg (1986) study. The CONTAM Panel is of the opinion that a change in only one parameter at only one time point without changes in other parameters in this study is not sufficient to identify neurotoxicity as a critical endpoint of the tested C16, or of CPs in general.

Stakeholder	Comment number	Chapter	Comment	EFSA response
	7	3.3. Dietary Exposure assessment	The EFSA exposure assessment is based on CP levels in fish. According to Swedish market basket studies, there are several food groups that contribute more to the dietary intake than fish (eg. sugar and sweets, fats and oils, dairy products), and fish/fish products will give less that 10% of the total CP intake from food (according th the same study; Swedish Market Basket Survey 2015, National Food Agency, report 26 - 2017). Thus, the CP intake for the European population may be considerably higher than that estimated in the EFSA document. If we add other exposure routes than food and other uncertainties in the performed estimations, the CP exposure calculation may not be very solid. If this leads to a possible erosion of the MOE, it will have consequences for the risk assessment.	The CONTAM Panel acknowledged in the Opinion that the exposure estimated from fish only is an underestimation of the exposure, as other food categories are expected to contribute to the exposure. Therefore, the Panel recommended the need for occurrence data in food for SCCPs, MCCPs and LCCPs to enable a robust human exposure assessment. Reference to the exposure estimated by a market basket study carried out in Sweden in 2015 (Yuan et al., 2017) and to the estimations by Krätschmer et al. (2019) has been made in Section 3.5.2 of the Opinion regarding the uncertainty in the exposure scenario/exposure model.
Federal Office of Consumer Protection and Food Safety (Germany)	8	Abstract	Abstract-Lines 24 to 26: As brought forward in the POPs meeting of 09.09.2019 and supported by the Netherlands, I would propose to adapt the wording of the sentence beginning with "*The panel concluded, that the MOEs do not indicate a health concern...*" as follows: "*Noting the uncertainty, based on a limited dietary exposure estimation for fish consumption only, the lack of toxicokinetic data for humans and that only a few CPs have been tested in the available toxicity studies, the Panel concluded, that there wouldn´t be for the time being a health concern.*"	The wording in the Abstract, Summary and other sections of the Opinion has now been modified in order to reflect better the conclusions and uncertainties in the risk assessment.

Stakeholder	Comment number	Chapter	Comment	EFSA response
UK Committee on the Toxicity of Chemicals in Food, Consumer Products and the Environment (COT)	9	General comments	These comments are submitted on behalf of the UK Committee on the Toxicity of Chemicals in Food, Consumer Products and the Environment (COT). Overall we agree with the analysis and conclusions and note the data gaps. Without sensitive and specific measurements it is not possible to accurately measure exposure to all congeners and extrapolate between different countries. The limited available information on toxicity and human exposure for a series with multiple homologues limits the ability to set standards. Toxicity studies have been restricted to only one/two homologues for SCCP, MCCP and LCCP so extrapolation is required possibly using a TEQ approach as adopted for dioxins and PCBs to other components. Also understanding the impact of chemical structure- degree of chlorination, chlorine position chain length on disposition and potential toxicity is important.	The CONTAM Panel acknowledges the comment. Regarding the possible grouping approach, please see reply to Comment 14.
	10	4.2.6. Conclusions – MOE approach	The use of the limited rodent toxicity studies for SCCP (kidney) and MCCP (kidney and thyroid) to define an MOE is appropriate but not LCCP (liver adaptive)	The CONTAM Panel acknowledges the comment.
Institute of Food Safety, Animal Health and Environment "BIOR" (Latvia)	11	General comments	Dear colleagues, The report provides a great deal of information in regards to the occurrence of chlorinated paraffins in food and feed and possible health risks for humans and animals related to these contaminants. The report is certainly more positive than negative by a large margin, although from the specific viewpoints of the risk assessment community there are two points of concern that need to be addressed. By our opinion the points of concern which should be taken into account for the preparation of the final report are: 1) According to the current draft version of the report the Panel concluded that the margin of exposure numbers (MOEs) do not indicate a health concern related to the presence of SCCPs and MCCPs in breast milk for breastfed infants. Although, the current report operates with the numbers observed for pooled breast milk samples without any consideration of probably considerable variations levels of CPs between individual samples. This point is of concern especially considering available data from other regions where large variations in CP levels in	The CONTAM Panel acknowledged that the exposure estimation performed for breastfed infants was done using pooled breast milk samples (see Section 3.5.2 of the Opinion) and thus recommended more data on variation of occurrence of CPs in human milk to enable a more robust exposure assessment for breastfed infants. This has now been made clearer in the

Stakeholder	Comment number	Chapter	Comment	EFSA response
			breast milk samples were observed. For example, according to data from China, the SCCP and MCCP concentrations in breast milk from different provinces varied by more than two orders of magnitude with the trend of increasing of CP concentrations over the time (D. Xia, et.al., Environment International 103 (2017) 1–7). The same variations are likely to be expected in the EU, especially considering the lipophilic properties of CPs and their uncontrolled usage in consumer goods. Such high variations could be supported by certain studies which report positive correlations between the levels of brominated flame retardants in matched samples of indoor dust and breast milk (e.g. J.D. Coakley et.al., Environment International 59 (2013) 255–261) especially considering bioaccumulative properties of CPs. Therefore in order to provide more realistic data, consideration of a range of contamination for the evaluation is highly recommended. Considering that some groups of people could be exposed to CPs to greater extent (e.g. people who involved in preparation of food in the kitchen) it is also could be recommended to perform separate risk assessment for these groups. 2) General tendency of increasing of CP usage in consumer goods should be also considered, especially taking into account positive temporal trends on the increasing of CP levels in breast milk. Therefore call for toxicological and occurrence data and further risk reevaluation is of high importance in case of CPs. Special concern should be paid also to the applying of CP containing formulations in technological processes for the preparation of food and feed. We are interested to bring attention to these concerns and ask that the EFSA considers these points for future discussions.	Summary, in Section 3.3.1, Section 3.4.1 and Conclusions of the Opinion. The CONTAM Panel made recommendations for more occurrence data in food and feed, and chronic toxicity studies for relevant CP mixtures. The presence of CPs in some common kitchen equipment, domestic plastic and food packaging was acknowledged by the Panel, and the fact that migration from plastic and kitchen equipment can contribute to the total CP exposure. A recommendation has now been made regarding the need of more data on the possible transfer of CPs from, e.g. kitchen equipment, into food.
Adrian Covaci, private capacity	12	Summary	P7, L273 - in general, we need toxicity studies in which more sensitive toxicity endpoints are studied. eventually studies in which biomarkers of effect are investigated, including omics biomarkers. P7, L278-279 - toxicity of specific CP congeners is also needed	The CONTAM Panel highlighted the need for chronic toxicity studies for relevant CP mixtures, as well as the need to identify which specific CP congeners are more relevant in terms of occurrence in food and of relevance for human health.

Stakeholder	Comment number	Chapter	Comment	EFSA response
	13	5. Recommendations	It certainly seems that there is a strong lack of data in all areas of the assessment. I imagine that much of the toxicology data from studies on rats and mice is from the 80s and 90s and until there are more studies looking a cellular level and endocrine disrupting effects I don't think much can be predicted. It also seems that LCCPs (for which there is almost no data) should be considered as a major portion of the assessment (rather than an emerging side note) as, at least in Europe, there is some evidence that these will likely make a substantial contribution to market share/production and consequent food chain contamination.	The CONTAM Panel made recommendations for more data in several areas of the risk assessment of CPs in order to reduce the uncertainties. The CONTAM Panel does not consider that LCCPs were a side note of the risk assessment. The assessment has considered the data available on all CPs, including LCCPs, for which considerations and limitations of the available data were discussed alongside those of SCCPs and MCCPs.
German Federal Institute for Risk Assessment (BfR)	14	General comments	As observed by the panel, chlorinated paraffins (CPs) are a very heterogeneous group of compounds. Please include an assessment, whether all members of the assessed CPs can be grouped together. To be transparent, the read-across assessment should follow the established guidelines such as ECHA's read across assessment framework (https://echa.europa.eu/support/registration/how-to-avoid-unnecessarytesting-on-animals/grouping-of-substances-and-read-across).	It was described in Section 3.1.6.1 of the Opinion that the CONTAM Panel is of the opinion that all CPs in general cannot be grouped together for a risk characterisation of CPs in food and feed: "*The toxicokinetic studies in rats and mice indicate that the toxicokinetics vary depending on carbon chain length, as well as on position and degree of chlorination (see Section 3.1.1.4). Therefore, the toxicokinetic and toxicity studies performed with only a few CPs can in principle only provide information on the CPs investigated. Read-across to other CPs, both within the same class as well as in other classes, is therefore problematic and will have high uncertainty.*" This message was also included in Section 3.5.4 about Other uncertainties. However, as an exposure assessment could be performed for SCCPs and MCCPs in fish, the CONTAM Panel decided to perform risk characterisations for these two groups of CPs acknowledging "*…that only a few CPs have been tested in the available toxicity studies*".

Stakeholder	Comment number	Chapter	Comment	EFSA response
	15	Abstract	Line 23ff: The Panel concluded that the MoEs do not indicate a health concern. Although EFSA noted the uncertainties of the Scientific Opinion, this overall conclusion should be re-phrased more cautiously as MoE is usually considered as a risk management tool.	The wording in the Abstract, Summary and other sections of the Opinion has now been modified in order to reflect better the conclusions and uncertainties in the risk assessment. The CONTAM Panel does not agree that the MOE approach for risk characterisation is a risk management tool. MOE as being the ratio between a toxicological reference point and the estimated exposure is part of risk assessment.
			Line 24: EFSA states (line 4196-4197) 'food could become more contaminated at the preparation stage as a result of transfer during contact (direct or secondary), and this is an important consideration when making exposure estimates'. Therefore, to use fish consumption only and to state 'that the MOEs do not indicate a health concern' (line 24) is misleading to the reader and to risk managers. It should either be clearly and explicitly stated in the Abstract that the MOE is valid for 'fish-only-eaters' only or EFSA should state in the abstract that the exposure for SCCP and MCCP is underestimated (similarly as in line 4872) and that a reliable MOE cannot be derived. A third option would be performing a rough estimate based on the limited exposure data on fish, dietary products and food processed using hand blenders together with an indication of the uncertainty.	The presence of CPs in some common kitchen equipment, domestic plastic and food packaging was acknowledged by the Panel, as well as the fact that migration from plastic and kitchen equipment can contribute to the total CP exposure (see Section 3.5.2 of the Opinion). A recommendation has now been made regarding the need of more data on the possible transfer of CPs from, e.g. kitchen equipment, into food.
	16	Summary	Lines 273-290: BfR forwarded data on the release on SCCP and MCCP from hand blenders into food simulant. Those findings were confirmed by Yuan et al. (doi:10.1016/j.envint.2017.09.014). Furthermore Gallistl et al. (doi: 10.1016/j.scitotenv.2017.09.112) quantified SCCPs and MCCPs in household ovens, used for the preparation of food. From our point of view food contact materials (FCM) like kitchen appliances may be a relevant source of dietary exposure to CP. Hence, data collection on the release of CP from such appliances and FCM into food should be investigated as well. The BfR suggests adding this to the list of recommendations (lines 273-290).	The CONTAM Panel thanks the BfR for the data submitted to EFSA on the release of SCCPs and MCCPs from hand blenders into food simulants, that is reported in Section 3.2.3 of the Opinion. A recommendation has now been made regarding the need of data on the possible transfer of CPs from, e.g. kitchen equipment, into food.

Stakeholder	Comment number	Chapter	Comment	EFSA response
	17	1.3.3.1. Biodegradation	Lines 652-681: Recently a dehydrohalogenase from *Sphingobium indicum* was characterised that eliminates HCl, thereby converting CPs to chlorinated olefins (Heeb et al. (doi:10.1016/j.chemosphere.2019.03.169)). In addition, enzymatic degradation of SCCP via dechlorination and carbon chain decomposition has been described in plants, like pumpkin and soy beans (Li et al. (doi:10.1016/j.yrtph.2019.04.010)). Degradation of chlorinated paraffins, not related to biological systems has been described and should be included in the discussion. It has been demonstrated that chlorinated paraffins in dough degrade to shorter congeners during baking at 200°C (Perkons et al. (doi:10.1016/j.foodchem.2019.125100)). These results were supported by an analysis on the decomposition of CP-52 (Xin et al. (doi:10.1016/j.jes.2018.05.022)). Data indicate that chlorinated paraffins degrade to shorter chain length congeners, thereby generating SCCPs. At temperatures between 200 400 °C, cyclisation and aromatisation can occur, thereby generating chlorinated PAHs.	The CONTAM acknowledges this information and notes that the sub-section on 'Biodegradation' under the Section on 'Environmental fate and levels' provides an overview of some aspects in the field, but does not claim for completeness as stated at the beginning of the section. The last update of the literature was done on 11 March 2019 and since that date, the literature was monitored to identify studies relevant for the risk assessment until the time of endorsement. The Panel however considers of interest the possible formation of chlorinated polycyclic aromatic hydrocarbons (PAHs) as described by Xin et al. (2019, available on-line 8 June 2019) and the dechlorination, chlorine rearrangement and carbon chain decomposition described by Li et al. (2019a, available on-line 17 May). Reference to these studies has now been made in Section 1.3.3 of the Opinion. The study by Perkons et al. (2019, available on-line 29 June) provides information of interest regarding the effects of processing (baking) on the levels of CPs, and reference to this study has now been made in Section 3.2.3 of the Opinion.
	18	1.3.3.3. Occurrence in the outdoor environment and wildlife	Lines 731-736: Diefenbacher and co-workers (doi:10.1021/acs.est.5b02153) reported concentrations, seasonal trends and spatial distributions of the SCCP in the outdoor air of Zürich (Switzerland) between 2011 and 2015. The SCCP concentrations in air ranged from 1.8 to 17 ng m−3 (spring 2011) and 1.1 to 42 ng m−3 (spring 2013) with medians of 4.3 and 2.7 ng m−3, respectively. Using a modelling approach the authors estimated that 218 312 kg of SCCP are emitted each year in the city of Zürich. Outdoor air concentrations in the UK were reported by Barber et al. (doi:10.1021/es047949w) and Peters et al. (doi.org/10.1016/S1352-2310(99)00479-3). The BfR suggests to add these data to this chapter.	The CONTAM acknowledges this information and notes that the sub-section on 'Occurrence in the outdoor environment and wildlife' under the Section on 'Environmental fate and levels' provides an overview of some aspects in the field, but does not claim for completeness as stated at the beginning of the section.

Stakeholder	Comment number	Chapter	Comment	EFSA response
	19	1.3.3.4. Occurrence in the outdoor environment	1.3.3.4. Occurrence in the indoor environment (transmission error: see correct header in the opinion) Lines 822-831: Data on indoor air concentrations of SCCP from Norwegian homes and two schools have been described by Sakhi et al (doi:10.1016/j.scitotenv.2019.04.086) and should be included to the opinion.	The CONTAM acknowledges this information and notes that the sub-section on 'Occurrence in the outdoor environment' under the Section on 'Environmental fate and levels' provides an overview of some aspects in the field, but does not claim for completeness as stated at the beginning of the section.
	20	2. Data and Methodologies	Using the RAPEX (Rapid Alert System for dangerous non-food products) data base a total of 141 SCCP containing consumer products were listed (see attachment). A baby sleeping bag contained 40 g/ kg (alert A12/0178/17), a garden hose contained 46.6 g/kg (alert A12/0318/19) and toys with up to 71 g/kg (alert A12 /0839/13) have been reported (see attached file). While RAPEX lists SCCP only according to its regulation, it clearly shows that chlorinated paraffins are ubiquitous distributed over a broad range of consumer related products. Other products were listed in the EFSA draft, but not considered for the exposure calculation. These are for example, CPs in oil-based dietary supplements (Sprengel et al. (doi:10.1016/j.envint.2019.04.065)). The BfR suggests to add the RAPEX data to the opinion in order to document the widespread exposure and to support identification of contaminated consumer products in future.	The CONTAM Panel thanks the BfR for this information and acknowledged the possible uses of CPs in Section 1.3.2 of the Opinion. The EFSA CONTAM Panel focuses on the estimation of the exposure from the diet, and made a rough estimation of the exposure via dust as a relevant non dietary source of exposure. Exposure via consumer products was not under the remit of the mandate.
	21	2.2. Occurrence data submitted to EFSA	Lines 1473-1475 Since the contribution of dietary supplements to exposure can be substantial (a mean daily intake of 5.5 µg SCCPs and 38 µg MCCPs, according to the authors) the discussion of these data without further integration into the exposure estimation is a severe short-coming of the opinion.	The outcome of the study by Sprengel et al. (2019) is reported in Section 3.2.2 and Section 3.3.2 of the Opinion. In addition, the authors submitted these data to EFSA, although these data could not be included on time in the EFSA Data warehouse for the current risk assessment and the estimates of exposure made by EFSA (see Section 2.2 of the Opinion). EFSA has acknowledged in its uncertainty analysis that other food categories contribute to the exposure, and recommended the need for more

Stakeholder	Comment number	Chapter	Comment	EFSA response
				occurrence data in food and feed to enable a robust exposure assessment.
	22	3.1.2.2.2. Repeated dose toxicity - MCCPs	Line 2153: '…these thyroidal effects were minimal to mild in nature' Comment: The effects of MCCP on the histopathology of different organs are described (Poon et al. 1995), using an average severity index (1, minimal; 2, mild; 3, moderate; 4, marked). The effects on the thyroid architecture reached a severity index of 2.5 at the highest dose. In contrast, the index for the thyroid epithelium (increased height) was 2.8 at the highest concentration in males and females, being closer to 'moderate' than to 'mild'. This is supported by the authors which state that 'with a mild to moderate degree of lesions detectable in the groups fed 50 ppm CP or higher' (page 462). The BfR suggests to change the thyroidal effects from 'minimal to mild' to 'minimal to moderate'. Unfortunately the authors did not report any thyroid hormone serum concentrations. Since the thyroid epithelial height reflects the hormonal activity of the gland, it is likely that the serum concentrations of T3 and T4 are affected. In contrast to Poon et al. (1995), the unpublished study (CXR, 2005b) on MCCP reported decreased T3 and T4 levels and an increase in plasma TSH (lines 2123-2128) and derived a NOAEL of 9.3 / 9.7 mg/kg bw per day, for males/females, respectively, based on these changes. According to the guidance document on endocrine disruptors (doi:10.2903/j.efsa.2018.5311) changes in the thyroid tissue and/or of circulating levels of T3 / T4 are adverse effects and request further studies.	The limitations of the Poon et al. (1995) study are clearly described in the Opinion, as well as the reasons for why the CONTAM Panel could not identify a NOAEL from this study (see Section 3.1.2.2.2 of the Opinion): "*It was not possible for the CONTAM Panel to obtain the scorings for individual animals from the study authors. Therefore, the Panel was not able to interpret the histopathological findings in the liver, kidney and thyroid, and thus not able to identify a NOAEL from this study.*" As described in section 3.1.6.1 of the Opinion, the CONTAM Panel identified a NOAEL of 10 mg/kg bw per day for MCCPs. This NOAEL is also the no-observed-effect level (NOEL) for changes in thyroid hormone plasma levels in the CXR (2005) study and therefore, the NOAEL of 10 mg/kg bw per day will also take into account the changes in thyroid hormone levels observed in the CXR (2005) study. The BfR suggested to change thyroidal findings to 'minimal to moderate' with a reference to page 462 in the Poon et al. (1995) manuscript. The CONTAM Panel noted that in the Result part of the manuscript (page 457) the thyroid changes are described as "*… changes were generally minimal to mild in nature*" and this is what is reflected in the Opinion. Text has now been revised slightly in the Opinion (see Section 3.1.2.2.2). The CONTAM Panel acknowledges the guidance document on endocrine disruptors. Due to the inconsistencies in thyroid hormone changes

Stakeholder	Comment number	Chapter	Comment	EFSA response
				between studies and between genders (MCCPs) the Panel considered that the changes in thyroid hormone levels could not to be used as a basis for deriving a reference point. Therefore, only the histopathological changes reported in studies with SCCPs have been considered as a basis for deriving a reference point. This has now been made clearer in the Opinion in Section 3.1.5.3 while discussing the mode of action for thyroid effects, Section 3.1.6.1 on Consideration of critical effects and Section 3.5.4 on uncertainties. The Panel also recognises that changes in thyroid hormone levels in rodents would be of potential concern regarding neurodevelopment in humans. However, no studies on potential neurodevelopmental effects of CPs in mammals were identified. This has now been made clearer in the Opinion in Section 3.1.5.3, in the uncertainty section (see Section 3.5.4 of the Opinion) and in the Recommendations in addition to the text already provided (see Section 5 of the Opinion).
	23	3.1.2.6.4. Summary on genotoxicity	The panel concluded that based on the weight of evidence the CPs would be 'not genotoxic'. Please include a complete weight of evidence assessment in line with EFSA's "Guidance on the use of the weight of evidence approach in scientific assessments". Currently, it is difficult to understand the reasons for that conclusion.	The EFSA Scientific Opinion on the Guidance on the use of the weight of evidence approach in scientific assessments (EFSA SC, 2017) indicates that the term 'weight of evidence' on its own is the extent to which evidence supports possible answers to a scientific question. This is what is assessed by weight of evidence assessment, and can be expressed qualitatively or quantitatively. As is evident from the Opinion, the majority of the genotoxicity tests are negative. The CONTAM Panel considered this as a qualitative weight of evidence assessment.

Stakeholder	Comment number	Chapter	Comment	EFSA response
	24	3.1.5.1.2. Mode of action – Effects in the liver - In vitro	General comment on in vitro studies: SCCP and MCCP have low water solubility (Gluege et al. (doi:10.1063/1.4802693)). The calculated solubility for MCCPs in water is between 0.02 µg/L (for a C17−CP with 70% chlorine) and 40.4 µg/L (for a C14−CP with 35% chlorine) (Gluege et al. (doi:10.1021/acs.est.7b06459)). Several in vitro studies were published and the modes of action of CP were discussed (Geng et al. (doi:10.1021/es505802x) and Ren et al. (doi: 10.1016/j.scitotenv.2019.05.388)). Care should be used in the interpretation of these studies, since either citation of the (commercial) source of the SCCP is missing (Geng et al. (doi:10.1021/es505802x)), there is a lack of data for those CPs synthesised (Wang et al. (doi:10.1016/j.envpol.2017.11.073)), and, likewise, absence of data on how CPs dissolved in cyclohexane were redissolved in DMSO (Ren et al. (doi:10.1016/j.scitotenv.2019.05.388)). Furthermore, none of the in vitro studies report a quantification of the effective doses of CP in the aqueous culture medium. This is a source of uncertainty. All authors reported, that CPs were dissolved in a DMSO stock solution. The final DMSO concentration in the culture was 0.05%. Hence, apparently the DMSO stock was diluted 2000-fold. Consequently the final concentration of CP must have been 200 mg/l (100 x 2000). It is questionable, if MCCP or LCCP (Ren et al. (doi:10.1016/j.scitotenv.2019.05.388)) can be completely dissolved at these concentrations in DMSO. Therefore, the effective concentrations given in the publications should be used with care.	The CONTAM Panel agrees with the comment, and no interpretation on a quantitative basis was made in the assessment. This has now been clarified in Section 3.1.5.1.2 of the Opinion.

Stakeholder	Comment number	Chapter	Comment	EFSA response
	25	3.1.5.1.3. Mode of action – effects in the liver - Summary on liver toxicity	EFSA excluded CAR and PPAR-alpha signalling as relevant MOA for human carcinogenicity (line 3179) and suggested that only hepatic cytotoxicity is the main MOA for hepatic carcinogenesis of SCCP. Comment to lines 3176-3180: SCCP, MCCP and LCCP show similar cytotoxic effects in HepG2 cells. All CPs induced significant increases of reactive oxygen species (ROS) and malondialdehyde (MDA) as well as a significant reduction in the ATP production. MCCP and SCCPs shared a most similar cytotoxicity and metabolic perturbation (Ren et al. (doi: 10.1016/j.scitotenv.2019.05.388)). MCCP are cytotoxic in vitro (Ren et al. (doi:10.1016/j.scitotenv.2019.05.388)) and in vivo. A 13-week exposure (Poon et al. 1995) resulted in significant hepatic changes as indicated by an increased pericentral homogeneity in males at 362.9 mg/kg b.w. per day and in females at and above 42.2 mg/kg b.w. per day. In addition, single-cell necrosis occurred in males and females at 362.9 and 418.9 mg/kg b.w per day. Therefore, it can be concluded, that MCCP are also hepatotoxic in rodent liver. Despite the absence of a rodent carcinogenicity study it cannot be excluded, that MCCP are hepatic cancerogens at high concentrations.	As mentioned in the reply to Comment 24, the CONTAM Panel agrees with the conclusion that no attempt should be made for a quantitative assessment of potency from *in vitro* studies. Therefore, it is considered too speculative to suggest that MCCPs may be carcinogenic. The Panel finds it inappropriate to 'not exclude' a possibility. However, the inability to conclude on the carcinogenicity of MCCPs because of insufficient data is noted elsewhere.

Stakeholder	Comment number	Chapter	Comment	EFSA response
	26	3.1.5.1.4. Mode of action – effects in the liver - Mode of action in liver carcinogenesis	Tumours were observed in several studies on various sites in mice and rats in tested SCCPs. Moreover, SCCPs (chlorinated paraffins C10-13 (SCCP), EC No: 287-476-5, CAS No: 85535-84-8) are legally classified as carcinogenic in humans. Several studies were performed on the clarification of the potential MoA of tumourgenesis. It was overall concluded that SCCPs are carcinogenic in rodents but the tumours observed in rats and mice were not relevant for humans. CAR activation and PPAR-alpha a MoA which was considered by the CONTAM Panel as not relevant for humans provided cytotoxicity does not occur. However, a proper WoE approach is lacking. Please include a complete weight of evidence assessment in line with EFSA's "Guidance on the use of the weight of evidence approach in scientific assessments". CAR and PPAR-alpha activation as assumed as MoA for liver tumours in rodents requires several key and associate events to support this assumption. Please provide a comprehensive human relevance assessment (https://www.who.int/ipcs/methods/harmonization/areas/cancer/en/) including a description of the molecular initiating event and the key events. It is noted that liver necrosis was seen in rats (NTP, 1986a; Bucher et al., 1987). This would indicate that cytotoxicity occurred.	The CONTAM Panel notes that the Opinion does not negate the potential importance of necrosis in rodent liver contributing to carcinogenicity (see Section 3.1.5.1.4 of the Opinion) it is fully recognised, and the dose dependency is noted regarding the relevance to humans. Modifications have been now included in Section 3.1.5.1.4 of the Opinion to clarify this. The EFSA Scientific Opinion on the Guidance on the use of the weight of evidence approach in scientific assessments (EFSA SC, 2017) indicates that the term 'weight of evidence' on its own is the extent to which evidence supports possible answers to a scientific question. This is what is assessed by weight of evidence assessment, and can be expressed qualitatively or quantitatively. In the CONTAM Panel assessment the mode of action for carcinogenicity in the rodent, liver has been established as potentially involving (1) CAR activation, (2) PPARα activation, (3) cytotoxicity; in the absence of evidence for genotoxicity. In the weight of evidence assessment these are considered along with a consideration of the relevance of the rodent liver effects to humans. Modifications have now been included in Section 3.1.5.1.4 of the Opinion to clarify this.

	27	3.1.5.3. Mode of action - Effects in the thyroid	Lines 3294-3296: '…the free fraction of the T4 is larger than in humans and total T4 half-life is shorter (around 24 h in rats, versus 5–6 days in humans) (Lewandowski et al., 2004).' Comment: This is a comparison between adult rats vs adult human. However, it should be kept in mind for any discussion about species-specific sensitivity towards endocrine disruptors of the thyroid-axis: (1) Depletion of the hormone reservoir as well as half-life in human newborns is much shorter than in adults. This has been shown for T4 plasma half-life (Lewander et al. (PMID: 2748253)) and turnover of the intrathyriodal T4 store (van den Hove et al. (doi: 10.1016/s0300-9084(99)80111-4)). This makes the young human population more vulnerable to declines in serum hormone levels. These are results of a 'round table discussion' organised by the Society of Toxicology (Li et al. (doi:10.1016/j.yrtph.2019.04.010)), which states that '… the human fetus /neonate has a lower storage capacity ….. and a shorter hormone half-life than do adults (e.g., T4 t1/2=3 4 days in fetuses and new-borns, 5-9 days in adults and 0.5-1 day in adult rats; …which makes them more vulnerable to serum hormone decline than adults'. Therefore, the risk assessment should include children and their sensitivity towards disturbed thyroxine serum levels. Lines 3303-3305: 'This is despite the fact that elevations of thyroid stimulating hormone have not been reported in humans for a range of drugs all of which cause hyperplasia or tumors in rats (Wu et al., 2006)'. Comment: This statement should be specified in more detail, since there are also reports about drug induced increased TSH levels in humans sometimes in combination with decreased fT4 levels (Eiris-Punal et al. (doi: 10.1111/j.1528-1157.1999.tb01595.x), Kim et al. (doi:10.1055/s-0032-1313913), Yilmaz et al. (doi:10.1016/j.seizure.2013.12.001)). Lines 3311-3314: 'However, the Panel considered that only when these hormonal changes are accompanied by histopathological changes in the thyroid, are these effects in rodents considered to be adverse and to be used in risk assessment.' Comment: Appropriate References supporting this approach should be included. This statement should be explained in more detail, since it	An additional sentence has been added in Section 3.1.5.3 of the Opinion to refer to the study by Li et al. (2019b). The CONTAM Panel recognises that changes in thyroid hormone levels observed in rodents would be of potential concern regarding neurodevelopment in humans. However, no studies on potential neurodevelopmental effects of CPs in mammals were identified. This has now been made clearer in the Opinion in Section 3.1.5.3, in the uncertainty section (see Section 3.5.4 of the Opinion) and in the Recommendations in addition to the text already provided (see Section 5 of the Opinion). Although there are further reports on changes in thyroid hormone levels in humans as suggested in the comment, the CONTAM Panel felt it appropriate only to refer to those changes that relate to chemicals that were proven tumourigenic in rodents since this is the comparison being made. The text regarding the Wu and Farreley (2006) study is still correct but has been modified to make it more detailed as suggested. See reply to comment 22 above.

			contradicts the EFSA/ECHA guidance document on endocrine disruptors (doi:10.2903/j.efsa.2018.5311), which states that (1) 'Substances inducing histopathological changes (i.e. follicular cell hypertrophy and/or hyperplasia and/or neoplasia) in the thyroid, with or without changes in the circulating levels of THs, would pose a hazard for human thyroid hormone insufficiency in adults as well as pre- and post-natal neurological development of offspring' and (2) 'substances that alter the circulating levels of T3 and/or T4 without histopathological findings would still present a potential concern for neurodevelopment.	
	28	3.1.5.3.1. Mode of action – effects in the thyroid - Additional thyroid effects investigated in zebrafish	Line 3342: …' might cause a hyperthyroid status in….' Comment: There seems to be a misprint, probably based on 'copy-and-paste'. In the cited work (Liu et al. (doi:10.1016/j.envpol.2016.09.016)) the authors detected reduced TT3 and sometimes reduced TT4 levels – this clearly indicates a hypothyroid state. At several occasions in their discussion, the authors similarly considered the findings indicative for a hypothyroid state. In their conclusion however, the term "hyperthyroid state" can be found which is most likely a misprint and was reproduced in the Draft of the EFSA. Therefore, the BfR suggests to change "hyperthyroid" to "hypothyroid".	The misprint has been corrected in Section 3.1.5.3.1 of the Opinion.
	29	3.1.5.4. Mode of action - Other tumour incidences in rodents treated with CPs	Several tumours were seen in studies with CPs. However, a proper WoE approach is lacking. Please include a complete weight of evidence assessment in line with EFSA's "Guidance on the use of the weight of evidence approach in scientific assessments". Please provide a comprehensive human relevance assessment (https://www.who.int/ipcs/methods/harmonization/areas/cancer/en/) including a description of the molecular initiating event and the key events.	The Opinion refers to the range of tumours reported and to the relevance to humans. The EFSA Scientific Opinion on the Guidance on the use of the weight of evidence approach in scientific assessments (EFSA SC, 2017) indicates that the term 'weight of evidence' on its own is the extent to which evidence supports possible answers to a scientific question. This is what is assessed by weight of evidence assessment, and can be expressed qualitatively or quantitatively. As is evident from the Opinion in Section 3.1.5.4, the CONTAM Panel considered this as a qualitative weight of evidence assessment, which included an assessment of the bases of the effects seen in rodents and the relevance to humans.

	30	3.1.6.2. Dose-response analysis (including BMD modelling)	It is unclear why a BMDL10 of 36 mg/kg bw/d was selected for MCCPs, knowing that the NOAEL in the range-finding 2-gen study was 9 mg/kg bw/d (reduced pup survival and subcutaneous haematoma /haemorrhages).	The comparison of a BMDL with a NOAEL from two different studies is not appropriate, since the NOAEL per se depends strongly on the dose selection. The correct comparison should be made between BMDLs from different studies. In this case, the NOAEL of the 2-generation dose-range finding study is particularly uncertain due to the rather wide inter-dose interval selected for the study. The application of the BMD analysis to the data on fetal toxicity resulted in a $BMDL_5$ of around 50 mg/kg bw per day. So overall the $BMDL_{10}$ of 36 mg/kg bw per day based on kidney weight changes is considered protective also towards the developmental effects.
	31	3.1.6.3. Derivation of a health-based guidance value / margin of exposure approach	Separate BMDLs were selected for SCCPs, MCCPs and LCCPs. Taking into account the heterogeneity of the toxicological data sets for each of the CP-groups, it might be possible to recommend the lowest PoD to be used for all CPs. This might also compensate for some of the uncertainties and difficulties of the chemical analyses to determine the contents in food and feed.	For clarification, BMDLs were not calculated for LCCPs (see Section 3.1.6.2 of the Opinion). It is described in Section 3.1.6.1 of the Opinion that the CONTAM Panel is of the opinion that all CPs in general cannot be grouped together for a risk characterisation of CPs in food and feed: "*The toxicokinetic studies in rats and mice indicate that the toxicokinetics vary depending on carbon chain length, as well as on position and degree of chlorination (see Section 3.1.1.4). Therefore, the toxicokinetic and toxicity studies performed with only a few CPs can in principle only provide information on the CPs investigated. Read-across to other CPs, both within the same class as well as in other classes, is therefore problematic and will have high uncertainty.*" And this message is also included in Section 3.5.4 of the Opinion on Other uncertainties. However, as an exposure assessment could be performed for SCCPs and MCCPs in fish, the CONTAM Panel decided to perform risk characterisations for these two groups of CPs acknowledging "*…that only a few CPs have been tested in the available toxicity studies*".

	32	3.3.2.6. Conclusions on the dietary exposure assessments reported in the literature	'Exposure from these products' (dietary supplements (BfRs comment)) 'could be in the same order of magnitude as from the consumption of fish meat'. Therefore it is not clear, why EFSA refused to add this exposure to the risk assessment. Even if this is a single study, the contribution to the exposure is substantial. This is not a '1 day exposure', since dietary supplements are taken often over a longer period of time. An additional uncertainty analysis can discuss the potential limitations of these data.	The outcome of the study by Sprengel et al. (2019) is reported in Section 3.2.2 and Section 3.3.2 of the Opinion. In addition, the authors submitted these data to EFSA, although these data could not be included on time in the EFSA Data warehouse for the current risk assessment and the estimates of exposure made by EFSA (see Section 2.2 of the Opinion). EFSA has acknowledged in its uncertainty analysis that other food categories contribute to the exposure, and recommended the need for more occurrence data in food and feed to enable a robust exposure assessment.
	33	3.4.1. Human health risk characterisation	The selected BMDL10s for SCCPs and MCCPs were used in the risk characterisation for breastfed infants (starting on line 4815). This population includes children with ages below 16 weeks. Please include an assessment in line with EFSA's "Guidance on the risk assessment of substances present in food intended for infants below 16 weeks of age" whether these BMDLs are applicable to/protective for infants.	The CONTAM Panel agrees that the $BMDL_{10}$s applied in the risk characterisation for breastfed infants do not apply without further considerations for this sub-population. However, the Panel considers that the risk characterisation performed for breastfed infants based on these $BMDL_{10}$s is protective for this sub-population for the following reasons: 1) these $BMDL_{10}$s are lower than the $BMDL_{10}$ derived for the haemorrhagic effects of the only tested MCCP; 2) the haemorrhagic effect observed in the rat pups and considered relevant for humans is due to deficiency in vitamin K and related clotting factors when the pups are reliant of these factors via the mother's milk, i.e. an indirect effect; 3) the exposure of the breastfed infants cannot be estimated; and 4) a lower reference margin of exposure (MOE) (500) would be applied for breastfed infants as the factor of 2 for extrapolation from sub-chronic studies to chronic exposure duration is not relevant for this sub-population.

	34	3.5.5. Summary of uncertainties	Table 37: "It is not clear whether changes in thyroid hormone levels in rodents via elevation of hepatic transporters and UDPGT in the absence of histopathological changes in the thyroid represents adversity in rodents" Comment: This has been discussed in the guidance document on endocrine disruptors of EFSA and ECHA (doi:10.2903/j.efsa.2018.5311) and uncertainties should be changed to '+/-'.	The CONTAM Panel acknowledges that liver enzyme induction as a mode of action for decreases in thyroid hormone levels (T4) has been addressed in the ECHA/EFSA (2018) Guidance for the identification of endocrine disruptors. A reference has been added (Bartsch et al., 2018) that discusses various reasons why thyroid hormone changes in rodents that are mediated through changes in hepatic metabolism appear to be much more pronounced than in humans. The Panel considerations on changes in thyroid hormone levels in the available CP studies have now been made clearer (see also reply to Comment 22). The entry in Table 37 on the Summary of uncertainties has been revised.
	35	4.2.2. Conclusions - Toxicity in experimental animals	The EFSA draft cites several studies with SCCP and/or MCCPs which detected reduced T3 and/or T4 levels in combination with histological findings in the thyroid. The study by Gong et al. (doi:10.1016/j.scitotenv.2017.12.251) reported decreased T3 and increased TSH levels after the exposure to SCCP. It is unclear why there were no histological changes in the thyroid despite increased TSH. Maybe the duration of the study was too short. Nonetheless, this study reports significant changes in the thyroid hormone system already at 10 mg SCCS /kg bw/d. The primary concern of altered thyroid hormone homeostasis is related to adverse effects on pre- and postnatal neuro-development (EFSA/ECHA guidance document (doi:10.2903/j.efsa.2018.5311)). Therefore, a change in thyroid hormone levels (and not changes in the thyroid gland itself i.e. hypertrophy/hyperplasia due to TSH feedback) is the more critical parameter and should be used here for risk assessment. Based on only these data and reflecting the above mentioned EFSA/ECHA guidance document a NOAEL of 1 mg SCCS / kg b.w./per day might be discussed for thyroidal and potential neurotoxic effects of SCCS (c.f see figure 1D and 1E in Gong et al. (doi:10.1016/j.scitotenv.2017.12.251)). A NOAEL of 9.3 mg/kg bw per day (CXR, 2005b) seems to be a reliable starting point, based on the EFSA /ECHA guidance document (doi:10.2903/j.efsa.2018.5311). The latter can be used to derive a tTDI. Standard uncertainty factors for toxicokinetic (10) and	Please see reply to Comment 22. The CONTAM Panel notes that a NOAEL approach is not the preferred approach in case a BMDL can be derived. The reasons not to derive health-based guidance value (HBGVs) for CPs

			toxicodynamic effect (10) should be included. An additional uncertainty factor of 10 seems to be plausible, using the arguments at line 180-187 in the EFSA Draft. Therefore, the tTDI for MCCP would be in the range of 9-10 µg/kg bw per day, based on changes in the thyroid and the related hormones.	are well discussed in the Opinion and are not dependent on the selected endpoint, therefore the derivation of a (temporary) tolerable daily intake (TDI) is not considered appropriate in this case.
	36	Appendix C – BMD modelling of rodent studies	For several findings a non-default benchmark response (BMR) was selected. The reasons are not transparent, why the higher BMR was considered more appropriate than the lower default BMRs. The reasons to deviate from the default values should be explained also citing references that support the deviation.	The CONTAM Panel concluded that a 5% change in absolute and relative kidney weights is of low biological relevance, considering that they are associated with histopathological changes at higher doses and these are modelled using a benchmark response (BMR) of 10% increase in the incidence (extra risk). A similar approach was used for kidney weight increase in several other EFSA opinions, e.g. Scientific opinion on the risks to public health related to the presence of bisphenol A (BPA) in foodstuffs (EFSA CEF Panel, 2015a, b).
	37	Appendix C.2. Incidence of nephritis in male rats exposed to SCCP (C10-12, 58% chlorination) (IRDC, 1984a)	The EFSA used this study to derive a BMDL10 value of 2.29 mg/kg bw per day, based on the increased incidence of nephritis. Comment: In general, the concentrations used in the studies of IRDC cited (1984a and 1984b) are spread over a very large concentration range; especially the doses in the lower and middle concentration. Such data sets are difficult for BMDL modelling and it is known that BMDL values might be artificially lowered. According to the EFSA guidance document (doi:10.2903/j.efsa.2017.4658) the BMDU/BMDL ratio reflects the uncertainty in the BMD estimate. This ratio is 33.36 (76.4/2.29, cf. line 6629) when modelling the endpoint "nephritis" in the study of the IRDC (1984a) and indicates a high uncertainty related to the BMDL10 derivation. Thus the data might not be informative enough to be used for derivation of a TDI. As stated in the above cited EFSA opinion, if related endpoints exist, for which the modelling results in significantly lower uncertainty (lower BMDU/BMDL relation), the application of these endpoints should be considered. When using the absolute kidney weights reported in the same study a BMDL10 of 38 mg/kg bw per day was derived. The corresponding BMDU/BMDL ratio was only 4.89 (186/38, line 6722) and thus has a much lower uncertainty. Alternatively, to be conservative, the NOAEL approach could be used to evaluate the study. This would result in a NOAEL of 10 mg/kg bw/day. Therefore, reasons to use a highly uncertain BMDL10	It should be noted that the BMD analysis is particularly useful in such situations since it helps to estimate the uncertainties around the Reference Point. In Table 23 of the Opinion it can be seen that in many cases the ratios BMDU/BMDL are in the same range or even higher than 33.36. In general, such a ratio is expectable considering the specific design of the study. Problematic datasets generally result in much wider BMDL-BMDU intervals of several orders of magnitude. The alternative proposal to use the NOAEL of 10 mg/kg bw instead of the $BMDL_{10}$ of 2.29 mg/kg bw gives a false presumption of precision since there is a lack of information on the uncertainty associated to the NOAEL. Note: the CONTAM Panel did not use the BMDL to derive a HBGV, i.e. a TDI (see Section 3.1.6.3 of the Opinion).

			value of 2.29 mg/ kg bw per day should be discussed in more detail. In addition, the BMDL10 of 38 mg/kg bw per day correlates well with a BMDL10, derived from another study (IRDC 1984b), which is 31.4 mg/ kg bw per day for males, bases on absolute kidney weights (EFSA line 6964). This finding decreases the uncertainty related to effects of SCCP in kidney.	
Euro Chlor (Cefic) Chloro Alkanes Product Group (Belgium)	38	General comments	In coordination with the chlorinated paraffins producers in the EU and U.S., the Chloro Alkanes Product Group (CAPG) and Chlorinated Paraffins Industry Association (CPIA) and have reviewed this document. CASG and CPIA had previously been contacted by EFSA and provided a large number of study reports in support of this research project. In general, we have found this report to be a thorough and well documented review of chlorinated paraffin toxicology. Presently, we do not have any specific comments to offer on the text though we will continue to review the document and share any comments with the study authors. Thank you for your efforts on this report.	The CONTAM Panel thanks Euro Chlor, CASG and CPIA for the unpublished study reports submitted to EFSA.
European Union Reference Laboratory for Halogenated POPs in Feed and Food	39	General comments	The EURL recognises the difficulties in data collection and interpretation met by the EFSA panel in the course of conducting this risk assessment. However, even if we agree with most of the data and conclusions presented in the document, we recommend a different approach to the way the conclusions and recommendations are presented in the draft opinion to avoid misunderstandings. We have been approached by institutions reading the draft opinion as meaning that CPs in general pose no health concern. This impression is supported by 1) the seemingly clear statement by EFSA concerning their evaluation of fish and human milk ["The Panel concluded that the MOEs do not indicate a health concern", ll. 24, 208, 222] and 2) a certain lack of elaboration on increasing risks from huge annual production volumes. As has recently been shown and concluded at the Dioxin 2019 symposium on halogenated POPs, chlorinated paraffins with their annual production volume of more than 1.3 million tons can certainly be classified as emerging POPs. In nearly all parts of the world, SCCPs and MCCPs present about 40% of the Stockholm Convention POPs found in human milk. In Europe at present, CPs present about 15% of the total Stockholm Convention POPs in human milk, with a higher contribution	The wording in the Abstract, Summary and other sections of the Opinion has now been modified in order to reflect better the conclusions and uncertainties in the risk assessment. Available CP production figures were reported in Section 1.3.2 of the Opinion.

			of the legacy industrial POPs used here, in particular caused by PCBs – however, a similar development in Europe to increasing proportions of CPs is likely in view of the wide variety of products containing CPs imported into the EU. Of particular concern would be a peak exposure which can derive from use of CPs in products used in households, in particular in the kitchen or for food and feed processing in general, as already addressed in the draft opinion. A new example for possible CP sources in households or food/feed production sites was presented at Dioxin 2019 where newly purchased polyurethane foams from the Netherlands were found to have CP levels ranging up to about 50% (w/w) with dominance of MCCPs and LCCPs. Test showed a transfer of these CPs onto skin and into air. The human milk results are based on pooled samples from 11 European countries analysed within WHO /UNEP coordinated surveys. According to the protocol of these surveys, pooled samples are prepared by mixing of representative individual samples. This is an extremely efficient way to receive information on the average contamination in countries with various POPs. However, ranges in individuals might comprise levels up to 10-fold higher. As shown in table 30 [p. 150, l. 4367], individual samples from Europe had SCCP contents up to 820 µg/kg fat (Thomas et al, 2006) and MCCP contents up to 903 µg/kg fat (Hilger et al., 2011) - this would lead, according to EFSA's calculations, to MOE <1000 for SCCPs. Therefore, peak exposure occurs also in humans and individual samples collected in Europe already have shown to be above the no-risk range or of possible health concern. EURL would like EFSA to comment on how to incorporate such findings into the risk assessment. As a result, an understanding of the draft EFSA opinion as meaning that CPs pose no health concern would have serious consequences for performance (planning and financing) of any further research in this field. Seemingly dismissing CPs altogether with respect to their possible impact on humans at this point in time seems premature. As the EFSA Panel rightfully recommended the collection of further data and further efforts to generate comparable analytical methods, we do not believe that this outcome would be in their (and the public's) best interest. We therefore propose that EFSA recommend a monitoring	The CONTAM Panel decided to use the more recent data available on human milk from that compiled in Table 30 of the Opinion in order to reflect better current concentrations and considering the development in the analytical methods. Thus, the Panel used the WHO/UNEP data to estimate the exposure for breastfed infants. The CONTAM Panel acknowledged that the estimation referred to pooled samples (Section 3.5.2 of the Opinion) and thus recommended more data on variation of occurrence of CPs in human milk to enable a more robust exposure assessment for breastfed infants. This has now been made clearer in the Summary, in Section 3.3.1, Section 3.4.1. and Conclusions of the Opinion. The CONTAM Panel recommends the generation of occurrence data in food and feed in order to perform a robust exposure assessment and for a complete risk characterisation. European and

			programme and mention this already in the abstract and summary part of the report.	national decision-makers will use EFSA's advice as well as other considerations to decide on the necessary measures. Due to the restricted number of words in the Abstract, the recommendations made by the Panel are generally not included in the Abstract, but are listed in the Summary.
	40	Abstract	Although EFSA quite extensively elaborates restrictions and limitations later on, line 17/18 present the reader two definitive BMDL10 values without any caveats. Based on the data and age/ reliability of the toxicological studies used, we propose to signal clearly that these BMDL10 values are more of a tentative nature – e.g. as "The Panel selected as reference points a provisional BMDL10 […] for some SCCPs and MCCPs, respectively." The second amendment is proposed as the toxicological studies only covered a very small segment of SCCPs or MCCPs, respectively, and the overall toxicological effects from other, not tested CPs were apparently derived from the available data by cross-reading different studies [p. 175-176, ll. 4898-4903]. Furthermore, we propose that the sentence "The Panel concluded that the MOEs do not indicate a health concern,…" might be amended as follows: "the Panel concluded that the MOEs derived for 'fish meat' do not presently indicate a health concern for this food group ,…". This way the caveats to this conclusion briefly mentioned in the second part of the sentence would become much clearer and misunderstandings as to the scope of the conclusion on a lack of health concern could be avoided more easily.	The wording in the Abstract, Summary and other sections of the Opinion has now been modified in order to reflect better the conclusions and uncertainties in the risk assessment. The CONTAM Panel does not establish provisional or temporary health-based guidance values or reference points. Limitations and uncertainties are described in the Opinion. In general terms, any health-based-guidance value or reference point will be revised if new evidence is available.
	41	Summary	In several places throughout the document CP congeners and congener patterns are mentioned. As fitting and familiar as this terminology might be when someone is used to dealing with PCBs and PCDD/Fs, in the case of CPs any derived patterns or profiles are most certainly pertaining to congener groups (also called homologues) instead of single congeners. Please consider amending your terminology accordingly. [p. 3, ll. 73-77] It should be noted that especially technical products from China never adhered to this three-tiered approach of classifying CPs by carbon chain length, so it is definitely not a recent development as stated in this passage. Additionally, the recent works of Zhou et al	The CONTAM Panel considers that where the term 'congener patterns' or 'congener profiles' is used, it is implicit that this refers to group patterns or profiles, and the use of this terminology is widely reflected in the literature. The text of the Opinion has been re-checked and modifications have been made in some places to clarify. Reference to very short chained CPs (vSCCPs) has been made in the corresponding section.

			and Xia et al on nonane-based CPs (part of a group called very short chained CPs, vSCCPs) should be mentioned, as they were found in significant percentages in Chinese wildlife already, with the current toxicological understanding of SCCPs placing them in a potentially harmful category [Zhou et al (2019), doi: 10.1016/j.envint.2019.104955 and Xia et al (2019), doi: 10.1016/j.jhazmat.2019.02.089]. The EURL is aware that there is not enough occurrence data and no toxicological data available yet but this development could become important in the future and should therefore not be omitted.	
			[p. 3, ll. 91-93] Did the panel consider the Chinese study on placental transfer of CPs? [Qiao et al (2018), doi: 10.1021/acs.est.8b02839] It is mentioned twice in the draft, but without further elaborations [p.56, ll 1711-1713, p. 148, ll. 4305-4312]. The study in question showed CPs from the mother (found in blood/milk) to blood drawn from the umbilical cord and neonate directly with somewhat matching homologue patterns. This would not only indicate the absorption of CPs to some degree, but also maternal transfer and might indicate some extent of metabolism. If this study was known but discarded by the panel, we would welcome a short statement as to why this was deemed irrelevant.	The CONTAM Panel has not discarded the Qiao et al. (2018) study, which is described in Section 3.1.1.2 (p. 57) and Section 3.2.4 (p. 154) of the Opinion. Text is Section 3.1.1.2 has now been amended.
			[p. 3, ll. 104-105] The EFSA Panel later on (p. 5, ll. 166-168; p.46 l. 1371, p. 119, ll.3492-3500) elaborates on the ECHA classification of one type of MCCPs as potentially harmful to breastfed infants due to vitamin K deficiency and respective studies with the conclusion that haemorrhagic effects are considered relevant to humans. The current text passage ("No studies on observations in humans of relevance for the risk assessment of CPs within the scope of this opinion were identified.") however seemingly dismisses this assessment without further explanation. As young children are clearly to be considered a vulnerable part of the population and both SCCPs and MCCPs have been found in European human milk, we ask the Panel to further elaborate on the decision to dismiss their own assessment.	The CONTAM Panel does not understand the comment that this information is dismissed. The effects on vitamin K deficiency have been shown in rat studies as described in the Opinion (Section 3.1.2.3.2 and Section 3.1.5.7). However, there are no human data on this effect. Nonetheless, the haemorrhaging effect is considered of relevance to humans, as described in Section 3.1.5.7 of the Opinion.
			[p. 4, ll. 116-119; 134-135] Keeping the BMDL10 of 36 mg/kg bw/d for MCCPs (endpoint: increased relative kidney weight) that the Panel concluded on in mind, the different studies named in the summary all conclude NOAELs around 9-10 mg/kg bw/d for increased kidney weight, decreased pup survival and subcutaneous haemorrhage. The EURL is aware that a BMD model is quite different to a derived NOAEL, but	As stated in Comment 30 the NOAEL gives a very partial view restricted to the doses that were tested in the study. The fact that a BMDL falls between the study NOAEL and LOAEL is not surprising and is actually much more informative about the dose at which a certain change is

			given the stark contrast to the very high BMDL10 value, we'd like to inquire if there might be a decimal error somewhere in the calculations. It seems unlikely that three studies in the same NOAEL range lead to a BMD model with a BMDL10 that is threefold higher than the NOAELs. [p. 5, ll. 189-192] "Due to the unavailability of sufficient occurrence data on foodstuffs other than fish, it was not possible to carry out a robust exposure assessment." In the interest of clear risk communication, this sentence definitely should be in the abstract, ideally instead of any comment on health concern, but otherwise at least heading up the section concerned with that conclusion.	expected to occur. It is unclear on which basis a BMDL that is only 3 times higher than the study NOAEL is defined as very high. The wording in the Abstract, as well as in the Summary and other sections of the Opinion, has now been modified in order to reflect better the conclusions and uncertainties in the risk assessment.
	42	3.1.6.3. Derivation of a health-based guidance value / margin of exposure approach	[p. 126, ll. 3718-3724] The uncertainty factor of 5 chosen by the panel for deficiencies in the database used for risk assessment was proposed by WHO/IPCS to reflect only minor deficiencies. The EURL does not agree that the currently available database, including all limitations already given in the cited text passage, has only minor deficiencies, but rather a major lack of data in all compartments: toxicology, metabolism and occurrence. The greater uncertainty factor of 10 seems therefore more prudent in this case.	According to the EFSA Scientific Committee Guidance on selected default values (EFSA SC, 2012a) an additional factor can be considered in case of deficiencies in the database on a case-by-case basis. A default value has not been proposed, as it will be directly dependent on the dataset available. WHO/IPCS (1994, 1999) has recommended a default factor of 3–5 for minor deficiencies in the dataset and a default factor of 10 for major deficiencies (lack of chronic/reprotoxicity studies). According to the ECHA (2012) Guidance on information requirements and chemical safety assessment, there is no scientific basis for a specific default factor for deficiencies in the database and a default factor of 1 is recommended. For the CPs, there are data regarding reprotoxicity, as well as chronic toxicity studies, including carcinogenicity for SCCPs and LCCPs. Although the available database is not considered sufficient, as reflected in the Recommendations, the CONTAM Panel is of the opinion that an uncertainty factor of 5 for deficiencies in the database is adequate.

	43	3.5. Uncertainty analysis	[p. 174 l. 4846] The EURL would like to point out that the data submission form provided by EFSA does not support reporting data on any specific CP congeners (or rather homologues as congener specific analysis is not feasible for CPs) at the present time. There is no matching analyte code available in the catalogue. Especially if there is to be a reassessment with more occurrence data in the future, this situation should be changed.	The Catalogue of EFSA is updated regularly according to the needs. A functional mailbox (Catalogues@efsa.europa.eu) is available where data providers can request missing parameter codes. New codes can be normally added in a short time (e.g. days) after indicating the need.
National Institute for Public Health and the Environment (RIVM)	44	General comments	RIVM would like to compliment EFSA on the work done and we would like to indicate our agreement with the general approach of the opinion. We agree that at this point in time, a risk characterization can only be performed for the consumption of fish. However, we feel that the conclusions based on this limited assessment could be formulated with more caution. Stating that there is no health concern, even while mentioning the uncertainties, could be interpreted as if these compounds could pose no harm while there is a lot of information missing. Therefore, we would suggest to reformulate the conclusions to illustrate the tentative nature of this risk assessment. This is also relevant as there are strong indications that bioaccumulation of CPs can occur in humans. In the opinion, it is indicated that elimination time decreases with increasing chain length and chlorination. In addition, in some species accumulation can be found (in fish; e.g. Fisk et al., 2000 and in poultry; e.g. Uebreschar et al., 2007) , especially in fat. Also, CPs have been detected in human milk in Europe in amounts comparable to well-known POPs. These signals are indicative of a 'POP' nature of the compound, warranting caution in formulating conclusions on their risk without using a body burden approach, especially considering the gaps in the current knowledge. We thank EFSA for the opportunity to comment on the draft opinion and we include some specific remarks and questions that may be of use in finalising it.	The wording in the Abstract, Summary and other sections of the Opinion has now been modified in order to reflect better the conclusions and uncertainties in the risk assessment.

	45	2.5. Exposure assessment	Paragraph 2.5, lines 1552 – 1553. 'Dietary exposure was assessed using overall European LB and UB mean occurrence of CPs'. For the exposure assessment, occurrence data from fatty fish and lean fish species have been combined. While we recognize that this is a pragmatic approach, a discussion point could be added that for countries where more fatty fish species are consumed, this results in an underestimation. For the countries with a predominantly lean fish consumption, this results in an overestimation.	Section 2.5 of the Opinion aims to describe the methodology used for the exposure assessment. Uncertainties related to the limitations of the occurrence data are listed under Section 3.5.2 'Exposure scenario' and Section 3.5.5 'Summary of uncertainties', where this issue is addressed: "Extrapolation of occurrence data on salmon, tuna and catfish to all other kinds of fish meat – Direction of the uncertainty: +/-".
	46	3.1.6.1. Consideration of critical effects	In lines 3537 – 3539, the conclusion is drawn that 'Liver toxicity observed consistently in rats and mice is considered secondary to an adaptive response and the associated energy costs, but could be relevant to humans at high dose levels (see Section 3.1.5.1).' In section 3.1.5.1.3 it is stated in lines 3164 – 3168 'Regarding the mode of action for liver toxicity, it is considered that enzyme induction and proliferation of the smooth endoplasmic reticulum leading to hypertrophy (and associated increases in liver size) is an adaptive physiological response to CPs. In addition, proliferation of rodent peroxisomes occurs mediated by PPARα. These responses could lead to toxicity if the energy balance to support this compensatory response becomes sufficiently perturbed so as to compromise the cell viability.' There is no mention of dose levels here. Could it be clarified how a perturbed energy balance relates to the mentioned possible relevance at 'high dose levels' for humans?	As discussed in Comment 24 and our response to it, we recognise the difficulty in extrapolating quantitative data from *in vitro* studies to effects *in vivo*, and in comparing concentrations achieved in cell culture between different studies in which the conditions of culture vary. Nevertheless, liver toxicity is seen *in vivo* and the *in vitro* studies show that energy imbalance provides a potential mechanism. In this way the cell culture studies have been very useful in helping to understand the mode of action. The CONTAM Panel noted the recent study by Geng et al. (2019, on-line 1 November 2019), that confirmed *in vitro* studies (see Section 3.1.5.1.2 of the Opinion) in demonstrating oxidative stress, PPARα activation and inhibition of energy metabolism produced by SCCPs in the liver of male rats. There was suppression of oxidative phosphorylation, glycolysis, and gluconeogenesis, reducing the levels of amino acids and nucleotides. Some of these effects on energy metabolism were produced at the lowest dose studies (0.01 mg/kg bw per day for 28 days). The authors noted the need for further studies to verify the impact on the energy metabolism. Whilst these findings demonstrate a mode of action in hepatotoxicity, the Panel could not conclude on a dose level whereby these

				changes lead to adversity. Text in the Opinion has now been amended.
	47	3.1.6.2. Dose-response analysis (including BMD modelling)	Lines 3684 – 3687: increased incidence of nephritis in male rats was chosen as critical effect for SCCP. Some studies indicate a higher sensitivity of the rat for nephritis as compared to mice (and possible other species). This could be discussed in more detail, we attach also an article for reference.	It is already noted in Section 3.1.5.2 of the Opinion that the rat is more sensitive than the mouse for kidney effects as follows: "*Repeated dose toxicity studies in rodents have revealed nephrotoxicity caused by CPs such as increased kidney weight, pigmentation in tubules, nephritis, and nephropathy. This includes tumours in male (but not female) rats, but not in mice treated with SCCPs*". It is noted that this relative sensitivity is common to other chemicals as shown in the reference by Lock and Hard (2004) but it is not felt that this alters the conclusion regarding SCCP, indeed it is in accord with the findings.
	48	3.1.6.3. Derivation of a health-based guidance value / margin of exposure approach	No body burden approach was applied, in the absence of TK models. There are strong indications that (at least) SCCP are behaving as POPs. In the opinion there are several studies indicating that SCCP accumulates in fish and in laying hen (Uebreschar et al., 2007), and elimination time increases with chlorination and chain length. Mostly, they are on the POP- list of UNEP. The possible need for a body burden approach could be discussed in more detail. In lines 3713 – 3724 it is indicated that a 'MOE higher than 1,000 might indicate that there is no health concern'. In this MOE, an uncertainty factor of 5 is used for 'deficiencies in the database'. It seems that differences in kinetics should be covered by the regular factor of 10 for interspecies differences. Because of the possible bioaccumulative properties as mentioned in our previous comment, it could be questioned if the regular factor of 10 for interspecies differences is sufficient to cover for these properties, even in combination with the extra factor of 5 as this factor was meant to cover other uncertainties. Elimination half-lives could not be derived but may vary largely. For illustration: for 2378-TCDD the half-life is 7 years in humans and 20 days in rats. It could be considered if an extra factor is needed for the uncertainty in bioaccumulation potential in different species.	There are no data to develop toxicokinetic (TK) models for CPs. A body burden approach would in principle be more appropriate for this type of compounds. Therefore, the CONTAM Panel gave the following recommendation in Section 5:"*The development of TK models would facilitate a body burden approach.*" The CONTAM Panel acknowledges that it could be questioned whether possible bioaccumulative properties are covered by the general default factor of 10 for interspecies differences. However, in case of no substance specific information regarding interspecies differences between experimental animals and humans , as is the case for the CPs, the default factor of 10 should be applied for interspecies differences. According to the EFSA Scientific Committee Guidance on selected default values (EFSA SC, 2012a) "*… the default value for extrapolating from subchronic to chronic toxicity studies*

				should not be applied when kinetic data show that the substance under consideration can accumulate, e.g. has a long biological half-life." According to the ECHA (2012) Guidance on information requirements and chemical safety assessment, "*A higher factor* [than the default factor of 2] *may be used if there are indications for potential accumulation. E.g. relevant for lipophilic substances, in which case the database needs to contain information on the rate of elimination to further explore the accumulation potential. If accumulation is likely, the toxicity studies need to be of sufficient length to cover the accumulation period (e.g. the time to reach a steady-state concentration). If there is limited information on these aspects, the assessor needs to consider whether the database may be inadequate, and to which extent this lack of information should affect the assessment factor.*" However, because of the limited substance specific information on bioaccumulative properties for the CPs, the Panel decided to apply the default factor of 2 for extrapolation from subchronic to chronic exposure duration and to apply an additional factor of 5 to take into account the limitations in the database. The Panel considered the additional factor of 5 as sufficient to take into account the limitations in the database, including the limitations regarding the possible bioaccumulative properties. The text in the Opinion has been amended.

	49	3.2.2.3. Conclusions on the occurrence data reported in the literature	Lines 4067 – 4095. In general, a lot of studies on occurrence of CPs in food have been extensively described but have not been used in the exposure assessment, while some studies may have had some use. E.g. measurements in meat, milk, fats and oils from Krätschmer et al. (2019a) could have been used for an indicative estimation of possible exposure from these food groups. The Swedish market basket study (Yuan et al. (2017) could possibly be used for a sensitivity analysis.	The CONTAM Panel acknowledged in the Opinion that the exposure estimated from fish only is an underestimation of the exposure, as other food categories are expected to contribute to the exposure. Therefore the Panel recommended the need for occurrence data in food for SCCPs, MCCPs and LCCPs to enable a robust human exposure assessment. Reference to the market basket study carried out in Sweden in 2015 (Yuan et al., 2017) and to the estimations by Krätschmer et al. (2019) has now been made in Section 3.5.2 of the Opinion regarding the uncertainty in the exposure scenario/exposure model.
	50	3.3.3. Non-dietary sources of exposure	Lines 4772 – 4774. The exposure assessment for dust has been performed with data from US-EPA, 20 and 50 mg per day for adults and children respectively, these are the 'central tendency values' (average estimates). These are much lower than the amounts that are being used in the framework of REACH Biocides, i.e. 50 and 100 mg per day for adults and children respectively (Oomen et al. 2008). The US EPA data are more recent, and if these data are therefore preferred over the REACH Biocides numbers, it could possibly be better to use the upper percentile from the US EPA data. Additionally, the use of the highest median value found Europe in the exposure scenario is not in agreement with the framework of REACH Biocides.	The assessment for dust in the Opinion is not meant as a robust exposure assessment, but is simply a rough estimate as stated, to put the dietary exposure estimates into context. The figures for exposure suggested by Oomen et al. (2008) are particularly relevant to biocides where products are purposely applied (e.g. by spraying). The CONTAM Panel considers that the values proposed by the US-EPA (2017) that were used in this Opinion are more appropriate in this context. The highest mean values were taken to reflect a high but feasible level of exposure. The values chosen for the rough estimate made in this Opinion are given, and the reader is able to make alternative calculations using other figures to represent different scenarios if they wish.

	51	3.5.5. Summary of uncertainties	Table 37, lines 4937 - 4939 presents the uncertainties of the different inputs of the risk assessment. The uncertainty 'Use of data from food consumption surveys covering only a few days to estimate high percentiles (95th) long-term (chronic) exposure' relates to the methodology used by the Panel to estimate the long-term exposure, and not to the underlying data. With the use of statistical models, this type of data would not necessarily need to result in an overestimation (+) of the long-term exposure. We would suggest rephrasing this uncertainty as 'methodology used to assess long-term exposure based on consumption surveys covering two or more days', as is being done by the FAF panel.	The entry in Table 37 of the Opinion has now been rephrased to address more accurately this issue.
	52	5. Recommendations	Lines 5129 – 5131. 'More information is needed on the toxicokinetics in humans and experimental animals, with respect to the impact of the degree of chlorination, chlorine position and carbon chain length. The development of TK models would facilitate a body burden approach.'. We refer to our comment to paragraph 3.1.6.3, and suggest to discuss the possible need for a body burden approach in the opinion.	The CONTAM Panel finds that this is adequately addressed in Section 5 of the Opinion under Recommendations.
	53	Appendix C - C.1. Introduction	Lines 6572-74 'In the case of quantal data,..... The 3-parameter model is selected if the difference in AIC is smaller than 5, otherwise the 4-parameter model is selected.'. It is unclear where this value of 5 AIC points comes from. In the EFSA BMD guidance (section 2.5.7) it is stated that "If nested models have been used (i.e. for continuous data), one single member is selected per model family: the one that resulted in the lowest AIC." Could it be clarified why the selection criterion of "the lowest AIC" is not applicable to nested models in case of quantal data?	The updated EFSA Guidance on the use of the benchmark dose approach in risk assessment (EFSA SC, 2017) does not provide guidance for the choice of the critical AIC value for quantal data. The value of 5 for the critical difference between the 3- or 5-parameter models, currently used in the Proast software, was chosen for the following reasons: (i) For biological reasons it is very unlikely that a quantal dose-response could level off below 100%. (ii) When the highest dose happens to result in an observed incidence that is similar to the previous dose (by sampling error), 5-parameters models can easily show an AIC which is more than 2 units lower than the 3-parameters model. In that case, model selection is potentially driven by (random, or maybe non-random) error in the data, which is not desirable. In such cases the two Latent Variable Models (LVM) Exponential and Hill could give quite different results from the other models, potentially impacting on the results of the model averaging.

Appendix 1: Explanatory note to Public Consultation

EFSA's Panel on Contaminants in the Food Chain (CONTAM) has launched an open consultation on the draft scientific opinion on the risks for animal and human health related to the presence of chlorinated paraffins in feed and food. This document presents an estimation of the human dietary exposure to chlorinated paraffins via the consumption of fish, and an assessment of the human health risks related to this dietary exposure. No risk assessment was possible for any of the farm animal species.

Interested parties are invited to submit written comments by 17 September 2019.

Please use the electronic template provided: https://ec.europa.eu/eusurvey/runner/PUBLIC_CONSULTATION_PCs to submit comments and refer to the line and page numbers. To submit additional data to support your comments or files, there is an upload function available in the tool (for a maximum size of 1Mb file). Otherwise you can also contact specific unit's functional mailbox: biocontam@efsa.europa.eu

Please note that comments will not be considered if they:

- are submitted after the closing date of the consultation
- are presented in any form other than what is provided for in the instructions and template
- are not related to the contents of the document
- contain complaints against institutions, personal accusations, irrelevant or offensive statements or material
- are related to policy or risk management aspects, which are out of the scope of EFSA's activity.

EFSA will assess all comments which are submitted in line with the criteria above. The comments will be further considered by the relevant EFSA Panel and taken into consideration if found to be relevant

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Publication of contributions

Contributions will be published (as part of an EFSA report published together with the final opinion) and may be re-used by EFSA in a different context. It should be noted that contributions submitted by individuals in a personal capacity will be published as such, indicating the author's first and family name, unless a substantial justification for protection is provided by the respondent. Contributions submitted on behalf of an organisation are also made publicly available and attributed to the organization in question.

Submit comments (deadline: 17 September 2019)

Published:

6 August 2019

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Abbreviations

BMD	benchmark dose (modelling)
BMDL	benchmark dose lower confidence limit
BMDU	benchmark dose upper confidence limit
BfR	German Federal Institute for Risk Assessment
BMR	benchmark response
BPA	Bisphenol A
b.w.	body weight
CAR	constitutive androstane receptor
CASG	Chloro Alkanes Product Group
CONTAM Panel	Panel on Contaminants in the Food Chain
CPs	chlorinated paraffins
CPIA	Chlorinated Paraffins Industry Association
EC	European Commission
ECHA	European Chemicals Agency
EFSA	European Food Safety Authority
EC	European Commission
HBGV	health-based guidance value
IARC	International Agency for Research on Cancer
IPCS	International Programme on Chemical Safety
IRCD	International Research and Development Center
LCCPs	long Chain Chlorinated Paraffins
LOAEL	lowest-observed adverse effect level
MCCPs	medium Chain Chlorinated Paraffins
MOE	margin of exposure
NOAEL	no-observed adverse effect level
NOEL	no-observed effect level
PAHs	polycyclic aromatic hydrocarbons
POPs	persistent organic pollutants
PPARα	peroxisome proliferator activated receptor α
REACH	registration, evaluation, authorisation and restriction of chemicals
RIVM	Dutch National Institute for Public Health and the Environment

SCCPs	short Chain Chlorinated Paraffins
T3	triiodothyronine
T4	thyroxine
TDI	tolerable daily intake
TH	thyroid hormone
TK	toxicokinetic
UDPGT	uridine 5'-diphospho-glucuronosyl transferase
UK	United Kingdom
UK-COT	UK-Committee on Toxicity
UNEP	United Nations Environment Programme
US-EPA	US-Environmental Protection Agency
vSCCPs	Very short chained CPs
WHO	World Health Organization