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Technical work: consideration of draft risk profiles: long-chain perfluorocarboxylic acids, their salts and related compounds

Comments and responses relating to the draft risk profile for long-chain perfluorocarboxylic acids, their salts and related compounds

Note by the Secretariat

As is mentioned in the note by the Secretariat on draft risk profile: long-chain perfluorocarboxylic acids, their salts and related compounds (UNEP/POPS/POPRC.18/6), the annex to the present note sets out a compilation of comments and responses relating to the draft risk profile for long-chain perfluorocarboxylic acids, their salts and related compounds, submitted by the chair of the intersessional working group on long-chain perfluorocarboxylic acids, their salts and related compounds. The present note, including its annex, has not been formally edited.

* UNEP/POPS/POPRC.18/1.

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Annex

Comments and responses relating to the draft risk profile for long-chain perfluorocarboxylic acids, their salts and related compounds

Minor grammatical or spelling changes have been made without acknowledgment. Only substantial comments are listed. Parts of the text with comments are indicated in bold. Suggested insertions and deletions are indicated in green text and in red strikethrough, respectively.

Source of Comment	Para	Comments on the 2nd draft risk profile for long-chain perfluorocarboxylic acids, their salts and related compounds	Response
Austria	Title	"Long-chain perfluorocarboxylic acids (PFCAs, C9-C21), their salts and related compounds" Proposal to mention already in the title C9-C21, since PFOA is also considered in most publications as a long chain PFCA.	Accepted.
Austria	18	"Compounds related to long-chain PFCAs are defined as **any substance that is a precursor and may degrade or transform to long-chain PFCAs**, where the perfluorinated alkyl moiety has the formula CnF2n+1 (where 8 ≤ n ≤ 20) and is directly bonded to any chemical moiety other than a fluorine, chlorine or bromine atom." Please clarify if fluoropolymers are also covered with this definition.	A non-exhaustive list of long-chain PFCAs, their salts and related compounds has been provided as a supporting information document to the draft risk profile. In Buck et al. (2011), a distinction is made between fluorinated polymers and fluoropolymers. Fluoropolymers are described as a distinct subset of fluorinated polymers, namely, those made by (co)polymerization of olefinic monomers, at least one of which contains fluorine bound to one or both of the olefinic carbon atoms, to form a carbon-only polymer backbone with fluorine atoms directly attached to it (e.g. polytetrafluoroethylene). Using this description, it is unlikely any fluoropolymer would be captured, as the number of fully fluorinated carbons is expected to exceed the upper limit in the definition (n=20).
Austria	21	"Substances **containing $F(CF_2)_n(CH_2)_2$- groups** can also be considered potentially related compounds to long-chain PFCAs, as they will likely result in the release of x:2 FTOHs in the environment (ECHA 2018a,b)." This definition could be used for some fluoropolymers as well – see previous comment.	Please see response to the previous comment to paragraph 18.
Austria	38	"As a result, long-chain **PFCAs may be present in certain products and articles as impurities**." Please address also emissions to the environment from thermolysis: https://www.nature.com/articles/35085548	Information on thermolysis has been added to the paragraph.
Austria	51	"C_9–C_{14}, C_{16} PFCAs and some related compounds, such as **monoPAPs (8:2** and 10:2) diPAPs (e.g. 8:2/8:2 and 8:2/10:2), FTOHs (8:2 and 10:2), fluorotelomer methacrylate (FTMAc) (8:2 and 10:2) and 8:2 FTSA, were reported to be found in cosmetics, sun creams, dental floss and/or body lotions (reviewed in ECHA 2018b; Blom and Hanssen 2015; Danish Environmental Protection Agency 2018; Guo et al. 2009; Whitehead et al.	Text has been added to paragraph 18 to indicate that some compounds related to long-chain PFCAs have also been identified as compounds related to PFOA.

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		2021; Swedish Chemicals Agency 2021; Schultes et al. 2018; Arcadis 2021).” Please indicate that some of the mentioned substances here are also PFOA-related	
Austria	67	“Field-derived BCFs and BAFs were variable depending on the species and ranged from 3.9 (C_9 PFCA) to 5 011 872 (C_{12} PFCA). Field-derived BCFs and BAFs also generally increased from C_9 PFCA to C_{14} PFCA and then declined at C_{15} PFCA (~~>~~59 – 224) (Kwadijk et al. 2010, Labadie and Chevreuil 2011, Murakami et al. 2011, Zhou et al. 2012, Naile et al. 2013, Fang et al. 2014, Pan et al. 2014, Ahrens et al. 2015, Gebbink et al. 2016, Liu et al. 2019a, Liu et al. 2019b, Munoz et al. 2019, Pan et al. 2019, Choi et al. 2020).” Please delete or did you mean <59 ?	The value of > 59 L/kg ww is cited from Gebbink et al. (2016). No other BCF or BAF values were reported for C15, therefore the text was updated to “up to 224” in order to avoid confusion of “greater than” values.
Austria	72	“Although it is unclear if this trend holds for compounds above C_{10} PFCA as Jackson et al. (2021) observed that binding to human serum albumin increased for C_4–C_9 PFCAs but then decreased for C_{10}–C_{12} PFCAs.” Maybe add Bischel et al. 2011 (https://doi.org/10.1002/etc.647) as an addtional reference, since they reported as well that the binding affinity of PFAAs to bovine serum albumin increases from C2-C8 and then decreases from C8-C12.	Sentence has been revised and Bischel et al. 2011 reference has been added.
Austria	85	“Human exposure” Please include the recent published biomonitoring data in teenager from HBM4EU cf. https://www.hbm4eu.eu/wp-content/uploads/2022/04/HBM4EU-Policy-Brief_PFAs.pdf	The HBM4EU report summarizes the data for all PFAS as opposed to only the long-chain PFCAs. Consequently, a general reference to the main EU HBM dashboard was added (instead of the suggested link) where individual data can be seen.
Austria	89	“**Maternal transfer** through cord blood and breastfeeding are sources of long-chain PFCAs for the fetus and for nursing infants/children.” Please include: Long-chain PFCAs can accumulate in the placenta; Kaiser et al. detected C9-C14 in the human placenta, as well as 8:2 diPAP (https://doi.org/10.1021/acs.est.1c00883). The exposure to long-chain PFAS in the placenta is of particular concern, since those compounds can probably **influence the function of the placenta**, which can have negative effects on the development of the fetus. Long-chain compounds can pass the placenta barrier more efficently than shorter congeners (Appel et al. 2022, https://pubmed.ncbi.nlm.nih.gov/34930098/)	References and text have been added.
Austria	92	“No overall temporal trends for C_9–C_{14} PFCAs were observed in German Biobank specimens for the period of 1982-2010 (Schröter-Kermani et al. 2013), although the time period of 2000 to 2009 showed increasing concentrations of C9–C10 PFCA (Yeung et al. 2013) and new information used to extend the dataset showed a decline in C9 PFCA from 2006 to 2019 (Göckener et al. 2020).”	References and text have been added..

Source of Comment	Para	Comments on the 2nd draft risk profile for long-chain perfluorocarboxylic acids, their salts and related compounds	Response
		Kaiser 2022 (PhD thesis), showed a decline of the PFNA concentration in pregnant women (third tremester) in Vienna from 2010/12 to 2017/19. https://repositorium.meduniwien.ac.at/obvumwhs/download/pdf/7001907?originalFilename=true Publication in progress, for information, publication in preparation	
Belgium	1.4	In reference to your call for comments we would like to provide you with some information regarding ongoing actions on PFAS in the Belgian region of Flanders. We highly recommend you to have a look at the Flemish PFAS website (https://www.vlaanderen.be/pfas-vervuiling) which has published several reports on PFAS in different environmental compartments. For example: Drinking water: https://assets.vlaanderen.be/image/upload/v1655130248/PFAS_-_VMM_-_PFAS_in_de_bronnen_-_juni_2022_y3xise.pdf Dust: https://assets.vlaanderen.be/image/upload/v1634302686/PFAS_Luchtmetingen_Oosterweel_tussentijds_rapport_oktober2021_ao3w3f.pdf Air deposition: https://assets.vlaanderen.be/image/upload/v1639515486/VMM_-_3M_en_Zwijndrecht_-_Tussentijdse_bevindingen_meetcampagne_PFAS_in_deposities_-_December_2021_axuuzd.pdf For an english summary you can access the following link: Summary of second interim report on the PFAS contamination | Vlaanderen.be Lastly the website includes an interactive map which gives an overview of PFAS contaminated sites and data on soil and water: https://www.dov.vlaanderen.be/portaal/?module=pfasverkenner&bm=8d3e98c9-7a44-4cf5-a5e6-2b64e0df0918	Information was reviewed and data on long-chain PFCAs in drinking water was included in INF/x.
China	General	I discussed with some colleagues in this industry and get some comments on the draft as follows: 1. Lack of enough date to show that the same toxicity profile exists with all substances included in the LC PFCAs especially the longer chains, and they urge a review to understand if this list is appropriate as it is or if it makes sense to split between the lower and the higher chains based on toxicity profiles. 2. Lists are starting to repeat substances - for instance PFOA related substances and the list of substances in the LC PFCAs may overlap, if that is the case industry may need guidance to understand which Annex etc. applies to the substance especially if each group falls within a different scope.	1. In our view, this homologous series of acids should be addressed as a single group in the draft risk profile. The high degree of structural similarity for the series, combined with the empirical data that is available for PFCAs up to C18, is strongly suggestive of similar persistence, bioaccumulation, long-range environmental transport and adverse effects characteristics. 2. Text has been added to paragraph 18 to the draft risk profile to acknowledge that compounds related to long-chain PFCAs have also been identified as PFOA-related substances. In our view, it would be reasonable to have an overlap between the PFOA listing and a potential long-chain PFCAs listing, since certain compounds have the

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			potential to be precursors to both PFOA and long-chain PFCAs.
Colombia	General	For this document, it is suggested that chapters “Production and trade” or “Uses”, include an indicative list of the more relevant commercial products that include the substances, as it is very focused on the production, trade and use of the LC-PFCAs as they are, but for many countries, these pollutants are present in products, usually as a mix, whose MSDS usually do not declare their presence and amount.	An indicative list of commercial products and mixtures containing long-chain PFCAs has not been added to the draft risk profile as this information is not readily available.
Denmark	General	The transformation of precursors to PFCAs is often described as a degradation process, both in the scientific literature and in this draft risk profile (e.g. paragraph no. 4). This term can be misunderstood, in my view, as it is usually associated with a break-down of the compounds. Instead, the C-F bond is so stable that there is no degradation of PFAS in the sense of a molecular break-down. Therefore, it may be more correct to use the term “transformation” or “reaction”.	The terminology used in the draft risk profile has been amended as suggested.
Denmark	General	Most empirical data cover LC-PFCAs with a chain length of up to 14 carbon atoms. Some data are available on longer chains, but hardly any on the molecules with 20 or 21 carbon atoms. This is clearly mentioned in the draft risk profile, as well as the fact that most conclusions for these longest chain lengths are based on analogies and read-across approaches. However, it could be useful to include more discussion of the possibilities and limitations of this approach, as this grouping and “risk assessment by analogy” could become a model approach for other compounds for which there currently are limited data.	Although further details on read-across, including possibilities and limitations, would be useful for the evaluation of future substances that could make use of read-across, it is felt that the present risk profile is not a suitable place for this type of general guidance information.
Denmark	69	Field-based biomagnification factors, as discussed in paragraph no. 69, were also determined for Baltic Sea biota by de Wit et al. (2020), however, with the caveat that predators and prey did not always match in location and time of sampling. de Wit, C.A.; Bossi, R.; Dietz, R.; Dreyer, A.; Faxneld, S.; Garbus, S.E.; Hellström, P.; Koschorreck, J.; Lohmann, N.; Roos, A.; Sellström, U.; Sonne, C.; Treu, G., Vorkamp, K.; Yuan, B.; Eulaers, I. (2020) Organohalogen compounds of emerging concern in Baltic Sea biota: levels, biomagnification potential and comparisons with legacy contaminants. Environ. Int.144, 106037	De Wit et al. (2020) does not report true BMFs, so it will not be included in paragraph 69.
Denmark	71	Paragraph no. 71 cites the detection of LC-PFCAs in livers of East Greenland polar bears (Greaves et al., 2013). However, the study by Greaves et al. (2013) mainly deals with the detection of LC-PFCAs (and some other PFAS) in polar bear brain, which could also be relevant to include in the draft risk profile.	This paragraph was modified, therefore, no changes were made based on this comment.
Denmark	2.2.4	The chapter on long-range transport states measurements from the Antarctic and the Canadian Arctic as examples of data from remote regions (in paragraph no. 76). I would like to add information from the contaminant monitoring programme in Greenland that also includes LC-	Results on 8:2 and 10:2 FTOHs from Bossi et al. (2016) were incorporated into paragraph 78, as suggested. Muir et al. (2019) is already cited in the draft risk profile.

Source of Comment	Para	Comments on the 2nd draft risk profile for long-chain perfluorocarboxylic acids, their salts and related compounds	Response
		PFAS and related compounds. For example, Bossi et al. (2016) reported on FTOHs monitored at Villum Research Station in Northeast Greenland. This could be relevant for paragraph no. 78 summarizing FTOH data with regard to long-range transport of precursors to LC-PFCAs. An update of these data is given in Muir et al. (2019), see below. Bossi, R.; Vorkamp, K.; Skov, H. (2016) Concentrations of organochlorine pesticides, polybrominated diphenyl ethers and perfluorinated compounds in the atmosphere of North Greenland. Environ. Pollut. 217, 4-10 Muir, D.; Bossi, R.; Carlsson, P.; Evans, M.; De Silva, A.; Halsall, C.; Rauert, C.; Herzke, D.; Hung, H.; Letcher, R.; Rigét, F.; Roos, A. (2019) Levels and trends of poly- and perfluoroalkyl substances in the Arctic environment – an update. Emerging Contaminants 5, 240-271	
Denmark	78	The draft risk profile refers to PFCA levels observed at the air monitoring stations of Alert (Canada) and Zeppelin (Svalbard), with reference to Wong et al. (2018). It could be relevant to mention that the authors ascribe the concentration difference observed between these two stations to a potential influence from sea spray, leading to higher inputs of PFCAs at Svalbard (because Alert is farther away from the shore).	The text was updated as suggested.
Denmark	84	Rigét et al. (2013) presented time trends for perfluoroalkylsubstances (PFAS), including LC-PFCAs, in wildlife from Greenland. These data were also updated in Muir et al. (2019). Biota time trends for the entire Arctic region were presented in Rigét et al. (2019). These data could be particularly relevant for paragraph no. 84. Rigét, F.; Bossi, R.; Sonne, C.; Vorkamp, K.; Dietz, R. (2013). Trends of perfluorochemicals in Greenland ringed seals and polar bears: indications of shifts to decreasing trends. Chemosphere 93, 1607-1614 Muir, D.; Bossi, R.; Carlsson, P.; Evans, M.; De Silva, A.; Halsall, C.; Rauert, C.; Herzke, D.; Hung, H.; Letcher, R.; Rigét, F.; Roos, A. (2019) Levels and trends of poly- and perfluoroalkyl substances in the Arctic environment – an update. Emerging Contaminants 5, 240-271 Rigét, F.F.; Bignert, A.; Braune, B.; Dam, M.; Dietz, R.; Evans, M.; Green, N.; Gunnlaugsdóttir, H.; Kucklick, J.; Letcher, R.; Muir, D.; Schuur, S.; Sonne, C.; Stern, G.; Tomy, G.; Vorkamp, K.; Wilson, S. (2019). Temporal trends of persistent organic pollutants in Arctic marine and freshwater biota. Sci. Total Environ. 649, 99-110	Rigét et al. (2013) and Muir et al. (2019) were added. Rigét et al. (2013) was also added to INF/x.
Denmark	2.2.4 2.3.1	Some recently published studies on LC-PFCAs from the Arctic include those by Sebastiano et al. (2020), Ask et al. (2021) and Jouanneau et al. (2022). An interesting example of potential biovector transport of LC-PFCAs is given by Hitchcock et al. (2019).	Sebastiano et al. (2020) was added to section 2.4 of the draft risk profile. Ask et al. (2021) was added to section 2.4 of INF/x, and Hitchcock et al. (2019) was added to the INF/x and INF/z. Jouanneau is already cited in INF/x.

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		Sebastiano, M.; Angelier, F.; Blévin, P.; Ribout, C.; Sagerup, K.; Descamps, S.; Herzke, D.; Moe, B.; Barbraud, C.; Bustnes, J.O.; Gabrielsen, G.W.; Chastel, O. (2020) Exposure to PFAS is associated with telomer length dynamics and demographic responses of an Arctic top predator. Environ. Sci. Technol. 54, 10217-10226 Ask, A.V.; Jenssen, B.M.; Tartu, S.; Angelier, F.; Chastel, O.; Gabrielsen, G.W. (2021) Per- and polyfluoroalkyl substances are positively associated with thyroid hormones in an Arctic seabird. Environ. Toxicol. Chem. 40, 820-831. Jouanneau, W.; Léandri-Breton, D.-J.; Corbeau, A.; Herzke, D.; Moe, B.; Nikoforov, V.A.; Gabrielsen, G.W.; Chastel, O. (2022) A bad start in life? Maternal transfer of legacy and emerging poly- and perfluoroalkyl substances to eggs in an Arctic seabird. Environ. Sci. Technol. 56, 6091-6102 Hitchcock, D.J.; Andersen, T.; Varpe, Ø.; Loonen, M.J.J.E.; Warner, N.A.; Herzke, D.; Tombre, I.M.; Griffin, L.R.; Shimmings, P.; Borgå, K. (2019) Potential effect of migration strategy on pollutant occurrence in eggs of Arctic breeding barnacle geese (Branta leucopsis). Environ. Sci. Technol. 53, 5427-5435	
Denmark	2.3.1	We presented levels and trends of PFAS, including LC-PFCAs, in peregrine falcon eggs from Greenland, with increasing trends for some LC-PFCAs (Vorkamp et al., 2019). While the reference is given in the Additional Information, I am not sure that these data are included. Vorkamp, K.; Falk, K.; Møller, S.; Bossi, R.; Rigét, F.; Sørensen, P.B. (2019) Perfluoroalkyl substances (PFASs) and polychlorinated naphthalenes (PCNs) add to the chemical cocktail in peregrine falcon eggs. Sci. Total Environ. 648, 894-901	Vorkamp et al. (2019) is included in INF/x and included in the data for Figure 1 of the draft risk profile.
Denmark	2.3.1	A review on PFAS in the Arctic, including LC-PFCAs was published by Muir et al. (2019), including a section dedicated to time trends. This peer-reviewed article also includes previously unpublished data on LC-PFCAs in snow from Villum Research Station (Greenland) as well as data from the Norwegian and Canadian monitoring programmes, which could provide relevant additional information. Muir, D.; Bossi, R.; Carlsson, P.; Evans, M.; De Silva, A.; Halsall, C.; Rauert, C.; Herzke, D.; Hung, H.; Letcher, R.; Rigét, F.; Roos, A. (2019) Levels and trends of poly- and perfluoroalkyl substances in the Arctic environment – an update. Emerging Contaminants 5, 240-271	Muir et al. (2019) has been added to the draft risk profile, as suggested by previous comment on paragraph 84.
Denmark	2.3.1	LC-PFCAs were reported to contribute significantly to total PFAS concentrations in whales studied in the Arctic (e.g. Reiner et al., 2011; Gebbink et al., 2016). Time trend data are available for some whale species as well, as reviewed by Muir et al. (2019).	Reiner et al. (2011) was added to paragraph 85 and to INF/x. Gebbink et al. (2016) is already included in INF/x (reference can be found in INF/z).

Source of Comment	Para	Comments on the 2nd draft risk profile for long-chain perfluorocarboxylic acids, their salts and related compounds	Response
		Reiner, J.L.; O'Connell, S.G.; Moors, A.J.; Kucklick, J.R.; Becker, P.R.; Keller, J.M. (2011) Spatial and temporal trends of perfluorinated compounds in beluga whales (Delphinapterus leucas) from Alaska. Environ. Sci. Technol. 45, 8129-8136 Gebbink, W.A.; Bossi, R.; Rigét, F.F.; Rosing-Asvid, A.; Sonne, C.; Dietz, R. (2016) Observation of emerging per- and polyfluoroalkyl substances (PFASs) in Greenland marine mammals. Chemosphere 144, 2384-2391 Muir, D.; Bossi, R.; Carlsson, P.; Evans, M.; De Silva, A.; Halsall, C.; Rauert, C.; Herzke, D.; Hung, H.; Letcher, R.; Rigét, F.; Roos, A. (2019) Levels and trends of poly- and perfluoroalkyl substances in the Arctic environment – an update. Emerging Contaminants 5, 240-271	Muir et al. (2019) was added to the draft risk profile, as suggested by previous comment on paragraph 84.
Denmark	Figure 1	Fish data from the Arctic do not currently seem to be included, as for example presented by Braune et al. (2014). These could also be included in a potential extension of Figure 1 to the Arctic, see comment below. Braune, B.M.; Gaston, A.J.; Elliott, K.H.; Provencher, J.F.; Woo, K.J.; Chambellant, M.; Ferguson, S.H.; Letcher, R.J. (2014) Organohalogen contaminants and total mercury in forage fish preyed upon by thick-billed murres in northern Hudson Bay. Mar. Pollut. Bull. 78, 258-266	Braune et al. (2014) is already included in Figure 1 (reference can be found in INF/z).
Denmark	Figure 1	Since Antarctica is presented separately in Figure 1, it could also be interesting to compile corresponding data for the Arctic.	Though it would be interesting to have Arctic data presented separately, it was decided that the Arctic data would be separated into their respective continents; therefore, this suggestion has not been accepted.
Equatorial Guinea	General	La Convención de Estocolmo, recientemente firmado 26/06/2019 y ratificado, todavía no dispone de mecanismos de control, evaluación y cumplimiento de ciertas acciones del Articulo 10, inciso 3 del Convenio. Concerniente a las revisiones de propuestas de enmiendas realizadas en el Comité sobre los riesgos que conlleva los productos químicos del Anexo A, B o C del Convenio: Dechlorane Plus; UV-328, Chlorpiryfos, Chlorinates parafines de cadena C14-17 y chlorination del nivel que excede 45% de nchlorine de peso y Long-chain perfluorocarboxylic acids(LC-PFCAs). Debido al desarrollo de su aplicabilidad en diversos campos en la agricultura, en los hospitales y su eco toxicidad no ha sido todavía estudiada en nuestro País en los mares y en los ríos como contaminantes orgánicos persistentes, por lo que, se caben evitar todos los posibles vertidos al medio ambiente dichas sustancias químicas. Tampoco Guinea Ecuatorial, no tiene elaborado un listando nacional que identifica los productos	Noted.

Source of Comment	Para	Comments on the 2nd draft risk profile for long-chain perfluorocarboxylic acids, their salts and related compounds	Response
		químicos en cuestión para un plan de acción de consentimiento fundamentado previo. En conclusión, el esfuerzo de nuestra Parte para utilizar, cuando es necesario, establecer los medios para incorporar dichas sustancias en los planes nacionales de aplicación relativo a los contaminantes orgánicos persistentes en sus documentos estratégicos de desarrollo sostenible; necesita **realizar una encuesta nacional sobre el uso e importación de referidos productos químicos en el País,** luego la aprobación de un proyecto de directrices técnico para la gestión ambiental en los tres Convenios sobre el uso de sus residuos tóxicos,	
European Union	General	This is to let you know that we do not have additional comments on the RP for LC-PFCAs. We notice that Canada has acknowledge our previous comments, and added the reference to the PFASs in fire-fighting foam EU restriction. The information included in the dossier seems extensive (apart from the higher chain-length C19 – C21, for which read-across is proposed) and clearly presented. For the next steps in the process, the ECHA colleagues will check “the non-exhaustive list of LC-PFCAs, their salts and related compounds” and look at potential overlaps with the lists of PFOA and PFOA-related compounds.	Noted.
Japan	1	“Compounds related to long-chain PFCAs are defined as any substance that ~~is a precursor and may~~ degrade ~~or transform~~ to long-chain PFCAs, where the perfluorinated alkyl moiety has the formula CnF2n+1 (where $8 \leq n \leq 20$) and is directly bonded to carbon ~~any chemical moiety other than a fluorine, chlorine or bromine~~ atom.” Reason for revision: The definition of long-chain PFCA-related compounds should be modified in the same way as the definition of PFOA-related substances. If C_8F_{17} bonds to non-carbon atoms, such compounds are covered by PFOA-related substances because it is expected that they will be degraded to PFOA. If there is no evidence that C8 or higher perfluoroalkyl groups bonded to non-carbon atoms, such as Si, does degrade to PFCAs, an atom which bonds to perfluoroalkyl groups should be limited to carbon atom only. Substances that degrade to PFOA should be excluded from the definition of long-chain PFCA to avoid duplication with PFOA-related substances, which is already subject to elimination by the Convention. (For refernce, PFOS is excluded in the definition of PFOA-related substances.)	This suggested edit has not been accepted. We agree that a number of compounds that would fall under the definition of compounds related to long-chain PFCAs are already covered by the PFOA listing, as these are expected to transform to PFCAs of various length, including C8 (PFOA) and ≥C9 PFCAs. For that reason, it would, in our view, be reasonable to have an overlap between the PFOA listing and a potential long-chain PFCAs listing. In addition, it would be important to cover both, as certain Parties may be bound by obligations to one of the listings but not the other. For these related compounds, any potential issues related to the alignment of the obligations for the two listings (i.e. exemptions) could be addressed at the Risk Management Evaluation stage, should this group of substances move forward in the POPRC review process.
Japan	Non-exhaustive list	In order to compare with the indicative list of PFOA, its salts and PFOA-related compounds, please highlight or emphasize the substances on	Due to time constraints, edits to the non-exhaustive list have not been considered at this time. This could be considered at the risk management evaluation stage,

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		this list that are already on the indicative list of PFOA-related substances. In order to immediately identify whether substances have scientific evidence of degradation to long-chain PFCAs or not, please highlight or emphasize substances that have those evidences (e.g. experimental data, QSAR or metabolic simulation results).	should this group of substances move forward in the review process.
Madagascar	General	Suite à la lettre en référence et relative à l'objet sus visé et après lecture des documents, le Ministère de l'Enseignement Supérieur et de la Recherche Scientifique n'a pas de commentaire ni d'observation par rapport à ces projets.	Noted.
Monaco	General	Please be informed that we have no comments regarding the 14 documents available.	Noted.
Sweden	General	"Long-chain PFCAs and their related compounds may also be released to the environment from landfills, incineration plants and wastewater treatment plants. C9–C18 PFCAs, FTOHs (8:2, 10:2 and 12:2), FTCAs (8:2 and 10:2), FTAs (8:2 and 10:2) and FTUCAs (8:2 and 10:2) have been measured in leachate, percolate or soil from landfills located in the USA, China, South Korea, Canada, Germany ~~and~~ Spain and Sweden (Lang et al. 2017; Liu et al. 2021; Sim et al. 2021; Benskin et al. 2012a; Busch et al. 2010; Fuertes et al. 2017; Kameoka et al. 2021; Weinberg et al. 2011)." A recent survey on PFASs in leachates from 117 landfills in Sweden found PFNA, PFDA, PFUnDA, PFDoDA and PFTeDA at levels >LOQ (Miljösamverkan Sverige (2022). https://www.miljosamverkansverige.se/wp-content/uploads/2022-01-27-Rapport-PFAS-vid-deponier.pdf (in Swedish)	The draft risk profile was amended as suggested, and the monitoring information was added to Table 4 of INF/x.
Switzerland	General	The BAFs determined in the following recent publications might be worth considering: *Field-Based Distribution and Bioaccumulation Factors for Cyclic and Aliphatic Per- and Polyfluoroalkyl Substances (PFASs) in an Urban Sedentary Waterbird Population* http://doi.org/10.1021/acs.est.2c01965	Szabo et al. (2022) was added to the draft risk profile and INF/x.
Switzerland	General	The drinking water concentrations of PFNA to PFTrDA from Table S7 of the following paper might be added to Table 6 of the INF document, even though the samples were not taken at the tap (treated water sampled at drinking water treatment plants): *A pilot study on extractable organofluorine and per- and polyfluoroalkyl substances (PFAS) in water from drinking water treatment plants around Taihu Lake, China: what is missed by target PFAS analysis?* https://doi.org/10.1039/D2EM00073C	Data and reference have been added to Table 8 of INF/x.
Switzerland	General	The following broad monitoring study might be worth including in the Excel database, even though only PFDA and PFUnDA were found in biota (see Table S2B):	Ng et al. (2022) study was not included in INF/z (Excel database) as it did not contain enough details on biota sampling for inclusion.

Source of Comment	**Para**	**Comments on the 2nd draft risk profile for long-chain perfluorocarboxylic acids, their salts and related compounds**	**Response**
		Target and suspect screening of 4777 per- and polyfluoroalkyl substances (PFAS) in river water, wastewater, groundwater and biota samples in the Danube River Basin https://doi.org/10.1016/j.jhazmat.2022.129276	
Switzerland	General	The occurrence data for PFNA to PFHxDA (PFODA: < LOD) from Table S6 of the following paper might be worth adding to the Excel database: *Determination of 56 per- and polyfluoroalkyl substances in top predators and their prey from Northern Europe by LC-MS/MS* https://doi.org/10.1016/j.chemosphere.2021.131775	Thank you for submitting the Androulakakis et al. (2022) study. These data were not included in INF/z (Excel database) as the database does not include pooled samples, which are summarised in the study.
Switzerland	Non-exhaustive list	What about renaming the caption “Fluoro ester” to e.g. “Polyfluorinated esters”, in line with other captions? BTW: Overall, there are several dozens of esters in this list.	We have made note of this suggestion. Due to time constraints, edits to the non-exhaustive list have not been considered at this time.
Switzerland	Non-exhaustive list	It would be helpful to link those CAS numbers to CAS Common Chemistry, of which there is an entry (e.g. 375-95-1). We have done so for the non-exhaustive list of PFOA, its salts und related compounds.	Due to time constraints, edits to the non-exhaustive list have not been considered at this time. This could be considered at the risk management evaluation stage, should this group of substances move forward in the review process.
Switzerland	Non-exhaustive list	The list might potentially be extended based on the work “PFASs and Fluorinated Compounds in PubChem Tree” (PubChem start page; video demonstration), if time allows.	Due to time constraints, we have not had the opportunity to consider expanding the non-exhaustive list based on this work. This could be considered at the risk management evaluation stage, should this group of substances move forward in the review process.
United Kingdom of Great Britain and Northern Ireland (UK)	30	Please add: “Although no specific information regarding the intentional manufacture of >C18 substances has been found, it is assumed that these chain lengths would be present as components or impurities within the C9-C18 materials.” We think the RP should be clear about the available information, but the current document does not provide specific data regarding >C18 chain lengths. Suggested text above reflects our understanding from the information presented in the production section.	The paragraph has been amended as suggested, with minor edits.
UK	67	“However, Burkhard (2021) reported that laboratory BCF measurements decline with increasing exposure concentration, rather than remaining constant.” Burkhard 2021 considers various PFAS. Does the text specifically relate to LC-PFCAs, if so, please state this? We note that the Inoue article states “The BCFs of test substances [LC-PFCAs] did not differ substantially between the 2 test concentrations, which differed by a factor of 10”.	Burkhard (2021) is a review and does not specifically discuss long-chain PFCAs for this trend.
UK	68	“The **moderate water solubility** of long-chain PFCAs causes a relatively high tendency to escape from the gills into water”	The moderate water solubility of long-chain PFCAs is correct. The previous paragraph refers to the low water solubility of very long-chain PFCAs. It is also noted in the document (paragraph

Source of Comment	Para	Comments on the 2nd draft risk profile for long-chain perfluorocarboxylic acids, their salts and related compounds	Response
		The previous paragraph (67) states field-derived BAF values for very long-chain PFCAs are not often reported because it is not feasible to measure these substances in water due to low water solubility causing the concentrations to be very low. Please address the inconsistency between the paragraphs: is the water solubility of the LC-PFCAs "moderate" or "low", and amend the text in both paragraphs accordingly?	88) that, as chain length increases, water solubility likely decreases.
UK	68	Following on from the previous comment, in the main Risk Profile or INF document, please provide the water solubility values for the different substances, so quantification of "low" and "moderate" is clear. We note that water solubility for C10 – C15 were provided in the Proposal document for POPRC-17, but are not sure where data for >C15 are? The water solubilities of these longer chain lengths is an important element of the read-across. Please also discuss the reliability of the values.	Available physical-chemical properties of C_9-C_{14} PFCAs, reported in the proposal, have been added to INF/x (Table 2). In addition, some of the physical-chemical properties of C_{15}-C_{19} PFCAs have been estimated using COSMOtherm and were added to Table 2 of INF/x.
UK	68	"As bioaccumulation in air-breathing organisms is driven primarily by volatility rather than polarity, the non-volatile nature of long-chain PFCAs promotes a relatively slow elimination to air, resulting in higher bioaccumulation potential in air-breathing organisms (Kelly et al. 2004). That is, fish gills provide an additional mode of elimination for long-chain PFCAs that species such as birds and terrestrial/marine mammals do not possess (Martin et al. 2003a)." Given the BCF values of up 17000 for the C12 and C13 substances determined by Inoue, how significant is fish gill elimination for the LC-PFCAs? Is it not likely be of decreasing significance with increasing chain length? A discussion of the water solubility trend would also help here.	The text was amended as suggested.
UK	68	"As such, field biomagnification factors (BMF, unitless) and trophic magnification factors (TMF, unitless) ~~are~~ may be more relevant in determining the overall bioaccumulation potential for long-chain PFCAs." Suggested amendment. The findings of Inoue suggest BCF is also important for the higher chain lengths (>C11). Note also the findings of Boisvert (2019) who comments (our emphasis) "Overall, longer chain PFCAs (C11 to C14; 60-80% of S13PFCA) dominated in bear fat and seal blubber, whereas as relatively shorter-chain PFCAs (C9 to C11; 85-90% of S13PFCA) dominated in the liver of the two species (Fig. 1). Fat and blubber deposition of PFCAs tended toward those with longer chains, which is consistent with the **increasing lipophilic character of longer chain PFCAs**. As discussed in Greaves et al. (2013), relationships between PFAA concentrations and lipid content are likely between longer-chain PFCAs (C10-C15) and	The text has been amended.

Source of Comment	Para	Comments on the 2nd draft risk profile for long-chain perfluorocarboxylic acids, their salts and related compounds	Response
		nonpolar free fatty acids (such as tri- glycerides, the dominant class of lipid in bear fat and seal blubber). Thus, these longer chain PFCAs are likely to biomagnify similar to lipophilic organohalogens such as PCBs and polybrominated diphenyl ether (PBDE) flame retardants as has been reported previously for East Greenland seals and bears (Letcher et al., 2009)."	
UK	68	"Nonetheless, whole body BCFs ~~that~~ have been derived in laboratories that exceed the BCF criteria in Annex D to the Convention." Suggested amendment to align with the data outlined in paragraph 66 as not all the values exceed the Annex D threshold.	The text has been amended as suggested.
UK	69	"Field biomagnification or trophic magnification studies on long-chain PFCAs (up to C1614 PFCA) that focused on multiple fish species and/or top predator species […] One study reported BMF values for C16 and C18 chain lengths, which were C16 (BMF = 2), and C18 (BMF = 1) for a seal liver – Polar bear liver comparison, although sample numbers were limited." Suggested amendment - as far as we understand the only study assessing >C14 was Boisvert et al. 2019.	The text was updated, with modifications.
UK	70	"However, it is ~~expected~~proposed that C_{17}–C_{21} PFCAs may ~~can~~ also biomagnify in birds and terrestrial/marine mammals." Suggested amendment	The text was amended as suggested, with modifications.
UK	70	"Additionally, the presence and metabolic transformation of compounds related to long-chain PFCAs in wildlife can add to the body burden of long-chain PFCAs (Nabb et al. 2007; Letcher et al. 2014)." For readability, please consider moving this text elsewhere in the section (maybe within the introduction discussing the analytical limitations or as part of the section conclusion?) as it is not specific to the homologues without bioaccumulation data, but the entire group that is being assessed. The remainder of paragraph 70 (merged with para 71) would then focuses on providing reading-across arguments.	This paragraph was modified, therefore, no changes were made based on this comment.
UK	70	"Although octanol-water partition coefficient (log K_{ow}) values are traditionally used as an indicator for bioaccumulation, meaningful log K_{ow} values cannot be reliably measured or modelled for surface-active and ionizing substances such as long-chain PFCAs. Only modelled K_{ow} values are available for long-chain PFCAs (e.g., Wang et al. 2011). Long-chain PFCAs tend to migrate to the interface of the organic (lipid) and aqueous phases rather than partition between the two phases (Houde et al. 2006; OECD 2002). Some portions of the perfluorinated molecule can interact with phospholipids (Armitage et al. 2012; Dassuncao et al. 2019; Droge 2019) but most studies show that	This paragraph was modified, therefore, no changes were made based on this comment.

Source of Comment	Para	Comments on the 2nd draft risk profile for long-chain perfluorocarboxylic acids, their salts and related compounds	Response
		protein-rich tissues (i.e., yolk, liver, and blood) are the primary repositories for long-chain PFCAs rather than lipids due to its highly hydrophobic tail and the polar headgroup that facilitates both hydrophobic and ionic interactions with proteins (Jones et al. 2003; Bischel et al. 2010; Woodcroft et al. 2010; Bischel et al. 2011; Ng and Hungerbuhler 2013; Cheng and Ng 2018; Zhong et al. 2019). Therefore, it is inappropriate to use log K_{ow} to characterize bioaccumulation and for predictive purposes (e.g., bioaccumulation models) for long-chain PFCAs (OECD 2002; Conder et al. 2008). Instead, empirical bioaccumulation data is more relevant. Refer to section 2.2.3 of UNEP/POPS/POPRC.18/INF/x for more details." For readability, please consider moving this text to the start of section 2.2.3 – it is not specific to the homologues without bioaccumulation data, but the entire group that is being assessed. The remainder of paragraph 70 (merged with para 71) then focuses on providing reading-across arguments.	
UK	71	Please re-order the paragraph so that physchem arguments come first. Please then include data for volatility, water solubility and molecular size across the entire group discussing any trends), then how any in trends in BMF or TMF support the read-across (for example are BMFs and TMFs generally similar amongst the data rich chain lengths, do they vary, do they peak, is there a difference depending on the tissue type (protein or fat) etc. – and how can this be extrapolated to the data poor chemicals). Given the breadth of perfluorinated carboxylic acids, we do not think "The high degree of chemical similarity for the series of acids has been described" can be stated without detailing the data used to make the assertion in this paragraph. The physchem arguments might potentially provide a stronger basis for reasoning why the >C16 chains might be bioaccumulative compared to the very limited empirical data.	This paragraph was modified, therefore, the paragraph was not reordered. Physical-chemical properties were added in Table 2 of INF/x. Predicted BCFs for the upper end of the range of acids has been included in the draft Risk Profile, which incorporate points raised in this comment.
UK	71	"PFCAs with linear perfluoroalkyl chains (effective diameter or Deff = 0.61 – 0.96 nm in C_8 to C_{18} PFCAs) can enable them to pass through biological membranes (Inoue et al. 2012)." We have now been able to access Inoue et al (2012), and note that the authors used OASIS to model the molecular size. This is the software used to define the 1.7 nm used as part of the EU criteria for limited uptake (see UK and EU comments in the previous commenting round). We would strongly suggest having a separate paragraph describing the data from the Inoue paper in more detail in the INF document to provide a read-across argument. As we stated in the previous commenting round, there would be benefit if OASIS data modelling Deff of the C19, C20 and C21 molecules could be	D_{eff} values were calculated for the C19, C20 and C21 molecules, and included in the paragraph.

Source of Comment	Para	Comments on the 2nd draft risk profile for long-chain perfluorocarboxylic acids, their salts and related compounds	Response
		included in the Risk Profile. We suggest the dossier submitter contacts observers or Parties to investigate who has access to the programme (unfortunately we do not).	
UK	71	"There is evidence of use/release of compounds related to C_{17}–C_{21} PFCAs. C_{17}–C_{21} PFCAs have been measured in snow and soil (Plassman and Berger 2013), C_9–C_{11}, C_{14} and C_{18} were measured in air samples in the Arctic (Wong et al. 2018) and C_{16}–C_{18} PFCAs have been measured in top predator species such as the peregrine falcon (Falco peregrinus) from the Great Lakes region (Canada) (Sun et al. 2020), and in the eggs of herring gulls (Larus argentatus) and Caspian tern (Hydroprogne caspia) from colony sites across the Great Lakes basin (Canada and the USA) (Letcher et al. 2015; Su et al. 2017), as well as in the liver of East Greenland polar bears (Greaves et al. 2013; Boisvert et al. 2019) and Hudson Bay polar bears (Letcher et al. 2018)." Please include text explaining how these data demonstrate the bioaccumulation of the >C17 chain lengths? Effectively are you able to connect the environmental exposure with the levels measured in the organisms?	This text is not meant to connect environmental exposure with levels measured in organisms, but instead to be indicators of environmental presence of longer chain PFCAs. The text was simplified to remove any confusion.
UK	INF para 10	"Where some studies found that BMF/TMFs decreased with increasing chain length (e.g., Zhang et al. 2015, Munoz et al. 2017b, Boisvert et al. 2019), other studies found that TMF increased with chain length (e.g., Tomy et al. 2009, Simonnet-Laprade et al. 2019b)." Please state which chain lengths each study reviewed, and which tissues.	The text was not updated as this information is already provided in the same paragraph.
United States of America (USA)	9	"However, read-across can be used to fill data gaps, particularly within a homologous series of substances." Where and how has this been demonstrated for PFCAs ?	This is discussed in para 16 of the draft risk profile.
USA	71	"**A read-across argument** can also be made to address data gaps." This paragraph provides evidence of read-across however it seems that more detail and explanation would strengthen the paragraph on how, where, why, what conditions, which species lead to successful application of read-across to describe conditions.	Predicted BCFs for the upper end of the range of acids have been included in the draft Risk Profile. The inputs include physical-chemical property estimates and partitioning information which may help address the provided comment.
USA	74	"Although information is lacking for the bioaccumulation of C12–C21 PFCAs in humans, a read-across argument can be made to address data gaps." Similar to above, the paragraph provides evidence of read-across however it seems that more detail and explanation would strengthen the paragraph on how, where, why, and what conditions lead to successful application of read-across to describe human bioaccumulation conditions.	As noted above, physical-chemical property estimates and partitioning information has been used in predicting bioaccumulation in ecological species, and can inform long-chain PFCA behaviour in other species.

Source of Comment	Para	Comments on the 2nd draft risk profile for long-chain perfluorocarboxylic acids, their salts and related compounds	Response
USA	90	"Long-chain PFCAs have been detected globally **in humans**." Information on exposure in urban areas would also be helpful.	To our knowledge, information on PFAS exposure as function of urban (vs rural) locations is not readily available.
USA	115	"However, increasing temporal concentration trends in wildlife, including top predator species, suggest that long-chain PFCAs can approach toxicity thresholds resulting in harm for wildlife populations in the future. In humans, the reported temporal concentration trends for long-chain PFCAs have been inconsistent. However, between 2011 and 2016-2017, concentrations of certain long-chain PFCAs have been reported to have increased in Canadian Nunavik pregnant women who rely on Arctic wildlife species for subsistence, while levels of these PFCAs were declining or stable in the general Canadian population. This suggests that certain populations are at risk of greater exposure to long-chain PFCAs." A description of the risk to urban populations would also be helpful.	To our knowledge, information on PFAS exposure as function of urban (vs rural) locations is not readily available.
Inuit Circumpolar Council (ICC)	80	"In addition, C_9–C_{13} PFCAs have been measured **in humans** living in locations distant from sources, such as Greenland and Northern Canada, highlighting the significance of the long-range environmental transport of PFASs to remote communities (Long et al. 2015; Wielsoe et al. 2017; Caron-Beaudoin et al. 2019; Caron-Beaudoin et al. 2020; Hjermitslev et al. 2020; Garcia-Barrios et al. 2021; Dubeau et al. 2022)." If this is referring to Arctic Indigenous Peoples (in particular Inuit), it would be good to mention that, since the Stockholm Convention has recognized Arctic Indigenous Peoples as particular vulnerable.	"Arctic Indigenous Peoples" has been added.
ICC	85	"Meanwhile, evidence suggests that wildlife species consumption, particularly top predator marine species, is the main pathway of exposure to long-chain PFCAs for ~~Circumpolar~~ Arctic Indigenous populations (Caron-Beaudoin et al. 2020, Aker et al. 2021, AMAP 2021)."	The text was amended as suggested, with modifications.
ICC	86	"This has the potential to lead to elevated levels in human populations relying on these species for subsistence, in particular Arctic Indigenous Peoples."	The text was amended as suggested, with modifications.
ICC	90	"Of note, concentrations of long-chain PFCAs in the serum/plasma of Indigenous Peoples, such as Nunavik adults, including pregnant Inuit women (C_9–C_{11}), First Nation Anishinabe youth (C_9) and seven Gwich'in and Dene First Nation communities (C_9) who live in very different areas across Canada (but all remote) were higher than CHMS values for comparable age and sex groups, and time periods (Caron-Beaudoin et al. 2019; Caron-Beaudoin et al. 2020; Aker et al. 2021;	The text was amended as suggested, with modifications.

Source of Comment	Para	Comments on the 2nd draft risk profile for long-chain perfluorocarboxylic acids, their salts and related compounds	Response
		AMAP 2021; Garcia-Barrios et al. 2021; Dubeau et al. 2022)."	
ICC	96	"As such, a direct cause-effect correlation is difficult to establish, as statistical correlations, by themselves, do not necessarily imply causal **relationships**. ~~Recognizing this uncertainty~~However, ~~several~~ the large number of field-based wildlife studies that have shown statistical correlations with observed effects for long-chain PFCA mixtures (from C_9 to C_{16}) in various wildlife species, including top predators are increasing the likelihood of a causal relationship […]" If correlations are observed in so many epidemiological studies, a causal relationship should be regarded as increasingly likely.	The text was updated, with modifications.
ICC	97	"There is a potential for further ecological effects to be caused by mixtures of long-chain PFCAs at environmental concentrations as well as interactions with other environmental stressors (including other contaminants), though these effects cannot currently be predicted." It should be kept in mind that PFCAS are only one class of contaminants found in organisms. This is on top of many other contaminants (in particular POPs), which are measured. Additive toxic effects are possible (and likely).	The text was updated, as suggested.
ICC	103	"While there are limitations to epidemiological studies, including the fact that the associations identified ~~are~~ may not necessarily be causal in nature, the large numbers of studies showing corellations, and then additionally ~~when~~ combined with toxicological data from experimental animals, the findings are more compelling and the overall evidence is strengthened." I don't think that causality can be ruled out. Particularly if it is a large number of studies, as pointed out above.	The text was amended as suggested, with modifications.
ICC	115	"This suggests that certain populations (such as Arctic Indigenous Peoples) are at risk of greater exposure to long-chain PFCAs."	Edit accepted.
International Pollutants Elimination Network and Alaska Community Action on Toxics (IPEN/ACAT)	97	"**There is a potential for further ecological effects to be caused by mixtures of long-chain PFCAs at environmental concentrations** as well as interactions with other environmental stressors, though these effects cannot currently be predicted." Since the long chain PFCAs are often detected as a mixture, and considering their similarities, it could be argued that it is even more relevant to assess these as mixtures rather than as individual substances. See e.g. this 2019 report from the Swedish government that outlines why this is the necessary progress for regulatory risk assessment https://www.government.se/4adb1a/contentassets/ee36b3e49c354bb8967f3a33a2d5ca50/future-chemical-risk-management---accounting-for-	This is well noted, and is supportive of the scope of the proposal, as C9-C21 PFCAs are expected to be co-produced and co-released into the environment as presented in the draft risk profile.

Source of Comment	Para	Comments on the 2nd draft risk profile for long-chain perfluorocarboxylic acids, their salts and related compounds	Response
		combination-effects-and-assessing-chemicals-in-groups-sou-201945	
IPEN/ACAT	103	"While there are limitations to epidemiological studies, including the fact that the associations identified ~~are~~ can not be proven to be causal in nature, when combined with toxicological data from experimental animals, the findings are more compelling and the overall evidence is strengthened." This sentence would benefit from clarification. We have therefore suggested an edit	Edits were made to this sentence in response to this and comments from the ICC.
IPEN/ACAT	116	"Long-chain PFCAs are persistent, bioaccumulative, have ~~evidence of~~ adverse effects on~~to~~ human health and/or the environment, and have the potential to undergo long-range environmental transport, in part due to the long-range atmospheric transport of compounds related to long-chain PFCAs." We suggest this revisions as an editorial, since there is strong evidence for all of the criteria (not only adverse effects).	Edits accepted.