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# Report of the Persistent Organic Pollutants Review Committee on the work of its eighteenth meeting

## Addendum

## Risk profile for long-chain perfluorocarboxylic acids, their salts and related compounds

At its eighteenth meeting, in decision POPRC-18/5, the Persistent Organic Pollutants Review Committee adopted a risk profile for long-chain perfluorocarboxylic acids, their salts and related compounds on the basis of the draft text contained in document UNEP/POPS/POPRC.18/6/Add.1, as revised during the meeting. The text of the risk profile as adopted is set out in the annex to the present addendum, without formal editing.

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**Annex***

# Long-chain perfluorocarboxylic acids (PFCAs, $C_9$-$C_{21}$), their salts and related compounds

# Risk profile

**September 2022**

* The studies and other information referred to in this document do not necessarily reflect the views of the Secretariat of the Stockholm Convention on Persistent Organic Pollutants, the United Nations Environment Programme (UNEP) or the United Nations. The designations employed and the presentation of the material in such studies and references do not imply the expression of any opinion whatsoever on the part of the Secretariat, UNEP or the United Nations concerning geopolitical situations or the legal status of any country, territory, area or city or its authorities.

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# Executive summary

1. The Persistent Organic Pollutants (POPs) Review Committee at its seventeenth meeting concluded that long-chain perfluorocarboxylic acids (PFCAs), their salts and related compounds fulfilled the screening criteria in Annex D (decision POPRC-17/6). This risk profile concerns the PFCAs with carbon chain lengths from 9 to 21 inclusive (i.e., $C_9$–$C_{21}$ PFCAs, hereafter referred to as long-chain PFCAs), their salts and related compounds. Long-chain PFCAs and their salts are a homologous series of substances with the molecular formula of $C_nF_{2n+1}CO_2H$ (where $8 \leq n \leq 20$). Compounds related to long-chain PFCAs are defined as any substance that is a precursor and may transform to long-chain PFCAs, where the perfluorinated alkyl moiety has the formula $C_nF_{2n+1}$ (where $8 \leq n \leq 20$) and is directly bonded to any chemical moiety other than a fluorine, chlorine or bromine atom.

2. Long-chain PFCAs, their salts and related compounds are used, or may have been used, in a range of applications, including in: industrial applications (e.g., as surfactants, and in the production of fluoropolymers); electronics; medical devices; printing inks and photographic materials; automotive care products; building and construction materials; cookware and food-contact materials; fire-fighting foams; ski waxes; and various consumers products (such as household products, personal care products, home textiles and apparel). In addition, long-chain PFCAs and their related compounds may be unintentionally produced during the manufacturing of per- and polyfluoroalkyl substances (PFASs).

3. Information in the public domain on the historic and current production of long-chain PFCAs, their salts and related compounds is limited, and estimated volumes vary in the literature. Estimates of the global production of the ammonium salt of $C_9$ PFCA (ammonium perfluorononanoate or APFN) have been reported to be in the range of 15 to 100 tonnes/year for the period between 1975 and 2004. The usage of APFN in Japan, Western Europe and the United States of America (USA) has been estimated to range between 8 and 107 tonnes/year for the years 1975 to 2015. Worldwide production of fluorotelomers (compounds related to long-chain PFCAs) was estimated at approximately 9100 tonnes in 2006. Another source estimated the global annual production of fluorotelomer-based products to range between 2500 and 20,000 tonnes for the years 1961 to 2004, and at 45,000 tonnes/year for the period 2005 to 2030. A geographical shift of industrial sources of PFCAs, as a result of the relocation of PFCA, fluoropolymer and other PFAS product production from the USA, Western Europe and Japan to emerging Asian economies, especially China, has been reported in the literature.

4. Long-chain PFCAs are released to the environment from direct and indirect sources. Direct sources include emissions from the production of PFCAs, as well as during the life cycle of products containing long-chain PFCAs. Indirect sources are those where compounds related to long-chain PFCAs emitted to the environment have transformed to long-chain PFCAs through biotic or abiotic transformation. Release of long-chain PFCAs, their salts and related compounds to the environment is documented by their detection in environmental matrices collected in proximity to production facilities and industrial areas; sites impacted by fire-fighting foam; wastewater, sludge and leachate from landfills, incineration plants and wastewater treatment plants; agricultural sites with a history of application of biosolids; snow and soil from skiing areas; indoor environments; and environments with no known direct sources, including Arctic regions.

5. Long-chain PFCAs, which are carboxylic acids bonded to a fully fluorinated carbon chain, are extremely persistent in the environment. The carbon-fluorine bond is one of the strongest covalent bonds (about 108–120 kcal/mole), making the bond extremely stable and generally resistant to degradation by acids, bases, oxidants, reductants, photolytic processes, microbes and metabolic processes. The strong carbon-fluorine bond and high density of electron-rich repellent fluorine atoms protect the carbon backbone and result in inertness to both heat and chemical reagents. A number of studies demonstrate that long-chain PFCAs do not degrade under environmentally relevant conditions. For example, $C_9$ PFCA did not biodegrade under the Organisation for Economic Co-operation and Development (OECD) 301F method. Other studies demonstrate some degradation of long-chain PFCAs, but not under environmentally relevant conditions.

6. Some measured bioconcentration factors and bioaccumulation factors greater than 5000 have been reported for $C_9$–$C_{14}$ PFCAs in freshwater and marine aquatic organisms. Trophic magnification factors and biomagnification factors greater than 1 have been reported for $C_9$–$C_{16}$ PFCAs in studies that focused on top predator species, such as birds and terrestrial/marine mammals, providing evidence that long-chain PFCAs biomagnify in air-breathing organisms. Although there are no biomagnification or trophic magnification data for long-chain PFCAs with chain lengths greater than $C_{18}$, PFCAs up to $C_{18}$ have been measured in top predator species, such as polar bears, herring gulls and peregrine falcons. In humans, long-chain PFCAs accumulate in the blood and well perfused tissues (e.g., liver, kidneys, lungs), and are eliminated very slowly from the body. The mean elimination half-lives for $C_9$ PFCA are estimated to range from 2.5 to 4.3 years in humans, whereas the mean half-lives for both $C_{10}$ and $C_{11}$ PFCA range from 4.5 to 12 years. Using a read-across approach on the basis of the high degree of chemical similarity for the long-chain PFCA $C_9$–$C_{21}$ series of acids, it is anticipated that long-chain PFCAs of up to 21 carbons have the potential to bioaccumulate in aquatic and terrestrial organisms, and in humans.

7. Global modelling indicates that long-chain PFCAs, their salts and/or related compounds have the potential to be transported over long distances. In addition, $C_9$–$C_{18}$ PFCAs have been measured in environmental media, biota and

human populations from remote sites, such as the Arctic and the Antarctic, indicating that long-chain PFCAs have the potential for long-range environmental transport. Furthermore, increasing temporal concentration trends in polar bears and humans from remote regions have been reported. Compounds related to long-chain PFCAs have also been measured in ambient air from various regions around the world, including in remote areas. Available research indicates that the presence of long-chain PFCAs in remote areas results from the atmospheric and oceanic transport of volatile precursors and/or the acids themselves. There is empirical evidence of the presence of long-chain PFCAs in locations distant from sources of long-chain PFCAs up to $C_{18}$. The high degree of chemical similarity across the series of acids suggests that long-chain PFCAs of up to 21 carbons may be expected to be present in remote environments. This may also be a result of the release of compounds related to long-chain PFCAs during their production and use in many applications, and the potential for these precursors to undergo long-range environmental transport.

8. Long-chain PFCAs have been detected globally, in all continents as well as in all environmental compartments, including biota, freshwater, saltwater, sediment, soil and rainwater. Increasing temporal trends for long-chain PFCAs (up to $C_{15}$ PFCA) have been reported in wildlife, including in top predator species, and in humans. In humans, $C_9$–$C_{18}$ PFCAs have been detected globally in various tissues and fluids. Exposure of the general population to long-chain PFCAs and their related products may take place through exposure to indoor dust, food, drinking water, indoor/outdoor air and consumer products. While the relative importance of each of these pathways for the general population remains unclear, evidence suggests that consumption of wildlife species, and particularly top predator species, may be the main pathway for Indigenous Peoples, including circumpolar populations and First Nations, who rely on traditional food for subsistence. Maternal transfer through cord blood and breastfeeding are sources of long-chain PFCAs for the fetus and for nursing infants/children. Occupational exposure to certain workers (e.g., firefighters, ski wax technicians) can lead to higher serum levels of long-chain PFCAs as compared to the general population.

9. Laboratory studies of ecological endpoints demonstrated developmental effects, behavioural effects, hepatotoxicity, immunotoxicity, neurotoxicity, changes in gene expression, genotoxicity and altered thyroid hormones. In addition, vitellogenin induction has occurred in juvenile rainbow trout after dietary exposure to $C_9$–$C_{11}$ PFCAs. Toxicological and epidemiological evidence indicates that long-chain PFCAs are associated with adverse effects in humans, including hepatotoxicity, developmental/reproductive toxicity, immunotoxicity, thyroid toxicity and altered cardiometabolic function. Data on the adverse effects of long-chain PFCAs is generally lacking for PFCAs with longer chain lengths (e.g., $C_{15}$, $C_{17}$ and $C_{19}$–$C_{21}$). However, read-across can be used to fill data gaps, particularly within a homologous series of substances. While introducing some uncertainties, this is a practical and efficient approach to address long-chain PFCAs. Long-chain PFCAs have a high degree of chemical similarity for the series of acids and existing data show effects on common endpoints. Data from homologues, including the extensively studied $C_8$ PFCA (perfluorooctanoic acid, PFOA) which has been listed to Annex A to the Convention, indicates the potential for adverse effects. Furthermore, several studies show that the activity/toxicity of PFCAs can increase with chain length. Therefore, it is anticipated that all long-chain PFCAs would have similar adverse effects on human health and the environment, and that the toxic potency may vary with chain length.

10. Long-chain PFCAs are persistent and remain in the environment for a very long time, which increases their probability, magnitude and duration of exposure to wildlife and humans. Long-chain PFCAs are also subject to long-range environmental transport, which can also result in regional and global contamination. As such, releases of long-chain PFCAs can lead to elevated concentrations in organisms over wide areas. Long-chain PFCAs may also biomagnify through the food chain, resulting in increased concentrations in top predator species. Several different long-chain PFCAs may be present simultaneously in the tissues of organisms, increasing the likelihood and potential severity of harm compared to looking at a single long-chain PFCA. 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 the 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, such as Indigenous Peoples, are at risk of greater exposure to long-chain PFCAs.

11. Due to the ongoing production and use of long-chain PFCAs, their salts and compounds related to PFCAs, long-chain PFCAs are directly or indirectly emitted into the environment from human activities. Long-chain PFCAs are globally ubiquitous in environmental compartments, including biota, freshwater, saltwater, sediment, soil and rainwater, and humans. Long-chain PFCAs are persistent, bioaccumulative, have adverse effects on 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. Increasing temporal concentration trends in wildlife, including top predator species, suggest that long-chain PFCAs can approach toxicity thresholds resulting in harm to wildlife populations. In humans, the high persistence of long-chain PFCAs can lead to widespread and increasing exposure, potentially resulting in adverse effects. Certain populations, such as Arctic Indigenous Peoples and those who rely on traditional foods for subsistence, are at risk of greater exposure and potential effects. Therefore, it is concluded that long-chain PFCAs, their salts and related compounds are likely, as a result of their long-range

environmental transport, to lead to significant adverse human health and/or environmental effects such that global action is warranted.

# 1. Introduction

12. In June 2021, Canada submitted a proposal to list long-chain ($C_9$–$C_{21}$) perfluorocarboxylic acids (PFCAs), their salts and related compounds in Annexes A, B and/or C to the Convention. The proposal (UNEP/POPS/POPRC.17/7) was submitted in accordance with Article 8 of the Convention and reviewed by the POPs Review Committee (POPRC) at its seventeenth meeting in January 2022.

13. Certain data gaps were noted for some members of the homologous series of long-chain PFCAs covered in this risk profile, most notably for biomagnification studies in the field and monitoring data for $C_{19}$–$C_{21}$ PFCAs. This may be the consequence of analytical challenges in measuring PFCAs at the upper end of the range (i.e., for $C_{15}$–$C_{21}$ PFCAs). Typical analysis (including standardized methods) for measuring PFCAs is by liquid chromatography-tandem mass spectrometry (LC-MS/MS) using electrospray ionization. Studies, such as those done by Androulakakis et al. 2022 and Gao et al. 2016, have shown that the instrument response decreases significantly for ≥$C_{14}$ PFCAs due to poor ionization efficiency. This is further demonstrated by standards for $C_{14}$–$C_{18}$ PFCAs. As a result, accredited analysis from commercial laboratories is restricted to $C_9$–$C_{14}$ PFCAs, which may limit the availability of data for $C_{15}$–$C_{21}$ PFCAs. Authentic reference standard mixtures of PFASs are widely employed in analytical methodology and the majority of these do not include >$C_{14}$ PFCAs (e.g., PFAC-MXH, EU-5813-NSS, EPA-533PAR, PFAC30PAR, PFC-MXA, PFAC-MXA, PFAC-24PAR, EPA-537PDS) (US EPA 2019, 2021a; Shoemaker et al. 2008; Wellington Laboratories 2022). These reference standards are commercially available mixtures designed to support standardized methods by the United States Environmental Protection Agency (US EPA) and European Union Council Directive.

14. Despite the outlined analytical challenges, analytical reliability for detected concentrations for $C_{14}$–$C_{18}$ PFCAs is robust, due to the availability of chemical standards for $C_{14}$, $C_{16}$, and $C_{18}$, and isotopically labeled standards for $C_{14}$, $C_{16}$, and $C_{18}$. The chemical standards are essential for accounting for matrix effects and recovery issues for >$C_{14}$. In addition, non-detects should not be interpreted as not present. Recovery of $C_{16}$ and higher is challenged by difficulty in extracting these PFCAs out of environmental matrices into organic solvents. Typical methods, originally developed to analyze perfluorooctyl substances (e.g., perfluorooctane sulfonic acid (PFOS) and PFOA), have been adapted to work for a larger suite of congeners. Due to differences in physical properties, the methods do not perform as well for PFAS ≤$C_4$ and ≥$C_{16}$. For ≥$C_{16}$ PFCAs, the substances have poor ionization efficiency using electrospray negative ionization instrumentation. Both the extraction method and instrumentation are analytical challenges that contribute to a high propensity of non-detects.

15. Lower incidence of detection for the longer-chain PFCAs may also be a result of the lower environmental loading of the longer-chain PFCAs, relative to those on the shorter end of the range. Nonetheless, the estimated worldwide production volumes of compounds related to long-chain PFCAs suggest that the environmental loading for PFCAs at the upper end of the range is significant (refer to section 2.1 for more details). Similarly, adverse effects data have largely focused on the shorter members of this homologous series (e.g., $C_9$–$C_{14}$ PFCAs).

16. To address data limitations, a read-across approach has been implemented in this document based on guidance on grouping of chemicals from the OECD (2014). According to this guidance, substances that have physicochemical, toxicological and ecotoxicological properties that are likely to be similar or follow a regular pattern as a result of structural similarity may be considered as appropriate for read-across. It is appropriate to take such an approach as the long-chain PFCAs are a homologous series of substances, with total carbon atoms ranging from 9 to 21. There is a high degree of structural similarity observed for all long-chain PFCAs; each acid contains a terminal carboxylic acid and an incremental and constant change of one additional –$CF_2$– throughout the series. This series can result from a common manufacturing method of telomerization (Buck et al. 2011) forming related compounds. These in turn are subject to common biotic and abiotic transformation mechanisms, to produce the acids (Butt et al. 2013; Ellis et al. 2004). Read-across is justified and has been adopted in certain portions of the document where data is lacking for specific long-chain PFCAs. While the information provided forms the basis of the justification for the use of read-across information, endpoint-specific considerations are reported in the appropriate sections of this document.

## 1.1 Chemical Identity

17. Long-chain PFCAs, their salts and related compounds are members of the per- and polyfluoroalkyl substances (PFASs) chemical class. The compounds included in the nomination of long-chain PFCAs, their salts and related compounds were defined in document UNEP/POPS/POPRC.17/7 and in decision POPRC-17/6 (UNEP/POPS/POPRC.17/13).

18. In line with decision POPRC-17/6, this risk profile concerns the PFCAs with carbon chain lengths from 9 to 21 inclusive, their salts and related compounds. Long-chain PFCAs and their salts are a homologous series of substances with the molecular formula of $C_nF_{2n+1}CO_2H$ (where $8 \leq n \leq 20$). Compounds related to long-chain PFCAs are defined as any substance that is a precursor and may transform to long-chain PFCAs, where the perfluorinated

alkyl moiety has the formula $C_nF_{2n+1}$ (where $8 \leq n \leq 20$) and is directly bonded to any chemical moiety other than a fluorine, chlorine or bromine atom. An indicative list of Chemical Abstracts Service (CAS) numbers for long-chain PFCAs, their salts and related compounds, comprising approximately 200 substances, is provided in UNEP/POPS/POPRC.18/INF/14. Some of the substances identified as compounds related to long-chain PFCAs have also been identified in the indicative list of substances covered by the listing of PFOA, its salts and PFOA-related compounds (UNEP/POPS/POPRC.17/INF/14/Rev.1) as compounds related to PFOA ($C_8$ PFCA).

19. The chemical identity of the long-chain PFCAs, and the available experimental and calculated physical and chemical data for this group are given in Tables 1 and 2 of UNEP/POPS/POPRC.18/INF/12.

20. Both linear and branched isomers are encompassed by the scope of the risk profile. Linear isomers have been reported to be predominant for long-chain PFCAs detected in biota (De Silva and Mabury 2004; Conder et al. 2008; Zhang et al. 2015). Conder et al. (2008) suggested that linear isomers may have significantly slower elimination rates and/or may be present at higher exposure concentrations than branched isomers. In a dietary exposure study using juvenile rainbow trout comparing linear $C_9$ PFCA (n-$C_9$ PFCA) and branched $C_9$ PFCA (i.e., iso-$C_9$ PFCA, with terminal isopropyl branching), the half-life in blood was 15.9 and 10.3 d, respectively, and in liver was 6.0 and 4.7 d, respectively (De Silva and Mabury 2009). In the same study, linear PFOA and seven branched PFOA isomers were also dosed. Two of the branched PFOA isomers had greater accumulation and longer half-lives than linear PFOA. The other branched PFOA isomers had less accumulation and shorter-half-lives. These data suggest that it is not possible to generalize the accumulation of branched isomers relative to linear isomers.

21. Related compounds to long-chain PFCAs include fluorotelomer alcohols (FTOHs) and fluorotelomer derivatives, including side-chain fluorinated polymers and polyfluoroalkyl phosphoric acid mono-/diesters (monoPAPs/diPAPs). Fluorotelomers are a subgroup of per- and polyfluorinated substances that are produced by a process called telomerization, which can produce a range of fluorocarbon chain lengths. FTOHs are not fully fluorinated, since they have a two or more hydrocarbon alkyl chains linked to the perfluorinated carbon chain (Environment Canada 2012). FTOHs with x number of perfluorinated carbons (where $x \geq 8$) produce intermediates such as fluorotelomer unsaturated carboxylates (x:2 FTUCA) and fluorotelomer carboxylic acids (x:2 FTCA) that can further transform to long-chain PFCAs (Environment Canada 2012). FTOHs are volatile and can also undergo atmospheric oxidation to yield long-chain PFCAs (Wallington et al. 2006). Substances containing $F(CF_2)_x(CH_2)_2$-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).

## 1.2 Conclusion of the POPs Review Committee regarding Annex D information

22. At its seventeenth meeting, the POPs Review Committee evaluated the proposal by Canada to list long-chain PFCAs, their salts and related compounds under the Convention. The Committee concluded that long-chain PFCAs, their salts and related compounds meet the screening criteria specified in Annex D (decision POPRC-17/6). It was decided to review the proposal further and to prepare a draft risk profile in accordance with Annex E to the Convention.

## 1.3 Data sources

23. The draft risk profile is based on the following data sources:

(a) The proposal to list long-chain PFCAs, their salts and related compounds submitted by Canada (UNEP/POPS/POPRC.17/7);

(b) Information submitted by Parties and observers according to Annex E to the Convention and in response to the invitation for comments on the draft risk profile. Annex E information was provided by: Austria, Belarus, Germany, Monaco, New Zealand, Norway, the Republic of Korea, Sweden, the United Kingdom of Great Britain and Northern Ireland, the United States of America (USA), the International Pollutants Elimination Network (IPEN) and Alaska Community Action on Toxics (ACAT), and Imaging and Printing Association Europe (I&P Europe). Additional information was provided by the Netherlands, Norway, the Health and Environment Justice Support (HEJSupport), the Helsinki Commission (HELCOM), IPEN/ACAT and the Nunavik Hunting Fishing and Trapping Association (NHFTA);

(c) Ecological Screening Assessment Report Long-Chain Perfluorocarboxylic Acids, their Salts and their Precursors prepared by Environment Canada (Environment Canada 2012);

(d) Opinions and related background document from the ECHA Committee for Risk Assessment and Committee for Socio-economic Analysis on an Annex XV dossier proposing restrictions on PFNA, PFDA, PFUnDA, PFDoDA, PFTrDA, PFTDA; their salts and precursors (ECHA 2018a,b, 2020);

(e) Tier II human health and environmental assessments of indirect precursors to long-chain PFCAs from the Australian National Industrial Chemicals Notification and Assessment Scheme (NICNAS 2017, 2019).

(f) The Toxicological Profile for Perfluoralkyls prepared by the Agency for Toxic Substances and Disease Registry (ATSDR 2021).

(g) Peer-reviewed scientific journals, as well as information from reports and other grey literature.

## 1.4 Status of the chemical under national or regional regulations

24. In Canada, an ecological risk assessment concluded that long-chain PFCAs, their salts and their precursors are entering or may enter the environment in a quantity or concentration or under conditions that have or may have an immediate or long-term harmful effect on the environment or its biological diversity (Environment Canada 2012). Consequently, long-chain PFCAs, their salts and their precursors were listed to Schedule 1–List of Toxic Substances of the *Canadian Environmental Protection Act*, 1999 (CEPA). Since 2016, the *Prohibition of Certain Toxic Substances Regulations, 2012* (Canada 2012) have prohibited the manufacture, use, sale, offer for sale or import of long-chain PFCAs, their salts and their precursors, and products containing them, with a limited number of exemptions. A consultation document, proposing regulatory amendments to these Regulations to further restrict long-chain PFCAs their salts and their precursors in Canada, was published in December 2018 (Canada 2018). The proposed *Prohibition of Certain Toxic Substances Regulations, 2022* (Canada 2022) were published in *Canada Gazette* Part I on 14 May 2022 for a 75-day public comment period.

25. In 2009, the US EPA published an Action Plan for addressing potential concerns with long-chain perfluorinated chemicals, including long-chain PFCAs, and identified long-chain PFCAs as persistent, bioaccumulative and toxic (PBT) (US EPA 2009). In July 2020, the US EPA released its final rule regarding a Significant New Use Rule (SNUR) under the Toxic Substances Control Act for long-chain perfluoroalkyl carboxylate (PFAC) and perfluoroalkyl sulfonate chemical substances. The term long-chain PFAC refers to the long-chain category of perfluoroalkyl carboxylate chemical substances with perfluorinated carbon chain lengths where $7 \leq n \leq 20$. The final rule amends previous SNURs for these substances, and requires manufacturers or importers of long-chain PFAC chemical substances, their salts and precursors to notify the US EPA before conducting certain activities (US EPA 2020). In October 2021, the US EPA published the PFAS Strategic Roadmap, which lays out the Agency's approach to addressing PFASs and sets timelines for taking actions (US EPA 2021b). In 2021, the Agency for Toxic Substances and Disease Registry (ATSDR) and the Environmental Protection Agency (EPA) in the United States developed a toxicological profile that characterizes the toxicologic and adverse health effects information for perfluoroalkyls, which include $C_9$–$C_{14}$ PFCAs.

26. In Australia, NICNAS (now the Australian Industrial Chemicals Introduction Scheme, AICIS) has developed an action plan to assess and manage chemicals that may degrade to PFCAs, perfluoroalkyl sulfonates and similar chemicals (NICNAS 2020), and published tier II human health and environmental risk assessments of precursors to long-chain PFCAs (NICNAS 2017, 2019). The precursors in this group were assessed as having the potential to cause adverse outcomes for the environment and human health. Consequently, it was recommended that NICNAS consult with industry and other stakeholders to consider strategies, including regulatory mechanisms available under the *Industrial Chemicals (Notification and Assessment) Act 1989*, to encourage the use of safer chemistry.

27. In Norway, long-chain PFCAs ($C_9$–$C_{14}$) were included on the national priority list in 2014 with the objective that emission and use of these hazardous substances must be eliminated (Annex E information 2022).

28. In the European Union (EU), $C_9$–$C_{14}$ PFCAs, their salts and related compounds are restricted since August 2021 under the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) Regulation (2021/1297), which will come into force in February 2023 (European Commission 2021). Furthermore, $C_9$ and $C_{10}$ PFCAs and their salts are classified[1] within the EU according to the Globally Harmonized System of Classification and Labelling of Chemicals (GHS) criteria provided under Regulation (EC) No 1272/2008 on classification, labelling and packaging of substances and mixtures (ECHA 2018b). In addition, six long-chain PFCAs and their salts were identified as Substances of Very High Concern (SVHC) and added to the REACH Candidate List, as they were identified as PBT and toxic for reproduction ($C_9$ and $C_{10}$ PFCAs), or very persistent and very bioaccumulative (vPvB) ($C_{11}$– $C_{14}$PFCAs) (ECHA 2018b). In Switzerland, an analogous regulation in the Chemical Risk Reduction Ordinance entered into force on 1 October 2022 (Swiss Federal Council 2022).

[1] $C_9$ and $C_{10}$ PFCAs and their salts are classified under the GHS for their carcinogenic potential (Carc. 2: Suspected of causing cancer), reproductive toxicity (Repr. 1B: Adverse effects on sexual function and fertility or on development) and effects on or via lactation. $C_9$ PFCA is also classified for its acute toxicity (Category 4), toxicity on the liver, thymus, and spleen (STOT RE 1: Specific target organ toxicity – repeat exposure) and eye damage (Category 1).

# 2. Summary of the information relevant to the risk profile

## 2.1 Sources

### 2.1.1 Production, trade, stockpiles

29. Estimates of the global production and consumption of long-chain PFCAs, their salts and related compounds have been reported in the literature. Worldwide total manufacturing volumes of the ammonium salt of $C_9$ PFCA (ammonium perfluorononanoate or APFN) for the production of primarily polyvinylidene fluoride (PVDF) for the years 1975 to 2004 was estimated to be in the range of 800 to 2300 tonnes (with production estimated to be in the range of 15 to 100 tonnes/year) (Prevedourous et al. 2006). For the year 2004, APFN volumes were estimated to range between 15 and 75 tonnes (PERFORCE 2004; Posner et al. 2009). Wang et al. (2014) estimated the APFN usage in Japan, Western Europe and the USA to range between 8 and 107 tonnes per year for the years 1975 to 2015. For the period of 2016–2030, the authors' assumption was that the use of APFN in PVDF production, and associated production of APFN in those countries, would cease as the major manufacturing companies committed to the US EPA Stewardship program.

30. In response to a survey conducted by the OECD for the year 2009 (OECD 2011), four companies in two countries[2] reported manufacture of long-chain PFCAs, their salts and related compounds, with perfluorinated chain lengths of 9 to 18 carbons. Twenty-three long-chain PFCAs ($C_9$–$C_{12}$), their salts and related compounds, including 10:2–18:2 fluorotelomers, were reportedly contained in products or mixtures, whether as part of the formulation or as residue (impurity). The total volume of these substances in products was approximately 16 tonnes. The majority of the substances were reported to have uses as raw materials (for surface treatment agents, water/oil repellents and soil repellents), fluoropolymer polymerisation aids or manufacturing intermediates (OECD 2011). Although no specific information regarding the intentional manufacture of substances with perfluorinated chain lengths greater than 18 carbons has been found, it is expected that these chain lengths would be present as components or impurities within the $C_9$–$C_{18}$ materials.

31. Worldwide production of fluorotelomers was estimated at approximately 9,100 tonnes (reported as 20 million pounds) in 2006 and, at that time, the USA was considered to account for more than 50 percent of the production (US EPA 2009). Textiles and apparel were considered to account for approximately 50 percent of the volume, with carpet and carpet care products accounting for the next largest share in consumer product uses. Coatings, including those for paper products, were identified as the third largest category of consumer product uses (US EPA 2009). For the years 2012 to 2015, annual national aggregate production volumes of < 454 tonnes were reported in the USA for each of the following FTOHs: 8:2, 10:2, 12:2 and 14:2 (CDR 2020).

32. Wang et al. (2014) estimated the global annual production of fluorotelomer-based products[3] to range between 2500 and 20,000 tonnes for the years 1961 to 2004, and production was estimated or projected at 45,000 tonnes per year for the period 2005 to 2030. The authors also reported that, since 2002, there has been a geographical shift of industrial sources of PFCAs as a result of the relocation of PFCA, fluoropolymer and other PFAS product production from the USA, Western Europe and Japan to emerging Asian economies, especially China.

33. Information collected for the years 2004 and 2005 indicate that eight products containing compounds related to long-chain PFCAs (i.e., used for automotive painting, glass treatment and ink cartridges, or as water/oil repellents for textiles, carpets and masonry/cement surfaces) were imported into Australia during that period, for a total volume of up to 33 tonnes (reported as 33,300 kg) per annum (NICNAS 2019). Two compounds related to PFCAs were also imported into Australia in 2005: a perfluorinated furan compound used as an analytical reagent (0.00025 tonnes) and a polymer containing a perfluoroalkylethyl ester moiety used to formulate coatings for wood boards of internal wall cladding (0.15 tonnes).

34. Based on two industry surveys conducted under the authority of the *Canadian Environmental Protection Act*, 1999 (CEPA) (Canada 1999) for the years 1997–2000, and 2004, long-chain PFCAs were not reported to be manufactured or imported into Canada. However, in both surveys, between 1 and 100 tonnes of a number of compounds related to the long-chain PFCAs were reported to be imported into Canada (Environment Canada 2001, 2005). In addition, substances imported within manufactured items, incidentally or not, were not accounted for as they were not reported through these surveys. Lastly, an average of 0.003 tonnes per year of long-chain PFCAs, their salts and/or related compounds were used for analysis, in scientific research or as a laboratory analytical standard, over the period of 2017 to 2021 (ECCC 2022).

35. No intentional manufacturing or use (including import and export) of $C_9$–$C_{14}$ PFCAs, their salts or related compounds above 1 tonne/annum have been identified in the EU as of June 2017 (ECHA 2018b). These substances were reported as being mainly manufactured unintentionally during the manufacturing of PFCAs containing a carbon

[2] The names of the companies and/or countries were not specified in the OECD report.

[3] "Fluorotelomer-based products" are described as comprising of non-polymers (e.g., FTOHs, fluorotelomer sulfonates (FTSAs) and diPAPs) and side-chain fluorinated polymers (e.g., acrylates) in Wang et al. (2004).

chain length of less than nine carbon atoms (ECHA 2018b). During the public consultation for the $C_9$–$C_{14}$ restriction proposal under the EU REACH regulation in 2018, one of the stakeholders reported that the production of $C_6$ fluorotelomers leads to production of an unavoidable fraction of $C_8$ and longer chain substances belonging to the $C_9$–$C_{14}$ substances to be restricted. This long-chain fraction is an unintentional byproduct occurring during production of the so-called "telomerisation process" (ECHA 2018c).

36. In their response to the request for Annex E information (2022), Belarus, Monaco, New Zealand, Norway and the Republic of Korea have indicated that long-chain PFCAs, their salts and related compounds are not manufactured in their countries. In addition, New Zealand has stated that none of the long-chain PFCAs or their salts appear in the New Zealand Inventory of Chemicals, but that a number of compounds related to long-chain PFCAs are present on the inventory, indicating they have been used as components in products approved for import into New Zealand.

### 2.1.2 Uses

37. Based on available information, long-chain PFCAs, their salts or related compounds are used, or may have been used, in a range of applications. Starting materials that may be used for the production of compounds related to long-chain PFCAs consist of FTOH mixtures of fluorinated chain lengths ranging from 4 to 20 carbons (Beatty 2003; Sherman et al. 2001). Based on the available commercial information, compounds at the upper end of this range (e.g., containing a total of 17 to 21 carbons) may represent a lower proportion of the mixtures (e.g., up to 4% by weight) compared to compounds at the lower end of the range (refer to Table 3 of UNEP/POPS/POPRC.18/INF/12 for details). Nonetheless, taking into account the estimated production volumes of fluorotelomers worldwide (as described in section 2.1.1), there is potential for significant loading of $C_9$–$C_{21}$ PFCAs into the environment.

38. Long-chain PFCAs and their related compounds may also be unintentionally produced during the manufacturing of PFASs, including those containing a carbon chain of less than nine carbon atoms (Prevedouros et al. 2006; ECHA 2018b, as described in section 2.1.2 of UNEP/POPS/POPRC.18/INF/12), in other industrial processes, such as the manufacture of polytetrafluoroethylene (PTFE) powders and the polymerisation of fluoropolymers (ECHA 2018b, 2020), and during thermolysis of fluorinated polymers, such as PTFE, in industrial or consumer high-temperature applications (e.g., ovens, non-stick cooking utensils and combustion engines) (Ellis et al. 2001). As a result, long-chain PFCAs may be present in certain products and articles as impurities.

39. Details on identified uses, as well as reported detections of long-chain PFCAs, their salts and related compounds in products and articles due to their intentional or unintentional inclusion in these products, are provided below. Note that, for the majority of the studies that reported the detection of long-chain PFCAs, the homologues with a higher number of carbons in the chain (i.e., > $C_{14}$ PFCAs) were not part of the analysis.

**Industrial applications**

40. APFN was identified as being used for surfactant applications and in the production of fluoropolymers, primarily PVDF (Prevedouros et al. 2006; OECD 2015). Fluoropolymers, such as PVDF, have many applications including use in cables, wires and electronics, as fire- or weather-resistant coatings for materials in construction-related applications, in the pulp and paper industry, and in nuclear waste processing (Banks 1994; Ebnesajjab 2013). PVDF polymers can contain an estimated residual content of 100–200 ppm APFN (Prevedouros et al. 2006).

41. Fluorotelomer epoxides, olefins or alcohols have been reported to be used as building blocks in the production of fluorotelomer-based substances. These substances are used in commercial products to provide oil-, grease-, water- and stain-repellent properties to other substrates. Some fluorotelomer-based substances can be further exploited as monomers (e.g., 10:2 fluorotelomer acrylate monomers (FTAcs)) to generate side-chain fluorinated polymers with the same characteristic properties (e.g., 10:2 fluorotelomer acrylate (FTA)) (Environment Canada 2012; Kannan et al. 2011). Some compounds related to long-chain PFCAs are also listed in the Substances in Preparations in Nordic Countries (SPIN) database for the manufacture of chemicals and chemical products, and patented as mould release agents (Glüge et al. 2020).

**Electronic articles, medical devices and photo-imaging**

42. Available patent information indicates that certain compounds related to long-chain PFCAs may be used in electronic articles (e.g., semiconductors) and medical devices (i.e., UV-hardened dental restorative materials, manufacturing of contact lenses) (Swedish Chemicals Agency 2015; ECHA 2018b). Other compounds related to long-chain PFCAs have also been used as functional fluids in computer and electronic product manufacturing (Glüge et al. 2020).

43. Based on information provided by I&P Europe and available patent information, long-chain PFCAs, their salts and their related compounds are used in photographic materials (I&P Europe Annex E information 2022; Glüge et al. 2020). The use of long-chain PFCAs and related compounds relates to the composition of commercial PFOA used by I&P Europe members in the manufacturing of some remaining photographic coatings applied to film, as they may contain homologues of PFOA and other substances that fulfill the definition of long-chain PFCAs and related substances. Because uses of PFOA and related compounds will be eliminated from all photographic coatings by July 2025 at the latest, this will automatically result in elimination of any long-chain PFCAs and related compounds

present in the few photographic materials concerned.

**Automotive care products**

44. $C_9$–$C_{14}$ and $C_{16}$ PFCAs have been detected in lubricants (i.e., engine oils, hydraulic fluids and greases) (Zhu and Kannan 2020; Arcadis 2021) and paint sealants (Arcadis 2021), and compounds related to long-chain PFCAs were reported to be, or to have been, used in products for motor vehicle repair (Nordic Council of Ministers 2015, as summarized in NICNAS 2019) and in automotive waxes and polishes (Glüge et al. 2020).

**Food-contact material, cookware and household products**

45. $C_9$–$C_{18}$ PFCAs and related compounds, such as 10:2 monoPAP, diPAPs (8:2 and 8:2/12:2) and FTOHs (8:2, 10:2, 12:2, 14:2, 16:2 and 18:2), have been detected in food contact materials (Schaider et al. 2017; Trier et al. 2011; Vestergren et al. 2015; Kotthoff et al. 2015; Blom and Hanssen 2015; Borg and Ivarsson 2017; Gebbink et al. 2013; Guo et al. 2009; Liu et al. 2014c; Granby and Tesdal Håland 2018; Schultes et al. 2019; Yuan et al. 2016) and $C_9$–$C_{12}$ PFCAs in plastic pet food packages (Chinthakindi et al. 2021). $C_{10}$ PFCA has also been measured in recycled paper food packaging materials (Curtzwiler et al. 2021). $C_9$–$C_{12}$ PFCAs were detected in non-stick cookware (Guo et al. 2009), and FTOHs (10:2 and 8:2) found in, and as emissions from, non-stick cookware (Sinclair et al. 2007; Herzke et al. 2012; Blom and Hanssen 2015).

46. $C_9$–$C_{12}$ PFCAs have been measured in household carpet care liquids and foams (Guo et al. 2009; Liu et al. 2014), and FTOHs (10:2 and 8:2) found in certain dish cleaning or rinsing agents (Kotthoff et al. 2015; Dinglasan-Panlilio and Mabury 2006; Blom and Hanssen 2015).

**Printing ink**

47. 8:2 FTOH has been detected in printer inks (Herzke et al. 2009).

**Building and construction materials**

48. Mono- and diPAPs are listed in the SPIN database for use in the building and construction sector (Glüge et al. 2020). $C_4$–$C_{14}$ PFCAs, FTOHs (8:2 and/or 10:2) and FTUCAs (10:2 and 8:2) were detected in building materials, such as coatings and foil for facades or glass-substituents, and window films (Janousek et al. 2019; Bečanová et al. 2016; Gewurtz et al. 2009). $C_9$–$C_{12}$ PFCAs have been detected in floor waxes and stone/tile/wood sealants, thread seal tapes and pastes (Guo et al. 2009; Liu et al. 2014; Arcadis 2021). Compounds related to long-chain PFCAs, such as FTOHs and side-chain fluorinated polymers, were measured in surfactants used in caulks, paints, coatings, adhesives and floor waxing (Dinglasan-Panlilio and Mabury 2006), and have been reported to be used in polishing agents, paints, lacquers and varnishes (Banks 1994; Nordic Council of Ministers 2015, as summarized in NICNAS 2019).

**Fire-fighting foam**

49. $C_9$–$C_{14}$ and $C_{18}$ PFCAs, FTA (8:2), FTCA (10:2), FTUCA (8:2 and 10:2), fluorotelomer sulfonate (FTSA) (8:2) and FTOHs (10:2 and 8:2) have been detected or reported to be used in aqueous film-forming foam (AFFF) (Herzke et al. 2009, 2012; Swedish Chemicals Agency 2015; Nordic Council of Ministers 2015, as summarized in NICNAS 2019; Favreau et al. 2017; ECHA 2022). $C_9$ and $C_{10}$ PFCAs have also been measured in fluorocarbon surfactants used for the preparation of AFFF (Mumtaz et al. 2019).

**Ski waxes**

50. $C_9$–$C_{21}$ PFCAs and 8:2 FTOHs have been measured in ski waxes/gliders or their raw materials (Kotthoff et al. 2015; Plassmann and Berger 2013; Blom and Hanssen 2015; Fang et al. 2020).

**Personal care and other consumer products**

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. 2021; Swedish Chemicals Agency 2021; Schultes et al. 2018; Arcadis 2021).

52. $C_9$–$C_{12}$ PFCAs, FTOHs (8:2, 10:2, 12:2, 14:2 and 16:2) and fluorotelomer ethoxylates (FTEOs, 8:2, 10:2, 12:2, 14:2 and 16:2) have been detected in anti-fog sprays and cloths (Herkert et al. 2022). $C_9$–$C_{14}$ and $C_{16}$ PFCAs, FTCAs (8:2 and 10:2), FTOHs (8:2 and 10:2) and FTAcs (8:2 and 10:2) have been measured in the fabric, foam and laminated composites of foam/fabric from children's car seats (Wu et al. 2021).

**Textiles and apparel**

53. Long-chain PFCAs ($C_9$–$C_{14}$, $C_{16}$), FTOHs (10:2 and 8:2), FTCAs and FTUCAs have been detected in apparel, including in adult and/or children outerwear and baby/children's bibs (Gremmel et al. 2016; Berger and Herzke 2006; Commission for Environmental Cooperation 2017; Borg and Ivarsson 2017; Liu et al. 2014), and membranes for apparel (Liu et al. 2014). A study conducted by Kotthoff et al. (2015) also reported detections of $C_9$–$C_{14}$ PFCAs

and/or FTOHs (10:2 and 8:2) in outdoor textiles (e.g., jackets, gloves) and leather samples. An analysis of the same samples conducted for a limited number of items indicated a correlation between FTOH (10:2 and 8:2) and PFCA ($C_{10}$ and $C_8$) concentrations ($r$=0.957; $p$=0.0013) (Kotthoff et al. 2015). $C_9$–$C_{12}$ PFCAs have been detected in medical garments (Guo et al. 2009; Liu et al. 2014) and firefighter turnout gear (Peaslee et al. 2020).

54. $C_9$–$C_{11}$ PFCAs and compounds related to long-chain PFCAs, such as FTOHs (8:2 and 10:2), FTA (8:2) and FTMAc (8:2), have been reported to be used in fabric protectors, textile impregnation agents and carpet protectors (Banks 1994; Nordic Council of Ministers 2015, as summarized in NICNAS 2019; Favreau et al. 2017). $C_9$–$C_{16}$ PFCAs and/or FTOHs (10:2 and 8:2) have been detected in home textiles (e.g., curtains, bed covers/linens, quilts, carpets, table cloths) (Commission for Environmental Cooperation 2017; Vestergren et al. 2015; Herzke et al. 2009, 2012; Blom and Hanssen 2015; Guo et al. 2009; Liu et al. 2014), outdoor textiles (Arcadis 2021), impregnation/water proofing agents (Herzke et al. 2012; Kotthoff et al. 2015; Borg and Ivarsson 2017; Arcadis 2021), and industrially applied polymeric materials (carpet protector) (Dinglasan-Panlilio and Mabury 2006). $C_4$–$C_{14}$ PFCAs and/or FTOHs (8:2 and/or 10:2) were also measured in other types of fabric/textiles (i.e., awning, seat cover for public transportation, maritime application) (Janousek et al. 2019).

55. Textiles and apparel have been considered to account for approximately 50 percent of the volume of fluorotelomers used globally, with carpet and carpet care products accounting for the next largest share in consumer product uses (US EPA 2009). During the early to mid-2000s, fluorotelomer-based side-chain fluorinated polymers replaced non-polymeric PFASs in treatments for carpets and rugs, and side-chain fluorinated polymers are now the most common carpet and rug treatments on the US market (FluoroCouncil 2017).

56. Upon entering the waste stream at the end of their life cycle these products may continue to be a significant source of $C_9$–$C_{21}$ PFCAs and related compounds in the environment.

### 2.1.3. Releases to the environment

57. There are no natural sources of long-chain PFCAs, their salts and related compounds (Kissa 1994). Their presence in the environment is due solely to human activity. Long-chain PFCAs can be released to the environment from direct and indirect sources. Direct sources include emissions from the production of PFCAs, as well as the life cycle (i.e., production, use and disposal) of products containing long-chain PFCAs, either as a main ingredient, or as residuals or chemical reaction impurities in products. Indirect sources are those where compounds related to long-chain PFCAs emitted to the environment have transformed to long-chain PFCAs through biotic or abiotic transformation (OECD 2015; Wang et al. 2014).

58. Long-chain PFCAs, their salts and related compounds have been detected in environmental and other matrices from various impacted sites. Details are provided below and in Table 4 of UNEP/POPS/POPRC.18/INF/12.

59. $C_9$–$C_{16}$ PFCAs, FTOHs (8:2 and 10:2), diPAP (8:2), FTUCAs (8:2 and 10:2) and FTSA (8:2, 10:2, 12:2, 14:2) have been measured in various environmental matrices (e.g., water, groundwater, soil, air, wastewater, sediment) collected in proximity to production facilities, electroplating industrial parks, a paper products factory and in industrial or urban areas located in India, China, South Korea, Germany, Norway and Japan (Chen et al. 2018a; Li and Hua 2021; Heydebreck et al. 2016; Lam et al. 2014; Sharma et al. 2016; Sim et al. 2021; Göckener et al. 2022; Takemine et al. 2014; Yu et al. 2022; Yao et al. 2016; Jiawei et al. 2019; Langberg et al. 2020; Kim et al. 2021). Yu et al. (2022) reported increasing temporal trends for $C_9$ and $C_{10}$ PFCAs concentrations in Taihu Lake, China, from 2009 and 2021.

60. $C_9$–$C_{12}$ PFCAs have also been measured in groundwater contaminated with AFFF collected at US military bases (Backe et al. 2013). $C_9$–$C_{14}$ and $C_{16}$ PFCAs, FTCAs (8:3, 9:3 and 11:3), 8:2 FTUCA and FTSAs (8:2, 10:2, 12:2 and 14:2) have also been detected in groundwater and/or soil sampled in AFFF-impacted sites from four Canadian airports (Liu et al. 2022).

61. Long-chain PFCAs and their related compounds may also be released to the environment from landfills, incineration plants and wastewater treatment plants. $C_9$–$C_{18}$ 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, 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; Miljösamverkan Sverige 2022). $C_9$–$C_{18}$ PFCAs and compounds related to long-chain PFCAs have also been detected in sludge, biosolids, influent and effluent from wastewater treatment plants located in various countries around the world (Lenka et al. 2021; Alder and von der Voet 2014; Loganathan et al. 2007; Rodríguez-Varela et al. 2021; Schultz et al. 2006; Bossi et al. 2008; Moodie et al. 2021; Pepper et al. 2021; Ahrens et al. 2011; Yao et al. 2016; Nguyen et al. 2022; Nordic Council of Ministers 2019; Austria Annex E information 2022; HELCOM 2022). In addition, $C_9$–$C_{14}$ PFCAs and 8:2 diPAPs have been measured in leachate, fly ash and bottom ash from municipal solid waste incineration plants (Liu et al. 2021). $C_9$–$C_{12}$ and $C_{14}$ PFCAs and FTOHs (8:2 and 10:2) have also been measured in air around wastewater treatment plants and landfills (Ahrens et al. 2011; Shoeib et al. 2016).

62. Land application of contaminated biosolids can also be a source of long-chain PFCA releases to the

environment. $C_9$–$C_{14}$ PFCAs have been detected in water (surface, well and ground) and soil from agricultural sites with a history of land application of biosolids (Lindstrom et al. 2011; Pepper et al. 2021; Sepulvado et al. 2011; Sim et al. 2021; Johnson 2022).

63. Ski wax has also been identified as a source emission of long-chain PFCAs and related compounds to the environment. $C_9$–$C_{21}$ PFCAs were measured in snow collected after cross-country ski competitions and/or in soil from skiing areas after snowmelt (Carlson and Tupper 2020; Plassmann and Berger 2013; Grønnestad et al. 2019).

64. Some uses of long-chain PFCAs, their salts and their related compounds may lead to releases to indoor environments. $C_9$–$C_{15}$ PFCAs have been detected in indoor air and/or dust samples from several countries at various locations including private homes, hotels, office buildings, vehicles and daycares (see section 2.3.2 and Table 9 in UNEP/POPS/POPRC.18/INF/12 for details).

65. Building on work by Prevedouros et al. (2006), Wang et al. (2014) estimated the global cumulative emissions of $C_4$–$C_{14}$ PFCAs for the years 1951 to 2030 (summarized in Table 5 of UNEP/POPS/POPRC.18/INF/12) from quantifiable sources[4] of these substances. These estimates were generated by combining data on products containing PFCAs and/or their precursors (including manufacturing processes, production volumes as a function of time, and use patterns) with estimated or empirically derived emission factors during each stage in the product life cycle. Uncertainties of the PFCA emissions were accounted for by defining lower and higher emission scenarios, which differed by a factor of eight approximately. Total estimated or projected global cumulative emissions of $C_9$–$C_{14}$ PFCAs, between 1951 and 2030, ranged from 342 to 3,041 tonnes (individual ranges are: 250–1,901 tonnes ($C_9$); 8–222 tonnes ($C_{10}$); 67–689 tonnes ($C_{11}$); 0–63 tonnes ($C_{12}$); 17–147 tonnes ($C_{13}$); 0–19 tonnes ($C_{14}$)). The sources of the estimated emissions differed between PFCA homologues, sometimes considerably, and the relative contributions of each source changed over time (refer to Figure 1 of UNEP/POPS/POPRC.18/INF/12 for more details).

## 2.2. Environmental fate

### 2.2.1 Persistence

66. Long-chain PFCAs are carboxylic acids bonded to a fully fluorinated carbon chain, with total carbon numbers from 9 to 21. This carbon-fluorine bond is one of the strongest covalent bonds (about 108–120 kcal/mole) (Dixon 2001; Parsons et al. 2008), making the bond extremely stable and generally resistant to degradation by acids, bases, oxidants, reductants, photolytic processes, microbes and metabolic processes. Fluorine also has the highest electronegativity of all elements in the periodic table. The presence of fluorine instead of hydrogen on the carbon chain alters the thermal, chemical and biological characteristics of the molecule. The strong carbon-fluorine bond and high density of electron-rich repellent fluorine atoms protects the carbon backbone and results in inertness to both heat and chemical reagents (Hakli et al. 2008; Colomban et al. 2014; Parsons et al. 2008). Moreover, this contributes to a high ionization potential, low polarizability, low inter- and intra-molecular interactions and low surface tension. Therefore, long-chain PFCAs are considered extremely stable in the environment. For example, $C_9$ PFCA did not biodegrade under the OECD 301F method (Stasinakis et al. 2008). Other studies demonstrate that long-chain PFCAs do not degrade under environmentally relevant conditions (e.g., Hori et al. 2005a; Hori et al. 2005b; Hori et al. 2008; Qu et al. 2016; Liu et al. 2017). Other studies, conducted under conditions considered not environmentally relevant, have reported some degradation of long-chain PFCAs (Taniyasu et al. 2013; Barisci and Suri 2020, refer to section 2.2.1 of UNEP/POPS/POPRC.18/INF/12 for details).

67. Long-chain PFCAs have met the regulatory criteria for persistence in different jurisdictions. In the EU, $C_9$–$C_{14}$ PFCAs have been concluded to meet the criteria of very persistent in accordance with the criteria set out in the REACH regulation (ECHA 2012a, b, c, d, 2015, 2016). In Canada, the ecological screening assessment for long-chain PFCAs, their salts and their precursors (Environment Canada 2012) concluded that long-chain PFCAs and their salts meet the criteria for persistence as set out in the *Persistence and Bioaccumulation Regulations* (Canada 2000). It is additionally recognized that transformation of precursors into stable long-chain PFCAs results in their increased presence in the environment. Further, the risk profile on PFOA (UNEP/POPS/POPRC.12/11/Add.2), a close homologue to long-chain PFCAs recognized as a POP and listed to the Stockholm Convention in 2019, concluded this substance to be persistent.

### 2.2.2 Bioaccumulation

68. Both bioconcentration and bioaccumulation empirical data are available for some long-chain PFCAs. Laboratory-derived bioconcentration factors (BCF, L/kg) and bioaccumulation factors (BAF, L/kg) have been reported (up to $C_{18}$ PFCA) in three freshwater fish species (i.e., zebrafish (*Danio rerio*), common carp (*Cyprinus carpio* L.) and rainbow trout (*Oncorhynchus mykiss*)) and one green mussel species (*Perna viridis*) as well as

[4] Historial and ongoing use of: (i) PFOA as processing aids in the (emulsion) polymerization of PTFE, fluorinated ethylene propylene, perfluoroalkoxyl polymer and PVDF; (ii) C9 PFCA as processing aids in the emulsion polymerization of PVDF; (iii) chemicals derived from perfluorooctane sulfonyl fluoride; and x:2 fluorotelomer-based substances.

saltwater species blackrock fish (*Sebastes schlegeli*) (Martin et al. 2003a; Martin et al. 2003b; Jeon et al. 2010; Liu et al. 2011a; Inoue et al. 2012; Goeritz et al. 2013; Chen et al. 2016; Menger et al. 2020). Laboratory BCF/BAF values were variable depending on the species and age of the test organism. For example, whole body BCFs in common carp were determined for $C_{11}$ PFCA (2300–3700), $C_{12}$ PFCA (10,000–16,000), $C_{13}$ PFCA (16,000–17,000), $C_{16}$ PFCA (4,700–4,800) and $C_{18}$ PFCA (320–430) (Inoue et al. 2012). BCF and BAF values generally increased from $C_9$ PFCA (<0.4–1514) to $C_{14}$ PFCA (17,000–363,078) and then decreased for $C_{16}$ to $C_{18}$ PFCAs (20–4,800). Field-derived BCFs and BAFs in freshwater and marine aquatic organisms have been reported up to $C_{15}$ PFCA. For example, BAFs were determined for common carp collected from a drainage canal near a sewage treatment plant outfall (Tokyo, Japan) with liver BAFs that ranged from 69 ($C_9$ PFCA) to > 26,000 ($C_{13}$ PFCA) and kidney BAFs that ranged from 2600 ($C_9$ PFCA) to > 40,000 ($C_{13}$ PFCA) (Murakami et al. 2011).

69. 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 (up to 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; Szabo et al. 2022). However, 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. In other studies, researchers have estimated BAFs using detection limits. For example, Zhang et al. (2019) derived BAFs for marine plankton by substituting non-detect concentrations in water with the detection limit. In a recent review of BCFs and BAFs of PFASs in aquatic species, Burkhard (2021) did not include any data that were based on concentrations below the detection limit in water or tissue, which therefore limited reporting to a maximum of $C_{10}$ chain length. This has been circumvented using lab-based exposures that are not limited by environmental concentrations, in order to empirically measure BCFs and BAFs for a larger range of chain lengths (i.e., all of those papers above). However, Burkhard (2021) reported that laboratory BCF measurements for some PFAS, including $C_{10}$ PFCA, decline with increasing exposure concentration, rather than remaining constant. It was postulated that PFASs body burden is controlled by both passive and active transport processes, the latter of which can be concentration dependent. At high doses the active protein-based transport becomes saturated resulting in more rapid elimination and lower accumulation (Liu et al. 2011a). As such, laboratory-derived BCFs using high concentrations are expected to be lower than a real-world scenario.

70. Extrapolating BCF/BAF data from fish and aquatic invertebrates to birds and terrestrial/marine mammals can underestimate the bioaccumulation potential for long-chain PFCAs. For neutral organic chemicals that are non-polar and non-volatile (e.g., polychlorinated biphenyls (PCBs)), bioaccumulation generally occurs by the same mechanism in water-breathing organisms (e.g., fish and aquatic invertebrates) and air-breathing organisms (e.g., terrestrial/marine mammals or birds). As neutral chemicals have low elimination rates to both water and air, this results in similar bioaccumulation potential for both air-breathing and water-breathing organisms (Kelly et al. 2004; Mackay and Fraser 2000). However, long-chain PFCAs that are ionizing, polar, and non-volatile have higher water solubility compared to neutral chemicals. For water-breathing organisms, this can result in a more rapid elimination of long-chain PFCAs to the water phase and a subsequent reduction in bioaccumulation potential. The moderate water solubility of long-chain PFCAs causes a relatively high tendency to escape from the gills into water, though this mechanism may be less significant for very long-chain PFCAs given their increasing lipophilic character. This is consistent with the observations of Boisvert et al. (2019) that longer chain PFCAs ($C_{11}$–$C_{14}$) dominate in polar bear fat and seal blubber whereas $C_9$–$C_{11}$ PFCAs dominate in liver of the two species. Conversely, the escaping tendency of long-chain PFCAs to the air, across the alveolar membrane of the lung, would be relatively low because of their low vapor pressure and negative charge. 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). Additionally, extrapolating BCF/BAF data from fish to marine/terrestrial mammals should not be performed due to the biological differences between higher and lower trophic levels (e.g., feeding rates, assimilation efficiency, and depuration rates) (Martin et al. 2003a). As such, field biomagnification factors (BMF, unitless) and trophic magnification factors (TMF, unitless) may be more relevant in determining the overall bioaccumulation potential for long-chain PFCAs. Nonetheless, whole body BCFs have been derived in laboratories that exceed the BCF criteria in Annex D to the Convention. Nevertheless, Boisvert et al. (2019) noted that fat and blubber deposition of PFCAs tended towards those with longer chains, which is consistent with the increasing lipophilic character of longer chain PFCAs.

71. Field biomagnification or trophic magnification studies on long-chain PFCAs (up to $C_{18}$ PFCA) that focused on multiple fish species and/or top predator species (i.e., birds or terrestrial/marine mammals) show high biomagnification potential (Martin et al. 2004, Houde et al. 2006a, Haukås et al. 2007, Butt et al. 2008, Powley et al. 2008, Kelly et al. 2009, Tomy et al. 2009b, Loi et al. 2013; Müller et al. 2011, Fang et al. 2014, Xu et al. 2014, Munoz et al. 2017b, Simonnet-Laprade et al. 2019b, Ren et al. 2022). Biomagnification factor and trophic magnification factor values above one are considered bioaccumulative. For example, a marine food web in Liaodong Bay, China,

with black-tailed gulls (*Larus crassirostris*) as the top predator species had TMFs that ranged from 1.78 to 4.88 for $C_9$–$C_{14}$ PFCAs, based on whole body concentration estimates using muscle and liver data (Zhang et al. 2015). The Orge River foodweb, in France, with eight freshwater fish species as top predators but with varying feeding behaviours had BMFs that ranged from 0.3 to 25.2 and TMFs that ranged from 1.5 to 3.0 for $C_{11}$–$C_{14}$ PFCAs (Simonnet-Laprade et al. 2019a). Five other riverine foodwebs in France with chub (*Squalius cephalus*) and common barbel (*Barbus barbus*) as top predator species had TMFs that ranged from 0.9 to 14.9 for $C_9$–$C_{14}$ PFCAs (Simonnet-Laprade et al. 2019b). Mean BMFs of about 2 to 3 were reported for $C_{16}$ and $C_{18}$ for a seal liver–polar bear liver comparison in Greenland, though sample numbers were limited. Measurable BMFs were much greater when using concentrations in seal blubber, as opposed to seal liver, which are more reflective of bear feeding patterns (Boisvert et al. 2019). TMF and BMF values have been reported for several food webs globally, and are detailed in section 2.2.3 of UNEP/POPS/POPRC.18/INF/12. Overall, TMF values available for $C_9$–$C_{14}$ ranged from 0.3 to 19.8 and BMF values available for $C_9$–$C_{16}$ ranged from 0.1 to 25.2 with top predator species (e.g., black-tailed gulls, egrets, carnivorous fish, ringed seal, beluga whales, polar bears and wolves) having values consistently above one.

72. There are no biomagnification or trophic magnification data for long-chain PFCAs with chain lengths greater than $C_{18}$ due to the analytical challenges of measuring these substances. However, considering the high BMFs in polar bears for $C_9$ to $C_{13}$ calculated using concentrations in seal blubber, in addition to the BMFs calculated for $C_{14}$ to $C_{18}$ which are above 1 (Boisvert et al. 2019), it is anticipated that that $C_{19}$–$C_{21}$ PFCAs can also biomagnify in marine mammals. 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). 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 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., $K_{ow}$ based 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/12 for more details.

73. The high degree of chemical similarity for the series of acids has been described earlier and is suggestive of similar bioaccumulation characteristics. It is noted that for shorter PFCAs such as PFOA, BCF is mitigated by low gill uptake rates and active renal clearance (Consoer et al. 2021). Longer chain PFCAs exhibit increased hydrophobic partitioning which may increase uptake efficiency and reduce renal clearance rates. In the absence of empirical bioaccumulation measurements for $C_{17}$–$C_{21}$, modeling of fish BCF values was conducted using BIONIC v3.0. This model was developed for ionogenic organic chemicals, and has been applied to a set of perfluoroalkyl acids (Armitage et al. 2013). This mechanistic model can address pH dependence of BCFs by incorporating the pKa and using specific partition coefficients relevant for ionic compounds, including storage lipid-water ($K_{slw}$), membrane-water ($K_{mw}$), blood serum albumin-water ($K_{saw}$) and structural protein-water ($K_{spw}$) partition coefficients. These inputs better account for the actual distribution of ionic compounds in fish, rather than traditional BCF models that focus only on storage lipid partitioning. Empirical partitioning input parameters for the modeled acids ($C_{17}$–$C_{21}$) are not available, and have therefore been developed based on observed partitioning of other long-chain PFCAs (Droge 2019; Allendorf et al. 2020). The BIONIC model also requires input of a metabolic rate constant ($k_M$) for fish, calculated using the mass balance method described in Arnot et al. (2009). All inputs are provided in Table 6 of UNEP/POPS/POPRC.18/INF/12. BCF predictions range from ~25,000 for $C_{17}$ PFCA to ~28,500 for $C_{21}$ PFCA. The predicted fish BCF values generally decline as chain length increases, however, all predictions exceed 5,000, supportive of the high bioaccumulation potential for $C_{17}$–$C_{21}$ PFCAs.

74. There is empirical evidence of bioaccumulation for long-chain PFCAs up to $C_{16}$. 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 (Plassmann 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 (Greaves et al. 2013; Letcher et al. 2015; Su et al. 2017; Letcher et al. 2018; Boisvert et al. 2019; Sun et al. 2020). PFCAs with linear perfluoroalkyl chains (effective diameter or $D_{eff}$ = 0.61–0.96 nm in $C_8$ to $C_{18}$ PFCAs) can enable them to pass through biological membranes (Inoue et al. 2012). The $D_{eff}$ for $C_{19}$ to $C_{21}$ have been predicted by Environment and Climate Change Canada (ECCC) using OASIS software (TIMES 2020) as 1.18, 1.22 and 1.25 nm respectively. Wang and Ober (1999) have suggested that the carbon-carbon conformation changes as the fluorocarbon chain length increases, with longer chains becoming more helical, resulting in reduced cross-sectional diameter molecules. These steric considerations lead to greater bioaccumulation potential than might be expected based on molecular weight and other physical chemical considerations (Anliker et al. 1988; Dimitrov et al. 2003). Recognizing that analytical limitations present challenges in

empirical determinations, it is concluded that $C_{17}$–$C_{21}$ PFCAs have the potential to bioaccumulate.

75. In humans, long-chain PFCAs accumulate in the blood and well perfused tissues such as the liver, kidneys and lungs (Pérez et al. 2013; Kudo 2015). Long-chain PFCAs are eliminated very slowly from the human body, likely due to their strong protein binding affinity and the reabsorption processes occurring at the hepatic, intestinal and renal level (EFSA 2020). The mean half-lives for $C_9$ PFCA are estimated to range from 2.5 to 4.3 years in humans whereas the mean half-lives for both $C_{10}$ and $C_{11}$ PFCA range from 4.5 to 12 years (Zhang et al. 2013). Several animal studies suggest that the longer the carbon chain length, the more slowly the PFCA is eliminated, and thus, the more bioaccumulative it is. These studies were conducted with $C_7$–$C_{10}$ PFCAs (Ohmori et al. 2003) $C_6$–$C_9$ PFCAs (Kudo et al. 2006), and $C_8$ and $C_{10}$ PFCAs (Yeung et al. 2009). In *in vitro* studies with $C_4$–$C_{10}$ PFCAs, compounds with longer carbon chains have been found to bind more strongly to proteins (Chen et al. 2020). However, it is unclear if this trend holds for all long-chain PFCAs as other studies have not identified the same increasing linear trend (Bischel et al. 2011; Jackson et al. 2021).

76. Bioaccumulation of long-chain PFCAs in humans is evidenced by biomonitoring studies which show increasing concentrations of long-chain PFCAs with age. For example, in a study of the general Canadian population, concentrations of $C_9$ and $C_{10}$ PFCAs were highest in the oldest age bracket (60–79 years) across the three cycles of monitoring (Health Canada 2021a,b). Similarly, in a health survey performed in 2017 of Inuit adults living in Nunavik, Canada, the sum of the plasma concentrations of $C_9$–$C_{11}$ PFCAs in males and females were found to significantly increase with age and were highest in the oldest age group (50 years and over) (Aker et al. 2021; Wielsøe et al. 2022; Aker et al. 2022a).

77. Although information is lacking for the bioaccumulation of $C_{12}$–$C_{21}$ PFCAs in humans, a read-across argument can be made to address some data gaps. The high degree of chemical similarity for the series of acids has been described earlier and is suggestive of similar bioaccumulation characteristics. There is direct evidence of the long half-lives of $C_9$, $C_{10}$ and $C_{11}$ PFCAs in humans and biomonitoring studies have shown blood concentrations of certain long-chain PFCAs to increase with age. In animal studies, there is evidence of slower elimination with increasing chain lengths ($C_4$–$C_{12}$). While there is also some *in vitro* evidence of increasing protein binding with increasing chain length, it is uncertain as to whether this trend holds true for all long-chain PFCAs. Consequently, it is anticipated that long-chain PFCAs of up to 21 carbons may bioaccumulate in humans, athough bioaccumulation may not necessarily increase with increasing chain length.

78. Long-chain PFCAs have met regulatory criteria for bioaccumulation in some jurisdictions. Long-chain PFCAs ($C_9$–$C_{14}$) have been assessed in the EU and identified as bioaccumulative ($C_9$ and $C_{10}$ PFCAs) or very bioaccumulative ($C_{11}$ to $C_{14}$ PFCAs) in accordance with the criteria set out in the REACH regulation (ECHA 2012a,b,c,d, 2015, 2016). In Canada, the ecological risk assessment for long-chain PFCAs, their salts and their precursors (Environment Canada 2012) used a weight of evidence approach based on BMF and TMF data to conclude that long-chain PFCAs and their salts accumulate and biomagnify in birds, and terrestrial/marine mammals.

### 2.2.3 Potential for long-range environmental transport

79. Long-chain PFCAs, their salts and related compounds are measured in both biotic and abiotic samples in remote areas, such as the Antarctic and the Canadian Arctic that are far from known manufacturing sites. Long-range environmental transport pathways include atmospheric and oceanic transport of long-chain PFCAs and/or related compounds. Examples of compounds related to long-chain PFCAs include fluorotelomer alcohols (e.g., 8:2 FTOH, 10:2 FTOH, 12:2 FTOH) and their fluorotelomer acid derivatives (e.g., 10:2 FTA; 10:2 FTUCA).

80. Global modelling indicates that long-chain PFCAs, their salts and/or related compounds have the potential to be transported over long distances (Wallington et al. 2006; Wania 2007; Yarwood et al. 2007; Thackray et al. 2020). The presence of long-chain PFCAs in remote areas can be partly attributed to related compounds (e.g., FTOH) emitted to the atmosphere ultimately yielding long-chain PFCAs through biotic or abiotic transformation. Wallington et al. (2006) used a three-dimensional global atmospheric chemistry model (IMPACT) to show that 8:2 FTOH transform in the atmosphere to form $C_9$ PFCA. Young et al. (2007) detected $C_9$ PFCA (0.005–0.246 ng/L), $C_{10}$ PFCA (ND–0.022 ng/L), and $C_{11}$ PFCA (ND–0.027 ng/L) on several Canadian High Arctic ice caps (Melville Ice Cap (Northwest Territories), Agassiz Ice Cap (Nunavut), and Devon Ice Cap (Nunavut)) and suggested that their presence is indicative of atmospheric oxidation of volatile precursors. Ellis et al. (2004b) showed that the atmospheric lifetime of FTOHs, as determined by their reaction with hydroxy radicals, was approximately 20 d, which would allow precursors to be slowly oxidized by atmospheric radical species to give fluorinated acids that would then be deposited in remote areas by precipitation (Waterland and Dobbs 2007). Atmospheric measurements confirm modelling results, in that volatile precursors can reach the Arctic and Antarctic latitudes where they may be transformed to long-chain PFCAs (Shoeib et al. 2006; Jahnke et al. 2007; Stock et al. 2007; Young et al. 2007; Cai et al. 2012a; Kwok et al. 2013; Wang et al. 2015b; Casal et al. 2017; MacInnis et al. 2019; Pickard et al. 2018; Wong et al. 2018; Joerss et al. 2020). Details are provided in Table 7 of UNEP/POPS/POPRC.18/INF/12.

81. Rauert et al. (2018) reported on long-chain PFCAs and related compounds at three Arctic sites, including the Canadian Arctic, for the years 2009–2015 under the Global Atmospheric Passive Sampling (GAPS) Network. The

levels of FTOHs (8:2 and 10:2) ranged from <2 to 121 pg/m$^3$ and of $C_9$–$C_{14}$ PFCAs ranged from <0.03 to 8 pg/m$^3$, with $C_9$ having the highest concentration. Wong et al. (2018) also summarized air concentrations and trends of PFCAs and related compounds at the Canadian High Arctic station of Alert, and at Zeppelin and Andøya stations in the Norwegian Arctic from 2006 to 2014. At Alert, concentration ranges of FTOHs (8:2 and 10:2) and FTAs (8:2 and 10:2) were <0.015 to 21 pg/m$^3$ and <0.033 to 0.71 pg/m$^3$, respectively. 8:2 and 10:2 FTOHs showed slow increasing trends with doubling times of 5.0 and 7.0 years, respectively. $C_9$–$C_{14}$, $C_{16}$ and $C_{18}$ showed concentrations of <0.0063 to 0.77 pg/m$^3$ at Alert, with $C_9$ having the highest concentrations. At Zeppelin and Andøya, $C_9$–$C_{11}$ PFCAs showed concentrations of <0.079 to 11 pg/m$^3$, with $C_9$ and $C_{10}$ showing the highest concentrations. Higher levels of PFCAs at Andøya and Zeppelin compared to Alert may be due to the fact that Andøya and Zeppelin are located 100 m and 2 km away from the ocean, respectively, and may receive additional PFCAs from sea spray aerosol compared to Alert, which is 4 km from the water (Wong et al. 2018). Stock et al. (2007) measured $C_9$–$C_{12}$ PFCAs (0.2–19 ng/L) and their FTOH acid derivatives (i.e., 8:2 FTUCA and 10:2 FTUCA) in Resolute Lake, Char Lake, and Amituk Lake on Cornwallis Island (Nunavut, Canada). Wong et al. (2021) reported that atmospheric levels of 8:2 and 10:2 FTOH increased between 2006 and 2012, followed by decreasing trends from 2012 to 2017, where the half-lives were derived as 4.0 and 3.0 years for 8:2 and 10:2 FTOH, respectively. Bossi et al. (2016) measured atmospheric levels of FTOHs (8:2 and 10:2) at Villum Research Station in North Greenland between 2008 and 2013. Concentrations ranged from <0.45 to 22.4 and <0.20 to 9.68 pg/m$^3$, for 8:2 and 10:2 FTOH, respectively. By modelling air mass transport densities and comparing temporal trends in deposition with production changes of possible sources, Pickard et al. (2018) determined that the deposition of long-chain PFCAs on the Devon Ice Cap (Nunavut) was dominated by atmospheric formation from volatile precursors. Pickard et al. (2018) sampled a 15-m ice core representing 38 years of deposition (1977–2015) from the Devon Ice Cap and detected $C_9$–$C_{13}$ PFCAs with concentrations that ranged from 0.00321 to 0.751 ng/L.

82. Oceanic transport is another long-range environmental transport mechanism for long-chain PFCAs. As perfluoroalkyl acids, their salts and conjugate bases are highly water-soluble with no appreciable vapor pressure, their presence in the atmosphere may be via sorption to air particulate or their transfer from the surface ocean by sea spray aerosols (Webster and Ellis 2010; Reth et al. 2011; Johansson et al. 2019). Reth et al. (2011) determined that their surface-active properties result in enrichment on the "*surface of bursting bubbles*". Reth et al. (2011) examined the water-to-air transfer of $C_6$–$C_{14}$ PFCAs in a laboratory-scale sea spray simulator and found that the sequestration of the perfluoroalkyl acids, their salts and conjugate bases out of bulk water to the air-water surface increased exponentially with the length of the perfluorinated alkyl chain. Sha et al. (2022) observed a strong correlation of long-chain PFCAs in sea spray aerosol and sodium ion, which is a marine tracer. Measurements of long-chain PFCAs in oceans suggest that oceanic transport does play a role in the transport of long-chain PFCAs to remote regions (Ahrens et al. 2010; Benskin et al. 2012b; Cai et al. 2012a; Cai et al. 2012b; Zhao et al. 2012; Gonzalez-Gaya et al. 2014; Casal et al. 2017; Yeung et al. 2017; Li et al. 2018; Gonzalez-Gaya et al. 2019; Zhang et al. 2019). Additionally, $C_9$–$C_{12}$ PFCAs were measured in air samples at two Norwegian coastal sites, and were positively correlated with sodium ion concentrations, which suggests that sea spray aerosols are a source of PFCAs to the atmosphere in coastal areas (Sha et al. 2022).

83. Long-chain PFCAs (primarily $C_9$ to $C_{18}$ PFCAs), have been measured in Antarctic and Arctic environmental matrices, including snow, ice caps, lake water, air, lichen, lake sediment and seawater, and biota, such as penguin (e.g., *Pygoscelis papua*), polar bear (*Ursus maritimus*), Arctic fox (*Vulpes lagopus*), caribou and reindeer (*Rangifer tarandus*), Alaskan sea otter (*Enhydra lutris kenyoni*) and muskox (*Ovibos moschatus*) (Bossi et al. 2005; Letcher et al. 2018; Smithwick et al. 2005a; Smithwick et al. 2005b; Smithwick et al. 2006; Tao et al. 2006; Butt et al. 2007a; Butt et al. 2007b; Butt et al. 2008; Dietz et al. 2008; Hart et al. 2009; Katz et al. 2009; Schiavone et al. 2009; Bengtson Nash et al. 2010; Müller et al. 2011; Greaves et al. 2012, 2013; Llorca et al. 2012; Rotander et al. 2012; Aas et al. 2014; Bossi et al. 2015; Lescord et al. 2015; Routti et al. 2015; Munoz et al. 2017a; Routti et al. 2016; Routti et al. 2017; Tartu et al. 2017; Boisvert et al. 2019; Costantini et al. 2019; Roscales et al. 2019; Roos et al. 2021). Refer to Table 7 of UNEP/POPS/POPRC.18/INF/12 for concentrations in biota. In addition, $C_9$–$C_{13}$ PFCAs have been measured in humans (including Arctic Indigenous Peoples) 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; Byrne et al. 2017; Wielsoe et al. 2017; Caron-Beaudoin et al. 2019; Caron-Beaudoin et al. 2020; Hjermitslev et al. 2020; Aker et al. 2021; Garcia-Barrios et al. 2021; Dubeau et al. 2022).

84. No measurements of $C_{19}$–$C_{21}$ PFCAs in environmental matrices or biota from locations distant from sources have been identified in the literature. However, the high degree of chemical similarity for the series of acids has been described earlier and is suggestive of similar transport mechanisms. Long-range environmental transport modeling of the 14:2 to the 20:2 FTOHs was conducted using the OECD long-range transport potential (LRTP) Screening Tool, V2.2 (OECD 2009; Wegman et al. 2009). Empirical input parameters for this model are not available and were predicted using *in silico* tools. Partition coefficients $LogK_{AW}$, $LogK_{OA}$ and $LogK_{OW}$ were predicted by COSMOtherm (personal communication, emails from Glüge to ECCC, dated 30 May 2022 and 14 June 2022; unreferenced). Atmospheric half-lives were estimated using AOPWIN v1.92, part of EPISuite™ (EPI Suite c2000-2012) and half-lives for water and soil were predicted using CATALOGIC™ biodegradation model v5.14.1 (CATALOGIC 2021). The air half-lives selected represent those at 65°N latitude with a 12-hour day. All inputs are described in Table 8 of

UNEP/POPS/POPRC.18/INF/12. Assuming 100% release to air, the model predicts characteristic travel distances range from 6,297 km with a transfer efficiency of 0.23% for the 14:2 FTOH, declining to 5,960 km with a transfer efficiency of 2.52% for the 20:2 FTOH. These predictions represent atmospheric travel distances supportive of the potential for long-range environmental transport of related compounds which can transform to PFCAs up of $C_{21}$.

85. There is empirical evidence of the presence of long-chain PFCAs in locations distant from sources of long-chain PFCAs up to $C_{18}$. While analytical limitations present challenges in empirical determination of certain long-chain PFCAs (refer to section 1), there is evidence of use/release of compounds related to $C_{19}$–$C_{21}$ PFCAs, as indicated by the chain length distribution of FTOH substances identified in the patent literature. The release of compounds related to long-chain PFCAs during their production and use in many applications is described in section 2.1.2. The potential for these precursors to undergo long-range environmental transport is supported by monitoring data and predictions of long characteristic travel distances in the atmosphere. Therefore, long-chain PFCAs of up to 21 carbons may be expected to be present in remote environments.

## 2.3 Exposure

### 2.3.1 Environmental monitoring data

86. Long-chain PFCAs were detected globally, in all continents as well as in all environmental compartments, including biota, freshwater, saltwater, sediment, soil and rainwater, as can be seen in Figure 1, representing concentrations measured from 1980 to 2019. Long-chain PFCAs with chain lengths $C_9$ to $C_{14}$ were measured in Africa, Antarctica, Asia, Europe, North America, Oceania and South America. Only one paper from Europe reported measurements of $C_{19}$–$C_{21}$, which were measured in snow from a ski area in Sweden (Plassmann and Berger 2013). However, the authors claimed that "All reported concentrations for C13–23 PFCAs should be considered as semi-quantitative estimations due to the lack of isotopically mass-labeled and/or authentic native standards of these compounds". $C_{18}$ was detected in biota, freshwater, saltwater, sediment and soil. In biota, mean concentrations of $C_{18}$ were measured in Adelie penguin (*Pygoscelis adeliae*) eggs from Antarctica up to 0.5 ng/g, and in freshwater fish (*Culter erythropterus)* muscle from China at 0.03 ng/g (Schiavone et al. 2009; Liu et al. 2018c). Maximum concentrations of $C_{18}$ were also measured in the livers of ringed seal (*Pusa hispida*) and polar bear (*Ursus maritimus*) from Greenland at 0.5 and 0.4 ng/g, respectively (Boisvert et al. 2019). The list of references used to generate Figure 1 is provided in UNEP/POPS/POPRC.18/INF/12. Details on the reported environmental concentrations of long-chain PFCAs are available on the Stockholm Convention website[5].

87. A further breakdown of worldwide concentrations of long-chain PFCAs is illustrated in Figure 2 of UNEP/POPS/POPRC.18/INF/12, which shows the occurrence of long-chain PFCAs by chain length, as well as measurements in seas and oceans. The compartments in which long-chain PFCAs were measured in all continents were biota, freshwater, and soil. Asia, Europe and North America reported concentrations of long-chain PFCAs in all environmental compartments, including ice/snow, rainwater and sediment. Biota was the compartment with the most reported measurements worldwide (n=3,780), followed by freshwater. Long-chain PFCAs were also measured in saltwater in coastal regions of Asia, Europe, North America, South America, and in seas and oceans. Birds/eggs were the only biota that were sampled in all continents (refer to Figure 3 of UNEP/POPS/POPRC.18/INF/12). The highest concentration of long-chain PFCAs in biota was measured in European starling eggs in Canada (PFDA=720 ng/g, Gewurtz et al. 2018). Birds/eggs were the most studied, followed by fish, mammals, invertebrates, reptiles, and then plants. Some of the highest measured concentrations of long-chain PFCAs were reported in freshwater at an industrial park in Taiwan, Province of China, at US Air Force sites in North America, and downstream of industrial sites in France (Anderson et al. 2016; Bach et al. 2017; Liu et al. 2012).

[5] http://www.pops.int/TheConvention/POPsReviewCommittee/Meetings/POPRC18/Overview/tabid/9165/Default.aspx.

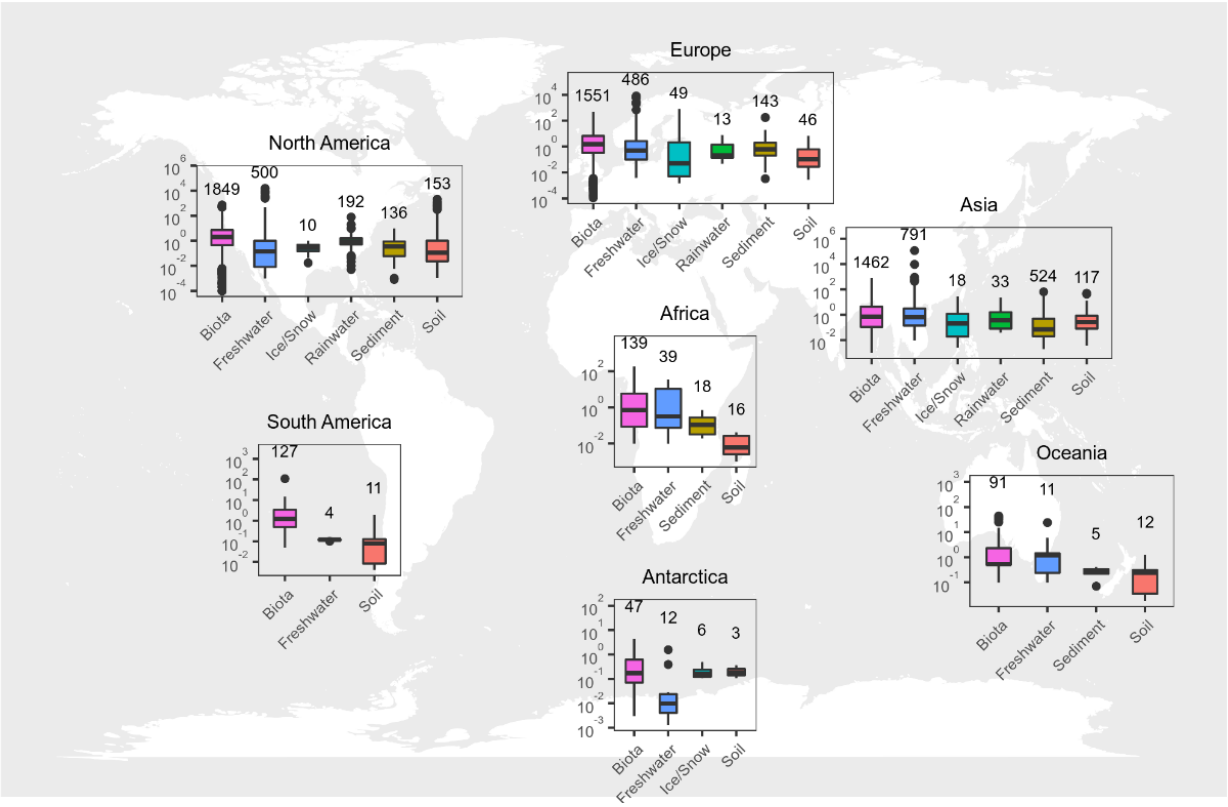


**Figure 1. Worldwide occurrence of long-chain PFCAs ($C_9$–$C_{21}$) in different environmental compartments. All measurements are in ng/L or ng/g, except for biota which are in ng/mL or ng/g.** Tukey box plots are interpreted as follows: the numbers above the bars indicate the number of data points and the lower and upper hinges (edges) of the box represent the first and third quantiles (Q1 and Q3), which are the 25th and 75th percentiles, respectively, while the black horizontal line within the box represents the second quantile, or the 50th percentile (median). The distance between the 25th and 75th percentile is called the interquartile range (IQR). The lower whisker represents the lowest data that are within the Q1–1.5 × IQR threshold, and the upper whisker represents the highest data that are within the Q3 + 1.5 × IQR threshold. Data exceeding these thresholds appear as circles. However, if the minimum and maximum are within these thresholds, they represent the lower and upper whiskers and no outliers are present.

88. Temporal trends for long-chain PFCAs (up to $C_{15}$ PFCA) have been reported in wildlife (including top predator species found in remote regions such as polar bears) (De Silva and Mabury 2004; Bossi et al. 2005; Letcher et al. 2015; Smithwick et al. 2005a; Smithwick et al. 2006; Butt et al. 2007a; Butt et al. 2007b; Verreault et al. 2007; Butt et al. 2008; Dietz et al. 2008; Tomy et al. 2009a; Holmström et al. 2010; O'Connell et al. 2010; Reiner et al. 2011; Rigét et al. 2013; Miller et al. 2015; Gewurtz et al. 2016; Lam et al. 2016; Dassuncao et al. 2017; Smythe et al. 2018; Falk et al. 2019; Gui et al. 2019; Muir et al. 2019; Wu et al. 2020; Soerensen and Faxneld 2020). From 1972 to 2002, mean doubling times for concentrations in polar bear livers from North American Arctic regions ranged from 5.8 to 9.1 years for $C_9$–$C_{11}$ PFCAs (Smithwick et al. 2006). From 1984 to 2006, 128 sub-adult (3–5 years old) Greenland polar bears showed annual increases for $C_9$ PFCA (6.1%), $C_{10}$ PFCA (4.3%), $C_{11}$ PFCA (5.9%), $C_{12}$ PFCA (52%), and $C_{13}$ PFCA (8.5%) (Dietz et al. 2008). From 1974 to 2007, $C_9$–$C_{15}$ PFCA doubling times ranged from 5.6 to 9.0 years in peregrine falcon (*Falco peregrinus*) eggs collected from Sweden (Holmström et al. 2010). Temporal trends for the harbor porpoise (*Phocoena phococena*) populations from the Baltic Sea and North Sea showed that $C_9$–$C_{13}$ PFCA concentrations increased significantly from 1991 to 2008 (Huber et al. 2012). Liver and serum mean concentrations of $C_9$ and $C_{10}$ PFCAs in the Baikal seal (*Pusa sibirica*) (Lake Baikal, Russia) collected in 2005 were 1.2 and 1.7-fold greater than liver and serum concentrations from 1992 (Ishibashi et al. 2008a). For the years 1980 to 2010, the ∑PFCAs (including $C_8$–$C_{12}$ PFCAs) in livers of male beluga whales (Nunavut, Canada) showed an annual increase of 1.8 ± 0.5 ng/g ww (Tomy et al. 2009). For the years 1986 to 2013, $C_9$–$C_{13}$ PFCA concentrations in the muscle tissue of North Atlantic male pilot whales (*Globicephala melas*) (caught in Faroe Islands) increased 2.8% to 8.3% per year (Dassuncao et al. 2017).

### 2.3.2 Human exposure

89. Humans may be exposed to long-chain PFCAs and their related products through food, drinking water, indoor/outdoor air, indoor dust and consumer products; however, the relative importance of each of these pathways for the general population remains unclear (ATSDR 2021). Meanwhile, evidence suggests that wildlife species consumption, particularly top predator marine species, is the main pathway of exposure to long-chain PFCAs for Arctic Indigenous Peoples (Caron-Beaudoin et al. 2020; Aker et al. 2021; AMAP 2021; Aker et al. 2022b).

90. The diet has been suggested as a principal exposure route for investigated long-chain PFCAs (Vestergren et al. 2012; Poothong et al. 2020). A number of studies have investigated the presence of long-chain PFCAs in market food items (see EFSA 2020 Annex A4; see section 2.3.2 and Table 11 of UNEP/POPS/POPRC.18/INF/12). However, overall, the detection frequencies of long-chain PFCAs in food items tend to be low. This is due in part to the methodological challenges associated with targeted analyses in varied and complex food matrices. When detected in foods, values for long-chain PFCAs are in the low pg/g to low ng/g range, with the highest concentrations being found in fish (or fish offal) and meats. Importantly, long-chain PFCAs are also being found in traditional food sources that are hunted and harvested from the wild (Ostertag et al. 2009; Byrne et al. 2017; Larter et al. 2017). This has the potential to lead to elevated levels in human populations, and in particular Arctic Indigenous Peoples, relying on these species for subsistence. For example, marine food consumption is likely a major contributor to long-chain PFCA exposure among Inuit in Nunavik, Canada (Aker et al. 2021) and the Yupik people of the northern Bering Sea in the Alaskan Arctic (Byrne et al. 2022). In addition, Ostertag et al. (2009) found that traditional foods contributed a higher percentage of PFASs to dietary exposure than market foods for Inuit in all age and gender groups.

91. Long-chain PFCAs have been infrequently measured and detected in tap water. This may be due in part to the fact that as the length of the perfluorinated chain increases, the water solubility of the PFCA molecule will likely decrease (Ellis et al. 2004a). Existing data for long-chain PFCAs in drinking water as measured at the tap are summarized in Table 10 in UNEP/POPS/POPRC.18/INF/12. $C_9$–$C_{14}$ PFCAs were recurrently detected in drinking water samples from Africa, Europe, Asia and the Americas in a study conducted during 2015 to 2016. $C_9$ PFCA was found in the highest concentrations with a maximum value of 4.5 ng/L (Kaboré et al. 2018). In the USA, data on $C_9$ PFCA was collected under the Third Unregulated Contaminant Monitoring Rule. The data showed that in 14 of the 4,920 public water systems (or 19 out of a total of 36,972 water samples), $C_9$ PFCA was detected above the minimum reporting level of 0.02 µg/L (US EPA 2017). Levels of $C_9$ PFCA in tap water were statistically significant predictors of plasma concentrations among individuals who drank more than 8 cups of tap water per day (Hu et al. 2019). In a Chinese study, women drinking bottled water had significantly lower (between 6% and 13%) blood concentrations of $C_9$–$C_{12}$ PFCA compared with those consuming mainly tap water (Zhou et al. 2019). Although the authors indicated that concentrations of PFASs have been found in previous studies to be higher in tap water as compared to bottled water, they did not measure long-chain PFCAs in tap or bottled water in their study. Drinking water may be an important source of exposure to long-chain PFCAs in areas contaminated with a point source of pollution. In a study of 29 public drinking water systems (PWS) in New Jersey, USA, $C_9$ PFCA was detected at two PWS at high concentrations of 72 ng/L and 96 ng/L. An industrial facility, where large quantities of $C_9$ PFCA were used as a processing aid in the manufacture of fluoropolymers, is located near the Delaware River about 2 miles from the site with the highest $C_9$ PFCA concentration and is a possible source of contamination at both of these two PWS (Post et al. 2013).

92. Analyses of major routes of exposure to long-chain PFCAs indicate that house dust ingestion and inhalation of indoor air can make important contributions to total intakes in the general population (Shoeib et al. 2011; Poothong et al. 2020). In a study of a Swedish population, the ingestion of house dust was estimated to account for >40% of the $C_9$, $C_{13}$ and $C_{14}$ PFCA uptake (Vestergren et al. 2012). Significant positive associations have been noted between levels of C9 PFCA in serum and levels in house dust or air (Makey et al. 2017; Poothong et al. 2020). Significant positive correlations were also noted between $C_9$ and $C_{11}$ PFCAs in serum samples and intakes of their precursor compounds (8:2 FTOH and 10:2 FTOH) from indoor air (Makey et al. 2017; Poothong et al. 2020). Studies have measured $C_9$–$C_{15}$ PFCAs in indoor air and/or dust samples from several countries at various locations, including private homes, hotels, office buildings, vehicles and daycares (see Table 9 in UNEP/POPS/POPRC.18/INF/12).

93. Maternal transfer through cord blood and breastfeeding are sources of long-chain PFCAs for the fetus and for nursing infants/children. Long-chain PFCAs have been detected in the placenta, which is of concern as these compounds could potentially influence the function of the placenta, and in turn may have negative effects on the development of the fetus (Kaiser et al. 2021). Long-chain PFCAs have also been detected in umbilical cord blood (Apelberg et al. 2007a, 2007b; Manzano-Salgado et al. 2015; Morello-Frosch et al. 2016), and studies show levels correlate with maternal blood/serum levels, indicating that these substances can cross the placental barrier resulting in *in utero* exposure (Manzano-Salgado et al. 2015; Yang et al. 2016). Further, long-chain PFCAs may cross the placental barrier more efficiently than compounds with intermediate chain length (Appel et al. 2022). $C_9$ PFCA has been the most frequently detected long-chain PFCA in umbilical cord blood/serum with concentrations as high as 2.24 ng/mL in cord serum (Manzano-Salgado et al. 2015). Relatively lower detection frequencies were reported for $C_{10}$–$C_{12}$ PFCAs with a maximum concentration of 1.9 ng/mL (Apelberg et al. 2007a, 2007b; Morello-Frosch et al. 2016). Studies from Europe, Asia and North America have detected $C_9$–$C_{18}$ PFCAs in human milk with values typically ranging from below the limit of detection to low pg/mL (see Table 12 of UNEP/POPS/POPRC.18/INF/12). Concentrations of a sum of seven PFASs (including $C_9$ PFCA) have been found to be significantly higher in the milk of first-time mothers as compared to multiparous women, which could be indicative of maternal transfer to the children either through breastfeeding or transfer to the fetus during pregnancy (Rawn et al. 2022). In addition to being an exposure source for infants, breastfeeding is also an elimination route for mothers. A study of Norwegian women showed that parous women had 62% lower $C_9$ PFCA levels as compared to nulliparous women and that the duration of breastfeeding was associated with decreased levels of $C_9$ PFCA in maternal serum (Brantsaeter et al. 2013). In

another study, each month of breastfeeding was associated with a 2% decline in $C_9$ PFCA levels in maternal serum (Mondal et al. 2014).

94. Long-chain PFCAs have been detected globally in humans. Plasma and serum concentrations reflect an integrated exposure to long-chain PFCAs regardless of the source (Sexton et al. 2004). Due in part to analytical challenges (see paragraph 13), much of the biomonitoring data is limited to the measurement of $C_9$–$C_{14}$ PFCAs. The $C_9$ PFCA typically has the highest detection frequencies, which are often close to 100%. Some studies have also measured and detected PFCAs up to $C_{18}$, however detection frequencies are low (e.g., less than 2% for $C_{14}$–$C_{16}$, $C_{18}$, Nystrom et al. 2022). Data from larger scale biomonitoring studies are available (see see Table 13 of UNEP/POPS/POPRC.18/INF/12 and HBM4EU 2022). The results from 29 biomonitoring studies in the EU showed $C_9$–$C_{11}$ PFCA serum concentrations to be in the high pg/mL to low ng/mL range, whereas $C_{12}$–$C_{14}$ PFCAs were relatively lower in the pg/mL range (ECHA 2018a). A similar range in values was noted for other larger scale biomonitoring studies in Asia, Australia and North America (see Table 13 of UNEP/POPS/POPRC.18/INF/12). In cycle 2 (2009–2011), cycle 5 (2016–2017) and cycle 6 (2018–2019) of the Canadian Health Measures Survey (CHMS), geometric mean plasma concentrations of $C_9$–$C_{11}$ PFCAs ranged from 0.12 to 0.82 µg/L in participants aged 12-79 (Health Canada 2021b). Of note, concentrations of long-chain PFCAs in the serum or plasma of Indigenous Peoples, including First Nation Anishinabe youth ($C_9$), Nunavik adults, as well as pregnant Inuit women in Nunavik ($C_9$–$C_{11}$), a Gwich'in community (Yukon, Canada) ($C_9$) and six Dene First Nation communities (Northwest Territories, Canada) ($C_9$) were higher than CHMS values for comparable ages, sex, and time periods (Caron-Beaudoin et al. 2019; Caron-Beaudoin et al. 2020; Aker et al. 2021; AMAP 2021; Garcia-Barrios et al. 2021; Dubeau et al. 2022). Specifically, children and youth aged 3 to 5, 6 to 11 and 12 to 19 years old from Anishinabe communities had $C_9$ PFCA geometric mean concentrations of 3.80 µg/L, 9.44 µg/L and 3.01 µg/L, respectively (Dubeau et al. 2022). These values are 8, 21 and 7 times higher, respectively, than CHMS cycle 5 values for the same age groups. Concentrations of $C_9$ and $C_{10}$ PFCA in pregnant women in Nunavik were 6.3 and 3.3 times higher, respectively, than women of a similar age in the CHMS (Caron-Beaudoin et al. 2020). Adults in Nunavik were found to have 4 to 7 times higher levels of $C_9$ to $C_{11}$ compared to adults in the CHMS (Aker et al. 2021). In addition, average $C_9$ PFCA concentrations in adults were found to be 1.8 and 2.8 times higher in Gwich'in and Dene communities, respectively, when compared to plasma concentrations of $C_9$ PFCA in adults in the CHMS. $C_9$–$C_{13}$ PFCAs have also been found in serum samples from Inuit women and men from Greenland at concentrations ranging from 0.031 to 38.6 ng/mL (µg/L) (Long et al. 2015; Wielsoe et al. 2017; Hjermitslev et al. 2020; Wielsoe et al. 2022). Results from these communities represent very different, but all remote areas, across Canada and elsewhere, and highlight the significance of long-range environmental transport of PFASs to northern communities. There is also evidence of an association between serum or plasma concentrations of certain long-chain PFCAs in Indigenous populations and biomarkers for the consumption of marine wildlife species (n-3/n-6 fatty acid ration), particularly top predator marine species, including marine mammals, fish and seabirds (Long et al. 2015; Caron-Beaudoin et al. 2020; Hjermitslev et al. 2020; Aker et al. 2021; Wielsoe et al. 2022). In these studies, serum concentrations of certain long-chain PFCAs have also been observed to be highest in the older age groups, possibly due to a number of factors, including continuous exposure since the 1950s, bioaccumulation, relatively long biological half-lives and renal resorption processes (Ji et al. 2012). In some cases, higher concentrations have been observed in older males than females, possibly due to the loss of PFASs through menstruation and the transfer of these pollutants from mothers to offspring via parturition and lactation (Ji et al. 2012; Seo et al. 2018). In Inuit populations, differences in PFAS concentrations between age groups and genders may also be reflective of the different types of wildlife species (or parts of animals) consumed across age and gender groups (Aker et al. 2021).

95. Occupational exposure can lead to higher serum levels of long-chain PFCAs. In a Swedish study of eight ski wax technicians, blood levels of $C_9$–$C_{11}$ PFCA were all higher in technicians as compared to representative populations from Sweden, China, and North America; $C_9$ PFCA was 15–270 times higher in the serum of ski wax technicians (Nilsson et al. 2010). Further, a significant correlation was found between the number of years in the ski wax profession and serum levels of $C_9$–$C_{13}$ PFCAs (Freberg et al. 2010; Nilsson et al. 2010). In a study of 86 female firefighters in the USA in 2014-2015, firefighters had 1.26 times higher geometric mean concentrations of $C_9$ PFCA (95% confidence interval (CI)=1.01, 1.58) and 1.83 times higher mean concentrations of $C_{11}$ PFCA (95% CI=0.97, 3.45) as compared to office workers. Firefighters that worked at the airport had $C_9$ PFCA levels that were two times higher compared to firefighters assigned to other stations (Trowbridge et al. 2020). Two other US studies (each with more than 100 firefighters) also found higher levels of certain long-chain PFCAs in firefighters compared to the general population as measured in the National Health and Nutrition Examination Survey (NHANES). Graber et al. (2021) found $C_9$ and $C_{10}$ PFCAs higher in volunteer firefighters whereas Dobraca et al. (2015) found elevated levels of $C_{10}$ PFCA in firefighters in California. In contrast to these findings, a study of 38 firefighters in the USA in 2009 noted that levels of $C_9$ and $C_{11}$ PFCA were significantly lower than the NHANES measurements (Khalil et al. 2020). In a study of eight male firefighters handling firefighting foam in Finland, serum levels of $C_9$ PFCA increased after three consecutive training sessions compared to the firefighters' individual baseline concentrations in samples taken two weeks before exposure. Concentrations were 0.43–6.69 ng/mL in the firefighters as compared to 0.35–1.66 ng/mL for the general Nordic population (Laitinen et al. 2014).

96. Although serum concentrations of other PFASs such as PFOA and PFOS generally appear to be declining

after the 2000s (when their production was phased-out or restricted nationally and internationally), time trends for the long-chain PFCAs have been inconsistent. For example, levels of $C_9$ and $C_{10}$ PFCAs increased from 1986 to 2007 in a Norwegian study, whereas levels of $C_{11}$ PFCA were stable (Berg et al. 2021). In a study of first time mothers in Sweden, levels of $C_9$ PFCA increased from 1996 to 2008, but then declined until 2019. An analysis of pregnant women in Vienna, Austria, also found levels of $C_9$ PFCA to decline from 2010/2012 to 2017/2019 (Kaiser 2021). Meanwhile, $C_{11}$ and $C_{13}$ PFCAs showed increasing temporal trends during the study period 1996-2019 (Gyllenhammar et al. 2020). Levels of $C_9$ and $C_{10}$ PFCAs in a cohort of Swedish children also demonstrated downward trends from 2008 to 2019 (Hedvall Kallerman et al. 2020). Conversely, a study of a cohort of senior adults reported an increase in $C_9$–$C_{11}$ PFCAs during 2001–2014 (Stubleski et al. 2006). For roughly the same period (2003–2014), data from the US NHANES study showed that levels of $C_9$ and $C_{10}$ PFCAs decreased (CDC 2018). 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 $C_9$–$C_{10}$ PFCA (Yeung et al. 2013) and new information used to extend the dataset showed a decline in $C_9$ PFCA from 2006 to 2019 (Göckener et al. 2020). Levels of $C_9$ and $C_{10}$ PFCAs declined from 2009 to 2019 in the general Canadian population while the detection frequency of $C_{11}$ PFCA remained stable between 2016 and 2019 (Health Canada 2021a,b). However, during the same time period, concentrations of $C_9$, $C_{10}$ and $C_{11}$ PFCA in pregnant women in Nunavik, Canada, increased by 19%, 13% and 21%, respectively (Caron-Beaudoin et al. 2020), with a chemical profile suggesting that these increasing levels of long-chain PFCAs result from the environmental transformation of FTOHs that are highly volatile and increasingly detected in the Arctic (Muir et al. 2019). A systematic review examining the phase out of PFASs worldwide found that, between roughly 1980 and 2013, $C_9$–$C_{14}$ PFCAs in humans were generally increasing, with no evidence of significantly declining trends in any global region (Land et al. 2018).

## 2.4 Hazard assessment for endpoints of concern

97. PFASs, in general, have been shown to activate the peroxisome proliferating receptors (PPARs) in multiple species (Ishibashi et al. 2008b; Hickey et al. 2009; Ishibashi et al. 2011; Kurtz et al. 2019; Routti et al. 2019a). PPAR-α plays a critical physiological role as a lipid sensor and a regulator of lipid metabolism. Within the cytochrome P450 enzymes, the CYP4A family members are integral to several metabolic functions, including detoxifying xenobiotic compounds. PPARs regulate CYP4A expression, which in turn acts as a modulator with other PPAR-α target genes involved in lipid homeostasis. Activation of the PPAR-α-CYP4A pathway could result in altered liver function, developmental toxicity, immunotoxicity, and feeding disorders (Kurtz et al. 2019; Kubota et al. 2011). $C_9$ and $C_{10}$ PFCAs have been shown to induce hepatic CYP4A-like proteins via PPAR-α signaling in Lake Baikal seals (Ishibashi et al. 2008b). PPAR-α mRNA expression and CYP4A protein expression in kidneys of cetaceans have also been positively correlated with $C_{10}$, $C_{11}$, $C_{13}$ and $C_{14}$ PFCAs (Kurtz et al. 2019).

98. In laboratory toxicity studies assessing aquatic organism endpoints such as growth, reproduction, and lethality, long-chain PFCAs (up to $C_{14}$ PFCA) show low to moderate toxicity depending on species sensitivity. Species tested include pelagic cladoceran (*Daphnia magna)*, benthic cladoceran (*Chydorus sphaericus*), rainbow trout, medaka (*Oryzias latipes*), green algae (*Chlorella vulgaris*), diatom (*Skeletonema marinoi*), blue-green algae (*Geitlerinema amphibium*), nematode (*Caenorhabditis elegans*), algae (*Scenedesmus obliquus*) and African clawed frog (*Xenopus laevis*) (Ding et al. 2012, Benninghoff et al. 2011, Ishibashi et al. 2008c, Hoke et al. 2012, Latala et al. 2009, Tominaga et al. 2004, Liu et al. 2008a, Kim et al. 2013). For example, for $C_9$–$C_{12}$ PFCAs, the 48h median effective concentration (EC50) values for immobilization for a pelagic cladoceran (*Daphnia magna)* and a benthic cladoceran (*Chydorus sphaericus*) ranged from 12.4 to 181 mg/L with the benthic cladoceran showing greater sensitivity (Ding et al. 2012). Refer to section 2.4 of UNEP/POPS/POPRC.18/INF/12 for detailed results.

99. In additional laboratory toxicity studies assessing the exposure to long-chain PFCAs (up to $C_{13}$ PFCA), endpoints where effects were observed also included developmental effects, behavioural effects, hepatotoxicity, immunotoxicity, neurotoxicity, genotoxicity, changes in gene expression, chemosensitivity and altered thyroid function. Species tested include common cormorant (*Phalacrocorax carbo*), zebrafish, rainbow trout, African clawed frog, rare minnow (*Gobiocypris rarus*), mussels (*Pema viridis*; *Mytilus californianus*) and chickens (*Gallus gallus*) (Matsubara et al. 2006; Stevenson et al. 2006; Liu et al. 2008a; Liu et al. 2008b; O'Brien et al. 2009; Wei et al. 2009; Yeung et al. 2009; Nobels et al. 2010; Tichy et al. 2010; Benninghoff et al. 2011; Liu et al. 2011b; Vongphachan et al. 2011; Benninghoff et al. 2012; O'Brien et al. 2013; Zhang et al. 2012a; Zhang et al. 2012b; Zheng et al. 2012; Kim et al. 2013; Ulhaq et al. 2013a; Ulhaq et al. 2013b; Jo et al. 2014; Liu et al. 2014a; Liu et al. 2014b; Yang et al. 2014; Liu et al. 2015; Lu et al. 2015; Gorrochategui et al. 2016; Jantzen et al. 2016a,b; Zhang et al. 2016; Guo et al. 2018; Zhang et al. 2018; Menger et al. 2020; Liu and Gin 2018). For example, embryo-larval zebrafish exposed to $C_9$ PFCA at 0.93 mg/L resulted in altered responses in locomotion and gene expression as well as biochemical and behavioural changes in young adult zebrafish exposed embryonically (Jantzen et al. 2016a; Jantzen et al. 2016b). Additionally, $C_9$ and $C_{10}$ PFCAs inhibited the p-glycoprotein in the marine mussel with average median inhibitory concentration (IC50) values of 2.2 mg/L and 3.7 mg/L, respectively, indicating that $C_9$ and $C_{10}$ PFCAs are chemo sensitizers (Stevenson et al. 2006). Refer to section 2.4 of UNEP/POPS/POPRC.18/INF/12 for detailed results.

100. For the field-based wildlife studies, it is difficult to uniquely distinguish effects from exposure to long-chain

PFCAs, as exposures from mixtures of other PFASs (e.g., PFOS, PFOA) and other contaminants cannot be excluded (Knudsen et al. 2007; Letcher et al. 2010; Bourgeon et al. 2017; Liu et al. 2018a; Routti et al. 2019b). PFASs (including related compounds) are also often summed as a group and statistically correlated with the effect observed. Thus, mixtures can be confounding when determining whether a singular substance or group of substances is affecting the health and condition of the wildlife species under investigation. 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, several field-based wildlife studies 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 (Houde et al. 2006b; Erikstad et al. 2009; Peng et al. 2010; Miljeteig et al. 2012; Houde et al. 2013; Aas et al. 2014; Ask 2015; Bustnes et al. 2015; Elliott et al. 2019; Persson and Magnusson 2015; Eggers Pedersen et al. 2016; Blévin et al. 2017; Soloff et al. 2017; Tartu et al. 2017; Bangma et al. 2018; Grønnestad et al. 2018; Lopez-Antia et al. 2019; Briels et al. 2019; Costantini et al. 2019; Groffen et al. 2019; Kurtz et al. 2019; Lasters et al. 2019; Blévin et al. 2020; Guillette et al. 2020; Sun et al. 2020, 2021; Choy et al. 2022). Refer to section 2.4 of UNEP/POPS/POPRC.18/INF/12 for detailed results. Additionally, Sebastiano et al. (2020) studied the influence of single PFAS congeners, including $C_9$–$C_{14}$, on telomer length and dynamics, and found that the effect of PFAS exposure may be tied to specific PFAS congeners instead of the total PFAS concentration.

101. Current environmental monitoring data indicate that concentrations for long-chain PFCAs are generally at the nanogram level (ng/g or ng/L) in biota. These concentrations are below the available tested toxicity thresholds, which are generally at the microgram (µg/g) or milligram level (mg/L) with varying sensitivity across species. 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. There are unique concerns about highly persistent and bioaccumulative substances such as long-chain PFCAs. Long-chain PFCAs are acknowledged to have the potential to cause serious and irreversible impacts to wildlife populations in the long-term due to their persistent nature (MacLeod et al. 2014; Ahrens and Bundschuh 2014). Long-chain PFCAs are persistent and remain in the environment for a very long time, which increases their probability, magnitude and duration of exposure to wildlife. Maternal transfer of long-chain PFCAs has also been demonstrated in wildlife (Houde et al. 2006b; Taylor et al. 2021; Grønnestad et al. 2017). Jouanneau et al. (2022) investigated maternal transfer of long-chain PFCAs ($C_9$–$C_{16}$) in black-legged kittiwakes (*Rissa tridactyla*) in Norway, and found that the longest chain PFCAs were preferentially transferred to eggs. Long-chain PFCAs are also subject to long-range environmental transport, which can also result in regional or global contamination. As such, releases of long-chain PFCAs can lead to elevated concentrations in organisms over wide areas. Long-chain PFCAs may also biomagnify through the food chain, resulting in increased internal concentrations for top predator species. Several different long-chain PFCAs may be present simultaneously in the tissues of organisms, increasing the likelihood and potential severity of harm compared to looking at a single long-chain PFCA. Increasing temporal concentration trends (i.e., doubling times) in wildlife (as discussed earlier in section 2.3.1), including top predator species, suggest that long-chain PFCAs can approach or exceed toxicity thresholds resulting in harm for wildlife populations in the future.

102. A number of mammalian toxicity studies in animal models are available for assessing the adverse effects of long-chain PFCAs. The most commonly observed effects in animal models include effects on liver, the immune system, on reproductive and developmental endpoints and on the thyroid. Further details on the studies investigating these endpoints are located in section 2.4 of UNEP/POPS/POPRC.18/INF/12. Other effects reported to a lesser extent in animal models include renal, cardiovascular and neurological effects, metabolic disruption, body and organ weight changes, and mortality.

103. *In vivo* data in rodents provide evidence of hepatotoxicity after acute, short-term and/or subchronic exposure to $C_9$–$C_{12}$, $C_{14}$, $C_{16}$ and $C_{18}$ PFCAs. Effects include liver weight alterations, hepatocellular hypertrophy, histopathological changes (including degeneration and necrosis), alterations in liver gene expression, and clinical chemistry changes (Zhang et al. 2008; Ding et al. 2009; Mertens et al. 2010; Fang et al. 2012a, 2012b, 2012c; Hirata-Koizumi et al. 2012; Takahashi et al. 2014; Fang et al. 2015; Hirata-Koizumi et al. 2015; Kato et al. 2015; Wang et al. 2015a; Frawley et al. 2018; NTP 2019; Costello et al. 2022). For example, hepatocyte necrosis and hepatomegaly were observed in rats treated with 0.5 mg/kg bw/d of $C_{10}$ PFCA for 28 days (Frawley et al. 2018).

104. Effects on the immune system induced by exposure to $C_9$–$C_{11}$ PFCAs are reported in rodents after acute, short-term and/or subchronic oral exposure (gavage or drinking water), or after intraperitoneal administration. The effects observed include splenic and thymic atrophy, reduced phagocytic function of macrophages, altered balance of immune cells, and inhibition of cytokine production (Fang et al. 2008, 2009, 2010; Rockwell et al. 2013; Bodin et al. 2016; Rockwell et al. 2017; Frawley et al. 2018; NTP 2019). For example, $C_9$-induced apoptosis was observed in rat splenocytes and the production of pro-inflammatory and anti-inflammatory cytokines was significantly increased and decreased respectively at exposures of 5 mg/kg bw/d for 14 days (Fang et al. 2010).

105. Several long-chain PFCAs ($C_9$, $C_{11}$, $C_{12}$, $C_{14}$, $C_{16}$ and $C_{18}$) have been shown to induce reproductive and developmental toxicity in rodents after short-term and/or subchronic oral exposure (gavage). Effects observed included reproductive organ weight alteration, testicular toxicity, and altered reproductive hormone levels.

Developmental effects included postnatal mortality, reduced body weight, and developmental delays (Harris and Birnbaum 1989; Shi et al. 2007; Feng et al. 2009; Lau et al. 2009; Shi et al. 2009; Wolf et al. 2010; Hirata-Koizumi et al. 2012; Rogers et al. 2014; Takahashi et al. 2014; Das et al. 2015; Hirata-Koizumi et al. 2015; Kato et al. 2015; Singh and Singh 2018; Chen et al. 2019; NTP 2019; Singh and Singh 2019a, 2019b, 2019c). For example, in rats exposed to 2.5 mg/kg bw/d of $C_{12}$ PFCA, only 1 of the 12 dams delivered live pups and decreases in pup body weight gain were noted (Kato et al. 2015). For repeated dose toxicity study using rats exposed to $C_{18}$ PFCA, no observed adverse effect level (NOAEL) was 40 mg/kg/day for hepatotoxicity (Hirata-Koizumi et al. 2012).

106. Short-term studies performed in rats and mice provide evidence that oral (gavage) exposure to $C_9$, $C_{10}$ and $C_{14}$ PFCAs induce altered thyroid weight and histopathological alterations in the thyroid gland as well as changes to thyroid hormone levels (Harris et al. 1989; Fang et al. 2009; Hirata-Koizumi et al. 2015; NTP 2019). For example, rats exposed up to 25 mg/kg bw/d of $C_9$ or $C_{10}$ PFCA for 28 days experienced altered thyroid weight and altered thyroid hormone levels (NTP 2019).

107. Over 200 epidemiological studies have investigated associations between exposure to long-chain PFCAs and various disease incidences or markers of effects. Although some studies have reported null, equivocal or even negative associations with exposure (i.e., protective effects), many studies have established positive associations between exposure to long-chain PFCAs and various health related outcomes. While there are limitations to epidemiological studies, including the fact that the associations identified may not be causal in nature, the large numbers of studies showing correlations, and then additionally, when combined with toxicological data from experimental animals, the findings are more compelling and the overall evidence is strengthened. Endpoints commonly investigated in epidemiological studies include effects on the liver, the immune system, cardiometabolic function, reproduction and development and effects on the thyroid.

108. Several epidemiological studies evaluated hepatic endpoints and noted associations between exposure to $C_9$–$C_{14}$ PFCAs and increased levels of serum lipid levels and changes to clinical biomarkers of liver function (e.g., EFSA 2020; ATSDR 202; Blomberg et al. 2021; Costello et al. 2022). With regards to the immune system, epidemiological studies noted positive associations between exposure to $C_9$–$C_{12}$, $C_{14}$ PFCAs and the incidence of infectious diseases, alterations of immune marker levels, asthma and allergic diseases (e.g., Dong et al. 2013; Zhu et al. 2016; Chen et al. 2018b; Impinen et al. 2018). The strongest evidence of immunotoxicity comes from investigations into antibody response to vaccines (Grandjean et al. 2012, 2017; Granum et al. 2013, Kielsen et al. 2016; Timmerman et al. 2020, 2022). Several studies evaluated possible associations between exposure to $C_9$–$C_{14}$ PFCAs and reproductive outcomes in adolescents/adults. Associations were noted with altered hormone levels and issues related to menstruation, menopause and female reproductive health (e.g., Taylor 2014; Jensen et al. 2015; Tsai et al. 2015; Ding et al. 2020). In terms of developmental endpoints, associations were also observed with birth size, bone development, reproductive outcomes, neurobehavioural and neuropsychological endpoints (e.g., Lind et al. 2016; Kwon et al. 2016; Buck Louis et al. 2018; Vuong et al. 2018a; 2018b). Effects on the thyroid were investigated in relation to $C_9$–$C_{14}$ PFCAs and associations were noted with outcomes including the incidence of congenital hypothyroidism and altered levels of thyroid hormones, thyroglobulin, and thyroid peroxidase antibodies in children and adults (e.g., Kim et al. 2016; Ballesteros et al. 2017; Aimuzi et al. 2019; Caron-Beaudoin et al. 2019; Itoh et al. 2019). Further details on some of the epidemiological studies investigating these endpoints are located in section 2.4 of UNEP/POPS/POPRC.18/INF/12. Comprehensive reviews of the data have concluded that the most convincing evidence exists for associations between exposure to $C_9$–$C_{10}$ PFCAs and increased serum lipid levels (ATSDR 2021; EFSA 2020), as well as for associations between $C_{10}$ PFCA and immune effects (decreased antibody responses to vaccines) (ATSDR 2021; Kirk et al. 2018).

109. Long-chain PFCAs are commonly detected together with a range of other PFASs in human blood samples. Although little is known about the mixture toxicity of long-chain PFCAs in serum, some studies have investigated synthetic mixtures in an attempt to describe mixture effects. In a cell viability study, human liver cells were exposed to mixtures of nine or eleven individual PFASs, including $C_9$–$C_{13}$ PFCAs. Mixtures of nine PFASs (including $C_9$–$C_{11}$ PFCAs) that had the same non-monotonic J-shaped response curves (i.e., response decreases and then increases with increasing concentration), showed synergistic effects. However, mixtures of eleven PFASs (including $C_9$–$C_{13}$ PFCAs), which included those with both J-shaped and classical S-shaped response curves (i.e., response increases with increasing concentration) showed only partial addition effects (Hu et al. 2014). Synergistic interactions were also observed in cytotoxicity studies in which human liver cells were exposed to binary, ternary, and multi-component combinations of PFASs (including $C_9$ and $C_{10}$ PFCAs). Binary mixtures of $C_9$ and $C_{10}$ PFCAs in particular demonstrated strong synergism under inhibitory concentrations ranging from 10 to 90% (Ojo et al. 2020). Synergistic effects were also observed when Chinese hamster ovary cells were exposed to a mixture of five PFASs, including $C_9$ and $C_{10}$ PFCA, and tested for anti-androgen activity (Kjeldsen and Bonefeld-Jørgensen 2013). Therefore, given the vast number and ubiquity of PFASs, it is reasonable to assume that cumulative effects could occur following exposure to PFASs.

110. Data on the adverse effects of long-chain PFCAs is generally lacking for PFCAs with longer chain lengths (i.e., $C_{15}$, $C_{17}$ and $C_{19}$–$C_{21}$). This is due in part to analytical difficulties in measuring longer chain PFCAs, as discussed earlier. However, predicting the hazard properties of chemicals in the absence of data is a well-established practice

and read-across can be used to fill data gaps. Long-chain PFCAs have a high degree of chemical similarity for the series of acids, and existing data show effects on common endpoints. Data from homologues, including the extensively studied $C_8$ PFCA (PFOA), which has been listed under Annex A of the Stockholm Convention, indicates the potential for adverse effects. Furthermore, several studies show that the activity/toxicity of PFCAs can increase with chain length. For example, in vivo studies in aquatic species and mammals indicate that the activity/toxicity of PFCAs tend to increase with chain length up to $C_{12}$ (Kudo et al. 2006; Ding et al. 2012; Liu et al. 2014a; Das et al. 2015; NTP 2019). In vitro data in mammalian cells indicate a similar trend of increasing activity/toxicity with increasing chain length up to $C_{18}$ (e.g., Buhrke et al. 2013; Gorrochategui et al. 2014; Rand et al. 2014; Yang et al. 2017; Lee and Kim 2018; Ojo et al. 2020; Reardon et al. 2021). Therefore, despite the lack of data for some substances, based on read-across, it is anticipated that all long-chain PFCAs could have similar adverse effects on human health and the environment, although the toxic potency may vary with chain length.

# 3. Synthesis of information

111. Long-chain PFCAs, their salts and related compounds are used, or may have been used, in a range of applications, including in: industrial applications; electronics; medical devices; printing inks and photographic materials; automotive care products; building and construction materials; cookware and food-contact materials; fire-fighting foams; ski waxes; and various other consumer products. In addition, long-chain PFCAs and their related compounds may be unintentionally produced during the manufacturing of PFASs.

112. Information in the public domain on the historic and current production of long-chain PFCAs, their salts and related compounds is limited, and estimated volumes vary between authors. Estimates of the global production of the ammonium salt of $C_9$ PFCA have been reported to be in the range of 15 to 100 tonnes/year for the period between 1975 and 2004. The usage of APFN in Japan, Western Europe and the USA has been estimated to range between 8 and 107 tonnes per year for the years 1975 to 2015. Worldwide production of fluorotelomers (compounds related to long-chain PFCAs) was estimated at approximately 9100 tonnes in 2006. Another source estimated or projected the global annual production of fluorotelomer-based products to range between 2,500 and 20,000 tonnes for the years 1961 to 2004, and at 45,000 tonnes/year for the period 2005 to 2030. A geographical shift of industrial sources of PFCAs, as a result of the relocation of PFCA, fluoropolymer and other PFAS product production from the USA, Western Europe and Japan to emerging Asian economies, especially China, has been reported in the literature.

113. Long-chain PFCAs are released to the environment from direct (i.e., production of PFCAs and during the life cycle of products containing long-chain PFCAs) and indirect sources (i.e., when compounds related to the long-chain PFCAs emitted to the environment have transformed to long-chain PFCAs). Release of long-chain PFCAs, their salts and related compounds to the environment is documented by their detection in: environmental matrices collected in proximity to production facilities and industrial areas; sites impacted by fire-fighting foam; wastewater, sludge and leachate from waste treatment facilities; agricultural sites with a history of application of biosolids; snow and soil from skiing areas; and indoor environments.

114. Long-chain PFCAs are extremely persistent in the environment. The carbon-fluorine bond is one of the strongest covalent bonds, and is extremely stable and generally resistant to degradation by acids, bases, oxidants, reductants, photolytic processes, microbes and metabolic processes. The strong carbon-fluorine bond and high density of electron-rich repellent fluorine atoms protect the carbon backbone and result in inertness to both heat and chemical reagents. A number of studies demonstrate that long-chain PFCAs do not degrade under environmentally relevant conditions. For example, $C_9$ PFCA did not biodegrade under the OECD 301F method. Other studies demonstrate some degradation of long-chain PFCAs, but not under environmentally relevant conditions.

115. Certain data gaps were noted for some members of the homologous series of long-chain PFCAs covered in this risk profile. This may be the consequence of analytical challenges (including lack of chemical standards) in measuring long-chain PFCAs at the upper end of the range (i.e., for $C_{15}$–$C_{21}$ PFCAs). To address data limitations, a read-across approach based on a high degree of chemical similarity, has been implemented in this document based on guidance on grouping of chemicals from the OECD (2014). While introducing some uncertainties, this is a practical and efficient approach to address long-chain PFCAs.

116. Some measured BCFs and BAFs greater than 5000 have been reported for $C_9$–$C_{14}$ PFCAs in freshwater and marine aquatic organisms. TMFs and BMFs greater than 1 have been reported for $C_9$–$C_{16}$ PFCAs in studies that focused on top predator species, providing evidence that long-chain PFCAs biomagnify in air-breathing organisms. PFCAs up to $C_{18}$ have been measured in top predator species, such as polar bears, herring gulls and peregrine falcons. In humans, long-chain PFCAs accumulate in the blood and well perfused tissues, and are eliminated very slowly from the body (i.e., estimated mean half-lives for $C_9$ PFCA range from 2.5 to 4.3 years, and mean half-lives for both $C_{10}$ and $C_{11}$ PFCA range from 4.5 to 12 years). Empirical information demonstrates the bioaccumulative nature of long-chain PFCAs up to and including $C_{16}$. Other information presented, including measured polar bear BMFs exceeding 1 for $C_9$–$C_{18}$, predicted BCFs for $C_{17}$–$C_{21}$ which exceed 5000, are supportive of the high bioaccumulation potential. It is reasonable to expect that long-chain PFCAs of up to 21 carbons have the potential to bioaccumulate in aquatic and terrestrial organisms, and in humans.

117. Global modelling indicates that long-chain PFCAs, their salts and/or related compounds have the potential to be transported over long distances. In addition, $C_9$–$C_{18}$ PFCAs have been measured in environmental matrices, biota and human populations from remote sites, such as the Arctic and the Antarctic, indicating that long-chain PFCAs have the potential for long-range environmental transport. Furthermore, increasing temporal concentration trends in polar bears and human populations from remote regions have been reported. Compounds related to long-chain PFCAs have also been measured in ambient air from various regions around the world, including in remote areas. Available research indicates that the presence of long-chain PFCAs in remote areas results from the atmospheric and oceanic transport of volatile precursors and/or the acids themselves. There is empirical evidence of the presence of long-chain PFCAs up to $C_{18}$ in locations distant from sources. $C_{19}$–$C_{21}$ PFCAs may also be expected to be present in remote environments as a result of the release of compounds related to long-chain PFCAs during their production and use in many applications, and the potential for these precursors to undergo long-range environmental transport, supported by predictions of long characteristic travel distances in the atmosphere.

118. Long-chain PFCAs are detected globally, in all continents as well as in all environmental compartments, including biota, freshwater, saltwater, sediment, soil and rainwater Increasing temporal trends for long-chain PFCAs (up to $C_{15}$ PFCA) have been reported in wildlife, including in top predator species, and in humans. In humans, $C_9$–$C_{18}$ PFCAs have been detected globally in various tissues and fluids. Exposure of the general population to long-chain PFCAs and their related products may take place through exposure to indoor dust, food, drinking water, indoor/outdoor air and consumer products. While the relative importance of each of these pathways for the general population remains unclear, evidence suggests that consumption of wildlife species, and particularly top predator species, may be the main pathway for exposure for Indigenous Peoples, including circumpolar populations and First Nations, who rely on traditional food for subsistence. Maternal transfer through cord blood and breastfeeding are sources of long-chain PFCAs for the fetus and for nursing infants/children. Occupational exposure to certain workers (e.g., firefighters, ski wax technicians) can lead to higher serum levels of long-chain PFCAs.

119. Laboratory studies of ecological endpoints demonstrated developmental effects, behavioural effects, hepatotoxicity, immunotoxicity, neurotoxicity, changes in gene expression, genotoxicity and altered thyroid hormones. In addition, vitellogenin induction has occurred in juvenile rainbow trout after dietary exposure to $C_9$–$C_{11}$ PFCAs. Toxicological and epidemiological evidence indicates that long-chain PFCAs are associated with adverse effects in humans, including hepatotoxicity, developmental/reproductive toxicity, immunotoxicity, thyroid toxicity and altered cardiometabolic functions. Further ecological effects of long-chain PFCAs may be possible but cannot yet be predicted by current science because the interactions of long-chain PFCAs in mixtures or with other environmental stressors is not fully understood. Data on the adverse effects of long-chain PFCAs is generally lacking for PFCAs with longer chain lengths (e.g., $C_{15}$, $C_{17}$ and $C_{19}$–$C_{21}$). However, read-across can be used to fill data gaps. Long-chain PFCAs have a high degree of chemical similarity for the series of acids, and existing data show effects on common endpoints. Data from homologues, including the extensively studied $C_8$ PFCA (PFOA), indicates the potential for adverse effects. Furthermore, several studies show that the activity/toxicity of PFCAs can increase with chain length. Therefore, it is anticipated that all long-chain PFCAs would have similar adverse effects on human health and the environment, although the toxic potency may vary with chain length.

120. Long-chain PFCAs are persistent and remain in the environment for a very long time, which increases their probability, magnitude and duration of exposure to wildlife and humans. Long-chain PFCAs are also subject to long-range environmental transport, which can also result in regional or global contamination. As such, releases of long-chain PFCAs can lead to elevated concentrations in organisms over wide areas. Long-chain PFCAs may also biomagnify through the food chain, resulting in increased concentrations for top predator species. Several different long-chain PFCAs may be present simultaneously in the tissues of organisms, increasing the likelihood and potential severity of harm compared to looking at a single long-chain PFCA. Current environmental monitoring data measure concentrations that are below the available tested toxicity thresholds. 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, concentrations of certain long-chain PFCAs have been reported to have increased in remote Canadian Indigenous populations, while levels of these PFCAs were declining or stable in the general Canadian population. This suggests that certain populations (such as Arctic Indigenous Peoples) are at risk of greater exposure to long-chain PFCAs.

# 4. Concluding statement

121. Due to the ongoing production and use of long-chain PFCAs, their salts and compounds related to PFCAs, long-chain PFCAs are directly or indirectly emitted into the environment from human activities. Long-chain PFCAs are globally ubiquitous in environmental compartments, including biota, freshwater, saltwater, sediment, soil and rainwater, and humans. Long-chain PFCAs are persistent, bioaccumulative, have adverse effects on 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. Increasing temporal concentration trends in wildlife, including top predator species, suggest that long-chain PFCAs can approach toxicity thresholds resulting in

harm to wildlife populations. In humans, the high persistence of long-chain PFCAs can lead to widespread and increasing exposure, potentially resulting in adverse effects. Certain populations, such as Arctic Indigenous Peoples and those who rely on traditional foods for subsistence, are at risk of greater exposure and potential effects. Therefore, it is concluded that long-chain PFCAs, their salts and related compounds are likely, as a result of their long-range environmental transport, to lead to significant adverse human health and/or environmental effects such that global action is warranted.

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