

# Long-chain perfluorocarboxylic acids (PFCAs), their salts and related compounds

## **RISK PROFILE**

Prepared by the intersessional working group of the  
Persistent Organic Pollutants Review Committee

**April 2022**

## **Table of contents**

[To be inserted]

## Executive summary

1. The Persistent Organic Pollutants Review Committee (POPRC) 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 (hereafter referred to as C9 – C21 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 degrade or 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 foam; ski waxes; and various consumer 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 (PFAS).
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 C9 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 LC-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 (particularly fluoropolymer production sites) 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 the long-chain PFCAs emitted to the environment have degraded to long-chain PFCAs through biotic or abiotic degradation. 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 aqueous film-forming 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.
5. Long-chain PFCAs, which are carboxylic acids bonded to a fully fluorinated carbon chain, are 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, C9 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 C9 – C14 PFCAs in freshwater and marine aquatic organisms. Trophic magnification factors and biomagnification factors greater than 1 have been reported for C9 – C16 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 C16, PFCAs up to C18 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, such as the liver and kidneys, and are eliminated very slowly from the body. The mean elimination half-lives for C9 PFCA are estimated to range from 2.5 to 4.3 years in humans, whereas the mean half-lives for both C10 and C11 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 series of acids, 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.

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, C9 – C18 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 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 C18. However, long-chain PFCAs of up to 21 carbons may 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.

8. Long-chain PFCAs have been detected globally, in all continents as well as in all environmental compartments, including biota, freshwater and saltwater, sediment, soil and rainwater. Increasing temporal trends for long-chain PFCAs (up to C15 PFCA) have been reported in wildlife, including in top predator species. In humans, C9 – C18 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; however, the relative importance of each of these pathways for the general population remains unclear. 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.

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 C9 – C11 PFCAs. Toxicological and epidemiological evidence indicates that long-chain PFCAs are associated with adverse effects in humans, including hepatotoxicity, developmental/reproductive toxicity, immunotoxicity and thyroid toxicity. Data on the adverse effects of long-chain PFCAs is generally lacking for PFCAs with longer chain lengths (e.g., C15, C17 and C19 – C21). However, read-across can be used to fill data gaps, particularly within a homologous series of substances. 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 C8 PFCA (perfluorooctanoic acid, PFOA) which has been listed to 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. Therefore, it is expected 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.

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. Long-chain PFCAs are also subject to long-range 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. Since they are widespread, several different long-chain PFCAs can be present simultaneously in the tissues of organisms, increasing the likelihood and potential severity of harm. 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, concentrations of certain long-chain PFCAs have been reported to have increased in Canadian Nunavik pregnant women between 2011 and 2016-2017, while levels of these PFCAs were declining or stable in the general Canadian population. This suggests that certain populations are at risk of greater exposure to long-chain PFCAs.

11. Due to the ongoing use of long-chain PFCAs, their salts and related compounds, 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 and saltwater, sediment, soil and rainwater, and humans globally. Long-chain PFCAs are persistent, bioaccumulative, have evidence of adverse effects to human health and/or the environment, and have

the potential to undergo long-range environmental transport, in part due to the long-range atmospheric transport of compounds related to long-chain PFCAs. 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 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 (C9 – C21) 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 C19 – C21 PFCAs. This may be the consequence of analytical challenges in measuring PFCAs at the upper end of the range (i.e. for C15 – C21 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 Androulakis et al. 2022 and Gao et al. 2016, have shown that the instrument response decreases significantly for  $\geq$ C14 PFCAs due to poor ionization efficiency. This is further demonstrated by standards for C14 – C18 PFCAs. As a result, accredited analysis from commercial laboratories is restricted to C9 – C14 PFCAs, which may limit the availability of data for C15 – C21 PFCAs. Authentic reference standard mixtures of PFAS are widely employed in analytical methodology and the majority of these do not include  $>$ C14 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 mixes designed to support standardized methods by the United States Environmental Agency (US EPA) and European Union Council Directive. Gaps in data 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.

14. To address data limitations, a read-across approach has been implemented in this document based on guidance on grouping of chemicals from the Organisation for Economic Co-operation and Development (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 chemical similarity. Each acid contains the same overall structure, with a terminal carboxylic acid and an incremental and constant change of one additional  $-\text{CF}_2$  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). A 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

15. Long-chain PFCAs, their salts and related compounds are members of the per- and polyfluoroalkyl substances (PFAS) 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).

16. 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  $\text{C}_n\text{F}_{2n+1}\text{CO}_2\text{H}$  (where  $8 \leq n \leq 20$ ). Compounds related to long-chain PFCAs are defined as any substance that is a precursor and may degrade or transform to long-chain PFCAs, where the perfluorinated alkyl moiety has the formula  $\text{C}_n\text{F}_{2n+1}$  (where  $8 \leq n \leq 20$ ) and is directly bonded to any chemical moiety other than a fluorine, chlorine or bromine atom. A non-exhaustive list of Chemical Abstracts Service (CAS) numbers for

long-chain PFCAs, their salts and related compounds is provided in UNEP/POPS/POPRC.18/INF/y.

17. 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.17/7. Information relating to the physicochemical properties is reported for C9 – C15 chain lengths.

18. Both linear and branched isomers are encompassed by the scope of the risk profile. Linear isomers appear to be predominant for long-chain PFCAs detected in biota as they may have significantly slower elimination rates and/or may be present at higher exposure concentrations than branched isomers (Conder et al. 2008).

19. 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 produce intermediates such as fluorotelomer unsaturated carboxylates (x:2 FTUCA) and fluorotelomer carboxylic acids (x:2 FTCA) that can further degrade to long-chain PFCAs (Environment Canada 2012). FTOHs, which are volatile, can also undergo atmospheric oxidation to yield long-chain PFCAs (Wallington et al. 2006). Substances containing  $F(CF_2)_n(CH_2)_2-$  groups can also be considered potentially related compounds to long-chain PFCAs, as they will likely result in the release of x:2 FTOHs in the environment (ECHA 2018a,b).

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

20. 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

21. 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 the following Parties and observers according to Annex E to the Convention: 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);

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

## 1.4 Status of the chemical under national regulations

22. 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 publication of the proposed regulatory amendments is anticipated to take place in 2022.

23. 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 PFAS and set timelines for taking actions (US EPA 2021b).

24. 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.

25. In Norway, long-chain PFCAs (C9 – C14) 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).

26. In the EU, C9 and C10 PFCAs and their salts are classified<sup>1</sup> according to the globally Harmonized System (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 Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) Candidate List, as they were identified as PBT and toxic for reproduction (C9 and C10 PFCAs), or very persistent and very bioaccumulative (vPvB) (C11 – C14 PFCAs) (ECHA 2018b). In August 2021, the European Commission published a Regulation (2021/1297) to restrict C9 – C14 PFCAs, their salts and related compounds under REACH, which will come into force in February 2023 (European Commission 2021).

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

### **2.1 Sources**

#### **2.1.1 Production, trade, stockpiles**

27. 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 ammonium salt of C9 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

---

<sup>1</sup> C9 and C10 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. C9 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).

manufacturing companies committed to the US EPA Stewardship program.

28. In response to a survey conducted by the OECD for the year 2009 (OECD 2011), four companies in two countries<sup>2</sup> 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 (C9 – C12), 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).

29. Worldwide production of fluorotelomers was estimated at approximately 9100 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).

30. Wang et al. (2014) estimated the global annual production of fluorotelomer-based products to range between 2500 and 20 000 tonnes for the years 1961 to 2004, and 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 (particularly fluoropolymer production sites) from the USA, Western Europe and Japan to emerging Asian economies, especially China.

31. 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).

32. 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).

33. No intentional manufacturing or use of C9 – C14 PFCAs, their salts or related compounds has been identified in the EU. These substances were reported as being mainly manufactured unintentionally during the manufacturing of PFCAs containing a carbon chain length of less than nine carbon atoms (ECHA 2018b).

34. 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

35. Based on available information, long-chain PFCAs, their salts their 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 fluorotelomer alcohol 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

---

<sup>2</sup> The names of the companies or countries were not specified in the OECD report.



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 1 of UNEP/POPS/POPRC.18/INF/x 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 C9 – C21 PFCAs into the environment.

36. Long-chain PFCAs and their related compounds may also be unintentionally produced during the manufacturing of PFAS, 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/x), and in other industrial processes, such as the manufacture of polytetrafluoroethylene (PTFE) powders and the polymerisation of fluoropolymers (ECHA 2018b, 2020). As a result, long-chain PFCAs may be present in certain products and articles as impurities.

37. Details on identified uses and reported detections of long-chain PFCAs, their salts and related compounds in products and articles are provided below. Note that, for the majority of the studies that reported the detection of long-chain PFCAs, the homologues at the end of range (i.e. > C14 PFCAs) were not part of the analysis.

### **Industrial applications**

38. 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).

39. 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**

40. 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).

41. 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<sup>3</sup> (I&P Europe Annex E information 2022; Glüge et al. 2020).

### **Automotive care products**

42. C9 – C12 PFCAs have been detected in automotive lubricants (i.e. engine oils, hydraulic fluids and greases) (Zhu and Kannan 2020), 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**

43. C9 – C18 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 (Schaidler et al. 2017; Xenia et al. 2011; Vestergren et al. 2015; Kotthoff et al. 2015; Blom and Hanssen 2015; Borg and Irvasson 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 C9 – C12 PFCAs in plastic pet food packages (Chinthakindi et al. 2021). C10 PFCA has also been measured in recycled paper food packaging materials (Curtzwiler et al. 2021). C9 – C12 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

---

<sup>3</sup> I&P Europe has indicated that companies in the photo-imaging industry in Europe are in the final stage of eliminating this use, with these materials no longer being in the market by July 2025.

(Sinclair et al. 2007; Herzke et al. 2012; Blom and Hanssen 2015).

44. C9 – C12 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**

45. 8:2 FTOH has been detected in printer inks (Herzke et al. 2009).

#### **Building and construction materials**

46. Mono- and diPAPs are listed in the SPIN database for use in the building and construction sector (Glüge et al. 2020). C4 – C14 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). C9 – C12 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). 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**

47. C9 – C14 PFCAs, FTA (8:2), fluorotelomer sulfonate (FTSA) (8:2) and FTOHs (10:2 and 8:2) have been detected or reported to be used in aqueous film-forming foams (Herzke et al. 2009, 2012; Swedish Chemicals Agency 2015; Nordic Council of Ministers 2015, as summarized in NICNAS, 2019; Favreau et al. 2017). C9 and C10 PFCAs have also been measured in fluorocarbon surfactants used for the preparation of aqueous film-forming foams (Mumtaz et al. 2019).

#### **Ski waxes**

48. C9 – C21 PFCAs and 8:2 FTOHs have been measured in ski waxes/gliders or their raw materials (Kotthoff et al. 2015; Plassman and Berger 2013; Blom and Hanssen 2015; Fang et al. 2020).

#### **Personal care and other consumer products**

49. C9 – C14, C16 PFCAs and some related compounds, such as monoPAP (8:2 and 10:2) diPAP (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).

50. C9 – C12 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). C9 – C14 and C16 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**

51. Long-chain PFCAs (C9 – C14, C16), FTOHs (10:2 and 8:2), FTCAs and FTUCAs have been detected in apparel, including in adults and/or children outerwear and baby/children's bibs (Gremmel et al. 2016; Berger and Herzke 2006; Commission for Environmental Cooperation 2017; Borg and Irvasson 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 C9 – C14 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 (C10 and C8) concentrations ( $r=0.957$ ;  $p=0.0013$ ) (Kotthoff et al. 2015). C9 – C12 PFCAs have been detected in medical garments (Guo et al. 2009; Liu et al. 2014) and firefighter turnout gear (Peaslee et al. 2020).

52. C9 – C11 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). C9 – C14 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), impregnation/water proofing agents (Herzke et al. 2012; Kotthoff et al. 2015; Borg and Irvasson 2017), and industrially applied polymeric (carpet protector) (Dinglasan-Panlilio and Mabury 2006). C4 – C14 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).

### 2.1.3. Releases to the environment

53. There are no known 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 the long-chain PFCAs emitted to the environment have degraded to long-chain PFCAs through biotic or abiotic degradation (OECD 2015; Wang et al. 2014).

54. 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 2 of UNEP/POPS/POPRC.18/INF/x.

55. C9 – C16 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. reported increasing temporal trends for C9 – and C10 PFCAs concentrations in Taihu Lake, China from 2009 and 2021 (Yu et al. 2022).

56. C9 – C12 PFCAs have also been measured in groundwater contaminated with aqueous film-forming foam (AFFF) collected at U.S. military bases (Backe et al. 2013). C9-C14 and C16 PFCAs, FTCAs (8:3, 9:3 and 11:3), 8:2 FTUCA and FTSA (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).

57. Long-chain PFCAs and their related compounds may also be released to the environment from waste treatment facilities, such as landfills, incineration plants and wastewater treatment plants. C9 – C18 PFCAs, FTOHs (8:2, 10:2 and 12:2), FTCAs (8:2 and 10:2), FTAs (8:2 and 10:2) and FTUCAs (8:2 and 10:2) have been measured in leachate, percolate or soil from landfills located in the United States (US), China, South Korea, Canada, Germany and Spain (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). C9-C18 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 (reviewed in 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). In addition, C9 – C14 PFCAs and 8:2 diPAPs have been measured in leachate, fly ash and bottom ash from a municipal solid waste incineration plants (Liu et al. 2021). C9-C12 and C14 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).

58. Land application of contaminated biosolids can also be a source of long-chain PFCAs releases to the environment. C9 – C14 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).

59. Ski wax has also been identified as a source emission of long-chain PFCAs and related compounds to the environment. C9 – C21 PFCAs were measured in snow collected after cross-country ski competitions and/or in soil from skiing areas after snowmelt (Carlson and Tupper 2020; Plassman and Berger 2013; Grønnestad et al. 2019).

60. Some uses of long-chain PFCAs, their salts and their related compounds may lead to releases to indoor environments. C9 – C15 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 5 in UNEP/POPS/POPRC.18/INF/x for details).

61. Building on early work by Prevedouros et al. (2006), Wang et al. estimated the global cumulative emissions of C4 – C14 PFCAs for the years 1951 to 2030 (summarized in Table 3 of UNEP/POPS/POPRC.18/INF/x) from quantifiable sources<sup>4</sup> of these substances (Wang et al. 2014). 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 approximately by a factor of eight. Total estimated or projected global cumulative emissions of individual C9 – C14 PFCAs, between 1951 and 2030, ranged from 0 to 1901 tonnes (i.e., 250 – 1901 tonnes (C9); 8 – 222 tonnes (C10); 67 – 689 tonnes (C11); 0 – 63 tonnes (C12); 17 – 147 tonnes (C13); 0 – 19 tonnes (C14)). 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/x for more details).

## 2.2. Environmental fate

### 2.2.1 Persistence

62. 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; Colombari 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 stable in the environment. For example, C9 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/x for details).

63. Long-chain PFCAs have met the regulatory criteria for persistence in different jurisdictions. In the European Union, C9 – C10 PFCAs have been identified as persistent and C11 – C14 PFCAs have been identified as 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.

### 2.2.3 Bioaccumulation

64. The unique characteristics and physicochemical properties of long-chain PFCAs are relevant to the potential for bioaccumulation. Long-chain PFCAs are non-volatile substances with combined properties of ionization, lipophobicity, hydrophobicity, and hydrophilicity over different portions of the molecule. The carboxylate functional group attached to the perfluorinated chain also imparts polarity to the molecule. Due to these properties, the hydrophobic and lipophilic interactions between long-chain PFCAs and the substrate are not the main mechanisms that govern their bioaccumulation, which is unlike most organic chemicals (Hekster et al. 2002). Hydrophobicity is unlikely to be the main driving force for partitioning to tissues, as the lipophobic tendencies oppose this partitioning process; instead, electrostatic interactions may be more important (Hekster et al. 2002). 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).

65. Although octanol-water partitioning 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

---

<sup>4</sup> Historial and ongoing use of: 1) PFOA as processing aids in the (emulsion) polymerization of PTFE, fluorinated ethylene propylene, perfluoroalkoxyl polymer and PVDF; 2) C9 PFCa as processing aids in the emulsion polymerization of PVDF; 3) chemicals derived from perfluorooctane sulfonyl fluoride; and x:2 fluorotelomer-based substances.

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 et al. 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., bioaccumulation models) for long-chain PFCAs (OECD 2002; Conder et al. 2008). Instead, empirical bioaccumulation data is more relevant. Refer to section 2.2.3 of UNEP/POPS/POPRC.18/INF/x for more details.

66. 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 C18 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 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 C11 PFCA (2300 – 3700), C12 PFCA (10 000 – 16 000), C13 PFCA (16 000 – 17 000), C16 PFCA (4700 – 4800) and C18 PFCA (320 – 430) (Inoue et al. 2012). BCF and BAF values generally increased from C9 PFCA (<0.4 – 1514) to C14 PFCA (17 000 – 363 078) and then decreased for C16 to C18 PFCAs (20 – 4800). Field-derived BCFs and BAFs in freshwater and marine aquatic organisms have been reported up to C15 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 (C9 PFCA) to > 26 000 (C13 PFCA) and kidney BAFs that ranged from 2600 (C9 PFCA) to > 40 000 (C13 PFCA) (Murakami et al. 2011). Field-derived BCFs and BAFs were variable depending on the species and ranged from 3.9 (C9 PFCA) to 5 011 872 (C12 PFCA). Field-derived BCFs and BAFs also generally increased from C9 PFCA to C14 PFCA and then declined at C15 PFCA (> 59 – 224) (Kwadijk et al. 2010, Labadie and Chevreuil 2011, Murakami et al. 2011, Zhou et al. 2012, Naile et al. 2013, Fang et al. 2014, Pan et al. 2014, Ahrens et al. 2015, Gebbink et al. 2016, Liu et al. 2019a, Liu et al. 2019b, Munoz et al. 2019, Pan et al. 2019, Choi et al. 2020). However, field-derived BAF values for very long chain PFCA are not often reported because it is not feasible to measure long PFCA in water due to low water solubility causing the concentrations to be very low. In other studies, researchers have estimated BAF using detection limits. For example, Zhang et al. derived BAF for marine plankton by substituting non-detect concentrations in water with the detection limit (Zhang et al. 2019). In a recent review of BCF and BAF of PFAS in aquatic species, Burkhard did not include any data that were based on concentrations below detection limit in water or tissue, which therefore limited reporting to a maximum of C10 chain length (Burkhard 2021). This has been circumvented using lab-based exposures that are not limited by environmental concentrations, in order to empirically measure BCF and BAF for a larger range of chain lengths (i.e. all of those papers above). However, Burkhard 2021 reported that laboratory BCF measurements decline with increasing exposure concentration, rather than remaining constant. It was postulated that PFAS body burden is controlled by both passive and active transport processes, the latter of which can be concentration dependent. As such, laboratory-derived BCF using high concentrations are expected to be lower than a real-world scenario.

67. 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., 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, whereas 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 PFCA 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 PFCA that 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) are more relevant in determining the overall bioaccumulation potential for long-chain PFCA.

68. Field biomagnification or trophic magnification studies on long-chain PFCA (up to C16 PFCA) that focused on multiple fish species and/or top predator species (i.e., birds or terrestrial/marine mammals) show higher 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, Boisvert et al. 2019, Simonnet-Laprade et al. 2019b). 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 C9 – C14 PFCA, 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 (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 C9 – C14 PFCA (Simonnet-Laprade et al. 2019b). 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/x. Overall, TMF values ranged from 0.3 to 19.8 and BMF values 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 1.

69. There are no biomagnification or trophic magnification data for long-chain PFCA with chain lengths greater than C16 due to the analytical challenges of measuring very long chain PFCA. However, it is expected that C17 – C21 PFCA can also biomagnify in birds and terrestrial/marine mammals. C17 – C21 PFCA have been measured in snow and soil (Plassman and Berger 2013), C9 – C11, C14 and C18 were measured in air samples in the Arctic (Wong et al. 2018) and C16 – C18 PFCA have been measured in top predator species such as the peregrine falcon (*Falco peregrinus*) from the Great Lakes region (Canada) (Sun et al. 2020), and in the eggs of herring gulls (*Larus argentatus*) and Caspian tern (*Hydroprogne caspia*) from colony sites across the Great Lakes basin (Canada and the U.S.) (Letcher et al. 2015; Su et al. 2017), as well as in the liver of East Greenland polar bears (Greaves et al. 2013; Boisvert et al. 2019) and Hudson Bay polar bears (Letcher et al. 2018).

70. A read-across argument can also be made to address 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 empirical evidence of bioaccumulation for long-chain PFCA up to C16. There is evidence of use/release of compounds related to C17 – C21 PFCA. PFCA with linear perfluoroalkyl chains ( $Deff = 0.61 - 0.96$  nm in C8 to C18 PFCA) can enable them to pass through biological membranes (Inoue et al. 2012). 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. This leads 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 C17 – C21 PFCA have the potential to bioaccumulate.

71. In humans, long-chain PFCA accumulate in the blood and well perfused tissues such as the liver and kidneys (Kudo 2015). Long-chain PFCA 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 C9 PFCA are estimated to range from 2.5 to 4.3 years in humans whereas the mean half-lives for both C10 and C11 PFCA range from 4.5 to 12 years (Zhang et al. 2013). In studies with C4 - C10 PFCA, compounds with longer carbon chains have been found to bind more strongly to proteins (Chen et al. 2020). Although it is unclear if this trend holds for compounds above C10 PFCA (Jackson et al. 2021). Several animal studies suggest that the longer the carbon chain length, the more slowly the PFAS is eliminated, and thus, the more bioaccumulative it is (Ohmori et al. 2003; Kudo et al. 2006; Yeung et al. 2009).

72. Although information is lacking for the bioaccumulation of C12 – C21 PFCA in humans, a

read-across argument can be made to address 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 C9, C10 and C11 PFCAs in humans, and in animal studies, there is evidence of slower elimination with increasing chain lengths. There is also evidence of increasing protein binding with increasing chain length for C4 – C10 PFCA, with some uncertainty acknowledged for longer PFCAs. Consequently, it is reasonable to expect that long-chain PFCAs of up to 21 carbons may bioaccumulate in humans.

73. Long-chain PFCAs have met regulatory criteria for bioaccumulation in some jurisdictions. Long-chain PFCAs (C9 – C14) have been assessed in the European Union and identified as bioaccumulative (C9 and C10 PFCAs) or very bioaccumulative (C11 to C14 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.

#### 2.2.4 Potential for long-range environmental transport

74. 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 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).

75. 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 attributed to related compounds (e.g., FTOH) emitted to the atmosphere ultimately yielding long-chain PFCAs through biotic or abiotic degradation. Wallington et al. (2006) used a three-dimensional global atmospheric chemistry model (IMPACT) to show that 8:2 FTOH degrades in the atmosphere to form C9 PFCA. Young et al. (2007) suggested that the presence of C9 – C11 PFCAs on several Canadian High Arctic ice caps (Melville Ice Cap (Northwest Territories), Agassiz Ice Cap (Nunavut), and Devon Ice Cap (Nunavut)) is indicative of atmospheric oxidation of volatile precursors. Young et al. (2007) detected C9 PFCA (0.005 – 0.246 ng/L), C10 PFCA (ND – 0.022 ng/L), and C11 PFCA (ND – 0.027 ng/L). Ellis et al. (2004) 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 biodegraded or 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 4 of UNEP/POPS/POPRC.18/INF/x.

76. 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 between <2 to 121 pg/m<sup>3</sup> and of C9 – C14 PFCAs ranged from <0.03 to 8 pg/m<sup>3</sup> with C9 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<sup>3</sup> and <0.033 to 0.71 pg/m<sup>3</sup>, respectively. 8:2 and 10:2 FTOHs showed slow increasing trends with doubling times of 5.0 and 7.0 years, respectively. C9-C14, C16 and C18 showed concentrations of <0.0063 – 0.77 pg/m<sup>3</sup> at Alert, with C9 having the highest concentrations. At Zeppelin and Andøya, C9 – C11 PFCAs showed concentrations of <0.079 to 11 pg/m<sup>3</sup>, with C9 and C10 showing the highest concentrations. Stock et al. (2007) measured C9 – C12 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. 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 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 C9 – C13 PFCAs with concentrations that ranged from 0.00321 – 0.751 ng/L.

77. Oceanic transport is another long-range environmental transport mechanism for long-chain PFCAs. As perfluorinated alkyl 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 results in enrichment on the “*surface of bursting bubbles*”. Reth et al. (2011) examined the water-to-air transfer of C6 – C14 PFCAs in a laboratory-scale sea spray simulator and found that the sequestration of the perfluorinated alkyl 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. observed a strong correlation of long-chain PFCA in sea spray aerosol and sodium ion, which is a marine tracer (Sha et al. 2022). 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, C9 – C12 PFCAs were measured in air samples at two Norwegian coastal sites, and were positively correlated with Na<sup>+</sup> ion concentrations, which suggests that sea spray aerosols are a source of PFCAs to the atmosphere in coastal areas (2022).

78. Long-chain PFCAs (primarily C9 to C18 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 4 of UNEP/POPS/POPRC.18/INF/x for concentrations in biota.

79. No measurements of C19 – C21 PFCAs in environmental matrices or biota from locations distant from sources have been identified in the literature. A read-across argument can be made to address these data gaps. The high degree of chemical similarity for the series of acids has been described earlier and is suggestive of similar transport mechanisms. There is empirical evidence of the presence of long-chain PFCAs in locations distant from sources of long-chain PFCAs up to C18. 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 C19 – C21 PFCAs, as indicated by the chain length distribution of FTOHs substances identified in the patent literature. As a result of the release of compounds related to long-chain PFCAs during their production and use in many applications (as described in section 2.1.2), and the potential for these precursors to undergo long-range environmental transport, long-chain PFCAs of up to 21 carbons may be expected to be present in remote environments.

## 2.3 Exposure

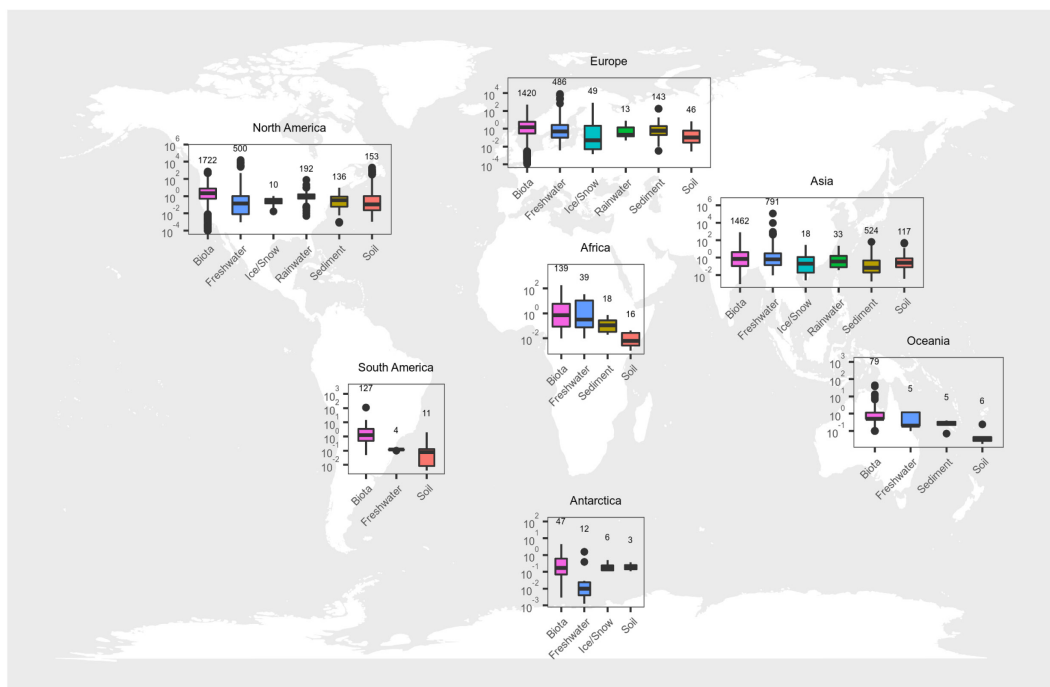
### 2.3.1 Environmental monitoring data

80. Long-chain PFCAs were detected globally, in all continents as well as in all environmental compartments, including biota, freshwater and saltwater, sediment, soil and rainwater, as can be seen in Figure 1, representing concentrations from 1980 to 2019. Long-chain PFCAs with chain lengths C9 to C14 were measured in Africa, Antarctica, Asia, Europe, North America, Oceania and South America. Only Europe reported measurements of C19 – C21 in the environment, which was measured in snow in Sweden (Plassman and Berger 2013). The list of references used to generate Figure 1 is provided in UNEP/POPS/POPRC.18/INF/x. Details on the reported environmental concentrations of long-chain PFCAs are provided in UNEP/POPS/POPRC.18/INF/z.

81. A further breakdown of worldwide concentrations of long-chain PFCAs is illustrated in Figure 2 of UNEP/POPS/POPRC.18/INF/x, 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=3780), 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/x). 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). Fish were the most studied biota after birds/eggs, followed by 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, 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).



**Figure 1. Worldwide occurrence of long-chain PFCAs (C9 – C21) 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  $Q1 - 1.5 \times IQR$  threshold, and the upper whisker represents the highest data that are within the  $Q3 + 1.5 \times IQR$  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.

82. Temporal trends for long-chain PFCAs (up to C15 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; 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; 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 C9 – C11 PFCAs (Smithwick et al. 2006). From 1984 to 2006, 128 sub-adult (3–5 years old) Greenland polar bears showed annual increases for C9 PFCA (6.1%), C10 PFCA (4.3%), C11 PFCA (5.9%), C12 PFCA (52%), and C13 PFCA (8.5%) (Dietz et al. 2008). From 1974 to 2007, C9 – C15 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 C9 – C13 PFCA concentrations increased significantly from 1991 to 2008 (Huber et al. 2012). Liver and serum mean concentrations of C9 and C10 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  $\Sigma$ PFCAs (including C8 – C12 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, C9 – C13 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

83. Humans may be exposed to long-chain PFCAs and their related products through indoor dust, food, drinking water, indoor/outdoor air and consumer products; however, the relative importance of each of these pathways for the general population remains unclear (ATSDR 2021).

84. 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 (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 C9, C13 and C14 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 C9, C11 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 analyzed for C9 – C15 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 5 in UNEP/POPS/POPRC.18/INF/x).

85. 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. 2004). However, some of these substances are still found in drinking water around the world (see Table 6 in UNEP/POPS/POPRC.18/INF/x). For example, C9 – C14 PFCAs were recurrently detected in drinking water samples from Africa, Europe, Asia and the Americas in a study conducted during 2015 to 2016. C9 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 C9 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) C9 PFCA was detected above the minimum reporting level of 0.02 µg/L (US EPA 2017). Levels of C9 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 C9 - C12 PFCA compared with those consuming mainly tap water (Zhou et al. 2019). 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, C9 PFCA was detected at two PWS at high concentrations of 72 ng/L and 96 ng/L. An industrial facility, where large quantities of C9 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 C9 PFCA concentration and is a possible source of contamination at both of these two PWS (Post et al. 2013).

86. The diet has been suggested as a principal exposure route for long-chain PFCAs (Vestergren et al. 2012; Poothong et al. 2020) and a number of studies have investigated the presence of long-chain PFCAs in food items (see EFSA 2020 Annex A4; see section 2.3.2 and Table 7 of UNEP/POPS/POPRC.18/INF/x). 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.

87. 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 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). C9 PFCA has been the most frequently detected 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 C10 – C12 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 C9 – C18 PFCAs in human milk with values typically ranging from below the LOD to low pg/mL (see Table 8 of UNEP/POPS/POPRC.18/INF/x). 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 C9 PFCA levels as compared to nulliparous women and that the duration of breastfeeding was associated with decreased levels of C9

PFCA in maternal serum (Brantsaeter et al. 2013). In another study, each month of breastfeeding was associated with a 2% decline in C9 PFCA levels in maternal serum (Mondal et al. 2014).

88. 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). Much of the biomonitoring data is limited to the measurement of C9 – C14 PFCAs, with C9 PFCA typically having the highest detection frequencies, which are often close to 100%. Some studies have also measured and detected up to C18 PFCAs, however detection frequencies are low (e.g., less than 2%, Nystrom et al. 2022). The results from 29 biomonitoring studies in the EU showed C9 – C11 PFCA serum concentrations to be in the high pg/mL to low ng/mL range, whereas C12 – C14 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 9 of UNEP/POPS/POPRC.18/INF/x). 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 C9 – C11 PFCAs ranged from 0.12 to 0.82 µg/L in participants aged 12–79 (Health Canada 2021). Of note, concentrations of long-chain PFCAs in the serum/plasma of Nunavik adults, including pregnant Inuit women (C9 – C11), First Nation Anishinabe youth (C9) and seven Gwich'in and Dene First Nation communities (C9) who live in very different areas across Canada (but all remote) were higher than CHMS values for comparable age and sex groups, and time periods (Caron-Beaudoin et al. 2019; Caron-Beaudoin et al. 2020; AMAP 2021; Garcia-Barrios et al. 2021; Dubeau et al. 2022). Specifically, C9 PFCA geometric mean concentrations among participants from Anishinabe communities aged 6 to 11 and 12 to 19 years old were 9.44 µg/L and 3.01 µg/L, respectively (Caron-Beaudoin et al. 2019). These values are 20 and 7 times higher respectively than CHMS cycle 5 values for the same age groups. Concentrations of C9 PFCA were up to seven times higher in Nunavik adults as compared to CHMS values (AMAP 2021). C9 – C13 PFCAs have also been found in serum samples from Inuit women from Greenland at concentrations ranging from 0.031 to 38.6 ng/mL (µg/L) (Long et al. 2015; Wielsoe et al. 2017; Hjermitsev et al. 2020), highlighting the significance of the long-range transport of PFAS to remote communities. Importantly, there is also evidence of an association between serum concentrations of long-chain PFCAs in Indigenous populations in these remote communities and biomarkers for the consumption of traditional foods (e.g., marine mammals) (Long et al. 2015; Caron-Beaudoin et al. 2020; Hjermitsev et al. 2020). Serum concentrations of long-chain PFCAs have been observed to increase with age, 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 but not all studies, higher concentrations have been observed in older males than females, possibly due to the loss of PFAS through menstruation and the transfer of these pollutants from mothers to offspring via parturition and lactation (Ji et al. 2012; Seo et al. 2018).

89. Occupational exposure can lead to higher serum levels of long-chain PFCAs. In a Swedish study of 8 ski wax technicians, blood levels of C9 – C11 PFCA were all higher in technicians as compared to representative populations from Sweden, China, and North America; C9 PFCA was 15–270 times higher in the 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 C9– C13 PFCAs (Freberg et al. 2010; Nilsson et al. 2010). In a study of 86 female firefighters in the USA, firefighters had 1.26 times higher geometric mean concentrations of C9 PFCA (95% CI = 1.01, 1.58) and 1.83 times higher mean concentrations of C11 PFCA (95% CI = 0.97, 3.45) as compared to office workers. Firefighters that worked at the airport had C9 PFCA levels that were two times higher compared to firefighters assigned to other stations (Trowbridge et al. 2020). Other U.S. studies of more than 100 firefighters also found higher levels of C9, C10 and C12 PFCAs in firefighters as compared to levels in the general population as measured in the National Health and Nutrition and Examination Survey (NHANES) (Dobraca et al. 2015; Graber et al. 2021). In contrast to these findings, a study of 38 firefighters in the U.S., noted that levels of C9 and C11 PFCA were significantly lower than the NHANES measurements (Khalil et al. 2020). In a study of eight male firefighters in Finland, levels of C9 PFCA 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).

90. Although serum concentrations of other PFAS 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 C9 and C10 PFCAs increased from 1986–2007 in a Norwegian study, whereas levels of C11 PFCA were stable (Berg et al. 2021). In a study of first time mothers in Sweden, levels of C9 PFCA increased from 1996–2008, but then declined until 2019. C11 and C13 PFCAs showed increasing temporal trends during the study period 1996–2019 (Gyllenhammar et al. 2020). Levels of C9 and C10 PFCAs in a cohort of Swedish children also demonstrated downward trends from 2008–2019 (Hedvall

Kallerman et al. 2020). Conversely, a study of a cohort of seniors reported an increase in C9 – C11 PFCA during 2001–2014 (Stubleski et al. 2006). For roughly the same period (2003–2014), data from the U.S. NHANES study showed that levels of C9 and C10 PFCA decreased (CDC 2018). No overall temporal trends for C9 – C14 PFCA were observed in German Biobank specimens for the period of 1982–2010 (Shroter-Kermani et al. 2013), although the time period of 2000 to 2009 showed increasing concentrations of C9 – C10 PFCA (Yeung et al. 2013) and new information used to extend the dataset showed a decline in C9 PFCA from 2006 to 2019 (Göckener et al. 2020). Levels of C9, C10 and C11 PFCA in the general Canadian population were declining or stable between 2011 and 2016–2017 (Health Canada, 2021). However, during the same time period, concentrations of C9, C10 and C11 PFCA in Canadian Nunavik pregnant women increased by 19%, 13% and 21%, respectively (Caron-Beaudoin et al. 2020). A systematic review examining the phase out of PFAS worldwide found that, between roughly 1980 and 2013, C9 - C14 PFCA 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

91. PFAS, 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- $\alpha$  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 $\alpha$  target genes involved in lipid homeostasis. Activation of the PPAR $\alpha$ –CYP4A pathway could result in altered liver function, developmental toxicity, immunotoxicity, and feeding disorders (Kurtz et al. 2019; Kubota et al. 2011). C9 and C10 PFCA have been shown to induce hepatic CYP4A-like proteins via PPAR- $\alpha$  signaling in Lake Baikal seals (Ishibashi et al. 2008b). PPAR- $\alpha$  mRNA expression and CYP4a protein expression in kidneys of cetaceans have also been positively correlated with C10, C11, C13 and C14 PFCA (Kurtz et al. 2019).

92. In laboratory toxicity studies assessing endpoints such as growth, reproduction, and lethality, long-chain PFCA (up to C14 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, C9 – C12 PFCA, the 48h EC50 values for immobilization for a pelagic cladoceran (*Daphnia magna*) and a benthic cladoceran (*Chydorus sphaericus*) ranged from 12.4 – 181 mg/L with the benthic cladoceran showing greater sensitivity (Ding et al. 2012). Refer to section 2.4.1 of UNEP/POPS/POPRC.18/INF/x for detailed results.

93. In additional laboratory toxicity studies assessing the exposure to long-chain PFCA (up to C13 PFCA), endpoints 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 (*Perna 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 C9 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). Refer to section 2.4.1 of UNEP/POPS/POPRC.18/INF/x for detailed results.

94. For the field-based wildlife studies, it is difficult to uniquely distinguish effects from exposure to long-chain PFCA, as exposures from mixtures of other PFAS (e.g., PFOS or 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). PFAS (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, as

statistical correlations, by themselves, do not imply causal relationships. Recognizing this uncertainty, several field-based wildlife studies have shown statistical correlations with observed effects for long-chain PFCA mixtures (from C9 to C16) 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). Refer to section 2.4.1 of UNEP/POPS/POPRC.18/INF/x for detailed results.

95. 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 ( $\mu\text{g/g}$ ) 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, 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. 2006; Taylor et al. 2019). Long-chain PFCAs are also subject to long-range 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. Since they are widespread, several different long-chain PFCAs can be present simultaneously in the tissues of organisms, increasing the likelihood and potential severity of harm. 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.

96. 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 2.4.2 of UNEP/POPS/POPRC.18/INF/x. 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.

97. *In vivo* data in rodents provide evidence of hepatotoxicity after acute, short-term and/or subchronic exposure to C9 – C12, C14, C16 and C18 PFCAs. Effects include liver weight alterations, hepatocellular hypertrophy, histopathological changes, 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).

98. Effects on the immune system induced by exposure to C9 – C11 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).

99. Several long-chain PFCAs (C9, C11, C12, C14, C16 and C18) 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).

100. Short-term studies performed in rats and mice provide evidence that oral (gavage) exposure to C9, C10 and C14 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).

101. 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 are not causal in nature, 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, reproduction and development and effects on the thyroid.

102. Several epidemiological studies evaluated hepatic endpoints and noted associations between exposure to C9 – C14 PFCAs and increased levels of serum lipid levels and changes to clinical biomarkers of liver function (e.g., EFSA 2020, ATSDR 2021 Blomberg et al. 2021). With regards to the immune system, epidemiological studies noted positive associations between exposure to C9 – C12, C14 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 C9 – C14 PFCAs and reproductive outcomes in adolescents/adults. Associations were noted with altered hormone levels, 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 C9 – C14 PFCAs and associations were noted with outcomes including the incidence of congenital hypothyroidism and altered levels of hormones, thyroglobulin, and thyroid peroxidase antibodies (e.g., Kim et al. 2016; Ballesteros et al. 2017; Aimuzi et al. 2019; Itoh et al. 2019). Further details on some of the epidemiological studies investigating these endpoints are located in Section 2.4.2 of UNEP/POPS/POPRC.18/INF/x. Comprehensive reviews of the data have concluded that the most convincing evidence exists for associations between exposure to C9 – C10 PFCAs and increased serum lipid levels (ATSDR 2021; EFSA 2020), as well as for associations between C10 PFCA and immune effects (decreased antibody responses to vaccines) (ATSDR 2021; Kirk et al. 2018).

103. Long-chain PFCAs are commonly detected together with a range of other PFAS 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 PFAS, including C9 – C13 PFCAs. Mixtures of nine PFAS (including C9 – C11) 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 PFAS (including C9 – C13), 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 PFAS (including C9 and C10 PFCAs). Binary mixtures of C9 and C10 PFCAs in particular demonstrated strong synergism under inhibitory concentrations ranging from 10-90% (Ojo et al. 2020). Synergistic effects were also observed when Chinese hamster ovary cells were exposed to a mixture of five PFAS including C9 and C10 PFCA and tested for anti-androgen activity (Kjeldsen and Bonefeld-Jørgensen 2013). Therefore, given the vast number and ubiquity of PFAS, it is reasonable to assume that cumulative effects could occur following exposure to PFAS.

104. Data on the adverse effects of long-chain PFCAs is generally lacking for PFCAs with longer chain lengths (e.g., C15, C17 and C19-21). 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 C8 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 C12 (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 C18 (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 expected 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

105. 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 PFAS.

106. 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 C9 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 LC-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 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 from the USA, Western Europe and Japan to emerging Asian economies, especially China, has been reported in the literature.

107. 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 degraded 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 aqueous film-forming 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.

108. Long-chain PFCAs are 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, C9 PFCA did not biodegrade under the OECD 301F method. Other studies demonstrate some degradation of long-chain PFCAs, but not under environmentally relevant conditions.

109. Some measured BCFs and BAFs greater than 5000 have been reported for C9 – C14 PFCAs in freshwater and marine aquatic organisms. TMFs and BMFs greater than 1 have been reported for C9 – C16 PFCAs in studies that focused on top predator species, providing evidence that long-chain PFCAs biomagnify in air-breathing organisms. PFCAs up to C18 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 C9 PFCA range from 2.5 to 4.3 years, and mean half-lives for both C10 and C11 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 series of acids, 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.

110. Global modelling indicates that long-chain PFCAs, their salts and/or related compounds have the potential to be transported over long distances. In addition, C9 – C18 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 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 C18 in locations distant from sources. Long-chain PFCAs of up to 21 carbons 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.

111. Long-chain PFCAs are detected globally, in all continents as well as in all environmental compartments, including biota, freshwater and saltwater, sediment, soil and rainwater. Increasing temporal trends for long-chain PFCAs (up to C15 PFCA) have been reported in wildlife, including in top predator species. In humans, C9 – C18 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; however, the relative importance of each of these pathways for the general population remains unclear. 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.

112. 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 C9 – C11 PFCAs. Toxicological and epidemiological evidence indicates that long-chain PFCAs are associated with adverse effects in humans, including hepatotoxicity, developmental/reproductive toxicity, immunotoxicity and thyroid toxicity. 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., C15, C17 and C19-21). 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 C8 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 expected 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.

113. 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. Long-chain PFCAs are also subject to long-range 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. Since they are widespread, several different long-chain PFCAs can be present simultaneously in the tissues of organisms, increasing the likelihood and potential severity of harm. 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, concentrations of certain long-chain PFCAs have been reported to increase in Canadian Nunavik pregnant women between 2011 and 2016-2017, while levels of these PFCAs were declining or stable in the general Canadian population. This suggests that certain populations are at risk of greater exposure to long-chain PFCAs.

#### **4. Concluding statement**

114. Due to the ongoing 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 and saltwater, sediment, soil and rainwater, and humans. Long-chain PFCAs are persistent, bioaccumulative, have evidence of adverse effects to human health and/or the environment, and have the potential to undergo long-range environmental transport, in part due to the long-range atmospheric transport of compounds related to long-chain PFCAs. 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 adverse human health and/or environmental effects such that global action is warranted.



## 5. References

- Aas CB, Fuglei E, Herzke D, Yoccoz NG, Routti H. 2014. Effect of body condition on tissue distribution of perfluoroalkyl substances (PFASs) in Arctic fox (*Vulpes lagopus*). *Environ Sci Technol.* 48: 11654–11661.
- Ahrens L, Xie Z, Ebinghaus R. 2010. Distribution of perfluoroalkyl compounds in seawater from northern Europe, Atlantic Ocean and Southern Ocean. *Chemosphere.* 78:1011–1016.
- Ahrens L, Shoeib M, Harner T, Lee SC, Guo R, Reiner EJ. 2011. Wastewater Treatment Plant and Landfills as Sources of Polyfluoroalkyl Compounds to the Atmosphere. *Environ. Sci. Technol.* 45:8098–8105.
- Ahrens L and Bundschuh M. 2014. Fate and effects of poly- and perfluoroalkyl substances in the aquatic environment: a review. *Environmental Toxicology and Chemistry.* 33(9):1921–1929.
- Ahrens L, Norstorm K, Viktor T, Cousins AP, Josefsson S. 2015. Stockholm Arlanda Airport as a source of per- and polyfluoroalkyl substances to water, sediment and fish. *Chemosphere.* 129: 33–38.
- Aimuzi R, Luo K, Chen Q, Wang H, Feng L, Ouyang F, Zhang J. 2019. Perfluoroalkyl and polyfluoroalkyl substances and fetal thyroid hormone levels in umbilical cord blood among newborns by prelabor caesarean delivery. *Environ Int.* 130:104929.
- Alder AC, van der Voet J. 2014. Occurrence and point source characterization of perfluoroalkyl acids in sewage sludge. *Chemosphere.* 129:62–73.
- [AMAP] Arctic Monitoring and Assessment Programme. 2021. Human Health in the Arctic Summary for Policy-makers. Tromsø, Norway. Available at <https://www.amap.no/documents/download/6756/inline>.
- Androulakis A, Alygizakis N, Gkotsis G, Nika M, Nikolopoulou V, Bizani E, Chadwick E, Cincinelli A, Claßen D, Danielsson S, Dekker Rene WRJ, Duke G, Glowacka N, Jansman HAH, Krone O, Martellini T, Movalli P, Persson S, Roosf A, O'Rourke E, Siebert U, Treu G, van den Brink NW, Walker LA, Deaville R, Slobodnik J, Thomaidis NS. 2022. Determination of 56 per- and polyfluoroalkyl substances in top predators and their prey from Northern Europe by LC-MS/MS. *Chemosphere* 287:131775
- Anliker R, Moser P, Doppinger D. 1988. Bioaccumulation of dyestuffs and organic pigments in fish. Relationships to hydrophobicity and steric factors. *Chemosphere.* 17:1631–1644.
- Anderson RH, Long GC, Porter RC, Anderson JK. 2016. Occurrence of select perfluoroalkyl substances at U.S. Air Force aqueous film-forming foam release sites other than fire-training areas: field validation of critical fate and transport properties. *Chemosphere.* 150:678–685.
- Apelberg BJ, Goldman LR, Calafat AM, Herbstman JB, Kuklennyik Z, Heidler J, Needham LL, Halden RU, Witter FR. 2007a. Determinants of fetal exposure to polyfluoroalkyl compounds in Baltimore, Maryland. *Environ.Sci.Technol.* 41(11): 3891-3897.
- Apelberg BJ, Witter FR, Herbstman JB, Calafat AM, Halden RU, Needham LL, Goldman LR. 2007b. Cord serum concentrations of perfluorooctane sulfonate (PFOS) and perfluorooctanoate (PFOA) in relation to weight and size at birth. *Environ.Health Perspect.* 115(11): 1670-1676.
- Armitage JM, Arnot JA, Wania F. 2012. Potential role of phospholipids in determining the internal tissue distribution of perfluoroalkyl acids in biota. *Environ Sci Technol.* 46:12285–12286.
- Arp HPH, Niederer C, Goss K-U. 2006. Predicting the partitioning behaviour of various fluorinated compounds. *Environ Sci Technol.* 40(23):7298–7304.
- Ask AG. 2015. Perfluoroalkyl and Polyfluoroalkyl Substances (PFASs) Affect the Thyroid Hormone System, Body Condition, and Body Mass in Two Arctic Seabird Species. [Master Thesis]. Trondheim: NTNU-Trondheim, Norwegian University of Science and Technology.
- [ATSDR] Agency for Toxic Substances and Disease Registry. 2021. Toxicological Profile for Perfluoroalkyls. U.S. Department of Health and Human Services, Public Health Service, Atlanta, GA.
- Bach C, Dauchy X, Boiteux V, Colin A, Hemard J, Sagres V, Rosin C, Munoz JF. 2017. The impact of two fluoropolymer manufacturing facilities on downstream contamination of a river and drinking water resources with per- and polyfluoroalkyl substances. *Environ Sci Pollut Res.* 24:4916–4925.

- Backe WJ, Day TC, Field JA. 2013. Zwitterionic, Cationic, and Anionic Fluorinated Chemicals in Aqueous Film Forming Foam Formulations and Groundwater from U.S. Military Bases by Nonaqueous Large-Volume Injection HPLC-MS/MS. *Environ. Sci. Technol.* 47:5226–5234.
- Ballesteros V, Costa O, Iñiguez C, Fletcher T, Ballester F, Lopez-Espinosa MJ. 2017. Exposure to perfluoroalkyl substances and thyroid function in pregnant women and children: A systematic review of epidemiologic studies. *Environ Int.* 99:15–28.
- Bangma JT, Reiner JL, Lowers RH, Cantu TM, Scott J, Korte JE, Scheidt DM, McDonough C, Tucker J, Back B, Adams DH, Bowden JA. 2018. Perfluorinated alkyl acids and fecundity assessment in striped mullet (*Mugil cephalus*) at Merritt Island national wildlife refuge. *Science of the Total Environment.* 619-620:740–747.
- Banks RE, Smart BE, Tatlow JC. *Organofluorine chemistry: principles and commercial applications.* Springer, 1994. ISBN: 978-0-306-44610-8. [As cited in OECD 2013]
- Bao J, Lee YL, Chen PC, Jin YH, Dong GH. 2014. Perfluoroalkyl acids in blood serum samples from children in Taiwan. *Environ.Sci.Pollut.Res.* 21(12): 7650-7655.
- Bao WW, Qian ZM, Geiger SD, Liu E, Liu Y, Wang SQ, Lawrence WR, Yang B-Y, Hu L-W, Zeng X-W, et al. 2017. Gender-specific associations between serum isomers of perfluoroalkyl substances and blood pressure among Chinese: Isomers of C8 Health Project in China. *Sci Total Environ.* 607-608:1304–1312.
- Barber JL, Berger U, Chaemfa C, Huber S, Jahnke A, Temme C, Jones KC. 2007. Analysis of per- and polyfluorinated alkyl substances in air samples from northwest Europe. *J.Environ.Monit.* 9(6): 530-541.
- Beatty RP, Inventor. E. I. du Pont de Nemours and Company, assignee. 2003 Apr 1. Fluorinated lubricant additives. United States Patent US 6541430. Available from: <https://patents.justia.com/patent/6541430> [Accessed: 23 February 2022]
- Bečanová J, Melymuk L, Vojta, Š. Komprdová, K. and Klánová, J. 2016. Screening for perfluoroalkyl acids in consumer products, building materials and wastes. *Chemosphere.* 164:322–329.
- Beneficemalouet S, Blancou H, Itier J, Commeyras A. 1991. An improved synthesis of perfluorocarboxylic acids. *Synthesis.* (Stuttg):647–648.
- Bengtson Nash S, Rintoul SR, Kawaguchi S, Staniland I, Hoff Jvd, Tierney M, Bossi R, 2010. Perfluorinated compounds in the Antarctic region: ocean circulation provides prolonged protection from distant sources. *Environ Pollut.* 158:2985–2991.
- Benninghoff AD, Bisson WH, Koch DC, Ehresman DJ, Kolluri SK, Williams DE. 2011. Estrogen-like activity of perfluoroalkyl acids in vivo and interaction with human and rainbow trout estrogen receptors in vitro. *Toxicol Sci.* 120(1):42–58.
- Benninghoff AD, Orner GA, Buchner CH, Hendricks JD, Duffy AM, Williams DE. 2012. Promotion of hepatocarcinogenesis by perfluoroalkyl acids in rainbow trout. *Toxicol Sci.* 125(1):69–78.
- Benskin JP, Li B, Ikononou MG, Grace JR, Li LY. 2012a. Per- and Polyfluoroalkyl Substances in Landfill Leachate: Patterns, Time Trends, and Sources. *Environ. Sci. Technol.* 46:11532–11540.
- Benskin JP, Muir DCG, Scott BF, Spencer C, De Silva AO, Kylin H, Martin JW, Morris A, Lohmann R, Tomy G, Rosenberg B, Taniyasu S, Yamshita N. 2012b. Perfluoroalkyl acids in the Atlantic and Canadian Arctic Oceans. *Environ Sci Technol.* 46(11):5815–5823.
- Berg V, Sandanger TM, Hanssen L, Rylander C, Nøst TH. 2021. Time trends of perfluoroalkyl substances in blood in 30-year old Norwegian men and women in the period 1986–2007. *Environ.Sci.Pollut.Res.* <https://doi.org/10.1007/s11356-021-13809-6>.
- Berger U, Herzke D. 2006. Per- and polyfluorinated alkyl substances (PFAs) extracted from textile samples. *Organohal Compds.* 68:2023–2026.
- Bernett MK, Zisman WA. 1959. Wetting of low-energy solids by aqueous solutions of highly fluorinated acids and salts. *J Phys Chem.* 63:1911–1916.
- Bischel HN, MacManus-Spencer LA, Luthy RG. 2010. Noncovalent interactions of long-chain perfluoroalkyl acids with serum albumin. *Environ Sci Technol.* 44:5263–5269.
- Bischel HN, MacManus-Spencer LA, Zhang C, Luthy RG. 2011. Strong associations of short-chain perfluoroalkyl acids with serum albumin and investigation of binding mechanism. *Environmental Toxicology and Chemistry.* 30(11):2423–30

- Blancou H, Moreau P, Commeyras A. 1976. Preparation of perfluoroalkane carboxylic and sulfonic-acid derivatives by the action of metallic couples on perfluoroalkyl iodides in dimethyl-sulfoxide. *J Chem Soc Chem Commun.* :885–886.
- Blévin P, Tartu S, Ellis HI, Chastel O, Bustamante P, Parenteau C, Herzke D, Angelier F, Gabrielsen GW. 2017. Contaminants and energy expenditure in an Arctic seabird: Organochlorine pesticides and perfluoroalkyl substances are associated with metabolic rate in a contrasted manner. *Environ Res.* 157:118–126.
- Blévin P, Shaffer SA, Bustamante P, Angelier F, Picard B, Herzke D, Moe B, Gabrielsen GW, Bustnes JO, Chastel O. 2020. Contaminants, prolactin and parental care in an Arctic seabird: Contrasted associations of perfluoroalkyl substances and organochlorine compounds with egg-turning behavior. *Gen Comp Endocrinol.* 291:113420.
- Blom C, Hanssen L. 2015. Analysis of per- and polyfluorinated substances in articles. Available from: <https://www.norden.org/en/publication/analysis-and-polyfluorinated-substances-articles> [Accessed: 24 February 2022]
- Blomberg AJ, Shih YH, Messerlian C, Jørgensen LH, Weihe P, Grandjean P. 2021. Early-life associations between per- and polyfluoroalkyl substances and serum lipids in a longitudinal birth cohort. *Environ.Res.* 200: 111400.
- Bodin J, Groeng EC, Andreassen M, Dirven H, Nygaard UC. 2016. Exposure to perfluoroundecanoic acid (PFUnDA) accelerates insulinitis development in a mouse model of type 1 diabetes. *Toxicol Rep.* 3:664–672.
- Boisvert G, Sonne C, Riget FF, Dietz R, Letcher RJ. 2019. Bioaccumulation and biomagnification of perfluoroalkyl acids and precursors in East Greenland polar bears and their ringed seal prey. *Environmental Pollution.* 252:1335–1343.
- Borg D, Ivarsson J. 2017. Analysis of PFASs and TOF in products. Available from: <https://norden.diva-portal.org/smash/get/diva2:1118439/FULLTEXT01.pdf> [Accessed: 24 February 2022]
- Bossi R, Riget FF, Dietz R. 2005. Temporal and spatial trends of perfluorinated compounds in ringed seal (*Phoca hispida*) from Greenland. *Environ Sci Technol.* 39:7416–7422.
- Bossi R, Strand J, Sortkjær O, Larsen MM. 2008. Perfluoroalkyl compounds in Danish wastewater treatment plants and aquatic environments. *Environment International.* 34:443–450.
- Bossi R, Dam M, Riget F. 2015. Perfluorinated alkyl substances (PFAS) in terrestrial environments in Greenland and Faroe Islands. *Chemosphere.* 129:164–169.
- Bourgeon S, Riemer AK, Tartu S, Aars J, Polder A, Jenssen BM, Routti H. 2017. Potentiation of ecological factors on the disruption of thyroid hormones by organo-halogenated contaminants in female polar bears (*Ursus maritimus*) from the Barents Sea. *Environ Res.* 158:94–104.
- Brantsæter AL, Whitworth KW, Ydersbond TA, Haug LS, Haugen M, Knutsen HK, Thomsen C, Meltzer HM, Becher G, Sabaredzovic A, et al. 2013. Determinants of plasma concentrations of perfluoroalkyl substances in pregnant Norwegian women. *Environ.Int.* 54: 74-84.
- Briels N, Torgersen LN, Castano-Ortiz JM, Løseth ME, Herzke D, Nygård T, Ciesielski TM, Poma G, Malarvannan G, Covaci A, Jaspers VLB. 2019. Integrated exposure assessment of northern goshawk (*Accipiter gentilis*) nestlings to legacy and emerging organic pollutants using non-destructive samples. *Environmental Research.* 178:108678.
- Buck RC, Franklin J, Berger U, Conder JM, Cousins IT, de Voogt P, Jensen AA, Kannan K, Mabury SA, van Leeuwenk SPJ. 2011. Perfluoroalkyl and Polyfluoroalkyl Substances in the Environment: Terminology, Classification, and Origins. *Integr. Environ. Assess. Manag.* 7(4):513–541.
- Buck Louis GM, Zhai S, Smarr MM, Grewal J, Zhang C, Grantz KL, Hinkle SN, Sundaram R, Lee S, Honda M, et al. 2018. Endocrine disruptors and neonatal anthropometry, NICHD Fetal Growth Studies - Singletons. *Environ Int.* 119:515–526.
- Buhrke T, Kibellus A, Lampen A. 2013. In vitro toxicological characterization of perfluorinated carboxylic acids with different carbon chain lengths. *Toxicol Lett.* 218(2): 97-104.
- Burkhard LP. 2021. Evaluation of Published Bioconcentration Factor (BCF) and Bioaccumulation Factor (BAF) Data for Per- and Polyfluoroalkyl Substances Across Aquatic Species. *Environmental Toxicology and Chemistry.* 40(6):1530–1543.

- Busch J, Ahrens L, Sturm R, Ebinghaus R. 2010. Polyfluoroalkyl compounds in landfill leachates. *Environmental Pollution*. 158:1467–1471.
- Bustnes JO, Bangjord G, Ahrens L, Herzke D, Yoccoz NG. 2015. Perfluoroalkyl substance concentrations in a terrestrial raptor: relationships to environmental conditions and individual traits. *Environmental Toxicology and Chemistry*. 34(1):184–191.
- Butt CM, Stock NL, Mabury SA, Muir DCG, Braune BM. 2007a. Prevalence of long-chain perfluorinated carboxylates in seabirds from the Canadian Arctic between 1975 and 2004. *Environ Sci Technol*. 41:3521–3528.
- Butt CM, Muir DCG, Stirling I, Kwan M, Mabury SA. 2007b. Rapid response of Arctic ringed seals to changes in perfluoroalkyl production. *Environ Sci Technol*. 41 (1): 42–49.
- Butt CM, Mabury SA, Kwan M, Wang X, Muir DCG. 2008. Spatial trends of perfluoroalkyl compounds in ringed seals (*Phoca hispida*) from the Canadian Arctic. *Environ Toxicol Chem*. 27(3):542–553.
- Butt CM, Muir DCG, Mabury SA. 2013. Biotransformation pathways of fluorotelomer-based polyfluoroalkyl substances: A review. *Environmental Toxicology and Chemistry*. 33(2):243–267.
- Cai M, Xie Z, Möller A, Yin Z, Huang P, Minggang C, Yang H, Sturm R, He J, Ebinghaus R. 2012a. Polyfluorinated compounds in the atmosphere along a cruise pathway from the Japan Sea to the Arctic Ocean. *Chemosphere*. 87:989–997.
- Cai M, Yang H, Xie Z, Zhao Z, Wang F, Lu Z, Sturm R, Ebinghaus R. 2012b. Per- and polyfluoroalkyl substances in snow, lake, surface runoff water and coastal seawater in Fildes Peninsula, King George Island, Antarctica. *Journal of Hazardous Materials*. 209-210: 335–342.
- Canada. 1999. *Canadian Environmental Protection Act, 1999*. S.C. 1999, c.33. Canada Gazette Part III, vol. 22, no. 3. Available from: <https://laws-lois.justice.gc.ca/eng/acts/C-15.31/> [Accessed: 14 April 2022]
- Canada. 2000. *Canadian Environmental Protection Act, 1999: Persistence and Bioaccumulation Regulations*. P.C. 2000-348, 23 March, 2000, SOR/2000-107. Available from: <https://laws-lois.justice.gc.ca/eng/regulations/SOR-2000-107/page-1.html> [Accessed: 14 April 2022]
- Canada. 2012. *Prohibition of Certain Toxic Substances Regulations, 2012*. SOR/2012-285. Available from: <https://laws-lois.justice.gc.ca/eng/regulations/SOR-2012-285/index.html> [Accessed: 14 April 2022]
- Canada. 2018. Dept. of the Environment. Dept. of Health. Consultation Document on Proposed Amendments to the Prohibition of Certain Toxic Substances Regulations, 2012 for PFOS, PFOA, LC-PFCAs, HBCD, PBDEs, DP and DBDPE (December 2018). Available from: <https://www.canada.ca/en/environment-climate-change/services/canadian-environmental-protection-act-registry/proposed-amendments-certain-toxic-substances-2018-consultation.html> [Accessed: 6 April 2022]
- Carlson GL, Tupper S. 2020. Ski wax use contributes to environmental contamination by per- and polyfluoroalkyl substances. *Chemosphere*. 261:128078.
- Caron-Beaudoin E, Ayotte P, Laouan Sidi EA; Community of Lac Simon; Community of Winneway – Long Point First Nation; CSSS Tshukuminu Kanani of Nutashkuan; Community of Unamen Shipu, Gros-Louis McHugh N, Lemire M. 2019. Exposure to perfluoroalkyl substances (PFAS) and associations with thyroid parameters in First Nation children and youth from Quebec. *Environ Int*. 2019 Jul;128:13-23.
- Caron-Beaudoin E, Ayotte P, Blanchette C, Muckle G, Avard E, Ricard S, Lemire M. 2020. Perfluoroalkyl acids in pregnant women from Nunavik (Quebec, Canada): Trends in exposure and associations with country foods consumption. *Environ Int*. 2020 Dec;145:106169.
- Casal P, Zhang Y, Martin JW, Pizzaro M, Jiménez B, Dachs J. 2017. Role of snow deposition of perfluoroalkylated substances at coastal Livingston Island (Maritime Antarctica). *Environ Sci Technol*. 51:8460–8470.
- [CDC] Centers for Disease Control and Prevention. 2018. Fourth National Report on Human Exposure to Environmental Chemicals. Updated Tables, March 2018, Volume One. Available at [https://www.cdc.gov/exposurereport/pdf/FourthReport\\_UpdatedTables\\_Volume1\\_Mar2018.pdf](https://www.cdc.gov/exposurereport/pdf/FourthReport_UpdatedTables_Volume1_Mar2018.pdf).
- [CDR]. Chemical Data Reporting. 2020. United States Environmental Protection Agency. [Accessed 6 July 2020] CAS No. 678-39-7; CAS No. 865-86-1; CAS No. 39239-77-5; CAS No. 60699-5106

- Chen F, Gong Z, Kelly BC. 2016. Bioavailability and bioconcentration potential of perfluoroalkyl-phosphinic and -phosphonic acids in zebrafish (*Danio rerio*): comparison to perfluorocarboxylates and perfluorosulfonates. *Science of the Total Environment*. 568:33–41.
- Chen H, Yao Y, Zhao Z, Wang Y, Wang Q, Ren C, Wang B, Sun H, Alder AC, Kannan K. 2018a. Multimedia Distribution and Transfer of Per- and Polyfluoroalkyl Substances (PFASs) Surrounding Two Fluorochemical Manufacturing Facilities in Fuxin, China. *Environ. Sci. Technol.* 52:8263–8271.
- Chen Q, Huang R, Hua L, Guo Y, Huang L, Zhao Y, Wang X, Zhang J. 2018b. Prenatal exposure to perfluoroalkyl and polyfluoroalkyl substances and childhood atopic dermatitis: a prospective birth cohort study. *Environ Health*. 17(1):8.
- Chen Y, Li H, Mo J, Chen X, Wu K, Ge F, Ma L, Li X, Guo X, Zhao J, et al. 2019. Perfluorododecanoic acid blocks rat leydig cell development during prepuberty. *Chem Res Toxicol*. 32(1):146–155.
- Chen H, Wang Q, Cai Y, Yuan R, Wang F, Zhou B. 2020. Investigation of the interaction mechanism of perfluoroalkyl carboxylic acids with human serum albumin by spectroscopic methods. *Int J Environ Res Public Health*. 17(4):1319–1330.
- Cheng W, Ng CA. 2018. Predicting relative protein affinity of novel per- and polyfluoroalkyl substances (PFASs) by an efficient molecular dynamics approach. *Environ Sci and Technol*. 52:7972–7980.
- Chinthakindi, S, Zhu, H, Kannan, K. 2021. An exploratory analysis of poly-and per-fluoroalkyl substances in pet food packaging from the United States. *Environmental Technology and Innovation*. 21:101247.
- Choi S, Kim J-J, Kim M-H, Joo Y-S, Chung M-S, Kho Y, Lee K-W. 2020. Origin and organ-specific bioaccumulation pattern of perfluorinated alkyl substances in crabs. 261: 114185.
- Colomban C, Kudrik EV, Afanasiev P, Sorokin AB. 2014. Catalytic defluorination of perfluorinated aromatics under oxidative conditions using N-bridged diiron phthalocyanine. *J Am Chem Soc*. 136: 11321–11330
- Commission for Environmental Cooperation. 2017. Furthering the Understanding of the Migration of Chemicals from Consumer Products – A Study of Per- and Polyfluoroalkyl Substances (PFASs) in Clothing, Apparel, and Children’s Items. Montreal, Canada: Commission for Environmental Cooperation. 201 pp.
- Conder JM, Hoke RA, de Wolf W, Russell MH, Buck RC. 2008. Are PFCAs bioaccumulative? A critical review and comparison with regulatory criteria and persistent lipophilic compounds. *Environ Sci Technol*. 42(4):995–1003.
- Costantini D, Blevin P, Herzke D, Moe B, Gabrielsen GW, Bustnes JO, Chastel O. 2019. Higher plasma oxidative damage and lower plasma antioxidant defences in an Arctic seabird exposed to longer perfluoroalkyl acids. *Environmental Research*. 168:278–285.
- Cui Q, Pan Y, Zhang H, Sheng N, Dai J. 2018. Elevated concentrations of perfluorohexanesulfonate and other per- and polyfluoroalkyl substances in Baiyangdian Lake (China): Source characterization and exposure assessment. *Environ.Pollut*. 241: 684–691.
- Curtzwiler GW, Silva P, Hall A, Ivey A, Vorst K. 2021. Significance of Perfluoroalkyl Substances (PFAS) in Food Packaging. *Integr Environ Assess Manag*. 17(1):7–12.
- Danish Environmental Protection Agency. 2018. Risk assessment of fluorinated substances in cosmetic products. Survey of chemical substances in consumer products No. 169. Available from: <https://www2.mst.dk/Udgiv/publications/2018/10/978-87-93710-94-8.pdf> [Accessed: 24 February 2022]
- Das KP, Grey BE, Rosen MB, Wood CR, Tatum-Gibbs KR, Zehr RD, Strynar MJ, Lindstrom AB, Lau C. 2015. Developmental toxicity of perfluorononanoic acid in mice. *Reprod Toxicol*. 51:133–44.
- Dassuncao C, Hu XC, Zhang X, Bossi R, Dam M, Mikkelsen B, Sunderland EM. 2017. Temporal shifts in poly- and perfluoroalkyl substances (PFASs) in North Atlantic pilot whales indicate large contribution of atmospheric precursors. *Environ Sci Technol*. 51:4512–4521.
- De Silva AO, Mabury SA. 2004. Isolating isomers of perfluorocarboxylates in polar bears (*Ursus maritimus*) from two geographical locations. *Environ Sci Technol*. 38:6538–6545.

- DeWitt J, Peden-Adams M, Keil D. (2015). Immunotoxic Effects of Perfluoroalkylated Compounds: Mechanisms of Action. In: Molecular Immunotoxicology. Corsini E and van Loveren H (eds.). Wiley-VCH Verlag GmbH & Co. KGaA, Germany. pp. 263-284.
- Dietz R, Bossi R, Riget FF, Sonne S, Born EW. 2008. Increasing perfluoroalkyl contaminants in east Greenland polar bears (*Ursus maritimus*): a new toxic threat to the Arctic bears. *Environ Sci Technol*. 42(7):2701–2707.
- Dimitrov SD, Dimitrova NC, Walker JD, Veith GD, Mekenyan OG. 2003. Bioconcentration potential predictions based on molecular attributes—an early warning approach for chemicals found in humans, birds, fish and wildlife. *QSAR Comb Sci*. 22:58–68.
- Ding L, Hao F, Shi Z, Wang Y, Zhang H, Tang H, Dai J. 2009. Systems biological responses to chronic perfluorododecanoic acid exposure by integrated metabolomic and transcriptomic studies. *J Proteome Res*. 8(6):2882–91.
- Ding G-H, Frömel T, van den Brandhof E-J, Baerselman R, Peijnenburg WJGM. 2012. Acute toxicity of poly- and perfluorinated compounds to two cladocerans, *Daphnia magna* and *Chydorus sphaericus*. *Environmental Toxicology and Chemistry*. 31 (3):605–610.
- Ding N, Harlow SD, Randolph Jr. JF, Loch-Carusio R, Park, SK. 2020. Perfluoroalkyl and polyfluoroalkyl substances (PFAS) and their effects on the ovary. *Hum Reprod Update*. 26(5):724–752.
- Dinglasan-Panlilio MJA, Mabury S. 2006. Significant Residual Fluorinated Alcohols Present in Various Fluorinated Materials. *Environ Sci Technol*. 40:1447–1453.
- Dixon DA. 2001. Fluorochemical decomposition process. Pacific Northwest National Laboratory, Richland WA
- Dobraca D, Israel L, McNeel S, Voss R, Wang M, Gajek R, Park JS, Harwani S, Barley F, She J, Das R. 2015. Biomonitoring in California firefighters: metals and perfluorinated chemicals. *J*. 57(1):88-97.
- Dong GH, Tung KY, Tsai CH, Liu MM, Wang D, Liu W, Jin YH, Hsieh WS, Lee YL, Chen PC. 2013. Serum polyfluoroalkyl concentrations, asthma outcomes, and immunological markers in a case-control study of Taiwanese children. *Environ Health Perspect*. 121(4):507–13.
- Duan Y, Sun H, Yao Y, Meng Y, Li Y. 2020. Distribution of novel and legacy per-/polyfluoroalkyl substances in serum and its associations with two glycemic biomarkers among Chinese adult men and women with normal blood glucose levels. *Environ Int*. 134:105295.
- Ebnesajjad S. 2013. Introduction to Fluoropolymers - Material, Technology, and Applications. Elsevier [As cited in ECHA 2018b]
- [ECHA] European Chemicals Agency. 2012a. Support Document for Identification of Henicosafluoroundecanoic Acid as a Substance of Very High Concern Because of its vPvB Properties. Available from: <https://echa.europa.eu/documents/10162/01986fb8-ede8-4458-b54e-12ff8a534b98> [Accessed: 23 October 2020]
- [ECHA] European Chemicals Agency. 2012b. Support Document for Identification of Heptacosafuorotetradecanoic Acid as a Substance of Very High Concern Because of its vPvB Properties. Available from: <https://echa.europa.eu/documents/10162/997efe1b-0564-4ca1-a012-bab93e518f25> [Accessed: 23 October 2020]
- [ECHA] European Chemicals Agency. 2012c. Support Document for Identification of Pentacosafuorotridecanoic Acid as a Substance of Very High Concern Because of its vPvB Properties. Available from: <https://echa.europa.eu/documents/10162/3fd11ee9-6925-475f-b328-d224d45219a4> [Accessed: 23 October 2020]
- [ECHA] European Chemicals Agency. 2012d. Support Document for Identification of Tricosafluorododecanoic Acid as a Substance of Very High Concern Because of its vPvB Properties. Available from: <https://echa.europa.eu/documents/10162/0d5abffa-6bbf-40c7-b6b1-1ca3736cf570> [Accessed: 23 October 2020]
- [ECHA] European Chemicals Agency. 2015. Support Document for Identification of Perfluorononan-1-oic Acid and its Sodium and Ammonium Salts as Substances of Very High Concern Because of their Toxic for Reproduction and PBT Properties. Available from: <https://echa.europa.eu/documents/10162/48ae5fe3-9436-4a10-a533-ed642b92ce47> [Accessed 23: October 2020]

- [ECHA] European Chemicals Agency. 2016. Support Document for Identification of Nonadecafluorodecanoic Acid (PFDA) and its Sodium and Ammonium Salts as a Substance of Very High Concern Because of its Toxic for Reproduction (Article 57 c) and Persistent, Bioaccumulative, and Toxic (PBT) (Article 75 D) Properties. Available from: <https://echa.europa.eu/documents/10162/d580f392-aadd-459c-5bfa-7a2e4dd86032> [Accessed: 23 October 2020]
- [ECHA] European Chemicals Agency. 2017. Annex XV Restriction Report. Proposal for a Restriction on C9-C14 PFCAs including their salts and precursors. Available from: <https://echa.europa.eu/documents/10162/2ec5dfdd-0e63-0b49-d756-4dc1bae7ec61> [Accessed: 23 October 2020]
- [ECHA] European Chemicals Agency. 2018a. Committee for Risk Assessment (RAC). Committee for Socio-economic Analysis (SEAC). Background document to the Opinion on an Annex XV dossier proposing restrictions on C9-C14 PFCAs including their salts and precursors. 29 November 2018. Available from: <https://echa.europa.eu/documents/10162/02d5672d-9123-8a8c-5898-ac68f81e5a72> [Accessed: 23 October 2020]
- [ECHA] European Chemicals Agency. 2018b. Committee for Risk Assessment (RAC). Committee for Socio-economic Analysis (SEAC). Opinion on an Annex XV dossier proposing restrictions on PFNA, PFDA, PFUnDA, PFDoDA, PFTrDA, PFTDA; their salts and precursors. Compiled version prepared by the ECHA Secretariat of RAC's opinion (adopted 14 September 2018) and SEAC's opinion (adopted 29 November 2018). Available from: <https://echa.europa.eu/documents/10162/5aabe3cc-a317-4b2f-5446-5fc22c522c31> [Accessed: 23 October 2020]
- [ECHA] European Chemicals Agency. 2020. Committee for Risk Assessment (RAC). Committee for Socio-economic Analysis (SEAC). Opinion related to the request by the Executive Director of ECHA under Art. 77(3)9(c) of REACH to prepare a supplementary opinion on : Proposed derogations from the restrictions on C9 – C14 perfluorocarboxylic acids (C9 – C14 PFCA), their salts and related substances and on Perfluorooctanoic acid (PFOA), its salts and PFOA-related substances. Compiled version prepared by the ECHA Secretariat of RAC's opinion (adopted 30 November 2020) and SEAC's opinion (adopted 10 December 2020). Available from: [https://echa.europa.eu/documents/10162/13579/art77\\_3c\\_pfoa\\_pfca\\_derogations\\_compiled\\_rac\\_seac\\_opinions\\_en.pdf/6582d9a1-56b2-3e88-a70f-cdf3ab33d421](https://echa.europa.eu/documents/10162/13579/art77_3c_pfoa_pfca_derogations_compiled_rac_seac_opinions_en.pdf/6582d9a1-56b2-3e88-a70f-cdf3ab33d421) [Accessed: 19 January 2021]
- [EFSA] European Food Safety Authority. 2020. Scientific Opinion on the Risk to Human Health Related to the Presence of Perfluoroalkyl Substances in Food. EFSA Journal. Available at <https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2020.6223>.
- Eggers Pedersen K, Letcher RJ, Sonne C, Dietz R, Styrishave B. 2016. Per- and polyfluoroalkyl substances (PFASs) – new endocrine disruptors in polar bears (*Ursus maritimus*)? *Environment International*. 96:180–189.
- Elliott SM, Route WT, DeCicco LA, VanderMeulen DD, Corsi SR, Blackwell BR. 2019. Contaminants in bald eagles of the upper Midwestern U.S.: a framework for prioritizing future research based on in-vitro bioassays. *Environmental Pollution*. 244:861–870.
- Ellis DA, Martin JW, De Silva AO, Mabury SA, Hurley MD, Sulbaek Andersen MP, Wallington TJ. 2004. Degradation of fluorotelomer alcohols : a likely atmospheric source of perfluorinated carboxylic acids. *Environ Sci Technol*. 38:3316–3321
- Environment Canada. 2001. Primary Report on PFAs from Section 71 survey prepared by Use Patterns Section, Chemicals Control Division, Commercial Chemicals Evaluation Branch. Gatineau (QC).
- Environment Canada. 2005. Report on PFCAs results of notice issued under Section 71 CEPA for 2004 calendar year.
- Environment Canada. 2012. Ecological Screening Assessment Report Long-Chain (C9–C20) Perfluorocarboxylic Acids, their Salts and their Precursors. Available from: <http://www.ec.gc.ca/ese-ees/default.asp?lang=En&n=CA29B043-1> [Accessed: 23 October 2020]
- [ECCC] Environment and Climate Change Canada. 2022. Personal communication.
- Ericson I, Domingo JL, Nadal M, Bigas E, Llebaria X, Van Bavel B, Lindström G. 2009. Levels of perfluorinated chemicals in municipal drinking water from Catalonia, Spain: Public health implications. *Arch. Environ. Contam. Toxicol*. 57(4): 631-638.

- Erikstad KE, Bustnes JO, Lorensten S-H, Reiersten TK. 2009. Sex ratio in lesser black-backed gull in relation to environmental pollutants. *Behav Ecol Sociobiol.* 63:931–938.
- European Commission. 2021. Commission Regulation (EU) 2021/1297 of 4 August 2021 amending Annex XVII to Regulation (EC) No 1907/2006 of the European Parliament and of the Council as regards perfluorocarboxylic acids containing 9 to 14 carbon atoms in the chain (C9-C14 PFCAs), their salts and C9-C14 PFCA-related substances. Available from: <https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32021R1297&from=EN> [Accessed: 8 December 2021]
- Fair PA, Romano T, Schaefer AM, Reif JS, Bossart GD, Houde M, Muir D, Adams J, Rice C, Hulseley TC, Peden-Adams M. 2013. Associations between perfluoroalkyl compounds and immune and clinical chemistry parameters in highly exposed bottlenose dolphins (*Tursiops truncatus*). *Environ Toxicol Chem.* 32(4):736–46.
- Falk S, Stahl T, Fliendner A, Rüdell H, Tarricone K, Brunn H, Koschorreck J. 2019. Levels, accumulation patterns and retrospective trends of perfluoroalkyl acids (PFAAs) in terrestrial ecosystems over the last three decades. *Environmental Pollution.* 246:921–931.
- Fang, X, Zhang L, Feng Y, Zhao Y, Dai J. 2008. Immunotoxic effects of perfluorononanoic acid on BALB/c mice. *Toxicol Sci.* 105(2):312–21.
- Fang X, Feng Y, Shi Z, Dai J. 2009. Alterations of cytokines and MAPK signaling pathways are related to the immunotoxic effect of perfluorononanoic acid. *Toxicol Sci.* 108(2):367–76.
- Fang X, Feng Y, Wang J, Dai J. 2010. Perfluorononanoic acid-induced apoptosis in rat spleen involves oxidative stress and the activation of caspase-independent death pathway. *Toxicology.* 267(1–3):54–9.
- Fang X, Zou S, Zhao Y, Cui R, Zhang W, Hu J, Dai J. 2012a. Kupffer cells suppress perfluorononanoic acid-induced hepatic peroxisome proliferator-activated receptor alpha expression by releasing cytokines. *Arch Toxicol.* 86(10):1515–25.
- Fang X, Gao G, Xue H, Zhang X, Wang H. 2012b. In vitro and in vivo studies of the toxic effects of perfluorononanoic acid on rat hepatocytes and Kupffer cells. *Environ Toxicol Pharmacol.* 34(2):484–494.
- Fang X, Gao G, Xue H, Zhang X, Wang, H. 2012c. Exposure of perfluorononanoic acid suppresses the hepatic insulin signal pathway and increases serum glucose in rats. *Toxicology.* 294(2–3):109–15.
- Fang S, Chen X, Zhao S, Zhang Y, Jiang W, Yang L, Zhu L. 2014. Trophic magnification and isomer fractionation of perfluoroalkyl substances in the food web of Taihu Lake, China. *Environ Sci*48:2173–2182.
- Fang, X, Gao G, Zhang X, Wang H. 2015. Perfluorononanoic acid disturbed the metabolism of lipid in the liver of streptozotocin-induced diabetic rats. *Toxicol Mech Methods.* 25(8):622–7.
- Fang S, Plassmann MM, Cousins IT. 2020. Levels of per- and polyfluoroalkyl substances (PFAS) in ski wax products on the market in 2019 indicate no changes in formulation. *Environ. Sci.: Processes Impacts.* 22:2142.
- Favreau P, Poncioni-Rothlisberger C, Place BJ, Bouchex-Bellomie H, Weber A, Tremp J, Field JA, Kohler M. 2017. Multianalyte profiling of per- and polyfluoroalkyl substances (PFASs) in liquid commercial products. *Chemosphere.* 171:491–501.
- Feng Y, Shi Z, Fang X, Xu M, Dai J. 2009. Perfluorononanoic acid induces apoptosis involving the Fas death receptor signaling pathway in rat testis. *Toxicol.Lett.* 190(2): 224-230.
- Fontell K, Lindman B. 1983. Fluorocarbon surfactants - phase-equilibria and phase structures in aqueous systems of a totally fluorinated fatty-acid and some of its salts. *J Phys Chem.* 87:3289–3297.
- Frawley RP, Smith M, Cesta MF, Hayes-Bouknight S, Blystone C, Kissling GE, Harris S, Germolec D. 2018. Immunotoxic and hepatotoxic effects of perfluoro-n-decanoic acid (PFDA) on female Harlan Sprague-Dawley rats and B6C3F1/N mice when administered by oral gavage for 28 days. *J Immunotoxicol.* 15(1):41–52.
- Freberg BI, Haug LS, Olsen R, Daae HL, Hersson M, Thomsen C, Thorud S, Becher G, Molander P, Ellingsen DG. 2010. Occupational exposure to airborne perfluorinated compounds during professional ski waxing. *Environ. Sci. Technol.* 44: 7723-7728
- Fuertes I, Gómez-Lavín S, Elizalde MP, Urriaga A. 2017. Perfluorinated alkyl substances (PFASs) in northern Spain municipal solid waste landfill leachates. *Chemosphere.* 168:399–407.



- Gao K, Gao Y, L Yi, Fu J, Zhang A. 2016. A rapid and fully automatic method for the accurate determination of a wide carbon-chain range of per- and polyfluoroalkyl substances (C4–C18) in human serum. *J. Chromatogr. A.* 1471:1–10.
- Gao S, Jing M, Xu M, Han D, Niu Q, Liu R. 2020. Cytotoxicity of perfluorodecanoic acid on mouse primary nephrocytes through oxidative stress: Combined analysis at cellular and molecular levels. *J Haz Mater.* 393:122444.
- Garcia-Barrios J, Drysdale M, Ratelle M, Gaudreau É, LeBlanc A, Gamberg M, Laird BD. 2021. Biomarkers of poly- and perfluoroalkyl substances (PFAS) in sub-arctic and arctic communities in Canada. *Int.J.Hyg.Enviroin.Health.* 235: 113754.
- Gebbink WA, Hebert CE, Letcher RJ. 2009. Perfluorinated carboxylates and sulfonates and precursor compounds in herring gull eggs from colonies spanning the Laurentian Great Lakes of North America. *Environ Sci Technol.* 43:7443–7449.
- Gebbink WA and Letcher RJ. 2012. Comparative tissue and body compartment accumulation and maternal transfer to eggs of perfluoroalkyl sulfonates and carboxylates in Great Lakes herring gulls. *Environmental Pollution.* 162:40–47.
- Gebbink WA, Ullah S, Sandblom O, Berger U. 2013. Polyfluoroalkyl phosphate esters and perfluoroalkyl carboxylic acids in target food samples and packaging—method development and screening. *Environ Sci Pollut Res.* 20:7949–7958.
- Gebbink WA, Glynn A, Darnerud PO, Berger U. 2015. Perfluoroalkyl acids and their precursors in Swedish food: The relative importance of direct and indirect dietary exposure. *Environ.Pollut.* 198: 108-115.
- Gebbink WA, Bignert A, Berger U. 2016. Perfluoroalkyl acids (PFAAs) and selected precursors in the Baltic Sea environment: do precursors play a role in food web accumulation of PFAAs? *Environ Sci50:6354–6362.*
- Gebbink WA, Van Asseldonk L, Van Leeuwen SPJ. 2017. Presence of emerging per- and polyfluoroalkyl substances (PFASs) in river and drinking water near a fluorochemical production plant in the Netherlands. *Environ.Sci.Technol.* 51(19): 11057-11065.
- Gewurtz SB, Bhavsar SP, Crozier PW, Diamond ML, Helm PA, Marvin CH, Reiner EJ. 2009. Perfluoroalkyl contaminants in window film: indoor/outdoor, urban/rural, and winter/summer contamination and assessment of carpet as a possible source. *Environ Sci Technol.* 43:7317–7323.
- Gewurtz SB, Martin PA, Letcher RJ, Burgess NM, Champoux L, Elliott JE, Weseloh DVC. 2016. Spatio-temporal trends and monitoring design of perfluoroalkyl acids in the eggs of gull (Larid) species from across Canada and parts of the United States. *Science of the Total Environment.* 565: 440–450.
- Gewurtz SB, Martin PA, Letcher RJ, Burgess NM, Champoux L, Elliott JE, Idrissi A. 2018. Perfluoroalkyl acids in European starling eggs indicate landfill and urban influences in Canadian terrestrial environments. *Environ Sci Technol.* 52: 5571–5580.
- Glüge J, Scheringer M, Cousins IT, DeWitt JC, Goldenman G, Herzke D, Lohmann R, Ng CA, Trieri X, Wang Z. 2020. An overview of the uses of per- and polyfluoroalkyl substances (PFAS). *Environ. Sci.: Processes Impacts.* 22:2345.
- Göckener B, Weber T, Rüdél H, Bücking M, Kolossa-Gehring M. 2020. Human biomonitoring of per- and polyfluoroalkyl substances in German blood plasma samples from 1982 to 2019. *Environ.Int.* 145: 106123.
- Göckener B, Flidner A, Rüdél H, Badry A, Koschorreck J. 2022. Long-Term Trends of Per- and Polyfluoroalkyl Substances (PFAS) in Suspended Particular Matter from German Rivers Using the Direct Total Oxidizable Precursor (dTOP) Assay. *Environ. Sci. Technol.* 56:208–217.
- Goeritz I, Falk S, Stahl T, Schafers C, Schlechtriem C. 2013. Biomagnification and tissue distribution of perfluoroalkyl substances (PFASs) in market-size rainbow trout (*Oncorhynchus mykiss*). *Environmental Toxicology and Chemistry.* 32 (9):2078–2088.
- Gonzalez-Gaya B, Dachs J, Roscales JL, Caballero G, Jimenez B. 2014. Perfluoroalkylated substances in the global tropical and subtropical surface oceans. *Environ Sci Technol.* 48:13076–13084.
- Gonzalez-Gaya B, Casal P, Jurado E, Dachs J, Jimenez B. 2019. Vertical transport and sinks of perfluoroalkyl substances in the global open ocean. *Environ Sci Process Impacts.* 21(11):1957–1969.

- Gorochategui E, Perez-Albaladejo E, Casas J, Lacorte S, Porte C. 2014. Perfluorinated chemicals: differential toxicity, inhibition of aromatase activity and alteration of cellular lipids in human placental cells. *Toxicol Appl Pharmacol.* 277(2): 124-30.
- Gorochategui E, Lacorte S, Tauler R, Martin FL. 2016. Perfluoroalkylated substance effects in *Xenopus laevis* A6 kidney epithelial cells determined by ATR-FTIR spectroscopy and chemometric analysis. *Chem Res Toxicol.* 29: 924–932.
- Goss K-U. 2008. The pKa values of PFOA and other highly fluorinated carboxylic acids. *Environ Sci Technol.* 42:456–458.
- Graber JM, Black TM, Shah NN, Caban-Martinez AJ, Lu SE, Brancard T, Yu CH, Turyk ME, Black K, Steinberg MB, Fan Z, Burgess JL. 2021. Prevalence and Predictors of Per- and Polyfluoroalkyl Substances (PFAS) Serum Levels among Members of a Suburban US Volunteer Fire Department. *Int. J. Environ. Res. Public Health.* 18(7):3730.
- Granby K, Tesdal Håland J. 2018. Per- and polyfluorinated alkyl substances (PFAS) in paper and board Food Contact Materials - Selected samples from the Norwegian market 2017. Technical University of Denmark. Available from : [https://www.mattilsynet.no/mat\\_og\\_vann/produksjon\\_av\\_mat/matkontaktmaterialer/rapport\\_fra\\_dtu\\_per\\_and\\_polyfluorinated\\_alkyl\\_substances\\_pfas\\_in\\_paper\\_and\\_board\\_food\\_contact\\_materials\\_2017.35382/binary/Rapport%20fra%20DTU%20Per-%20and%20polyfluorinated%20alkyl%20substances%20\(PFAS\)%20in%20paper%20and%20board%20Food%20Contact%20Materials,%202017](https://www.mattilsynet.no/mat_og_vann/produksjon_av_mat/matkontaktmaterialer/rapport_fra_dtu_per_and_polyfluorinated_alkyl_substances_pfas_in_paper_and_board_food_contact_materials_2017.35382/binary/Rapport%20fra%20DTU%20Per-%20and%20polyfluorinated%20alkyl%20substances%20(PFAS)%20in%20paper%20and%20board%20Food%20Contact%20Materials,%202017) [Accessed: 6 April 2022]
- Grandjean P, Andersen EW, Budtz-Jørgensen E, Nielsen F, Mølbak K, Weihe P, Heilmann C. 2012. Serum vaccine antibody concentrations in children exposed to perfluorinated compounds. *JAMA.* 307(4): 391-397.
- Grandjean P, Heilmann C, Weihe P, Nielsen F, Mogensen UB, Budtz-Jørgensen E. 2017. Serum vaccine antibody concentrations in adolescents exposed to perfluorinated compounds. *Environ Health Perspect.* 125(7): 077018.
- Granum B, Haug LS, Namork E, Stølevik SB, Thomsen C, Aaberge IS, van Loveren H, Løvik M, Nygaard UC. 2013. Pre-natal exposure to perfluoroalkyl substances may be associated with altered vaccine antibody levels and immune-related health outcomes in early childhood. *J.Immunotoxicol.* 10(4): 373-379.
- Greaves AK, Letcher RJ, Sonne C, Dietz R, Born EW. 2012. Tissue-specific concentrations and patterns of perfluoroalkyl carboxylates and sulfonates in East Greenland polar bears. *Environ Sci Technol.* 46:11575–11583.
- Greaves AK, Letcher RJ, Sonne C, Dietz R. 2013. Brain region distribution and patterns of bioaccumulative perfluoroalkyl carboxylates and sulfonates in East Greenland polar bears (*Ursus maritimus*). *Environmental Toxicology and Chemistry.* 32(3):713–722.
- Gremmel C, Frömel T, Knepper TP. 2016. Systematic determination of perfluoroalkyl and polyfluoroalkyl substances (PFASs) in outdoor jackets. *Chemosphere.* 160:173–180.
- Groffen T, Lasters R, Lopez-Antia A, Prinsen E, Bervoets L, Eens M. 2019. Limited reproductive impairment in a passerine bird species exposed along a perfluoroalkyl acid (PFAA) pollution gradient. *Science of the Total Environment.* 652:718–728.
- Grønnestad R, Villanger GD, Polder A, Kovacs KM, Lydersen C, Jenssen BM, Borgå K. 2018. Effects of a complex contaminant mixture on thyroid hormones in breeding hooded seal mothers and their pups. *Environmental Pollution.* 240:10–16.
- Grønnestad R, Vázquez VP, Arukwe A, Jaspers VLB, Jenssen BN, Karimi M, Lyche JL, Krøkje Å. 2019. Levels, Patterns, and Biomagnification Potential of Perfluoroalkyl Substances in a Terrestrial Food Chain in a Nordic Skiing Area. *Environ. Sci. Technol.* 53:13390–13397.
- Gui D, Zhang M, Zhang T, Zhang B, Lin W, Sun X, Yu X, Liu W, Wu Y. 2019. Bioaccumulation behaviour and spatiotemporal trends of per- and polyfluoroalkyl substances in Indo-Pacific humpback dolphins from the Pearl River Estuary, China. *Science of the Total Environment.* 658:1029–1038.
- Guillette TC, McCord J, Guillette M, Polera ME, Rachels KT, Morgeson C, Kotlarz N, Knappe DRU, Reading BJ, Strynar M, Belcher SM. 2020. Elevated levels of per- and polyfluoroalkyl substances in Cape Fear River striped bass (*Morone saxatilis*) are associated with biomarkers of altered immune and liver function. *Environment International.* 136:105358.

- Guo Z, Liu X, Krebs KA, Roache NF. 2009. Perfluorocarboxylic acids content in 166 articles of commerce. EPA/600/R-09/033. Available from: [https://cfpub.epa.gov/si/si\\_public\\_record\\_report.cfm?Lab=NRMRL&dirEntryId=206124](https://cfpub.epa.gov/si/si_public_record_report.cfm?Lab=NRMRL&dirEntryId=206124) [Accessed: 24 February 2022]
- Guo X, Zhang S, Lu S, Zheng B, Xie P, Chen J, Li G, Wu Q, Cheng H, Sang N. 2018. Perfluorododecanoic acid exposure induced developmental neurotoxicity in zebrafish embryos. *Environ Pollut.* 241:1018–1026.
- Gyllenhammar I, Benskin JP, Plassmann M, Sandblom O, Hedvall Kallerman P, Lampa E, Ankarberg EH. 2020. Levels of perfluoroalkyl substances (PFAS) in individual serum samples from first-time others in Uppsala, Sweden: results from year 2017-2019, and temporal trends for the time period 1996-2019. Report to the Swedish EPA (Health-Related Environmental Monitoring Program) Contract no. 215-18-001.
- Hakli O, Ertekin K, Ozer MS, Aycan S. 2008. Determination of pKa values of clinically important perfluorochemicals in non aqueous media. *Journal of Analytical Chemistry.* 63(11):1051–1056
- Hare EF, Shafrin EG, Zisman WA. 1954. Properties of films of adsorbed fluorinated acids. *J Phys Chem.* 58(3):236–239.
- Harris MW and Birnbaum LS. 1989. Developmental toxicity of perfluorodecanoic acid in C57BL/6N mice. *Fundam.Appl.Toxicol.* 12(3): 442-448.
- Harris MW, Uraih LC, Birnbaum LS. 1989. Acute toxicity of perfluorodecanoic acid in C57BL/6 mice differs from 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Toxicol.Sci.* 13(4): 723-736.
- Hart K, Gill VA, Kannan K. 2009. Temporal trends (1992-2007) of perfluorinated chemicals in northern sea otters (*Enhydra lutris kenyoni*) from south-central Alaska. *Arch Environ Contam Toxicol.* 56:607–614.
- Haukås M, Berger U, Hop H, Gulliksen B, Gabrielsen GW. 2007. Bioaccumulation of per- and polyfluorinated alkyl substances (PFAS) in selected species from the Barents Sea food web. *Environ Pollut.* 148:360–371.
- Health Canada. 2021. Sixth Report On Human Biomonitoring of Environmental Chemicals in Canada. Results of the Canadian Health Measures Survey Cycle 6 (2018–2019). Available at <https://www.canada.ca/en/health-canada/services/environmental-workplace-health/reports-publications/environmental-contaminants/sixth-report-human-biomonitoring.html>.
- Hedvall Kallerman P, Benskin JP, Plassmann M, Sandblom O, Halldin Ankarberg E, Gyllenhammar I. 2020. Temporal trends of poly- and perfluoroalkyl substances (PFASs) in serum from children at 4, 8, and 12 years of age, in Uppsala 2008-2019. Report to the Swedish EPA (Health-Related Environmental Monitoring Program) Contract no. 215-18-001.
- Hekster FM, de Voogt P, Pijnenburg AMCM, Laane RWPM. 2002. Perfluoroalkylated substances — aquatic environmental assessment. Report RIKZ/2002.043. Prepared at the University of Amsterdam and RIKZ (The State Institute for Coast and Sea), July 1, 2002. 99 pp.
- Herbst L, Hoffmann H, Kalus J, Reizlein K, Schmelzer U, Ibel K. 1985. Small-angle neutron-scattering on nematic lyotropic liquid-crystals. *Berichte der Bunsengesellschaft für physikalische Chemie.* 89(10):1050–1064.
- Herkert NJ, Kassotis CD, Zhang S, Han Y, Pulikkal VF, Sun M, Ferguson PL, Stapleton HM. 2022. Characterization of Per- and Polyfluorinated Alkyl Substances Present in Commercial Anti-fog Products and Their In Vitro Adipogenic Activity. *Environ. Sci. Technol.* 56:1162–1173.
- Herzke D, Posner S, Olsson E. 2009. Survey, screening and analyses of PFCs in consumer products. Swerea IVF Project report 09/41. Available from: <https://www.miljodirektoratet.no/globalassets/publikasjoner/klif2/publikasjoner/2578/ta2578.pdf> [Accessed: 24 February 2022]
- Herzke D, Olsson E, Posner S. 2012. Perfluoroalkyl and polyfluoroalkyl substances (PFASs) in consumer products in Norway – A pilot study. *Chemosphere.* 88: 980–987.
- Heydebreck F, Tang J, Xie Z, Ebinghaus R. 2016. Emissions of Per- and Polyfluoroalkyl Substances in a Textile Manufacturing Plant in China and Their Relevance for Workers' Exposure. *Environ. Sci. Technol.* 50:10386–10396.
- Hickey NJ, Crump D, Jones SP, Kennedy SW. 2009. Effects of 18 perfluoroalkyl compounds on mRNA expression in chicken embryo hepatocyte cultures. *Toxicological Sciences.* 111(2):311–320.

- Higgins CP, Luthy RG. 2006. Sorption of perfluorinated surfactants on sediments. *Environ Sci Technol.* 40:7251–7256.
- Hirata-Koizumi M, Fujii S, Furukawa M, Ono A, Hirose A. 2012. Repeated dose and reproductive/developmental toxicity of perfluorooctadecanoic acid in rats. *J Toxicol Sci.* 37(1):63–79.
- Hirata-Koizumi M, Fujii S, Hina K, Matsumoto M, Takahashi M, Ono A, Hirose A. 2015. Repeated dose and reproductive/developmental toxicity of long-chain perfluoroalkyl carboxylic acids in rats: perfluorohexadecanoic acid and perfluorotetradecanoic acid. *Fundamental Toxicological Sciences.* 2(4):177–190.
- Hjermitslev MH, Long M, Wielsøe M, Bonefeld-Jørgensen EC. 2020. Persistent organic pollutants in Greenlandic pregnant women and indices of foetal growth: The ACCEPT study. *Sci. Tot. Environ.* 698: 134118.
- Hoke RA, Bouchelle LD, Ferrell B, Buck RC. 2012. Comparative acute freshwater hazard assessment and preliminary PNEC development for eight fluorinated acids. *Chemosphere.* 87:725–733.
- Holmström KE, Johansson A-K, Bignert A, Lindberg P, Berger U. 2010. Temporal trends of perfluorinated surfactants in Swedish peregrine falcon eggs (*Falco peregrinus*) 1974-2007. *Environ Sci Technol.* 44 (11):4083–4088.
- Hori H, Yamamoto A, Hayakawa E, Taniyasu S, Yamashita N, Kutsuna S, Kiatagawa H, Arakawa R. 2005a. Efficient decomposition of environmentally persistent perfluorocarboxylic acids by use of persulfate as a photochemical oxidant. *Environ Sci Technol.* 39:2383–2388.
- Hori H, Yamamoto A, Katsuna S. 2005b. Efficient photochemical decomposition of long-chain perfluorocarboxylic acids by means of an aqueous/liquid CO<sub>2</sub> biphasic system. *Environ Sci Technol.* 39:7692–7697.
- Hori H, Nagaoka Y, Murayama M, Kutsuna S. 2008. Efficient decomposition of perfluorocarboxylic acids and alternative fluorochemical surfactants in hot water. *Environ Sci Technol.* 42(19):7238–7443.
- Houde M, Martin JW, Letcher RJ, Solomon KR, Muir DG. 2006a. Biological monitoring of polyfluoroalkyl substances: a review. *Environ Sci Technol.* 40:3463–3473.
- Houde M, Balmer BC, Brandsma S, Wells RS, Rowles TK, Solomon KR, Muir DCG. 2006b. Perfluoroalkyl compounds in relation to life-history and reproductive parameters in bottlenose dolphins (*Tursiops truncatus*) from Sarasota Bay, Florida, USA. *Environmental Toxicology and Chemistry.* 25(9):2405–2412.
- Houde M, Douville M, Despatie SP, De Silva AO, Spencer C. 2013. Induction of gene responses in St. Lawrence River northern pike (*Esox lucius*) environmentally exposed to perfluorinated compounds. *Chemosphere.* 92(9):1195–200.
- Hu J, Li J, Wang J, Zhang A, Dai J. 2014. Synergistic effects of perfluoroalkyl acids mixtures with J-shaped concentration-responses on viability of a human liver cell line. *Chemosphere.* 96: 81-88.
- Hu XC, Andrews DQ, Lindstrom AB, Bruton TA, Schaidler LA, Grandjean P, Lohmann R, Carignan CC, Blum A, Balan SA, et al. 2016. Detection of poly- and perfluoroalkyl substances (PFASs) in U.S. drinking water linked to industrial sites, military fire training areas, and wastewater treatment plants. *Environ.Sci.Techno.Lett.* 3(10): 344-350.
- Hu XC, Tokranov AK, Liddie J, Zhang X, Grandjean P, Hart JE, Laden F, Sun Q, Yeung LWY, Sunderland EM. 2019. Tap water contributions to plasma concentrations of poly- and perfluoroalkyl substances (PFAS) in a nationwide prospective cohort of U.S. women. *Environ.Health Perspect.* 127(6): 67006.
- Huang B-N, Haas A, Lieb M. 1987. A new method for the preparation of perfluorocarboxylic acids. *J Fluor Chem.* 36:49–62.
- Huang M, Jiao J, Zhuang P, Chen X, Wang J, Zhang Y. 2018. Serum polyfluoroalkyl chemicals are associated with risk of cardiovascular diseases in national US population. *Environ Int.* 119:37–46.
- Huber S, Ahrens L, Bardsen B-J, Siebert U, Bustnes JO, Vikingsson GA, Ebinghaus R, Herke D. 2012. Temporal trends and spatial differences of perfluoroalkylated substances in livers of harbour porpoise (*Phocoena phocoena*) populations from Northern Europe, 1991 – 2008. *Science of the Total Environment.* 419:216–224.
- Hurley MD, Sulbaek Andersen MP, Wallington TJ. 2004. Atmospheric chemistry of perfluorinated carboxylic acids: reaction with OH radicals and atmospheric lifetimes. *J Phys Chem* 108: 615-620.

- Ikawa Y, Tsuru S, Murata Y, Okawauchi M, Shigematsu M, Sugihara G. 1988. A pressure and temperature study on solubility and micelle formation of sodium perfluorodecanoate in aqueous-solution. *J Solution Chem.* 17:125–137.
- Impinen A, Nygaard UC, Lodrup Carlsen KC, Mowinckel P, Carlsen KH, Haug LS, Granum B. 2018. Prenatal exposure to perfluoroalkyl substances (PFASs) associated with respiratory tract infections but not allergy- and asthma-related health outcomes in childhood. *Environ Res.* 160:518–523.
- Inoue Y, Hashizume N, Yakata N, Murakami H, Suzuki Y, Kikushima E, Otsuka M. 2012. Unique physicochemical properties of perfluorinated compounds and their bioconcentration in common carp *Cyprinus carpio* L. *Arch Environ Contam Toxicol.* 62:672–680.
- Ishibashi H, Kim E-Y, Iwata H. 2011. Transactivation potencies of the Baikal seal (*Pusa sibirica*) peroxisome proliferator-activated receptor  $\alpha$  by perfluoroalkyl carboxylates and sulfonates: estimation of PFOA induction equivalency factors. *Environ Sci Technol.* 45:3123–3130.
- Inoue Y, Hashizume N, Yakata N, Murakami H, Suzuki Y, Kikushima E, Otsuka M. 2012. Unique physicochemical properties of perfluorinated compounds and their bioconcentration in common carp *Cyprinus carpio* L. *Arch Environ Contam Toxicol.* 62:672–680.
- Ishibashi H, Iwata H, Kim E-Y, Tao L, Kannan K, Amano M, Miyazaki M, Tanabe S, Batoev VB, Petrov EA. 2008a. Contamination and effects of perfluorochemicals in Baikal seal (*Pusa sibirica*). 1. residue level, tissue distribution and temporal trend. *Environ Sci Technol.* 42(7):2295–2301.
- Ishibashi H, Iwata H, Kim E-Y, Tao L, Kannan K, Tanabe S, Batoev VB, Petrov EA. 2008b. Contamination and effects of perfluorochemicals in Baikal seal (*Pusa sibirica*). 2. molecular characterization, expression level, and transcriptional activation of peroxisome proliferator-activated receptor  $\beta$ . *Environ Sci Technol.* 42(7):2302–2308.
- Ishibashi H, Yamauchi R, Matsuoka M, Kim J-W, Hirano M, Yamaguchi A, Tominaga N, Arizono K. 2008c. Fluorotelomer alcohols induce hepatic vitellogenin through activation of the estrogen receptor in male medaka (*Oryzias latipes*). *Chemosphere.* 71:1853–1859.
- Ishikawa N, Takahashi M, Sato T, Kitazume T. 1983. Ultrasound-promoted direct carboxylation of perfluoroalkyl iodides. *J Fluor Chem.* 22:585–587.
- Itoh S, Araki A, Miyashita C, Yamazaki K, Goudarzi H, Minatoya M, Ait Bamai Y, Kobayashi S, Okada E, Kashino I, et al. 2019. Association between perfluoroalkyl substance exposure and thyroid hormone/thyroid antibody levels in maternal and cord blood: The Hokkaido Study. *Environ Int.* 133(Pt A):105139.
- Jackson TW, Scheibly CM, Polera ME, Belcher SM. 2021. Rapid Characterization of Human Serum Albumin Binding for Per- and Polyfluoroalkyl Substances Using Differential Scanning Fluorimetry. *Environ Sci Technol.* 55(18):12291-12301
- Jahnke A, Berger U, Ebinghaus R, Temme C. 2007. Latitudinal gradient of airborne polyfluorinated alkyl substances in the marine atmosphere between Germany and South Africa (53° N-33°S). *Environ Sci Technol.* 41(9):3055–3061.
- Janousek RM, Lebertz S, Knepper TP. 2019. Previously unidentified sources of perfluoroalkyl and polyfluoroalkyl substances from building materials and industrial fabrics. *Environ Sci Processes Impacts.* 21:1936–1945.
- Jantzen CE, Annunziato KM, Cooper KR. 2016a. Behavioral, morphometric, and gene expression effects in adult zebrafish (*Danio rerio*) embryonically exposed to PFOA, PFOS, and PFNA. *Aquat Toxicol.* 180:123–130.
- Jantzen CE, Annunziato KA, Bugel SM, Cooper KR. 2016b. PFOS, PFNA, and PFOA sub-lethal exposure to embryonic zebrafish have different toxicity profiles in terms of morphometrics, behavior and gene expression. *Aquat Toxicol.* 175:160–70.
- Jensen TK, Andersen LB, Kyhl HB, Nielsen F, Christesen HT Grandjean P. 2015. Association between perfluorinated compound exposure and miscarriage in Danish pregnant women. *PLoS One.* 10(4):e0123496.
- Joel J, Kanna K, Lim HK, Moon HB, Kim SD. 2010. Bioconcentration of perfluorinated compounds in blackrock fish, *Sebastes schlegelii*, at different salinity levels. *Environ Toxicol Chem.* 29(11):2529–2535.

- Ji K, Kim S, Kho Y, Paek D, Sakong J, Ha J, Kim S, Choi K. 2012. Serum concentrations of major perfluorinated compounds among the general population in Korea: Dietary sources and potential impact on thyroid hormones. *Environ.Int.* 45: 78–85.
- Jiawei T, Yizhen Z, Jiajun S, Xuelu S, Chao S, Chunhui Z. 2019. Occurrence and characteristics of perfluoroalkyl substances (PFASs) in electroplating industrial wastewater. *Water Sci Technol.* 79(4):731–740.
- Jo A, Ji K, Choi K. 2014. Endocrine disruption effects of long-term exposure to perfluorodecanoic acid (PFDA) and perfluorotridecanoic acid (PFTrDA) in zebrafish (*Danio rerio*) and related mechanisms. *Chemosphere.* 108:360–366.
- Joensen UN, Veyrand B, Antignac JP, Blomberg Jensen M, Petersen JH, Marchand P, Skakkebaek NE, Andersson AM, Le Bizec B, Jørgensen N. 2013. PFOS (perfluorooctanesulfonate) in serum is negatively associated with testosterone levels, but not with semen quality, in healthy men. *Hum.Reprod.* 28(3): 599–608.
- Joerss H, Xie Z, Wagner CC, Wilken JvA, Sunderland EM, Ebinghaus R. 2020. Transport of legacy perfluoroalkyl substances and the replacement compound HFPO-DA through the Atlantic Gateway to the Arctic Ocean – is the Arctic a sink or a source? *Environ Sci Technol.* 54(16):9958–9967.
- Johansson JH, Salter ME, Acosta Navarro JC, Leck C, Nilsson ED, Cousins IT. 2019. Global transport of perfluoroalkyl acids via sea spray aerosol. *Environmental Science: Processes & Impacts.* 21(4):635–649.
- Johnson GR. 2022. PFAS in soil and groundwater following historical land application of biosolids. *Water Research.* 211:118035.
- Jones PD, Hu W, De Coen W, Newsted JL, Giesy JP. 2003. Binding of perfluorinated fatty acids to serum proteins. *Environmental Toxicology and Chemistry.* 22 (11):2639–2649.
- Kaboré HA, Vo Duy S, Munoz G, Méité L, Desrosiers M, Liu J, Sory TK, Sauvé S. 2018. Worldwide drinking water occurrence and levels of newly-identified perfluoroalkyl and polyfluoroalkyl substances. *Sci.Total Environ.* 616-617: 1089-1100.
- Kaiser MA, Larsen BS, Kao C-P, Buck RC. 2005. Vapor pressures of perfluorooctanoic, -nonanoic, -decanoic, -undecanoic, and -dodecanoic acids. *J Chem Eng Data.* 50:1841–1843.
- Kameoka H, ItoK, Ono J, Banno A, Matsumura C, Haga Y, Endo K, Mizutani S, Yabuki Y. 2021. Investigation of perfluoroalkyl carboxylic and sulfonic acids in leachates from industrial and municipal solid waste landfills, and their treated waters and effluents from their closest leachate treatment plants. *Journal of Material Cycles and Waste Management.* 24:287–296.
- Kannan K. 2011. Perfluoroalkyl and polyfluoroalkyl substances: current and future perspectives. *Environ Chem.* 8:333–338.
- Kärrman A, Ericson I, VanBavel B, Ola Darnerud P, Aune M, Glynn A, Ligneli S, Lindström G. 2007. Exposure of perfluorinated chemicals through lactation: Levels of matched human milk and serum and a temporal trend, 1996-2004, in Sweden. *Environ.Health Perspect.* 115(2): 226-230.
- Kärrman A, Domingo JL, Llebaria X, Nadal M, Bigas E, van Bavel B, Lindström G. 2010. Biomonitoring perfluorinated compounds in Catalonia, Spain: Concentrations and trends in human liver and milk samples. *Environ.Sci.Pollut.Res.Int.* 17(3): 750-758.
- Kato H, Fujii S, Takahashi M, Matsumoto M, Hirata-Koizumi M, Ono A, Hirose A. 2015. Repeated dose and reproductive/developmental toxicity of perfluorododecanoic acid in rats. *Environ Toxicol.* 30(11):1244–1263.
- Katz S, Muir D, Gamberg M. 2009. Bioaccumulation of perfluorinated compounds in the vegetation-caribou-wolf food chain In: Smith S, Stow J, Edwards J, editors. *Synopsis of research conducted under the 2008-2009 Northern Contaminants Program.* Ottawa, Ontario: Department of Indian Affairs and Northern Development. p. 215–220.
- Kauck EA, Diesslin AR. 1951. Some properties of perfluorocarboxylic acids. *Ind Eng Chem.* 43:2332–2334.
- Kelly BC, Gobas FAPC, McLachlan MS. 2004. Intestinal absorption and biomagnification of organic contaminants in fish, wildlife and humans. *Environ Toxicol Chem.* 23(10):2324–2336.

- Kelly BC, Ikonomidou MG, Blair JD, SurrIDGE B, Hoover D, Grace R, Gobas FAPC. 2009. Perfluoroalkyl contaminants in an arctic marine food web: Tropic magnification and wildlife exposure. *Environ Sci Technol.* 43:4037–4043.
- Kelly BC, Ikonomidou MG, Blair JD, SurrIDGE B, Hoover D, Grace R, Gobas FAPC. 2019. Perfluoroalkyl contaminants in an Arctic marine food web: trophic magnification and wildlife exposure. *Environ Sci Technol.* 43:4037–4043.
- Khalil N, Ducatman AM, Sinari S, Billheimer D, Hu C, Littau S, Burgess JL. 2020. Per-and polyfluoroalkyl substance and cardio metabolic markers in firefighters. *J.Occup.Environ.Med.* 62(12): 1076-1081.
- Kielsen K, Shamim Z, Ryder LP, Nielsen F, Grandjean P, Budtz-Jørgensen E, Heilmann C. 2016. Antibody response to booster vaccination with tetanus and diphtheria in adults exposed to perfluorinated alkylates. *J.Immunotoxicol.* 13(2): 270-273.
- Kim M, Son J, Park MS, Ji Y, Chae S, Jun C, Bae J-S, Kwon TK, Choo Y-S, Yoon H, Yoon D, Ryoo J, Kim S-H, Park M-J, Lee H-S. 2013. In vivo evaluation and comparison of developmental toxicity and teratogenicity of perfluoroalkyl compounds using *Xenopus* embryos. *Chemosphere.* 93(6):1153–60.
- Kim DH, Kim UJ, Kim HY, Choi SD, Oh JE. 2016. Perfluoroalkyl substances in serum from South Korean infants with congenital hypothyroidism and healthy infants--its relationship with thyroid hormones. *Environ.Res.* 147: 399-404.
- Ki Yong Kim 1 , Mlamuli Ndabambi 1 , Sol Choi, Jeong-Eun Oh. 2021. Legacy and novel perfluoroalkyl and polyfluoroalkyl substances in industrial wastewater and the receiving river water: Temporal changes in relative abundances of regulated compounds and alternatives. *Water Research.* 191:116830.
- Kirk M, Smurthwaite K, Braunig J, Trevenar S, D'Este C, Lucas R, Lal A, Korda R, Clements A, Mueller J, et al. 2018. The PFAS Health Study – Systematic Literature Review. Canberra: Australian National University.
- Kissa E. 1994. Fluorinated Surfactants. Synthesis Properties Applications. New York (NY): Marcel Dekker, Inc.
- Kjeldsen LS and Bonefeld-Jørgensen EC. 2013. Perfluorinated compounds affect the function of sex hormone receptors. *Environ.Sci.Pollut.Res.Int.* 20(11): 8031-8044.
- Klevens HB, Raison M. 1954. Association dans les perfluoroacides. III. Etudes des tensions superficielles. *J Chim Phys Physicochim Biol.* 51.
- Knudsen LB, Borgå K, Jørgensen EH, van Bavel B, Schlabach M, Verreault J, Gabrielsen GW. 2007. Halogenated organic contaminants and mercury in northern fulmars (*Fulmarus glacialis*): levels, relationships to dietary descriptors and blood to liver comparison. *Environmental Pollution.* 146:25–33.
- Kotthoff M, Müller J, Jüriling H, Schlummer M, Fiedler D. 2015. Perfluoroalkyl and polyfluoroalkyl substances in consumer products. *Environ Sci Pollut Res.* 22:14546–14559.
- Kubota A, Stegeman JJ, Goldstone JV, Nelson DR, Kim E-Y, Tanabe S, Iwata H. 2011. Cytochrome P450 CYP2 genes in the common cormorant: Evolutionary relationships with 130 diapsid CYP2 clan sequences and chemical effects on their expression. *Comparative Biochemistry and Physiology Part C: Toxicology & Pharmacology.* 153(3):280–289.
- Kudo N. 2015. Metabolism and pharmacokinetics. In: Dewitt J, editor. Toxicological effects of perfluoroalkyl and polyfluoroalkyl substances. Switzerland: Springer International Publishing. p. 151-175.
- Kudo N, Suzuki-Nakajima E, Mitsumoto A, Kawashima Y. 2006. Responses of the liver to perfluorinated fatty acids with different carbon chain length in male and female mice: in relation to induction of hepatomegaly, peroxisomal beta-oxidation and microsomal 1-acylglycerophosphocholine acyltransferase. *Biol Pharm Bull.* 29(9):1952–1957.
- Kunieda H, Shinoda K. 1976. Krafft points, critical micelle concentrations, surface tension, and solubilizing power of aqueous solutions of fluorinated surfactants. *J Phys Chem.* 80(22):2468–2470.
- Kurtz AE, Reiner JL, West KL, Jensen BA. 2019. Perfluorinated alkyl acids in Hawaiian cetaceans and potential biomarkers of effect: peroxisome proliferator-activated receptor alpha and cytochrome P450 4A. *Environ Sci Technol.* 53:2830–2839.

- Kwadijk CJAF, Korytar P, Koelmans AA. 2010. Distribution of perfluorinated compounds in aquatic systems in the Netherlands. *Environ Sci*44:3746–3751.
- Kwok KY, Yamazaki E, Yamashita N, Taniyasu S, Murphy MB, Horii Y, Petrick G, Kallerborn R, Kannan K, Murano K, Lam PKS. 2013. Transport of perfluoroalkyl substances (PFAS) from an arctic glacier to downstream locations: implications for sources. *Science of the Total Environment*. 447:46–55.
- Kwon EJ, Shin JS, Kim BM, Shah-Kulkarni S, Park H, Kho YL, Park EA, Kim YJ, Ha EH. 2016. Prenatal exposure to perfluorinated compounds affects birth weight through GSTM1 polymorphism. *J. Occup. Environ. Med.* 58(6): e198-205.
- Labadie P, Chevreuil M. 2011. Partitioning behaviour of perfluorinated alkyl contaminants between water, sediment and fish in the Orge River (nearby Paris, France). *Environ Pollut.* 159(2):391–397.
- Laitinen JA, Koponen J, Koikkalainen J, Kiviranta H. 2014. Firefighters' exposure to perfluoroalkyl acids and 2-butoxyethanol present in firefighting foams. *Toxicol. Lett.* 231(2): 227-232.
- Lam H, Cho C, Lee JS, Soha H, Lee B, Lee JA, Tatarozako N, Sasaki K, Saito N, Iwabuchi K, Kannan K, Cho H. 2014. Perfluorinated alkyl substances in water, sediment, plankton and fish from Korean rivers and lakes: A nationwide survey. *Science of the Total Environment*. 491–492:154–162.
- Lam JCW, Lyu J, Kwok KY, Lam PKS. 2016. Perfluoroalkyl substances (PFASs) in marine mammals from the South China Sea and their temporal changes 2002-2014: concern for alternatives of PFOS? *Environ Sci Technol.* 50:6728–6736.
- Land M, de Wit CA, Bignert A, Cousins I, Herzke D, Johansson JH, Martin JW. 2018. What is the effect of phasing out long-chain per- and polyfluoroalkyl substances on the concentrations of perfluoroalkyl acids and their precursors in the environment? A systematic review. *Environ Evid* 7, 4.
- Lang JR, Allred BM, Field JA, Levis JW, Barlaz MA. 2017. National Estimate of Per- and Polyfluoroalkyl Substance (PFAS) Release to U.S. Municipal Landfill Leachate. *Environ. Sci. Technol.* 51:2197–2205.
- Langberg HA, Breedveld GD, Slinde GA, Grønning HM, Høisæter Å, Jartun M, Rundberget T, Jenssen BM, Hale SE. 2020. Fluorinated Precursor Compounds in Sediments as a Source of Perfluorinated Alkyl Acids (PFAA) to Biota. *Environ. Sci. Technol.* 54:13077–13089.
- Lasters R, Groffen T, Lopez-Antia A, Bervoets L, Eens M. 2019. Variation in PFAA concentrations and egg parameters throughout the egg-laying sequence in a free-living songbird (the great tit, *Parus major*): implications for biomonitoring studies. *Environmental Pollution*. 246:237–248.
- Latala A, Nedzi M, Stepnowski P. 2009. Acute toxicity assessment of perfluorinated carboxylic acids towards the Baltic microalgae. *Environmental Toxicology and Pharmacology*. 28:167–171.
- Lau C, Das KP, Tatum K, Zehr D, Wood CR, Rosen MB. 2009. Developmental toxicity of perfluorononanoic acid in the mouse. *Toxicologist*. 108:417.
- Lee JK, Kim SH. 2018. Correlation between mast cell-mediated allergic inflammation and length of perfluorinated compounds. *J Toxicol Environ Health A*. 81(9): 302-313.
- Lehmler H-J, Oyewumi M-O, Jay M, Bummer PM. 2001. Behaviour of partially fluorinated carboxylic acids at the air-water interface. *J Fluor Chem*. 107:141–146.
- Lescord GL, Kidd KA, De Silva AO, Williamson M, Spencer C, Wang X, Muir DCG. 2015. Perfluorinated and polyfluorinated compounds in lake food wens from the Canadian High Arctic. *Environ Sci Technol.* 49:2694–2702.
- Letcher RJ, Bustnes OJ, Dietz R, Jenssen BM, Jørgensen EH, Sonne C, Verreault J, Vijayan MM, Gabrielsen GW. 2010. Exposure and effects assessment of persistent organohalogen contaminants in Arctic wildlife and fish. *Science of the Total Environment*. 408:2995–3043.
- Letcher RJ, Chu SG, McKinney MA, Tomy GT, Dietz R, Sonne C. 2014. Comparative hepatic in vitro depletion and metabolite formation of major perfluorooctane sulfonate precursors in polar bear, ringed seal and beluga whale. *Chemosphere*. 112:225–231.
- Letcher, R.J., Su, G., Moore, J.N., Williams, L.L., Martin, P.A., de Solla, S.R. and Bowerman, W.W. 2015. Perfluorinated sulfonate and carboxylate compounds and precursors in herring gull eggs from across the Laurentian Great Lakes of North America: Temporal and recent spatial comparisons and exposure implications. *Science of the Total Environment* 538, 468-477.



- Letcher, RJ, Morris, AD, Dyck, M, Sverko, E., Reiner, E, Blair, DAD, Chu, SG and Shen, L. 2018. Legacy and new halogenated persistent organic pollutants in polar bears from a contamination hotspot in the Arctic, Hudson Bay Canada. *Science of the Total Environment* 610-611, 121-136.
- Li L, Zheng H, Wang T, Cai M, Wang, P. 2018. Perfluoroalkyl acids in surface seawater from the North Pacific to the Arctic Ocean: Contamination, distribution and transportation. *Environ Pollut.* 238:168–176.
- Li J, Cai D, Chu C, Li Q, Zhou Y, Hu L. 2020a. Transplacental transfer of per- and polyfluoroalkyl substances (PFASs): differences between preterm and full-term deliveries and associations with placental transporter mRNA expression. *Environ Sci Technol.* 54(8):5062–5070.
- Li Y, Yu N, Du L, Shi W, Yu H, Song M. 2020b. Transplacental transfer of per- and polyfluoroalkyl substances identified in paired maternal and cord sera using suspect and non-target screening. *Environ Sci Technol.* 54(6):3407–3416.
- Li X, Hua Z. 2021. Multiphase distribution and spatial patterns of perfluoroalkyl acids (PFAAs) associated with catchment characteristics in a plain river network. *Chemosphere.* 263:128284.
- Lindstrom AB, Strynar MJ, Delinsky AD, Nakayama SH, McMillan L, Libelo EL, Neill M, Thomas L. 2011. Application of WWTP Biosolids and Resulting Perfluorinated Compound Contamination of Surface and Well Water in Decatur, Alabama, USA. *Environ. Sci. Technol.* 45:8015–8021.
- Lind V, Priskorn L, Lassen TH, Nielsen F, Kyhl HB, Kristensen DM, Christesen HT, Steener J, Grandjean P, Jensen TK. 2016. Prenatal exposure to perfluoroalkyl substances and anogenital distance at 3 months of age as marker of endocrine disruption. *Reprod Toxicol.* S0890-6238(16):30265–9.
- Liu W, Chen S, Quan, X, Jin Y-H. 2008a. Toxic effect of serial perfluorosulfonic and perfluorocarboxylic acids on the membrane system of a freshwater alga measured by flow cytometry. *Environ Toxicol Chem.* 27(7):1597–1604.
- Liu Y, Wang J, Wei Y, Zhang H, Xu M, Dai J. 2008b. Induction of time-dependent oxidative stress and related transcriptional effects of perfluorododecanoic acid in zebrafish liver. *Aquat Toxicol.* 89(4):242–50.
- Liu C, Gin KYH, Chang VWC, Goh BPL, Reinhard M. 2011a. Novel perspectives on the bioaccumulation of PFCs – the concentration dependency. *Environ Sci and Technol.* 45:9758–9764.
- Liu Y, Wang J, Fang X, Zhang H, Dai, J. 2011b. The thyroid-disrupting effects of long-term perfluorononanoate exposure on zebrafish (*Danio rerio*). *Ecotoxicology.* 20(1): 47–55.
- Liu WL, Ko YC, Hwang BH, Li ZG, Yang TCC, Lee MR. 2012. Determination of perfluorocarboxylic acids in water by ion-pair dispersive liquid-liquid microextraction and gas chromatography-tandem mass spectrometry with injection port derivation. *Analytica Chimica Acta.* 726:28–34.
- Liu C, Chang VWC, Gin KYH, Nguyen VT. 2014a. Genotoxicity of perfluorinated chemicals (PFCs) to the green mussel (*Perna viridis*). *Science of the Total Environment.* 487: 117–122.
- Liu C, Chang VWC, Gin KYH. 2014b. Oxidative toxicity of perfluorinated chemicals in green mussel and bioaccumulation factor dependent quantitative structure-activity relationship. *Environmental Toxicology and Chemistry.* 33 (10): 2323–2332.
- Liu X, Guo Z, Krebs KA, Pope RH, Roache NF. 2014c. Concentrations and trends of perfluorinated chemicals in potential indoor sources from 2007 through 2011 in the US. *Chemosphere.* 98:51–57.
- Liu H, Sheng N, Zhang W, Dai J. 2015. Toxic effects of perfluorononanoic acid on the development of zebrafish (*Danio rerio*) embryos. *J Environ Sci.* 32: 26–34.
- Liu J, Qu R, Wang Z, Mendoza-Sanchez I, Sharma VK. 2017. Thermal- and photo-induced degradation of perfluorinated carboxylic acids: kinetics and mechanism. *Water Research.* 126:12–18.
- Liu Y, Richardson ES, Derocher AE, Lunn NJ, Lehmler J, Li X, Zhang Y, Cui JY, Cheng L, Martin JW. 2018a. Hundreds of unrecognized halogenated contaminants discovered in polar bear serum. *Angew Chem Int Ed.* 57:16401–16406.
- Liu G, Dhana K, Furtado JD, Rood J, Zong G, Liang L, Qi L, Bray GA, DeJonge L, Coull B, et al. 2018b. Perfluoroalkyl substances and changes in body weight and resting metabolic rate in response to weight-loss diets: A prospective study. *PLoS Med* 15(2):e1002502.

- Liu C and Gin KY. 2018. Immunotoxicity in green mussels under perfluoroalkyl substance (PFAS) exposure: reversible response and response model development. *Environ Toxicol Chem.* 37(4):1138-1145.
- Liu J, Zhao X, Liu Y, Qiao X, Wang X, Ma M, Jin X, Liu C, Zheng B, Shen J, Guo R. 2019a. High contamination, bioaccumulation and risk assessment of perfluoroalkyl substances in multiple environmental media at the Baiyangdian Lake. *Ecotoxicology and Environmental Safety.* 182:109454.
- Liu W, He W, Wu J, Qin N, He Q, Xu F. 2019b. Residues, bioaccumulations and biomagnification of perfluoroalkyl acids (PFAAs) in aquatic animals from Lake Chaohu, China. *Environmental Pollution.* 240:607–614.
- Liu G, Zhang B, Hu Y, Rood J, Liang L, Qi L. 2020. Associations of perfluoroalkyl substances with blood lipids and apolipoproteins in lipoprotein subspecies: the POUNDS-lost study. *Environ Health.* 19(1):5.
- Liu S, Zhao S, Liang Z, Wang F, Sun F, Chen D. 2021. Perfluoroalkyl substances (PFASs) in leachate, fly ash, and bottom ash from waste incineration plants: Implications for the environmental release of PFAS. *Science of the Total Environment* 795:148468.
- Liu M, Munoz G, Duy SV, Sauvé S, Liu J. 2022. Per- and Polyfluoroalkyl Substances in Contaminated Soil and Groundwater at Airports: A Canadian Case Study. *Environ. Sci. Technol.* 56: 885–895.
- Llorca M, Farre M, Tavano MS, Alonso B, Koremblit G, Barcel OD. 2012. Fate of a broad spectrum of perfluorinated compounds in soils and biota from Tierra del Fuego and Antarctica. *Environ Pollut.* 163:158–166.
- Loganathan BG, Sajwan KS, Sinclair E, Kumar KS, Kannan K. 2007. Perfluoroalkyl sulfonates and perfluorocarboxylates in two wastewater treatment facilities in Kentucky and Georgia. *Water Research.* 41:4611–4620.
- Loi EIH, Yeung LWY, Taniyasu S, Lam PKS, Kannan K, Yamashita N. 2011. Trophic magnification of poly- and perfluorinated compounds in a subtropical food web. *Environ Sci Technol.* 45:5506–5513.
- Loi EIH, Yeung LWY, Mabury SA, Lam PKS. 2013. Detections of commercial fluorosurfactants in Hong Kong marine environment and human blood: A Pilot Study. *Environ Sci*47(9): 4677–4685. doi:10.1021/es303805k.
- Long M, Knudsen AKS, Pedersen HS, Bonefeld-Jørgensen EC. 2015. Food intake and serum persistent organic pollutants in the Greenlandic pregnant women: The ACCEPT sub-study. *Sci.Total Environ.* 529: 198-212.
- Loos R, Locoro G, Bidoglio G, Contini S, Rimaviciute E, Gawlik BM. 2009. EU-wide survey of polar organic persistent pollutants in European river waters. *Environmental Pollution.* 157(2):561–568.
- Loos R, Locoro G, Gomero S, Contini S, Schwesig D, Werres F, Balsaa P, Gans O, Weiss S, Blaha L, Bolchi M, Gawlik BM. 2010. Pan-European survey on the occurrence of selected polar organic persistent pollutants in ground water. *Water Research.* 44(14):4115–4126.
- Lopez-Antia A, Groffen T, Lasters R, AbdElgawad H, Sun J, Asard H, Bervoets L, Eens M. 2019. Perfluoroalkyl acids (PFAAs) concentrations and oxidative status in two generations of Great Tits inhabiting a contamination hotspot. *Environ Sci Technol.* 53:1617–1626
- Lu GH, Liu JC, Sun LS, Yuan LJ. 2015. Toxicity of perfluorononanoic acid and perfluorooctane sulfonate to *Daphnia magna*. *Water Science and Engineering.* 8(1):40–48.
- Lum KJ, Sundaram R, Barr DB, Louis TA, Buck Louis, GM. 2017. Perfluoroalkyl chemicals, menstrual cycle length, and fecundity: findings from a prospective pregnancy study. *Epidemiology.* 28(1):90–98.
- MacInnis JJ, Lehnerr I, Muir DCG, St. Pierre KA, St. Louis VL, Spencer C, De Silva AO. 2019. Fate and transport of perfluoroalkyl substances from snowpacks into a lake in the High Arctic of Canada. *Environ Sci Technol.* 53(18):10753–10762.
- Mackay D, Fraser A. 2000. Bioaccumulation of persistent organic chemicals: mechanism and models. *Environmental Pollution.* 110:375–391.
- MacLeod M, Breitholtz M, Cousins IT, de Wit CA, Persson LM, Rudén C, McLachlan MS. 2014. Identifying chemicals that are planetary boundary threats. *Environ Sci Technol.* 48: 11057–11063.

- Makey CM, Webster TF, Martin JW, Shoeib M, Harner T, Dix-Cooper L, Webster GM. 2017. Airborne precursors predict maternal serum perfluoroalkyl acid concentrations. *Environ. Sci. Technol.* 51 (13): 7667-7675.
- Manzano-Salgado CB, Casas M, Lopez-Espinosa MJ, Ballester F, Basterrechea M, Grimalt JO, Jiménez AM, Kraus T, Schettgen T, Sunyer J, et al. 2015. Transfer of perfluoroalkyl substances from mother to fetus in a Spanish birth cohort. *Environ.Res.* 142: 471-478.
- Martin JW, Mabury SA, Solomon KR, Muir DCG. 2003a. Dietary accumulation of perfluorinated acids in juvenile rainbow trout (*Oncorhynchus mykiss*). *Environ Toxicol Chem.* 22:189-195.
- Martin JW, Mabury SA, Solomon KR, Muir DCG. 2003b. Bioconcentration and tissue distribution of perfluorinated acids in rainbow trout (*Oncorhynchus mykiss*). *Environ Toxicol Chem.* 22:196-204.
- Martin JW, Whittle M, Muir DCG, Mabury SA. 2004. Perfluoroalkyl contaminants in a food web from Lake Ontario. *Environ Sci* 38:5379-5385.
- Matsubara E, Harada K, Inoue K, Koizumi A. 2006. Effects of perfluorinated amphiphiles on backward swimming in *Paramecium caudatum*. *Biochemical and Biophysical Research Communication.* 339:554-561.
- Menger F, Pohl J, Ahrens L, Carlsson G, Örn S. 2020. Behavioural effects and bioconcentration of per- and polyfluoroalkyl substances (PFASs) in zebrafish (*Danio rerio*) embryos. *Chemosphere.* 245:125573.
- Mertens JJ, Sved DW, Marit GB, Myers NR, Stetson PL, Murphy SR, Schmit B, Shinohara M, Farr CH. 2010. Subchronic toxicity of S-111-S-WB in Sprague Dawley rats. *Int J Toxicol.* 29(4):358-71.
- Miljeteig C, Gabrielsen GW, Strøm H, Gavrilov MV, Lie E, Jenssen BM. 2012. Eggshell thinning and decreased concentrations of vitamin E are associated with contaminants in eggs of ivory gulls. *Science of the Total Environment.* 431:92-99.
- Miller A, Elliott JE, Elliott KH, Lee S, Cyr F. 2015. Temporal trends of perfluoroalkyl substances (PFAS) in eggs of coastal and offshore birds: increasing PFAS levels associated with offshore bird species breeding on the Pacific coast of Canada and wintering near Asia. *Environmental Toxicology and Chemistry.* 34 (8):1799-1808.
- Mobacke I, Lind L, Dunder L, Salihovic S, Lind PM. 2018. Circulating levels of perfluoroalkyl substances and left ventricular geometry of the heart in the elderly. *Environ Int.* 115:295-300.
- Mondal D, Weldon RH, Armstrong BG, Gibson LJ, Lopez-Espinosa MJ, Shin HM, Fletcher T. 2014. Breastfeeding: A potential excretion route for mothers and implications for infant exposure to perfluoroalkyl acids. *Environ.Health Perspect.* 122(2): 187-192.
- Moodie D, Coggan T, Berry K, Kolobaric A, Fernandes M, Lee E, Reichman S, Nugegoda D, Clarke BO. 2021. Legacy and emerging per- and polyfluoroalkyl substances (PFASs) in Australian biosolids. *Chemosphere.* 270:129143.
- Morello-Frosch R, Cushing LJ, Jesdale BM, Schwartz JM, Guo W, Guo T, Wang M, Harwani S, Petropoulou S-E, Duong W, et al. 2016. Environmental chemicals in an urban population of pregnant women and their newborns from San Francisco. *Environ.Sci.Technol.* 50(22): 12464-12472.
- Moroi Y, Yano H, Shibata O, Yonemitsu T. 2001. Determination of acidity constants of perfluoroalkanoic acids. *Bull Chem Soc Jpn.* 74:667-672.
- Mukerjee P, Handa T. 1981. Adsorption of fluorocarbon and hydrocarbon surfactants to air-water, hexane-water, and perfluorohexane-water interfaces - relative affinities and fluorocarbon-hydrocarbon nonideality effects. *J Phys Chem.* 85:2298-2303.
- Müller CE, De Silva AO, Small J, Williamson M, Wang X, Morris A, Katz S, Gamberg M, Muir DCG. 2011. Biomagnification of Perfluorinated Compounds in a Remote Terrestrial Food Chain: Lichen - Caribou - Wolf. *Environ Sci Technol.* 45:8665-8673.
- Mehvish Mumtaz, Yixiang Bao, Liquan Liu, Jun Huang,\* Giovanni Cagnetta,\* and Gang Yu. 2019. Per- and Polyfluoroalkyl Substances in Representative Fluorocarbon Surfactants Used in Chinese Film-Forming Foams: Levels, Profile Shift, and Environmental Implications. *Environ. Sci. Technol. Lett.* 6:259-264.
- Mumtaz M, Bao Y, Liu L, Huang J, Cagnetta G, Yu G. 2019. Per- and Polyfluoroalkyl Substances in Representative Fluorocarbon Surfactants Used in Chinese Film-Forming Foams: Levels, Profile Shift, and Environmental Implications. *Environ. Sci. Technol. Lett.* 6:259-264.

- Munoz G, Budzinski H, Babut M, Drouineau H, Lauzent M, Le Menach K, Lobry J, Selleslagh J, Simonnet-Laprade, Labadie P. 2017b. Evidence for the trophic transfer of perfluoroalkylated substances in a temperate macrotidal estuary. *Environ Sci Technol.* 51:8450–8459.
- Munoz G, Labadie P, Geneste E, Pardon P, Tartu S, Chastel O, Budzinski H. 2017a. Biomonitoring of fluoroalkylated substances in Antarctica seabird plasma: development and validation of a fast and rugged method using on-line concentration liquid chromatography tandem mass spectrometry. *Journal of Chromatography A.* 1513:107–117.
- Munoz G, Budzinski H, Babut M, Lobry J, Selleslagh J, Tapie N, Labadie P. 2019. Temporal variations of perfluoroalkyl substances partitioning between surface water, suspended sediment, and biota in a macrotidal estuary. *Environ Sci Technol.* 53:319–326.
- Murakami M, Adachi N, Saha M, Morita C, Takada H. 2011. Levels, temporal trends, and tissue distribution of perfluorinated surfactants in freshwater fish from Asian countries. *Arch Environ Contam Toxicol.* 61:631–641.
- Nabb DL, Szostek B, Himmelstein MW, Mawn MP, Gargas ML, Sweeney LM, Stadler JC, Buck RC, Fasano WJ. 2007. In vitro metabolism of 8-2 fluorotelomer alcohol: interspecies comparisons and metabolic pathway refinement. *Toxicological Sciences.* 100(2):333–344.
- Naile JE, Khim JS, Hong S, Park J, Kwon B-O, Ryu JS, Hwang JH, Jones PD, Giesy JP. 2013. Distributions and bioconcentration characteristics of perfluorinated compounds in environmental samples collected from the west coast of Korea. *Chemosphere.* 90:387–394.
- Ng CA, Hungerbuhler K. 2013. Bioconcentration of perfluorinated alkyl acids: how important is specific binding? *Environmental Science and Technology.* 47:7214–7223.
- Ng CA, Hungerbuhler K. 2014. Bioaccumulation of perfluorinated alkyl acids: observations and models. *Environ Sci Technol.* 48:4637–4648.
- Nguyen HT, McLachlan MS, Tschärke B, Thai P, Braeunig J, Kaserzon S, O'Brien JW, Mueller JF. 2022. Background release and potential point sources of per- and polyfluoroalkyl substances to municipal wastewater treatment plants across Australia. *Chemosphere.* 293:133657.
- Nian M, Li QQ, Bloom M, Qian ZM, Syberg KM, Vaughn MG, Wang SQ, Wei Q, Zeeshan M, Gurrain N, et al. 2019. Liver function biomarkers disorder is associated with exposure to perfluoroalkyl acids in adults: Isomers of C8 Health Project in China. *Environ Res.* 172:81–88.
- [NICNAS] National Industrial Chemicals Notification and Assessment Scheme. 2017. Indirect precursors of long-chain perfluorocarboxylic acids (PFCAs): Human health tier II assessment. Available from: [https://www.nicnas.gov.au/chemical-information/imap-assessments/imap-group-assessment-report?assessment\\_id=1811](https://www.nicnas.gov.au/chemical-information/imap-assessments/imap-group-assessment-report?assessment_id=1811) [Accessed: 22 June 2020]
- [NICNAS] National Industrial Chemicals Notification and Assessment Scheme. 2019. Indirect precursors to perfluorocarboxylic acids: Environment tier II assessment. Available from: <https://www.nicnas.gov.au/chemical-information/imap-assessments/imap-assessments/tier-ii-environment-assessments/indirect-precursors-to-perfluorocarboxylic-acids> [Accessed: 25 May 2020]
- [NICNAS] National Industrial Chemicals Notification and Assessment Scheme. 2020. Data requirements for notification of new chemicals containing a perfluorinated carbon chain. Available from: <https://www.nicnas.gov.au/notify-your-chemical/data-requirements-for-new-chemical-notifications/data-requirements-for-notification-of-new-chemicals-containing-a-perfluorinated-carbon-chain> [Accessed: 26 June 2020]
- Nilsson H, Kärman A, Westberg H, Rotander A, van Bavel B, Lindström G. 2010. A time trend study of significantly elevated perfluorocarboxylate levels in humans after using fluorinated ski wax. *Environ. Sci. Technol.* 44:2150–2155.
- Nobels I, Dardenne F, De Coen W, Blust R. 2010. Application of a multiple endpoint bacterial reporter assay to evaluate toxicological relevant endpoints of perfluorinated compounds with different functional groups and varying chain length. *Toxicology in Vitro.* 24:1768–1774.
- Nordic Council of Ministers. 2015. Substances in Preparations in Nordic Countries (SPIN). Chemical Group, Nordic Council of Ministers, Copenhagen, Denmark. Accessed 17 March 2015. [As cited in NICNAS 2019]
- Nordic Council of Ministers. 2019. PFASs in the Nordic environment. Screening of Poly- and Perfluoroalkyl Substances (PFASs) and Extractable Organic Fluorine (EOF) in the Nordic

Environment. Available from: PFASs in the Nordic environment (diva-portal.org) [Accessed: 6 April 2022]

[NTP] National Toxicology Program. 2019. NTP technical report on the toxicity studies of perfluoroalkyl carboxylates (perfluorohexanoic acid, perfluorooctanoic acid, perfluorononanoic acid, and perfluorodecanoic acid) administered by gavage to Sprague Dawley (Hsd:Sprague Dawley SD) rats. Research Triangle Park (NC): U.S. Department of Health and Human Services, National Toxicology Program. Toxicity Report 97.

Nystrom J, Benskin JP, Plassmann M, Sandblom O, Glynn A, Lampa E, Gyllenhammar I, Moraeus L, Lignell S. 2022. Demographic, life-style and physiological determinants of serum per- and polyfluoroalkyl substance (PFAS) concentrations in a national cross-sectional survey of Swedish adolescents. *Res.* 208:112674.

O'Brien JM, Crump D, Mundy LJ, Chu S, McLaren KK, Vongphachan V, Letcher RJ, Kennedy SW. 2009. Pipping success and liver mRNA expression in chicken embryos exposed in ovo to C8 and C11 perfluorinated carboxylic acids and C10 perfluorinated sulfonate. *Toxicology Letters.* 190:134–139.

O'Brien JM, Williams A, Yauk CI, Crump D, Kennedy SW. 2013. In vitro microarray analysis identifies genes in acute-phase pathways that are down-regulated in the liver of chicken embryos exposed in ovo to PFUDA. *Toxicology in Vitro.* 27:1649–1658.

O'Connell SG, Arendt M, Segars A, Kimmel T, Braun-McNeil J, Avens L, Schroeder B, Ngai L, Kucklick JR, Keller J. 2010. Temporal and spatial trends of perfluorinated compounds in juvenile loggerhead sea turtles (*Caretta caretta*) along the east coast of the United States. *Environ Sci Technol.* 44:5202–5209.

[OECD] Organization of Economic Cooperation and Development. 2002. Co-operation on existing chemicals. Hazard assessment of perfluorooctane sulfonate (PFOS) and its salts. Environment Directorate. Joint meeting of the Chemicals Committee and the Working Party on Chemicals, Pesticides and Biotechnology. ENV/JM/RD(2002)17/FINAL (Unclassified).

[OECD] Organisation for Economic Co-operation and Development. 2011. PFCS: Outcome of the 2009 Survey on the production, use and release of PFOS, PFAS, PFOA PFCA, their related substances and products/mixtures containing these substances. Available from: [http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono\(2011\)1&doclanguage=en](http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono(2011)1&doclanguage=en) [Accessed: 23 October 2020]

[OECD] Organisation for Economic Co-operation and Development. 2013. OECD/UNEP Global PFC Group, Synthesis paper on per- and polyfluorinated chemicals (PFCs), Environment, Health and Safety, Environment Directorate, OECD. Available from: [https://www.oecd.org/env/ehs/risk-management/PFC\\_FINAL-Web.pdf](https://www.oecd.org/env/ehs/risk-management/PFC_FINAL-Web.pdf) [Accessed: 23 October 2020]

[OECD] Organisation for Economic Co-operation and Development. 2014. Guidance on grouping of chemicals, second edition. Environment, Health and Safety Publications Series on Testing and Assessment. No. 194. Available from: [http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono\(2014\)4&doclanguage=en](http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono(2014)4&doclanguage=en) [Accessed: 21 February 2022]

[OECD] Organisation for Economic Co-operation and Development. 2015. Working towards a global emission inventory of PFASs: focus on PFCAs - status quo and the way forward. OECD Environment, Health and Safety Publications Series on Risk Management. No. 30. Available from: <https://www.oecd.org/chemicalsafety/Working%20Towards%20a%20Global%20Emission%20Inventory%20of%20PFAS.pdf> [Accessed: 24 February 2022]

[OECD] Organisation for Economic Co-operation and Development. 2020. Portal on Per and Polyfluorinated Chemicals. Country Information. Available from: <https://www.oecd.org/chemicalsafety/portal-perfluorinated-chemicals/> [Accessed: 23 October 2020]

Ohmori K, Kudo N, Katayama K, Kawashima Y. 2003. Comparison of the toxicokinetics between perfluorocarboxylic acids with different carbon chain length. *Toxicology.* 184(2-3):135–140.

Ojo AF, Peng C, Ng JC. 2020. Combined effects and toxicological interactions of perfluoroalkyl and polyfluoroalkyl substances mixtures in human liver cells (HepG2). *Environmental Pollution.* 263: 114182.

Oshida K, Vasani N, Thomas RS, Applegate D, Rosen M, Abbott B, Lau C, Guo G, Aleksunes LM, Klaassen, et al. 2015. Identification of modulators of the nuclear receptor peroxisome proliferator-

- activated receptor  $\alpha$  (PPAR $\alpha$ ) in a mouse liver gene expression compendium. PLOS ONE. 10(2): e0112655.
- Pan C-G, Zhao J-L, Liu Y-S, Zhang Q-Q, Chen Z-F, Lai H-J, Peng F-J, Liu S-S, Ying G-G. 2014. Bioaccumulation and risk assessment of per- and polyfluoroalkyl substances in wild freshwater fish from rivers in the Pearl River Delta region, South China. *Ecotoxicology and Environmental Safety*. 107:192–199.
- Pan Y, Zhang H, Cui Q, Sheng N, Yeung LWY, Sun Y, Guo Y, Dai J. 2018. Worldwide distribution of novel perfluoroether carboxylic and sulfonic acids in surface water. *Environmental Science and Technology*. 52(14):7621-7629.
- Pan X, Ye J, Zhang H, Tang J, Pan D. 2019. Occurrence, removal, and bioaccumulation of perfluoroalkyl substances in Lake Chaohu, China. *Int J Environ Res Public Health*. 16:1692.
- Parsons JR, Saez M, Dolfing J, de Voogt P. 2008. Biodegradation of perfluorinated compounds. *Reviews of Environmental Contamination and Toxicology*, Vol 196. D.M. Whitacre (ed.), Springer-Science + Business Media LLC
- Peaslee GF, Wilkinson JT, McGuinness SR, Tighe M, Caterisano N, Lee S, Gonzales A, Roddy M, Mills S, Mitchell K. 2020. Another Pathway for Firefighter Exposure to Per- and Polyfluoroalkyl Substances: Firefighter Textiles. *Environ. Sci. Technol. Lett.* 7:594–599.
- Peng H, Wei Q, Wan Y, Giesy JP, Li L, Hu J. 2010. Tissue distribution and maternal transfer of poly- and perfluorinated compounds in Chinese sturgeon (*Acipenser sinensis*): implications for reproductive risk. *Environ Sci Technol*. 44:1868–1874.
- Pepper IL, Brusseau ML, Prevatt FJ, Escobar BA. 2021. Incidence of PFAS in soil following long-term application of class B biosolids. *Science of the Total Environment*. 793:148449.
- PERFORCE. 2004: Perfluorinated substances in the European environment, EU project FP6-NEST-508967. [As cited in ECHA 2018b]
- Persson S and Magnusson U. 2015. Environmental pollutants and alterations in the reproductive system in wild male mink (*Neovison vison*) from Sweden. *Chemosphere*. 120:237–45.
- Pickard HM, Criscitiello AS, Spencer C, Sharp MJ, Muir DCG, DeSilva AO, Young CJ. 2018. Continuous non-marine inputs of per- and polyfluoroalkyl substances to the High Arctic: a multi-decadal temporal record. *Atmos Chem Phys*. 18 (7):5045–5058.
- Plassman and Berger. 2013. Perfluoroalkyl carboxylic acids with up to 22 carbon atoms in snow and soil samples from a ski area. *Chemosphere*. 91:832-837.
- Poothong S, Papadopoulou E, Padilla-Sánchez JA, Thomsen C, Haug LS. 2020. Multiple pathways of human exposure to poly- and perfluoroalkyl substances (PFASs): From external exposure to human blood. *Environ.Int.* 134: 105244.
- Posner S, Roos S, and Olsson E. 2009. Survey of the extent of use and occurrence of PFNA (perfluorononanoic acid) in Norway, Swerea IVF, Project report 09/46. TA-2562/2009. [As cited in ECHA 2018b]
- Post GB, Louis JB, Lippincott RL, Procopio NA. 2013. Occurrence of perfluorinated compounds in raw water from new jersey public drinking water systems. *Environ.Sci.Technol.* 47(23): 13266-13275.
- Powley GR, George SW, Russell MH, Hoke RA, Buck RC. 2008. Polyfluorinated chemicals in a spatially and temporally integrated food web in the Western Arctic. *Chemosphere*. 70:664–672.
- Prevedouros K, Cousins IT, Buck RC, Korzeniowski SH. 2006. Sources, fate, and transport of perfluorocarboxylates. *Environ Sci Technol*. 40:32–44.
- Qu R, Liu J, Li C, Wang L, Wang Z, Wu J. 2016. Experimental and theoretical insights into the photochemical decomposition of environmentally persistent perfluorocarboxylic acids. *Water Research*. 104:34–43.
- Rahman ML, Zhang C, Smarr MM, Lee S, Honda M, Kannan K, Tekola-Ayele F, Buck Louis GM. (2019). Persistent organic pollutants and gestational diabetes: A multi-center prospective cohort study of healthy US women. *Environ Int.* 124: 249–258.
- Rand AA, Rooney JP, Butt CM, Meyer JN, Mabury SA. 2014. Cellular toxicity associated with exposure to perfluorinated carboxylates (PFCAs) and their metabolic precursors. *Chem Res Toxicol*. 27(1): 42-50.

- Rand AA, Mabury SA. 2017. Is there a human health risk associated with indirect exposure to perfluoroalkyl carboxylates (PFCAs)? *Toxicology*. 375:28-36.
- Rauert, C., Shoieb, M., Schuster, J. K., Eng, A., & Harner, T. 2018. Atmospheric concentrations and trends of poly- and perfluoroalkyl substances (PFAS) and volatile methyl siloxanes (VMS) over 7 years of sampling in the Global Atmospheric Passive Sampling (GAPS) network. *Environmental Pollution*, 238, 94-102.
- Reardon AJF, Rowan-Carroll A, Ferguson SS, Leingartner K, Gagne R, Kuo B, Williams A, Lorusso L, Bourdon-Lacombe JA, Carrier R, Moffat I, Yauk CL, Atlas E. 2021. Potency Ranking of Per- and Polyfluoroalkyl Substances Using High-Throughput Transcriptomic Analysis of Human Liver Spheroids. *Toxicol. Sci.* 184(1):154–169.
- Ren XM, Qin WP, Cao LY, Zhang J, Yang Y, Wan B, Guo LH. 2016. Binding interactions of perfluoroalkyl substances with thyroid hormone transport proteins and potential toxicological implications. *Toxicology*. 366-367: 32-42.
- Reth M, Berger U, Broman D, Cousins IT, Nilsson ED, McLachlan MS. 2011. Water-to-air transfer of perfluorinated carboxylates and sulfonates in a sea spray simulator. *Environmental Chemistry*. 8(4):381–388.
- Rockwell CE, Turley AE, Cheng X, Fields PE, Klaassen CD. 2013. Acute immunotoxic effects of perfluorononanoic acid (PFNA) in C57BL/6 mice. *Clin Exp Pharmacol. Suppl* 4:S4–002.
- Rockwell CE, Turley AE, Cheng X, Fields PE, Klaassen CD. 2017. Persistent alterations in immune cell populations and function from a single dose of perfluorononanoic acid (PFNA) in C57BL/6 mice. *Food Chem Toxicol*. 100:24–33.
- Rodríguez-Varela M, Durán-Álvarez JC, Jiménez-Cisneros B, Zamora O, Prado B. 2021. Occurrence of perfluorinated carboxylic acids in Mexico City's wastewater: A monitoring study in the sewerage and a mega wastewater treatment plant. *Science of the Total Environment* 774:145060.
- Rogers JM, Ellis-Hutchings RG, Grey BE, Zucker RM, Norwood J Jr, Grace CE, Gordon CJ, Lau C. 2014. Elevated blood pressure in offspring of rats exposed to diverse chemicals during pregnancy. *Toxicol Sci.* 137(2):436–46.
- Roos AM, Gamberg M, Muir D, Kärrman A, Carlsson P, Cuyler C, Lind Y, Bossi R, Rigét F. 2021. Perfluoroalkyl substances in circum-Arctic *Rangifer*: caribou and reindeer. *Environ Sci Pollut Res*. doi:10.1007/s11356-021-16729-7.
- Roscales JL, Vicente A, Ryan PG, Gonzalez-Solis J, Jimenez B. 2019. Spatial and interspecies heterogeneity in concentrations of perfluoroalkyl substances (PFASs) in seabirds of the Southern Ocean. *Environ Sci Technol*. 53:9855–9865.
- Rosen MB, Das KP, Rooney J, Abbott B, Lau C, Corton JC. 2017. PPARalpha-independent transcriptional targets of perfluoroalkyl acids revealed by transcript profiling. *Toxicology*. 387: 95-107.
- Rotander A, Karrman A, van Bavel B, Polder A, Rigét F, Audousson GA, Vikingsson G, Gabrielsen GW, Bloch D, Dam M. 2012. Increasing levels of long-chain perfluorocarboxylic acids (PFCAs) in Arctic and North Atlantic marine mammals, 1984-2009. *Chemosphere*. 86:278–285.
- Routti H, Krafft BA, Herzke D, Eisert R, Oftedal O. 2015. Perfluoroalkyl substances detected in the world's southernmost marine mammal, the Weddell seal (*Leptonychotes weddellii*). *Environmental Pollution*. 197:62–67.
- Routti H, Gabrielsen GW, Herzke D, Kovacs KM, Lydersen C. 2016. Spatial and temporal trends in perfluoroalkyl (PFASs) in ringed seals (*Pusa hispida*) from Svalbard. *Environmental Pollution*. 214: 230–238.
- Routti H, Aars J, Fuglei E, Hanssen L, Lone K, Polder A, Pedersen A, Tartu S, Welker JM, Yoccoz NG. 2017. Emission changes dwarf the influence of feeding habits on temporal trends of per- and polyfluoroalkyl substances in two Arctic top predators. *Environ Sci Technol*. 51:11996–12006
- Routti H, Berg MK, Lille-Langey R, Øygarden L, Harju M, Dietz R, Sonne C, Goksey A. 2019a. Environmental contaminants modulate the transcriptional activity of polar bear (*Ursus maritimus*) and human peroxisome proliferator-activated receptor alpha (PPARA). *Scientific Reports*. 9:6918.
- Routti H, Atwood TC, Bechshoft T, Boltunov A, Ciesielski TM, Desforges J-P, Dietz R, Gabrielsen GW, Jenssen BM, Letcher RJ, McKinney MA, Morris AD, Rigét FF, Sonne C, Styriehave B, Tartu S.

- 2019b. State of knowledge on current exposure, fate and potential health effects of contaminants in polar bears from the circumpolar Arctic. *Science of the Total Environment*. 664:1063–1083.
- Salihovic S, Stubleski J, Karrman A, Larsson A, Fall T, Lind L, Lind PM. 2018. Changes in markers of liver function in relation to changes in perfluoroalkyl substances - A longitudinal study. *Environ Int*. 117:196–203.
- Schaider LA, Balan SA, Blum A, Andrews DQ, Strynar MJ, Dickinson ME, Lunderberg DM, Lang JR, Peaslee GF. 2017. Fluorinated Compounds in U.S. Fast Food Packaging. Supporting Information. *Environ Sci Technol. Lett* 4:105–111.
- Schiavone A, Corsolini S, Kannan K, Tao L, Trivelpiece W, Torres D, Focardi S. 2009. Perfluorinated contaminants in fur seal pups and penguin eggs from South Shetland, Antarctica. *Sci Total Environ*. 407:3899–3904.
- Schröter-Kermani C, Müller J, Jüriling H, Conrad A, Schulte C. 2013. Retrospective monitoring of perfluorocarboxylates and perfluorosulfonates in human plasma archived by the German Environmental Specimen Bank. *Int.J.Hyg.Environ.Health*. 216(6): 633-640.
- Schultz MM, Higgins P, Huset CA, Luthy RG, Barofsky DF, Field JA. 2006. Fluorochemical Mass Flows in a Municipal Wastewater Treatment Facility. *Environ. Sci. Technol*. 40:7350–7357.
- Schultes L, Vestergren R, Volkova K, Westberg E, Jacobsonc T, Benskin JP. 2018. Per- and polyfluoroalkyl substances and fluorine mass balance in cosmetic products from the Swedish market: implications for environmental emissions and human exposure. *Environ. Sci.: Processes Impacts*. 20:1680.
- Schultes L, Peaslee GF, Brockman JD, Majumdar A, McGuinness SR, Wilkinson JT, Sandblom O, Ngwenyama RA, Benskin JP. 2019. Total Fluorine Measurements in Food Packaging: How Do Current Methods Perform? *Environ. Sci. Technol. Lett*. 6:73–78.
- Scinicariello F, Buser MC, Balluz L, Gehle K, Murray HE, Abadin HG, Attanasio, R. 2020. Perfluoroalkyl acids, hyperuricemia and gout in adults: Analyses of NHANES 2009–2014. *Chemosphere*. 259:127446.
- Seo SH, Son MH, Choi SD, Lee DH, Chang YS. 2018. Influence of exposure to perfluoroalkyl substances (PFASs) on the Korean general population: 10-year trend and health effects. *Environ. Int*. 113: 149-161.
- Sha B, Johansson JH, Tunved P, Bohlin-Nizzetto P, Cousins IT, Salter ME. 2022. Spray Aerosol (SSA) as a source of perfluoroalkyl acids (PFAAs) to the atmosphere: Field Evidence from long-term air monitoring. *Environ. Sci. Technol*. 56(1):228–238.
- Sexton K, Needham LL, Pirkle JL. 2004. Human biomonitoring of environmental chemicals: Measuring chemicals in human tissues is the “gold standard” for assessing people’s exposure to pollution. *American Scientist*. 92(1): 38-45.
- Sharma BM, Bharat GK, Tayal S, Larssen T, Bečanová B, Karásková P, Whitehead PG, Futter MN, Butterfield D, Nizzetto L. 2016. Perfluoroalkyl substances (PFAS) in river and ground/drinking water of the Ganges River basin: Emissions and implications for human exposure. *Environmental Pollution*. 208:704–713.
- Sherman MA, Kirchner JR, Del Pesco TW, Huang H, inventors. E. I. du Pont de Nemours and Company, assignee. 2001. Fluorochemical oil and water repellents. World Intellectual Property Organization Patent WO 01/10922 A1. Available from: <https://patents.google.com/patent/WO2001010922A1/en?q=WO2001010922A1> [Accessed: 23 February 2022]
- Shi Z, Zhang H, Liu Y, Xu M, Dai J. 2007. Alterations in gene expression and testosterone synthesis in the testes of male rats exposed to perfluorododecanoic acid. *Toxicol Sci*. 98(1):206–15.
- Shi Z, Ding L, Zhang H, Feng Y, Xu M, Dai J. 2009. Chronic exposure to perfluorododecanoic acid disrupts testicular steroidogenesis and the expression of related genes in male rats. *Toxicol Lett*. 188(3):192–200.
- Shoeib M, Harner T, M. Webster G, Lee SC. 2011. Indoor sources of poly- and perfluorinated compounds (PFCS) in Vancouver, Canada: Implications for human exposure. *Environ.Sci.Technol*. 45(19): 7999-8005.



- Shoeib M, Schuster J, Rauert C, Su K, Smyth S, Harner H. 2016. Emission of poly and perfluoroalkyl substances, UV-filters and siloxanes to air from wastewater treatment plants. *Environmental Pollution*. 218:595–604.
- Shoemaker JA, Grimmett P, Boutin B. 2008. Determination of Selected Perfluorinated Alkyl Acids in Drinking Water by Solid Phase Extraction and Liquid Chromatography/Tandem Mass Spectrometry (LC/MS/MS). U.S. Environmental Protection Agency, Washington, DC. Available from: [https://cfpub.epa.gov/si/si\\_public\\_record\\_report.cfm?Lab=NERL&dirEntryId=198984&simpleSearch=1&searchAll=EPA%2F600%2FR-08%2F092](https://cfpub.epa.gov/si/si_public_record_report.cfm?Lab=NERL&dirEntryId=198984&simpleSearch=1&searchAll=EPA%2F600%2FR-08%2F092) [Accessed: 25 March 2022]
- Simonnet-Laprade C, Budzinski H, Maciejewski K, Le Menach K, Santos R, Alliot F, Goutte A, Labadie P. 2019a. Biomagnification of perfluoroalkyl acids (PFAAs) in the food web of an urban river: assessment of the trophic transfer of targeted and unknown precursors and implications. *Environ Sci*. 21:1864–1874.
- Sim W, Park H, Yoon J, Kim J, Oh J. 2021. Characteristic distribution patterns of perfluoroalkyl substances in soils according to land-use types. *Chemosphere* 276:130167.
- Simonnet-Laprade C, Budzinski H, Babut M, Le Menach K, Munoz G, Lauzent M, Ferrari BJD, Labadie P. 2019b. Investigation of the spatial variability of poly- and perfluoroalkyl substance trophic magnification in selected riverine ecosystems. *Science of the Total Environment*. 686:393–401.
- Sinclair E, Kim SK, Akinleye HB, Kanna K. 2007. Quantitation of Gas-Phase Perfluoroalkyl Surfactants and Fluorotelomer Alcohols Released from Nonstick Cookware and Microwave Popcorn Bags. *Environ Sci Technol*. 41:1180–1185.
- Singh S, Singh SK. 2018. Chronic exposure to perfluorononanoic acid impairs spermatogenesis, steroidogenesis and fertility in male mice. *J Appl Toxicol*. 39(3):420–431.
- Singh S, Singh SK. 2019a. Effect of gestational exposure to perfluorononanoic acid on neonatal mice testes. *J Appl Toxicol*. 39(12):1663–1671.
- Singh S, Singh SK. 2019b. Acute exposure to perfluorononanoic acid in prepubertal mice: Effect on germ cell dynamics and an insight into the possible mechanisms of its inhibitory action on testicular functions. *Ecotoxicol Environ Saf*. 183:109499.
- Singh S, Singh SK. 2019c. Prepubertal exposure to perfluorononanoic acid interferes with spermatogenesis and steroidogenesis in male mice. *Ecotoxicol Environ Saf*. 170:590–599.
- Smithwick M, Mabury SA, Solomon KR, Sonne C, Martin JW, Born EW, Dietz R, Derocher AE, Letcher RJ, Evans TJ, et al. 2005a. Circumpolar study of perfluoroalkyl contaminants in polar bears (*Ursus maritimus*). *Environ Sci Technol*. 39:5517–5523.
- Smithwick M, Muir DCG, Mabury SA, Solomon KR, Martin JW, Sonne C, Born EW, Letcher RJ, Dietz R. 2005b. Perfluoroalkyl contaminants in liver tissue from east Greenland polar bears (*Ursus maritimus*). *Environ Toxicol Chem*. 24:981–986.
- Smithwick M, Norstrom RJ, Mabury SA, Solomon K, Evans TJ, Stirling I, Taylor MK, Muir DCG. 2006. Temporal trends of perfluoroalkyl contaminants in polar bears (*Ursus maritimus*) from two locations in the North American Arctic, 1972–2002. *Environ Sci Technol*. 40(4):1139–1143.
- Smythe TA, Loseto LS, Bignert A, Rosenberg B, Budakowski W, Halldorson T, Pleskach K, Tomy GT. 2018. Temporal trends of brominated and fluorinated contaminants in Canadian Arctic beluga (*Delphinapterus leucas*). *Arctic Science*. 4:388–404.
- Soerensen AL, Faxneld S. 2020. The Swedish National Monitoring Programme for Contaminants in marine biota (until 2019 year's data) – Temporal trends and spatial variations. Stockholm (SE): Swedish Museum of Natural History. Report No.: NV-00362-19.
- Soloff AC, Wolf BJ, White ND, Muir D, Courtney S, Hardiman G, Bossart GD, Fair PA. 2017. Environmental perfluorooctane sulfonate exposure drives T cell activation in bottlenose dolphins. *J Appl Toxicol*. 37(9):1108–1116
- Stanifer JW, Stapleton HM, Souma T, Wittmer A, Zhao X, Boulware LE. 2018. Perfluorinated chemicals as emerging environmental threats to kidney health: A scoping review. *Clin J Am Soc Nephrol*. 13(10):1479–1492.
- Stasinakis AS, Petalas AV, Mamais D, Thomaidis NS. 2008. Application of the OECD 301F respirometric test for the biodegradability assessment of various potential endocrine disrupting chemicals. *Bioresource Technology*. 99:3458–3467.

- Stevenson CN, MacManus-Spencer LA, Luckenbach T, Luthy RG, Epel D. 2006. New perspectives on perfluorochemical ecotoxicology: inhibition and induction of an efflux transporter in the marine mussel, *Mytilus californianus*. *Environ Sci Technol*. 40: 5580–5585.
- Stock NL, Furdui VI, Muir DCG, Mabury SA. 2007. Perfluoroalkyl contaminants in the Canadian Arctic: evidence of atmospheric transport and local contamination. *Environ Sci Technol*. 41:3529–3536.
- Stubleski J, Salihovic S, Lind L, Lind PM, van Bavel B, Kärrman A. 2016. Changes in serum levels of perfluoroalkyl substances during a 10-year follow-up period in a large population-based cohort. *Environ.Int*. 95: 86-92.
- Su, G., Letcher, R.J., Moore, J.N., Williams, L.L. and Grasman, K. 2017. Contaminants of emerging concern in herring gull compared to and Caspian tern eggs from United States colony sites in the Great Lakes of North America. *Environmental Pollution* 222, 154-164.
- Sun J, Letcher RJ, Eens M, Covaci A, Fernie KJ. 2020. Perfluoroalkyl acids and sulfonamides and dietary, biological and ecological associations in peregrine falcons from the Laurentian Great Lakes Basin, Canada. *Environmental Research*. 191:110151–110160.
- Swedish Chemicals Agency. 2015. Chemical Analysis of Selected Fire-fighting Foams on the Swedish Market 2014. [As cited in ECHA 2018b]
- Swedish Chemicals Agency. 2021. PM 91: PFASs in Cosmetics. Available from: <https://www.kemi.se/en/publications/pms/2021/pm-9-21-pfass-in-cosmetics> [Accessed: 21 January 2022]
- Takahashi M, Ishida S, Hirata-Koizumi M, Ono A, Hirose A. 2014. Repeated dose and reproductive/developmental toxicity of perfluoroundecanoic acid in rats. *J Toxicol Sci*. 39(1):97–108.
- Takemine S, Matsumura C, Yamamoto K, Suzuki M, Tsurukawa M, Imaishi H, Nakano T, Kondo A. 2014. Discharge of perfluorinated compounds from rivers and their influence on the coastal seas of Hyogo prefecture, Japan. *Environmental Pollution*. 184:397–404.
- Tao L, Kannan K, Kajiwara N, Costa MM, Fillmann G, Takahashi S, Tanabe S. 2006. Perfluorooctanesulfonate and related fluorochemicals in albatrosses, elephant seals, penguins, and polar skuas from the Southern Ocean. *Environ Sci Technol*. 40:7642–7648.
- Tartu S, Bourgeon S, Aars J, Andersen M, Lone K, Jenssen BM, Polder A, Thiemann GW, Torget V, Welker JM, Routti H. 2017. Diet and metabolic state are the main factors determining concentrations of perfluoroalkyl substances in female polar bears from Svalbard. *Environmental Pollution*. 229:146–158.
- Taylor KW, Hoffman K, Thayer KA, Daniels JL. 2014. Polyfluoroalkyl chemicals and menopause among women 20-65 years of age (NHANES). *Environ.Health Perspect*. 122(2): 145-150.
- Taylor S, Terkildsen M, Stevenson G, de Araujo J, Yu C, Yates A, McIntosh RR, Gray R. 2021. Per and polyfluoroalkyl substances (PFAS) at high concentrations in neonatal Australian pinnipeds. *Sci Total Environ*. 786:147446.
- Temkin AM, Hocevar BA, Andrews DQ, Naidenko OV, Kamendulis LM. 2020. Application of the Key Characteristics of Carcinogens to Per and Polyfluoroalkyl Substances. *Int J Environ Res Public Health*. 17(5):1668.
- Thackray CP, Selin NE, Young CJ. 2020. A global atmospheric chemistry model for the fate and transport of PFCAs and their precursors. *Environ Sci Process Impacts*. 22(2):285–293.
- Tichy M, Valigurova R, Cabala R, Uzlova R, Rucki M. 2010. Toxicity of perfluorinated carboxylic acids for aquatic organisms. *Interdisc Toxicol*. 3(2):73–75.
- Timmermann CAG, Pedersen HS, Weihe P, Bjerregaard P, Nielsen F, Heilmann C, Grandjean P. 2022. Concentrations of tetanus and diphtheria antibodies in vaccinated Greenlandic children aged 7–12 years exposed to marine pollutants, a cross sectional study. *Environ.Res*. 203:111712.
- Timmermann CAG, Jensen KJ, Nielsen F, Budtz-Jørgensen E, van der Klis F, Benn CS, Grandjean P, Fisker AB. 2020. Serum perfluoroalkyl substances, vaccine responses, and morbidity in a cohort of Guinea-Bissau children. *Environ.Health Perspect*. 128(8): 1-11.

- Tominaga N, Kohra S, Iguchi T, Arizono, K. 2004. Effects of perfluoro organic compound toxicity on nematode *Caenorhabditis elegans* fecundity. *J Health Sci.* 50:545–550.
- Tomy G, Pleskach K, Rosenberg B, Stern G. 2009a. Temporal trends of halogenated chemicals of emerging concern in beluga whales (*Delphinapterus leucas*) from Hendrickson Island and Pangnirtung In: Smith S, Stow J, Edwards J, editors. Synopsis of research conducted under the 2008-2009 Northern Contaminants Program. Ottawa, Ontario: Department of Indian Affairs and Northern Development. p. 99–107.
- Tomy GT, Pleskach K, Ferguson SH, Hare J, Stern G, MacInnis G, Marvin CH, Loseto L. 2009b. Trophodynamics of some PFCs and BFRs in a western Canadian Arctic marine food web. *Environ Sci Technol.* 43:4076–4081.
- Trowbridge J, Gerona RR, Lin T, Rudel RA, Bessonneau V, Buren H, Morello-Frosch R. 2020. Exposure to perfluoroalkyl substances in a cohort of women firefighters and office workers in San Francisco. *Environ.Sci.Technol.* 54(6): 3363-3374.
- Tsai MS, Lin CY, Lin CC, Chen MH, Hsu SH, Chien KL, Sung FC, Chen PC, Su TC. 2015. Association between perfluoroalkyl substances and reproductive hormones in adolescents and young adults. *Int J Hyg Environ Health.* 218(5):437–43.
- Ulhaq M, Örn S, Carlsson G, Morrison DA, Norrgren L. 2013a. Locomotor behavior in zebrafish (*Danio rerio*) larvae exposed to perfluoroalkyl acids. *Aquat Toxicol.* 144–145: 332–40.
- Ulhaq M, Carlsson G, Örn S, Norrgren L. 2013b. Comparison of developmental toxicity of seven perfluoroalkyl acids to zebrafish embryos. *Environmental Toxicology and Pharmacology.* 36(2):423–426.
- [US EPA] United States Environmental Protection Agency. 2009. Long-Chain Perfluorinated Chemicals (PFCs) Action Plan. Available from: [https://www.epa.gov/sites/production/files/2016-01/documents/pfcs\\_action\\_plan1230\\_09.pdf](https://www.epa.gov/sites/production/files/2016-01/documents/pfcs_action_plan1230_09.pdf) [Accessed: 23 October 2020]
- [US EPA] U.S. Environmental Protection Agency. 2017. The Third Unregulated Contaminant Monitoring Rule (UCMR 3): Data Summary, January 2017. Available at <https://www.epa.gov/sites/default/files/2017-02/documents/ucmr3-data-summary-january-2017.pdf>.
- US EPA. 2019. Method 533: Determination of per- and polyfluoroalkyl substances in drinking water by isotope dilution anion exchange solid phase extraction and liquid chromatography/tandem mass spectrometry. Available from: <https://www.epa.gov/sites/default/files/2019-12/documents/method-533-815b19020.pdf> [Accessed: 25 March 2022]
- [US EPA] United States Environmental Protection Agency. 2020. Final Rule. Long-Chain Perfluoroalkyl Carboxylate and Perfluoroalkyl Sulfonate Chemical Substances; Significant New Use Rule. Available from: <https://www.govinfo.gov/content/pkg/FR-2020-07-27/pdf/2020-13738.pdf> [Accessed: 23 October 2020]
- [US EPA] United States Environmental Protection Agency. 2021a. Draft Method 1633. Analysis of Per- and Polyfluoroalkyl Substances (PFAS) in Aqueous, Solid, Biosolids, and Tissue Samples by LC-MS/MS. Available from: [https://www.epa.gov/system/files/documents/2021-09/method\\_1633\\_draft\\_aug-2021.pdf](https://www.epa.gov/system/files/documents/2021-09/method_1633_draft_aug-2021.pdf) [Accessed: 25 March 2022]
- [US EPA] United States Environmental Protection Agency. 2021b. PFAS Strategic Roadmap: EPA's Commitments to Action 2021-2024. Available from: PFAS Strategic Roadmap: EPA's Commitments to Action 2021-2024 | US EPA [Accessed: 31 March 2022]
- Verreault J, Berger U, Gabrielsen GW. 2007. Trends of perfluorinated alkyl substances in herring gull eggs from two coastal colonies in northern Norway: 1983–2003. *Environ Sci Technol.* 41(19):6671–6677.
- Vestergren R, Berger U, Glynn A, Cousins IT. 2012. Dietary exposure to perfluoroalkyl acids for the Swedish population in 1999, 2005 and 2010. *Environ.Int.* 49: 120-127.
- Vestergren R, Herzke D, Wang T, Cousins IT. 2015. Are imported consumer products an important diffuse source of PFASs to the Norwegian environment? *Environmental Pollution.* 198:223–230.
- Vongphachan V, Cassone CG, Wu D, Chiu S, Crump D, Kennedy SW. 2011. Effects of perfluoroalkyl compounds on mRNA expression levels of thyroid hormone-responsive genes in primary cultures of avian neuronal cells. *Toxicological Sciences.* 120(2):392–402.

- Vuong AM, Braun JM, Yolton K, Wang Z, Xie C, Webster GM, Ye X, Calafat AM, Dietrich KN, Lanphear BP, Chen A. 2018a. Prenatal and childhood exposure to perfluoroalkyl substances (PFAS) and measures of attention, impulse control, and visual spatial abilities. *Environ Int.* 119: 413-420.
- Vuong AM, Yolton K, Wang Z, Xie C, Webster GM, Ye X, Calafat AM, Braun JM, Dietrich KN, Lanphear BP, Chen A. 2018b. Childhood perfluoroalkyl substance exposure and executive function in children at 8 years. *Environ Int.* 119: 212-219.
- Wallington TJ, Hurley MD, Xia J, Wuebbles DJ, Sillman S, Ito A, Penner JE, Ellis DA, Martin J, Mabury SA, Nielsen OJ, Sulbaek Andersen MP. 2006. Formation of C7F15COOH (PFOA) and other perfluorocarboxylic acids during the atmospheric oxidation of 8:2 fluorotelomer alcohol. *Environ Sci Technol.* 40:924–930.
- Wang J, Ober CK. 1999. Solid state crystalline and liquid crystalline structure of semifluorinated 1-bromoalkane compounds. *Liq Cryst.* 26:637.
- Wang Y, Fu J, Wang T, Liang Y, Pan Y, Cai Y, Jiang G. 2010. Distribution of perfluorooctane sulfonate and other perfluorochemicals in the ambient environment around a manufacturing facility in China. *Environ.Sci.Technol.* 44(21): 8062-8067.
- Wang Z, MacLeod M, Cousins IT, Scheringer M, Hungerbühler K. 2011. Using COSMOtherm to predict physicochemical properties of poly- and perfluorinated alkyl substances (PFASs). *Environ Chem.* 8(4):389–98.
- Wang Z, Cousins IT, Scheringer M, Buck RC, Hungerbühler K. 2014. Global emission inventories for C4–C14 perfluoroalkyl carboxylic acid (PFCA) homologues from 1951 to 2030, Part I: production and emissions from quantifiable sources. Supplementary Information. *Environment International.* 70:62–75.
- Wang J, Yan S, Zhang W, Zhang H, Dai J. 2015a. Integrated proteomic and miRNA transcriptional analysis reveals the hepatotoxicity mechanism of PFNA exposure in mice. *J Proteome Res.* 14(1):330–41.
- Wang Z, Xie Z, Mi W, Möller A, Wolschke H, Ebinghaus R. 2015b. Neutral poly/per-fluoroalkyl substances in air from the Atlantic to the Southern Ocean and in Antarctic snow. *Environ Sci Technol.* 48: 7770–7775.
- Wang Y, Zhong Y, Li J, Zhang J, Lyu B, Zhao Y. 2018. Occurrence of perfluoroalkyl substances in matched human serum, urine, hair and nail. *J Environ Sci (China).* 67:191–197.
- Wania F. 2007. A global mass balance analysis of the source of perfluorocarboxylic acids in the Arctic Ocean. *Environ Sci Technol.* 41:4529–4535.
- Waterland and Dobbs. 2007. Atmospheric chemistry of linear perfluorinated aldehydes: dissociation kinetics of C<sub>n</sub>F<sub>2n+1</sub>CO radicals. *J. Phys. Chem A.* 111:2555–2562.
- Webster E and Ellis DA. 2010. Potential role of sea spray generation in the atmospheric transport of perfluorocarboxylic acids. *Environmental Toxicology and Chemistry.* 29(8):1703–1708.
- Wei Y, Shi X, Zhang H, Wang J, Zhou B, Dai J. 2009. Combined effects of polyfluorinated and perfluorinated compounds on primary cultured hepatocytes from rare minnow (*Gobiocypris rarus*) using toxicogenomic analysis. *Aquatic Toxicology.* 95:27–36.
- Weinberg I, Dreyer A, Ebinghaus R. 2011. Landfills as sources of polyfluorinated compounds, polybrominated diphenyl ethers and musk fragrances to ambient air. *Atmospheric Environment.* 45: 935–941.
- Wellington Laboratories Inc. 2022. <https://well-labs.com/> [Accessed: 25 March 2022]
- Whitehead HG, Venier M, Wu Y, Eastman E, Urbanik S, Diamond ML, Shalin A, Schwartz-Narbonne H, Bruton TA, Blum A, Wang Z, Green M, Tighe M, Wilkinson JT, McGuinness S, Peaslee GF. 2021. Correction to “Fluorinated Compounds in North American Cosmetics”. *Environ Sci Technol Lett.* 8(7):538–544.
- Wielsoe M, Kern P, Bonefeld-Jørgensen EC. 2017. Serum levels of environmental pollutants is a risk factor for breast cancer in Inuit: A case control study. *Environ.Health Global Access Sci.Sour.* 16(1):56.
- Wolf CJ, Zehr RD, Schmid JE, Lau C, Abbott BD. 2010. Developmental effects of perfluorononanoic Acid in the mouse are dependent on peroxisome proliferator-activated receptor- $\alpha$ . *PPAR Res.* 2010:282896.

- Wolf CJ, Schmid JE, Lau C, Abbott, BD. 2012. Activation of mouse and human peroxisome proliferator-activated receptor-alpha (PPARalpha) by perfluoroalkyl acids (PFAAs): further investigation of C4-C12 compounds. *Reprod Toxicol.* 33(4): 546-551.
- Wong F, Shoeib M, Katsoyiannis A, Eckhardt S, Stohl A, Bohlin-Nizzetto P, Li H, Fellin P, Su Y, Hung H. 2018. Assessing temporal trends and source regions of per- and polyfluoroalkyl substances (PFASs) in air under the Arctic Monitoring and Assessment Programme (AMAP). *Atmospheric Environment.* 172:65–73.
- Wong F, Hung H, Dryfhout-Clark H, Aas W, Bohlin-Nizzetto P, Breivik K, Nerentorp Mastromonaco M, Brorström Lundén E, Ólafsdóttir K, Sigurðsson Á, Vorkamp K, Bossi R, Skov H, Hakola H, Barresi E, Sverko E, Fellin P, Li H, Vlasenko A, Zapevalov M, Samsonov D, Wilson S. 2021. Time trends of persistent organic pollutants (POPs) and chemicals of emerging arctic concern (CEAC) in Arctic air from 25 years of monitoring. *Sci Total*775:145109.
- Woodcroft MW, Ellis DA, Rafferty SP, Burns DC, March RE, Stock NL, Trumpour JY, Munro K. 2010. Experimental characterization of the mechanism of perfluorocarboxylic acids liver protein bioaccumulation: the key role of the neutral species. *Environmental Toxicology and Chemistry.* 29(8): 1669–1677.
- Wu M, Sun R, Wang M, Liang H, Ma S, Han T. 2017. Analysis of perfluorinated compounds in human serum from the general population in Shanghai by liquid chromatography-tandem mass spectrometry (LC-MS/MS). *Chemosphere.* 168:100–105.
- Wu J, Junaid M, Wang Z, Sun W, Xu N. 2020. Spatiotemporal distribution, sources, and ecological risk of perfluorinated compounds (PFCs) in the Guanlan River from the rapidly urbanizing areas of Shenzhen, China. *Chemosphere.* 245: 125637.
- Wu Y, Miller GZ, Gearhart J, Peaslee G, Venier M. 2021. Side-chain fluorotelomer-based polymers in children car seats. *Environ Pollut.* 268:115477.
- Xenia T, Granby K, Christensen JH. 2011. Polyfluorinated surfactants (PFS) in paper and board coatings for food packaging. *Environ Sci Pollut Res.* 18:1108–1120.
- Xu J, Guo C-S, Zhang Y, Meng W. 2014. Bioaccumulation and trophic transfer of perfluorinated compounds in an eutrophic freshwater food web184: 254–261.
- Yang CH, Glover KP, Han X. 2010. Characterization of cellular uptake of perfluorooctanoate via organic anion-transporting polypeptide 1A2, organic anion transporter 4, and urate transporter 1 for their potential roles in mediating human renal reabsorption of perfluorocarboxylates. *Toxicol Sci.* 117(2): 294-302.
- Yang S, Liu S, Ren Z, Jiao X, Qin S. 2014. Induction of oxidative stress and related transcriptional effects of perfluorononanoic acid using an in vivo assessment. *Comparative Biochemistry and Physiology. Part C.* 160:60–65.
- Yang L, Li J, Lai J, Luan H, Cai Z, Wang Y, Zhao Y, Wu Y. 2016. Placental transfer of perfluoroalkyl substances and associations with thyroid hormones: Beijing prenatal exposure study. *Sci.Rep.* 6: 21699.
- Yang Y, Lv QY, Guo LH, Wan B, Ren XM, Shi YL, Cai YQ. 2017. Identification of protein tyrosine phosphatase SHP-2 as a new target of perfluoroalkyl acids in HepG2 cells. *Arch Toxicol.* 91(4): 1697-1707.
- Yao Y, Chang S, Sun H, Gan Z, Hu H, Zhao Y, Zhang Y. 2016. Neutral and ionic per- and polyfluoroalkyl substances (PFASs) in atmospheric and dry deposition samples over a source region (Tianjin, China). *Environmental Pollution.* 212:449–456.
- Yarwood G, Kemball-Cook S, Keinath M, Waterland RL, Korzeniowski SH, Buck RC, Russell MH, Washburn ST. 2007. High-resolution atmospheric modelling of fluorotelomer alcohols and perfluorocarboxylic acids in the North American troposphere. *Environ Sci Technol.* 41: 5756–5762
- Yeung LW, Loi EI, Wong VY, Guruge KS, Yamanaka N, Tanimura N. 2009. Biochemical responses and accumulation properties of long-chain perfluorinated compounds (PFOS/PFOA/PFOA) in juvenile chickens (*Gallus gallus*). *Arch Environ Contam Toxicol.* 57(2):377–386.
- Yeung LW, Robinson SJ, Koschorreck J, Mabury SA. 2013. Part I. A temporal study of PFCAs and their precursors in human plasma from two German cities 1982-2009. *Environ.Sci.Technol.* 47(8): 3865-3874.

- Yeung LWY, Dassuncao C, Mabury S, Sunderland EM, Zhang X, Lohmann R. 2017. Vertical profiles, sources, and transport of PFASs in the Arctic Ocean. *Environ Sci Technol.* 51(12):6735–6744.
- Young CJ, Furdui VI, Franklin J, Koerner RM, Muir DCG, Mabury SA. 2007. Perfluorinated acids in Arctic snow: new evidence for atmospheric formation. *Environ Sci Technol.* 41:3455–3461.
- Yu L, Liu X, Hua Z, Zhang Y, Xue H. 2022. Spatial and temporal trends of perfluoroalkyl acids in water bodies: A case study in Taihu Lake, China (2009–2021). *Environmental Pollution.* 293:118575.
- Yuan G, Peng H, Huang C, Hu J. 2016. Ubiquitous occurrence of fluorotelomer alcohols in eco-friendly paper-made food-contact materials and their implication for human exposure. *Environ.Sci.Technol.* 50(2): 942-950.
- Zeng XW, Qian Z, Emo B, Vaughn M, Bao J, Qin XD, Zhu Y, Li J, Lee YL, Dong GH. 2015. Association of polyfluoroalkyl chemical exposure with serum lipids in children. *Sci Total Environ.* 512-513: 364-370.
- Zhang H, Shi Z, Liu Y, Wei Y, Dai J. 2008. Lipid homeostasis and oxidative stress in the liver of male rats exposed to perfluorododecanoic acid. *Toxicol Appl Pharmacol.* 227(1):16–25.
- Zhang W, Liu Y, Zhang H, Dai J. 2012a. Proteomic analysis of male zebrafish livers chronically exposed to perfluorononanoic acid. *Environ Int.* 42: 20–30.
- Zhang W, Zhang Y, Zhang H, Wang J, Cui R, Dai J. 2012b. Sex differences in transcriptional expression of FABPs in zebrafish liver after chronic exposure to perfluorononanoic acid exposure. *Environ Sci Technol.* 46:5175–5182.
- Zhang Y, Beesoon, Zhu L, Martin JW. 2013. Biomonitoring of perfluoroalkyl acids in human urine and estimates of biological half-life. *Environ Sci Technol.* 47(18):10619–27.
- Zhang Z, Peng H, Wan Y, Hu J. 2015. Isoner-specific trophic transfer of perfluorocarboxylic acids in the marine food web of Liaodong Bay, North China. *Environ Sci Technol.* 49:1453–1461.
- Zhang W, Sheng N, Wang M, Zhang H, Dai J. 2016. Zebrafish reproductive toxicity induced by chronic perfluorononanoate exposure. *Aquat Toxicol.* 175:269–76.
- Zhang S, Guo X, Lu S, Li G, Xie P, Liu C, Zhang L, Xing Y. 2018. Exposure to PFDa causes disruption of the hypothalamus-pituitary-thyroid axis in zebrafish larvae. *Environmental Pollution.* 235:974–982.
- Zhang X, Lohmann R, Sunderland EM. 2019. Poly- and perfluoroalkyl substances in seawater and plankton from the Northwestern Atlantic Margin. *Environ Sci Technol.* 53(21):12348–12356.
- Zhao Z, Xie Z, Möller A, Sturm R, Tang J, Zhang G, Ebinghaus R. 2012. Distribution and long-range transport of polyfluoroalkyl substances in the Arctic, Atlantic Ocean and Antarctic coast. *Environmental Pollution.* 170:71–77.
- Zheng X-M, Liu H-L, Shi W, Wei S, Giesy JP, Yu H-X. 2012. Effects of perfluorinated compounds on development of zebrafish embryos. *Environ Sci Pollut Res Int.* 19:2498–2505.
- Zhong W, Zhang L, Cui Y, Chen M, Zhu L. 2019. Probing mechanisms for bioaccumulation of perfluorinated acids in carp (*Cyprinus carpio*): impacts of protein binding affinities and elimination pathways. *Science of the Total Environment.* 647:992–999.
- Zhou Z, Shi Y, Li W, Xu L, Cai Y. 2012. Perfluorinated compounds in surface water and organisms from Baiyangdian Lake in North China: sources, profiles, bioaccumulation, and potential risk. *Bull Environ Contam Toxicol.* 89:519–524.
- Zhou W, Zhao S, Tong C, Chen L, Yu X, Yuan T, Aimuzi R, Luo F, Tian Y, Zhang J. 2019. Dietary intake, drinking water ingestion and plasma perfluoroalkyl substances concentration in reproductive aged Chinese women. *Environ.Int.* 127: 487-494.
- Zhu Y, Qin XD, Zeng XW, Paul G, Morawska L, Su MW, Tsai CH, Wang SQ, Lee YL, Dong GH. 2016. Associations of serum perfluoroalkyl acid levels with T-helper cell-specific cytokines in children: By gender and asthma status. *Sci Total Environ.* 559:166–173.
- Zhu H, Kannan K. 2020. A pilot study of per- and polyfluoroalkyl substances in automotive lubricant oils from the United States. *Environ Technol & Innovat.* 19:100943.