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State of Per- and Polyfluoroalkyl Substances (PFAS) Report

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Content

Executive Summary

Per- and polyfluoroalkyl substances (PFAS) are a class of thousands of human-made substances. These substances have a wide range of uses in products available to consumers, and in commercial and industrial applications. The widespread use of these substances and their extreme persistence in the environment, propensity for accumulation, and mobility has led to PFAS being commonly detected in the environment and humans. Despite data having largely been generated on a limited suite of well-studied PFAS, there is an increasing body of evidence that exposure to other PFAS can lead to adverse effects on the environment and human health. Cumulative effects from co-exposure to multiple PFAS may also occur.

This report provides a qualitative assessment of the fate, sources, occurrence, and potential impacts of PFAS on the environment and human health to inform decision-making on PFAS in Canada. The Draft State of PFAS Report was published in May 2023, followed by the Updated Draft State of PFAS Report which was published in July 2024. Both documents were open for a 60-day public consultation. This report has taken into consideration the comments received and information submitted during both consultation periods or identified from other sources.

The common chemical characteristic of PFAS is their perfluoroalkyl moiety, which is extremely stable in the environment, to the extent that PFAS have often been termed “forever chemicals.” Simple PFAS are highly persistent, whereas more complex molecules transform into stable PFAS. In this report, the term PFAS refers to the broad chemical definition by the Organisation for Economic Co-operation and Development (OECD) [2021], which is: “fluorinated substances that contain at least one fully fluorinated methyl or methylene carbon atom (without any H/Cl/Br/I atom attached to it), that is, with a few noted exceptions, any chemical with at least a perfluorinated methyl group ($–CF_3$) or a perfluorinated methylene group ($–CF_2–$) is a PFAS.” The class of PFAS is comprised of substances meeting this definition. The definition captures substances with a wide range of structures and properties, from discrete chemicals, such as perfluorocarboxylic acids, perfluorosulfonic acids, and fluorotelomer alcohols, to side-chain fluorinated polymers, perfluoropolyethers and fluoropolymers. Some PFAS on the market also possess structural attributes other than perfluoroalkyl chains (for example inclusion of ether linkages or chlorine atoms in the fluorinated hydrocarbon chains).

The properties of PFAS (including their oil and water repellency, high chemical, physical and thermal resistance to degradation, and low surface tension) have led to their use in a wide range of products available to consumers and in commercial and industrial applications. Some typical uses of PFAS include surfactants, lubricants, and repellents (for dirt, water, and grease). PFAS can also be found in certain firefighting foams (for example aqueous film-forming foams [AFFF]), food packaging materials, drugs (including natural health products and non-prescription drugs), medical devices, cosmetics, pesticides, textiles (for example carpets, furniture, and clothing), vehicles and electronics.

There are many potential sources of PFAS in Canada that can lead to human exposure and releases to the environment. Humans can be exposed to PFAS from various sources such as food and food packaging materials, cosmetics, products available to consumers, ambient air, indoor air and dust, and drinking water. Furthermore, PFAS-impacted contaminated sites represent “hot spot” areas across Canada where people and the environment may be exposed to elevated concentrations of PFAS. Such sites include those associated with the use of AFFF, typically released during activities associated with fighting liquid fuel fires, training activities and maintenance of firefighting equipment, including at airports and military facilities. As it is not possible to separate PFAS-containing waste

from the general waste stream, PFAS-containing products can be found in municipal solid waste (MSW) landfills or are destined for MSW incineration. Composting of PFAS-containing food packaging materials, releases into wastewater treatment systems, and the application of biosolids to land provide additional pathways of PFAS exposure to the environment. It should be noted that PFAS contamination is present throughout Canada and is not limited to a few sources or areas.

Once PFAS are released into the environment, their physical and chemical properties influence their fate and behaviour. Neutral PFAS (for example fluorotelomer alcohols) may be more volatile and therefore more likely to be found in the atmosphere. Fluorotelomer alcohols as well as other polyfluoroalkyl substances and side-chain fluorinated polymers can undergo transformation to form other more stable PFAS that are extremely persistent in the environment under ambient conditions. Ionic PFAS (which are predominantly ionized at environmental pH), such as perfluorocarboxylic acids and perfluorosulfonic acids, are water soluble and non-volatile, and thus partition predominantly to water where they can mobilize. Some shorter-chain PFAS, adopted in place of prohibited long-chain PFAS, have proven to be even more mobile on a local scale, potentially leading to transfer to food crops and drinking water. Some PFAS are also capable of undergoing long-range transport in the atmosphere (that is, for neutral, volatile PFAS) or in global ocean currents (that is, for ionic PFAS), as evidenced by their widespread distribution around the world, including in remote regions. Experience with contaminated sites management has also indicated that PFAS are challenging to remediate from contaminated sites and it is not possible to remove them from the broader environment.

Globally, PFAS can be found in virtually all environmental compartments, including air, surface and groundwater, oceans, soils, and biota, as well as in wastewater influent and effluent, landfill leachate, sewage sludge, and biosolids. The highest reported concentrations are typically in proximity to known sources of PFAS that may be released into the environment, such as contaminated sites where concentrations of PFAS may occur at levels which can pose negative human health and/or environmental effects. PFAS are also routinely reported in locations far removed from these sources. Similarly, although the highest concentrations of PFAS in organisms have been noted in proximity to known releases, their ubiquitous presence has been noted in tissue samples collected from organisms worldwide. While the number of PFAS that have been examined in studies to date has been limited, studies have increasingly noted the frequent detection of a range of PFAS. Monitoring and research activities in Canada are being conducted to better understand trends in PFAS occurrence in Canadian ecosystems and wildlife. Thus far, these activities have confirmed the ubiquitous presence of PFAS throughout Canada.

Depending on the substance’s physical and chemical properties, certain PFAS have been found to bioaccumulate in biota. PFAS have also been reported to significantly biomagnify (that is, to accumulate to increasingly higher levels up the food chain) in air-breathing organisms (for example mammals, birds), which can increase the likelihood of adverse effects being observed. Ecotoxic effects such as immunotoxicity and neurotoxicity as well as effects on growth, reproduction, and development have been reported in the literature, although there are still significant data gaps for certain species, groups of PFAS, and types of effects studied.

Currently, only a small number of PFAS are monitored in human biomonitoring surveys. Certain PFAS have been found in the blood (plasma or serum) of the general population in Canada and internationally. PFAS can also be transferred through the placenta, and infants and children can be exposed to PFAS through ingestion of human milk. Certain subpopulations were identified as having potential for greater exposure to PFAS. Compared to the general population, some northern

Indigenous communities (as measured in adults, including pregnant women) as well as Indigenous youth and children in other parts of Canada were considered to have higher levels of certain PFAS; however, other PFAS (for example perfluorooctanoic acid [PFOA]) have been noted to be lower. Firefighters internationally were also found to have elevated levels of certain PFAS. Canadian firefighters and people living in the vicinity of sites contaminated with PFAS (for example associated with the use of AFFF) may also be disproportionately exposed to higher levels of PFAS, although specific Canadian biomonitoring information was not available for these subpopulations.

In humans, some well-studied PFAS have been demonstrated to be readily absorbed in the body and bind to proteins in the blood. These PFAS can then be distributed through the bloodstream and accumulate in well perfused tissues (for example liver and kidneys). Some of the studied PFAS have been shown to be eliminated very slowly from the human body. Toxicological (*in vitro* and *in vivo*) and human epidemiological information is only available for a limited number of PFAS and recent information on well-studied PFAS, particularly PFOA and perfluorooctane sulfonate (PFOS), shows negative effects on human health at lower levels than reported in previous studies. Effects commonly reported in animal studies include effects on the liver, kidney, thyroid, immune system, nervous system, metabolism, body weight, reproduction, and development. Outcomes of human epidemiological studies involve similar organs, systems, or endpoints. Based on this information, it is evident that exposure to PFAS has the potential to cause effects to multiple organs and systems.

Although the vast majority of toxicology and epidemiology studies have focused on the effects from exposure to a single PFAS, biota and humans typically experience exposure to many PFAS at a given time, as can be seen from environmental sampling and biomonitoring data. A limited number of studies have evaluated the interactive effect of multiple PFAS on different endpoints; however, given the vast number and ubiquity of PFAS, it is reasonable to expect that cumulative effects may occur. The Government of Canada has been actively studying the ecological and human health effects associated with exposure to PFAS, including the use of new approach methods to characterize multiple PFAS in biological and environmental media at the same time. These studies confirm the environmental presence of PFAS mixtures that include many substances that are not targeted in typical monitoring and surveillance studies. In addition to specific initiatives, there are ongoing environmental and human monitoring and surveillance programs to address subpopulations that may be more susceptible or highly exposed, including pregnant people, children, Indigenous and northern communities in Canada, and firefighters.

Canada has acted to address certain PFAS for which early evidence had indicated potential concerns for the environment or human health. A limited number of PFAS are subject to risk management controls in Canada. The manufacture, use, sale, offer for sale, and import of PFOS, PFOA, long-chain perfluorocarboxylic acids (LC-PFCAs), and their salts and precursors, and products that contain them, are prohibited under the *Prohibition of Certain Toxic Substances Regulations, 2012* with a limited number of exemptions. Proposed regulations that would repeal and replace the *Prohibition of Certain Toxic Substances Regulations, 2012*, were also published in May 2022, which propose to further restrict these PFAS by removing or providing time limits for most remaining exemptions. Some PFAS notified under the *New Substances Notification Regulations (Chemicals and Polymers)* have also been subject to prohibitions, ministerial conditions, and significant new activity provisions under the *Canadian Environmental Protection Act, 1999* (CEPA). It has been observed that shorter-chain PFAS have been used as substitutes for long-chain PFAS (carbon chain length of 8 or more) following the implementation of regulatory restrictions on the latter.

Other domestic activities that target certain PFAS include developing water and soil guidelines for the protection of human health and the environment by the Government of Canada or through the Canadian Council of Ministers of the Environment (CCME); reducing risks from known federal contaminated sites through the Federal Contaminated Sites Action Plan; and reducing the anthropogenic release of chemicals of mutual concern into the Great Lakes under the Great Lakes Water Quality Agreement. Regulations for the import, export, and manufacture of certain ozone-depleting substances and concerning halocarbon alternatives are also set out under the *Ozone-depleting Substances and Halocarbon Alternatives Regulations*. In October 2024, the Canadian Food Inspection Agency (CFIA) implemented an interim standard for PFAS in biosolids as part of the Government of Canada's coordinated suite of risk mitigation measures intended to minimize human and environmental exposure to PFAS throughout the product's life cycle from manufacture to disposal. The CFIA has been working with the provinces and will continue to engage with the provinces, municipalities, and the biosolids industry in implementing the interim standard. Also in October 2024, Innovation Science and Economic Development Canada (ISED) launched a challenge under the Innovation Solutions Canada Program, focused on advancing the destruction of PFAS compounds in contaminated media. This initiative seeks to identify innovative, cost-effective, safe, and scalable solutions that lead to the destruction of PFAS across various contaminated solid or aqueous media. The Government of Canada works with other governments internationally on initiatives that address PFAS, including through the OECD and the Stockholm Convention on Persistent Organic Pollutants. For example, Canada has successfully nominated LC-PFCAs, their salts, and related compounds for addition to the Stockholm Convention.

The broad use of PFAS, their ability to move locally and over long ranges, and their consequent ubiquitous presence in the environment have resulted in continuous environmental and human exposure to multiple PFAS, with well-studied PFAS demonstrating the potential to affect multiple systems and organs in both humans and wildlife. Certain PFAS may bioaccumulate and biomagnify in food webs to an extent that can cause adverse effects in biota at low environmental concentrations. Recent information on well-studied PFAS, particularly PFOA and PFOS, also shows negative human health effects at lower levels than indicated by previous studies. As a result of the extreme persistence of PFAS, their potential for bioaccumulation in organisms and biomagnification through the food chain, and the impossibility of their removal from the broader environment, presence in the environment and uptake by biota and humans will continue and potentially increase in the absence of intervention. The potential for cumulative exposure and effects are important considerations as most wildlife and human exposures involve an unknown mixture of PFAS.

There are uncertainties associated with understanding the characteristics of substances across the range of PFAS structures from toxicological, epidemiological and monitoring datasets that are focused on a limited number of PFAS. However, there is a growing body of evidence suggesting that concerns identified for well-studied PFAS are more broadly applicable to other PFAS than previously believed. Similarly, while the specific hazards associated with mixtures of PFAS are largely unknown, there are many potential sources of PFAS that can lead to exposure and it is reasonable to expect that cumulative effects may occur from exposure to multiple PFAS.

To be protective of the environment and human health, and to apply precaution when addressing gaps in information, it is reasonable to anticipate that the concerns identified for PFAS that have been well studied may also be inherent in other substances in the class.

However, there is evidence to suggest that fluoropolymers may have significantly different exposure and hazard profiles when compared with other PFAS in the class. Fluoropolymers are defined as polymers made by polymerization or copolymerization of olefinic monomers (at least 1 of which contains fluorine bonded to 1 or both of the olefinic carbon atoms) to form a carbon-only polymer backbone with fluorine atoms directly bonded to it. Given information suggesting their differences from the other PFAS in the class, additional work on fluoropolymers is warranted. PFAS meeting the definition of fluoropolymers are not addressed within this report and are planned for consideration in a separate assessment.

Owing to the extreme persistence of PFAS and their potential to cause adverse effects, impacts on the environment are expected to increase if entry to the environment continues. On the basis of what is known about well-studied PFAS and the potential for other PFAS to behave similarly, and on the expectation that combined exposures to multiple PFAS increase the likelihood of detrimental impacts, it is concluded that the class of PFAS, excluding fluoropolymers as defined in this report, meets the criteria under paragraph 64(*a*) of CEPA as these substances are entering or may enter the environment in a quantity or concentration or under conditions that have or may have immediate or long-term harmful effects on the environment or its biological diversity. However, it is concluded that the class of PFAS, excluding fluoropolymers as defined in this report, does not meet the criteria under paragraph 64(*b*) of CEPA as these substances are not entering the environment in a quantity or concentration or under conditions that constitute or may constitute a danger to the environment on which life depends.

Owing to the widespread use of PFAS combined with their ubiquitous presence in the environment, humans are continuously exposed to multiple PFAS, which has the potential to cause effects of concern. On the basis of what is known about well-studied PFAS and the potential for other PFAS to behave similarly, and on the expectation that combined exposures to multiple PFAS increase the likelihood of detrimental impacts, it is concluded that the class of PFAS, excluding fluoropolymers as defined in this report, meets the criteria under paragraph 64(*c*) of CEPA as these substances are entering or may enter the environment in a quantity or concentration or under conditions that constitute or may constitute a danger in Canada to human life or health.

Therefore, it is concluded that the class of PFAS, excluding fluoropolymers as defined in this report, meets 1 or more of the criteria set out in section 64 of CEPA.

Well-studied PFAS meet the persistence criteria as set out in *the Persistence and Bioaccumulation Regulations* of CEPA. Based on available information and structural similarities, it is expected that other substances within the class of PFAS are also highly persistent or transform to persistent PFAS. It is therefore determined that the class of PFAS meets the persistence criteria as set out in the *Persistence and Bioaccumulation Regulations* of CEPA. Given that fluoropolymers have been excluded from this assessment, they are also excluded from this determination with regard to *the Persistence and Bioaccumulation Regulations* of CEPA.

There is a high concern identified for the biomagnification and trophic magnification potential of well-studied PFAS in air-breathing organisms; however, the numeric criteria for bioaccumulation, outlined in the *Persistence and Bioaccumulation Regulations*, are based on bioaccumulation data for freshwater aquatic species which do not account for biomagnification potential. Therefore, application of the criteria would not reflect the concern for dietary-based biomagnification, the primary route of food web exposure identified for well-studied PFAS. Therefore, the bioaccumulation potential of PFAS

cannot reasonably be determined according to the regulatory criteria set out in the *Persistence and Bioaccumulation Regulations* of CEPA.

1 Introduction

Pursuant to section 68 of the *Canadian Environmental Protection Act, 1999* (CEPA) (Canada 1999), the Minister of the Environment and the Minister of Health have prepared a report on the class of per- and poly-fluoroalkyl substances (PFAS) to provide an overview of the sources, fate, occurrence, and potential impacts of PFAS on the environment and human health. This class of substances was considered a priority on the basis that scientific evidence to date indicates that the other groups of PFAS, including those used to replace regulated PFAS (that is, perfluorooctane sulfonate [PFOS] and its salts and precursors, perfluorooctanoic acid [PFOA] and its salts and precursors, and long-chain perfluorocarboxylic acids [LC-PFCAs] and their salts and precursors), may also be associated with environmental or human health effects. This report and its conclusion are intended to inform decision-making on PFAS as a class in Canada.

PFAS are a large class of human-made substances that include a very broad range of chemicals from discrete fluorosurfactants to polymeric PFAS such as side-chain fluoroalkyl polymers (SCFPs), including larger precursors that can transform in the environment to produce simpler PFAS.

The common chemical characteristic of PFAS is the perfluoroalkyl moiety, which is extremely stable, rendering it resistant to degradation. As a result of this stability, PFAS have often been termed “forever chemicals” due to their long persistence in the environment. The extreme persistence of the fluorocarbon moiety combined with the propensity for environmental accumulation and mobility of many PFAS has resulted in the ubiquitous presence of PFAS globally, even in remote regions like the Arctic (Kwiatkowski et al. 2020). It has been argued that the ongoing release of these highly persistent substances will result in increased concentrations and increased probabilities of known and unknown effects (Cousins et al. 2020).

The widespread use of these substances has led to the detection of certain PFAS in humans and nearly all environmental compartments, including ambient air, surface water, groundwater, marine water, and soil as well as in landfill leachate, wastewater influent, effluent, sludge, and biosolids (see, for example, ECHA 2022c). Globally, several groups of PFAS have been found in the environment near point sources, such as manufacturing plants and sites where firefighting foams have been used, including airports and military bases (see, for example, Hu et al. 2016; Lanza et al. 2016). If the concentrations of PFAS are above various guideline levels, locations may be identified as contaminated sites. PFAS can also be released to the environment through consumer use and disposal of PFAS-containing products. Therefore, landfills and wastewater treatment facilities (including associated waste products such as biosolids) are potential pathways of PFAS entry into the environment (see, for example, Gewurtz et al. 2013; Lakshminarasimman et al. 2021). Once in the environment, certain PFAS move readily through water and soil and can contaminate large areas (see, for example, Bhavsar et al. 2016; CCME 2021a). Significant costs are associated with assessing and remediating contaminated soil and drinking water sources (Kwiatkowski et al. 2020). This is because PFAS do not readily break down, and treatment and destruction technologies at commercial scales are still quite limited. Many PFAS have been shown to be transported long distances through the atmosphere, waterbodies, and within groundwater. Long-range transport of PFAS has resulted in these

substances being found in the Arctic in air, ice, and both fresh and salt water as well as in wildlife such as polar bears, whales, seals, and birds (Muir et al. 2019). Certain PFAS have also been found in higher concentrations in northern First Nations and Inuit communities compared with the rest of the Canadian population (see, for example, Caron-Beaudoin et al. 2020; Garcia-Barrios et al. 2021).

In Canada, 3 well-defined subgroups of PFAS (that is, PFOS, PFOA, and LC-PFCAs, and their salts and precursors) were assessed under Canada's Chemicals Management Plan (CMP) (EC 2006, 2012; EC, HC 2012). These groups were added to Schedule 1 of CEPA on the basis of risks to the environment due in large part to their persistence and bioaccumulation potential and are regulated under the *Prohibition of Certain Toxic Substances Regulations, 2012* (PCTSR). This risk management measure addresses 94 PFAS on the Domestic Substances List (DSL)[1] (Canada 1999). Given that these subgroups are defined using a description of the perfluorinated moiety, the risk management measures also apply to any PFAS meeting the description, even those not known to be used in commerce in Canada. Approximately 100 of the more than 290 PFAS notified under the *New Substances Notification Regulations (Chemicals and Polymers)* (NSNR) have also been subject to regulations and/or prohibitions, ministerial conditions, or significant new activity (SNAc) provisions under CEPA. Many of the actions under the NSNR have been rescinded and/or replaced by the introduction of other regulations, which cover the same substances and prevent risk to human health and/or the environment (for example, the *Ozone-Depleting Substances and Halocarbon Alternatives Regulations* [ODSHAR]).

A quantitative risk analysis and management approach on discrete substances, subgroups, or groups of existing PFAS (that is, with risk conclusions drawn and management actions taken separately for each substance/group) has been recognized as an inefficient way to manage the class of PFAS. Many scientists (Helsingør, Madrid, and Zürich Statements [Scheringer et al. 2014; Blum et al. 2015; Ritscher et al. 2018; DeWitt et al. 2024]) recommend a preventive and precautionary approach to this class of substances, with management actions undertaken on broad subgroups or on the class in its entirety despite a lack of scientific certainty regarding the majority of PFAS, which remain poorly studied. In addition, multilateral organizations and agreements, such as the Organisation for Economic Co-operation and Development (OECD) and the United Nations' Stockholm Convention on Persistent Organic Pollutants (POPs), have recognized the potential for regrettable substitution within the PFAS family. Many jurisdictions, including some states in the United States (US) and the European Union (EU), have acted or are considering to take action on PFAS as a class.

In April 2021, the Government of Canada published a Notice of Intent, signaling an intent to move forward with activities to address PFAS as a class (ECCC, HC 2021). The Draft State of

[1] The Domestic Substances List (DSL) is an inventory of substances manufactured in or imported into Canada on a commercial scale. It was originally published in the *Canada Gazette*, Part II on May 4, 1994, and included approximately 23 000 substances deemed to have been in Canadian commerce between January 1984 and December 1986. The DSL is amended, on average, 12 times per year to add, update, or delete substances. It now contains more than 28 000 substances and can be accessed through Substances Search.

PFAS Report was published in May 2023 (ECCC, HC 2023) followed by an Updated Draft State of PFAS Report in July 2024 (ECCC, HC 2024).

The State of PFAS Report is a qualitative assessment of the fate, sources, occurrence, and potential impacts of PFAS on the environment and human health, including the basis for a class-based approach and application of precaution, to inform decision-making on PFAS in Canada. It includes information collected through literature searches, including key information submitted by stakeholders in response to the *Notice of Intent to Address the broad class of PFAS* (ECCC, HC 2021), and during a 60-day public comment period following both the publication of the Draft State of PFAS Report on May 20, 2023 and the Updated Draft State of PFAS Report on July 13, 2024. The majority of relevant data were identified up to March 2022, with additional data identified up to September 2024. This report has undergone external review. Comments were received from reviewers at Tetra Tech during the development of the Draft and Updated Draft State of PFAS Reports. While external comments were taken into consideration, the final content and outcome of this report remain the responsibility of Health Canada (HC) and Environment and Climate Change Canada (ECCC).

This report focuses on information to support a conclusion under section 64 of CEPA by examining scientific information, including information on subpopulations who may have greater susceptibility or greater exposure and cumulative effects[2], if available, and incorporating a weight of evidence approach and precaution. This report presents the critical information and considerations on which the conclusion is based.

1.1 Chemical scope

The class of PFAS encompasses a broad range of structures (for example, ethers, polymers), including those with varying degrees of fluorination and chain length (Buck et al. 2011; Wang Z et al. 2017; ITRC 2020a; OECD 2021). This is illustrated by the 2018 OECD list of over 4700 PFAS (OECD 2018a) or other lists such as the US Environmental Protection Agency (US EPA) CompTox Chemicals Dashboard (CompTox 2021, 2022) which lists approximately 15,000 substances.

This report defines the class of PFAS according to the OECD (2021) definition for PFAS, which is **"fluorinated substances that contain at least one fully fluorinated methyl or methylene carbon atom (without any H/Cl/Br/I atom attached to it), that is with a few noted exceptions, any chemical with at least a perfluorinated methyl group (–CF_3) or a perfluorinated methylene group (–CF_2–) is a PFAS."** In this report, the class of PFAS is comprised of substances meeting the OECD definition and, as such, the class of PFAS meets

[2] The consideration of cumulative effects under CEPA may involve an analysis, characterization and possible quantification of the combined risks to health or the environment from exposure to multiple chemicals.

the definition for a class of substances under CEPA as they contain the same portion of chemical structure[3].

This chemical definition captures substances with a wide range of structures, properties, and use patterns. The fluorocarbon moiety is frequently functionalized, commonly as carboxylic or sulfonic acids (for example, PFOA or PFOS) or as fluorotelomer alcohols (FTOHs). These functionalized molecules may be used to chemically link the fluorocarbon moiety to more complex molecules, such as side-chain fluorinated polymers or sulfonamidoethanol compounds.

The OECD (2021) definition of PFAS is broader than the approach used to compile the OECD list of PFAS in 2018, which focused on those PFAS that contain a perfluoroalkyl moiety with 3 or more carbons or a perfluoroalkylether moiety with 2 or more carbons; consequently, the use of the OECD (2021) definition increases the number of individual PFAS beyond the approximately 4700 PFAS originally identified by OECD in 2018 (OECD 2018 a,b). The OECD (2021) definition also results in the inclusion of certain substances used in drugs and pesticides, and substances that are regulated in Canada under the ODSHAR, such as chlorofluorocarbons (CFCs), hydrochlorofluorocarbons (HCFCs), and hydrofluorocarbons (HFCs). Trifluoracetic acid (TFA), a transformation product formed in the atmosphere from some of the ODSHAR-regulated substances as well as hydrofluoroolefins (HFOs) and hydrochlorofluoroolefins (HCFOs) (UNEP 2016), is also captured by the OECD definition. Other jurisdictions have also identified a larger number of PFAS; for example, the European Chemicals Agency (ECHA, 2023b) and the US EPA CompTox Chemicals Dashboard (CompTox 2021, 2022) list more than 10,000 and approximately 15,000 substances, respectively.

This report uses the 2021 OECD chemical definition of PFAS, given the concern with the stability of the fluorocarbon moiety, which results in persistence in the environment. For PFAS that experience some transformation, the fluorinated portion of the molecule is typically preserved, resulting in stable PFAS transformation products. The class of PFAS is comprised of substances meeting this definition. While the general definition of PFAS is based on chemical structure, the OECD (2021) report notes that individual jurisdictions may develop working definitions for PFAS, which may be established by combining the general definition of PFAS with additional considerations (for example, specific properties or use areas). Such working definitions may be beneficial when contemplating regulatory or non-regulatory approaches to reduce exposure.

PFAS acronyms that are frequently used in this report are defined in Appendix A. This State of PFAS Report often refers to long-chain (LC) and short-chain (SC) PFAS, where long-chain refers to a carbon chain length of 8 (C8) or higher and short-chain refers to a carbon chain length of 7 (C7) or lower. Although the definition of long-chain PFAS used in this report is consistent with reports by many other authors for perfluorinated carboxylic acids (for example,

[3] Subsection 3(3) of CEPA states that a class of substances are substances for the purpose of the Act where, as stated in the definition of the term *class of substances* in subsection 3(1), as any 2 or more substances that: (a) contain the same portion of chemical structure; (b) have similar physical-chemical or toxicological properties; or (c) have similar types of use.

the OECD, US EPA), other authors may sometimes refer to perfluorinated sulfonates with 6 (C6) or more fully fluorinated carbons (for example, perfluorohexane sulfonic acid [PFHxS]) as being long-chain PFAS. The definitions of short-chain and long-chain PFAS used in this report are consistent with other Government of Canada publications. Moreover, reference to perfluoroalkyl acids (PFAAs) includes the PFAAs (for example, perfluorocarboxylic acids [PFCAs], perfluorosulfonic acids [PFSAs], perfluoroalkyl phosphonic acids [PFPAs], perfluoroalkyl phosphinic acids [PFPiAs]) and perfluoroalkylether acids (for example, per- and polyfluoroalkyl ether carboxylic acids [PFECAs], per- and polyfluoroalkyl ether sulfonic acids [PFESAs]).

1.1.1 Polymeric PFAS

PFAS are sometimes classified on the basis of whether they are polymeric or non-polymeric (Buck et al. 2011; OECD 2021). The most commonly identified groups of polymeric PFAS include side-chain fluorinated polymers (SCFPs), perfluoropolyethers (PFPEs), and fluoropolymers.

SCFPs are polymeric PFAS that do not have perfluorinated or polyfluorinated polymer backbones and are instead composed of variable composition backbones with polyfluoroalkyl (and possibly perfluoroalkyl) side chains (Buck et al. 2011). SCFPs can be categorized according to the type of PFAS moieties present on the side chains (for example, n:2 fluorotelomers) or the structural repeating units in the polymer backbone (for example, acrylates, oxetanes, urethanes) (OECD 2022). It is well-established that SCFPs can undergo abiotic or biotic degradation to release non-polymeric PFAS (that is, via cleavage of the side chains) (OECD 2022; Lohmann and Letcher 2023), which can then transform to stable PFAS (for example, PFCAs, PFSAs) that are bioavailable. For example, acrylate and urethane side-chain fluorinated polymers can undergo ester bond cleavage. In addition, the polymer backbone may also break to form small oligomeric species that subsequently undergo ester bond cleavage (OECD 2022; Lohmann and Letcher 2023). A recent study by Matsukami et al. (2024) assessed the tendency of SCFPs in commercially available durable water repellents (DWRs) to degrade and form PFAAs and PFAA-precursors and found increased concentrations of PFBS (a PFAA), and the PFAA-precursors MeFBSE, fluorotelomer olefins, and FTOHs following alkaline hydrolysis. The authors also concluded that the composition of DWRs containing SCFPs has shifted over the years towards the use of short-chain SCFPs (that is, C_4F_9- and C_6F_{13}-SCFPs), following regulations placed on long-chain PFAAs.

PFPEs have an ether polymer backbone with F atoms directly attached, having backbone units such as -CF_2-, -CF_2CF_2-, and -$CF(CF_3)CF_2$- units separated by oxygen atoms (Buck et al. 2011). The OECD Synthesis Report on PFPEs (2024) has noted that many PFPEs have low molecular weight, even below 1000 Daltons in some cases. Molecules with molecular weight less than 1000 Daltons can be considered to be bioavailable (US EPA 2013), as such, lower molecular weight PFPEs have the potential to be bioavailable. These lower molecular weight PFPEs can be volatile (Young et al. 2006; OECD 2024) and may demonstrate some degree of solubility at ppm levels (DelRaso et al. 1996; ECHA 2020; OECD 2024), indicating potential for mobility in the environment. For PFPEs with the same functional end-groups, their volatility decreases with increasing molecular weight (OECD 2024).

PFPEs are generally considered to be stable under natural conditions (OECD 2024). However, under use-related conditions, PFPEs have been shown to degrade at elevated temperatures (such as those that may be encountered in industrial applications) to form non-polymeric PFAS (OECD 2024). The fate of PFPEs (including degradation rate) is dependent on the nature of the application, the molecular weight, and end-groups of the PFPE (OECD 2024).

Lower molecular weight, linear PFPEs are considered to be structurally similar to per- and polyfluoroalkyl ether carboxylic acids (PFECAs) with 4 or 5 ether repeat units (oligomers) and molecular weights of approximately 500 Daltons; these PFECAs contain the same type of repeating backbone ether linkage found in PFPEs and may demonstrate similar effects as lower molecular weight PFPEs. These PFECAs can bioaccumulate (Burkhard 2021; Li Y et al. 2021) and have been reported to display acute embryotoxicity in fish (Gebreab et al. 2020; Wang et al. 2020; Gui et al. 2023). In addition, these PFECAs have been associated with effects on the liver in animal studies (Guo et al. 2019; Chen et al. 2021; Conley et al 2024; Jackson et al. 2024) and have been measured in human serum samples (Kotlarz et al. 2020; 2024). Separately, no treatment-related effects were observed for a PFPE (molecular weight of 3,200 Daltons) in an animal study (Malinverno et al. 1996).

Fluoropolymers are defined as polymers made by polymerization or copolymerization of olefinic monomers (at least 1 of which contains fluorine bonded to 1 or both of the olefinic carbon atoms) to form a carbon-only polymer backbone with fluorine atoms directly bonded to it (Buck et al. 2011). Additionally, a version of this definition has been used by ECHA (2023c), and a simplified version that retains the description of the final polymeric structure has been used by the OECD (2015a, 2021). Certain ionomers, which consist of a fluoropolymer backbone with side-chains of perfluoroethers terminating with an ionizable group such as a sulfonic or carboxylic acid (for example, Mauritz and Moore 2004), are considered to be fluoropolymers (see section 3.2.3).

Compared with SCFPs and PFPEs, fluoropolymers have C-F bonds on a carbon-only backbone. Fluoropolymers do not appear to degrade under natural environmental conditions (Huber et al. 2009; Gangal and Brothers 2015; Geertinger et al. 2019); however, there may be potential for the leaching of non-polymeric PFAS (for example, processing aids, monomers and oligomers) throughout the fluoropolymer lifecycle (Lohmann et al. 2020). Fluoropolymers with high molecular weight and low solubility may not be mobile or bioavailable (Korzeniowski et al. 2023; Lohmann and Letcher 2023). In comparison, other PFAS in the class are expected to be mobile in the environment (including potentially undergoing long-range environmental transport) and are found to be bioavailable, given their physical-chemical properties. Fluoropolymers may have significantly different exposure and hazard profiles when compared with other PFAS.

In order to further examine these differences, additional work is warranted. PFAS meeting the definition of fluoropolymers as defined in this report are therefore planned for consideration in a separate assessment and are not considered further within this report. Other fluorinated polymers, including SCFPs and PFPEs, remain within the scope of this report.

2 Uses and sources of exposure

KEY POINTS ON USES AND SOURCES OF EXPOSURE

- PFAS are used in many commercial applications and industrial sectors and are found in a wide range of products, including certain firefighting foams (for example, aqueous film-forming foams [AFFF]), food packaging materials, surfactants, lubricants, drugs (including natural health products and non-prescription drugs), medical devices, cosmetics, pesticides, textiles, vehicles, repellents and electronics.
- Some other uses of PFAS include solvents; processing aids; oil/water repellents in packaging; levelling agents in paints, ink, and adhesive formulations; and refrigerants / blowing agents.
- Contaminated sites associated with the use of PFAS-containing AFFF represent “hot spot” areas where elevated concentrations of PFAS may be found in the environment.
- PFAS releases from municipal solid waste (MSW) landfills, MSW incineration, composting of PFAS-containing food packaging materials, wastewater treatment systems, and the application of biosolids to land are potential pathways of PFAS exposure to the environment.
- PFAS contamination is present throughout Canada and is not limited to a few sources and areas.
- Experience with PFAS-contaminated sites has shown that remediation and management of these sites are challenging and complex; additionally, the removal of PFAS from the broader environment is not possible.

2.1 Uses of PFAS

PFAS possess practical traits that are useful in a broad spectrum of applications, such as:

- oil and water repellency, which provides stain resistance, soil repellency, and non-stick properties;
- high resistance to chemical, physical, and thermal degradation; and
- low surface tension, resulting in the use of PFAS as surfactants and lubricants.

Due to their properties, PFAS are used in many commercial applications and industrial sectors and are found in a wide range of products, including certain firefighting foams, food packaging materials, surfactants, lubricants, drugs (including natural health products and non-prescription drugs), medical devices, cosmetics, pesticides, textiles, vehicles, repellents and electronics. A study published in 2020 (Glüge et al. 2020) identified more than 200 current uses within 64 use categories for more than 1400 PFAS and presents in detail their functions and the related sectors.

PFAS-containing firefighting foams are used during emergencies to extinguish Class B fires, involving flammable and combustible liquids and gases, including petroleum greases, tars, oils and gasoline, solvents, and alcohols. In the past, these foams were widely used for training purposes, but users have progressively started to employ training foams that do not contain PFAS (ITRC 2020b). PFAS surfactants help to cut off the oxygen from the fire by contributing to the formation of a foam blanket and, more uniquely, a water film that glides over the surface of

the burning liquid. Aqueous film-forming foam (AFFF) is the most widely used and available of these foams and, for this reason, PFAS-containing firefighting foams are often simply referred to as AFFF, including in this report. There are, however, other types of PFAS-containing firefighting foams with slightly different compositions used in specialized applications, such as alcohol-resistant AFFF (AR-AFFF) for polar solvents, and film-forming fluoroprotein foam (FFFP) for an added burn back resistance for deeper pool fires.

In Canada, AFFF that contain certain regulated PFAS are prohibited under the PCTSR with a few exemptions (Canada 2016). Since 2016, these exemptions have accommodated the transition to alternatives to PFOA and/or LC-PFCAs and the residual levels of PFOS that remain in firefighting equipment from historical use of the substance. However, these regulations are currently being revised, and the proposed *Prohibition of Certain Toxic Substances Regulations, 2022* would further restrict these exemptions (Canada 2022a), and would lead to the phase-out of the use of AFFF-containing PFOA and/or LC-PFCAs. Certain shorter length PFAS have been used as replacements for regulated PFAS in this application. The dispersive use of AFFF during training and fire events broadly releases PFAS and have greatly contributed to PFAS contaminated sites in Canada, which is further discussed in section 2.3.

In Canada, although there are regulations in place prohibiting PFOS, PFOA, LC-PFCAs, their salts, and their precursors, these regulations currently include a limited number of exemptions such as manufactured items. As a result, these substances may remain in circulation (refer to section 8.1.1 for additional information on risk management under CEPA). Furthermore, longer-chain PFAS are often produced as impurities during the manufacturing process of shorter-chain length replacements, and they may still be present in the effluents of manufacturing plants and in finished products (Prevedouros et al. 2006).

Eight different Canadian surveys to gather information on commercial activity in Canada, issued pursuant to section 71 of CEPA since the year 2000, have included a total of 269 PFAS, with a number of these PFAS being included in more than 1 survey (Canada 2005a, 2005b, 2012, 2015, 2017, 2018, 2020a). Of the 269 PFAS that have been surveyed, responses were received for 87 PFAS from 27 different companies. Of these 269 PFAS surveyed, 169 have been prohibited by the PCTSR since they were last surveyed.

Only very limited information is available on the type and concentrations of PFAS used in products available to consumers sold in Canada, including products intended for children (Beesoon et al. 2012; Kim et al. 2015; Xia et al. 2022).

2.1.1 Uses notified to the Government of Canada

Knowledge of the many uses of PFAS in Canada has been informed by New Substances Notifications received under the NSNR of CEPA, Cosmetic Notifications received under the *Cosmetic Regulations* of the *Food and Drugs Act*, and voluntary submissions received by HC that are related to food packaging materials.

2.1.1.1 *New Substances Notification Regulations (Chemicals and Polymers) (NSNR)*

New substances that are imported into or manufactured in Canada are subject to notification requirements tiered to annual import/manufacture quantity. Notification requires substance-specific information such as identity, use, hazard, and ecotoxicity information in order to assess the potential for risk to humans and the environment. Over 290 new PFAS have been notified to Canada under the NSNR since 1994 (half of which are polymers). Of these PFAS, approximately 30 have been identified as intended to be manufactured in Canada, generally with limitations (for example, identified as contained site-limited intermediates, contained for export only, subject to the ODSHAR, or subject to the SNAc provisions of CEPA).

These New Substances Notifications have indicated a wide range of potential uses (Figure 1). Some typical uses notified for chemical PFAS include processing aids (for example, mold release agents for plastics); oil/water repellents in packaging, carpet, leather, fabric, and tile; levelling agents in paints, ink, and adhesive formulations; grease-proof coating for food packaging materials (that is, food contact materials); refrigerants / blowing agents; firefighting foams (surfactants in AFFF); or as active ingredients in human and veterinary drug products. New PFAS polymers were notified mostly with the intended use of anti-stain and water/oil repellency, with some intended uses as levelling agents, processing aids, surfactants, and lubricants. Uses in the “other” category for new PFAS include antistatic agents, colourants, electrolytes, cosmetic ingredients, tracers, marine paints, and herbicide safeners.

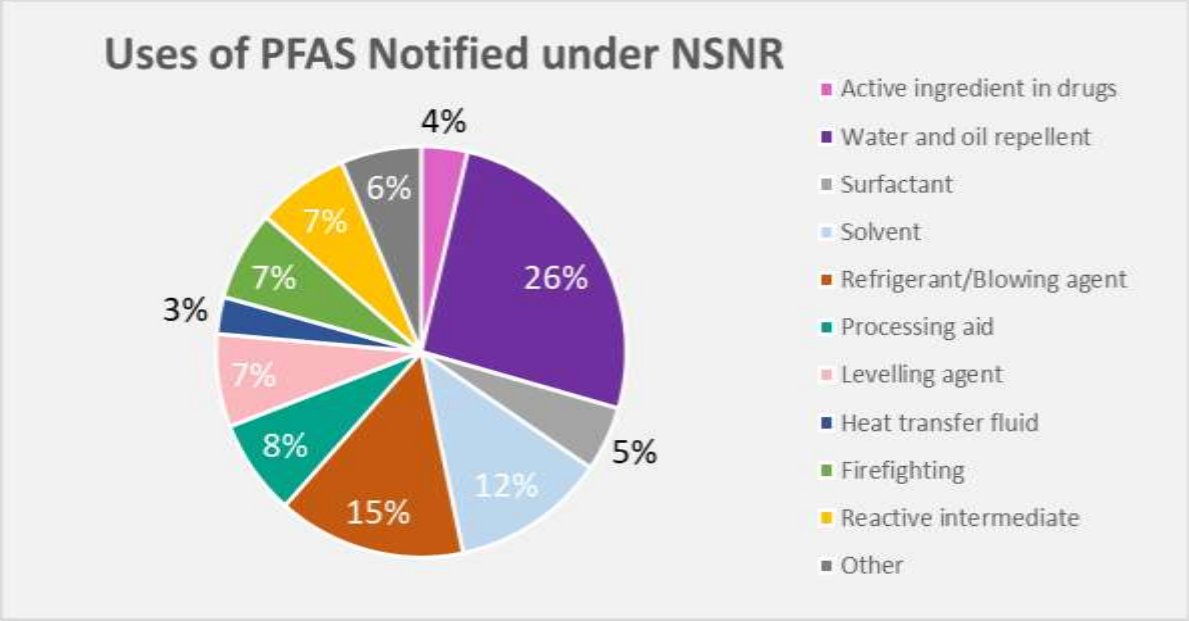

Figure 1. Uses of new PFAS notified under the NSNR since 1994. Percentage of total notified uses in PFAS New Substances Notifications.

Approximately 90 PFAS notified under the NSNR have been added to the DSL. Once a substance is added to the DSL, it may be used for any purpose unless it is subject to risk management measures.

Prior to 2016, many refrigerants and blowing agents notified under the NSNR were later added to the DSL with or without risk management measures, including measures imposed by the New Substances program; however, as of December 2016, these substances have been regulated under the ODSHAR (see section 8.1).

Although the intended uses notified by importers and manufacturers under the NSNR are largely industrial, some of the same PFAS may be used in other types of products, such as cosmetics. Analysis has shown that 15 PFAS notified under the NSNR for industrial uses, including some not on the DSL, have also been notified for cosmetic use in Canada under the *Cosmetic Regulations* and are presently used in cosmetics. Therefore, PFAS that were reported to have industrial uses at the time of notification (such as an industrial foam stabilizer) may be subsequently used in non-industrial products that result in greater direct human exposure (such as cosmetics).

2.1.1.2 Cosmetics

PFAS are intentionally added to some cosmetics, such as foundations, moisturizers, lotions, and creams, to improve the penetration of other ingredients into the skin, enhance brightness, and increase the durability of makeup. Section 30 of the *Cosmetic Regulations* requires that all manufacturers and importers of cosmetics submit a Cosmetic Notification form to HC at the latest 10 days after they first sell their cosmetic in Canada. The Cosmetic Notification form must include, among other things, a list of all the ingredients and, for each ingredient, its exact concentration or the concentration range (Canada 2019). Between January 1993 and July 2024, a total of 3,648 cosmetic products notified to Health Canada contained 1 or more PFAS. Approximately 78% of these notifications were for leave-on products such as makeup and moisturizers, which are intended to be used on the body, face, lips, and eye areas. Most (87%) of these products contain listed PFAS at or below a concentration of 3%; in about 4% of the products, PFAS ingredients are notified above a concentration of 10%. A trend analysis of the Cosmetic Notification data indicated that the annual number of notifications of new PFAS-containing cosmetics introduced in the Canadian market increased between 1993 and 2017, reaching a maximum of 487 in 2017. Notifications of new PFAS-containing cosmetics have been declining since then to approximately 157 in 2023. Over the last 5 years, Health Canada has received approximately 268,000 Cosmetic Notifications for cosmetics such as cleansers, conditioners, exfoliators, foundations, body creams, and makeup products. PFAS-containing Cosmetic Notifications represent less than 1% of the total Cosmetic Notifications received.

As of July 2024, 67 unique PFAS ingredients have been notified in cosmetics in Canada. These PFAS ingredient names are notified using the International Nomenclature of Cosmetic Ingredients (INCI) naming convention. Among these, 10 (perfluorodecalin, trifluoroacetyl tripeptide-2, polyperfluoromethylisopropyl ether, perfluorononyl dimethicone, polyperfluoroethoxymethoxy difluoroethyl PEG phosphate, perfluorohexylethyl triethoxysilane, tetradecyl aminobutyroylvalylaminobutyric urea trifluoroacetate, methyl perfluorobutyl ether, methyl perfluoroisobutyl ether, perfluorohexane) were the most frequently notified PFAS ingredients. Given that PFOA and PFOS are prohibited substances under the PCTSR, they were not notified as cosmetic ingredients per se; however, cosmetics containing polymeric

PFAS, FTOHs, and polyfluoroalkyl phosphate esters (PAPs) may be potential sources of PFOA, PFOS, and other PFAAs (Fujii et al. 2012; Harris et al. 2022; Bălan et al. 2024).

The identification and measurement of PFAS in cosmetics is still an emerging area internationally. Using chromatographic methods, several research groups have investigated cosmetic products for specific PFAAs and their precursors (Danish EPA 2018; Whitehead et al. 2021; Harris et al. 2022). A recent study confirmed several PFAAs and PAPs at concentrations ranging from ng/g to mg/g in cosmetics purchased in Canada that listed the presence of fluorinated ingredients (Harris et al. 2022). However, the concentration of individual PFAS detected varied widely between tested samples. PFAS were also detected in cosmetics that did not list their presence on product labels, although at much lower concentrations ranging from ng/g to μg/g (Whitehead et al. 2021; Harris et al. 2022). In addition, several researchers have studied the total fluorine and extractable organic fluorine content in cosmetic products using methods that do not identify/differentiate between different kinds of fluorine-containing substances and which may include non-PFAS (Fujii et al. 2013; Schultes et al. 2018; Whitehead et al. 2021). The results from these studies indicate that the sum of the concentrations of individually identified PFAS measured in cosmetics was substantially lower than their respective total fluorine content, in many cases accounting for only about 1% of the total fluorine. Consequently, the lack of mass balance observed in these studies indicates the presence of many unknown fluorinated substances in cosmetics, some of which may be PFAS. The availability of a wide spectrum of fluorinated ingredients and lack of analytical standards make it challenging to screen for individual PFAS in cosmetics.

2.1.1.3 Food packaging Materials

In Canada, all food packaging materials, including domestic and imported materials, must comply with the safety provisions under Division 23 of the *Food and Drug Regulations*. Division 23 prohibits the sale of food in a package that could transfer a chemical to the food that may be harmful to the health of the consumer. The responsibility to ensure that the materials used in contact with foods are in compliance with regulatory requirements lies with the food seller (for example, the food manufacturer, packager, or distributor).

To date, HC has evaluated and issued Letters of No Objection concerning 16 polymeric PFAS (that is, perfluoropolyethers and side-chain fluorinated [co]polymers), the most recent of which was provided in 2018. These uses are consistent with the use of PFAS approved in food contact materials internationally (European Commission 2020a; OECD 2020; US FDA 2022a).

Given the existing risk management actions in Canada (see section 8.1.1), the US, and Europe (US EPA 2009; OECD 2015b, 2020), the presence of PFOS-based food packaging materials on the Canadian marketplace is not expected. The proposed amendments to the PCTSR will further restrict the import, use and sale of manufactured items containing PFOA and LC-PFCAs in Canada (Canada 2022a).

Since treated paper and paperboard may enter recycled paper feedstock, it is possible that untreated paper products made from recycled feedstock will contain detectable concentrations of PFAS. Xu Y et al. (2013) report that the sum concentration of 7 perfluorocarboxylates (that is, PFHxA, PFHpA, PFOA, PFNA, PFDA, PFUnDA, and PFDoDA) were detected at concentrations

ranging from 700 µg/kg to 2220 µg/kg of paper (0.7 ppm to 2.2 ppm) in 2 commercially available food contact papers, while PFBS, PFHxS and PFOS were not detected. According to Curtzwiler et al. (2021), the PFCA (that is, PFBA, PFHxA, PFOA, and PFDA) concentration threshold in recycled paper packaging materials, associated with functional performance gains, ranged from 30 ppm for PFDA to 1238 ppm for PFBA. Minet et al. (2022) estimate that 2% of Canadian food packaging materials contains intentionally added PFAS.

Given the known use of polymeric PFAS in paper/paperboard food packaging materials, it is expected that some PFAS will be detected in paper and paperboard food packaging materials on the retail market. For example, Schaider et al. (2017) found detectable levels of fluorine in 33% of paper and paperboard food wrappers and related food packaging materials at fast-food restaurants from various regions of the US. Overall, Schaider et al. (2017) report that detectable levels of fluorine were more common amongst grease-proof products compared with products holding liquids or not intended to come into contact with food. According to Schwartz-Narbonne et al. (2023), 45% of fast-food packaging in samples from Toronto, Canada, contained detectable levels of total fluorine with the highest concentration of fluorine being detected in molded fibre bowls (Schwartz-Narbonne et al. 2023).

2.2 Occurrence in retail foods

PFAS have been reported at very low concentrations in various retail foods in Canada, the US, Australia, New Zealand, and Europe (Tittlemier et al. 2006, 2007; Ostertag et al. 2009; EFSA 2020; FSANZ 2021; US FDA 2021a). The European Food Safety Authority (EFSA; 2020) indicates that the source of PFAS detected in retail foods (for example, PFOS and LC-PFAS) appears to primarily be from PFAS that have bioaccumulated through aquatic and terrestrial food chains, not direct migration from food packaging materials. Food Standards Australia and New Zealand (FSANZ; 2017) also reports that PFSAs, PFCAs, and fluorotelomer sulphonates were not detected in various packaged foods in Australian supermarkets.

In collaboration with the Canadian Food Inspection Agency (CFIA), HC monitors the levels of certain PFAS in food. Tittlemier et al. (2007) reported that only 9 out of 54 composite samples (4 meat-containing, 3 fish and shellfish, 1 fast food, and 1 microwave popcorn) from the Canadian Total Diet Study (TDS) between 1992 and 2004 contained detectable levels of perfluorinated compounds. PFOS and PFOA were detected the most frequently (in all 9 composites), with concentrations ranging from 0.5 ppb to 4.5 ppb. Among this small data set, the consumption of beef contributed to more than 80% of the average total dietary PFAS exposure (that is, total PFCA and PFOS).

Tittlemier et al. (2006) analyzed 151 TDS composite food samples from 1992 to 2004 for a series of perfluoroalkane sulfonamides (FASAs) including perfluorooctanesulfonamide (PFOSA) and a number of N-alkyl perfluorooctanesulfonamides, namely N-ethylperfluorooctanesulfonamide, N,N-diethylperfluorooctanesulfonamide, N-methylperfluorooctanesulfonamide, and N,N-dimethylperfluorooctanesulfonamide. Out of a total of 541 individual results, 73% were below the limits of detection (LODs). At least 1 FASA was detected in a sample from each of the food groups tested (baked goods and candy, dairy, eggs, fast food, fish, meat, and foods to be prepared in packaging). The most frequently detected

FASA was N-ethylperfluorooctanesulfonamide with a detection rate of approximately 52%. The highest concentrations of the sum of FASA compounds analyzed in this study were found in fast food composites, ranging from less than the LOD to 27.3 ppb.

Ostertag et al. (2009) reported the detection of 6:2 fluorotelomer unsaturated carboxylate (in cold cuts at 1.26 ppb), PFHpA (in cookies, cheese, pizza, and frozen beef dinner at ≤0.59 ppb), PFOA (in cookies, cheese, peppers, canned lunchmeats, and pizza at ≤0.77 ppb), PFNA (in cold cuts and cookies at ≤3.75 ppb), PFDA (in peppers at 1.02 ppb), and PFOS (in cheese at ≤1.14 ppb) in samples collected in 1998 from stores and restaurants in Whitehorse, Yukon Territory, Canada.

The CFIA has conducted targeted surveys for PFOS and PFOA in various foods (root vegetables, potato products, seafood products, frozen vegetables, flour and cereals) sampled from 2013 to 2016. None of the more than 3,200 food samples had levels of PFOS or PFOA above the LOD of 0.25 ng/g (CFIA 2016).

HC analyzed samples from the 2016, 2017 (CANLINE 2020-), and 2019 TDS for between 27 and 30 PFAS analytes including sulfonates, sulfonamides, carboxylates, and fluorotelomer carboxylates. A total of 154 composite food samples of meats (for example, poultry, beef, lamb, and pork), eggs, fish, dairy, fruits, vegetables, prepared foods, fats and oils, and baby foods were analyzed, which generated 4606 individual results, 92% of which were below the LODs (0.004 ppb to 2.13 ppb). Among the composite food samples, PFOS and PFOA were the most frequently detected analytes as they were found at concentrations above their LODs in roughly 65% and 25% of samples, respectively. Positive PFOS concentrations ranged from 0.011 ppb (chocolate milk) to 0.255 ppb (marine fish), while positive PFOA concentrations ranged from 0.039 ppb (peppers) to 0.21 ppb (cured pork). The highest single analyte concentrations were for ethylperfluorooctanesulfonamide (EtFOSA) in samples of luncheon meats (9.39 ppb), marine fish (4.23 ppb), freshwater fish (1.86 ppb), and canned fish (1.80 ppb).

An assessment conducted by EFSA noted that more than 90% of the results for PFAS in foods analyzed as part of European dietary surveys, conducted from 2000 to 2016, were below the limit of quantification (LOQ) or LOD (EFSA 2020). In the surveys reported in this assessment, high concentrations (95th percentile >10 ppb) of some PFAS were reported in edible offal from game animals and a number of fish species. According to EFSA, 4 PFAS (PFOA, PFNA, PFHxS, and PFOS) combined contributed a median of 46% (range of 33% to 56%) of the sum of all adult dietary exposures to PFAS. The relative median contributions were 9%, 2%, 4%, and 30% for PFOA, PFNA, PFHxS, and PFOS, respectively. Other PFAS that contributed more than 5% were PFBA (16%) and PFHxA (15%). Due to the high proportion of non-detects, EFSA cautioned that the exposure estimates should be ‘interpreted with caution’; nevertheless, for the combined exposure to PFOA, PFNA, PFHxS and PFOS, ‘Fish meat’, ‘Fruit and fruit products’ and ‘Eggs and egg products’, were the main contributing food categories to dietary exposure for all population groups. EFSA indicated that the concentrations of PFOS and PFOA in food appeared to be decreasing.

FSANZ (2021) report that of the 30 PFAS analyzed in their 27th Australian TDS (covering years 2019–2020), PFOS was the only congener found to have detectable concentrations in the

regional and national food samples analyzed. PFOS was detected in eggs, fish fillets (saltwater), liver or other offal (non-poultry), prawns (cooked), and canned tuna. PFOS was most frequently detected in liver or other offal at concentrations ranging from <0.05 ppb to 5.5 ppb. All other concentrations of PFOS detected were below 0.2 ppb. In the previous 24th Australian TDS (Phase 2, covering year 2011) of a smaller subset of food samples and analytes (that is, PFOA and PFOS only), FSANZ (2016a) reported that PFOS was only detected in 2 of 50 samples (that is, PFOS was detected in fish fillets and beef sausages at concentrations ≤1 ppb).

The US Food and Drug Administration (US FDA) has conducted analyses for PFAS in foods grown or produced in contaminated geographic areas as well as in foods from the general food supply (Young et al. 2012, 2013; US FDA 2021a, 2022a; Genualdi et al. 2022). PFAS occurrence data from the general food supply (US FDA 2021a) were obtained from the analysis of samples collected from the US FDA's TDS, which included a wide variety of foods such as fruits and vegetables, bread, meats, fish, dairy products, processed foods, and baby foods, as well as from targeted surveys on bottled water (2016), seafood (2013), and milk (2012). In the first 5 sets of TDS samples (available as of February 2022 on the US FDA website)[4], the US FDA analyzed 4 sets of TDS samples for 16 PFAS (PFBA, PFPeA, PFHxA, PFHpA, PFOA, PFNA, PFDA, PFBS, PFPeS, PFHxS, PFHpS, PFOS, ADONA, HFPO-DA, 11Cl-PF3OUdS, 6:2 Cl-PFESA [F53B]) and 1 set of TDS samples for 20 PFAS (PFUnDA, PFDoA, PFTrDA, and PFTeDA, in addition to the 16 PFAS analyzed in the other data sets; US FDA 2022b). In all 5 combined TDS data sets, only 10 of the 532 total samples analyzed had detectable levels of PFAS. PFOS was detected in ground turkey (85.7 parts per trillion [ppt]), tilapia (3 samples; 87, 83, and 28 ppt), pre-cooked shrimp (216 ppt), baked cod (98 ppt), protein powder (140 ppt), and frozen fish sticks/patties (33 ppt). PFNA was detected in samples of frozen fish stick/patties (50 ppt) and baked cod (2 samples; 233 ppt and 87 ppt). PFDA was detected in canned tuna (72 ppt) and baked cod (23 ppt). PFUnDA was detected in pre-cooked shrimp (233 ppt) and baked cod (151 ppt), and PFDoA was detected in pre-cooked shrimp (71 ppt). The bottled water survey analyzed for PFOS and PFOA and none of the 30 samples had detectable levels of either PFAS (US FDA 2021a). In the seafood survey, 11 of 46 samples had detectable levels of at least 1 type of PFAS, and PFOS was the most widely detected (in 9 of 11 positives), with generally higher concentrations (0.97 ppb to 6.29 ppb) (Young et al. 2013). In the milk survey, 1 of 12 raw milk samples had detectable levels of PFAS, while none of the 49 retail milk samples did (Young et al. 2012). The lone sample with detectable PFAS (PFOS at 0.16 ppb) came from a dairy farm that had applied PFAS-containing biosolids to its fields. Although the US FDA has not presented PFAS exposure estimates based on the above results, they have stated that these results do not suggest any need to avoid particular foods because of concerns regarding PFAS contamination (US FDA 2021b). The US FDA (2021b) has limited the assessment of human health risk to PFOA, PFNA, PFBS, PFHxS, and PFOS.

[4] TDS results from the US FDA are now available after February 2022, on their website.

The US FDA also conducted a targeted survey in 2021 and 2022 for 20 PFAS in 8 types of seafood (primarily imported): tuna, salmon, tilapia, crab, shrimp, cod, pollock, and clam (US FDA 2022c). The US FDA determined that the levels of PFOA in the canned clam samples were likely a health concern. Subsequently, the 2 distributors of the canned clams in question initiated a voluntary product recall (US FDA 2022d).

A study by Ruffle et al. (2020) analyzed 70 samples of fish fillets (from purchased whole fish) and shellfish commercially available in the US for 26 PFAS compounds. Up to 10 PFAS were detected in 21 samples, with PFOS as the predominant compound found. Total PFAS concentrations were generally single digit or sub-ppb level (0.6 to 4.4 ppb) except for fish from the Great Lakes area, with higher levels reported in whitefish, walleye, and yellow perch (1.2 ppb to 21.6 ppb).

Although food-related PFAS occurrence data from Canada, Europe, Australia and New Zealand, and the US are growing, the scope of existing data is still limited compared with the number of PFAS included under this broad class. Notably, targeted analysis and quantification in the varied and complex matrices of food present methodological challenges. Due to analytical limitations associated with measuring substances in complex food matrices, much of the occurrence data show a very high frequency of non-detect concentrations (that is, below the LOD), rendering exposure estimates highly uncertain. EFSA (2020) recommended that improved analytical methods for a broader range of PFAS in a broader range of foods are needed in order to reduce the uncertainty in the dietary exposure assessment. In an effort to improve dietary exposure estimates, food research organizations, including the Food Research Division of HC's Food and Nutrition Directorate, continue to work to develop occurrence data in various food matrices (for example, fish, meat, fast foods) using methods that have recently been developed (Rawn et al. 2022a).

2.3 Sites contaminated with Aqueous Film-Forming Foams (AFFF)

Notwithstanding the fact that PFAS are ubiquitous in the environment, contaminated sites where PFAS-containing AFFF have been or are being used (for example, firefighting training areas) represent "hot spot" areas where elevated levels of PFAS may be found in the environment. PFAS contamination may pose risks to human health and the environment not only at the contaminated site (that is, on-site), but also off-site due to the potential for migration via surface water and groundwater or by wind transport or overspray of the AFFF product during use. PFAS have demonstrated the ability to travel long distances (several kilometres) in the subsurface (groundwater) and surface water, which can lead to a large area of impact from a single point source of PFAS (Bhavsar et al. 2016; Weber et al. 2017; CCME 2021a). An example of a contaminated site impacted by PFAS, an airport firefighting training area, is illustrated in the conceptual site model below in Figure 2 (HC 2021). It highlights examples of potential human and ecological receptors (for example, wildlife) exposure pathways for a PFAS-impacted site as a result of historical AFFF use. These pathways may include: direct contact (ingestion, inhalation, and/or dermal) with soil, surface water, groundwater, sediment, dust, and/or other environmental media, notably ingestion of impacted drinking water and indirect contact through the consumption of agricultural or country foods (hunted/harvested foods from the land).

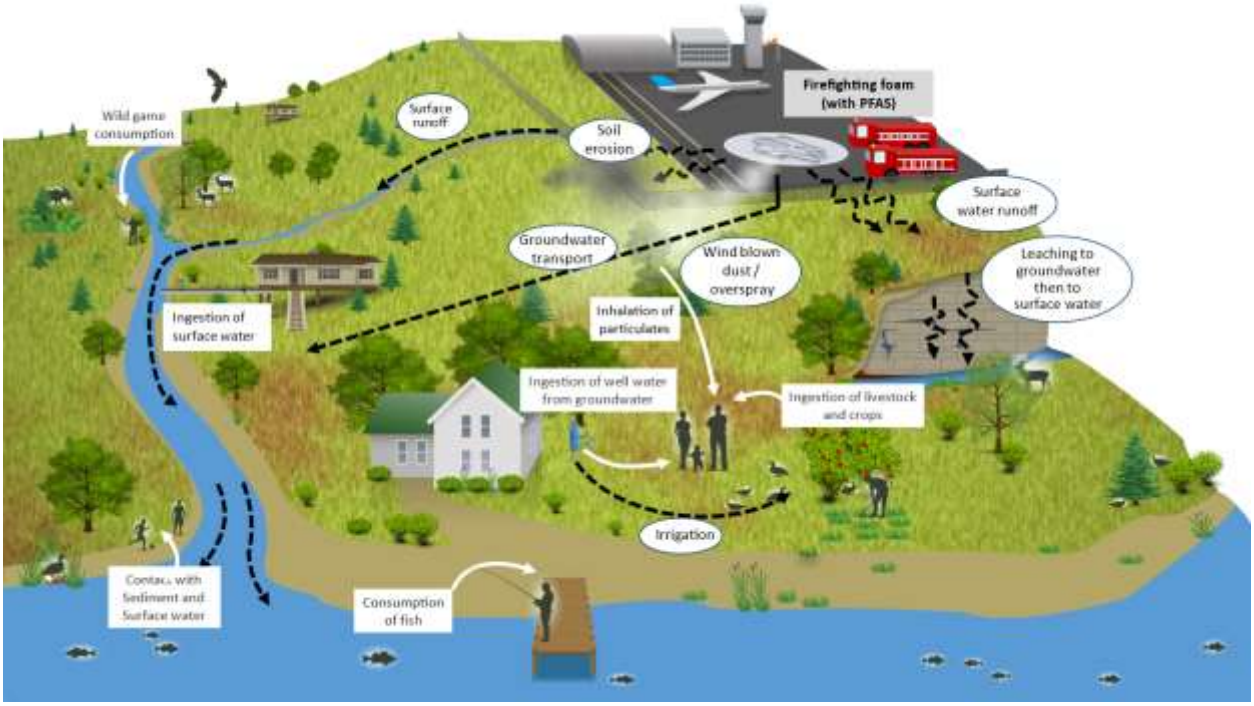

Figure 2. Conceptual site model for a PFAS-impacted contaminated site due to historical AFFF use and associated human and ecological receptor exposure pathways to be assessed in a human health and ecological risk assessment.

Federal contaminated sites are located on land owned or leased by the federal government, or on land where the federal government has accepted responsibility for the contamination. There are over 100[5] federal contaminated sites with confirmed or suspected PFAS contamination. As shown in Figure 3, such sites exist in all provinces and territories. Most of these sites are associated with past and/or current use of AFFF, typically during activities associated with fighting liquid fuel fires, including training activities and maintenance of firefighting equipment at airports and military facilities. Several PFAS (PFBA, PFPeA, PFHxA, PFHpA, PFOA, PFNA, PFBS, PFHxS, and PFOS) were detected in groundwater at former firefighting training areas in British Columbia, Alberta, Nova Scotia, Quebec, and Ontario (Paterson et al. 2008; Environmental Sciences Group 2015; Milley et al. 2018; Liu M et al. 2022). Other ways that PFAS may contaminate sites may include migration of landfill leachate or land application of wastewater treatment biosolids contaminated with PFAS, which are discussed in section 2.6. Many PFAS-impacted federal contaminated sites are located in areas where there is reliance on local resources (for example, consumption of drinking water from private groundwater wells,

[5] There are over 100 federal contaminated sites with active or suspected PFAS contamination across the country, as displayed in Figure 3. However, the Federal Contaminated Sites Inventory (FCSI) does not currently contain all the PFAS-contaminated sites as this category was newly developed in the 2024-2025 fiscal year. The inventory will be updated yearly to ensure that sites with confirmed or suspected PFAS contamination are entered in the database. As of November 6, 2024, there were 81 PFAS-contaminated sites registered in FCSI.

hunting, gathering, fishing, small-scale and/or commercial farming, gardening, and recreational activities).

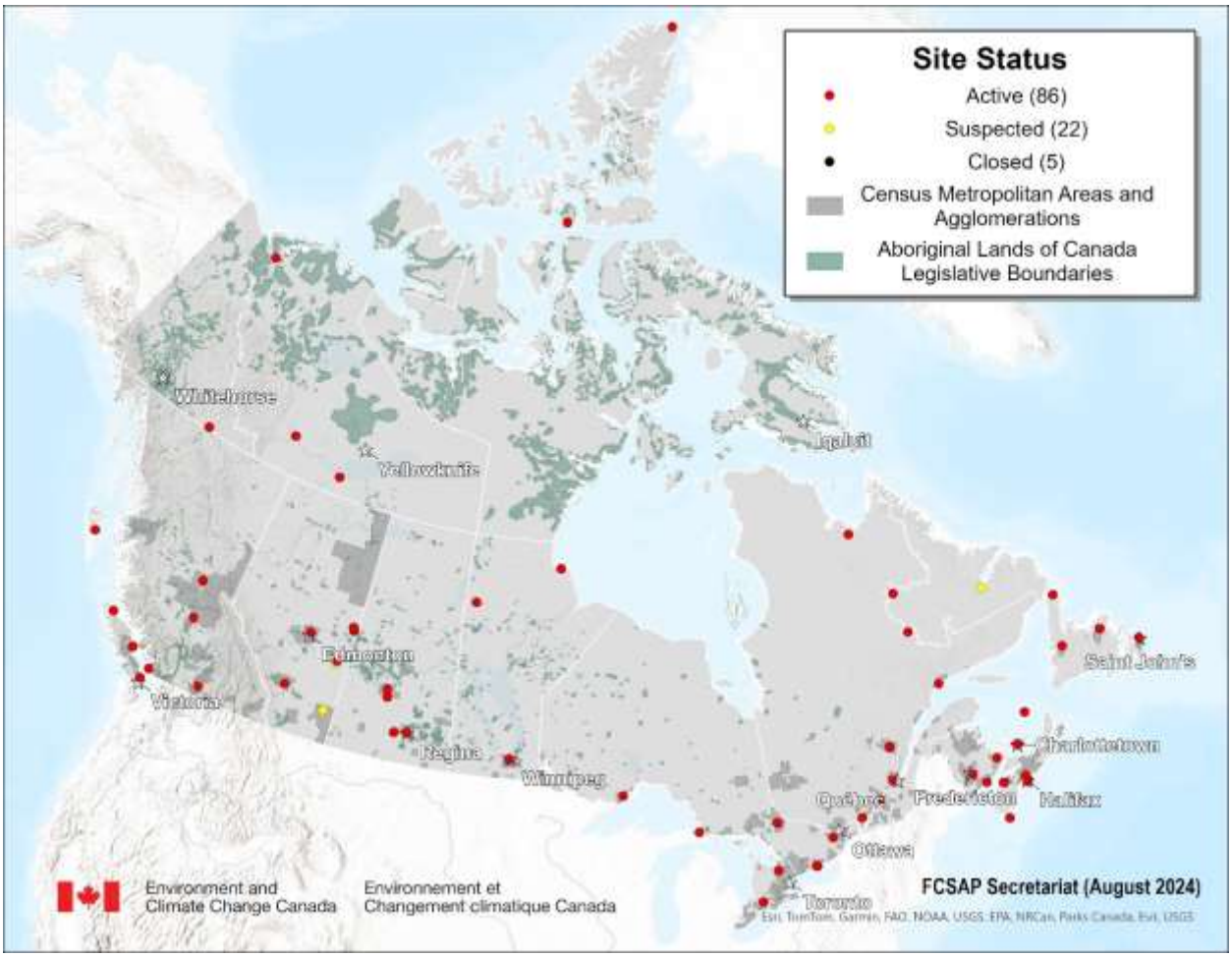

Figure 3. Federal contaminated sites with confirmed or suspected PFAS contamination, as of August 2024. Site status (that is, Suspected, Active, and Closed) applies to the entire site and is not specific to PFAS contamination.

Non-federal PFAS-contaminated sites also exist in Canada. For example, AFFF are used in the oil and gas industry, mining industry, and by municipal firefighting departments. Contamination on non-federal lands is under the jurisdiction of the province/territory and/or the local health authority (refer to section 8.1.4).

As illustrated in Figure 2, PFAS detected in groundwater or surface water at a contaminated site can be considered mobile and are likely migrating via the groundwater or surface water flow. Other plausible transport pathways for off-site migration of PFAS may also include (but are not limited to) the migration of impacted surface soils, sediment, dust, stormwater/snow melt runoff (depending on local topography), and/or migration of firefighting foam from historical site use (for example, overspray and wind transport).

Sites contaminated with AFFF have the potential to impact plants and animals that may be consumed by people. Section 6.1 discusses plant uptake of PFAS and bioaccumulation in animals.

2.4 Drinking water

As of 2024, the validated and standardized analytical methods available for the quantitation of PFAS in drinking water can measure a combined total of 29 compounds (US EPA 2020a, 2020b). There is also a validated standardized method that can measure 40 PFAS in aqueous samples such as surface water and groundwater (US EPA 2024). Although many other PFAS may be present, they cannot currently be measured by commercial laboratories with these specific methods. However, new methods that will measure a greater number of compounds are under development in many countries.

PFAS may be present in both private drinking water wells and public drinking water supplies. In terms of public supplies, PFAS are not regularly monitored at water treatment plants in Canada. Therefore, although the body of evidence is growing, only limited data are available for municipally supplied drinking water. Where monitoring data exists, it is often for a limited number of PFAS. Further, there is variability in the type of PFAS studied, the analytical methods used, the detection limits, the sampling frequency and the general study designs. Consequently, it is challenging to get an accurate picture of the concentrations of PFAS in drinking water across Canada. The information below includes a summary of data from the scientific literature.

At 7 sites in Quebec, source and treated water samples were collected monthly between April 2007 and March 2008. 13 PFAS were analyzed. PFOA was detected in 75% of treated water samples (method detection limit [MDL] of 0.3 ng/L to 0.6 ng/L), with a median value of 2.5 ng/L and a maximum value of 73.0 ng/L. PFOS was detected in 52% of treated samples (MDL of 0.3 ng/L to 0.6 ng/L), with a median value of 1.0 ng/L and a maximum value of 12.0 ng/L. PFNA and PFUDA were also detected in some samples (Berryman et al. 2012).

Between 2016 and 2021, samples were collected from 41 drinking water treatment systems in Quebec and tested for 18 PFAS (PFBA, PFPeA, PFHxA, PFHpA, PFOA, PFNA, PFDA, PFUnDA, PFBS, PFHxS, PFHpS, PFOS, PFDS, 6:2 FTUCA, 8:2 FTUCA, 4:2 FTSA, 6:2 FTSA, 8:2 FTSA). Both surface and groundwater systems were sampled, with the latter being added in 2018 (MELCC 2022). Detection limits ranged from 0.5 ng/L to 5 ng/L for raw water samples and from 0.3 ng/L to 5 ng/L for treated water samples. Among the 18 PFAS analyzed, 6 (PFPeA, PFHxA, PFHpA, PFOA, PFNA, and PFOS) were detected in 10% or more of the samples taken. The 2016 data showed a reduction in the maximum concentrations of PFOA and PFOS (6 ng/L and 3 ng/L, respectively) when compared with the maximum surface water concentrations from the same sites sampled in 2007–2008 (66 ng/L for PFOA and 8.8 ng/L for PFOS). In the St. Lawrence River and other rivers, 5 substances (PFHxA, PFHpA, PFOA, PFNA, and PFOS) were detected in at least 30% of the samples. PFOA and PFHxA were detected at the highest frequency (72% and 59%, respectively); both had a maximum concentration of 6 ng/L. In Lac Memphrémagog, PFOA (maximum 2 ng/L) and PFHxA (maximum 3 ng/L) were detected in raw water; both were detected in treated drinking water at a maximum of 1 ng/L each. In groundwater sources, PFPeA (maximum 48 ng/L) and PFHxA (maximum 30 ng/L) were found in 14% and 17% of samples, respectively, while PFOA (maximum 4 ng/L) and PFOS (maximum 3 ng/L) were found in 6% and 4% of samples (MELCC 2022).

Between 2018 and 2021, a total of 463 tap water samples were taken from within 376 municipalities in Quebec and examined for the presence of PFAS. Targeted analyses identified 31 PFAS in the water samples, while an additional 23 PFAS were identified using non-target screening. Individual detection limits ranged from 0.001 ng/L to 0.082 ng/L. 99% of the tap water samples contained PFAS, and the concentrations of total PFAS in each sample ranged from below the detection limit to 108 ng/L (median: 2 ng/L; 95th percentile: 13 ng/L). The most frequently detected PFAS included PFOA (88%, median: 0.27 ng/L; max: 8.1 ng/L) and PFOS (80%, median: 0.15 ng/L; max: 13 ng/L). In addition, short-chain (C3-C6) perfluoroalkane sulfonamides were frequently detected (for example, FBSA detection = 50%) but at lower concentrations (<1 ng/L). Of note, this study also reported the presence of emerging PFAS, such as 6:2 FTSAS-sulfone and 5:1:2 FTB, which were present at concentrations greater than 1 ng/L but were not widely detected. In addition, PFAS that have never been measured in drinking water before (for example, HO-x:2 FTSA, fluorotelomer thioether amido sulfonate-related compounds, N-sulfopropyl dimethylammoniopropyl perfluoroalkyl sulfonamide-related compounds, trimethylammoniopropyl perfluoroalkyl sulfonamides, x:3 FTB, and x:1:2 FTB) were detected in some of the samples. Overall, concentrations of PFAS were higher in tap water samples that had a surface water source compared with tap water samples that had a groundwater source. However, of the top 10 most contaminated locations, 6 had groundwater as their water source (Munoz et al. 2023).

In a study that included 5 tap water samples from Niagara-on-the-Lake, Ontario, PFOA and PFOS were found at concentrations of 2.1 ng/L and 3.3 ng/L (arithmetic means), respectively. PFBA, PFPeA, PFHxA, PFHpA, PFNA, PFDA, PFUnDA, PFHxS, and PFEtS were also detected in the samples. The limits of quantification ranged from 0.004 to 1.6 ng/L (Mak et al. 2009).

Between 2012 to 2016, the Ontario Ministry of the Environment, Conservation and Parks measured the occurrence and concentrations of 14 PFAS (PFBA, PFPeA, PFHxA, PFHpA, PFOA, PFNA, PFDA, PFUnDA, PFDoDA, PFBS, PFHxS, PFOS, PFDS, and PFOSA) in 25 drinking water systems in Ontario (Kleywegt et al. 2020). MDLs ranged from 0.5 ng/L to 1 ng/L, and results less than the MDL were substituted with a value of half of the MDL. PFUnDA, PFDoDA, PFDS, and PFOSA were not detected in either the source water or treated drinking water samples. The most frequently detected compounds in Ontario drinking water were PFOA (73%; median 1.1 ng/L), PFBA (67%; median 2.4 ng/L), PFHxA (54%; median 1.3 ng/L), PFPeA (51%; median 1.0 ng/L), and PFOS (50%; median 0.63 ng/L).

Similar median concentrations of PFBA, PFPeA, PFHxA, PFOA, and PFOS were reported in samples of drinking water sourced from 19 sites around Lake Ontario and the St. Lawrence River (n=8) and other lakes and small rivers in Canada (n=11). Maximum concentrations of PFAS ranged from 0.1 ng/L (PFDA) to 4.1 ng/L (PFOS) in the Great Lakes-St. Lawrence samples, and 0.1 ng/L (PFUnDA) to 4.9 ng/L (PFOA) for the rest of the Canadian tap water samples. PFHxA was detected in all Canadian tap water samples from this study. Other PFAS that were frequently detected included PFBA (95%) and PFHxS and PFOS (both 89%), while PFPeA, PFHpA, PFOA, PFNA, PFDA, and PFBS were detected in at least 84% of the samples. Compounds detected less frequently in Canadian tap water included FOSA (53%), 6:2 FTSA

(37%), and 5:3 FTCA (11%) as well as PFUnDA, PFDoDA, and 7:3 FTCA, which were each detected in less than 10% of samples. A qualitative screening approach indicated that FBSA, FHxSA, PFECHS, and PFPeS were occasionally present in tap water (concentrations ranged from below the limit of detection to 1.2 ng/L), whereas PFEtS, PFPrS, and PFPeS were below the limit of detection for all Canadian samples. The limits of detection for tap water ranged from 0.01 ng/L to 0.08 ng/L (Kaboré et al. 2018).

In a 2023 pilot study involving 14 water treatment plants, the Government of Canada measured PFAS concentrations in paired source and treated water samples collected during the winter season. Samples were analyzed using a method developed to measure 38 PFAS compounds. The MDLs for this method ranged from 0.01 to 0.23 ng/L. The PFAS detected at the highest frequency in drinking water were PFBA, PFPeA, PFHxA, PFHpA, PFOA, PFNA, PFBS, PFPeS, PFHxS, PFHpS, and PFOS. Median concentrations for individual PFAS, estimated from graphs, ranged from 0.05 to 0.80 ng/L for raw water and from 0.06 to 0.35 ng/L for treated water (Fan 2023).

2.5 Indoor air and dust

PFAS compounds have been measured in indoor air and dust in residential and non-residential environments (for example, childcare facilities, fire stations) in Canada and other countries (for example, the US, Ireland, Belgium, Italy, Spain, Norway, Finland, Japan, and China) (Haug et al. 2011; Winkens et al. 2018; Yao et al. 2018; de la Torre et al. 2019; Harrad et al. 2019; Wu et al. 2020; Zheng et al. 2020; Lin et al. 2022a; Eichler et al. 2023; Li and Kannan, 2024). These studies were mostly conducted on a regional scale and reported approximately 70 PFAS in total. Sources of PFAS in indoor environments include rugs and carpets, treated floor waxes and stone/wood, food packaging materials, cosmetics, building materials, furnishings, paper products, clothing, insecticides, and electronics (Liu et al. 2015; Morales-McDevitt et al. 2021; Savvaides et al. 2021; Eichler et al. 2023). Additionally, PFAS present in ambient air from outdoor sources can enter indoors through ventilation and infiltration (Lin et al. 2022a; Li and Kannan 2024).

In Canada, 4 studies examined the airborne PFAS concentrations in 271 residential homes in 3 cities (Ottawa, Vancouver, Edmonton) from 2002 to 2008 (Shoeib et al. 2005, 2011; Beesoon et al. 2012; Makey et al. 2017). Overall, the data suggest that FTOHs (8:2, 6:2, and 10:2 FTOH), followed by the FOSAs (MeFOSA, EtFOSA), and FOSEs (MeFOSE, EtFOSE) appear to be the most prominent in the air samples collected from Canadian homes.

For PFAS in dust, 6 studies measured PFAS concentrations in household dust in 308 Canadian homes in 3 cities (Ottawa, Toronto, Vancouver) from 2002 to 2015 (Kubwabo et al. 2005; Shoeib et al. 2005, 2011; De Silva et al. 2012; Eriksson and Kärrman 2015; Karásková et al. 2016). When comparing exposure through inhalation and ingestion of dust, inhalation was identified as the primary exposure pathway for neutral and ionic PFAS for adults, whereas for toddlers, intake via dust ingestion is more relevant due to the higher frequency of hand-to-mouth activities (Shoeib et al. 2005, 2011). The most abundant PFAS in indoor dust were diPAPs, PFOS, PFOA, PFNA, PFHxA, PFHpA, PFDS, PFHxS, PFDoDA, MeFOSE, EtFOSE, MeFOSA, EtFOSA, 6:2 FTOH, 8:2 FTOH, and 10:2 FTOH. For diPAPs, the dominating homologues were

6:2 diPAP, 6:2/8:2 diPAP, 8:2 diPAP, 8:2/12:2 diPAP, and 10:2 diPAP (De Silva et al. 2012; Eriksson and Kärrman 2015).

2.6 Waste/end of life product management

PFAS are present in a wide variety of consumer and industrial products. The expected fate of these products is either disposal, at a Municipal Solid Waste (MSW) landfill or by incineration, or recycling. The responsibilities for waste management in Canada are discussed in section 8.1.5.

2.6.1 Landfills

The disposal of products and materials that contain PFAS, including PFAS-contaminated soils and biosolids, into landfills can become an indirect pathway of release to the environment. PFAS may leach out of these products and materials and accumulate in landfill leachate and eventually be released to the environment, even if that leachate is sent to a wastewater treatment system. Other solid waste facilities, such as organic processing facilities, scrapyards, and recycling facilities, may also be a source of release to the environment. Concentrations of PFAS in landfill leachate are discussed in section 4.2.3.

The leachate from most landfill sites undergoes some form of treatment prior to being released to the environment. Approximately 87% of the leachate generated by large landfills in Canada, that is, those permitted to receive more than 40 000 tonnes of MSW per year, is directed to municipal wastewater treatment plants (WWTPs), and 7% is treated on site prior to release. The remainder of leachate generated (approximately 6%), typically from small, unengineered landfills that have limited environmental controls, is released directly into the environment via groundwater or surface water without treatment.

MSW landfills are a known source of groundwater contamination, with leachate-impacted plumes that may extend greater than 1 km (Christensen et al. 2001). Modern Canadian landfills are designed with groundwater protection systems and contingencies to address this problem; however, there is currently limited information available on their long-term reliability. Recent research indicates that PFAS in leachate can diffuse through some types of landfill liners (Rowe et al. 2023). Many contaminants of emerging concern, including PFAS, have been found in the leachate of both operating and closed MSW landfills and are described in section 4.2.3.

Ahrens et al. (2011) collected samples in ambient air near landfills and found higher levels than at reference sites of FTOHs, a category of PFAS that have been used as replacements for compounds such as PFOA and PFOS in commerce. Unlike PFOA and PFOS, FTOHs are highly volatile and are likely to be present in landfill gas. Therefore, FTOHs in uncollected landfill gas may be a relevant emission source, as well as any FTOHs in collected landfill gas that are not destroyed by their combustion. Furthermore, a recent study conducted at 3 municipal solid waste landfills in Florida measured neutral PFAS in landfill gas and ionic PFAS in landfill leachate, to compare the relative mobility between the 2 pathways. Results showed that the mass of fluorine leaving in landfill gas was comparable to or greater than the mass leaving in landfill leachate, suggesting that landfill gas serves as a major pathway for the mobility of PFAS from landfills. (Lin et al. 2024).

2.6.2 Incineration

PFAS may not fully degrade from incineration at temperatures below 1000ºC, which may result in the formation of other volatile fluorinated compounds. Data suggest that temperatures of 1000ºC and above, such as those found in MSW incinerators, are expected to sufficiently destroy (that is, mineralize) many fluorinated compounds; however, further data are needed regarding the optimal residence times for sufficient and/or complete destruction of PFAS, including the breakdown of the highly stable $–CF_2–$ moieties, while avoiding the formation of other compounds (Yamada et al. 2005).

Due to the wide variety of products that contain these substances, it is reasonable to assume that the fraction of PFAS that is incinerated is equal to the total fraction of waste incinerated in Canada. A 2012 study by Cheminfo Services Inc. indicated that the percentage of MSW being disposed of in landfills in Canada (for 2008) was 96%, while 4% was disposed of through incineration. Since this figure is likely representative of current data, it can be assumed that 4% of PFAS are incinerated, while the remaining 96% are sent to landfills where they are potentially released to the environment (Cheminfo Services Inc. 2012). Note that these figures do not include biosolids, only MSW.

2.6.3 Wastewater treatment systems and biosolids

Municipal wastewater treatment systems act as pathways of PFAS to aquatic environments through the discharge of treated effluent, and to the terrestrial environment when biosolids are applied to land as soil amendments. Both pathways can subsequently impact groundwater, for example, through riverbank filtration and soil water infiltration, respectively. The wastewater sector has no control over chemicals that enter its treatment systems, including PFAS. Municipal WWTPs are generally designed to remove oxygen demand, suspended material, pathogenic organisms, and nutrients (Metcalf & Eddy Inc. 2003). Treatment of trace contaminants such as PFAS is not a design criterion for Canadian WWTPs. Therefore, persistent chemicals such as PFAS that enter WWTPs will end up in wastewater effluent and/or biosolids. Although the terms “biosolids” and “sludge” are sometimes used interchangeably, in this document they have distinct definitions as per the Water Environment Federation (Wilson 2014). Specifically, biosolids are the primarily organic solid product of wastewater treatment that can be beneficially used. Sludge or sewage sludge is the unprocessed (that is, unstabilized) solid material and is generally unsuitable for beneficial use.

ECCC’s National Wastewater Monitoring Program gathers data on levels of certain PFAS entering municipal WWTPs, evaluates the fate of PFAS through the liquid and solids trains of typical treatment process types used in Canada, and determines levels of PFAS being discharged in WWTP effluents and solids residuals. These are described in section 4.2.4. On-site wastewater treatment (that is, septic systems) releases liquid effluent via a subsurface drain field, while sludge from septic holding tanks can also be land-applied; both pathways have the potential to impact groundwater.

Many PFAS have been measured in WWTP influent and effluent (Guerra et al. 2014; Lenka et al. 2021), septic system effluent (Subedi et al. 2015; Schaider et al. 2016), and WWTP biosolids (EFSA 2020; Lakshminarasimman et al. 2021). PFAAs can also be formed during wastewater

treatment, likely as a result of the transformation of unmeasured precursors entering WWTPs (Guerra et al. 2014). The amount of PFAAs formed is dependent on process temperature and treatment type, with higher rates of formation in biological WWTPs operating at higher hydraulic retention times and temperatures (Guerra et al. 2014). In addition, concentrations of some PFAAs are higher in final stabilized biosolids than in raw sludge at some WWTPs, likely due to the transformation of unmeasured precursors during biosolids treatment (Lakshminarasimman et al. 2021). Concentrations of both PFOS and PFOA may increase during biological treatment processes due to the incomplete transformation of their precursors (Sinclair and Kannan 2006; Guerra et al. 2014; Lenka et al. 2021). Transformation of PFAS is described in section 3.2.3.

Only 15% of the 989 kilo tonnes of biosolids generated annually in Canada is incinerated; 27% is landfilled, while over 50% is applied to agricultural land (35% for crop production and 23% for grazing) (Doucette 2013; B.C. Ministry of Environment 2023; M&M 2023). PFAS can be taken up by plants grown in agricultural fields, with accumulation dependent on soil and groundwater concentrations, chain length of the PFAS, functional group, plant species and variety, and soil and applied biosolids characteristics (Ghisi et al. 2019) (see section 6.1). EFSA (2020) reported that PFBS, PFHpA, and PFBA have been shown to be available to plants via the root system, with reported uptake into pea shoots and/or celery grown in soil amended with biosolids; however, as noted in section 2.2, concentrations of 17 PFAS in retail foods were predominantly (93.5%) found to be below the LOQ or LOD. Uptake of PFAS by plants is discussed further in section 6.1.

2.6.4 Compost

Compost made from PFAS-containing food packaging materials, single-use paper products, or food waste is expected to be contaminated with PFAS. PFAS persist when composted, may accumulate in the soil or leach into groundwater, and may be taken up by certain crops (see section 6.1) as well as taken into the natural food chain.

A study by Lazcano et al. (2020) found 17 PFAS, including PFOA and PFOS, to be present in 13 commercially available biosolids-based products, 6 organic composts (manure, mushroom, peat, and untreated wood), and 1 food and yard waste compost. Biosolids-based products had concentrations of PFAS ranging from 9 to 199 micrograms per kilogram (µg/kg, ppb), while composts made from various combinations of food scraps, yard trimmings, and other organic products had PFAS concentrations of between 0.1 µg/kg and 18.5 µg/kg.

2.6.5 Potential PFAS removal and treatment technologies

PFAS are widely used because they are resistant to heat and chemical extremes, but these same characteristics make most conventional treatment technologies ineffective for PFAS removal or destruction both at contaminated sites (see section 2.3) and for drinking water treatment. Experience with PFAS-contaminated sites has shown that the remediation and management of these sites are complex and present unique challenges. This often leads to cleanup and monitoring costs that are higher than those associated with sites contaminated with other substances. The field of PFAS treatment and remediation is rapidly evolving and advancing, with new information becoming available as experience is gained through conducting activities at contaminated sites. Detailed information regarding PFAS remediation at

contaminated sites is available from the Interstate Technology & Regulatory Council (ITRC) (2020c).

PFAS are generally resistant to physical, biological, and chemical processes and are typically unaffected by conventional treatments used for landfill leachate and wastewater (see section 2.6). This has been demonstrated for PFOA, PFNA, PFDA, PFUnDA, PFHxS, and PFOS (Sinclair and Kannan 2006; Xiao et al. 2013).

Separation technologies are most commonly used for the treatment of environmental media contaminated with PFAS, although destructive technologies are under active research.

The effectiveness of drinking water treatment for PFAS removal depends on several factors, including source water characteristics, as well as the concentration and type of the PFAS, treatment goals, and proper operation of the system. Conventional treatment is not effective for PFAS removal. The most effective treatment technologies for the removal of PFAS (including PFOS and PFOA) are, alone or combined, granular activated carbon, membrane filtration (reverse osmosis and nanofiltration), and anion exchange (Appleman et al. 2013, 2014; Dickenson and Higgins 2016; Lin et al. 2021), although there are technical challenges associated with short-chain PFAS breakthrough (Li F et al. 2020). To reduce the release of PFAS into the environment, spent filtration and ion exchange media require specialized disposal (for example, high temperature regeneration/destruction). Similarly, membrane technologies require treatment and disposal of the concentrate residual stream (US EPA 2020c).

Results from studies on PFOS and PFOA show that sonochemical degradation can be an effective and rapid process to treat these substances in landfill leachate (EC 2014). PFOS and PFOA have a tendency to partition into sludges and have been found to be resistant to treatment of the sludge (Gómez-Canela et al. 2012; Sun et al. 2012). Other newly developing technologies for treatment of PFAS-impacted soil or sand (possibly biosolids) include ball milling (for example, Battye et al. 2022) and smoldering technologies (for example, Duchesne et al. 2020).

All of these treatments are limited in their ability to be widely used, such that PFAS remediation is currently limited to specific locations where deploying one or more of these technologies is economically and logistically feasible. As a result, removing PFAS from the broader environment is not possible.

Since PFAS removal and treatment technologies are not specific to individual PFAS, the measurement of total PFAS would allow for more comprehensive remediation and treatment planning by providing more information on the total “PFAS load” that requires treatment/removal to ensure that the strategies used are appropriate. The use of analytical total oxidizable precursors (TOP) assays is beneficial as a line of evidence in this application.

2.7 Substitution trends

Restrictions on PFOS, PFOA and LC-PFCAs have brought about a shift from the use of legacy long-chain PFAS to the use of short-chain PFAS. Key substitutions observed with respect to fluorosurfactants have included the move to perfluorohexyl-based fluorotelomer substances

from variable chain length LC-PFCA precursors, and the use of PFBS-based products as PFOS replacements (ACC 2022; 3M 2002). Polyfluorinated ether acid surfactants, such as ADONA and GenX (that is, HFPO-DA and its ammonium salt), have also been substituted for the use of PFOA as a fluoropolymer processing aid (ITRC 2020d).

New Substances Notifications may provide insight into new substances being introduced as potential substitutes Retrospectively analyzing substances notified for import into or manufacture in Canada under the NSNR can highlight when substitutions have occurred over the years and illustrates how industry is acting to substitute hazardous substances (also known as informed substitution). Other data collection methods (for example, CEPA section 71 surveys) may be used by the Government of Canada to obtain new use information that can inform future assessments and risk management actions.

Following the prohibitions put in place on 4 new fluorotelomer-based substances (PFCA precursors) in 2004, no further perfluoroalkyl substances with carbon chain lengths equal to or greater than C8 were notified under the NSNR (Figure 4). This could indicate that industry had already transitioned to replace those substances by the time the Perfluorinated Carboxylic Acids (PFCAs) and Precursors: An Action Plan for Assessment and Management and the PCTSR amendments were published in 2006 and 2016, respectively. Substitution for these substances was observed through an increase in notifications of short-chain PFAS.

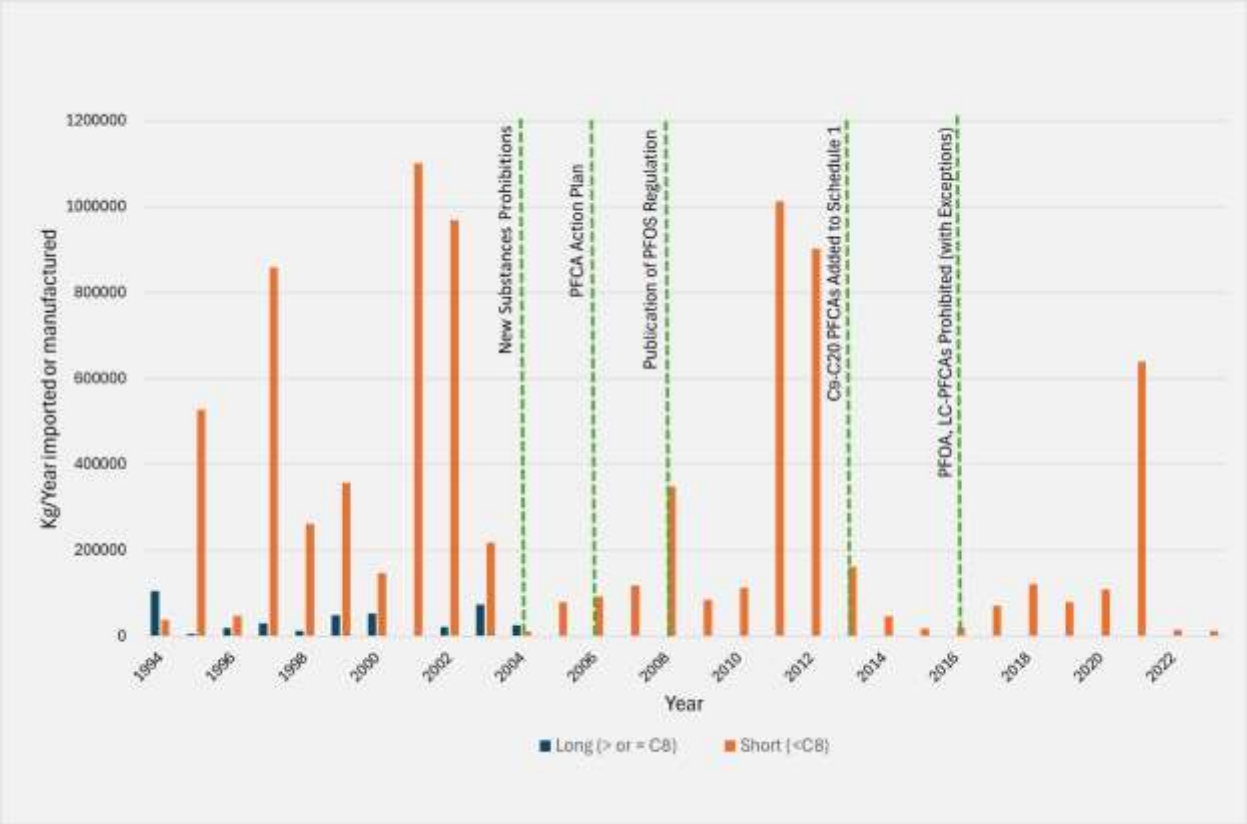

Figure 4. Quantities (kilograms per year) of chemical and polymeric PFAS notified under the NSNR per year, separated by long and short carbon chain lengths.

When a new substance is notified under the NSNR, the importer or manufacturer must indicate the expected quantity of substance to be imported into or manufactured in Canada. These values are provided for the year of notification and, when known, the maximum amount in a 12-month period in the next 3 years. Apart from the quantities notified for blowing agents and refrigerants, which tend to be high in certain years, the quantities of new chemical and polymeric PFAS notified under the NSNR are generally relatively constant at roughly 30,000 kg/year or less for each new PFAS being imported into or manufactured in Canada.

3 Key characteristics and environmental behaviour

KEY POINTS ON ENVIRONMENTAL BEHAVIOUR

- The physical and chemical properties of PFAS influence their fate and behaviour in the environment.
- PFAS are highly persistent in the environment due to the stability of carbon-fluorine bonds.
- Ionic PFAS (that is, PFAS that are predominantly ionized at environmental pH) such as PFCAs and PFSAs are highly water-soluble and non-volatile, and thus partition predominantly to water where they are more easily transported.
- Neutral PFAS such as FTOHs may be volatile and thus are more likely to be found in the atmosphere.
- Various PFAS including FTOHs, as well as other polyfluoroalkyl substances and side-chain fluorinated polymers, can undergo transformation to form more stable PFAS that are extremely persistent in the environment under ambient conditions.
- Some shorter-chain PFAS have proven to be even more mobile on a local scale than longer chain PFAS.
- Some PFAS are also capable of undergoing long-range transport in the atmosphere (that is, for neutral, volatile PFAS) or in global ocean currents (that is, for ionic PFAS), as can be seen by their widespread distribution around the world, including to remote regions.

The purpose of this section is to summarize the key physical/chemical and fate properties of PFAS. The concept of PFAS precursor substances (PFAS that are capable of transforming into simpler environmentally stable PFAS, such as PFAAs), is also discussed. The general properties of these PFAS contribute to their environmental partitioning, persistence, mobility, and long-range environmental transport characteristics.

Fluorine has high electronegativity, low polarizability, and a small atomic radius. The combined effect produces a strong carbon-fluorine bond (about 108–120 kcal/mol), making it extremely stable. Fluorocarbon substances are resistant to heat and biological and chemical attack. With low surface energy and weak intermolecular interactions, they are both hydrophobic and lipophobic. It is these characteristics that provide desirable performance in many applications where surface protection, chemical resistance, thermal stability, and non-stick properties are sought.

Complex PFAS molecules, such as side-chain perfluoroalkyl polymers or sulfonamidoethanol compounds, contain the persistent perfluoroalkyl moiety, although other portions of the molecule may undergo transformation and liberate a stable PFAS acid. Complex PFAS that can yield simpler persistent PFAS are referred to as precursor substances.

Although the precursor substances may exhibit a range of physical/chemical properties dependent in part on the non-fluorinated parts of the molecule, the simpler PFAS have physical/chemical properties that result in fate characteristics that are better understood. These properties will be highlighted in section 3.1.

3.1 Select physical and chemical properties

Water solubility: Various estimates for the pKa (that is, acid dissociation constant) of PFOA have been generated (for example, by Brace 1962; Goss et al. 2008; Steinle-Darling and Reinhard 2008; Vierke et al. 2013), though the actual value is believed to be within the range of 1 to 2. Consequently, PFOA is predominantly found in the environment in the form of its conjugate base, the perfluorooctanoate anion. The water solubility of this conjugate base is 3.5 g/L at 20°C (EC, HC 2012). Similarly, the PFOS conjugate base anion, perfluorooctane sulfonate, is the most common form at pH values in the environment and human body. The water solubility for the potassium salt of PFOS is reported as being 519 mg/L to 680 mg/L (EC 2006). Liu and Lee (2005, 2007) reported water solubilities of 974, 18.8, 0.224 and 0.011 mg/L at 22°C for 4:2, 6:2, 8:2, and 10:2 FTOH, respectively. A review by Ding and Peijnenburg (2013) reported experimentally determined water solubilities for select PFAS ranging from 0.011 mg/L to 5.66×10^4 mg/L.

With a hydrophobic and lipophobic fluorocarbon tail and a polarized head, these PFAS acids exhibit surfactant behaviour and can aggregate in micelles above the critical micelle concentration.

Log*Kow*: Because PFAS acids behave as surfactants, the octanol/water partition coefficient (Log*Kow*) values are difficult to determine experimentally since the molecules aggregate at the octanol/water interface. Many reported Log*Kow* values are calculated for the neutral form of the molecules. As the neutral form is not present under normal environmental conditions, these values are of limited use in describing their environmental fate or bioaccumulation potential.

Log*Koc*: For PFAS acids, the values for the organic carbon-water adsorption/desorption coefficient are in part dependent upon the length of the fluorocarbon chain. Shorter-chain PFAS acids tend to have lower Log*Koc* values, indicating a greater affinity for water, while longer-chain PFAS acids may partition preferentially to soil and sediments. For these reasons, shorter-chain PFAS have greater mobility via groundwater. Log*Koc* values are also dependent on the polar head group. For example, PFSAs tend to sorb more strongly to soil and sediments than doPFCAs (Pereira et al. 2018).

Vapour pressure and Henry's law constant: The vapour pressure of the PFOS potassium salt is 3.31×10^{-4} Pa at 20°C and its Henry's law constant is 3.45×10^{-4} Pa m^3/mol (EC 2006), indicating a low likelihood to partition to and be transported by air. For the acid form of PFOA, the calculated vapour pressure and Henry's law constant are 2.2 Pa and 2.4 Pa m^3/mol, respectively, indicating a low likelihood of atmospheric transport (EC, HC 2012).

While the acids themselves are not susceptible to atmospheric transport, volatile precursor substances contribute to environmental transport. For example, although PFOS has low volatility, several PFOS precursors are considered volatile, such as N-EtFOSE alcohol, which has a vapour pressure of 0.5 Pa and Henry's law constant of 1930 Pa m^3/mol. When present in products or used in industrial processes, volatile PFAS precursors can volatize into the atmosphere and travel long distances before transforming into non-volatile forms such as

PFAAs. These volatile precursors contribute to the widespread environmental occurrence of PFAS, including in remote areas such as the Arctic (Muir et al. 2019).

Fluorotelomer alcohols are precursors to perfluorocarboxylic acids (PFCAs, which include PFOA). Vapour pressures of C_6-C_{12} FTOHs range from 144 Pa to 992 Pa at 25°C (Stock et al. 2004), with the Henry's law constant for 8:2 FTOH estimated at 3506 Pa m^3/mol (Xie et al. 2013). These volatile precursors are globally distributed and also subject to transformation to PFCAs through reaction with hydroxyl radicals (Ellis et al. 2004), contributing to the wide dispersion of the resulting acids.

3.2 Environmental fate and behaviour

The environmental fate and behaviour of PFAS describes what happens to these substances when they are released into the environment. The behaviour of these substances in the environment can be influenced by their physical and chemical properties, which can vary between different PFAS. This section examines the fate and distribution of PFAS in various media, their persistence, and transport of these substances within and between media, including long-range environmental transport. Focus is given to PFAS that are well studied in terms of their environmental fate and behaviour. Some emerging PFAS (for example, PFPAs, PFPiAs, PAPs) are much less understood in terms of their environmental fate (Guo et al. 2020); therefore, these PFAS are not discussed in detail in this section.

3.2.1 Environmental fate

As a result of the fluorinated alkyl tail and polar head group of ionic PFAS (which are predominantly ionized at environmental pH, such as PFAAs), the partitioning properties and electrostatic interactions of ionic PFAS can dictate their partitioning and distribution in the environment. Because of their hydrophilic head, PFAAs can exhibit high water solubility, which can allow the chemical to interact and disperse in water. This, combined with a negligible vapour pressure, explains why PFAAs primarily partition to surface waters, soil water, and groundwater (Prevedouros et al. 2006). Partitioning of PFAS to ice surfaces has also been reported. Garnett et al. (2021) found that long-chain PFAS were enriched in bulk sea-ice up to 3-fold more than short-chain PFAS, which has been attributed to hydrophobic interactions. PFAAs also tend to accumulate at the air-water interface as a result of their surfactant-like properties (that is, their hydrophilic head group dissolves in water, while their hydrophobic tail orients itself to the air; Costanza et al. 2019), leading to retention in soils and upper layers of the subsurface (the unsaturated zone). Some studies have also shown that PFAAs display significantly higher enrichment in the sea surface microlayer (1 µm to 1000 µm thickness) (Ju et al. 2008; Wang S et al. 2015). Moreover, transport to the deep ocean and sediment burial are considered to be environmental sinks for PFAAs, given that they have a very long residence time in the environment (Prevedouros et al. 2006).

The organic carbon content in soil and sediment and alkyl chain length are strongly correlated to the sorption of many PFAS, which demonstrates the importance of hydrophobic interactions (Liu and Lee 2005; Higgins and Luthy 2006). In general, sorption to organic carbon increases with fluoroalkyl chain length in the ionic, non-volatile PFAS. Zhao et al. (2016) examined the distribution of PFAS in a river and found that short-chain PFAAs were predominantly found in

water, whereas the long-chain PFAAs were present in suspended particulate matter and sediment. A study of sediment cores by Ahrens et al. (2009) also determined that short-chain PFCAs were only found in pore water, whereas longer-chain PFCAs (C ≥ 11) were exclusively found in sediment. Moreover, partitioning and sorption is dependent on the properties of the functional groups present (ITRC 2020a). At a pH of above 3, most PFAAs exist in the anionic state in the environment; PFAAs in the environment therefore tend to repel negatively charged natural soils and sorb to positively charged minerals. For example, Higgins and Luthy (2006) determined that sorption of PFAS such as PFCAs, PFSAs, and FASAs to sediment increased at higher Ca^{2+} concentrations. However, differences have been noted in the sorption of PFAAs depending on their functional groups, such as PFPAs which tend to be more sorptive than PFCAs at equal chain lengths in soil (Lee and Mabury 2017; ECHA 2022b). Sorption of cationic and zwitterionic PFAS to soil and sediment have been far less investigated in comparison with anionic PFAS species; however, recent studies have shown that cationic and zwitterionic PFAS sorb more strongly to soil and sediment than do anionic PFAS because of their electrostatic interactions (Barzen-Hanson et al. 2017; Xiao et al. 2019; Nickerson et al. 2021). It is important to note that trends in sorption potential (that is, chain length and functional group) evidenced by different PFAS do not indicate that there is no sorption occurring with some PFAS but rather that sorption may occur to a lesser extent compared with more strongly sorbing PFAS.

Ionic PFAS are not commonly found in air because of their high solubility in water, low vapour pressure, and low Henry's law constant. In their anionic, less volatile form, PFAAs can adsorb to airborne particulate matter (ITRC 2021a). Moreover, other neutral PFAS (for example, fluorotelomer-based substances) may have a greater volatility due to the functional groups that they possess (for example, alcohols) and may therefore be more likely to be found in the atmosphere.

3.2.2 Persistence

Broadly speaking, PFAS are extremely persistent in the environment (that is, they have long half-lives[6]) as fluorocarbon moieties (fundamentally $-CF_2-$ and $-CF_3$) are very stable with resistance to biodegradation, hydrolysis, photolysis, and thermolysis. This extreme persistence of PFAS is due to their carbon-fluorine bonds which, as previously described, are the strongest carbon-halogen bonds in nature. The carbon-fluorine bond contributes to the low polarizability and high bond energies of PFAS, which increase as the degree of fluorination increases.

Most of the current persistence data have focused on the limited number of well-studied PFAS. As such, the information presented in this section is focused on PFOS and PFOA; however, substances of the same PFAS group can be considered to be equally persistent (ECHA 2022b). Further, the vast majority of these so-called "forever chemicals" are non-degradable or, in cases where these transformation mechanisms may act upon other parts of more complex PFAS molecules, the stable PFAS transformation products are environmentally persistent (Cousins et

[6] According to the *Persistence and Bioaccumulation Regulations of CEPA*, half-life refers to the period that the concentration of a substance takes to be reduced by half, by transformation, in a medium.

al. 2020a). As such, it is expected that the substances in the class of PFAS are highly persistent or transform to persistent PFAS.

For PFOS, half-lives in water were determined to be >41 years via hydrolysis, estimated by varying pH from 1.5 to 11.0 and at a temperature of 50°C to facilitate hydrolysis (Stockholm Convention on Persistent Organic Pollutants 2006). No biodegradation has been found in studies of PFOS in activated sludge, sediment cultures, and soil cultures. Moreover, PFOA is not expected to significantly photodegrade under environmental conditions, undergo significant biotic or abiotic degradation, or hydrolyze (EC, HC 2012). PFOA was also determined to have a half-life of about 235 years in water via hydrolysis (3M 2001, as cited in the Stockholm Convention on Persistent Organic Pollutants 2016). Short-chain PFAA substitutes are just as persistent in the environment as legacy long-chain PFAAs (Manojkumar et al. 2023). Although there are a limited number of studies from the literature, it is expected that PFECAs and PFESAs (other alternatives to long-chain PFAAs) are also likely to be highly persistent in the environment (Wang Z et al. 2015). As is discussed in further detail in section 3.2.3, some PFAS are capable of releasing PFAAs into the environment upon transformation; however, this process may be slow for some precursors under abiotic conditions. Washington and Jenkins (2015) tested the abiotic hydrolysis of a commercial fluorotelomer-based acrylate side-chain fluorinated polymer, which yielded half-lives ranging from 55 to 89 years. The current data suggest that many PFAS will remain in the environment for long periods, with the result being that they can reach significantly higher concentrations in comparison with short-lived chemicals released in the same quantities (Cousins et al. 2019).

3.2.3 Transformation

Polyfluoroalkyl substances (for example, fluorotelomers, polyfluoroalkyl ethers, perfluoroalkane sulfonamides) and SCFPs (for example, fluorinated urethane polymers, fluorinated acrylate/methacrylate polymers, fluorinated oxetane polymers) can be considered to be “precursors” and undergo abiotic or biotic transformation in multi-step processes to form more stable perfluoroalkyl transformation products that do not degrade under ambient environmental conditions (Buck et al. 2011). This can occur as a result of the nonfluorinated bond(s) (for example, carbon-hydrogen, carbon-oxygen) in the structure of these polyfluoroalkyl substances and side-chain fluorinated polymers, which can create a “weak” point in the chemical structure that can be broken to release a perfluoroalkyl moiety (ITRC 2021a). Studies have shown that fluorotelomer-based substances can undergo atmospheric oxidation (Ellis et al. 2004; Wallington et al. 2006) and aerobic transformation (Liu et al. 2010; D’Agostino and Mabury 2017) to form PFCAs. The atmospheric oxidation of HFCs, HFOs and HCFOs can also form trifluoroacetic acid (Young and Mabury 2010), which falls within the definition of PFAS used in this document. The biotransformation of HFO-1234yf was also observed to a low extent in rats, mice, and rabbits (Schuster et al. 2010).

The precursors FOSA, FOSAA, FTOHs, and fluorotelomer sulfonic acids (FTSAs) have been observed in wastewater and can transform to PFAAs via biological or chemical treatment in WWTPs (Vo et al. 2020; Thompson et al. 2022). Landfill conditions are favourable for the anaerobic biotransformation of PFAS (Reinhart et al. 2023). Polyfluorinated precursor transformation was evidenced by simultaneous precursor disappearance and accumulation of

PFAAs in the leachate (Coffin et al. 2023). Liu Y et al. (2021) found that PFAS began to undergo transformations prior to arriving at the landfill; transformation of diPAPs and FTSAs to intermediary products such as FTCAs already occurring at curbside collection. 6:2 FTSA has also been detected following biotransformation from polyfluorinated substances in AFFF (Thompson et al. 2022). Metabolic transformation of PFAS precursors can also be a source of PFAAs (Ahrens and Bundschuh 2014).

A study reported that the main PFAS components in Scotchgard fabric protector products made before and after the year 2002 were identified as side-chain perfluorooctane sulfonamide-urethane polymer and side-chain perfluorobutane sulfonamide-urethane polymer, respectively (Chu and Letcher 2014). Furthermore, the same study, using a model microsomal *in vitro* assay (Wistar-Han rat liver microsomes), reported that the rapidly formed metabolites were FOSA and perfluorobutane sulfonamide (FBSA), respectively.

Petre et al. (2023) identified 4 biotransformation products of PFOA in common carp (Cyprinus carpio): PFBA, PFPeA, PFHxA, and PFHpA. Carp *in vivo* studies found both C8 PFPA and PFOA, which were presumed to have come from the biotransformation of PFPiA following exposure (Kolanczyk et al. 2023). Moreover, PFPiA was found to metabolize into PFPA and C8 PFPA in rats and rainbow trout.

Biotransformation of FTOH to PFCAs has been observed in rainbow trout, rat, chicken, pig, zebrafish, and aerobic soil (EC, HC 2012; Kolanczyk et al. 2023). Furthermore, the largest collection of metabolized FTOH products, including PFUnA, PFDA, PFHxA, and PFPeA, were present in wheat samples of the root and shoots (Kolanczyk et al. 2023).

In another study using a liver microsomal *in vitro* assay performed on polar bear (from Iceland), Wistar-Han rats, and ringed seal and beluga whale (Canadian Arctic), N-ethyl-perfluorooctanesulfonamide (N-EtFOSA) was found to be dealkylated rapidly to FOSA by polar bears and rats, more slowly by ringed seals, and very slowly by beluga whales (Letcher et al. 2014). In a medaka *in vivo* study, N-EtFOSA transformed into an intermediary form of FOSA and a final product of PFOS. The transformation of FOSA to PFOS was also observed in rainbow trout, zebrafish embryo, rat, earthworm, aerobic soil, wheat, pumpkin, and soybean (Kolanczyk et al. 2023; LaFond et al. 2023).

3.2.4 Mobility

In general, PFAS are capable of being transported from point sources to other locations as a result of their physical-chemical properties. Volatile PFAS (which generally have a neutral charge at environmental pH, such as FTOHs) are also capable of undergoing airborne transport from release sources (for example, stack emissions) and are capable of being dispersed by the wind. Atmospheric studies conducted surrounding waste management sites found that volatile PFAS (such as FTOH and their transformation intermediates) are dispersed via landfill gas emissions (Lin et al. 2022b, 2024; Reinhart et al. 2023). Ismail et al. (2023) suggest that sand and dust storms are also capable of mobilizing PFAS in areas with arid and semi-arid climates. Eventually, some PFAS can be removed by atmospheric deposition and accumulate in soil, groundwater, and surface water. This can occur both by wet deposition (that is, precipitation)

and dry deposition (that is, removal of particles from the atmosphere due to gravity). Shimizu et al. (2021) concluded that wet deposition is able to remove PFAS from the atmosphere more effectively than dry deposition.

Ionic, short-chain PFAAs are considered to possess greater mobility in the aquatic environment and soils due to their increased water solubility and lower sorption potential to solids (ECHA 2017; Ghisi et al. 2019). Although some major manufacturers have phased out the production of long-chain PFAAs and have turned to homologues with shorter chains, research has demonstrated that short-chain PFAAs are capable of being even more mobile in the aquatic environment (Kwiatkowski et al. 2020). Advection, which is the transport of a chemical by a fluid, can be considered a primary driver of PFAS transport, such as in a groundwater plume or downstream in a river (ITRC 2020e). Moreover, Lohmann et al. (2013) determined that vertical eddy diffusion is also capable of moving PFAAs from the ocean surface water to the deep ocean.

Ionic, non-volatile PFAS tend to associate with the organic carbon fraction of soil and air-water interfaces, often accumulating within the vadose zone (between ground surface and the water table; including soil layers). These PFAS can also be leached downward by infiltrating water to underlying groundwater systems, where they may form groundwater contaminant plumes, particularly in areas with point sources such as fire-fighting training areas (Weber et al. 2017) and landfills (Abunada et al. 2020). Xiao et al. (2015) found increasing levels of PFOS and PFOA with increasing depth in subsurface soils, indicating that there is potential for the substances to contaminate the groundwater. Additionally, downward migration of PFAS throughout a concrete pad was observed following historical use of AFFF, with PFAS being present along the entire length of cores drilled through the entire thickness of the pad (11 cm to 17 cm) (Williams et al. 2023).

3.2.5 Long-range environmental transport

Some PFAS are also capable of undergoing long-range environmental transport, as evidenced by their widespread distribution around the globe, even to remote regions. It is believed that this can occur via both atmospheric transport and global ocean currents (Zhao et al. 2012). In general, long-range atmospheric transport tends to occur more quickly in comparison with transport through water, which could take decades (Young and Mabury 2010).

In the case of releases of PFAS to air (for example, stack emissions, volatilization from products) and the potential for air to disperse PFAS over long distances in all wind directions, airborne transport becomes a relevant migration pathway. More specifically, neutral volatile precursors (for example, FTOHs) have been found in remote regions due to their high volatility (Wania 2007). These neutral volatile precursors are often the most prevalent PFAS present in the gas phase (Wang Z et al. 2014). The long-range transport and transformation of PFAS and PFAS precursors has been seen as a potential cause for the presence of PFAAs in remote regions, as precursors can be subject to transformation processes and be deposited via precipitation. For example, a study by Stock et al. (2007) found evidence to support the transformation of volatile precursors in the Canadian Arctic. Another study by Young and Donaldson (2007) found that 8:2 FTOH can transform to PFOA within the atmosphere and be

deposited in distant environments, such as the polar regions. Other FTOHs, short-chain FOSAs, and FOSEs are also potential sources of PFCAs and PFSAs via atmospheric transformation (ATSDR 2021). Although not in polar regions, remote/rural sampling sites in other Canadian locations (Golden, BC; Egbert, ON) that are distant from emission sources have identified FTOHs and PFCAs in surface water (Loewen et al. 2008) and ambient air (Gawor et al. 2014). Although there is currently no field evidence identifying the presence of HFPO-DA in remote locations, modelled data support its potential for long-range transport similar to legacy PFAS (Mahoney et al. 2022).

Ionic PFAS (for example, PFAAs) are mainly distributed in surface waters and are believed to be predominantly transported globally by marine ocean currents due to their higher water solubility (Yamashita et al. 2008; Zhao et al. 2012). It is also believed that PFAAs can be transported from the ocean to the atmosphere via sea spray aerosols, which can occur with breaking waves and rough sea conditions (Prevedouros et al. 2006). Johansson et al. (2019) estimated the annual global emissions of PFOA and PFOS to the atmosphere via sea spray aerosols to be 122 tonnes/year and 183 tonnes/year, respectively. It has been suggested that sea spray aerosols are capable of circulating significant amounts of PFAAs between the ocean and atmosphere and can be considered a possible contributor to the long-range transport of PFAAs (Prevedouros et al. 2006; Johansson et al. 2019; Sha et al. 2022). Furthermore, tracer analysis conducted by Persaud et al. (2024) suggests that marine aerosols and mineral dust can act as transport vectors for PFAAs to the Arctic region.

This global cycling of PFAAs in the world's hydrosphere, combined with their extreme persistence, will lead to levels of PFAAs in atmospheric deposition that are poorly reversible. Measurements of 4 PFAS (PFOA, PFOS, PFHxS, and PFNA) in various global environmental media (rainwater, soils, and surface waters) showed the ubiquitous exceedance of several guideline values (see section 4.1). Consequently, the authors stressed the importance of rapidly restricting uses and emissions of PFAS due to the "poor reversibility of exposure and their associated effects" (Cousins et al. 2022).

3.3 Considerations for hydrofluoroolefins (HFOs) and hydrochlorofluoroolefins (HCFOs)

Hydrofluoroolefins (HFOs) are unsaturated organic compounds composed of hydrogen, fluorine, and carbon, while hydrochlorofluoroolefins (HCFOs) are unsaturated organic compounds composed of hydrogen, fluorine, carbon, and chlorine. Many HFOs and HCFOs contain at least 1 fully fluorinated carbon atom and are considered to be PFAS on the basis of the OECD (2021) definition. HFOs and HCFOs have a much lower global warming potential than hydrofluorocarbons (HFCs) and hydrochlorofluorocarbons (HCFCs) and are not ozone-depleting substances (ODS). As a result, HFOs and HCFOs have been increasingly used as alternatives to other organofluoro compounds for certain applications in the manufacture, servicing, and maintenance of refrigeration and air-conditioning equipment; as blowing agents in the manufacture of foam products, such as insulation; as propellants in aerosol products; and as solvents.

HFOs and HCFOs that are PFAS are known to undergo atmospheric photodegradation to trifluoroacetic acid (TFA) (ECHA 2023c; UNEP 2023a). Estimates of TFA molar conversion rates for individual HFOs and HCFOs vary widely depending on the predicted degradation pathways. HFO-1234yf, which has begun replacing HFC-134a in vehicle air conditioning units in Canada and is predicted to be increasingly adopted globally, has a conversion efficiency to TFA of 100% via intermediate degradation to trifluoroacetyl fluoride (ECHA 2023c; UNEP 2023a). It is also predicted to become the predominant source of anthropogenic TFA inputs into the environment (ECHA 2023c; UNEP 2023a). It was previously proposed that degradation via trifluoroacetaldehyde intermediates did not yield TFA (for example, WMO 2014); however, the assumptions underlying these estimates have been questioned (Umwelt Bundesamt 2021) and the current consensus is that trifluoroacetaldehyde is expected to degrade to TFA, albeit with much lower estimated conversion rates than for trifluoroacetyl fluoride (WMO 2022; ECHA 2023c; UNEP 2023a). TFA is considered to be a PFAS on the basis of the OECD (2021) definition and is highly persistent.

There are a number of other anthropogenic sources of TFA in the environment in addition to HFOs and HCFOs. These include the transformation of other PFAS, including certain pharmaceuticals and pesticides, industrial releases from PFAS manufacturing, and incineration of PFAS during end-of-life (UNEP 2023a; Madronich et al. 2024). Many of the releases associated with these activities/uses of PFAS may act as point sources of TFA into the environment, but it is difficult to predict their contribution to locally elevated concentrations of TFA. While the incremental contributions of TFA in the environment from various anthropogenic sources are uncertain, HFOs and HCFOs (particularly HFO-1234yf) are predicted to become an increasingly important source of TFA in the environment as the transition away from other organofluoro compounds continues (UNEP 2023a).

TFA is detected nearly ubiquitously in the environment. For example, TFA has been detected in North American pine needles, precipitation, rivers, lakes, oceans, snow and ice, soils, and water columns (Scott et al. 2005a, 2005b, 2006; Yeung et al. 2017; Pickard et al. 2020; Hartz et al. 2023). Pickard et al. (2020) noted that chlorofluorocarbon replacements (such as HFOs) introduced following the Montreal Protocol are likely a major source of TFA in the Arctic owing to increased depositional fluxes of TFA starting around 1990. While it is generally agreed that TFA found in freshwaters, the atmosphere, and the terrestrial environment originates from anthropogenic sources, there is some debate as to whether TFA can occur naturally in deep oceans. A number of references have concluded that TFA is naturally present in deep oceans based on measured concentrations that are higher than they contend are possible from anthropogenic sources alone and/or concentrations of TFA are elevated in proximity to undersea hydrothermal vents (Frank et al. 2002; Scott et al. 2005a; Lindley 2023). However, others have identified data quality issues in the TFA analyses performed in these studies and have also noted that the presence of TFA in the deep ocean is not enough evidence to conclude the existence of natural TFA without considering other explanations in the absence of a reasonable natural mechanism for TFA formation (Joudan et al. 2021).

A recent report by the Environmental Effects Assessment Panel (EEAP) under the United Nations Environment Programme (UNEP) concluded that environmental concentrations of TFA

resulting from the degradation of HFOs are expected to be well below thresholds for adverse effects in humans and the environment (UNEP 2023a). However, this evaluation only accounted for TFA concentrations in oceans. On the other hand, atmospheric deposition of TFA resulting from the degradation of HFOs and HCFOs is expected to be more localized than was previously observed for TFA derived from other organofluoro compounds due to shorter atmospheric half-lives of HFOs and HCFOs (UNEP 2023a).

While TFA deposited locally will eventually migrate to terminal sinks (that is, oceans, large lakes), local surface water concentrations and migration rates are expected to vary depending on precursor transformation rates, precipitation patterns and effects of seasonality, other releases of TFA, and local hydrology (for example, flow rates, retention times). The combination of these and other factors, including persistence, may contribute to locally elevated concentrations of TFA. For example, some recent studies have reported significant increases in TFA concentrations at various sites, including an average 6-fold increase in surface water concentrations at sites in Northern California and Alaska between 1998 and 2021 (Cahill 2022). Additionally, a study by Scheurer et al. (2017) found elevated concentrations of TFA of more than 100 µg/L in a major German river during potable and surface water screening in southwest Germany. Further research also indicates that both the detection and concentrations of TFA found in drinking water are increasing (Neuwald et al. 2022; Albers and Sültenfuss 2024; Arp et al. 2024; Garavagno et al. 2024). While the ultimate fate of TFA produced as a persistent secondary pollutant through the photo-degradation of HFOs and HCFOs is unclear, it is believed that large bodies of water (lakes, oceans) serve as sinks for TFA (UNEP 2023a).

TFA has been found to be moderately toxic to certain biota (Solomon et al. 2016; ECHA c2020); however, data are limited or missing for certain groups of organisms (for example, marine macrophytes, terrestrial mammals). Additionally, most evaluations have not considered the potential for TFA to contribute to cumulative effects nor has TFA toxicity been evaluated at environmentally occurring concentrations. While TFA is not expected to bioaccumulate significantly (ECHA c2020, Garavagno et al. 2024), it is commonly detected alongside other PFAS in plant and animal tissues, including at concentrations exceeding other measured PFAS (for example, Lan et al. 2020; Guckert et al. 2023; Herzke et al. 2023).

Given the potential for TFA to cause adverse effects and its ubiquitous presence in the environment and organisms alongside other PFAS, the potential for TFA to contribute to cumulative effects of PFAS in organisms is of concern. As such, HFOs and HCFOs that are PFAS according to the definition of the class of PFAS are within the scope of this report.

4 Environmental occurrence

KEY POINTS ON ENVIRONMENTAL OCCURRENCE

- Globally, PFAS are routinely detected in virtually all environmental compartments and in the tissues of numerous species.
- The highest concentrations of PFAS are usually found in proximity to points of release; however, PFAS are ubiquitous in precipitation and global soils, including in remote areas.
- Because environmental monitoring studies have focused on limited subsets of PFAS, total PFAS concentrations and the extent of cumulative exposure are uncertain and likely underestimated.
- In Canada, PFAS are routinely detected in various environmental samples collected from coast to coast to coast, including ambient air, aquatic ecosystems, landfill leachate, wastewater, and biosolids as well as aquatic and terrestrial wildlife.
- The Government of Canada conducts a variety of monitoring programs and research studies to understand trends in PFAS occurrence in Canadian ecosystems and wildlife.

4.1 Overview of environmental occurrence

As might be expected on the basis of the mobility and long-range transport potential of PFAS, numerous studies and reviews have documented the presence of PFAS globally within a wide variety of ecosystems and biota, including in remote areas far from locations where PFAS are initially discharged to the environment (for example, Lau et al. 2007; Houde et al. 2008; Gewurtz et al. 2013; Letcher et al. 2018; Muir et al. 2019; Ankley et al. 2021; Muir and Miaz 2021; Cousins et al. 2022). The highest PFAS concentrations have generally been found in proximity to points of release of AFFF and industrial activities (for example, Moody et al. 2002; Hu et al. 2016; Lanza et al. 2016; Carrizo et al. 2023) as well as in landfill leachates (for example, Hamid et al. 2018) and wastewater treatment plant effluents (for example, Arvaniti and Stasinakis 2015). However, measurable concentrations have also been reported in ecosystems at varying distances from these locations, including but not limited to stormwater runoff (for example, Saifur and Gardner 2021), agricultural land and crops (for example, Ghisi et al. 2019), the Amazon rainforest (for example, Kourtchev et al. 2024), the Great Lakes (for example, Houde et al. 2008, Xia et al. 2024), oceans and coastal waters (for example, Muir and Miaz 2021), and the Arctic and Antarctic (for example, MacInnis et al. 2017; Pickard et al. 2018; Muir et al. 2019; Wong et al. 2021; Persaud et al. 2024).

PFAS are also routinely found in the blood and tissues of a wide variety of organisms, both those in close proximity to points of PFAS release (for example, near sites where AFFF have been used in firefighting activities) and in remote locations. For example, an early study by Giesy and Kannan (2001) examined select fluorinated organic compound (FOC) concentrations in tissues of aquatic mammals, birds, fish, and amphibians collected during the 1990s as part of monitoring studies in the US, Canada, and internationally. They found that while few samples contained PFOSA, PFHxS, or PFOA above the LOQ, PFOS was detectable in most samples, including those collected from remote marine regions (for example, the Arctic Ocean). Houde et al. (2011) also reviewed post-2005 monitoring information on perfluorinated compounds in

aquatic biota. PFOS was determined to be the most predominant substance, likely due to a combination of its high biomagnification potential, persistence, and the continued international use of PFOS precursors. However, the ubiquity of PFCAs was also noted across tissue samples. Recognition of the ubiquity of PFOS, PFOA, and LC-PFCAs in global environments and biota has been a key driver in regulatory action both in Canada (EC 2006, 2012; EC, HC 2012) and internationally, which includes the listing of PFOS, PFOA, and recommended listing of LC-PFCAs, and related substances as Persistent Organic Pollutants under the Stockholm Convention.

PFAS have also been detected in crops and livestock, as outlined below. The Ontario Ministry of the Environment, Conservation and Parks recently carried out studies examining short-chain (PFBA, PFPeA, PFHxA, PFHpA, and PFBS) and long-chain (PFOA, PFNA, PFDA, PFUnDA, PFDoDA, PFHxS[7], PFOS, PFDS, and PFOSA) uptake into tomatoes, lettuce, and beets following irrigation with PFAS-contaminated surface water. The result of this study demonstrated that irrigation water impacted by AFFF-contaminated sites has the potential to impact crops irrigated with contaminated water, particularly for the short-chain PFAS (McDonough et al. 2021). This study also demonstrated elevated concentrations of short-chain PFAS in the tomato flower, which may have implications for pollinators (McDonough et al. 2021). In 2018, a herd of approximately 5000 dairy cattle in the US was discovered to have been chronically exposed to elevated PFAS (that is, PFOA and PFOS as well as other PFCAs and PFSAs) from contaminated feed and water (Lupton et al. 2022). Milk and cheese from the affected farm were analyzed by the US FDA. PFOS was the dominant PFAS detected in milk, which was discarded and did not enter the food supply (US FDA 2021a). The US FDA analyzed multiple collections of milk samples from the affected farm, showing that PFOS concentrations steadily decreased over time between 2018 and 2021 (US FDA 2021a). Using plasma and skin samples from a small sample of the affected animals, Lupton et al. (2022) determined that bioaccumulation of four- to nine-carbon PFCAs did not occur in plasma or skin, but PFSAs longer than 4 carbons accumulated in both plasma and skin.

Recently, the ECHA completed an extensive review of the European and global environmental occurrence of PFAS (ECHA 2022c). The occurrence and concentration of individual PFAS were highly variable depending on location; however, PFAS were found in surface waters, groundwater, soil, contaminated sites, wastewater influent, effluent, sludge and biosolids in virtually all locations that were examined. PFAS were also found to be present in nearly all organisms tested worldwide.

A number of studies and reviews have noted declines in environmental concentrations of regulated PFAS (for example, De Silva et al. 2021; Muir and Miaz 2021), supporting the effectiveness of regulatory actions. However, this trend is not universal, and some studies have reported different (or a lack of) temporal trends within a single study species and/or the same geographic region depending on sampling location (for example, see section 4.2.2). A review

[7] McDonough et al. (2021) categorized PFHxS as a long-chain PFAS. While the State of PFAS Report categorizes PFHxS as a short-chain (C6) PFAS, it is included in this list of long-chain PFAS for consistency with the cited study as it reported results based on total short-chain and long-chain PFAS concentrations.

from Lohmann et al. (2024) found that PFOS concentrations have increased in East Greenland subadult and adult polar bears from 2013 to 2014 until the most recent measurement in 2021. This followed a period of decline from 2006 until 2013 to 2014. The authors suggested that this increase may be related to climate change effects. This trend was not found in East or West Hudson Bay polar bears; however, subadult ringed seals in western Hudson Bay found decreasing concentrations of PFOS prior to an increase around 2008 to 2011, and then decreasing again. A review by Cousins et al. (2022) found that concentrations of select PFAAs in global rainwater samples routinely exceeded US EPA lifetime drinking water health advisories for PFOS and PFOA; the Danish Environmental Protection Agency drinking water limit value for the sum of PFOS, PFOA, PFNA, and PFHxS; and the EU freshwater environmental quality standard (EQS) for PFOS, including in remote and sparsely populated regions. Some urban rainwater levels reported in this study for PFOA and PFOS also exceeded the Canadian Objective of 30 ng/L for the sum of 25 PFAS in drinking water. Though data for soils from remote regions remain sparse, the authors concluded that 1 outcome of these findings is the global contamination of soils due to the environmental ubiquity and poor reversibility of PFAAs in atmospheric deposition.

Recent studies have also noted increases in the concentrations of short-chain PFAS (for example, Manojkumar et al. 2023, section 4.2), presumably due to the use of these substances as replacements for regulated long-chain PFAS. Additionally, TFA, which is produced via decomposition of HFOs/HCFOs and may be produced during manufacture and/or incineration of other PFAS, has been detected globally in surface water, precipitation, sediment, soils, ice cores, and plant tissues (for example, Boutonnet et al. 1999; Scott et al. 2005a, 2005b, 2006; Pickard et al. 2020; Umwelt Bundesamt 2021; Freeling et al. 2022, 2023; ECHA 2023c; Hartz et al. 2023). TFA has been detected in soil and precipitation samples in various locations across Canada, as well as in Canadian conifer needles sampled in the Banff, Alberta and Guelph, Ontario regions (Scott et al. 2005b). TFA was ubiquitously found in soil and precipitation samples in Germany and was also detected in a variety of sampled plant species (Umwelt Bundesamt 2021; Freeling et al. 2022). The majority of species and sampling locations in the study showed increasing levels of TFA over time, which the authors concluded was likely the result of increasing emissions of gaseous TFA precursors (Freeling et al. 2022).

Additionally, SCFPs have been found in Canadian biosolids, aquatic sediments from the Great Lakes basin, and sludge from WWTPs in Sweden (Chu and Letcher 2017; Letcher et al. 2020; Fredriksson et al. 2022).

As environmental monitoring has typically focused on limited suites of the class of PFAS (for example, OECD 2018b; Buck et al. 2021; De Silva et al. 2021), and as the detection of a broader spectrum of PFAS is dependent on the development of new analytical methods, it is expected that the number and distribution of PFAS in the environment, as well as total PFAS concentrations, are underestimated in the current body of literature. This is a critical limitation as manufacturing has shifted to other perfluorinated substances (for example, see section 2.7). The limited scope of monitoring was illustrated in a review by Xiao (2017), in which it was determined that aquatic studies published between 2009 and 2017 identified 455 new PFAS in natural waters, fish, sediments, wastewater, activated sludge, soils, AFFF, and commercial fluorinated polymer surfactants. The narrow scope of most existing monitoring data has also led

to concerns regarding the potential for higher than anticipated concentrations of currently unquantified, common transformation products from multiple precursors.

While historically the scope of PFAS examined in many studies has largely been limited, studies have increasingly noted the broad occurrence of and co-exposure to a range of PFAS. Broad and/or non-target analyses have detected a variety of PFAS in various substrates, including, for example, Northern European and Arctic sea waters (Joerss et al. 2020), Arctic lake and air samples (Stock et al. 2007), surface waters (Hensema et al. 2021; Ulrich et al. 2024), biosolids (Letcher et al. 2020) and organic waste (Munoz et al. 2022a; Saha et al. 2024), and urban air particulate matter (Yu et al. 2018). Examples of broad detection of co-occurring PFAS in organism tissues include presence in marine mammals (Spaan et al. 2020; Barrett et al. 2021), sea birds (Letcher et al. 2015; Su et al. 2017; Robuck et al. 2020), tree bark, and fish species from various regions (for example, Pignotti et al. 2017; Liu and Gin 2018; Baygi et al. 2021). This evidence of broad PFAS co-exposure among such varied regions, environmental media, and organisms suggests that widespread co-occurrence is increasingly the norm and that studies that do not account for a broader (and possibly unanticipated) suite of PFAS may not adequately describe cumulative exposure. To this end, a number of techniques to detect total PFAS in environmental samples are being investigated, including total organic fluorine (TOF), extractable organic fluorine (EOF), and total oxidizable precursors (TOP) methods (see, for example, Nikiforov 2021; Rehman et al. 2023). Significantly, studies that measured PFAS concentration using TOF and EOF in different environmental compartments have shown that the majority of PFAS measured are unidentified (Manojkumar et al. 2023), which supports the belief that concentrations of PFAS in the environment are underestimated. It is hoped that, in the future, these or other newly developed methods may be used to provide a more complete understanding of PFAS diversity and concentrations in the environment and organisms.

4.2 Environmental monitoring in Canada

In addition to monitoring international trends and developments regarding the environmental occurrence of PFAS, the Government of Canada conducts a variety of monitoring programs to understand trends in PFAS occurrence in Canadian ecosystems and wildlife. The data generated from these monitoring programs are routinely published on the Government of Canada Open Data Portal as well as in the peer-reviewed literature. A summary of results generated to date is provided in this section.

4.2.1 Ambient air

The Government of Canada has monitored PFAS (including C4-C14, C16, C18 PFCAs, and C4, C6, C8, C10 PFSAs and their precursors) in air at the Canadian High Arctic Station of Alert, Nunavut, since 2006 with high volume active air samplers (AMAP 2014, 2017; Wong et al. 2018, 2021). PFOA and PFOS concentrations in air at Alert increased between 2006 and 2013. After 2013, the concentrations of PFOA and PFOS have steadily declined (Wong et al. 2021). PFHxS appeared to decline from 2013 onwards but this was probably driven by the few high measurements in 2013 and low measurements in 2017. PFNA showed non-changing trends, while PFDA and PFUnDA showed increasing trends. It should be noted that the evaluation of trends for PFAAs other than PFOA and PFOS at Alert has been hampered by low detection frequencies and inconsistent blank levels (Wong et al. 2021). The AMAP (2017) report also

included several new PFAS compounds, including perfluoroethylcyclohexane sulfonic acid (PFECHS, an analog of PFOS), perfluorobutane sulfonamide (FBSA, a precursor of PFBS), and 6:2-chloro-polyfluorinated ether sulfonic acid (6:2-Cl-PFAES or F-53B, a chlorinated polyfluorinated ether sulfonic acid).

Research projects have also been conducted on the atmospheric deposition of PFAS in remote areas through the analysis of PFAAs (including C4-C14 PFCAs, C4, C6, C8, C10 PFSAs, PFECHS, FOSA) in Arctic snow, glaciers (MacInnis et al. 2019a), and ice cores (MacInnis et al. 2017; Pickard et al. 2018; Persaud et al. 2024). These studies have confirmed the ubiquitous presence of PFAAs in remote regions. These abiotic samples are pertinent as they demonstrate higher concentrations of short-chain PFAAs that are not prevalent in biota. Analyses in sectioned and dated ice cores were used to calculate annual fluxes of PFAAs via atmospheric deposition. Furthermore, PFCA congener analysis was consistent with long-range environmental transport of fluorotelomer precursors followed by atmospheric deposition. PFCAs were frequently detected in an ice core from Ellesmere Island, Nunavut, after the 1990s and have been increasing over time (Persaud et al. 2024). Results suggest that PFAAs are carried by marine aerosols and mineral dust reaching the remote Arctic.

In the Great Lakes Basin, PFAS (including C4 to C12 PFCAs and C4, C6, and C8 PFSAs) have been monitored in precipitation since 2006 at Point Petre on the coast of Lake Ontario, Evansville on Lake Huron, and Sibley on Lake Superior (Gewurtz et al. 2019; Government of Canada 2021). PFOS and PFOA concentrations generally decreased in Great Lakes precipitation. However, concentrations of shorter-chained PFAAs, which are not regulated in Canada, did not decrease, while those of PFHxA and PFBA recently increased (since approximately 2010 to 2016 depending on the location), which could be due to their use as replacements since the longer-chained PFAAs are being phased out by industry (Gewurtz et al. 2019). A recent study estimating the mass budget for PFBA, PFBS, PFOS and PFOA for the 5 lakes (Xia et al. 2024) using measured concentrations in precipitation, air and water samples indicated atmospheric deposition is an important PFAS source to the lakes, especially for Lake Superior. PFAAs were not strongly associated with human population density around each Great Lakes sampling site, in contrast to other legacy contaminants (that is, polycyclic aromatic hydrocarbons [PAHs], pesticides, and polybrominated diphenyl ethers [PBDEs]), all of which were associated with population density. This indicates that PFAAs in precipitation may not reflect localized sources as observed for other contaminants. PFAS have been monitored in air at Point Petre since October 2018 and at Evansville since July 2019.

The Government of Canada monitors PFAS (C4-C14, C16, C18 PFCAs and C4, C6, C8, C10 PFSAs and their precursors) in passive air samples under the Global Atmospheric Passive Sampling (GAPS) network (initiated in 2004) at 13 Canadian sites (Rauert et al. 2018; Saini et al. 2023). Over the 9 years between 2009 and 2017, FTOHs and fluorinated sulfonamides and sulfonamidoethanols (FOSAs and FOSEs) in general, had weak decreasing trends or stable levels. However, PFSA concentrations including PFBS, PFHxS, and PFOS increased significantly over the same period at some Canadian sites. Total PFCA concentrations, including PFHxA, PFHpA, PFOA, PFNA, and PFDA, also showed an increase in 2017, but such changes need to be confirmed with additional monitoring, particularly in order to characterize

the effectiveness of control measures for these regulated substances. The results from passive air samplers (Rauert et al. 2018; Saini et al. 2023) are consistent with those from high volume air samplers described above (AMAP 2014, 2017; Wong et al. 2018, 2021).

PFAS emissions from the waste sector (that is, WWTPs and landfills) to air have also been investigated (Ahrens et al. 2011; Shoeib et al. 2016). Ahrens et al. (2011) collected PFAS air samples on and around 1 WWTP and 2 solid waste landfills in Ontario in 2009. The samples were analyzed for 5 groups of PFAS (FTOHs, FOSAs, FOSEs, PFSAs, and PFCAs). Compared with the reference sites, the total PFAS concentrations in air were 3 to 15 times higher within the WWTP and 5 to 30 times higher at the landfill sites. The emissions of FTOHs (6:2 FTOH was dominant at the WWTP, and 8:2 FTOH was dominant at landfill sites) were about 2 orders of magnitude higher than the other PFAS classes evaluated in this study. Among the PFSAs and PFCAs, PFOS and PFBA represented the highest emissions to the atmosphere from the WWTP, and PFBA emissions were highest at the landfill sites.

4.2.2 Aquatic ecosystems and wildlife

The Government of Canada carries out freshwater monitoring at sites across Canada. From 2013 to 2020, 29 sites were sampled for PFAS to determine concentrations and trends in ambient surface waters. This work did not target specific releases from industrial sources. Sampling sites were located in every province with the exception of Alberta and Prince Edward Island, as well as none of the 3 Territories; PFAS were detected in the surface water of every province tested. Overall, 13 PFAS were measured in 566 Canadian freshwater samples, with concentrations ranging from below the laboratory detection limit (LOD range: 0.4 ng/L to 1.6 ng/L) to a maximum of 138 ng/L (for PFBS). While PFOS and PFOA concentrations were declining over this time period, other compounds such as PFBA and PFPeA increased (Lalonde and Garron 2022). PFOS concentrations in surface water samples collected between 2007 and 2010 (ECCC 2018) and 2016 and 2017 (ECCC 2019) from drainage regions across Canada were all below the Federal Environmental Quality Guideline (FEQG) for PFOS in surface water (ECCC 2018). In the Great Lakes, median concentrations of PFAS in water were lowest in Lake Superior (1.3 ng/L) and approximately 10-fold higher in Lake Ontario (11 ng/L) (Xia et al. 2024). Concentrations of regulated PFAS such as PFOS and PFOA have generally declined in concentration; whereas those shorter chain PFAS that have been used as replacements have not, with PFBA being the most abundant (Xia et al. 2024). This same study estimated the mass budget of PFAS compounds in the Great Lakes basin using available datasets and found that, overall, the upper lakes (Superior and Huron) are accumulating PFAS and the lower lakes (Erie and Ontario) are net exporters of PFAS.

PFAS (including C8-C12 PFCAs and C7, C8 PFSAs) are measured in whole body homogenates of fish from water bodies across Canada (Burniston et al. 2011; Gewurtz et al. 2012; Chu et al. 2016; McGoldrick and Murphy 2016; ECCC 2019; ECCC, US EPA 2022). This monitoring provides information on the presence and accumulation of PFAS in the aquatic environment. Concentrations of PFOS in Lake Ontario lake trout increased from the 1990s to early 2000s, declining subsequently, although concentrations remain above federal guidelines for mammalian diet at Great Lakes sites (McDaniel et al. 2021; ECCC, US EPA 2022), and above the FEQGs for the protection of mammals and birds that eat fish (ECCC 2019). In

contrast, increasing concentrations of PFCAs were seen within the past decade in Lake Huron lake trout, whereas concentrations declined in Lake Ontario (McDaniel et al. 2021). These data were measured in whole fish including non-edible portions such as digestive organs, blood and bones; concentrations do not necessarily reflect contaminant concentrations in edible portions of fish tissue. (ECCC, US EPA 2022).

Surveillance studies of PFAS (including C4 to C14, C16, C18 PFCAs and C6, C8, C10, PFSAs) in Arctic and Subarctic locations are performed as part of the Northern Contaminants Program (NCP) core Environment Monitoring and Research (EMR) projects (Braune and Letcher 2013; Letcher et al. 2014, 2018; Lucia et al. 2015; AMAP 2016, 2017, 2018; CIRNAC 2018; Muir et al. 2019; Routti et al. 2019a; Sonne et al. 2021). Under these projects, Arctic seawater has been analyzed each year since 2011 and constitutes the longest continuous data set for this medium; PFOS and PFCAs have declined in seawater collected in more recent years (CIRNAC 2018). Ringed seals and Arctic char have been analyzed every year since the 1990s and constitute the longest continuous temporal data set for these media. Declining trends for total (C7 to C14) PFCA were observed in ringed seals from 4 locations in the Canadian Arctic for the period 2005 to 2010 (Muir et al. 2019). However, more recent trends indicate an increase in these PFCAs in ringed seals from 2 of the locations, Hudson Bay and Lancaster Sound (Muir et al. 2019). C7 to C14 PFCAs in landlocked Arctic char from Lake Hazen, Char Lake, and Amituk Lake appear to be declining from their peak during the period 2006 to 2009 (Muir et al. 2019). PFAAs were analyzed in the food web of Lake Melville, NL (including in ringed seals), where local residents are concerned about contaminant levels in the country foods they harvest (CIRNAC 2018). PFAA concentrations in Lake Melville ringed seal pups increased annually from 2013 to 2016 (CIRNAC 2018). Efforts are underway to evaluate the influence of local vs long-range inputs to ringed seals in Lake Melville, which is in close proximity to major land development. Concentrations of PFAA in Arctic char have generally declined since the period 2008 to 2009 but the trends vary among the High Arctic lakes evaluated and among specific chemicals (CIRNAC 2018; Muir et al. 2019). PFAS were measured in the blood of adult thick-billed murres, a marine Arctic seabird that preys on fish, in southern Hudson Bay. This research has provided additional information on the presence and possible effects of PFAS on this migratory Arctic seabird in the marine environment but have yet to be validated by peer review. PFAS were assessed in polar bears from different populations in Hudson Bay and correlated with liver metabolites. Temporal trends were also assessed in polar bears along with their diet in the Hudson Bay region (Pedersen et al. 2016; Letcher et al. 2018; Morris et al. 2019; Muir et al. 2019). There were no obvious increasing or decreasing trends in total PFCA and PFOS concentrations in the liver tissue of 2 subpopulations of polar bears from the southern and western Hudson Bay (Nunavut) over the 2007 to 2016 period (INAC 2017; CIRNAC 2018; Muir et al. 2019).

Outside of the NCP, Government of Canada researchers have led research projects on PFAS in Arctic and Subarctic environments. Analyses of short-chain and long-chain PFCAs and PFSAs in High Arctic icefields (MacInnis et al. 2017; Pickard et al. 2018, 2020), snow melt, permafrost thaw and glacier melt (Cabrerizo et al. 2018; MacInnis et al. 2019a) are relevant to the aquatic environment due to accelerated melting mediated by climate change. This was supported by the PFAA depth profile in a dated sediment core from Lake Hazen, Nunavut, and its correlation with

glacial discharge (MacInnis et al. 2019b). PFAAs have also been measured in Arctic water (Lescord et al. 2015; Cabrerizo et al. 2018; MacInnis et al. 2019a) and lake sediment (Lescord et al. 2015).

The Government of Canada monitors, among other chemicals, PFAS in fish and wildlife across Canada as part of research and monitoring programs under the CMP. These include analysis of C4 to C16 PFCAs, C4 to C10 PFSAs, and novel PFAS (for example, perfluoroalkyl phosphinic acids, zwitterionic and cationic PFAS) in fish and birds from the Great Lakes and St. Lawrence River (Houde et al. 2013; De Silva et al. 2016; Munoz et al. 2022b) and in beluga whales from the St. Lawrence Estuary (Barrett et al. 2021). Seventy AFFF-derived PFAS were analyzed in fish collected downstream of an active fire-training area at an international civilian airport in Ontario (Carrizo et al. 2023). PFOS largely dominated the PFAS profile, with record-high concentrations in Brook Sticklebacks (*Culaea inconstans*) from the creek (16,000–110,000 ng/g wet weight whole-body) (Carrizo et al. 2023). Time trends were also evaluated in beluga whales from the St. Lawrence Estuary, where a general decline in regulated legacy PFAA and PFOSA was observed after the mid-2000s (Barrett et al. 2021). However, unregulated short-chain PFAS alternatives, single-hydrogenated perfluorocarboxylic acids (H-PFCAs; detected for the first time in this study), and odd-chain fluorotelomer-based carboxylic acids (FTCA) were found to increase over time (Barrett et al. 2021). Eggs from aquatic (gull species) and terrestrial wildlife (European Starlings) have been monitored for PFAS in the Atlantic provinces, St. Lawrence River, Great Lakes, prairies, Pacific coast, and the Subarctic (Letcher et al. 2015; Miller et al. 2015, 2020; Gewurtz et al. 2016, 2018; Su et al. 2017; Elliott et al. 2021). Eggs of these species have been collected annually since 2008 and analyzed for PFAS that include C4 to C14, C16, and C18 PFCAs and C4, C6, C8, and C10 PFSAs. There was evidence of decreasing trends for concentrations of PFOS (comprising >90% of total PFSA) and total long-chain PFCAs in eggs collected from 14 of 39 sites/colonies monitored from 2008 to 2021. For the unregulated short-chain PFAS, which were found at relatively lower concentrations, there was no evidence of a temporal change in concentrations at these sites/colonies, with the exception of a few sites where either an increase (2 sites) or decrease (3 sites) in total PFBS and PFHxS concentrations were found during this period. A nationwide survey of European starling eggs across Canada indicated elevated concentrations of PFAS, including both PFCAs and PFSAs, at landfill sites compared with urban/industrial and rural sites (Gewurtz et al. 2018). However, the concentrations were not related to the quantity of waste received at those landfills.

PFAS were measured in the eggs and blood of nestling peregrine falcons, a terrestrial predator of other avian species, in southern Ontario and the north shore of Lake Superior (Sun et al. 2020, 2021). A total of 22 PFAA and 4 FASA were determined; the PFSA were PFBS, PFHxS, PFEtCHxS, PFOS, and PFDS, and the PFCAs (C4 to C14, C16, and C18) were PFBA, PFPeA, PFHxA, PFHpA, PFOA, PFNA, PFDA, PFUdDA, PFDoDA, PFTrDA, PFTeDA, PFHxDA, and PFODA. PFSA (including PFHxS, PFOS, and PFDS) were detected in most eggs and plasma samples. In addition, 11 PFCAs (C5 to C14, C16) were detected in most egg samples, and 8 PFCAs (C8 to C14, C16) were detected in most plasma samples. PFPiAs, PFCAs, and PFSAs were surveyed in fish, dolphins, and birds from various freshwater and marine locations in North America (De Silva et al. 2016). This was the first report of PFPiAs in fish, dolphin, and bird plasma. Total PFPiA levels were 1 to 2 orders of magnitude lower than those of PFCAs and

PFSAs in the same samples. PFAS concentrations were measured in turtles, invertebrates, and water samples in rural and urban environments and downstream of an airport in southern Ontario (de Solla et al. 2012). The PFAS evaluated included C4 to C15 PFCAs, C4, C6, C8, and C10 PFSAs, several PFAA precursors (for example, PFOSA), and PFECHS (a cyclic PFAS used in aircraft hydraulic fluid). This study found elevated levels of PFAS downstream of the airport compared with the other locations evaluated (de Solla et al. 2012). PFAS were also measured in crayfish and water collected upstream and downstream of 6 airports, 3 WWTPs, and along the Grand River in southern Ontario, on an annual basis starting in 2018.

In addition, PFOA and PFOS have been identified as contaminants of concern for 3 species of at-risk whales: the Southern Resident Killer Whale, the St. Lawrence Estuary Beluga, and the North Atlantic Right Whale. As part of the Initiative to Protect and Recover Endangered Whale Populations, the Government of Canada has committed to increasing monitoring and research to improve understanding of the sources and possible impacts of contaminants on whales and their prey. This initiative includes air and freshwater monitoring within whale habitat as well as monitoring of potential land-based contaminant sources.

4.2.3 Landfill leachate

Landfill leachate was collected at 13 selected large (permitted to receive 40,000 tonnes of municipal solid waste annually) MSW landfills across Canada between 2008 and 2014 under the CMP Environmental Monitoring and Surveillance program. PFAS (C4 to C12 PFCAs, C4, C6, and C8 PFSAs, PFOSA) were analyzed in the leachate samples collected between 2009 and 2011 at 12 different landfills (EC 2013; Gewurtz et al. 2013). The total concentration of PFAS measured in leachate ranged from 320 ng/L to 9,400 ng/L before any treatment (median of 3,227 ng/L) and from 800 ng/L to 14,201 ng/L (median of 4,498 ng/L) after on-site leachate treatment. The total concentration of PFAS measured in leachate generally increased after on-site leachate treatment (discussed further in section 2.6.4).

The Government of Canada recently completed a research project that investigated the presence of various contaminants of emerging concern, including 17 PFAS (C4 to C14 PFCAs, C4, C6, C8 and C10 PFSAs, PFECHS, FOSA), within 48 samples of leachate-impacted groundwater from 20 historic landfills (with closing dates from the 1920s to early 1990s; few have leachate collection systems) in Ontario, Canada (Propp et al. 2021). Several of these landfills, closed in the 1960s or later, had total PFAS concentrations similar to those reported for modern landfills, with a maximum of 12,700 ng/L. Subsequently, a set of field-based investigations was conducted (ending 2022) at 2 of these historic landfill sites where a surface water aquatic ecosystem (1 a pond and 1 a stream) was receiving discharge from groundwater plumes contaminated with landfill leachate. The investigations assessed exposure to various contaminants, including PFAS. These projects were supported through an agreement with the Province of Ontario’s Ministry of Environment, Conservation and Parks.

Ad hoc analysis of PFAS sampled and analyzed by the Government of Canada included 29 PFAS analytes that were measured in 6 leachate samples in 2019 to 2020 (2 consecutive days at 3 sites) at operational landfills. Many of the 29 analytes were detected frequently. Only 8

analytes (4:2 FTSA, N-EtFOSA, N-MeFOSA, PFDoS, PFDS, PFNS, PFTeDA, and PFTrDA) were seldom detected.

As part of the Initiative to Protect and Recover Endangered Whale Populations, the Government of Canada sampled leachate from 10 operational MSW landfills in Canada over a four-year period (2019 to 2022) to determine the presence and concentration of specific substances, including certain PFAS, in landfill leachate. 9 PFAS were regularly detected in the raw leachate samples: PFNA (52%), 6:2 FTSA (66%), PFOS (74%), PFBS (84%), PFHxS (90%), PFHpA (94%), PFPeA (98%), PFOA (98%), and PFHxA (99%) (SNC-Lavalin 2023). The effects of leachate treatment in removing PFAS varied widely between the different analytes, the type of leachate treatment, and the number of processes used for onsite treatment. Generally speaking, treatment appeared to be less effective with shorter-chain compounds such as PFBS and PFPeA, which were often present in higher concentrations in the treated effluents than in the raw leachate.

PFAS emissions to air from the waste sector are described in section 4.2.1.

4.2.4 Wastewater and biosolids

The Government of Canada gathers data on levels of PFAS entering municipal WWTPs, evaluates the fate of PFAS through the liquid and solids trains of typical treatment process types used in Canada, and determines levels of PFAS being discharged in WWTP effluents and solids residuals (EC 2013; Gewurtz et al. 2013, 2020, 2024; Guerra et al. 2014; Government of Canada 2021; Lakshminarasimman et al. 2021). The Government of Canada has developed partnerships with municipalities throughout Canada in order to evaluate typical Canadian WWTP types (including primary, secondary, advanced, and lagoon treatment) and geographic regions (mountain, prairie, Great Lakes/St. Lawrence, coastal). As discussed in section 2.6.4, PFAAs are formed during wastewater treatment, which is likely a result of transformation of unmeasured precursors (Guerra et al. 2014).

Guerra et al. (2014) examined the fate and behaviour of 13 PFAS (including C4 to C12 PFCAs, C4, C6, and C8 PFSAs, PFOSA) in influent, effluent, and solids samples collected from 15 Canadian WWTPs. Of the PFAA measured, PFOA was the predominant PFAA in wastewater, with concentrations ranging from 2.2 ng/L to 150 ng/L in influent and 1.9 ng/L to 140 ng/L in effluent. PFOS was the predominant compound in primary sludge, waste biological sludge, and treated biosolids, with concentrations ranging from 6.4 ng/g to 2,900 ng/g dry weight, 9.7 ng/g to 8,200 ng/g dry weight, and 2.1 ng/g to 17,000 ng/g dry weight, respectively. More recently, Gewurtz et al. (2024) monitored the fate and behaviour of 42 PFAS in 27 Canadian WWTPs. They found that some PFAS concentrations generally decreased over time, which can be attributed to industrial production phase-outs and regulations. PFOS did not decrease over time in wastewater, indicating that regulatory action and industrial phase-outs of PFOS are slow to be reflected in wastewater. Concentrations of short-chain PFCAs and PFSAs in wastewater influent and effluent consistently increased between 2009 and 2021, which reflect the use of short-chain PFAS as replacements for phased-out and regulated longer-chained PFAS.

Lakshminarasimman et al. (2021) evaluated the formation and removal of 13 PFAS (including C4 to C12 PFCAs, C4, C6, and C8 PFSAs, PFOSA) in 9 different sludge treatment systems. Of the 13 target PFAS, only 4 (PFOA, PFDA, PFDoDA, and PFOS) were detected appreciably (>1%) in both raw sludge and biosolids samples. The concentrations of PFOA and PFOS ranged from below the laboratory reporting limit to 4.8 ng/g and 27 ng/g dry weight in raw sludge and ranged from below the laboratory reporting limit to 23 ng/g and 25 ng/g dry weight in biosolids, respectively.

A Government of Canada research project reported on the distribution of selected PFAS (including ionizable PFAS such as PFOS and PFOA and their precursors) in aquatic sediment and agricultural soils where WWTP-sourced biosolids application occurred, and in samples from sites in the Great Lakes basin (Chu and Letcher 2017). 13 soil samples were collected (2015) from a WWTP-biosolids applied and 2 non-biosolids applied farm field sites in southern Ontario. Novel side-chain fluoroalkyl (co)polymers (SCFPs) were also evaluated in this study. The SCFPs were detected in 100% of the soil samples from biosolid-augmented agricultural sites and at concentrations much greater than in the aquatic sediment samples. The concentrations of SCFPs in soil and sediment samples were also much greater than the total concentration of other PFAS that were measured (including PFOS and PFOA). For the same project, SCFPs and established PFAS were detected in biosolids samples from 20 Canadian WWTPs, and the novel fluorinated polymers were at much higher concentrations than those of other commonly monitored PFAS (including PFOS and PFOA) (Letcher et al. 2020). Gottschall et al. (2017) monitored concentrations of 13 PFAS (including C4 to C12 PFCAs, C4, C6, and C8 PFSAs, PFOSA) in groundwater, tile drainage, soil, and crop grain following application of municipal biosolids to a field. They found that although PFAAs were detected post-application in groundwater, tile water, and soil throughout the study period, overall, statistically significant post-application increases were detected only for tile drainage water and soil. Studies conducted outside of Canada on agricultural fields where biosolids have been applied have found varying results with some reporting an increase in PFAS concentrations (Brusseau et al. 2020; Johnson 2022) and some finding no difference compared to sites that did not receive biosolids (Pepper et al. 2021). Some studies have shown that PFAS can be taken up from soil by plants and can be transferred to animals and humans through the consumption of crops (Costello and Lee 2020; Scearce et al. 2023). However, as has been discussed in greater detail in section 2.3, the overall process of PFAS uptake and accumulation in plants and crops has not been fully determined, and concentrations of PFAS in retail foods tend to be below the LOD.

Please refer to section 8.1.5 for information on the CFIA’s interim standard for biosolids.

5 Human biomonitoring

KEY POINTS ON HUMAN BIOMONITORING

- Few PFAS (typically PFCAs and PFSAs) have been commonly monitored in past human biomonitoring (HBM) surveys. Although, the number of PFAS analytes examined continues to grow, in general, well-studied PFAS (for example, PFOA, PFNA, PFHxS and PFOS) continue to demonstrate the highest concentrations and detection frequencies.
- Between 2007 and 2019, Canadian HBM data, obtained through several cycles of the Canadian Health Measures Survey (CHMS), have shown that there was a statistically significant decreasing trend over time in PFOA (by 52%), PFNA (by 47%), PFDA (by 36%), PFHxS (by 64%) and PFOS (by 67%) concentration in the general population of Canada aged 12 or 20 to 79.
- Canadian HBM data demonstrate that, at any given time, Canadians are exposed to multiple PFAS.
- Canadian HBM data have demonstrated that, although there are statistically decreasing trends over time observed for certain PFAS (for example, PFOA, PFOS, and PFHxS), these PFAS are present in almost 100% of the Canadian population (in blood) despite risk management measures being in place in Canada for several years. Other PFAS (PFDA and PFUnDA) are commonly detected in over 50% of the population.
- 4 cycles of CHMS have shown a trend of higher concentrations of PFOA, PFHxS, and PFOS in the plasma of males compared to females, and concentrations of PFAS were generally higher in adults than in children in the Canadian population.
- Results in the CHMS, a nationally representative PFAS data set for children, demonstrate that children as young as 3 can be exposed to multiple PFAS.
- Certain population groups in Canada were reported to have higher levels of certain PFAS in blood than the general population. For example, Anishinabe children (ages 3 to 5, 6 to 11) and youth (ages 12 to 19) were reported to have elevated levels of PFNA, up to 21-fold higher, compared with similar age groups (for similar time periods) in the CHMS. Adults (male and female) and pregnant women in Nunavik also were reported to have PFNA levels that were 7- and 6.3-fold higher than comparable populations in the CHMS (for similar time periods). Certain PFAS (for example, PFOA) were reported to be lower in certain Indigenous populations when compared with the CHMS.
- Concentrations of certain PFAS were reported to have increased in certain populations of Canada; specifically, concentrations of PFNA in the serum of pregnant women in Nunavik increased in the 5 years between 2011 to 2012 and 2016 to 2017.
- In the most recent CHMS survey of the general population (ages 3 to 79 years) in Canada, as well as in specific subpopulations (for example, adults and pregnant women in Nunavik, adults in Dene communities in the Dehcho region of the Northwest Territories [NWT]), more than 25% of the sampled group report concentration levels above an international HBM guidance value developed by EFSA (for women of reproductive age) combined exposure to PFOA, PFNA, PFHxS, and PFOS.
- Internationally, firefighters appear to have elevated levels of PFHxS, PFOS, PFDA, and PFOA when compared to the general population.

5.1 Introduction to human biomonitoring and PFAS

Human biomonitoring (HBM) is the measure of a chemical, its metabolites, or reaction products in biological matrices (for example, blood, urine). It provides a biologically relevant, integrated measure of systemic exposure to environmental chemicals that may occur across multiple routes (for example, oral, dermal, and inhalation) and sources (for example, natural and anthropogenic, environmental media, diet, and frequent or daily use products) (Sexton et al. 2004; Haines and Murray 2012; Zidek et al. 2017). However, HBM data also have limitations. HBM data from population-level biomonitoring surveillance programs alone cannot provide information on the source of exposure and have uncertainty in identifying the period of exposure, especially for substances with longer half-lives. However, HBM data can be used to establish reference concentrations of chemicals representing the upper margins of background exposures in people in Canada, which allows the identification of individuals or subpopulations with an increased level of exposure compared with the background exposure (Haines et al. 2017). In this report, HBM comparisons included populations within Canada (for example, individuals living in Northern Canada and the Canadian Health Measures Survey [CHMS] general population) and comparison with other countries. Additionally, if data from multiple sample collection periods are available, HBM data support the identification of levels of or trends for chemicals in populations using factors such as sex, age, and time (HC 2023a). While HBM data are increasingly used in the characterization of exposure and risks from a number of chemical substances (HC 2016a, 2016b), this data may also be readily screened in a risk context through direct comparisons with health-based biomonitoring guidance values such as biomonitoring equivalents and the German HBM values (St-Amand et al. 2014; Faure et al. 2020). HBM data can also be used in assessing the effectiveness of risk management actions (Canada 2020b, 2020c, 2021; ECCC 2020) and identifying future research needs, such as potential links between exposure to certain chemicals and specific health effects (Eykelbosh et al. 2018; HC 2020).

Few PFAS (typically PFCAs and PFSAs) have been commonly monitored in past HBM surveys; however, more recent biomonitoring studies have examined a larger number of PFAS analytes (for example, 25 to 60 PFAS analytes examined in Cioni et al. (2023), Reardon et al. (2023), Borghese et al. (2024)). Available HBM studies have demonstrated that certain PFAS, particularly PFOA, PFNA, PFHxS, and PFOS, are ubiquitous, while others (for example, PFDA, PFUnDA) are commonly found in the blood (plasma or serum) of the general population of countries where the surveys have taken place (for example, Canada, the US, France and Sweden) (Bjermo et al. 2013; Fillol et al. 2021; CDC 2022; HC 2023b). In a scoping review of analytical methods for PFAS in human matrices, Comito et al. (2023) noted that PFBA, PFHxA, PFHpA, and PFBS were the short chain PFAS that were the most commonly detected in human samples, although the detection rates were highly variable. Table B-1 of Appendix B provides a summary of the most frequently detected PFAS in blood in Canada and internationally, including studies that are national, regional, or small in scale; some studies are birth-cohorts (that is, examining a group of people born at a similar time). In addition, PFAS have also been reported in cord blood and human milk in various parts of the world, for example, Canada, the US, France, Spain, Korea, Japan, and China (Monroy et al. 2008; Fujii et al. 2012; Arbuckle et al.

2013; Kubwabo et al. 2013; Cariou et al. 2015; Fisher et al. 2016; Kang et al. 2016; Lorenzo et al. 2016; Cai et al. 2020; Zheng et al. 2021; LaKind et al. 2022; Rawn et al. 2022b).

Due to the persistence, high bioavailability in the environment, and widespread use (current and historical) of PFAS, people can be exposed to multiple PFAS at any given time from various sources (HBM4EU 2019; Bil et al. 2021). The relative contributions of different PFAS vary between people, for example, between children and adults (EFSA 2020), however, the most prominent PFAS in human serum and plasma (both in terms of contribution to sum of PFAA concentration levels as well as number of samples above detection limits) are consistently found to be PFOA, PFNA, PFDA, PFHxS, and PFOS.

5.2 Factors to consider when using HBM data to assess PFAS exposures

To evaluate whether and how HBM data can be used to consider exposure to a substance, the adequacy of the biomarker, quality of the data, and appropriateness of the data set should be examined (Zidek et al. 2017). Chemical-specific information that is important to consider for the use of HBM data include: appropriateness of the biomarker(s), appropriateness of the biological matrix, and knowledge of biological half-lives. Study-specific information related to the use of HBM data include detection limits, geographic location of sampled population, timing of sample collection, age of study, subpopulation(s) monitored, and sample size. The following sections provide more details on chemical-specific factors. Study-specific information is described in later sections where PFAS-specific biomonitoring results are discussed (sections 5.4, 5.5, and 5.6).

5.2.1 Biomarkers

Many PFAS may degrade to PFAAs (including PFCAs and PFSAs) under environmentally relevant conditions; these PFAAs are considered to be stable end products (Bil et al. 2021). Serum or plasma concentrations of PFCAs or PFSAs (for example, PFOA or PFOS) have been considered appropriate biomarkers for PFAS, representing either direct exposure to these PFCAs or PFSAs or exposure to precursor compounds that are then degraded or metabolized to these terminal acids. PFAS that are commonly monitored in biomonitoring studies include PFOA, PFNA, PFDA, PFUnDA, PFHxS, and PFOS.

Uncertainty may arise, however, given that the number and concentrations of co-occurring, unidentified precursors in serum of the general population is unknown (McDonough et al. 2022). No precursor substances were examined in the CHMS; however, certain substances have been included in some international biomonitoring studies and in small-scale studies (Table B-1 of Appendix B). In past HBM studies, precursors were not typically measured; however, expansion of the number of PFAS analytes has resulted in more precursors being monitored (for example, in studies by Ao et al. 2022; Aro et al. 2022; Borghese et al. 2024). Some intermediate metabolites of PFCA or PFSA precursors have been noted to have higher toxicity than the final PFCA or PFSA degradation products (Rand et al. 2014; Rice et al. 2020). Studies have indicated that some of the intermediate short-chain PFAS metabolites, such as 5:3 FTCA, may biopersist and bioaccumulate (Kabadi et al. 2018, 2020; Rice et al. 2024).

In recent years, ultra-short chain PFAAs (including TFA and PFPeA) have been detected in human blood, cord blood, and urine (Duan et al. 2020; Aro et al. 2021; Jia et al. 2023; Zheng et al. 2023).

Uncertainty exists regarding the comprehensiveness and comparability of HBM studies due to differences in approaches to identify and quantify biomarkers (Perera et al. 2024). Optimization of methods to identify or quantify a larger scope of PFAS may be complicated due to the range of PFAS that may be present and the variability in their properties; choices in approaches may result in bias toward certain types of PFAS (for example, most sample preparation procedures were developed for selected anionic and neutral PFAS). These areas of uncertainty apply to analytical approaches that are targeting specific PFAS analytes as well as non-specific approaches (for example, total organic fluorine). The most widely used method for identification and quantitation in biological samples is liquid chromatography with tandem mass spectrometry (LC MS/MS) (Perera et al. 2024; Perovani et al. 2024); however, LC-based techniques may overlook neutral and volatile PFAS. Application of gas chromatography may aid in detection of more volatile PFAS (Perera et al. 2024). Methods to integrate ultra-short chain PFAS into existing methods of measurement in human plasma and serum are also being explored (Liang and Steimling, 2024). It has been noted that analytical techniques developed for TFA and other ultra-short chain PFAAs have different strengths and limitations compared to other PFAS in the class (Björnsdotter et al. 2020).

Advances have been made using LC MS/MS approaches, in particular by expanding the target analyte list (for example, up to 60 PFAS analytes), however, these added analytes generally result in minor contributions to total identified PFAS and, as such, have not resulted in substantive changes to understanding the total potential PFAS burden (Perera et al. 2024). Some techniques are available to address the knowledge gap between the specific PFAS that are currently monitored in biomonitoring studies and a larger proportion of PFAS substances that may be present (De Silva et al. 2021). These include the use of fluorine mass balance, total fluorine, extractable organic fluorine (EOF), total oxidizable precursors (TOP) and targeted PFAS analyses (Cioni et al. 2022). The TOP assay assumes that the unknown compounds will oxidize to PFAAs; however, as some precursors are not fully converted to PFAA, the TOP assay can only provide semi-quantitative estimates of oxidizable precursors in human serum and likely underestimate precursor burdens (Cioni et al. 2022; Perera et al. 2024). EOF determination may represent an estimate of organic fluorinated chemicals but may contain organofluorine compounds other than PFAS (Aro et al. 2022). When combined with targeted analyses, EOF has been used to identify the fraction of unexplained organic fluorine which may include: PFAS precursors or replacements, ultra short PFAS that have not typically been included in biomonitoring studies, organofluorine pharmaceuticals (some of which may meet the definition for PFAS), and other organofluorine compounds (for example, pesticides) that also may meet the definition for PFAS (Pennoyer et al. 2023).

There is growing use and interest in methods such as TOP and EOF with the inclusion of ultra short PFAAs and efforts should be made to increase the performance of existing methods in terms of extraction recovery, repeatability and reproducibility. Björnsdotter et al. (2020) have noted that certain aspects of TOP assays may complicate the quantitative determination of

ultra-short chain PFAAs. Perera et al. (2024) also indicates that more work is needed to identify additional overlooked PFAS and that additional analytical approaches are needed to expand the chemical space captured by PFAS analysis to close the unidentified EOF gap.

5.2.2 Biological matrix

In the past, most biomonitoring studies have measured PFAS concentrations in either blood plasma (for example, the CHMS and Maternal-Infant Research on Environmental Chemicals study [MIREC]) or serum (for example, the US National Health and Nutrition Examination Survey [NHANES], MIREC). Individuals occupationally exposed to PFOA and PFOS and individuals living near a PFOA manufacturing facility have been observed to have much higher plasma or serum concentrations in comparison with the general population, suggesting that plasma and serum are appropriate matrices to measure biomarkers of exposure (ATSDR 2021). PFAS are also measured in whole blood in some biomonitoring studies (EFSA 2020; ATSDR 2021). Whole blood has the additional advantage of representing the entire circulating fluid (EFSA 2020). Some studies have shown that whole blood is the most appropriate matrix for PFOSA and PFHxA (Poothong et al. 2017; EFSA 2020). ATSDR (2021) further reported that only PFHxA, and not PFHxS, enters the cellular components of blood.

The ratio of most PFAS in serum to plasma is assumed to be approximately 1:1. Poothong et al. (2017) identified the median serum-to-plasma ratios of certain PFAS (PFOA, PFNA, PFUnDA, PFHxS, PFOS, PFBS, and 6:2 diPAP) as ranging from 0.8 to 1.3; however, other PFAS demonstrated wider serum-to-plasma ratios, such as PFTrDA (2.9) and PFDS (2.5). Similarly, median serum (or plasma) to whole blood ratios of PFOA, PFNA, PFUnDA, PFHxS, and PFOS were approximately 2 (Poothong et al. 2017; EFSA 2020). However, the ratios were variable for PFDA, PFDoDA, PFTrDA, PFBS, PFHpS, and PFDS, probably as a result of differences in distribution in the blood compartments. Additionally, these substances are generally found in low concentrations in the body, resulting in analytical uncertainties (EFSA 2020). Less invasive approaches to biological monitoring in whole blood are being developed including remote sampling approaches for quantifying PFAA collected using volumetric absorptive microsamplers (Carignan et al. 2023).

PFAS are also measured in human milk, but the levels in human milk are substantially lower than in serum, with concentrations ranging from 1 to several orders of magnitude lower (EFSA 2020; ATSDR 2021).

Individual PFAS can also be measured via other less invasive biological matrices, such as in umbilical cord blood, semen, hair, and nails (Comito et al. 2023; Di Giorgi et al. 2024). However, it is still unclear how to interpret these results (EFSA 2020; ATSDR 2021). EOF analysis have also been performed on tissues such as cord serum and placenta (Kaiser et al. 2021).

PFAS with shorter biological half-lives (for example, PFBA, PFHxA) are more efficiently eliminated in urine than long-chain PFAS with longer half-lives (Calafat et al. 2019; ATSDR 2021). Calafat et al. (2019) demonstrated that when paired serum-urine data for 12 PFAS from 2273 participants in the US NHANES were analyzed for serum and urine concentrations, PFAS was rarely detected in urine compared with serum. At that time, the authors concluded that the

findings of this study do not support biomonitoring of urine as a preferred biomarker for PFAS (including short-chain PFAS) for the general population. Similar observations were reported by multiple authors that examined paired urine-serum samples from other regions, for example, South Korea and China (Zhang et al. 2015; Kato et al. 2018, as cited in EFSA 2020).

Despite these observations, both Perera et al. (2024) and Comito et al. (2023) note that urine may be an informative matrix for exposure monitoring of short-chain PFAS in populations with ongoing exposures. Hartmann et al. (2023) investigated 14 PFAS in urine as part of the Austrian Children's Biomonitoring Survey (2020) and noted that more than 50% of samples were above LOQ for 4 PFCAs (PFPeA, PFHxA, PFHpA, PFOA) with the highest median concentration of 0.0044 µg/L for PFHxA. In a study conducted by Plassmann et al. (2022), urine was used as a matrix to examine PFAS including ultra-short chain PFAAs; TFA was observed in 40% of samples and others detected less frequently. The authors concluded that urine might not be an efficient biomonitoring matrix for ultra short PFAS, at least at the volumes used in their study (approximately 2 mL). This information suggests that data on the utility of urine as a biological matrix for PFAS exposure is equivocal and may be influenced by PFAS chain length or biological half-life. Zheng et al. (2023) found detection frequencies greater than 50% for PFPrA, PFBA and PFPeA and suggested that frequent detection of shorter-chain PFAAs compared to longer-chain PFAAs may be attributed to their higher water solubility.

5.2.3 Biological half-lives of PFAS

Section 7.1 discusses toxicokinetics and elimination half-lives in more detail. This section notes that, in general, the half-life values represent the time for half the original concentration to be cleared by the body through excretion (for example, urine, feces); in some cases, half-lives have been based on declines in human serum over time. As studies have used various approaches, half-lives are not necessarily directly comparable. PFAS with half-lives of years-to-decades (for example, PFOA, PFNA, PFHxS, and PFOS, on the basis of declines in serum PFAS in humans over time) are well suited for population-level biomonitoring surveys, such as the CHMS, as the levels measured are indicative of long-term steady-state serum or plasma concentrations. In contrast to these PFAS, certain SC-PFAS are more rapidly excreted, with serum or plasma half-lives of several days to several weeks. For example, mean half-lives are on the scale of days (for example, 72 to 87 hours on the basis of serum decline in humans) for PFBA (Chang et al. 2008), and weeks (for example, up to 49 days on the basis of decline in human whole blood) for PFHxA (Russell et al. 2013). Available data also shows that humans are less effective in eliminating PFHxA compared to laboratory rodent species (ECHA 2024a). This is consistent with the general observation of differences in the elimination rates of PFAS between species in which the longest half-lives are often observed in humans and the shortest in rodents (as noted in section 7.1). An elimination half-life for TFA was identified to be around 34 hours for elimination from blood in rabbits (Dekant and Dekant 2023). Some of these SC-PFAS are less commonly detected in population-level biomonitoring surveys compared to those with longer half-lives, but have been found in smaller biomonitoring studies (often with lower limits of detection) (Poothong et al. 2017; CA OEHHA 2020).

5.3 Existing HBM guidance values

A health-based HBM guidance value is an important tool in interpreting HBM data or as a screening value to assist in the evaluation of general or specific population biomonitoring data. HBM guidance values for general population exposure for 2 individual PFAS have been published in several reports and journal articles, including Borg et al. (2013), ECHA (2015), EFSA (2018), and the German Human Biomonitoring Commission (HBM Commission) (Umwelt Bundesamt 2015; Hölzer et al. 2021; Schümann et al. 2021). Key chronic HBM guidance values identified in the literature, derived by international organizations, are summarized in Table 1 below. HBM guidance values derived by different organizations vary depending on the selected critical effect level, selected uncertainty factors, and the derivation method.

In a 2020 assessment, the EFSA Panel on Contaminants in the Food Chain derived a Tolerable Weekly Intake (TWI) using a benchmark dose level ($BMDL_{10}$) of 17.5 µg/L for the sum of 4 frequently detected PFAS (PFOA, PFNA, PFHxS, and PFOS) in serum. As certain PFAS are known to be persistent in the body, the EFSA (2020) derived a TWI rather than a Tolerable Daily Intake (TDI). The critical study selected by the EFSA for derivation of their TWI is based on the sum of 4 prevalent PFAS, which suggests that this approach acknowledges potential co-exposures of the general population to PFAS at any given time.

The $BMDL_{10}$ used by the EFSA for the derivation of their TWI was based on decreased immune responses (that is, reduction in antibody titres against diphtheria) observed in 1-year-old children. The EFSA then estimated a serum level in mothers that would result in levels in human milk leading to serum levels in infants that would be associated with decreased immune response. Using physiologically-based pharmacokinetic (PBPK) modelling and assuming 12 months of breastfeeding, the $BMDL_{10}$ of 17.5 µg/L in infants was converted into a serum concentration of 6.9 µg/L in mothers at 35 years of age, which corresponded to an oral PFAS intake of 0.63 ng/kg bw/day (TWI of 4.4 ng/kg bw/week) by mothers (EFSA 2020). Thus, these serum concentrations (that is, 17.5 µg/L and 6.9 µg/L for infants and women of reproductive age, respectively) were used as the basis for the EFSA TWI values and are referred to as “reference serum levels” in this document.

There are uncertainties associated with the EFSA guidance values (EFSA 2020), such as the use of PFOA and PFOS PBPK modelling to derive the intake of the PFAS mixture by mothers that would result in serum levels in the 1-year-old infant at the effect level, or the assumption of equal potencies for effects of the 4 PFAS on immune outcomes. Mixture effects of PFAS and uncertainties of approaches are further discussed in section 7.5.

The HBM Commission of the Federal Environment Agency (UBA) of Germany has established human biomonitoring values (HBM-I and HBM-II) for PFOA and PFOS in serum or plasma (Hölzer et al. 2021; Schümann et al. 2021). According to the German HBM Commission, “the HBM-I value represents the concentration of a substance in a body matrix at and below which, according to the HBM Commission’s current assessment, adverse health effects are not expected and therefore, no exposure reduction measures are necessary” (Hölzer et al. 2021). The HBM-II is defined as the “the concentration in human biological material which, when exceeded, may lead to health impairment which is considered as relevant to exposed

individuals" (Schümann et al. 2021). The HBM-I and HBM-II values for PFOA and PFOS are primarily based on human studies considering the following effects: developmental toxicity, reduced birth weights, reduced fertility, immune system/reduced antibody formation, increased cholesterol concentration, and Type II diabetes/gestational diabetes (Hölzer et al. 2021; Schümann et al. 2021).

ECHA (2015) identified several different internal derived-no-effect-level ($DNEL_{internal}$) values for PFOA using animal data and human data and for different endpoints. According to the EU's Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) Annex 1 Section 1.0.1, a DNEL is defined as "a level of exposure to the substance above which humans should not be exposed" (ECHA 2012). The lowest $DNEL_{internal}$ values were based on reduced birth weight in a human study and increased total cholesterol and low-density lipoprotein (LDL) in human serum. These values are presented in Table 1.

The German HBM-I and HBM-II values examined key health effects (for example, pregnancy and fertility, birth weight, lipid metabolism, immunological effects) observed in a large number of epidemiological and animal studies, including the 2 critical epidemiological studies (that is, Fei et al. 2009; Steenland et al. 2009) that form the basis of the ECHA $DNEL_{internal}$ values.

Guidance values have also been derived for workers. ECHA (2015) derived a $DNEL_{internal}$ value for PFOA for workers, which is described below in Table 1.

The German Research Foundation, also known as Deutsche Forschungsgemeinschaft (DFG), also derived health-based guidance values for workers, which they designate as BAT (Biologischer Arbeitsstoff-Toleranz-Wert) values, for PFOA and PFOS (DFG 2017, 2019, 2021). The BAT values for PFOA and PFOS were based on critical effect levels from animal studies since the DFG considered that internal concentrations associated with health effects could not be determined based on existing epidemiological studies (DFG 2017, 2019). The derived BAT values for PFOA and PFOS were 5 000 µg/L and 15 000 µg/L in serum, respectively. The difference between the PFOA German BAT value and the ECHA PFOA $DNEL_{internal}$ for workers (ECHA 2015) was due to the derivation methods used. The ECHA $DNEL_{internal}$ was based on a critical effect level from a human study and included an uncertainty factor for intra-individual variation, whereas the German BAT value for PFOA was related to a critical effect level identified from an animal toxicity study and an uncertainty factor was not included; therefore, this reference value is not used further in this section.

Table 1. Available chronic health-based biomonitoring guidance values for PFOA, PFNA, PFHxS, and PFOS

Organization (year)	PFAS	Critical endpoint	Critical dose level (in serum/plasma)	HBM guidance value (µg/L)
EFSA (2020)	Sum of PFOA, PFNA, PFHxS, and PFOS	Decreased antibody titres for diphtheria of 1-year-old infants (Abraham et al. 2020 as cited in EFSA 2020)	$BMDL_{10}$ = 17.5 µg/L (serum concentration infants) used by EFSA to derive TWI	Reference serum level = 17.5 (children)[a]
EFSA (2020)	Sum of PFOA, PFNA, PFHxS, and PFOS	Decreased antibody titres for diphtheria of 1-year-old infants (Abraham et al. 2020 as cited in EFSA 2020)	$BMDL_{10}$ = 17.5 µg/L (serum concentration infants) used by EFSA to derive reference serum level in women of reproductive age	Reference serum level = 6.9 (women of reproductive age)[a,b]
German HBM values (Umwelt Bundesamt 2015; Hölzer et al. 2021; Schümann et al. 2021)	PFOS	Based on weight of evidence from epidemiology data and animal data	1–15 µg/L plasma	HBM-I = 5
German HBM values (Umwelt Bundesamt 2015; Hölzer et al. 2021; Schümann et al. 2021)	PFOS	Based on weight of evidence from epidemiology data and animal data	1–30 µg/L plasma	HBM-II = 10 (women of childbearing age)
German HBM values (Umwelt Bundesamt 2015; Hölzer et al. 2021; Schümann et al. 2021)	PFOS	Based on weight of evidence from epidemiology data and animal data	1–30 µg/L plasma	HBM-II = 20 (all other population groups)
German HBM values (Umwelt Bundesamt 2015; Hölzer et al. 2021; Schümann et al. 2021)	PFOA	Based on weight of evidence from epidemiology data and animal data	1–10 µg/L plasma (for HBM-I)	HBM-I = 2

Organization (year)	PFAS	Critical endpoint	Critical dose level (in serum/plasma)	HBM guidance value (µg/L)
German HBM values (Umwelt Bundesamt 2015; Hölzer et al. 2021; Schümann et al. 2021)	PFOA	Based on weight of evidence from epidemiology data and animal data	3–10 µg/L plasma (for HBM-II)	HBM-II = 5 (women of childbearing age)
German HBM values (Umwelt Bundesamt 2015; Hölzer et al. 2021; Schümann et al. 2021)	PFOA	Based on weight of evidence from epidemiology data and animal data	3–10 µg/L plasma	HBM-II = 10 (all other population groups)
ECHA 2015	PFOA-related substances	Reduced birth weight in a human study (Fei et al. 2009 as cited in ECHA 2015)	3.9 µg/L (serum concentration)	$DNEL_{internal}$ = 0.7 (general population)[c]
ECHA 2015	PFOA-related substances	Reduced birth weight in a human study (Fei et al. 2009 as cited in ECHA 2015)	3.9 µg/L (serum concentration)	$DNEL_{internal}$ = 1.3 (workers)[d]
ECHA 2015	PFOA-related substances	Increased total cholesterol and LDL in human serum (Steenland et al. 2009 as cited in ECHA 2015)	13.1 µg/L (serum concentration)	$DNEL_{internal}$ = 2.2 (general population)[c]
ECHA 2015	PFOA-related substances	Increased total cholesterol and LDL in human serum (Steenland et al. 2009 as cited in ECHA 2015)	13.1 µg/L (serum concentration)	$DNEL_{internal}$ = 4.4 (workers)[d]

LOAEL = lowest observed adverse effect level; NOAEL = no observed adverse effect level; BMD = benchmark dose; BMDL = 95% lower confidence limit on the BMD; $DNEL_{internal}$ = derived no effects level (internal); HBM-I; II = human biomonitoring value-1, 2

[a] "No additional uncertainty factors (UF) need to be applied, because $BMDL_{10}$ is based on infants which are expected to be a sensitive population group, as is true for many immunotoxic chemicals (EFSA 2020).

[b] Using a PBPK model, and assuming 12 months of breast feeding, EFSA estimated that the $BMDL_{10}$ in infants corresponds to an intake by the mother of 0.63 ng/kg bw per day for the sum of the 4 PFAS. Such intake would result in a serum level in the mother of 6.9 µg/L at 35 years of age (EFSA 2020).

[c] Uncertainty factor (UF) = 6 for intra-individual variation

[d] Uncertainty factor (UF) = 3 for intra-individual variation

5.4 Summary of human biomonitoring data on PFAS in Canada

5.4.1 PFAS measured in Canadian (CHMS, MIREC) and regional biomonitoring studies

In Canada, 9 PFAS have been measured as part of the CHMS. Carried out since 2007, the CHMS is a cross-sectional national survey in which many environmental chemicals or their metabolites are measured in the blood or urine of people in Canada. It is an ongoing survey conducted in 2-year cycles and is representative of the general population in Canada. The population surveyed in cycles 1 and 2 of the CHMS included persons living in the 10 provinces and 3 territories of Canada. Subsequent cycles of CHMS did not include the territories. The target population of CHMS excludes persons living on reserves and in other Indigenous settlements in the provinces, full-time members of the Canadian Forces, institutionalized populations, and residents of certain remote regions. All together, these exclusions represent less than 4% of the population in Canada. In addition to the nationally representative data for PFAS available through the CHMS, published Canadian PFAS biomonitoring data are available for certain populations not included in the CHMS, for example, persons living on reserves, in certain communities (for example, Innu and Anishinabe communities, communities in Nunavik) and in the territories (for example, Dene communities in the Dehcho region of the Northwest Territories and Gwich'in community in the Yukon) (AFN 2013; Caron-Beaudoin et al. 2019, 2020; Aker et al. 2021; Garcia-Barrios et al. 2021). These data are discussed in the next section.

CHMS biomonitoring data on PFAS are available for 4 cycles from 2007 to 2019 (HC 2023b). Cycle 1 (2007 to 2009) included PFOA, PFHxS, and PFOS. CHMS cycles 2 (2009 to 2011), 5 (2016 to 2017), and 6 (2018 to 2019) measured 9 PFAS, specifically PFBA, PFHxA, PFOA, PFNA, PFDA, PFUnDA, PFBS, PFHxS, and PFOS (Appendix B, Table B-2). A summary of the PFAS plasma concentrations from cycles 1, 2, 5, and 6 is presented in Table B-3 of Appendix B.

Results from the CHMS demonstrate a statistically significant decreasing trend ($p<0.001$) in PFOA, PFNA, PFDA, PFHxS, and PFOS concentrations in people in Canada aged 12 or 20 to 79 years (HC 2023a). Between 2007 and 2019, plasma concentrations of PFOA and PFOS declined significantly, with a 52% decline for PFOA and a 67% decline for PFOS, on the basis of geometric mean values found in the data from the CHMS for people aged 20 to 79 years. Despite these declines, PFOA and PFOS continue to be detectable in almost all of the population. The most recent cycle of the CHMS (cycle 6) reported that both PFOA and PFOS were detected in the plasma of over 99% of the population aged 3 to 79 years on the basis of an LOD of 0.066 µg/L for PFOA and 0.43 µg/L for PFOS (Table B-3 of Appendix B). Consistent with results found in other regional and national biomonitoring surveys, results for the general population in Canada aged 3 to 79 years from CHMS cycle 6 have shown that, compared to other monitored PFAS, PFOS is found in the highest concentrations (geometric mean [GM] = 2.5 µg/L) in the plasma, followed by PFOA (GM = 1.2 µg/L) (Table B-3 of Appendix B). This illustrates that despite risk management measures being in place in Canada for several years (for example, PFOS has been regulated since 2008; PFOA and LC PFCAs were added to PCTSR in 2016), these PFAS are still ubiquitous in people in Canada.

Comparison of the levels of PFHxS across the 4 cycles of the CHMS has shown that geometric mean plasma concentrations declined significantly (by 64%) between 2007 and 2019 in people in Canada aged 20 to 79 years (HC 2023a). PFHxS was still detected in over 99% of the population aged 3 to 79 years in cycle 6, with geometric mean plasma concentrations reported to be 0.76 µg/L (LOD = 0.063 µg/L).

Other trends observed over the course of the 4 cycles of CHMS include higher concentrations of PFOA, PFHxS, and PFOS in the plasma of males compared to females and concentrations of PFAS were generally higher in adults than in children in the Canadian population (HC 2023a).

PFNA, PFDA, and PFUnDA were monitored in CHMS cycles 2, 5, and 6. In cycle 6, PFNA was detected in over 98% (LOD of 0.13 µg/L) of the population (3 to 79 years). The geometric mean plasma concentration of PFNA was 0.44 µg/L, the fourth-highest plasma concentration of measured PFAS among CHMS participants after PFOS, PFOA, and PFHxS (Table B-3 of Appendix B). Although PFDA was found in lower concentrations (GM of 0.12 µg/L) in cycle 6, the substance is still very prevalent, with a detection frequency of over 65% (LOD of 0.092 µg/L) in 3 to 79 year olds. PFUnDA was less prevalent than PFOA, PFNA, PFDA, PFHxS, and PFOS (36% detection frequency with an LOD of 0.12 µg/L) in cycle 6, and, consequently, a geometric mean was not calculated (>40% of samples are below LOD). Between 2009 and 2019, plasma concentrations of PFNA and PFDA declined by 47% and 36%, respectively, on the basis of geometric mean values in the Canadian population aged 12 to 79 years. However, unlike PFOA, PFHxS, and PFOS, plasma concentrations of PFNA and PFDA were similar between sexes (HC 2023a).

Throughout cycles 2, 5, and 6 of the CHMS, detection frequencies of PFBA, PFHxA and PFBS were generally low (for example, in cycle 6, PFBA was at 5.4%, PFHxA at 1.0%, and PFBS at 0.3%). In the CHMS, when over 40% of samples are below the LOD, geometric means are not calculated, which was the case for PFBA, PFHxA, and PFBS (Table B-3 of Appendix B). PFBA, PFHxA, and PFBS have shorter biological half-lives, which may be associated with lower detection frequencies for these PFAS; however, other studies with lower detection limits have demonstrated that a higher proportion of samples were found to be above the detection limit. For example, PFBS was measured in both plasma and serum of adults in a small-scale study in Oslo, Norway, resulting in percentages above the method detection limit (MDL) of 100% and 51%, respectively, on the basis of an MDL of 0.018 (plasma) and 0.009 (serum) µg/L (Poothong et al. 2017). The plasma and serum detection limits from these studies are both lower than 0.066 µg/L (the LOD of PFBS in cycle 6 of the CHMS).

MIREC is a research initiative conducted in Canada which focuses on investigating the potential health effects of environmental chemicals on pregnant women and their children. From 2008-2011, the MIREC study enrolled a large cohort of pregnant women from 10 sites across Canada. There have since been many follow-up studies of the MIREC children and mothers. Borghese et al. (2024) have reported on Canadian biomonitoring data for PFAS that were part of a 2018-2021 follow-up study (MIREC 2024). In Borghese et al. (2024) serum samples from 289 adult female participants, which represent a subset of participants from 8 of the 10 original sites, were analyzed for 40 PFAS. Most of the 40 PFAS were not included in previous cycles of

the CHMS, however, some have been examined in the US NHANES. The limits of detection used in the Borghese et al. (2024) study were generally much lower than those used in many previous biomonitoring studies including the CHMS. As a result, a wider range of PFAS was detected, including some PFAS that had not been previously detected in people living in Canada.

Of the 40 PFAS analyzed by Borghese et al. (2024), 17 were detected in more than 50% of samples and 7 of these (PFOA, PFNA, PFHxS, PFOS, N-EtFOSE, PFOSA, 7:3 TFCA) were reported to be above the limit of detection in more than 97% of samples. In addition, 10 of the 17 PFAS (that is, PFPeA, PFHpS, N-EtFOSE, N-MeFOSE, N-MeFOSAA, PFOSA, 7:3 FTCA, 4:2 FTS, 6:2 TFS, PFMBA) had not previously been reported to be measured in people living in Canada. The geometric mean serum concentrations of these less commonly reported PFAS (besides PFOA, PFNA, PFDA, PFHxS, PFOS) ranged from 0.001 µg/L (PFMBA) to 0.064 µg/L (PFBA).

Other notable findings include PFAS that were reported to have fewer than 50% of samples above detection limits but have not been commonly detected in biomonitoring studies, including HFPO-DA, ADONA, 9Cl-PF3ONS, and perfluoroether compounds (NFDHA, PFMPA, PFMBA, PFEESA). Authors noted that concentrations for several of these substances were lower than reporting limits in used in previous studies. HFPO-DA and ADONA have rarely been detected in populations without an occupational source, however, in this study HFPO-DA and ADONA were detected in 47% and 16% of participants, respectively. 9Cl-PF3ONS was reported to have a 15% detection rate. The perfluoroether compounds were reported to have 95th percentile serum concentrations ranging from 0.002 µg/L (PFEESA and PFDoS) to 0.174 µg/L (PFTeDA) µg/L.

A series of studies from the Alberta Pregnancy Outcomes and Nutrition cohort examined 25 PFAAs in maternal plasma (from blood samples collected between 2009 and 2012) in the second trimester of participants (Reardon et al. 2019, 2023; Soomro et al. 2023, 2024). In this population, well-studied PFAAs, including PFOA, PFNA, PFDA, PFUnDA, PFHxS and PFOS were highly detected, ranging from 89 to 100% of samples. However, shorter-chain PFBA, PFPeA, PFHxA (MDLs from 0.02-0.04 ng/mL) and PFBS (MDL 0.4 ng/mL) were reported to be below method detection limits, and 67% of samples had detectable levels of PFHpA, but with a geometric mean that was close to the method detection limit (MDL = 0.02 ng/mL; GM = 0.04). Although PFDoA was detected in 56% of samples, longer-chain PFTrDA, FTeDA as well as PFDS were not detected. Reardon et al. (2023) also included 10 branched isomers of PFOS and PFOA in addition to linear PFAS.

5.4.2 PFAS measured in First Nations (on-reserve) populations, Inuit communities, and other Indigenous or northern communities

Data are available on PFAS concentrations measured in plasma or serum of First Nations (on-reserve) people, Inuit communities, and other Indigenous or northern communities in Canada (AFN 2013; Caron-Beaudoin et al. 2019, 2020; Aker et al. 2021; Garcia-Barrios et al. 2021). When results from these studies are compared to CHMS plasma concentration values for similar age and sex subpopulations during similar time periods (for example, cycle 5), notable observations may be made for certain long-chain PFCAs and PFSAs.

Caron-Beaudoin et al. (2020) examined 9 PFAS (PFBA, PFHxA, PFOA, PFNA, PFDA, PFUnDA, PFBS, PFHxS, and PFOS) in serum of pregnant Inuit women (16 to 40 years) from communities in Nunavik participating in the Nutaratsaliit Qanuingisiarningit Niqituinnanut (NQN) Pregnancy Wellness with Country Food Project (2016 to 2017). The authors found that maternal serum levels of PFOA, PFHxS, and PFOS showed statistically significant downward trends ($p<0.0001$) between 2007 (PFOA and PFHxS) or 2004 (PFOS) and 2017, similar to those observed for the Canadian general population in the CHMS. PFOA and PFHxS were lower in the NQN than in cycle 5 of the CHMS.

Despite these declining trends, when the data from the NQN project study were compared with geometric mean plasma concentrations in females of childbearing age (18 to 40 years) from cycle 5 of the CHMS (2016 to 2017), Caron-Beaudoin et al. (2020) noted that geometric mean serum concentrations of certain PFAS (specifically PFNA, PFDA, PFUnDA, and PFOS) were higher in the pregnant Inuit women from communities in Nunavik (Figure 5 and Table B-4 of Appendix B). Indeed, PFNA, PFDA, and PFOS in the NQN participants were 6.3, 3.3, and 1.8 times higher, respectively, than in the CHMS participants (Caron-Beaudoin et al. 2020). In addition, PFUnDA was detected in 100% of samples in pregnant Inuit women from Nunavik (LOD = 0.1 µg/L), whereas it had a detection frequency of less than 40% in cycle 5 of the CHMS (LOD = 0.12 µg/L). Additionally, maternal serum concentrations of PFNA, PFDA, and PFUnDA in pregnant Inuit women in Nunavik increased by 19%, 13%, and 21%, respectively, between 2011 to 2012 and 2016 to 2017, while the levels of PFNA and PFDA in the general population (CHMS) decreased over a similar time period of 2009 to 2019 (Caron-Beaudoin et al. 2020; see Table B-4 of Appendix B). A trend could not be assessed for PFUnDA in the CHMS due to the low number of samples with detection (detection frequency was less than 40% in CHMS cycles 5 (2016 to 2017) and 6 (2018 to 2019); HC 2023b). Caron-Beaudoin et al. (2020) noted that LC-PFCAs concentrations, particularly for PFNA, of pregnant Inuit women from Nunavik in 2016 to 2017 were among the highest compared to other recently reported PFNA concentrations in the circumpolar region (AMAP 2021). It may be noted that the comparison of PFAS concentrations in serum or plasma of pregnant women with non-pregnant women of childbearing age may have uncertainty associated with differences in plasma volumes (Aguree and Gernand 2019).

Figure 5 below presents the geometric mean serum or plasma concentrations of PFOA, PFNA, PFDA, PFUnDA, PFHxS, and PFOS from both pregnant Inuit women (aged 16 to 40 years) in the NQN study and females of childbearing age (18 to 40 years) from cycle 5 of the CHMS.

Aker et al. (2021) reported results from the Qanuilirpitaa? 2017 Health Survey for PFAS in plasma from adults (18+ years, sampled in 2017) from the 14 Inuit communities in Nunavik. These results were also compared with CHMS values (18 to 79 years) from cycle 5 and are presented in Figure 5. These data demonstrate higher levels of PFNA (7-fold), PFDA (3-fold), and PFOS (1.5-fold) in the adults sampled in Nunavik as well as the variability in levels of certain PFAS among subpopulations in Canada. The figure below describes data for the 6 PFAS included in both surveys or studies and does not capture all PFAS to which individuals may be exposed. In this population group, the study authors identified country foods (hunted/harvested foods from the land) as an exposure source of certain PFAAs, however,

other work is planned to examine PFAS in other media (for example drinking water) in Nunavik (Aker et al. 2024).

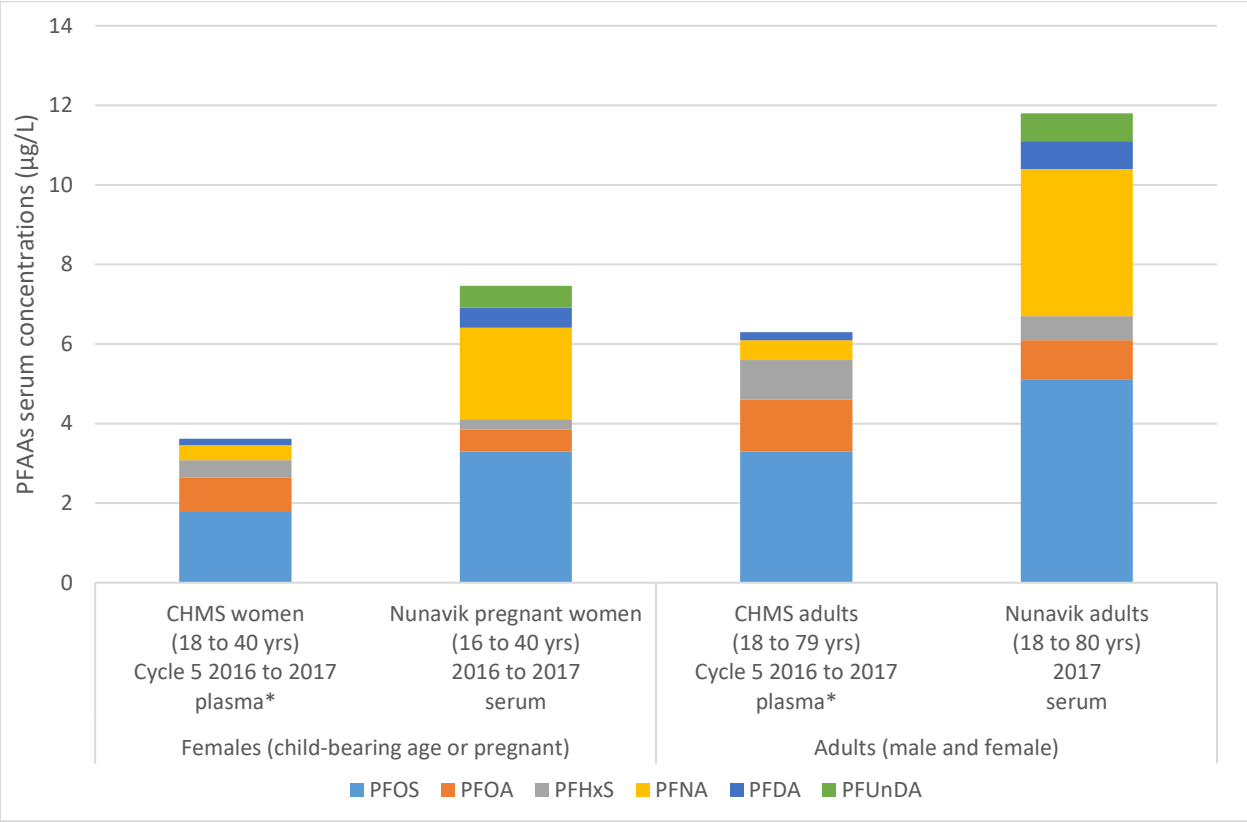

*Figure 5. Comparison of geometric mean plasma or serum concentrations of 6 PFAS (PFOA, PFNA, PFDA, PFUnDA, PFHxS, PFOS) in females (18 to 40 years) in CHMS cycle 5 (2016 to 2017) with pregnant Inuit women (16 to 40 years) from Nunavik (2016 to 2017), and comparison of geometric mean plasma or serum concentrations of these 6 PFAS in adults (18 to 79 years) in CHMS cycle 5 (2016 to 2017) with adults (18 to 80 years) from Nunavik (2017). *CHMS does not report GM if >40% of samples are below the LOD, resulting in no reported concentration for PFUnDA in CHMS populations (Caron-Beaudoin et al. 2020; Aker et al. 2021; HC 2023b).*

Other northern communities have also demonstrated elevated levels of PFNA compared to levels detected in the CHMS (based on comparisons of similar age groups and time periods). Garcia-Barrios et al. (2021) reported PFAS in serum or plasma of people residing in several northern communities, specifically Old Crow (Yukon) and 6 nations in the Dehcho region of the Northwest Territories. Average PFNA concentrations in adults were found to be 1.8 times higher in a Gwich'in community and 2.8 times higher in the Dehcho region when compared to plasma concentrations of PFNA in adults in the CHMS cycle 5 (2016-2017). These results are summarized in Table B-5.

Results from the First National Biomonitoring Initiative (FNBI) carried out in 2011 indicated that concentrations of PFOA, PFHxS, and PFOS were higher in adults (20 to 79 years) in CHMS cycle 2 (2009 to 2011) when compared to plasma concentrations found in the First Nation on-reserve population (aged 20 years and older) (AFN 2013; HC 2023a).

There are also studies available that have analyzed PFAS in Indigenous youth and children. O'Brien et al. (2012) collected blood samples from young Inuit children (mean age 2.1 years) attending childcare centres in Nunavik from 2006 to 2008 to document benefits of a nutrition program and detected PFOA, PFHxS, and PFOS in 100%, 50%, and 100% of samples, respectively (LODs of 0.3 µg/L). In a later study conducted in 2015 and examining Indigenous youth aged 3 to 19 years old from 4 First Nation communities in Quebec, serum PFNA concentrations in Anishinabe participants were 7 to 21 times higher than plasma concentrations of PFNA for the same age groups (3 to 5, 6 to 11 and 12 to 19 years) in CHMS cycle 5 (2016 to 2017) (Caron-Beaudoin et al. 2019; Lemire et al. 2019; Dubeau et al. 2022). These results are presented in Figure 6 and are also summarized in Table B-5 of Appendix B.

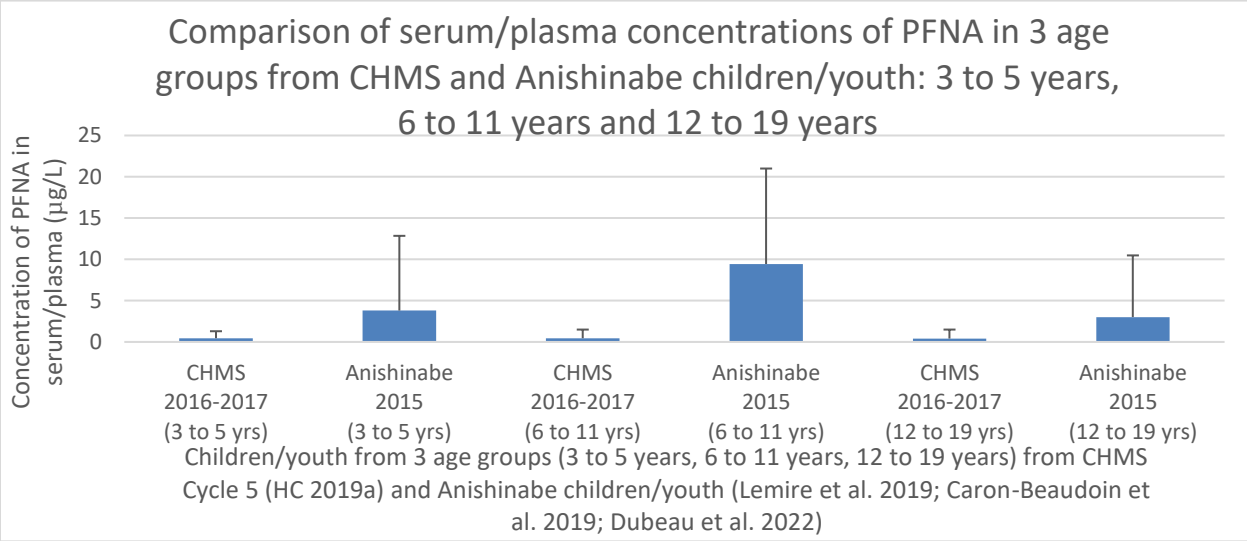

Figure 6. Geometric mean (whiskers are the 95th percentile) concentrations of PFNA in plasma or serum of children from the following age groups: 3 to 5 years, 6 to 11 years, and 12 to 19 years each from CHMS cycle 5 (2016 to 2017) (HC 2023b) and Anishinabe children/youth (2015) (Caron-Beaudoin et al. 2019; Lemire et al. 2019; Dubeau et al. 2022).

5.4.3 PFAS measured in cord blood and human milk

PFOA, PFHxS, and PFOS were measured in the plasma and cord blood plasma of approximately 2000 pregnant women from 10 cities across Canada between 2008 to 2011 as part of the MIREC study (Fisher et al. 2016). These maternal plasma results were somewhat similar to CHMS cycle 1 (2007 to 2009) and to data from CHMS cycle 2 (2009-2011) results for women (aged 20 to 39 years) as per Health Canada (2023a). PFOA, PFHxS, and PFOS were also found in cord plasma. The presence of PFAS in cord blood suggests that children are exposed to PFAS in utero.

Few Canadian studies have examined PFAS in human milk. However, a study by Kubwabo et al. (2013) focused on improving analytical detection methods for measuring a broad range of PFAS in human milk. In this study, 5 PFCAs, 2 PFSAs, and 8 diPAPs (polyfluoroalkyl phosphate diesters) were analyzed in 13 human milk samples collected between 2003 and 2004 from a study population in Kingston, Ontario. Of the PFCAs and PFSAs analyzed, only PFOA was

detected in 85% of the samples (LOD = 0.24 µg/L). Only 4 diPAPs were quantifiable in 3 to 8 of the 13 samples. Kubwabo et al. (2013) concluded that diPAPs are present in human milk. Additionally, these authors note that low detection levels or variability in detection of PFAS in human milk may be due to several factors, including the lack of standardization of methods used for determination of PFAS in milk, the complexity of the matrix, and PFAS being strongly bound to the protein fraction in human blood. In addition, 13 PFAS were analyzed in human milk samples from 553 to 664 women in Canada participating in the MIREC study. While some PFAS were not detected in these samples (PFHpA, PFDA, PFUnDA, PFDoDA, PFTeDA, PFHpS, and PFDS), PFOS and PFOA (linear and branched isomers) were highly detected in these samples (87.7% to 99.5%) and were the dominant contributors to the overall sum of PFAS concentrations. PFNA and PFHxS were less frequently detected (61.0% and 62.5%, respectively), while PFHxA and PFBS were infrequently detected (0.7% and 0.9%, respectively) (Rawn et al. 2022b). Results from these studies indicate that infants in Canada may be exposed to multiple PFAS through the consumption of human milk.

5.5 Summary of international human biomonitoring data on PFAS

5.5.1 PFAS measured in serum, plasma, whole blood, or urine

There are many studies varying in scope and purpose that examine human biomonitoring of PFAS in various populations around the world. Certain studies are national, others are regional or small in scale, while others examine birth cohorts (studies examining children or infants born around the same time). NHANES has measured a range of PFAS since 1999 and 2000 with up to 21 PFAS (including isomers of PFOA and PFOS) being examined. Some caveats associated with comparing these results include variation between sampling years and matrices (for example, plasma or serum), and methodological differences. In addition, national surveys such as the CHMS and NHANES are weighted to provide population-level detection frequencies, whereas smaller studies simply report the percentage of samples above the LOD or LOQ. Results from several PFAS biomonitoring studies representing a range of geographical regions (for example, the US, France, Sweden, South Korea, Germany, Norway, Denmark [Greenland, the Faroe Islands], and Japan) demonstrate that, at a given time, multiple PFAS occur consistently in many regions (Table B-1, Appendix B). Table B-1, Appendix B includes up to 24 PFAS that have been included in the analysis of various biomonitoring studies.

PFOA, PFNA, PFHxS, and PFOS were the most commonly detected PFAS, with percentage of samples detected or population-level detection frequencies generally ranging from 90% to 100%; PFDA and PFUnDA were the next most commonly detected PFAS in these studies. PFBA, PFHxA, PFHpA, PFDoDA, PFTrDA, PFHpS, PFDS, and PFOSA generally have low detection frequencies in national surveys; however, they were each reported to be detected in over 50% of samples in at least 2 studies.

As with Canadian national biomonitoring data, other national biomonitoring data show similar trends over time, that is, decreases in the most commonly monitored long-chain PFCA and PFSA concentrations. As examples, NHANES has shown downward trends for PFOA, PFNA, PFDA, PFHxS and PFOS from 1999 to 2018 (Sonneberg et al, 2023). In another example, Australian human biomonitoring data has also shown declines in PFOS, PFOA and PFHxS

between 2003-2004 to 2017-2018; PFNA initially increased before subsequently declining (Taucare et al. 2024).

Certain short-chain PFCAs and PFSAs have been reported to have shorter elimination half-lives than LC-PFAS (ECHA 2023c); however, it is noted that these PFAS are detected in some smaller-scale studies, which in some cases may be attributed to issues such as greater sensitivity of the analytical method. Other factors that may contribute to the variation in detection frequencies across studies are the cohort characteristics (for example, dietary preferences or use of traditional remedies; CA OEHHA 2020). Other PFAS have been measured in specific biomonitoring studies internationally (often at sites of PFAS contamination). As noted in section 1.1.1 of this report, PFO4DA and PFO5DA have been detected in serum samples of adults in an area near a fluorochemical manufacturing facility (Kotlarz et al. 2020; 2024).

As with Canadian data, in biomonitoring studies examining serum, plasma or whole blood, PFOA, PFNA, PFOS, PFHxS are the predominant PFAS quantified. Aro et al. (2021) examined whole blood and noted that long chain PFAAs (including PFHxS) made up 98% of the sum of 63 PFAS whereas short-chain PFAAs (along with the other PFAS analytes) were found to contribute a minimal amount. In HBM studies examining serum, similar results (that is PFOA, PFNA, PFOS and PFHxS being predominant amongst quantified PFAS) have been noted (for example, Duffek et al. 2020; Borghese et al. 2024).

Ultra-short chain PFAAs (for example, TFA and PFPrA) have been qualitatively (due to lack of suitable internal standards) reported in whole blood (detected in 62% and 22% of the samples, respectively) by Aro et al. (2021). Duan et al. (2020) also noted TFA above method detection limits in most samples of serum in adults in China in 2017, despite analytical limitations in reporting (for example, LOQ not reported, PFBA as internal standard). A study in the US found TFA to be the predominant PFAA in human serum samples, comprising 57% of the total PFAA concentration and was found to be significantly correlated with TFA in house dust and drinking water (Zheng et al. 2023). As noted in section 5.2.1, analytical techniques developed for TFA and other ultra-short chain PFAAs have challenges (Björnsdotter et al. 2020).

Several international studies have analyzed exposure to PFAS in children, infants, and fetuses (for example, Rappazzo et al. 2017; Dassuncao et al. 2018; Mamsen et al. 2019; Li J et al. 2020a). Rappazzo et al. (2017) conducted a systemic review of the literature available on PFAS exposure and child health outcomes. The studies were predominately conducted in the US, Taiwan, the United Kingdom, Denmark, and Norway. Study designs were primarily cohort or cross-sectional, and measurements of PFAS were primarily in serum. Mamsen et al. (2019) measured the concentrations of 6 PFAS (PFOA, PFNA, PFDA, PFUnDA, PFHxS, PFOS) in maternal serum and human embryonic and fetal organs from first, second, and third trimester pregnancies in Denmark and Sweden. Mamsen et al. (2019) found that, in general, PFAS concentrations in embryo/fetal tissue were lower than maternal serum but similar to placenta concentrations, suggesting that human fetuses were intrinsically exposed to a mixture of PFAS throughout gestation and PFAS deposit to embryo and fetal tissues. Li J et al. (2020a) detected 16 of 32 PFAS in 50% to 100% of maternal serum and cord serum samples of participants from the Maoming Birth cohort study (China) between 2015 and 2018, not only demonstrating

transplacental transfer of PFAS but also identifying differences in transfer in preterm and full-term deliveries (Li J et al. 2020a).

Hartmann et al. (2023) examined 14 PFAS in 85 children from Austria, ages 8 to 10 years, using single void urine and found 9 PFAS were detected, with PFHxA, PFOA, PFHpA, PFPeA, PFOS and PFNA having the highest detection rates (60% to 100%) and the highest median concentration of 0.04 µg/L for PFHxA.

As only a relatively small number of PFAS have been monitored, there are concerns that human exposure may be underestimated. Studies have tried to address this uncertainty. Several biomonitoring studies have examined total fluorine, including extractable organic fluorine, total oxidizable precursors or targeted analyses to try to better understand unidentified PFAS.

Examination of trends in total fluorine over time have shown varying results. Cioni et al. (2023) did not find significantly different total fluorine levels in pooled serum between 1986 and 2015, whereas Miaz et al. (2020) found declining trends in total fluorine in pooled serum between 1996 and 2017.

Using fluorine mass balance approaches, studies have shown that targeted PFAS have only accounted for a portion of the EOF in serum. Varying trends in unidentified PFAS over time have been reported. Miaz et al. (2020) suggested that recent samples had a larger fraction of unknown EOF compared to older samples on the basis of declines in target PFAS contribution over time and lack of trend for EOF. Cioni et al. (2023) found varying levels of unidentified EOF across 3 time periods (1986, 2007, and 2015) but proposed that precursors with more than 4 perfluorinated carbons were minor contributors to EOF. In a subsequent study, Cioni et al. (2024) found that the unidentified EOF portion was largely explained by 3 fluorinated pharmaceuticals (two PFAS and one non-PFAS) and their metabolites. Cioni et al. (2024) suggest that target PFAA analysis might be sufficient to describe human exposure to PFAS with more than 3 perfluorinated carbons. They also noted that CF_3-containing pharmaceuticals were expected to yield TFA after oxidation in the TOP assay, however, no TFA was observed. As such, contribution of certain CF_3-containing substances may not be identified using the TOP assay. The authors suggest that careful investigation of PFAS precursors that contain -CF_3 is needed.

Pennoyer et al. (2023) also explored the pharmaceutical contribution to EOF in serum of 20 adults in the US using fluorine mass balance. The authors found that the majority of identified EOF in serum was PFOS, PFHxS and PFOA, although 44 PFAS analytes were included in the analysis, and that these 3 PFAS (PFOS, PFHxS and PFOA) accounted for 14-85% EOF in serum. Pennoyer et al. (2023) found that although organofluorine pharmaceuticals (some of which are PFAS) contributed to EOF in serum, a substantial amount of EOF remained unexplained. They also noted that EOF may be underestimated due to extraction techniques.

EOF and targeted PFAS were measured in pooled maternal serum, placental tissue and cord serum samples in Austria and levels of unidentified EOF were found to be higher in placental tissue compared to maternal and cord serum (Kaiser et al. 2021).

5.5.2 PFAS measured in human milk

Several international studies have examined PFAS in human milk with analysis of samples collected from the US, France, Japan, China, Sweden, Spain, Korea, Austria and South Africa (Tao et al. 2008; Fujii et al. 2012; Cariou et al. 2015; Kang et al. 2016; Lorenzo et al. 2016; Zheng et al. 2021, 2022; Macheka et al. 2022; Hartmann et al. 2024). A review in 2023 also focused on 4 PFAS (PFOA, PFNA, PFHxS, PFOS) in human milk, with samples collected from Europe, Asia, Africa and North America (LaKind et al. 2023). In 2019, Zheng et al. (2021) recruited 50 women residing in Seattle in the US. The analysis included 39 PFAS, 12 (PFHxA, PFHpA, PFOA, PFNA, PFDA, PFUnDA, PFDoDA, PFTrDA, PFHxS, PFHpS, PFOS, and PFNS) of which were found to have detection frequencies ranging from 58% to 100%. PFOA and PFOS were found in 86% and 100% of samples and were the predominant PFAS (median concentrations of 0.014 µg/L and 0.03 µg/L, respectively). Zheng et al. (2021) noted that when compared with levels in human milk from a previous study based in the US (Tao et al. 2008), levels of PFOA and PFOS in human milk appear to have declined since 1996. Zheng et al. (2021) also compared their results with currently available data on SC-PFAS in human milk and demonstrated that the number of samples above detection limits (normalized to the highest detection limit reported for each individual PFAS across the studies included in the analysis) of short-chain (C4 to C7) PFAS has increased since the early 2000s, doubling every 4.1 years for all of the C4 to C7 PFAS included in the analysis.

Detection frequencies and concentration ranges of the PFAS tested varied widely across the studies. It is possible that differences in analytical sensitivity (for example, detection or quantification limits) may be a factor in the variability of these results.

Overall, data from various studies suggest that infants may be exposed to at least a dozen PFAS through the consumption of human milk.

5.6 Occupational HBM data - Firefighters

Certain occupations, including firefighters, have been identified as having potential exposure to PFAS (Christensen and Calkins, 2023; Lucas et al. 2023). Firefighter exposure to PFAS is of particular interest as PFAS have been used in certain types of firefighting foams. PFAS have also been intentionally used, detected in or released from firefighters' protective clothing and may be released from burning products treated with or containing PFAS (ITRC 2020b; Peaslee et al. 2020; Muensterman et al. 2022; Graber et al. 2021; Aranda-Rodriguez et al. 2024; NIST, 2024).

There are no available Canadian studies examining biomonitoring levels of PFAS in firefighters. However, 13 studies examining serum levels of various PFAS in firefighters were identified in the available literature. 10 of the studies were carried out in the US (Jin et al. 2011; Shaw et al. 2013; Dobraca et al. 2015; Khalil et al. 2020; Leary et al. 2020; Trowbridge et al. 2020; Goodrich et al. 2021a; Graber et al. 2021; Barton et al. 2022; Burgess et al. 2022), while 2 studies examined firefighters in Australia (Rotander et al. 2015; Nilsson et al. 2022a), and 1 sampled firefighters in Finland (Laitinen et al. 2014). All studies took place between 2005 and 2019. Although 13 studies were considered, 1 study, Burgess et al. (2022), included 5 separate data sets of serum PFAS concentrations (4 data sets on male firefighters and 1 set on female

firefighters) from 4 municipal fire departments; this resulted in the examination of a total of 17 separate data sets of PFAS in serum of firefighters.

Varying suites of specific PFAS were examined in the studies, with perfluorinated carbon chain lengths ranging from 3 (for example, PFBA) to 13 (for example, PFTeDA); however, PFOA, PFNA, PFHxS, and PFOS were examined in all 13 studies. Certain short-chain PFCAs and PFSAs (for example, PFBA, PFPeA, and PFHpS) were not detected in any of the firefighter serum samples (Shaw et al. 2013; Dobraca et al. 2015; Rotander et al. 2015; Khalil et al. 2020; Barton et al. 2022). Although PFBS was detected in only 1 of the studies, it was detected in 73% of samples in that study (Trowbridge et al. 2020). PFHxA and PFHpA were detected more frequently across studies, with the percentage of samples above detection limits ranging from 50% to 92% (Shaw et al. 2013; Dobraca et al. 2015; Rotander et al. 2015; Trowbridge et al. 2020).

Serum levels of PFAS from the firefighter studies were compared with concentrations in the general population. The ratios resulting from this comparison for 6 of the most commonly detected PFAS in firefighters and the general population are shown in Figure 7. In the 10 studies that examined firefighters in the US, the firefighter serum concentrations were compared with serum concentrations from NHANES (representing the general population of the US). In the 3 studies that were not carried out in the US (that is, in Australia and Finland), the firefighter serum concentrations were compared to relevant PFAS plasma concentrations from the CHMS (that is, people in Canada). These comparisons were done for similar years of serum/plasma sampling, similar age groups (for example, age 20 to 60), and similar sexes. Although a statistically rigorous comparison could not be done to compare the firefighter data and the general population data, geometric mean concentration values from each of the studies were compared to the upper confidence interval (CI) of the geometric mean from the general population. For each of the 6 PFAS, the ratios (GM firefighter serum values/upper Cl of the GM of the general population) were calculated for each study and PFAS-specific average ratios were calculated. The average ratios for each PFAS are presented in Figure 7. PFOA, PFDA, PFHxS, and PFOS had average ratios >1.1, suggesting that, on average across the 13 studies, firefighter serum geometric mean values were higher than the geometric mean values of these PFAS in the general population (based on a similar time of sampling, similar age group, and similar sex). PFHxS had the largest ratio, suggesting a larger difference in the firefighter serum concentrations compared to the general population for this specific PFAS.

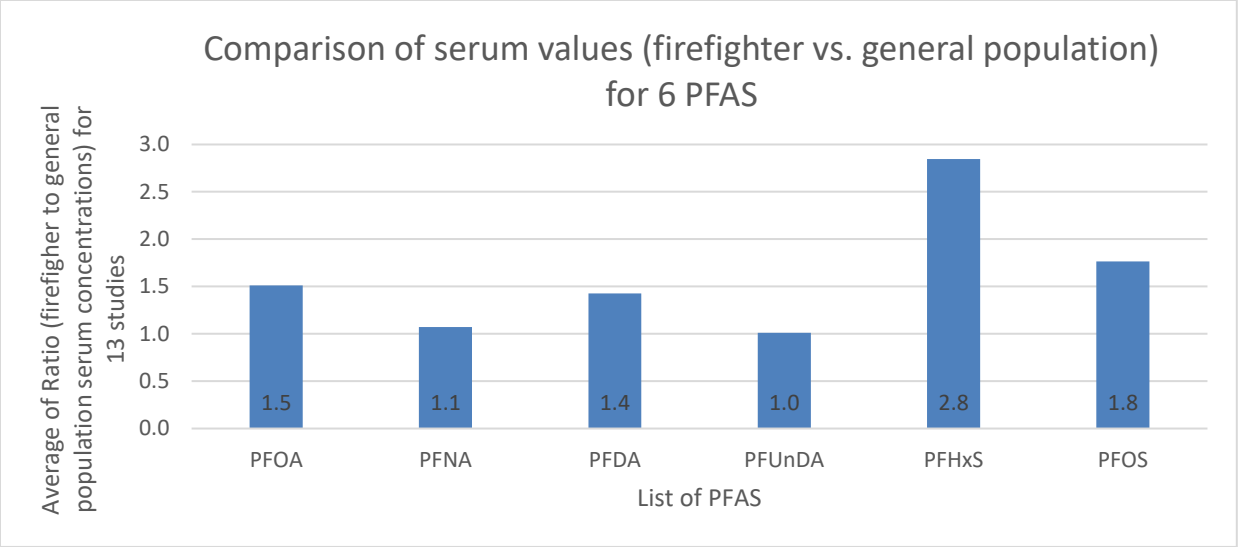

Figure 7. Average of ratios of geometric mean (or lower CI of GM) firefighter serum levels to upper CI of geometric mean serum (or plasma) levels in the general population averaged across 13 studies (representing 17 data sets) (each ratio is derived from similar time period, sex, and age group comparison between study population and general population biomonitoring values). Information on the GM (CI) of firefighter serum values, GM (CI) for reference populations, and ratios for each of the 6 PFAS are found in Table D-1.

5.7 Interpretation of HBM data

5.7.1 Canadian general population and Indigenous communities

In this section, biomonitoring values from various populations groups in Canada were compared to the EFSA reference value for the sum of 4 PFAS (PFOA, PFNA, PFHxS, and PFOS) and the HBM-I and HBM-II values for PFOA and PFOS identified in Table 1 of section 5.3.

Canadians are likely co-exposed to multiple PFAS due to the widespread use of these substances in products and the presence of PFAS in the environment. Additionally, people can be co-exposed to several PFAS due to the long biological half-lives of certain PFAS in humans and their historical uses. The concentration of co-occurring, unidentified PFAS in serum or plasma in the general population is not known. According to the CHMS data on PFAS (HC 2023b) the highest plasma concentrations reported in the Canadian population among those PFAS that were measured were for PFOS, PFOA, PFHxS, and PFNA (Table B-3 of Appendix B). Also, as noted previously, the CHMS demonstrate a statistically significant decreasing trend ($p<0.001$) in PFOA, PFNA, PFDA, PFHxS, and PFOS concentrations in people in Canada aged 12 or 20 to 79 years (HC 2023a).

As described above, EFSA (2020) identified reference serum levels of 6.9 µg/L and 17.5 µg/L for women of reproductive age and infants, respectively (see Table 1) for the sum of exposure to 4 PFAS (that is, PFOA, PFNA, PFHxS, and PFOS). In Figure 8, the EFSA reference serum level for women of reproductive age was compared with box plots identifying the 25th to 75th percentile values for the sum of 4 PFAS (PFOA, PFNA, PFHxS, and PFOS) in 6 population groups, that is, cycle 6 of the CHMS (all population, ages 3 to 79), cycle 6 of the CHMS (women of childbearing age, ages 18 to 40), pregnant women in Nunavik, adults in Dene communities in

the Dehcho region of NWT, adults in a Gwich'in community in the Yukon, and adults in Nunavik (Caron-Beaudoin et al. 2020; Aker et al. 2021; Garcia-Barrios et al. 2021; personal communication, emails from the Population Studies Division, HC, to the Existing Substances Risk Assessment Bureau, HC, May 4, 2022 and May 5, 2022; unreferenced). See Table C-1 in Appendix C for details.

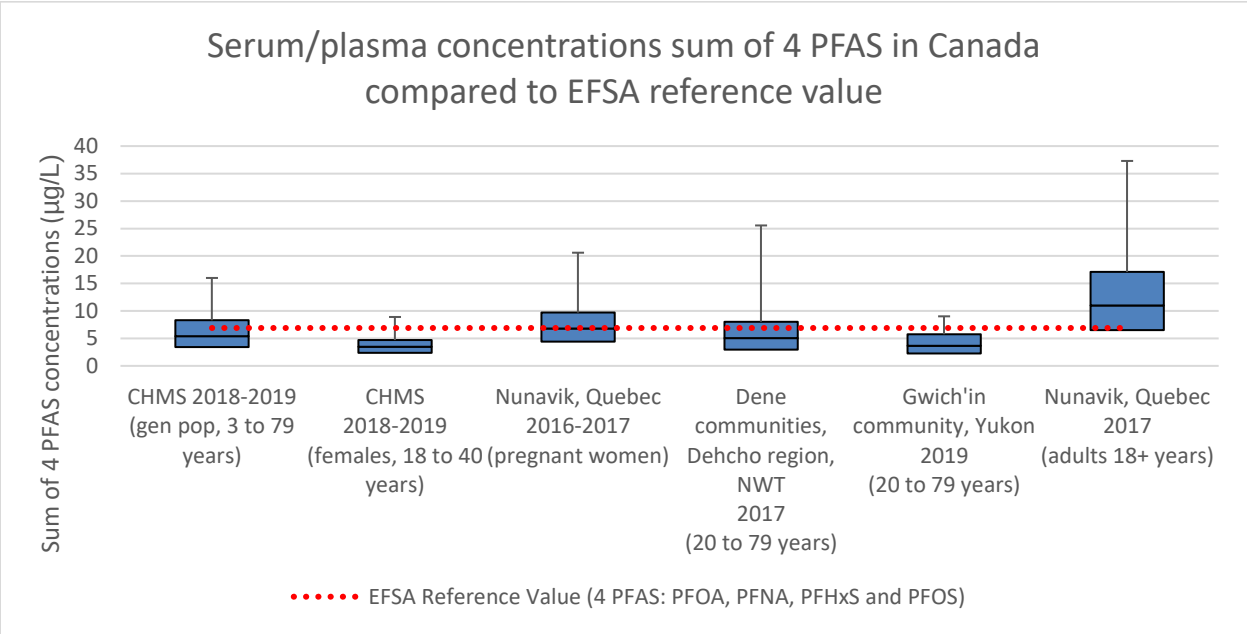

Figure 8. Comparison of the EFSA reference value of 6.9 µg/L with box plots identifying the 25th to 75th percentiles including geometric means (lines) and 95th percentile (whiskers) of the sum of 4 PFAS concentrations (in µg/L) in 6 population groups: CHMS cycle 6 total population (3 to 79 years; HC 2023b), CHMS cycle 6 females (18 to 40; personal communication, HC Population Studies Division, 2022; unreferenced), Nunavik pregnant women (16 to 40 years; Caron-Beaudoin et al. 2020), adults living in the Dehcho region of the Northwest Territories (20 to 79 years), adults living in a Gwich'in community, Yukon (20 to 79 years; Garcia-Barrios et al. 2021), and Inuit adults (18+ years) living in 14 communities in Nunavik (Aker et al. 2021).

The geometric mean of the sums of PFOA, PFNA, PFHxS, and PFOS in serum of pregnant Inuit women in Nunavik (6.8 µg/L in serum) was very close to the EFSA reference level (6.9 µg/L), indicating that approximately 50% of the sampled population was above the reference value. In adults in Nunavik, close to 75% of the sampled population was above the EFSA reference value. In the other population groups, a proportion of the sampled population (approximately 35% or less) was above the reference level.

The German HBM Commission's HBM-I and HBM-II values for PFOS and PFOA were also examined in relation to biomonitoring data for the Canadian population.

In Figures 9 and 10, HBM-I and HBM-II values for PFOS and PFOA were presented in relation to box plots outlining the 25th to 75th percentile concentrations for PFOA and PFOS in 6 population groups, specifically: CHMS cycle 6 (general population aged 3 to 79 years), pregnant women in Nunavik, on-reserve populations of Indigenous adults across Canada (aged 20+ years), First Nations people (aged 20 to 79 years) living in Dene communities in the Dehcho

region of the Northwest Territories, First Nations people (aged 20 to 79 years) living in a Gwich'in community in the Yukon, and Inuit adults living in 14 communities in Nunavik (AFN 2013; Caron-Beaudoin et al. 2020; Aker et al. 2021; Garcia-Barrios et al. 2021; personal communication, emails from Population Studies Division, HC, to Existing Substances Risk Assessment Bureau, HC, May 2022; unreferenced). As noted earlier, CHMS data represents PFOA and PFOS exposure in the general population of Canada; Figures 9 and 10 include smaller-scale studies examining specific populations of people that were not represented in the CHMS.

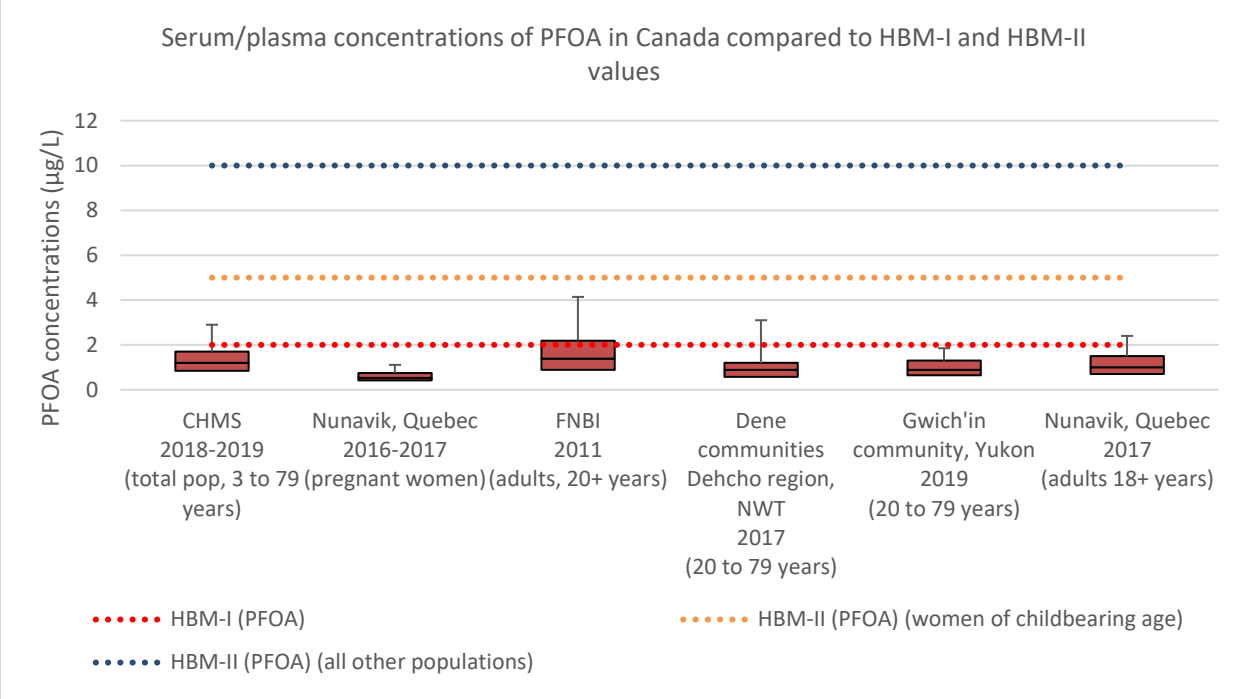

Figure 9. Box plots identifying the 25th to 75th percentiles (including geometric means [lines] and 95th percentile [whiskers]) of the PFOA concentrations (in µg/L) in 6 population groups: CHMS cycle 6 total population (3 to 79 years; HC 2023b; personal communication, emails Population Studies Division, HC, to Existing Substances Risk Assessment Bureau, HC, May 2022; unreferenced), Nunavik pregnant women (16 to 40 years; Caron-Beaudoin et al. 2020), Indigenous on-reserve populations across Canada (20+ years; FNBI; AFN 2013), adults living in the Dehcho region of the Northwest Territories (20 to 79 years), adults living in a Gwich'in community in the Yukon (20 to 79 years; Garcia-Barrios et al. 2021), and Inuit adults (18+ years) living in 14 communities in Nunavik (Aker et al. 2021), presented in relation to PFOA HBM-I, HBM-II (women of childbearing age), and HBM-II (other population groups) values (Holzer et al. 2021; Schümann et al. 2021) (data in Appendix C-Table C-2).

According to Figure 9, the geometric means of PFOA concentrations in all 6 groups (AFN 2013; Caron-Beaudoin et al. 2020; Aker et al. 2021; Garcia-Barrios et al. 2021; HC 2023b) were below the HBM-I and HBM-II values. The 95th percentiles of PFOA concentrations for all populations assessed, except for pregnant women in Nunavik and the Gwich'in community in the Yukon, exceeded the HBM-I value but were lower than the HBM-II (women of childbearing age) value.

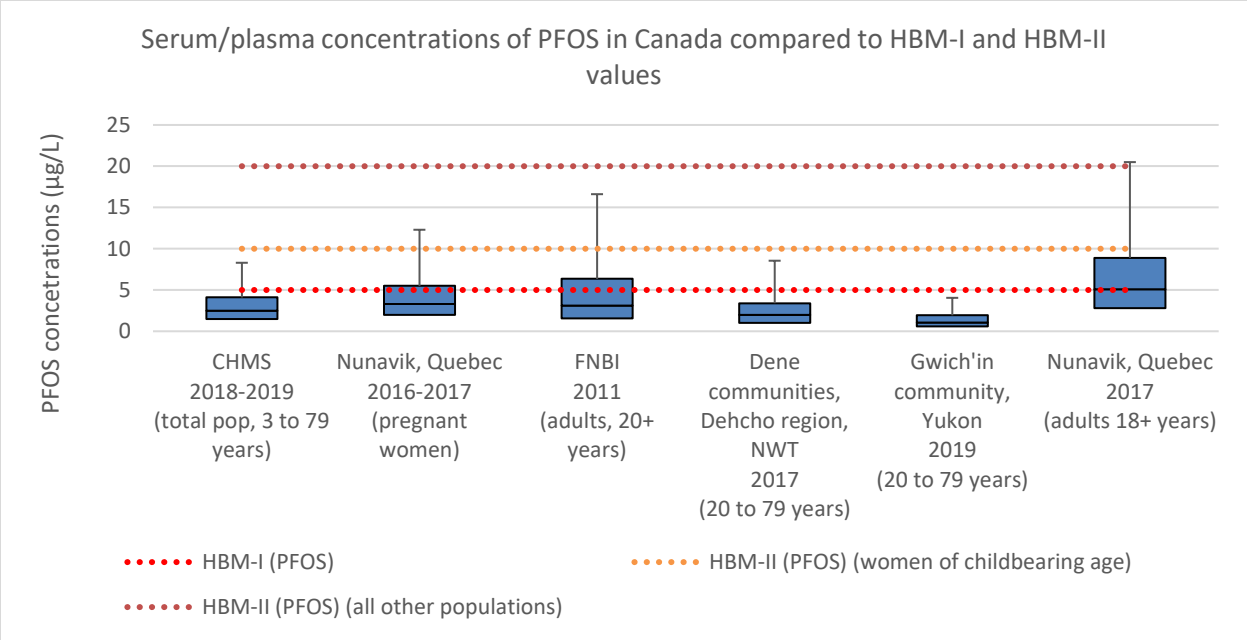

Figure 10. Box plots identifying the 25th to 75th percentiles (including geometric means [lines] and 95th percentile [whiskers]) of PFOS concentrations (in µg/L) in 6 population groups: CHMS cycle 6 total population (3 to 79 years; HC 2023b, personal communication, emails Population Studies Division, HC, to Existing Substances Risk Assessment Bureau, HC, May 2022; unreferenced), pregnant Nunavik women (16 to 40 years; Caron-Beaudoin et al. 2020), Indigenous on-reserve populations across Canada (20+ years; AFN 2013), adults living in the Dehcho region, Northwest Territories (20 to 79 years), adults living in a Gwich'in community, Yukon (20 to 79 years; Garcia-Barrios et al. 2021), and Inuit adults (18+ years) living in 14 communities in Nunavik (Aker et al. 2021) in relation to PFOS HBM-I, HBM-II (women of childbearing age), and HBM-II (other population groups) values (Holzer et al. 2021; Schümann et al. 2021) (data in Appendix C-Table C-2).

Although the geometric means of PFOS concentration in all the population groups were below the HBM-I value, certain portions of each of these populations were above it. In Figure 10 the following can be observed: (1) the 75th percentiles of 3 groups are above the HBM-I value, that is, pregnant women in Nunavik, Indigenous adults living on reserve (sampled in 2011), and adults living in Nunavik, (2) a portion of these 3 groups was above the HBM-II value (women of childbearing age), (3) the 95th percentile of adults in Nunavik was above the HBM-II value (population groups other than women of childbearing age; 20 µg/L), and (4) the 95th percentiles of PFOS concentrations in the CHMS group and in the plasma of First Nations people living in Dene communities in the Dehcho region of the Northwest Territories fell between HBM-I and HBM-II values.

According to the German HBM Commission, if measured concentrations are found to exceed the HBM-I level, the causes of the increase should be investigated, and sources of exposure should be reduced or eliminated to the extent possible (Holzer et al. 2021), whereas exceedance of the HBM-II values requires immediate attention as indicated by the German HBM Commission (Umwelt Bundesamt 2015; Schümann et al. 2021).

In summary, although geometric means of the concentrations of PFOS and PFOA in the general population in Canada and in the Indigenous populations living in northern communities and south of the 60th parallel are generally below the HBM-I guidance values, and although these

substances have risk management in place, the geometric mean of PFOS concentrations in adults in Nunavik is above the HBM-I value (5.1 µg/L vs. 5 µg/L, respectively). The 95th percentile concentration levels for PFOA and PFOS in most populations also exceed the HBM-I value. In pregnant women in Nunavik, the 95th percentile of PFOS in serum exceeds the HBM-II value for childbearing women. The geometric mean of the sums of 4 PFAS in pregnant Inuit women in Nunavik was slightly below the EFSA (2020) serum reference level, indicating that a proportion of the population is above this reference level. The 95th percentile of the sum of the 4 PFAS exceeded the EFSA (2020) serum reference level.

5.7.2 Firefighters

As noted in section 5.6, there are no available Canadian studies examining biomonitoring levels of PFAS in firefighters. Geometric mean (or median) concentrations of PFOA and PFOS found in 13 international studies examining firefighters (see section 5.6; Jin et al. 2011; Shaw et al. 2013; Dobraca et al. 2015; Rotander et al. 2015; Goodrich et al. 2021a; Graber et al. 2021; Barton et al. 2022; Burgess et al. 2022; Khalil et al. 2020; Laitinen et al. 2014; Leary et al. 2020; Nilsson et al. 2022a; Trowbridge et al. 2020) were considered in relation to the HBM-II values for PFOA and PFOS (Figures 11 and 12). As noted in section 5.6, 1 study examined 5 separate data sets, bringing the total number of data sets used in the analyses to 17.

The HBM-II value is not derived with the intention of interpreting occupational biomonitoring data; however, it was considered to be the most appropriate reference level of those available for comparison with firefighters' exposure to PFOA and PFOS. HBM-II is a concentration in a human biological material, above which there is an increased risk for adverse health effects and an acute need for exposure reduction measures and the provision of biomedical advice.

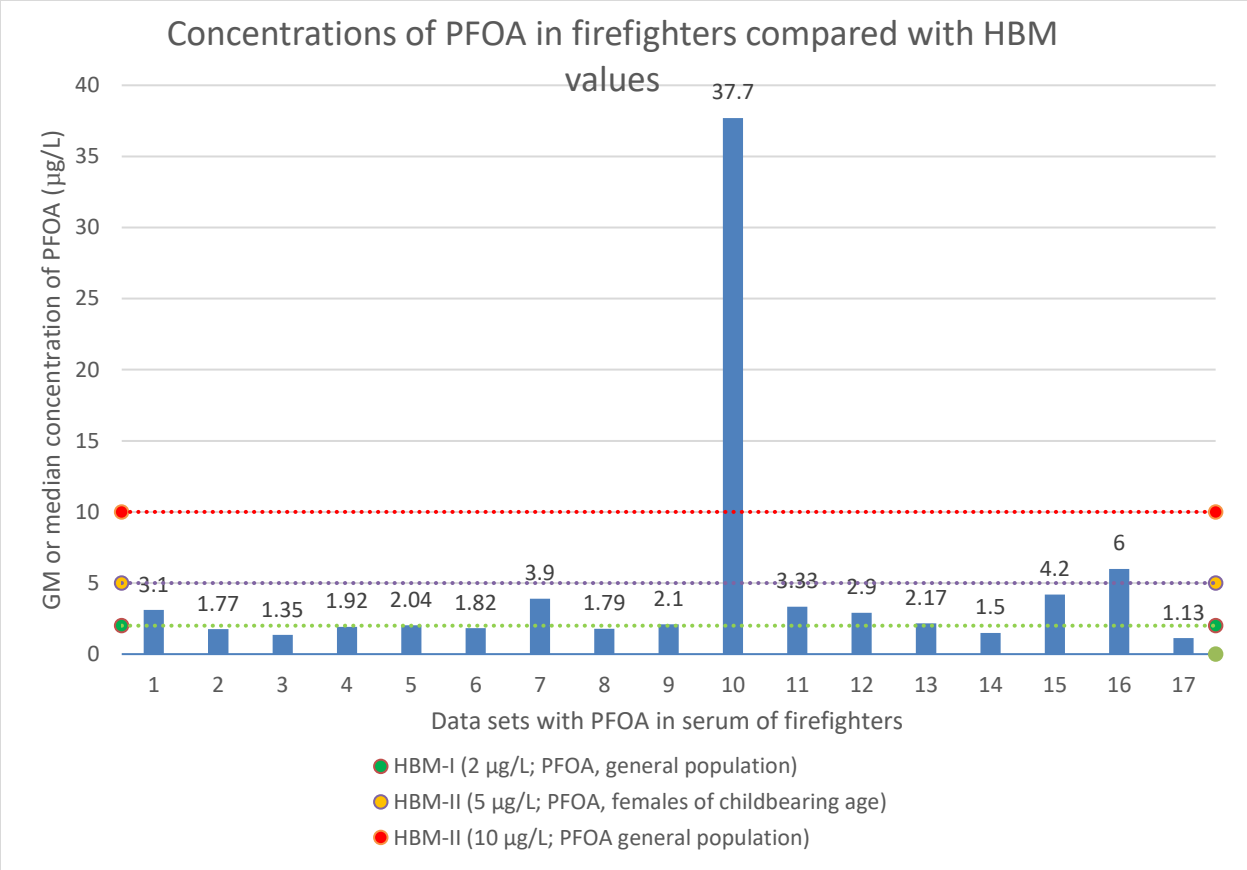

Figure 11. Geometric mean (or median) concentrations of PFOA in serum of firefighters (sampling year ranging from 2005 to 2019) from 17 data sets obtained from 13 studies (data in Appendix D-Table D-1) compared to HBM-I and HBM-II values for PFOA. Value 1=Barton et al. 2022; Values 2,3,4,5,6=Burgess et al. 2022 (Stations A (males), A (females), B (males), C (males), D (males), respectively); Value 7=Dobraca et al. 2015; Value 8=Goodrich et al. 2021a; Value 9=Graber et al. 2021; Value 10=Jin et al. 2011; Value 11=Khalil et al. 2020; Value 12=Laitenen et al. 2014; Value 13=Leary et al. 2020; Value 14=Nilsson et al. 2022a; Value 15=Rotander et al. 2015; Value 16=Shaw et al. 2013; Value 17=Trowbridge et al. 2020 (Values 6 and 17 are based on females and should be compared to HBM-II [5 µg/L, females of childbearing age]).

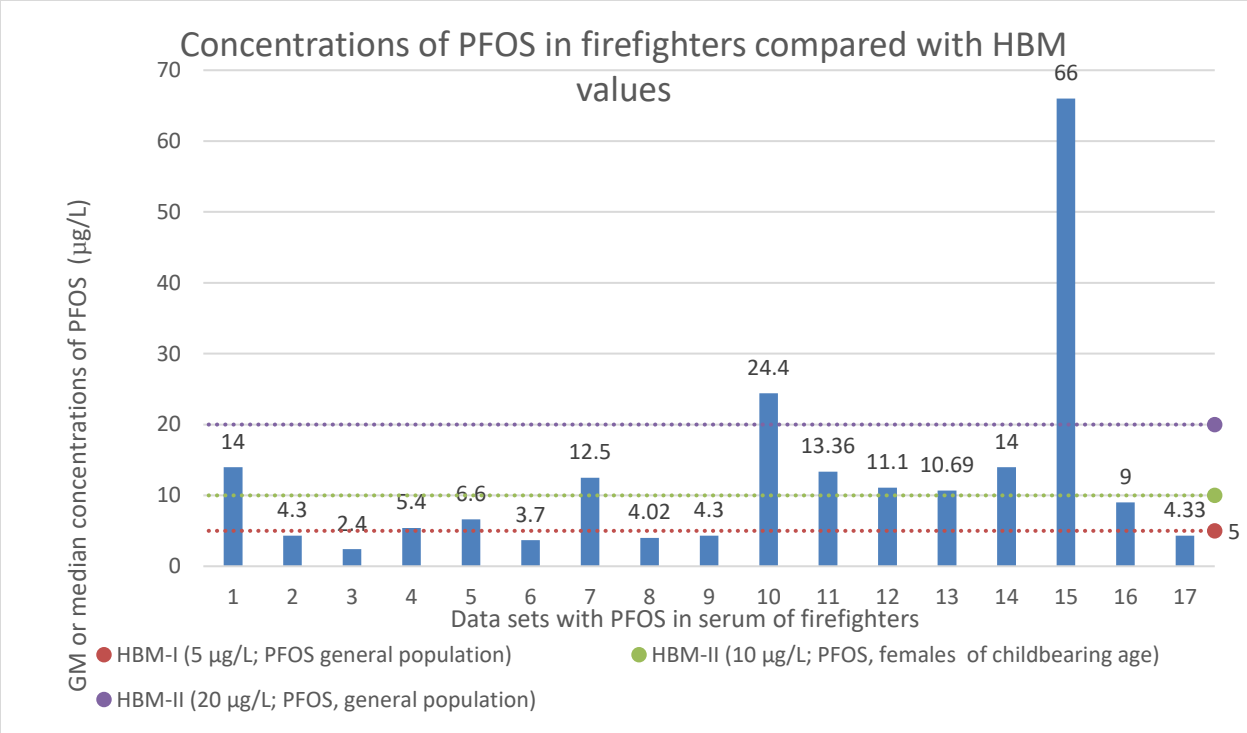

Figure 12. Geometric mean (or median) concentrations of PFOS in serum of firefighters (sampling year ranging from 2005 to 2019) from 17 data sets from 13 studies (data in Appendix D-Table D-1) compared to HBM-I and HBM-II values for PFOS. Value 1=Barton et al. 2022; Values 2,3,4,5,6=Burgess et al. 2022 (Stations A (males), A (females), B (males), C (males), D (males), respectively); Value 7=Dobraca et al. 2015; Value 8=Goodrich et al. 2021a; Value 9=Graber et al. 2021; Value 10=Jin et al. 2011; Value 11=Khalil et al. 2020; Value 12=Laitenen et al. 2014; Value 13=Leary et al. 2020; Value 14=Nilsson et al. 2022a; Value 15=Rotander et al. 2015; Value 16=Shaw et al. 2013; Value 17=Trowbridge et al. 2020 (Value 11 based on females and should be compared to HBM-II female of childbearing age).

Overall, 3 studies demonstrated geometric mean results above HBM-II (general population) values for PFOA or PFOS: 1 study for PFOA (Jin et al. 2011) and 2 studies for PFOS (Jin et al. 2011; Rotander et al. 2015). Jin et al. (2011) collected samples from 2005 to 2006 as part of a project implemented after the drinking water near a DuPont facility in West Virginia was contaminated, which made this population group considered likely to have higher background levels of PFAS. In 2013, Rotander et al. (2015) sampled firefighters working at AFFF training facilities in Australia. Of note, Trowbridge et al. (2020) and Burgess et al. (2022) (Value 3 in Figures 11 and 12) examined female firefighters separately, highlighting the importance of taking into consideration the HBM-II value for women of childbearing age for PFOA and PFOS.

As many studies report geometric mean values above the HBM-I values for PFOA and PFOS, this analysis suggests that exposure to PFOA and PFOS in firefighters is higher than in the general population and is above reference values. Because the biomonitoring data for firefighters are not specifically Canadian, they may have limitations (for example, some studies took place several years prior to restrictions being imposed on certain PFAS). However, firefighters in North America (and perhaps Europe and Australia) may have similar PFAS exposures as a result of working with AFFF containing PFAS, and these considerations may

mean that firefighter exposure to PFAS is not unique to each country. Therefore, even with limitations, these studies may have relevance for Canada.

6 Ecotoxicity

KEY POINTS ON ECOTOXICITY

- Some well-studied PFAS have been shown to bioaccumulate in wildlife and plants. Air-breathing organisms (for example, mammals, birds) have been reported to have a high potential for biomagnification, which may increase the likelihood of adverse toxicological effects being observed.
- Well-studied PFAS have been demonstrated to cause apical (for example, growth, reproduction, development) and mechanistic (for example, immunotoxicity, neurotoxicity) endpoint effects in biota.
- On the basis of the available data, the magnitude of ecotoxicity (including bioaccumulation) in organisms appears to vary with the structural features of PFAS (for example, chain length, functional groups); however, this does not indicate a lack of hazard for some PFAS (for example, short-chain PFAS).
- There are significant data gaps in the literature available for certain species (for example, amphibians, reptiles, birds, mammalian wildlife) and types of effects studied (for example, multigenerational effects, cumulative effects), which makes it difficult to identify and understand trends in ecotoxicity.
- While most ecotoxicology studies have focused on the effects seen with exposure to a single PFAS, organisms are typically exposed simultaneously to multiple PFAS in the environment, which has the potential to increase impacts on them. Recent studies investigating cumulative effects of PFAS and mechanisms of action for PFAS mixtures have shown complex and varied effects.
- Uncertainties in ecological hazard can be reduced through further study and possibly through the use of new approach methods (NAMs).

The following section provides an overview of the available literature on PFAS bioaccumulation and biomagnification, as well as ecotoxicity in invertebrates (including aquatic and terrestrial), vertebrates (including fish, birds, mammals, and amphibians/reptiles), and plants (including aquatic and terrestrial). Where available, discussions on mode/mechanism of action and multigenerational effects in species are included in the ecological effects section. This section is not intended to be a comprehensive review of the current literature and does not include a critical review of each study. Most studies in the literature focus on PFAAs (more specifically, PFOS and PFOA) and studies in aquatic organisms (that is, fish, aquatic invertebrates). Fewer studies are available on the other groups of PFAS (for example, PFPEs and SCFPs) and on terrestrial species (that is, terrestrial invertebrates, amphibians, reptiles, birds, mammalian wildlife). A more in-depth review of the toxicological effects of PFAS is provided in Ankley et al. (2021), who have compiled ecotoxicity data for PFAS in different species from the available literature. Where applicable, other studies are included to supplement and/or support the information.

6.1 Bioaccumulation

The use of logK_{ow} to predict bioaccumulation potential is based on the assumption that the main mechanisms governing partitioning are the hydrophobic and lipophilic interactions (EC 2006). However, this assumption cannot be easily applied to many PFAS (for example, PFAAs) due to their surfactant-like properties. As PFAS generally have the combined properties of oleophobicity, hydrophobicity, and hydrophilicity over different portions of their chemical structure, logK_{ow} is not considered to be an appropriate metric of bioaccumulation potential. The combination of a hydrophobic fluorinated alkyl chain paired with a polar functional group in PFAA resembles the structure of a fatty acid, which facilitates both hydrophobic and ionic interactions with proteins (Bischel et al. 2010). It is important to note that rather than accumulating in lipids, some of these substances preferentially bind to proteins and are therefore found in protein-rich tissues such as liver and blood.

In Canada, the regulatory criteria for bioaccumulation potential, as set out in the *Persistence and Bioaccumulation Regulations* of CEPA (Canada 2000), are met when the bioaccumulation factor (BAF) or bioconcentration factor (BCF) is ≥ 5000 or logK_{ow} is ≥ 5. However, as these threshold criteria were based on historical experience with neutral, non-metabolized organic substances and many PFAS tend to preferentially bind to proteins, the regulatory paradigm based on low logK_{ow} value cannot be applied for this class of substances (EC, HC 2012). The application of BAF and BCF data is only 1 component of the overall weight of evidence in identifying the potential of a substance to bioaccumulate in organisms. Even if regulatory criteria are not met, a substance can still be deemed as having bioaccumulation potential.

A literature search for studies on PFAS bioaccumulation in aquatic species was performed by Burkhard (2021). In this paper, data from 22 taxonomic classes were compiled to determine median BAF and BCF values and to assess the availability of such data in the literature. A summary of the available BCFs and BAFs for fish is provided in Table 2. It should be noted, however, that empirical BCF and BAF data alone cannot be used to reliably determine bioaccumulation potential for PFAS as results for typically tested model organisms (that is fish, daphnia, and algae) may underestimate bioaccumulation potential (ECCC 2023). Moreover, the available BCF and BAF data from the literature are also limited. In general, PFAAs are relatively data rich for aquatic species, whereas data are limited or nonexistent for other PFAS such as fluorotelomers. In addition, PFAAs with very short (C<5, including TFA) or very long (C>12) alkyl chain lengths also appear to be data scarce (Burkhard 2021). Based on the experimental data compiled by Burkhard (2021), a recent paper by Kowalska et al. (2024) developed a predictive quantitative structure-property relationship model to determine BCF and implemented it to predict the BCF values for 2209 PFAS. The *in silico* analysis indicated that approximately 47.3% of the substances had BCF values below 2,000, 9.4% had log BCF values between 2,000 and 5,000, and 43.3% had BCF values above 5,000.

Table 2. Select median bioconcentration factors and bioaccumulation factors in fish (adapted from Burkhard 2021)

PFAS group	Chemical name	Median whole body BCF (L/kg ww)	Median whole body BAF (L/kg ww)
PFCAs	PFBA	15.1 (n=2)	144.5 (n=6)
PFCAs	PFPeA	0.9 (n=1)	55.0 (n=5)
PFCAs	PFHxA	9.5 (n=3)	25.1 (n=11)
PFCAs	PFHpA	18.2 (n=1)	63.1 (n=10)
PFCAs	PFOA	24.0 (n=14)	144.5 (n=48)
PFCAs	PFNA	602.6 (n=6)	631.0 (n=41)
PFCAs	PFDA	6,166.0 (n=3)	2,818.4 (n=43)
PFCAs	PFUnDA	3,715.4 (n=5)	2,951.2 (n=21)
PFCAs	PFDoDA	4,365.2 (n=8)	151.4 (n=1)
PFCAs	PFTrDA	21,877.6 (n=2)	NA
PFCAs	PFTeDA	25,118.9 (n=4)	NA
PFCAs	PFHxDA	4,786.3 (n=2)	NA
PFCAs	PFOcDA	371.5 (n=2)	NA
PFSAs	PFBS	11.5 (n=7)	100.0 (n=5)
PFSAs	PFHxS	117.5 (n=6)	199.5 (n=25)
PFSAs	PFOS	1,023.3 (n=21)	3,311.3 (n=81)
PFECAs	F-53B	707.9 (n=6)	21,379.6 (n=5)
FASAs and derivatives	FOSA	NA	5,011.9 (n=12)
FT-based substances	4:2 FTSA	NA	13,803.8 (n=1)
FT-based substances	6:2 FTSA	34.7 (n=3)	NA
FT-based substances	8:2 FTSA	NA	72,443.6 (n=2)
PFPiAs	C6/C6 PFPiA	131,825.7 (n=2)	NA
PFPiAs	C6/C8 PFPiA	22,908,676.5 (n=2)	NA
PFPiAs	C8/C8 PFPiA	199,526,231.5 (n=2)	NA
PFPiAs	C6/C10 PFPiA	331,131,121.5 (n=2)	NA
PFPiAs	C8/C10 PFPiA	616,595.0 (n=2)	NA
PFPiAs	C6/C12 PFPiA	1,995,262.3 (n=2)	NA

Abbreviations: NA, not available; ww, wet weight.

The chain length and functional group(s) present in PFAS seem to determine the extent of bioaccumulation in animals. Studies have shown that sulfonates (that is, PFSA) and PFAS with a long perfluoroalkyl chain (that is, C ≥ 9) tend to accumulate more in water-breathing organisms (for example, fish, aquatic invertebrates) than do carboxylates (that is, PFCAs) and substances with shorter chain lengths (C < 9) (Martin et al. 2003; Dai et al. 2013). Additionally, based on published field studies compiled in the Supporting Document: Ecological State of the Science Report on Short-chain PFCAs, Short-chain PFSAs, and Long-chain PFSAs (ECCC 2023), air-breathing organisms (for example, terrestrial mammals, marine mammals, birds) are more likely to accumulate certain PFAS in comparison to water-breathing organisms. The BCF and BAF values for ionic PFAS (that is, PFAA) in fish are relatively low, likely due to their polar and non-volatile nature. PFAAs tend to have a high water solubility, which can lead to a more

rapid elimination of the substances in the water phase via gill exchange in fish. However, higher levels of PFAA bioaccumulation may occur in air-breathing organisms as their bioaccumulation potential is primarily driven by the low volatility of PFAA (that is, respiration is not a viable loss mechanism) and the polarity of PFAA facilitates protein binding in the body. This is also consistent with the findings of Khan et al. (2023) on the basis of their review of 143 publications on PFAA accumulation in marine environments published between 2000 and 2020. It should be noted that these trends do not imply that there is no potential for bioaccumulation for some PFAS and in some aquatic organisms but rather that it may occur to a lesser extent.

Yun et al. (2023) studied the bioaccumulation of 14 PFAS in 3 freshwater benthic macroinvertebrates: worms (*Lumbriculus variegatus*), mussels *(Elliptio complanata*), and snails (*Physella acuta*). Among these species, worms exhibited the highest BAFs and BSAFs, which could be a result of their ability to breathe through their skin, supported by a more developed dorsal blood vessel system. Furthermore, the BSAF values for 8:2 FTSA were the highest among the tested PFAS for all species. In another study of the St. Lawrence River near a major metropolitan area in Quebec, Canada, it was found that certain PFAS had high BAFs across various fish and invertebrate species (Munoz et al. 2022b). This included long-chain PFCAs (PFDA: 4,169 to 69,599; PFUnDA: 20,544 to 225,861; PFTrDA: 9,096 to 180,905), PFDS (1,110 to 45,020), and FOSA (2,156 to 14,667) (Munoz et al. 2022b). Newly monitored PFAS were found to be moderately bioaccumulative: FBSA (BAF of 145 to 1,612) and PFECHS (BAF of 33 to 1,438).

Biomagnification can also be observed in the food chain, often with the top predators having the highest levels of PFAS. This is especially of concern when concentrations reach levels that can cause adverse effects in organisms. In the Canadian Arctic, Kelly et al. (2009) found a high degree of PFAA biomagnification in upper trophic level wildlife (that is, whales, polar bears, and seals). They also noticed no biomagnification occurring in aquatic organisms, which they attributed to the high solubility of PFAA. These findings align with Canada's past screening assessments of PFOS, PFOA, and LC-PFCAs and their salts and precursors, which concluded that air-breathing mammals and avians have higher biomagnification factors (BMFs) and trophic magnification factors (TMFs[8]) in comparison with water-breathing organisms (EC 2006, 2012; EC, HC 2012). For example, in the case of PFOS, food webs involving air-breathing mammals were determined to have a TMF of about 20, while aquatic piscivorous food webs in Lake Ontario yielded TMFs ranging from 1.9 to 5.9 (De Silva et al. 2021). Recent studies have also reported trophic transfer of short-chain PFAS (for example, PFBS, PFBA, and PFHxS) (Huang K et al. 2022) and long-chain PFECAs (Li Y et al. 2022a, 2023). Further, Munoz et al. (2022b) reported biomagnification occurring in fish and invertebrate species in the St. Lawrence River, with BMFs for PFTrDA, PFTeDA, PFDS, and FOSA reaching as high as 14.8, 12.1, 32.5, and

[8] The BMF is defined as the ratio of a chemical in an organism divided by the concentration of chemical in its food (that is, prey or diet). The TMF is an extension of this concept, in which BMFs are adjusted according to stable isotopes of carbon and nitrogen (ITRC 2021a). TMFs are often believed to be a more objective metric in terms of biomagnfication between multiple organisms along a trophic chain. Moreover, BMF and TMF values greater than 1 are widely considered to be good indicators of biomagnification (Franklin 2016).

13.0, respectively. Biomagnification of PFOS and LC-PFCAs between apex piscivorous fish and prey fish has also been reported in Great Lakes aquatic food webs (George et al. 2023; Ren et al. 2023). It should be noted, however, that there is a considerable degree of variability in the literature for BMFs and TMFs of any specific PFAS (Franklin 2016). Lewis et al. (2022) found that PFAS concentration, dissolved organic matter, sediment organic matter, and biotransformation of precursor PFAS significantly contribute to the variation of bioaccumulation metrics seen in the literature.

PFAS can also be absorbed by plants and crops from sources of releases such as contaminated compost (see section 2.6.4) and biosolids (see section 2.6.3). For this reason, consumption of plants is a possible contributor to the PFAS concentrations seen in animals and humans (Ghisi et al. 2019). For example, Lan et al. (2020) found that the concentrations of TFA in locusts were significantly correlated with TFA concentrations in poplar and maize leaves. Unlike the definition used in animal studies, plant uptake studies define BAF and BCF[9] as the PFAS concentration in plant divided by the concentration in soil (ITRC 2021a). In general, terrestrial plant uptake of PFAA seems to vary with chain length and functional group. In contrast to what is seen in animals, longer-chained PFAS generally have lower levels of accumulation in plants than do shorter-chained PFAS (Blaine et al. 2014; Krippner et al. 2015; Liu Z et al. 2019), which may be a function of their water solubility and root uptake (Lesmeister et al. 2021; Adu et al. 2023). For example, Lan et al. (2020) reported that BAFs for TFA were generally higher than values for PFOS, PFOA and 6:2 Cl-PFESA. TFA has also been shown to be bioaccumulated by vascular plants via soil water, rain, and fog (Benesch and Gustin 2002; Lan et al. 2020), as well as via uptake of airborne TFA (Tian et al. 2018). Consequently, even in isolated and remote areas, the presence of TFA in dry and wet atmospheric deposition causes a broad contamination of terrestrial ecosystems (Freeling et al. 2022). Qian et al. (2023) and Xu et al. (2022) also note that long-chain PFAS tend to be adsorbed and retained on the root epidermis of plants, whereas short-chain PFAS are translocated across tissue above the ground and stored in the shoot. PFSAs have also displayed lower levels of bioaccumulation than PFCAs have. Recent studies have also reported that GenX and 6:2 FTSA can bioaccumulate in plants (Chen C-H et al. 2020; Zhi et al. 2022).

The extent of PFAS uptake by plants or crops is highly dependent on several factors, including soil properties and characteristics (pH, organic matter, salinity, temperature), plant type, and physiology (Wang et al. 2020; Lesmeister et al. 2021; Adu et al. 2023). Differences in PFAS accumulation between species may be attributed to various factors such as protein content, root system surface area, and biomass accumulation (Ghisi et al. 2019). Plants tend to display a high level of accumulation in the vegetative compartments (for example, leaves, stems) in comparison to reproductive and storage organs, which may be a result of their root uptake mechanism (Lesmeister et al. 2021; Liu Z et al. 2019). Moreover, Li Y et al. (2021) found that leafy vegetables had the highest BAF values for PFBA and PFOA, followed by fruit vegetables and root vegetables. This is consistent with the findings of the review by Xu et al. (2022), which

[9] A BAF or BCF of 1 indicates no net accumulation from soil to plant; however, this is not indicative of equilibrium.

found that the BAF values of vegetables were greatest in leaf vegetables, followed by root vegetables, flowers, vegetables, and shoot vegetables. They also note that the BAF values of vegetables were mostly higher than those of cereals (for example, wheat, maize, oat).

Overall, the bioaccumulation potential of PFAS, as well as its persistence (section 3.2.2), indicate an increased potential for risk to the environment. PFAS can remain in the environment for long periods as a result of their persistence, which contributes to global presence and increases the likelihood of organism exposure. Moreover, some PFAS have been demonstrated to have the potential to bioaccumulate and biomagnify in food webs to a degree that could allow them to reach levels that can cause adverse effects in organisms. Ultimately, bioaccumulation could result in an increased potential for toxicity in organisms.

6.2 Ecological effects

6.2.1 Invertebrates

6.2.1.1 Aquatic invertebrates

Several studies have examined PFAS toxicity in aquatic invertebrates. In general, toxicity in aquatic invertebrates is higher for PFAS with a longer fluoroalkyl chain, with crustaceans commonly being the most sensitive taxa (Ankley et al. 2021). It has also been determined that PFSAs are typically more hazardous than PFCAs. For example, Li (2009) found that PFOS had a higher acute toxicity than PFOA in all of the aquatic invertebrates tested. There are also more acute toxicity studies for aquatic invertebrates available in the literature than chronic toxicity studies (ITRC 2021b). Ankley et al. (2021) determined that the 50% effective concentration (EC50) and 50% lethal concentration (LC50) values from chronic exposures ranged from 0.03 mg/L to >100 mg/L and were generally in the same order of magnitude as values from acute exposures for the same species. The aqueous toxicity of PFOA was evaluated in chronic tests with *Hyalella azteca* (amphipod) by Bartlett et al. (2021), where it was found that environmental concentrations of PFOA in global surface waters were generally below those that caused toxicity in this study (LC50 = 51 mg/L).

Effects on growth, development, and reproduction have been reported with PFAS exposure in aquatic invertebrates (Boudreau et al. 2003; Fabbri et al. 2014; Seyoum et al. 2020; Wang N et al. 2023; Kadlec et al. 2024). In general, developmental effects tend to be seen at lower concentrations than growth and reproductive endpoints (Ankley et al. 2021). Moreover, PFAS have been shown to cause oxidative stress and affect immune-related cell viability. Liu and Gin (2018) observed measurable reductions in the immune fitness of green mussel (*Perna viridis*) following exposure to PFAS, as shown through significant decreases in biomarker responses (that is, neutral red retention, phagocytosis, and spontaneous cytotoxicity of hemocytes). In a study of adult Eastern oyster, *Crassostrea virginica*, exposed to a technical mixture of PFOS (linear and branched isomers) by Aquilina-Beck et al. (2020), no significant damage to lipid membranes or the glutathione phase II enzyme system was observed; however, significant cellular lysosomal damage was observed. Genotoxic effects have also been seen, where Liu et al. (2014) observed irreversible genetic damage caused by elevated concentrations of PFAAs in green mussels. Additionally, neurotoxic effects, such as altered brain morphology and reductions in locomotor velocity, have been observed in planaria (*Dugesia japonica*; Ankley et

al. 2021). Foguth et al. (2020) found that PFOS is capable of significantly affecting the expression of genes that are important for neuronal development in planaria in a dose- and time-dependent manner. Furthermore, it was suggested that PFECHS has endocrine disruption potential in chronically exposed *Daphnia magna* at concentrations higher than levels reported in the aquatic environment (Houde et al. 2016). PFAAs have also been found to cause multigenerational effects among aquatic invertebrates, where reductions in growth and individual fitness were seen across generations by Marziali et al. (2019) and Jeong et al. (2016), respectively.

In order to study the toxicity of PFAS replacing those subject to restriction, sublethal exposures of PFOS, PFOA, and GenX to *Daphnia magna* were evaluated. In a study by Labine et al. (2022), PFOA and GenX (carboxylic acid-bearing PFAS) led to a greater number of perturbations in the metabolic profile of *Daphnia magna* than did PFOS. More specifically, GenX and PFOA significantly disrupted more metabolic pathways and led to downregulation of nucleosides and nucleotides. GenX exposure also led to significant shifts in individual amino acids.

6.2.1.2 Terrestrial invertebrates

In comparison to the toxicological studies on aquatic invertebrates, fewer studies have been conducted with terrestrial invertebrates. Using a high-throughput system with nematodes (*Caenorhabditis elegans*), Ankley et al. (2021) noted that developmental toxicity generally increased with longer-chain PFAS. Various studies have also found behavioural, reproductive, growth, developmental, and neurotoxic effects when nematodes were exposed to PFAAs (Sammi et al. 2019; Foguth et al. 2020; Chowdhury et al. 2021; Sana et al. 2021; Currie et al. 2023). Currie et al. (2023) noted that larval stages of *Caenorhabditis elegans* were most susceptible to PFAS exposure. In European honeybees (*Apis mellifera*), PFOS exposure caused brood development to cease entirely and led to adverse behavioural effects (that is, colony activity, temperament, hive maintenance, defense; Sonter et al. 2021). Moreover, in earthworms (*Eisenia fetida*), Xu D et al. (2013) found that exposure to PFOS can induce DNA damage and oxidative stress. The toxicity of PFOS was also assessed in 2 invertebrates (*Collembolan Folsomia candida* and mites, *Oppia nitens*) in 2 soil types to assess the inclusion of these 2 study species in the risk assessment of PFOS in soil (Princz et al. 2018). A recent study highlights the harmful effects of PFHxS contamination on the terrestrial environment, which leads to reduced microbial activity. PFHxS also affected earthworm (*Eisenia fetida*) mortality in a concentration-dependent manner (Samarasinghe et al. 2023). Furthermore, Delor et al. (2023) studied the chronic ecotoxicity of PFOA and PFOS, both individually and in mixture, at environmentally relevant concentrations on the earthworm *Aporrectodea caliginosa.* Even at soil concentrations as low as 0.3 mg/kg, PFOA, PFOS, and their combination were found to impair growth and induce genotoxic effects. The toxicity of PFOA and PFOS was observed to increase with co-exposure.

A review of the toxicity of per- and polyfluoroalkyl substances to nematodes (*Caenorhabditis elegans*) revealed that GenX induced physiological effects, including developmental and progeny production delay, behaviour and locomotive effects, and transcriptional effect in these organisms (Ma et al. 2023).

6.2.2 Vertebrates

6.2.2.1 Fish

Several studies have examined PFAS toxicity in fish species, with freshwater Cyprinidae—more specifically zebrafish (*Danio rerio*)—having the most data available (Ankley et al. 2021). More studies have also been completed on freshwater species than on marine fish. In general, PFAS have a relatively lower acute toxicity to fish compared to aquatic invertebrates (Ankley et al. 2021). Acute toxicity in fish species seems to vary with chain length and functional group. In most of the fish families studied, short-chain PFAAs as well as sulfonates have been shown to display lower LC50s than long-chain PFAAs and carboxylates. A similar trend was also seen in chronic toxicity studies.

A review by Lee et al. (2020) compiled the existing literature on the adverse effects of PFAA on fish and other aquatic organisms. Exposure to PFAAs has been found to cause effects on reproduction, growth/development, mobility, behaviour, and survival. For example, studies have shown that PFAA exposure in zebrafish larvae can lead to decreased body length, decreased locomotor speed, decreased hatching rate, increased mortality, and disruption in larval morphology (for example, uninflated swim bladder, less developed gut, curved spine) (Chen et al. 2014; Guo et al. 2018; Zhang S et al. 2018a). Moreover, PFAAs can induce oxidative stress and alter the regulation of genes and nuclear receptors related to xenobiotic, lipid, and carbohydrate metabolism in fish (Lee et al. 2020). Effects on the endocrine and reproductive system have also been reported, such as by Zhang W et al. (2016), who found that chronic exposure of zebrafish to PFNA can lead to dysfunction in the hypothalamic-pituitary-gonadal-liver axis and sex hormone synthesis as well as a decrease in gonadosomatic index (a measure of sexual maturity) and fertility. In terms of neurotoxicity, Foguth et al. (2020) reported altered levels of norepinephrine, epinephrine, and acetylcholine following PFBS exposure to marine medaka (*Oryzias melastigma*). Hawkey et al. (2023) reported behavioural changes and neurobehavioural toxicity in zebrafish exposed to PFOA and PFOS. Molecular pathway analyses of transcriptomics data showed that the most enriched pathways for PFOA and PFBA in zebrafish were cancer-related (Wasel et al. 2022). Additionally, multigenerational studies have noted that PFAA exposure can impact mortality, fecundity, gonad development, and swimming rate in fish offspring (Ji et al. 2008; Wang et al. 2011; Lee et al. 2017) in addition to affecting the thyroid endocrine system (Chen L et al. 2018), lipid pathways, and behaviour (Haimbaugh et al. 2022).

Recently, more studies have been conducted on short-chain PFAS, which have been used as replacements for PFOA and PFOS. Ulhaq and Tse (2023) reported that PFHxS accumulated in zebrafish embryos causing developmental toxicities and induced oxidative stress. In addition, Rericha et al. (2022) noted abnormal larval and juvenile zebrafish behaviour in the F1 generation (F0 zebrafish were exposed to PFHxA contaminated diets for 42 days). Dunn et al. (2024) reported that GenX and PFBS exposure to zebrafish resulted in metabolomic changes related to growth and development. Furthermore, PFBA and PFBS may act as endocrine disruptors, alter lipid composition, and accumulate in the tissues of fish species (Ivantsova et al. 2024).

Toxicity of HFPO-DA was compared with PFOA using embryo-larval zebrafish and the results suggested that HFPO-DA was less toxic than PFOA on the basis of the exposure-effect concentrations (Satbhai et al. 2022). However, the internal effect concentrations were similar when the differences in bioconcentrations were accounted for, suggesting similar toxic potencies between HFPO-DA and PFOA (Satbhai et al. 2022). However, Mahoney et al. (2022) hypothesizes that HFPO-DA may be more toxically potent at acute levels of exposure compared to PFOA based on several fish studies. Wang Y et al. (2023) also found that zebrafish embryos exposed to HFPO-DA and HFPO-TA induced effects on the disorder of lipid metabolism, hypothalamic–pituitary–thyroid axis, and neurodevelopment.

6.2.2.2 Amphibians and reptiles

Similar to what has been observed in fish, PFAS have relatively lower acute toxicity in amphibians compared to aquatic invertebrates following acute exposure. The toxicity of PFAS in amphibians also seems to vary with fluoroalkyl chain length and functional group. For instance, when examining the acute toxicity of PFAA in amphibian species, Tornabene et al. (2021) and Flynn et al. (2019) determined that PFOS was more hazardous than PFOA. Moreover, PFAS has been observed to have impacts on the growth and development of early amphibian life stages (Ankley et al. 2021; Degitz et al. 2024). In northern leopard frog (*Rana pipiens*) larvae, Flynn et al. (2021) observed that exposure to PFOS and PFOA under environmentally relevant conditions led to developmental delays. Flynn et al. (2019) also found reductions in snout-vent length when American bullfrog (*Rana catesbeiana*) tadpoles were exposed to a mixture of PFOS and PFOA. Flynn et al. (2022) determined that chronic exposure to PFAS can have a negative effect on amphibian body condition and development at concentrations as low as 10 µg/L but noted that these effects were species-dependent, with frogs and salamanders being more sensitive than toads. A review of 16 amphibian studies which consisted of experiments using PFOS, PFOA, PFHxS, and 6:2 fluorotelomer sulfonate showed that body mass was the most sensitive endpoint (Pandelides et al. 2023).

Although the majority of amphibian studies have focused on the earlier aquatic life stages, it has also been found that PFAS can induce sublethal effects on post-metamorphic amphibians (Abercrombie et al. 2021). More specifically, these authors found that exposure to PFOS, PFOA, PFHxS, or 6:2 fluorotelomer sulfonate can impact final snout-vent length and scaled mass index (a measure of relative body condition) in juvenile American toads (*Anaxyrus americanus*), eastern tiger salamanders (*Ambystoma tigrinum*), and northern leopard frogs (*Rana pipiens*); however, the observed effects were dependent on the species and chemical tested. Lin et al. (2022b, 2022c, 2022d) reported PFAS-induced lipid metabolism disorders, liver damage, endrocrine disruption, immunosuppression, and hepatotoxicity in black-spotted frogs (*Rana nigromaculata*).

In a recent study, Rohonczy et al. (2024a) found that chronic exposure to 0.1 to 100 µg/L of PFBA and PFHxA significantly affected tadpole growth, but not development in northern leopard frogs. Furthermore, a shift in the sex ratio to a greater proportion of males was observed at 1 µg/L of PFBA. Rohonczy et al. (2024b) found that at 0.1 µg/L of PFHxS there was a higher likelihood for phenotypic females, however, further histological assessment is required to confirm if PFBA and PFHxS may affect sex differentiation. Rohonczy et al. (2024b), also found

that northern leopard frog tadpole hepatic health and lipid metabolism was affected by exposure to PFSAs. Hence, short-chain carboxylic and sulfonic acids, designed as replacements for their longer-chain counterparts can exert negative effects on northern leopard frogs with some evidence to suggest endocrine disrupting potential.

Even fewer studies have examined reptilian species, with recent investigations focusing on turtles and alligators. Some impacts seen in turtles include reduced emergence success of hatchlings following exposure to long-chain PFCAs (Wood et al. 2021), negative correlations between PFAA exposure and body mass (Bangma et al. 2019), and negative metabolic impacts from PFAS mixtures (Beale et al. 2022). Blood concentrations of PFAS (long- and short-chain PFAAs, perfluoroalkyl ether acids, and 6:2 FTS) in American alligators (*Alligator mississippiensis*) were reported to be associated with disrupted immune functions, resulting in autoimmune-like pathology (Guillette et al. 2022).

6.2.2.3 Mammalian wildlife

There are very few existing studies on PFAS toxicity in mammalian wildlife. Although Ankley et al. (2021) did not identify any laboratory toxicity studies on mammalian wildlife, there are some field studies that point to a significant association between PFAS exposure and the expression of biomarkers of effects. Pedersen et al. (2015) found that PFSA and PFCA concentrations in East Greenland polar bears (*Ursus maritimus*) could lead to alterations in their neurochemistry. In the bottlenose dolphin (*Tursiops truncatus*), plasma PFAA concentrations were observed to have a statistically significant association with hematologic, biochemical, and immunologic endpoints (Fair et al. 2013). As mentioned previously in section 6.1, air-breathing organisms are more likely to accumulate ionic PFAS in comparison to water-breathing organisms because of their low volatility and protein binding mechanism in tissue. As a result, it is expected that these substances would have a greater potential for exposure in air-breathing organisms (including birds, discussed in the following section) due to their significant bioaccumulation potential, which can lead to adverse effects (ECCC 2023).

Due to the lack of research on PFAS toxicity in mammalian wildlife, studies on laboratory mammals (for example, rodents, rabbits, monkeys) may be used as surrogates for toxicity in mammalian wildlife as this has been the focus of many studies from the current literature. Exposure to PFAS has the potential to cause adverse effects on multiple systems and organs (for example, liver, kidney, immune system, reproduction, endocrine system, and nervous system), according to studies of laboratory mammals (refer to section 7.2 for key health effect findings in laboratory animals). In addition, toxicity seems to vary with fluoroalkyl chain length in studies of laboratory mammals exposed to PFAA (Ankley et al. 2021). According to the findings of rat studies, the lowest observed adverse effects levels (LOAELs) for ecologically relevant endpoints were between 1.0 mg/kg bw/d (PFUnDA) and 200 mg/kg bw/d (PFHxA) for the PFCAs and between 1.6 mg/kg bw/d (PFOS) and 1,000 mg/kg bw/d (PFBS) for the PFSA. It is expected that adverse effects similar to those seen in laboratory animals could be seen in mammalian wildlife. However, it should be noted that the effects demonstrated and the magnitude of effects displayed in mammals can vary between mammalian species. Furthermore, most toxicokinetic data on mammalian species focus on laboratory animals and are discussed in section 7.1.

Some effects (for example, hepatotoxicity) of PFAS exposure in mammals are believed to be mediated in part through activation of the peroxisome proliferator-activated receptor alpha (PPARα), which plays a role in lipid and glucose metabolism. This mechanism is well studied in laboratory animals (that is, rodents) and is discussed further in section 7.4. Some studies of mammalian wildlife have also reported this mechanism of action, including studies on cetaceans (Kurtz et al. 2019), polar bears (Routti et al. 2019b), and seals (Ishibashi et al. 2008). PPARα-independent transcript regulation in mammals following PFAS exposure is also possible (Rosen et al. 2017) and is discussed further in section 7.4.

6.2.2.4 Birds

The available literature on bird toxicity of PFAS is quite limited. Toxicity reference values and predicted no effect concentrations (PNECs) have been established for serum (1,700 and 1,000 ng/mL, respectively), egg yolk (1,700 and 1,000 ng/mL, respectively), and liver (600 and 350 ng/g, respectively) on the basis of acute and chronic dietary exposures of PFOS in northern bobwhite quail (*Colinus virginianus*) and mallard (*Anas platyrhynchos*) (Newsted et al. 2005). In a study of chronic PFOS exposure in northern bobwhite quail, Dennis et al. (2021) established species- and tissue-specific chronic toxicity values, associated with a LOAEL threshold of 226, 50.4, and 92.4 ng/g wet weight in adult liver tissue, offspring liver tissue, and whole egg, respectively. More recently, chronic toxicity values of 92.4, 49.6 and 43.7 ng/g egg have been proposed, corresponding to chronic exposure to PFOS, PFOS + PFHxS and PFOS + PFHxA, respectively, in northern bobwhite quails (Dennis et al. 2022).

In avian species, it has been found that fluoroalkyl chain length and functional groups are key factors that appear to determine the toxicity of PFAS (Ankley et al. 2021). Broadly speaking, compounds with 8 carbons as well as sulfonates were found to be more hazardous than short-chain PFAS and carboxylates. Both PFOS and PFOA were determined to be more hazardous than PFBS on the basis of LC50 values obtained from northern bobwhite (*C. virginianus*) and Japanese quail (*Coturnix japonica*) acute toxicity studies (Ankley et al. 2021). Moreover, Bursian et al. (2021) concluded that PFOS exhibits a higher subacute toxicity in Japanese quail compared to PFOA and that this effect may be additive.

Studies of the peregrine falcon (*Falco peregrinus*) in the Laurentian Great Lakes have also found that exposure to PFAA can lead to potential physiological impacts on nestlings and impaired immune function (Sun et al. 2020, 2021). The toxicity of PFUnDA was determined using genomic responses in exposed liver cells of embryonic chicken (O'Brien et al. 2013). Furthermore, hatching success and toxicogenomic responses were assessed in chicken embryos following exposure to PFHxS and PFHxA (Cassone et al. 2012a, 2012b). Other avian studies have observed reductions in body weight, increases in liver weight, endocrine and metabolism disruptions, reduced hatching success, increased oxidative stress, and effects on genes related to the fat metabolism and immunological system of birds (Molina et al. 2006; Newsted et al. 2007; Custer et al. 2013; Tartu et al. 2014; Jacobsen et al. 2018; Costantini et al. 2019; Dennis et al. 2021; Bursian et al. 2021; Lopez-Antia et al. 2023; Sebastiano et al. 2023).

6.2.3 Aquatic and terrestrial plants

Most studies that have examined the toxicity of PFAS in aquatic and terrestrial plants have been limited to PFOS and PFOA. According to data summarized by the ITRC (2021b), studies that examined PFOS toxicity in aquatic plants had no observed effect concentration (NOEC) values ranging from 7 mg/L to 30 mg/L for acute exposures and from 0.3 mg/L to 11.4 mg/L for chronic exposures. Reviews by Li J et al. (2022a) and Adu et al. (2023) have examined the phytotoxic effects of PFAS on various plants from a physiological, biochemical, and molecular standpoint. At the physiological level, PFAS can cause damage to cell morphology, impact the content of photosynthetic pigments, and alter plant phenotype (Li J et al. 2022a). Elevated levels of PFOS have been found to cause damage to the root cell ultrastructure in wetland plants (Li R et al. 2020). In algae (*Chlorella pyrenoidosa*), tested concentrations of PFOA and its substitute GenX were found to inhibit growth and negatively affect photosynthetic activity (Li Y et al. 2021). Niu et al. (2019a) also reported that environmentally relevant concentrations of 6:2 Cl-PFESA, HFPO-DA and PFECHS reduced the growth of marine *Chlorella* sp. In addition, Ebinezer et al. (2022) treated hydroponically-grown maize plants with a mixture of 11 different PFAAs and found a significant reduction in the relative growth rate and fresh weight of leaves and roots. Moreover, PFAS exposure can also induce the overgeneration of reactive oxygen species (ROS; reactive chemicals derived from molecular oxygen), perturb the expression of genes, regulate the proteins involved in photosynthesis, and disturb some major pathways in energy metabolism (Li J et al. 2022a). A study by Lin et al. (2020) examined the phytotoxicity of Cl-PFESAs in wheat seedlings, which demonstrated higher levels of root membrane permeability and ROS, as well as a reduction in antioxidant enzyme activity. Wheat seedlings exposed to environmentally relevant levels of PFBA showed an increase in ROS, an increase in enzymatic and non-enzymatic antioxidants, as well as down-regulated plant-pathogen interaction genes (Wang et al. 2024). Further, the transcriptional and cellular responses of the green alga *Chlamydomonas reinhardtii* to PFPAs were evaluated where potential impacts to the antioxidant defensive system were observed, such as gene regulation expression (Sanchez et al. 2015). Sun et al. (2022) also found that PFBS altered the expression of genes associated with phytohormone signalling pathways in *Arabidopsis thaliana.*

6.2.4 Mixtures and cumulative effects in the environment

Although the vast majority of ecotoxicology studies have focused on the effects seen with exposure to a single PFAS, organisms are typically exposed simultaneously to multiple PFAS in the environment, as can be seen from environmental occurrence and monitoring data. Even very low or negligible concentrations of individual components may contribute to combined effects (Altenburger et al. 2013). Therefore, it is important to consider that combined exposure to multiple PFAS is likely to be a more accurate representation of exposure circumstances, which can increase the likelihood of detrimental impacts in organisms and presents a broader concern with the class of PFAS.

Some field-based wildlife studies also group PFAS together, sometimes with other chemicals, and examine the effects observed in the organism (ECCC 2023). The Supporting Document: Ecological State of the Science Report on Short-chain PFCAs, Short-chain PFSAs, and Long-chain PFSAs (ECCC 2023) provides a compilation of published cumulative effect studies for

certain PFAS in various wildlife species. Hoover et al. (2019) reported that cytotoxicity results of mixtures of PFASs were approximately additive and that certain mixtures of PFAS may have increased toxicity potential. Synergistic effects have also been observed in PFOS and PFOA mixtures (Yang et al. 2019; Hoover et al. 2019).

However, the interactive effects of PFAS mixtures (that is, whether they are additive, synergystic, or antagonistic) and the extent of the effect may depend on various factors. Rodea-Palomares et al. (2012) found that PFOS and PFOA showed complex interactive effects that had additive, synergistic and antagonistic effects depending on molar ratios of PFOS. Flynn et al. (2019) reported that the interactive effects (additive and synergistic effects) and relative toxicity of PFAS mixtures may depend on biological endpoints considered.

More recent studies have investigated the impact of PFAS mixtures in the environment. Maternal health effects and changes in placenta morphology and gene expression in a rabbit pregnancy model have been reported with exposure to an environmentally-relevant mixture of 10 PFAAs (Crute et al. 2022). Behavioural changes and untargeted gene expression across zebrafish generations were found following exposure to a mixture of PFOS and PFOA (Haimbaugh et al. 2022). Chronic exposure of PFAA mixtures to rainbow trout at environmentally relevant doses showed effects on peroxisome proliferator activated receptors, metabolic dysregulation, immunotoxicity, and neurotoxicity (Pollard et al. 2024). Lech et al. (2022) also examined the impact of various PFAS mixtures (variations containing PFOS, PFOA, PFHxS, PFHxA and/or PFPeA) on host-parasite interactions (that is, larval American bullfrogs to echinostomes) and found an increased parasite load in all treatments compared to when bullfrogs were not exposed to PFAS. As a result, PFAS were found to increase host susceptibility to parasites. However, mixtures were found to have a lesser effect on host susceptibility to parasites when compared to PFOS-only treatments. Furthermore, mechanism-of-action has been explored such as in Liu X et al. (2022) which demonstrated a synergistic toxicity effect in algae exposed to a PFBS-FBSA mixture at environmental concentrations.

6.2.5 New approach methods for ecotoxicity

The evolving landscape of chemical production has rendered toxicological testing using vertebrate animals impractical, and advances in science coupled with ethical concerns have resulted in government agencies, including in the US (US EPA 2021a), EU (ECHA 2023a; Cattaneo et al. 2023), and Canada (ECCC, HC 2024), committing to replace, reduce or refine the use of vertebrate animals in toxicity testing, whenever possible. New approach methods (NAMs) are broadly described as any technology, method, approach, or a combination of these that can be used to replace, reduce, or refine, vertebrate animal testing and allow more rapid or effective prioritization and/or assessment of chemicals (ECCC 2023). These methods may include the use of computer models or assays with biological molecules, cells, tissues, or organs as well as exposure prediction approaches.

The evolution and advantages of NAMs for ecological risk assessment of PFAS are reviewed in Ankley et al. (2021). Similar to NAMs for human health risk assessment, a major focus has been on measures of bioactivity, the rationale being that this could lead to a mechanistic understanding of PFAS toxicity to aid in the identification of susceptible species and endpoints,

and to support cross-species extrapolation. A number of studies have aimed to identify the biological pathways affected by PFAS by evaluating changes in gene or protein expression in non-mammalian test systems (Ankley et al. 2021). However, a review of adverse effects of PFAA on aquatic organisms determined that toxicity involves diverse metabolic processes, highlighting the challenge of elucidating linkages and interactions among metabolic pathways (Lee et al. 2020). Combining molecular information with computational models could be used to inform adverse outcome pathways to confidently identify PFAS-specific molecular initiating events and changes at higher levels of biological organization (that is, key events) to elucidate how these changes translate into adverse effects and outcomes (that is, apical endpoints; Ankley et al. 2010).

7 Human health hazard

KEY POINTS ON HUMAN HEALTH HAZARD

- Toxicological and epidemiological information is available for approximately 50 PFAS with most research focused on PFOA and PFOS.
- Recent information on well-studied PFAS, particularly PFOA and PFOS, shows negative effects on human health at lower levels than previous studies.
- Some well-studied PFAS have been demonstrated to be readily absorbed into the body and are eliminated very slowly. Consequently, some PFAS can accumulate and persist in the body for years.
- Exposure to PFAS can affect multiple organs and systems. The main targets include the liver, immune system, kidney, reproduction, development, endocrine disruption (thyroid), nervous system, and metabolism (lipids, glucose homeostasis, body weight). Effects on most of these endpoints have been observed in both animal and human studies.
- Since humans are typically exposed to mixtures of PFAS, it is reasonable to expect that cumulative effects may occur. However, the specific hazards associated with these mixtures are largely unknown.
- New approach methods (NAMs) can help fill gaps in the data by generating information using time- and resource-efficient techniques, including high-throughput screening.

7.1 Toxicokinetics

Toxicokinetic data are available primarily for PFAAs. Available data on specific PFAAs indicate that these substances are readily absorbed following oral ingestion and, although data on inhalation and dermal exposure are extremely limited, available studies indicate that absorption occurs by these routes as well (ATSDR 2021; Sanexen 2024; Weatherly et al. 2024a, 2024b). The extent to which PFAS are absorbed by the different routes (for example dermal absorption) may vary by substance (Ragnarsdóttir et al. 2024). Once absorbed, the studied PFAAs bind to serum protein albumin and other proteins in the blood, which serve as the primary transport mechanism of these substances within the body (Forsthuber et al. 2020; Louisse et al. 2023; Fischer et al. 2024; Smeltz et al. 2024). Information on studied PFAAs indicates that they are distributed throughout the body and accumulate in the blood and well-perfused tissues such as the liver and kidneys (Kudo 2015). A number of PFAS (for example, PFAAs and FOSA) have been shown to cross the placental barrier, resulting in in utero exposure to the developing fetus (Wang Y et al. 2019a; McAdam et al. 2023; Liu et al. 2024). They can also be transferred to infants and children via human milk (VanNoy et al. 2018; Rawn et al. 2022b; Zheng et al. 2022; Hoadley et al. 2023). Many PFAS, including PFAAs, are not metabolized in the body, likely because of their high stability and low reactivity of carbon-fluorine bonds (ATSDR 2021). However, precursors such as FTOHs and PAPs can be biotransformed to several metabolites including PFAAs (Butt et al. 2014).

Some PFAS have been shown to be eliminated very slowly from the human body, likely due to their interaction with transporters involved in renal, hepatic, and intestinal reabsorption processes (Yang et al. 2010; EFSA 2020). As a result, these substances persist and

accumulate in humans and can take a very long time to be cleared from the body. Biological half-lives have been identified for 40 PFAS in humans and/or animal models (Table 3). These values represent the time it takes for half of the original concentration of the substance to be cleared by the body through excretion (for example, urine, feces). As these values were derived for different groupings of individuals using various methodological approaches and with different statistics, the half-lives are not necessarily directly comparable. However, there are clear species differences in the elimination rates of PFAS, with the longest half-lives often being observed in humans and the shortest in rodents. In humans, C8 to C11 PFCAs, C6 to C8 PFSAs, and several ether-PFAS have the longest half-life values (years to decades). It is noted that there is some uncertainty in the human values since the washout studies typically used for determining half-lives in animal studies are not used to determine half-lives in humans (FSANZ 2016b). The determination of half-lives in humans is more complicated because other parameters, such as continuous exposure, need to be considered (Russell et al. 2015a). For some PFAS such as PFCAs (C4 to C12) and PFSAs (C4 to C8), the longer the chain length, the more slowly the PFAS is eliminated from the body (Kudo 2015). Studied PFAS are excreted primarily in the urine and feces and, to a lesser extent, in human milk and menstrual fluid (ATSDR 2021). The latter excretion routes may contribute to sex differences observed in some human monitoring studies (Mondal et al. 2014; Wong et al. 2014; Jain and Ducatman 2022; Upson et al. 2022).

Table 3. Biological half-lives for PFAS in animals and humans (adapted from Sanexen 2021, 2024)

PFAS group	PFAS	Mouse	Rat	Monkey	Pig	Human	References
PFCAs	PFBA	hours[a]	hours–days	days	-	days	Chang et al. 2008; Russell et al. 2015b
PFCAs	PFPeA	-	hours	-	-	-	Choi et al. 2020
PFCAs	PFHxA	hours	minutes–hours	hours–days	days	days–years	Noker 2001; Himmelstein et al. 2008; Chengelis et al. 2009a, 2009b; Gannon et al. 2009; Iwai 2011; Russell et al. 2013; Numata et al. 2014; Russell et al. 2015b Dzierlenga et al. 2020; Xu Y et al. 2020; ECHA 2024a
PFCAs	PFHpA	-	hours	-	months	months–years	Ohmori et al. 2002; Zhang et al. 2013; Numata et al. 2014; Russell et al. 2015b; Xu Y et al. 2020
PFCAs	PFOA[b]	weeks	hours–weeks	weeks-months	months	years–decades	Hanhijärvi et al. 1988; Vanden Heuvel et al. 1991; Kudo et al. 2002; Kemper 2003; Ohmori et al. 2003; Olsen et al. 2003; Butenhoff et al. 2004a; Lau et al., 2005; Lieder et al. 2006; Olsen et al., 2007; Benskin et al. 2009; Costa et al. 2009; and others[c]
PFCAs	PFNA[d]	months	days–months	-	-	years	Ohmori et al. 2003; Benskin et al. 2009; De Silva et al. 2009; Tatum-Gibbs et al. 2011; Zhang et al. 2013; Chiu et al. 2022
PFCAs	PFDA[d]	-	months	-	-	years	Ohmori et al. 2003; Zhang et al. 2013
PFCAs	PFUnDA	-	-	-	-	years–decades	Zhang et al. 2013
PFCAs	PFDoDA	-	months	-	-	-	Kawabata et al. 2017a
PFSAs	PFBS	hours	hours	hours-days	months	weeks–months	Chengelis et al. 2009a; Olsen et al. 2009; Numata et al. 2014; Rumpler et al. 2016; Huang et al. 2019a; Lau et al. 2020; Xu Y et al. 2020
PFSAs	PFPeS	-	-	-	-	Months-years	Xu Y et al. 2020; Li Y et al. 2022b

PFAS group	PFAS	Mouse	Rat	Monkey	Pig	Human	References
PFSAs	PFHxS	weeks	days–weeks	months	years	years–decades	Olsen et al. 2007; Benskin et al. 2009; Zhang et al. 2013; Numata et al. 2014; Fu et al. 2016; Kim et al. 2016; Worley et al. 2017; Li Y et al. 2018; Huang et al. 2019a; Sundstrom et al. 2012; Xu Y et al. 2020; Chiu et al. 2022; and others[e]
PFSAs	PFHpS[d]	-	-	-	years	years	Numata et al. 2014; Xu Y et al. 2020; Li Y et al. 2022b; Nilsson et al. 2022a
PFSAs	PFOS[d,f]	weeks–months	weeks–months	months	years	years–decades	Seacat et al. 2002; Noker and Gorman 2003; Olsen et al. 2007; Benskin et al. 2009; De Silva et al. 2009; Chang et al. 2012; Zhang et al. 2013; Numata et al. 2014; Wong et al. 2014; Fu et al. 2016; Kim et al. 2016; Shi et al. 2016; and others[g]
FASAs and derivatives	FOSA	-	days	-	-	-	Ross et al. 2012
FT-based substances	8:2 FTOH	-	hours	-	-	-	Fasano et al. 2006; Huang et al. 2019b
FT-based substances	5:3 Acid	-	weeks–months	-	-	months	Russell et al. 2015b; Kabadi et al. 2020
PFPAs	C6 PFPA	-	days	-	-	-	D'eon and Mabury 2010
PFPAs	C8 PFPA	-	hours–days	-	-	-	D'eon and Mabury 2010; Joudan et al. 2017
PFPAs	C10 PFPA	-	days	-	-	-	D'eon and Mabury 2010
PFPIAs	C6/C6 PFPiA	-	days	-	-	-	D'eon and Mabury 2010
PFPIAs	C6/C8 PFPiA	-	days	-	-	-	D'eon and Mabury 2010; Joudan et al. 2017
PFPIAs	C6/C10 PFPiA	-	days	-	-	-	D'eon and Mabury 2010
PFPIAs	C6/C12 PFPiA	-	days–weeks	-	-	-	D'eon and Mabury 2010
PFPIAs	C8/C8 PFPiA	-	days	-	-	-	D'eon and Mabury 2010; Joudan et al. 2017

PFAS group	PFAS	Mouse	Rat	Monkey	Pig	Human	References
PFPIAs	C8/C10 PFPiA	-	days–weeks	-	-	-	D'eon and Mabury 2010
PAPs	4:2 diPAP	-	days	-	-	-	D'eon and Mabury 2011
PAPs	6:2 diPAP	-	days	-	-	-	D'eon and Mabury 2011
PAPs	8:2 diPAP	-	days	-	-	-	D'eon and Mabury 2011
PAPs	10:2 diPAP	-	days	-	-	-	D'eon and Mabury 2011
Ether-PFAS (PFESAs)	6:2 Cl-PFESA	-	days	-	-	years–decades	Shi et al. 2016; Yi et al. 2021
Ether-PFAS (PFESAs)	6:2 H-PFESA	-	days	-	-	-	Yi et al. 2021
Ether-PFAS (Cl-PFECAs)	Cl-PFECAs	-	days-months[h]	-	-	years[i]	RTC 2016; Solvay 2019
Ether-PFAS (PFECAs)	ADONA	hours	hours–weeks	hours	-	weeks	3M 2007a, 2008a, 2008b, 2008c, 2010; Harlan Laboratories Ltd 2010
Ether-PFAS (PFECAs)	EEA-NH4	-	hours	hours–days	-	-	AGC Chemical 2007a, 2007b
Ether-PFAS (PFECAs)	HFPO-DA	hours–days	hours–days	hours–days	-	days	DuPont 2008b, 2011; Gannon et al. 2016; ECHA 2021b
Ether-PFAS (PFECAs)	PFO4DA	hours	-	-	-	-	Kotlarz et al. 2020; Chen et al. 2021; NJDEP 2021
Ether-PFAS (PFECAs)	PFO5DoDA	months	-	-	-	-	Chen et al. 2021
Ether-PFAS (PFECAs)	PFO5DoA	-	-	-	-	months[j]	Kotlarz et al. 2024
Ether-PFAS (PFECAs)	C6O4[k]	-	-	-	-	days	Fustinoni et al. 2023
Other	3,890 individual PFAS	-	-	-	-	hours-years[k]	Dawson et al. 2023

[a] Time frames: hours = up to 24 hours; days = >1 to 7 days; weeks = >7 to 31 days; months = >1 to 12 months; years = >1 year; decades = >10 years.
[b] PFOA was also tested in dogs, with a half-life in the order of weeks.
[c] De Silva et al. 2009; Lou et al. 2009; Bartell et al. 2010; Brede et al. 2010; Seals et al. 2011; Zhang et al. 2013; Numata et al. 2014; Fu et al. 2016; Gomis et al.

2016, 2017; Kim et al. 2016; Worley et al. 2017; Li et al. 2018a; Dzierlenga et al. 2020; Xu Y et al. 2020; Chiu et al. 2022; Li Z et al. 2022a; Nilsson et al. 2022a; Rosato et al. 2024.

[d] PFNA, PFDA, PFHpS and PFOS, were also tested in cattle, with half-life in the order of weeks to months (Drew et al. 2022).

[e] Li Y et al. 2022b; Nilsson et al. 2022a; Rosato et al. 2024.

[f] PFOS was also tested in rabbits, with a half-life in the order of months.

[g] Tarazona et al. 2016; Gommis et al. 2017; Worley et al. 2017; Li Y et al. 2018; Huang et al. 2019a; Xu Y et al. 2020; Chiu et al. .2022; Li Y et al. 2022b; Nilsson et al. 2022a; Rosato et al. 2024.

[h] Data is based on CAS RN 330809-92-2 which contained a mixture of 5 Cl-PFECAs congeners (8-, 10-, 11-, 13- and 14-carbon).

[i] Data is based on workers who were exposed to Cl-PFECA sodium (CAS RN 220207-15-8) and ammonium (CAS RN 330809-92-2) salts. These forms dissociate to the anion (CAS RN 329238-24-6) in the environment and in biological systems.

[j] The median decrease in serum levels across 44 participants over 6 months was 27.4%.

[k] Dawson et al. (2023) used machine learning to predict the human half-lives ($t_{1/2}$) of 3,890 PFAS, and classified the PFAS into 4 bins. 56% of the PFAS were classified into Bin 4 ($t_{1/2}$ > 2 months, median 3.3 years), 7% were classified into Bin 3 (1 week < $t_{1/2}$ < 2 months, median 33 days), 37% were classified into Bin 2 (12 h < $t_{1/2}$ < 1 week, median 2.2 days) and 0% of PFAS were classified into Bin 1 (12 h < $t_{1/2}$).

7.2 Health effects

Although there is a vast amount of research on the health effects associated with PFAS, the majority of research is focused on PFCAs and PFSAs, particularly PFOA and PFOS. Fewer data exist for other PFAS, although research on these substances, including by the Government of Canada (see section 8.1.2.2), is increasing. Toxicological and epidemiological data currently exist for approximately 50 individual PFAS. A number of international agencies and journal publications have reviewed the human health hazards associated with these PFAS (for example, EFSA 2020; ATSDR 2021; Fenton et al. 2021; ECHA 2022a, 2022b, 2023c; Polcher et al. 2023). In contrast, limited or no data exist for the majority of PFAS, including many PFAS that are known to be present in commercial products or that have been found in the environment. These include C1 to C3 PFSAs and PFCAs, other FT-based substances (for example, containing phosphorus or a thioether), cyclic PFAS, side-chain fluorinated polymers, or perfluoropolyethers.

When examining the toxicity data available for PFAS, it is evident that, on the basis of the available information, exposure to these substances has the potential to affect multiple systems and organs. To gain a better understanding of the key health endpoints, the Government of Canada commissioned a report to summarize the available data (Sanexen 2024). The purpose of the report was to provide an overview of the publicly available science and to highlight commonalities across the studied PFAS. It did not include a critical review of the individual studies (for example, evaluation of study design, strengths, weaknesses, biases). The Government of Canada has reviewed the report in detail and noted that data on recurrent health effects were available for 50 PFAS, including perfluorinated compounds (PFCAs, PFSAs), polyfluorinated compounds (FT-based substances, FASAs, and derivatives) as well as per/polyfluoroalkyl ether compounds (PFESAs, PFECAs, C6O4, Cl-PFECAs), one perfluorinated substance with an aromatic moiety (OBS), and HQ-115. Although several PFAS subgroups (for example, LC-PFCAs or LC-PFSAs) were well represented with a number of studies and health endpoints available for several compounds, other PFAS subgroups were limited to data for a single substance or were limited in terms of the amount and type of data available for each substance. In addition, a separate examination of unpublished studies and published reviews for TFA was conducted (Solomon et al. 2016; Dekant and Dekant 2023; ECHA 2023d, 2024b). Exposure of laboratory animals to high doses of TFA has been associated primarily with liver effects (increased liver weight, hepatocellular hypertrophy, increased alanine aminotransferase (ALT)), although increased kidney weight, decreased white blood cells, reduced weight of reproductive organs, litter loss, reduced body weight of offspring, and malformations have also been observed (ECHA 2023b, 2023d, 2024b).

Table 4 provides an overview of the information available for the various PFAS groups and subgroups. Both toxicological data (studies in laboratory animal models) and epidemiological data (studies in humans) are available for most of the PFAS groups/subgroups. The exceptions were for C1 to C3 PFCA (that is, TFA and PFPrA), C1 to C3 PFSA (that is, TFMS, trifluoromethane sulfonic acid), FT-based substances, C6O4, OBS, and HQ-115 for which only animal data were available, and for FASAs, for which only human data were available. Overall, and despite the lack of equivalency in the level of information between PFAS groups/subgroups,

the main systems/organs/targets identified as being affected include the liver, immune system, kidney, reproduction, development, endocrine disruption (thyroid), the nervous system, and metabolism (lipids, glucose homeostasis, body weight). For most of these systems/organs/targets, recurrent effects were associated with PFAS exposure in both animal and human studies. The exception is for effects in the adrenal glands, which were reported in animal studies only.

While there are limitations to epidemiological studies—including the fact that it is often not possible to definitively determine causality for the associations observed—when they are combined with toxicological data from experimental animals, the findings are more compelling, and the overall evidence of effect is strengthened.

The sections below provide an overview of the information available for each of the recurrent health endpoints (see Appendix E for supporting references). This overview is not a comprehensive critical review of the health effects caused by PFAS, nor does it present all the toxicity data required to assess the hazard of, or weight of evidence available for, individual substances. Rather, the purpose of this section is to highlight the commonalities between PFAS and summarize the effects on the most recurrent endpoints, organs and systems. Although the data indicate that statistically significant effects or associations were identified for these endpoints, it is recognized that other studies may have found no such effect or association. While the information in this section focuses on studies where effects were seen, there are also some studies that demonstrate null effects for specific PFAS under certain conditions (for example, Arbuckle et al. 2020; Chen Z et al. 2020). These null findings are not detailed in the summaries below.

Table 4. Summary of the recurrent health effect endpoints examined in human and animal studies

PFAS groups	PFAS subgroups	Number of PFAS with data	Effect on body weight	Effect on kidney	Effect on immune system	Effect on liver (except serum lipids)	Effect on reproduc-tion (except ED)	Effect on development (except ED and neurotoxicity)	Effect on nervous system or neuro-development	Effect on endocrine system - ED during develop-ment	Effect on endocrine system - Reproductive hormones	Effect on endocrine system - Thyroid gland or hormones	Effect on endocrine system - Adrenal gland or hormones	Metabolic disruption - Serum lipids	Metabolic disruption - Glucose homeo-stasis
PFCAs	C1-C3	≤2	-	**A +**	A +	A +	A +	**A +**	-	-	-	**-**	-	-	-
PFCAs	C4–C7	≤4	H + A +	**H ++** **A ++**	H ++ A +	H+ A ++	H + A +	**H ++** **A ++**	A ++	A +	H +	**H ++** **A ++**	-	A ++	H ++
PFCAs	≥C8	≤9	**H ++** **A ++**	**H ++** **A ++**	**H ++** **A ++**	**H ++** **A ++**	**H ++** **A ++**	**H ++** **A ++**	**H ++** **A ++**	**H ++** **A ++**	**H ++** **A ++**	**H ++** **A ++**	A ++	**H ++** **A ++**	**H ++** **A ++**
PFSAs	C1–C3	≤1	-	-	-	A +	A +	-	-	-	-	-	-	A +	A +
PFSAs	C4–C7	≤3	**H ++** **A ++**	H + A ++	**H ++** **A ++**	**H ++** **A ++**	H ++ A +	**H ++** **A ++**	H + A +	H + A +	H ++ A+	**H ++** **A ++**	A +	**H ++** **A ++**	H ++
PFSAs	≥C8	≤2	H + A +	H ++ A +	H + A +	H + A +	H + A +	H + A +	H + A +	H ++ A +	H + A +	H + A +	A +	H + A +	H + A +
FASAs and derivatives	FASA	≤1	H +	-	H +	-	H +	H +	H +	-	-	-	-	-	-
FASAs and derivatives	Derivatives	≤6	H ++ A +	H + A +	A +	A ++	H + A ++	A ++	-	-	H+	H ++ A +	-	A ++	H +
FT-based substances	FTSA (n:2)	≤1	A +	A +	-	A +	-	-	-	-	-	-	-	-	-
FT-based substances	FTOH (n:2)	≤2	A ++	A ++	A ++	A ++	A +	A +	A +	-	-	A ++	-	A +	-
FT-based substances	FTCA (n:2 and n:3)	≤2	A +	A +	A +	A ++	-	-	-	-	-	A +	-	A +	-
Ether-PFAS	PFESA	≤2	A +	H +	A +	H + A +	A +	H +	-	H +	-	A +	-	H + A +	H +
Ether-PFAS	PFECA	≤12	A ++	**H ++** **A ++**	A ++	**H ++** **A ++**	A +	A ++	-	-	H +	A ++	A ++	**H ++** **A ++**	A ++

PFAS groups	PFAS subgroups	Number of PFAS with data	Effect on body weight	Effect on kidney	Effect on immune system	Effect on liver (except serum lipids)	Effect on reproduc-tion (except ED)	Effect on development (except ED and neurotoxicity)	Effect on nervous system or neuro-development	Effect on endocrine system - ED during develop-ment	Effect on endocrine system - Reproductive hormones	Effect on endocrine system - Thyroid gland or hormones	Effect on endocrine system - Adrenal gland or hormones	Metabolic disruption - Serum lipids	Metabolic disruption - Glucose homeo-stasis
Ether-PFAS	Cl-PFECAs	≥ 1	A+	A+	H+	A+	A+	-	-	-	H+	H+ A+	-	A+	A+
Ether-PFAS	C6O4	≤ 1	-	-	-	A +	A +	A +	-	-	-	A +	-	-	-
Other	OBS	≤ 1	-	-	-	-	-	-	-	A+	-	-	-	A+	-
Other	HQ-115	≤ 1	A +	A +	-	A +	A +	A +	A +	-	-	A +	-	A +	-

A: animal data (statistically significant effect and/or adverse effect induced by PFAS); ED: endocrine disruption; H: human data (significant association with exposure to PFAS).

- No retrieved data indicating a PFAS-induced effect (A) or an association with exposure to PFAS (H) (that is, effect/association not observed, not evaluated, or not retrieved).

\+ Recurrent effect in the target observed for a single PFAS within the subgroup.

++ Recurrent effect in the target observed for more than 1 PFAS within the subgroup.

Bold Indicates cases where (++) were attributed to both human and animal data.

Source: Information for TFA (C1-C3 PFCAs) was taken from ECHA (2023c, 2024b). Information for all other PFAS was adapted from Sanexen (2024)

7.2.1 Liver

Effects on the liver are one of the most investigated endpoints, and data have been reported in humans and/or animals for 40 PFAS. In epidemiological studies, exposure to PFOS and PFHxS was associated with an increased risk of certain liver diseases (for example, non-alcoholic fatty liver disease, cholelithiasis, biliary duct disorders, lobular and portal inflammation, liver fibrosis). Changes in serum levels of enzymes and bilirubin were the most common biomarkers of liver damage investigated in both epidemiological and laboratory studies. Increased liver enzyme levels were reported for 10 PFCAs, 3 PFSAs, 2 FT-based substances, 8 ether-PFAS, and HQ-115, while inconsistent alterations to bilirubin levels were reported for 6 PFCAs, 3 PFSAs, 2 FT-based substances, and 4 ether-PFAS, indicating the possibility that bilirubin may not be a consistent biomarker for liver effects in these cases. In laboratory studies, liver weight and histopathological endpoints were often examined as evidence of hepatotoxicity. Altered liver weights and/or histopathological findings such as hepatocellular hypertrophy, hyperplasia, and necrosis were noted following exposure to 13 PFCAs, 4 PFSAs, 2 FASA derivatives, 5 FT-based substances, 14 ether-PFAS, and HQ-115. In addition, alterations to lipid homeostasis in the liver were examined in animal studies, and data were reported for 5 PFCAs, 3 PFSAs, and 4 ether-PFAS. Both increasing and decreasing levels of hepatic triglycerides and/or total cholesterol levels were reported. Currently, the relationship between changes in these parameters following PFAS exposure and lipid homeostasis is not clearly understood (Das et al. 2017).

7.2.2 Kidney

The long biological half-lives of certain PFAS are attributed in part to renal reabsorption processes (Louisse et al. 2023). PFAS can accumulate in renal tissues and effects on the kidney have been reported in humans and/or animals for 32 PFAS. In epidemiological studies, exposure to PFBA, PFOA, PFHxS, and PFOS was associated with an increased risk of chronic kidney disease and/or gout. In addition, altered glomerular filtration rates were also associated with exposure to 9 PFCAs, 4 PFSAs, and N-MeFOSA. Of note is that reverse causality is a possibility for this endpoint, meaning that decreased glomerular filtration (for example, due to a pre-existing condition) may result in increased PFAS levels, as opposed to the increased levels of PFAS potentially causing the decreased filtration rates. The kidneys remove waste products such as uric acid, urea and creatinine from the blood. These parameters can act as biomarkers of renal function and indicators of increased risk for disease. In epidemiological and/or laboratory studies exposure to 11 PFCAs, 3 PFSAs, and 5 ether-PFAS was mostly associated with increases in these biomarkers. In animal studies, altered kidney weights were reported for 7 PFCAs, 3 PFSAs, N-MeFOSE, 3 FT-based substances, 4 ether-PFAS, and HQ-115. For most PFAS, increased kidney weights were noted; however, for some PFAS, decreased kidney weights were also reported. Nephrotoxicity as indicated by histopathological findings in animal models included tubular hypertrophy, degeneration and/or necrosis/dilation, papilloma necrosis/fibrosis as well as cortical and/or medullary congestion. Such findings were reported for 5 PFCAs, 2 PFSAs, 4 FT-based substances, and 3 ether-PFAS.

7.2.3 Immune system

The immune system can be a sensitive target for environmental contaminants; immune effects associated with PFAS exposure have been reported in human and/or animal studies for 26 PFAS. In epidemiological studies, as well as studies in animal models, both immunosuppression and immunoenhancement have been investigated.

In epidemiological studies, immunosuppression mainly refers to reduced antibody responses to vaccination (for example, rubella, tetanus, diphtheria) and to increased incidence of infectious diseases (for example, throat/airway/ear infections, gastroenteritis, croup). Immunosuppression was noted following exposure to 6 PFCAs, 3 PFSAs, and FOSA. In animal studies, immunosuppression referring mainly to decreased antibody response to antigens (T-cell-dependent or -independent antibody responses) was reported following exposure to PFOA, PFOS, and HFPO-DA. In addition, the modulation of cytokine levels (increased and/or decreased) was noted following exposure to 3 PFCAs, PFOS, 8:2 FTOH, and 6:2 Cl-PFESA. Reduced levels, proliferation, and/or activity of white blood cells was noted as a result of exposure to 4 PFCAs, PFOS, 8:2 FTOH, and 3 ether-PFAS, and an increased incidence of infectious disease was noted following exposure to PFOS. Published reviews, particularly on PFOS and PFOA, show epidemiological findings to be concordant with animal studies indicating the importance of immunosuppression as a key endpoint (NTP 2016; Dewitt 2019).

In terms of immunoenhancement, which refers to allergic sensitization and/or hypersensitivity (for example, asthma, rhinitis, atopic dermatitis), this endpoint was examined in epidemiological studies and reported to be associated with exposure to 8 PFCAs and 4 PFSAs. Changes in immune system organ weights and histopathological alterations have also been investigated in laboratory studies in relation to PFAS exposure. Studies have noted decreased spleen, thymus, and/or lymph node weights, often in association with histopathological findings (decreased size and/or cellularity, necrosis, and hyperplasia) in these organs and/or in the bone marrow. At least one of these findings was reported following exposure to 6 PFCAs, 2 PFSAs, N-EtFOSE, 3 FT-based substances, and 3 ether-PFAS.

7.2.4 Reproduction

Reproductive effects associated with PFAS exposure have been investigated in human and/or animal studies for 28 PFAS. In epidemiological studies, lower fecundability (that is, the probability of conception in a menstrual cycle) and higher infertility (that is, a time to pregnancy longer than 12 months) were related to exposure to 4 PFCAs and 2 PFSAs. In addition, preeclampsia and/or pregnancy-induced hypertension were found to be associated with exposure to 5 PFCAs and 3 PFSAs. In animal studies, a decreased number of pregnancies, reduced fertility and gestational indexes, possible changes in the estrous cycle, and increased pre-coital time and implantation loss were observed following exposure to HQ-115. Increased gestational weight gain was noted in epidemiological and/or animal studies as being associated with exposure to PFOA, PFOS, N-EtFOSAA, and HFPO-DA. Both laboratory and epidemiological studies have investigated the effects on reproductive hormones following PFAS exposure. Altered serum levels (increased or decreased) of estradiol, testosterone, progesterone, follicle-stimulating hormone, and/or prolactin were the most recurrent endpoints and were associated with exposure to 7 PFCAs, 3 PFSAs, N-EtFOSA, and Cl-PFECAs. In

terms of male reproductive outcomes, abnormal sperm morphology, decreased semen volume, and decreased sperm motility, concentration, and/or count were noted in epidemiological and/or animal studies as being associated with exposure to 7 PFCAs, 3 PFSAs, and FOSA. In addition, altered reproductive organ weights (that is, seminal vesicles, testes, and/or epididymides) were reported in animal studies following exposure to 4 PFCAs, 2 PFSAs, 2 FASA derivatives, 6:2 FTOH, and 3 ether-PFAS.

7.2.5 Development

Information on developmental toxicity associated with PFAS exposure was noted in human and/or animal studies for 28 PFAS. Different exposure scenarios were considered, including maternal exposure before or during gestation (that is, *in utero* exposure), lactational exposure, postnatal exposure, or a combination of these. The most commonly investigated endpoints were prenatal and postnatal growth outcomes such as decreased birth weight, birth length, ponderal index, and head circumference. These outcomes were observed in epidemiological and/or animal studies as being associated with exposure to 10 PFCAs, 3 PFSAs, 2 FASAs and derivatives, 6:2 FTOH, 7 ether-PFAS, and HC-115. Laboratory studies further noted increased prenatal and postnatal mortality following exposure to many of these same PFAS. In laboratory studies, delayed ossification and other skeletal variations (increased incidence of tail, sternal, and limb defects) were reported following exposure to PFOA, 2 PFSA, N-EtFOSE, 6:2 FTOH, and HFPO-DA. The occurrence of cleft palate was also noted following PFOS exposure. Delayed eye opening was a recurrent finding in animal studies with exposure to 4 PFCAs and 2 PFSAs. Malformations predominately affecting the eyes were also noted following exposure to TFA. In epidemiological studies, increased risk of septal defects and/or conotruncal defects in the heart were associated with exposure to PFDA, PFDoDA and PFOS. Alterations in the development of the reproductive system were noted in relation to exposure to 8 PFCAs, 4 PFSAs, and HFPO-DA. In epidemiological studies, this was related to altered anogenital distance, altered hormone levels, and changes to the mean age of puberty onset. In laboratory animals, the most recurrent reproductive effects observed included altered hormone levels, decreased Leydig cell development, altered ovarian function, altered anogenital distance, delayed puberty, and abnormal mammary gland development.

7.2.6 Endocrine function (thyroid)

Some PFAS may act as endocrine disruptors and, more specifically, may have effects on thyroid function. Effects on the thyroid and adrenal glands were reported in studies for 28 PFAS. In epidemiological studies, an increased risk of thyroid diseases (for example, hyperthyroidism, hypothyroidism) was associated with exposure to PFOA, PFHxS, and PFOS. Alterations (increase and/or decrease) in the serum levels of thyroid-stimulating hormone, triiodothyronine, and thyroxine levels were the most recurrent evidence of PFAS endocrine disruption. These effects were examined in both epidemiological and laboratory studies and PFAS exposure was associated with these effects in juvenile and adult populations as well as in pregnant women (epidemiological studies only). In laboratory studies, alterations to thyroid gland weight (mainly increases but also decreases) and/or adrenal gland weight were reported following exposure to 5 PFCAs, 3 PFSAs, 2 FT-based substances, and 3 ether-PFAS. Histopathological alterations to the thyroid gland (mainly hypertrophy and hyperplasia but also adenoma and altered colloids) were reported following exposure to 4 PFCAs, PFHxS, N-EtFOSE, 2 FT-based substances, and

3 ether-PFAS, whereas histopathological alterations to the adrenal glands (including hypertrophy, hyperplasia, necrosis, atrophy, and vacuolation) were reported after exposure to 2 PFCAs and HFPO-DA.

7.2.7 Nervous system

Effects on the nervous system have not been studied as widely as other endpoints. However, recurrent effects have been associated with PFAS exposure in humans and/or animals for 14 PFAS. Both neurodevelopmental effects and neurological effects (observed during adulthood) have been investigated. In terms of neurodevelopmental effects, epidemiological studies have examined outcomes in relation to 7 PFCAs, 3 PFSAs, and FOSA. The studies found that exposure to these PFAS was associated with mixed effects on behaviour (for example, attention deficit hyperactivity disorder, autism spectrum disorder) and cognition (for example, learning, reading skills). In animal studies, neurodevelopmental effects such as behavioural deficits, altered spontaneous behavior, cognitive function, and/or altered motor activity in rodent offspring were reported following exposure to 3 PFCAs and 2 PFSAs. In terms of neurological effects, laboratory studies with 7 PFCAs, 2 PFSAs, 6:2 FTOH, and HQ-115 identified neurotoxicity (including cachexia, lethargy, delay in bilateral pupillary reflex, and tonic convulsions in response to stimuli), impaired cognition, and/or impaired motor activity (including grip strength and locomotor activity) in animal models. In epidemiological studies, exposure to PFOA was associated with cognitive impairment, and exposure to PFBS and PFOS in pregnant women was associated with decreased sleep quality.

7.2.8 Metabolism and body weight

Some PFAS have a structure similar to fatty acids, which activate peroxisome proliferator-activated receptors (PPARs). Since PPARs regulate lipid and glucose metabolism, it is thought that PFAS may also have an effect on body weight regulation and the development of diabetes. Results of studies investigating these endpoints in humans and/or animals were reported for 35 PFAS. In epidemiological studies, an increased prevalence of gestational diabetes and/or increased levels of diabetes biomarkers (for example, insulin resistance, serum levels of insulin and/or glucose) reported during pregnancy were found to be associated with exposure to 6 PFCAs and 3 PFSAs. However, these outcomes were inconsistently observed in youth and (non-pregnant) adults exposed to PFAS. In laboratory studies, increased levels of diabetes biomarkers were reported in adult animals following exposure to 4 PFCAs, PFOS, and 5 ether-PFAS. Levels were also increased in dams and juveniles exposed to PFOS.

In terms of body weight, in epidemiological studies in adults, exposure to 3 PFCAs, 3 PFSAs, and 2 FASA derivatives was associated with an increased incidence of obesity and/or obesity biomarkers (for example, waist circumference, body mass index). In children, the results were not as consistent; exposure to 7 PFCAs, 3 PFSAs, FOSA, and 8:2 Cl-PFESA was associated at times with increased body weights and at other times with decreased body weights and/or obesity biomarkers. In animal studies, decreased body weights were observed in most studies, although increased body weights were also reported for several PFAS, especially at low doses. Data were available for 9 PFCAs, 3 PFSAs, N-EtFOSE, 4 FT-based substances, 5 ether-PFAS, and HQ-115.

Alterations (mostly increases) in serum triglycerides and/or cholesterol levels were also associated with PFAS exposure in several epidemiological studies, including exposure to 4 PFCAs, 3 PFSAs, and 5 ether-PFAS. Conversely, serum lipid levels were mostly decreased in animal studies following exposure to 8 PFCAs, 4 PFSAs, 2 FASA derivatives, 3 FT-based substances, and 6 ether-PFAS. It has been suggested that the differences in the modulation of lipid homeostasis between humans and animals may be due to the large differences in exposure doses between humans and animals (Fragki et al. 2021).

7.2.9 Carcinogenicity

Although a number of epidemiological and animal studies have examined the association between exposure to PFAS and the occurrence of cancer, the data are limited primarily to PFOA and PFOS, with less data for a small number of other PFAS, including PFCAs, PFSAs, and FASAs. Recently, the International Agency for Research on Cancer (IARC) classified PFOA as being carcinogenic to humans (Group 1) and PFOS as possibly carcinogenic to humans (Group 2B) (Zahm et al. 2024). The findings for PFOA were based on sufficient evidence in experimental animals, strong mechanistic evidence (for epigenetic alterations and immunosuppression, as well as several other key characteristics of carcinogens), and limited evidence in humans (renal cell carcinoma and testicular cancer). The findings for PFOS were based on strong mechanistic evidence (for epigenetic alterations and immunosuppression, as well as several other key characteristics of carcinogens), limited evidence in experimental animals and inadequate evidence in humans. In terms of other PFAS, some individual epidemiological studies have noted increased risks for cancer (ATSDR 2021). For example, a study examining prostate cancer found an association between serum levels of PFHxS, PFDA, and PFUnDA and prostate cancer in men with a hereditary risk factor (first degree relative with prostate cancer) (Hardell et al. 2014). Another study found diagnoses in women (melanoma and uterine cancer) to be related to concentrations of PFNA, PFDA, and PFUnDA in their serum (Cathey et al. 2023). However, for the most part, the associations between exposure to PFAS other than PFOA and PFOS and the risk of cancer remains inconsistent. A further study investigated the health effects in a large population of the Veneto region of Italy where the surface, ground and drinking water had been contaminated with numerous PFAS. Researchers found increased mortality from malignant neoplastic diseases, including kidney cancer and testicular cancer in the exposed population (Biggeri et al. 2024).

Temkin et al. (2020) applied a weight of evidence approach (consideration of epidemiological data, *in vivo* data in animals, and *in vitro* data) using the Key Characteristics of Carcinogens framework for cancer hazard identification to evaluate 26 PFAS. The authors found that multiple PFAS exhibited several of the key characteristics of carcinogens (for example, induces oxidative stress, is immunosuppressive, alters cell proliferation, exhibits epigenetic alterations). They found that well-studied PFAS, such as PFOA and PFOS, exhibited up to 5 key characteristics.

7.3 Overview of the lowest observed adverse effect levels (LOAELs)

Table 5 provides a summary of the lowest doses at which adverse effects have been observed following oral exposure to PFAS in animal studies. With a focus on common endpoints of concern, data were found for 43 PFAS. The LOAELs refer to external experimental doses in

mg/kg bw/day that are associated with statistically significant adverse changes for a given endpoint. The compilation of values is not exhaustive, particularly for data-rich PFAS, where the focus was on the lower values. Toxicity studies in various animal models with various designs (for example, dose regimens, study duration, statistics) were identified and considered. The determination of a critical effect level depends in part on the selection of doses tested in a toxicity study and whether a no observed adverse effect level (NOAEL) was identified. Several of the LOAELs presented in Table 5 were the lowest dose tested in a study (that is, a NOAEL could not be determined). The lowest dose tested sometimes varied by more than an order of magnitude between studies.

To date, there has been no consensus among scientists on the most sensitive endpoints in animal studies for any one PFAS. This has resulted in various endpoints being selected as points of departure for risk assessments and is in part responsible for the wide array of toxicological reference values seen across governments and organizations worldwide. Recent assessments have concluded that effects on the immune system, which is the effect associated with the lowest serum PFAS levels in both animals and humans, are critical (EFSA 2020; US EPA 2022a, 2022b). However, the science is rapidly evolving and, as has been observed in the past, it is possible that new data may continue to show effects on other endpoints at lower levels.

Table 5. Overview of the lowest LOAELs (lowest observed adverse effect levels) identified for various endpoints of concern following oral exposure to PFAS in laboratory animals

Target	Health endpoint	Range of LOAELs [a] (mg/kg bw per day)	Number of PFAS[b]	References
Liver	Non-neoplastic histopathological lesions	0.01 to 300	20	IRDC 1978; NOTOX 1999; Covance Laboratories Inc. 2001; 3M 2008d; Butenhoff et al. 2002, 2009, 2012a; Perkins et al. 2004; Kirkpatrick 2005; DuPont 2008a, 2008b, 2008c, 2008d, 2008e, 2010a, 2010b, 2010c, 2012, 2013a, 2013b; Loveless et al. 2008, 2009; Stump et al. 2008; Ladics et al. 2008; Chengelis et al. 2009b; Gordon 2011; Hirata-Koizumi et al. 2012, 2015; Serex et al. 2014; Takahashi et al. 2014; Caverly Rae et al. 2015; Filgo et al. 2015; Kato et al. 2015; Mukerji et al. 2015; Quist et al. 2015; Xing 2016; Sheng et al. 2017; Wang J et al. 2017; ,; Chang et al. 2018;

Target	Health endpoint	Range of LOAELs [a] (mg/kg bw per day)	Number of PFAS[b]	References
				NTP 2019a; Wang X et al. 2019; Blake et al. 2020; Zhou et al. 2020; ECHA 2021a; Wang G et al. 2021
Liver	Neoplastic lesions	0.1 to 500	2	Butenhoff et al. 2012a; DuPont 2013b; Caverly Rae et al. 2015
Liver	Increased liver weight (sometimes concomitant with increased serum enzymes and/or altered liver lipid/glycogen contents)	0.002 to 300	26	Kennedy 1987; Harris and Birnbaum 1989; Kawashima et al. 1995; Liu et al. 1996; Covance Laboratories Inc. 1999, 2000; 3M 2001; Seacat et al. 2002; York 2003; Butenhoff et al. 2004b, 2012b; Kirkpatrick 2005; Luebker et al. 2005a; Miyata 2007; Das et al. 2008, 2015; DuPont 2008a, 2008b, 2008c, 2008d, 2008e, 2009a, 2010c; Lefebvre 2008; Son et al. 2008; Zhang et al. 2008, 2018b; Ding et al. 2009; Dong et al. 2009b; Lieder et al. 2009a; Xie et al. 2009; Mertens et al. 2010; Wolf et al. 2010; Fang et al. 2012a; Wan et al. 2014; Wang J et al. 2015; Zhong et al. 2016; Rushing et al. 2017; Zheng et al. 2017; Chang et al. 2018; Frawley et al. 2018; Huck et al. 2018; Lai et al. 2018; NCDPH 2018; Sheng et al. 2018; Wu et al. 2018; Conley et al. 2019, 2021; Guo et al. 2019, 2021a, 2021b; NTP 2019a, 2019b; Chen et al. 2021; Woodlief et al. 2021
Kidney	Increased kidney weight and/or altered clinical chemistry	0.13 to 1,000	18	Covance Laboratories Inc. 1999; NOTOX 1999; Butenhoff et al. 2004b, 2009; Kirkpatrick 2005; Asahi Glass 2006; Miyata 2007; DuPont 2008a, 2008b, 2008c, 2008d, 2008e, 2009a, 2010a, 2010b, 2010c, 2012, 2013a; Stump et al. 2008; Chengelis et al. 2009b; Ding et al. 2009; Dong et al. 2009; Loveless 2009; Gordon 2011; Hirata-Koizumi et

Target	Health endpoint	Range of LOAELs [a] (mg/kg bw per day)	Number of PFAS[b]	References
				al. 2012, 2015; Serex et al. 2014; Takahashi et al. 2014; Kato et al. 2015; Mukerji et al. 2015; Xing et al. 2016; NCDPH 2018; NTP 2019a, 2019b; Blake et al. 2020; ECHA 2021a
Kidney	Histopathological lesions	5 to 300	5	York 2003; Kirkpatrick 2005; Ladics et al. 2008; Lieder et al. 2009a; DuPont 2010a, 2010b, 2010c, 2013b; Caverley Rae et al. 2015; Klaunig et al. 2015; ECHA 2021b
Immune function	Altered immune response (reduced antibody response to an antigen, reduced resistance to disease, and/or altered cytokine response)	0.0004 to 100	5	Peden-Adams et al. 2008; Dong et al. 2009, 2011; Guruge et al. 2009; Fair et al. 2011; Bodin et al. 2016; DeWitt et al. 2016; Zhong et al. 2016; Rushing et al. 2017; Wang X et al. 2019, 2021
Immune function	Histopathological lesions or altered splenic cell subpopulations	0.03 to 315	11	Griffith and Long 1980; Covance Laboratories Inc. 2002; Kirkpatrick et al. 2005; Fang et al. 2008; Son et al. 2009; Hirata-Koizumi et al. 2015; Kato et al. 2015; Zhong et al. 2016; Rushing et al. 2017; Frawley et al. 2018; Guo et al. 2021c; Woodlief et al. 2021
Immune function	Decreased spleen and/or thymus weights	1 to 125	9	Yang et al. 2001; Kirkpatrick 2005; DuPont 2008a, 2008b, 2008c, 2008d, 2008e, 2009, 2012; Lieder et al. 2009b; Loveless et al. 2008; Fang et al. 2009, 2010; Kato et al. 2015; DeWitt et al. 2016; Zhong et al. 2016; NTP 2019a, 2019b; Rushing et al. 2017
Immune function	Reduced globulin levels, increased A/G ratio, and/or	0.2 to 250	7	DuPont 2007, 2008a, 2008b, 2008c, 2008c, 2008d, 2008e, 2013b; Lefebvre et al. 2008;

Target	Health endpoint	Range of LOAELs [a] (mg/kg bw per day)	Number of PFAS[b]	References
	reduced immunoglobulin G1 level			Loveless et al. 2009; Caverly Rae et al. 2015; NTP 2019a, 2019b
Immune function	Altered white blood cell counts	1 to 100	2	Gordon 2011; DuPont 2013a
Reproduction	Altered male reproductive system	0.01 to 500	14	Argus Research Laboratories Inc. 1999a; Covance Laboratories Inc. 1999; HC 2006; Miyata et al. 2007; Shi et al. 2007; DuPont 2008a, 2008b, 2008c, 2008d, 2008e, 2013a; Feng et al. 2009, 2010; Loveless et al. 2009; Shi et al. 2009a; Serex et al. 2014; Hirata-Koizumi et al. 2015; Kato et al. 2015; Mukerji et al. 2015; Li L et al. 2018; Singh and Singh 2018, 2019a; Zhou et al. 2018, 2020; NTP 2019a; ATSDR 2021; Yan et al. 2021
Reproduction	Altered female reproductive system	0.2 to 1,000	7	DuPont 2008a, 2008b, 2008c, 2008d, 2008e, 2013; Fair et al. 2011; Hirata-Koizumi et al. 2012; Kato et al. 2015; Miyata 2007; Mukerji et al. 2015; Chen et al. 2017; NTP 2019b; Wang X et al. 2018; Cao et al. 2020
Reproduction	Altered serum levels of reproductive hormones (testosterone, estradiol, LH, FSH, and/or progesterone)	0.2 to 200	7	Cook et al. 1992; Liu et al. 1996; Biegel et al. 2001; Seacat et al. 2002; Shi et al. 2007, 2009a, 2009b; Feng et al. 2009; Zhao et al. 2010; Li L et al. 2018; Chen et al. 2019; NTP 2019a; Singh and Singh 2019a; Cao et al. 2020; Yan et al. 2021
Reproduction	Adverse outcomes during gestation and/or lactation	0.4 to 1,000	10	Riker Laboratories Inc 1981; Argus Research Laboratories Inc. 1999a, 1999b, 1999c, 2000; Case et al. 2001; Luebker et al. 2005b; Das et al. 2008; Wolf et al. 2010; White et al. 2011; Hirata-Koizumi et al. 2012; DuPont 2013a; O'Connor et al. 2014; Kato et al. 2015; Lee et al. 2015; Mukerji et

Target	Health endpoint	Range of LOAELs [a] (mg/kg bw per day)	Number of PFAS[b]	References
				al. 2015; Chang et al. 2018; Blake et al. 2020
Development	Reduced postnatal survival	0.3 to 1.6	4	Stump et al. 1997; Butenhoff et al. 2004b; Luebker et al. 2005b; Abbott et al. 2007; Wolf et al. 2010; Xia et al. 2011; White et al. 2011; Chen et al. 2012
Development	Altered prenatal and/or postnatal growth (low birth weight, reduced body weight gain, delayed eye opening, reduced ossification, skeletal alterations)	0.3 to 1,000	14	Riker Laboratories Inc. 1980; Hazleton Laboratories America Inc. 1983; Harris and Birnbaum 1989; Argus Research Laboratories Inc. 1999d, 1999e, 1999f; Luebker et al. 2005a, 2005b; Lau et al. 2006; Das et al. 2008, 2015; Loveless et al. 2009; DuPont 2010c; Hu et al. 2010; Onishchenko et al. 2011; Gordon 2011; Hirata-Koizumi et al. 2012, 2015; Asahi Glass 2014; Iwai and Hoberman 2014; Rogers et al. 2014; Takahashi et al. 2014; Koskela et al. 2016; Feng et al. 2017
Development	Altered development of the reproductive system (altered sexual hormones, delayed puberty, decreased weight and/or function of male organs, altered function/morphology of female organs)	0.01 to 200	8	Lau et al. 2006; Macon et al. 2011; Das et al. 2015; Tucker et al. 2015; Zhong et al. 2016; Feng et al. 2017; Ramhøj et al. 2018, 2020; Song P et al. 2018; Conley et al. 2019; Singh and Singh 2019a; Li C et al. 2021, Li Z et al. 2021; Zhang et al. 2021a
Development	Altered thyroid hormones	0.4 to 200	3	Lau et al. 2003; Luebker et al. 2005a; Feng et al. 2017; Ramhøj et al. 2020
Development	Increased fetal/pup liver	0.01 to 10	6	Harris and Birnbaum 1989; Hines et al. 2009; Stump et al. 2008;

Target	Health endpoint	Range of LOAELs [a] (mg/kg bw per day)	Number of PFAS[b]	References
	weight(s) and/or metabolic alterations (altered serum cholesterol, glucose, insulin and/or leptin level, increased body weight, reduced fetal liver glycogen accumulation)			Wan et al. 2014; Das et al. 2015; Quist et al. 2015; Zhong et al. 2016; Chang et al. 2018; Conley et al. 2019, 2021
Endocrine	Adrenal gland (altered weight(s), increased cortisol or corticosterone, histopathologic al changes)	0.01 to 100	8	3M 2007b; DuPont 2008a, 2008b, 2008c, 2008d, 2008e, 2010a, 2010b, 2010c; Fang et al. 2008, 2009; Gordon 2011; Hirata-Koizumi et al. 2015; Kato et al. 2015; Hadrup et al. 2016; NTP 2019a, 2019b
Endocrine	Thyroid gland (altered weight(s), altered T3, T4 and/or TSH, histopathologic al changes)	0.1 to 125	18	Harris et al. 1989; Covance Laboratories Inc. 2001; Butenhoff et al. 2002, 2009, 2012a, 2012b; Seacat et al. 2002; Lau et al. 2003; Thibodeaux et al. 2003; Kirkpatrick 2005; Luebker et al. 2005a; 3M 2007b; DuPont 2007, 2012; Ladics et al. 2008; Loveless et al. 2009; Yu et al. 2009; Gordon 2011; Serex et al. 2014; Hirata-Koizumi et al. 2015; Feng et al. 2017; Ramhøj et al. 2018, 2020; Wang X et al. 2018; Conley et al. 2019, 2021; NTP 2019a, 2019b; Cao et al. 2020; Hong et al. 2020; ECHA 2021b
Nervous system	Decreased grip strength, decreased motor activity, alterations in the	0.5 to 150	7	Griffith et al. 1980; Miyata 2007; Butenhoff et al. 2012b; Hirata-Koizumi et al. 2015; Kato et al. 2015; Salgado et al. 2016; Kawabata et al. 2017b

Target	Health endpoint	Range of LOAELs [a] (mg/kg bw per day)	Number of PFAS[b]	References
	dopaminergic system, delayed pupillary reflex, hypoactivity, and prostration			
Nervous system	Neurodevelopmental alterations (spontaneous and/or cognitive behaviour, alteration in the hippocampus)	0.3 to 9.2	3	Johansson et al. 2008; Onishchenko et al. 2011; Zeng et al. 2011; Viberg et al. 2013; Wang Y et al. 2015; Koskela et al. 2016; Goulding et al. 2017; Mshaty et al. 2020
Metabolism and body weight	Effects on glucose homeostasis	0.01 to 1,000	12	Ding et al. 2009; Hines et al. 2009; Gordon 2011; Fang et al. 2012b; Hirata-Koizumi et al. 2012; Serex et al. 2014; Wan et al. 2014; Kato et al. 2015; Bodin et al. 2016; Zheng et al. 2017; Huck et al. 2018; Lai et al. 2018; NCDPH 2018; Wu et al. 2018; Zhou et al. 2020; Chen et al. 2021
Metabolism and body weight	Increased serum lipids	0.01 to 125	6	Butenhoff et al. 2002; Shi et al. 2007, 2009; Huck et al. 2018; Wu et al. 2018; Chen et al. 2021; Conley et al. 2021
Metabolism and body weight	Decreased serum lipids	0.01 to 1,000	23	Covance Laboratories Inc. 1999, 2001, 2002; Seacat et al. 2002; Kirkpatrick 2005; Luebker et al. 2005a; Ladics et al. 2008; Loveless et al. 2008, 2009; Chengelis et al. 2009b; Ding et al. 2009; DuPont 2009a,b, 2010a, 2010b, 2010c, 2012, 2013a; Bijland et al. 2011; Gordon 2011; Butenhoff et al. 2012a, 2012b; Fang et al. 2012a; Hirata-Koizumi et al. 2012; Takahashi et al. 2014; Kato et al. 2015; Quist et al. 2015; Wang J et al. 2017; Chang et al. 2018; Lai et al. 2018; NCDPH 2018; Sheng et al. 2018; Singh and Singh 2018; Wu et al. 2018; Zhang H et al. 2018; Conley et al.

Target	Health endpoint	Range of LOAELs [a] (mg/kg bw per day)	Number of PFAS[b]	References
				2019, 2021; NTP 2019a, 2019b; Blake et al. 2020; Zhou et al. 2020; ECHA 2021a
Metabolism and body weight	Increased body weight	0.01 to 100	6	Hines et al. 2009; Loveless et al. 2009; Zhang H et al. 2018; Blake et al. 2020; Chen et al. 2021
Metabolism and body weight	Decreased body weight	0.4 to 1,000	18	Griffith and Long 1980; Hazleton Laboratories America Inc. 1983; Harris and Birnbaum 1989; Permadi et al. 1993; Kawashima et al. 1995; Argus Research Laboratories Inc. 1998, 1999a, 1999b, 1999d; NOTOX 1999; Case et al. 2001; Luebker et al. 2005a; Shi et al. 2007, 2009; Ladics et al. 2008; Lefebvre et al. 2008; Loveless et al. 2008, 2009; Stump et al. 2008; Ding et al. 2009; Dong et al. 2009; Fang et al. 2009; Xie et al. 2009; DuPont 2012, 2013b; Hirata-Koizumi et al. 2012, 2015; Asahi Glass 2014; O'Connor et al. 2014; Takahashi et al. 2014; Caverly Rae et al. 2015; Das et al. 2015; Kato et al. 2015; Lee et al. 2015; Mukerji et al. 2015; Wang Z et al. 2015; Hadrup et al. 2016; Xing et al. 2016; Kawabata et al. 2017b; Frawley et al. 2018; Sheng et al. 2018; Conley et al. 2019, 2021; NTP 2019a, 2019b; Blake et al. 2020; NTP 2020; ECHA 2021b; Wang G et al. 2021

A/G: albumin/globulin; FSH: follicle-stimulating hormone; LH: luteinizing hormone; T3: triiodothyronine; T4: thyroxine; TSH: thyroid-stimulating hormone

[a] The indicated LOAEL was the lowest dose tested that yielded a response. Therefore, the actual LOAEL may not have been observed and could be lower.

[b] The number of PFAS represents the number of different substances for which data have been found. There may be more than 1 study with an identified LOAEL for a given PFAS.

Source: Sanexen (2021)

7.4 Mode of action

The mechanisms of action for PFAS-induced effects are not well understood. Many of the different effects induced by PFAS are believed to be mediated in part by the activation of peroxisome proliferator-activated receptor alpha (PPARα), which modulates lipid and glucose homeostasis, cell proliferation and differentiation, and inflammation. However, studies in animals in which the expression of PPARα has been removed have also shown adverse effects for some endpoints such as liver steatosis (Das et al. 2017) and developmental toxicity in mice (Abbott et al. 2009), suggesting that mechanisms other than PPARα activation are also involved. It is more likely that multiple nuclear receptors, including constitutive activated/androstane receptor (CAR), play a role in mediating PFAS-induced effects in the various target organs (Elcombe et al. 2010). In high-throughput *in vitro* studies, the US EPA's Tox21 (a US federal research collaboration) data set shows that short- and long-chain PFCAs, PFSAs, and FTOHs can interact with around 2 dozen different nuclear receptors, with the number of receptors varying depending on the individual PFAS (Goodrum et al. 2021). In a more recent study using Tox21 screening data, 32 PFAS were evaluated for their bioactivity in more than 75 assay endpoints (for example nuclear receptors, stress response, and metabolism) to better understand the effect of PFAS on targets and pathways. An enrichment analysis comparing PFAS to non-PFAS compounds in the Tox21 compound library found that PFAS are enriched in the assays targeting nuclear receptors (that is, estrogen receptor α, retinoid X receptor, peroxisome proliferator-activated receptors γ and δ, mitochondrial membrane potential), stress response (that is, aromatase, antioxidant response element, p53) and metabolism (that is, a high affinity for CYP2C9) (Ooka et al. 2024).

Several studies have begun investigating adverse outcome pathways (AOPs) relevant to PFAS exposure, although none have yet been endorsed by the OECD. AOPs describe a molecular initiating event (MIE) that can be linked to an adverse outcome (AO) through multiple key events (KE) connected by key event relationships (KER) occurring successively at different levels of biological organization (Ankley 2010). Kaiser et al. (2022) used data from epidemiological studies as well as molecular events and AOs identified in *in vivo* and *in vitro* studies to explore the relationship between PFAS exposure and metabolic outcomes. They found aspects of 3 existing AOPs could be connected with exposure to PFAS: 1) hypertension, through peptide oxidation (MIE); 2) increased hypertension through inhibition of the serotonin transporter activity (MIE) leading to increased intracellular calcium (KE) and activated phospholipase C (KE); and 3) obesity through epigenetic modification of PPARγ (MIE) leading to activation of PPARγ (KE) and increased adipogenesis (KE). Lu et al. (2023) proposed 5 new AOPs for male reproductive toxicity following exposure to perfluoroalkyl acids: 1) changes in membrane permeability leading to reduced sperm motility; 2) disruption of mitochondrial function leading to sperm apoptosis; 3) decreased gonadotropin-releasing hormone expression in hypothalamus leading to reduced testosterone production in male rats; 4) activation of the p38 signaling pathway leading to disruption of the blood-testis barrier in mice; 5) inhibition of p-FAK-Tyr407 activity leading to the destruction of the blood-testis barrier. Neagu et al. (2021) have suggested that the mode of action of PFAS immunotoxicity involves DNA methylation, altered gene expression and altered cytokine regulation. Perfluorinated chemicals have also been linked with an AOP that describes

adverse human neurodevelopmental effects resulting from xenobiotic interference with thyroid serum binding protein transthyretin (Janus et al. 2023).

In terms of the mode of action and carcinogenicity of PFAS, there is little evidence to suggest that PFAS are directly mutagenic. Rather PFAS linked to cancer likely act through non-genotoxic mechanisms. In a review, Pesonen and Vähäkangas (2024) investigated tissue-specific mechanisms potentially responsible for tumour formation in the liver, kidney, testicles and breast following PFAS exposures. The observed molecular changes included the disturbance of signaling via nuclear receptors, the disruption of lipid metabolism and endocrine balance and the induction of oxidative stress and epigenetic changes. Similarly, Boyd et al. (2022) reviewed the mechanisms of action in relation to PFAS exposure and proposed 3 major pathways of action for PFAS carcinogenicity: metabolic alteration, endocrine disruption, and epigenetic perturbation. Studies of firefighters in the US found serum PFAS concentrations to be linked with accelerated epigenetic age and locus-specific DNA methylation. These toxicity biomarkers are associated with many diseases, including cancer (Goodrich et al. 2021a).

7.5 Mixtures and cumulative effects on human health

On the basis of environmental sampling and biomonitoring data, it is evident that humans are typically exposed to multiple PFAS. Despite a lack of toxicity data for many PFAS, it is also evident that studied PFAS have the potential to have effects on similar organs and systems (for example, liver, immune system, thyroid, serum lipids). Given the combined exposure to multiple PFAS and the similarity of affected endpoints, there are concerns that exposure to PFAS could be associated with cumulative effects (ECHA 2022a). Most toxicology and epidemiology studies have evaluated the effects associated with exposure to a single PFAS, but, though this approach is useful in providing robust, specific, and unbiased information on potential health effects, these studies are not typically designed to assess the potential for interaction, non-additivity of effects, or cumulative effects at lower doses. The hazards of exposure to PFAS mixtures are largely unknown. A limited number of *in vivo* and *in vitro* studies have evaluated the interactive effect of multiple PFAS on different endpoints (see Ojo et al. 2021 for a summary as well as Addicks et al. 2023). Antagonistic, synergistic, and additive effects have all been observed in different studies and may be dependent on the species, dose levels, dose ratios, duration of exposure, and mixture components (Ojo et al. 2021).

Epidemiological studies have traditionally been limited with respect to the study of chemical mixtures (for example, mixtures of multiple PFAS) because many of the individual chemicals are correlated with one another (that is, people exposed to higher levels of one are often also exposed to higher levels of another). This makes it difficult to identify unique contributions of individual chemicals or to examine cumulative effects (Braun et al. 2016). In recent years, several novel statistical tools have been developed to overcome these limitations (Carrico et al. 2015; Bobb et al. 2018; Keil et al. 2019). Using these novel and continually emerging tools, epidemiologists are beginning to provide evidence for the cumulative health effects of exposure to PFAS mixtures (Borghese et al. 2022; Rosato et al. 2022; Goodman et al. 2023; Palaniyandi et al. 2023; Kuiper et al. 2024). This work is also expected to help identify whether there are individual PFAS within a mixture that may be the “bad actors” driving a mixture effect. An ongoing challenge in this area is the identification of important statistical mixtures—that is,

mixtures of PFAS to which humans are actually exposed—as opposed to those for which biomonitoring data are correlated for other reasons (for example, shared physiological processes, such as distribution and excretion pathways).

7.6 New approach methods (NAMs) for human health hazard

NAMs (described previously in section 6.2.5) provide a time- and resource-efficient alternative to traditional animal testing and are increasingly being used to provide hazard and risk information for chemical prioritization and human health risk assessment, reducing the reliance on mammalian models. Recently, frameworks outlining fit-for-purpose criteria to evaluate and achieve credibility in the use of NAMs in regulatory contexts have been developed to address data-poor chemicals (such as PFAS) and establish confidence in the scientific underpinning of NAMs among international stakeholders (Ball et al. 2022; van der Zalm et al. 2022; Magurany et al. 2023; ICCVAM 2024).

The utility of screening thousands of chemicals using high-throughput *in vitro* toxicity testing (US EPA) has been demonstrated under the existing toxicity forecasting (ToxCast) program (Judson et al. 2010; Reif et al. 2010; US EPA 2015) and increasingly through collaborative efforts such as the Accelerating the Pace of Chemical Risk Assessment (APCRA) initiative (Paul Friedman et al. 2020). Multiple PFAS are currently listed within the ToxCast chemical inventory, which reveals characteristics that could be used to identify PFAS based on their potential for immunotoxicity (Naidenko et al. 2021), carcinogenicity (Singh and Hsieh 2021), or target organ toxicity (Massarsky et al. 2022).

PFAS (with the exception of PFOS and PFOA) are largely considered to be data-poor, making this group a suitable candidate for high-throughput screening (HTS) and NAM-based approaches to gain a better understanding of distinct features across the class. NAMs have been used to generate information using HTS techniques for related subsets of chemicals with varied characteristics (that is, physicochemical and structural properties) and used to model and characterize hazards, such as for the purpose of read-across (Kuseva et al. 2021). Implementing *in vitro* and *in silico* analyses to investigate mechanistic properties of PFAS has indicated direct interaction with the nuclear receptor peroxisome proliferator activated receptor (PPAR) and other transcription factors (Azhagiya Singam et al. 2020, 2024; Behr et al. 2020; Almeida et al. 2021; Houck et al. 2021; Tachachartvanich et al. 2022; Sadrabadi et al. 2023; Barutcu et al. . However, PPAR activation alone does not fully explain the toxicity of PFAS. Additional mechanisms leading to effects such as disrupted cholesterol metabolism and regulation, immunotoxicity, and carcinogenicity have also been identified as playing a role, wherein NAMs are being developed to identify *in vitro* proxies to characterize and quantify these outcomes (Naidenko et al. 2021; Singh and Hsieh 2021). Government of Canada efforts to use NAMs to fill data gaps for PFAS are further described in section 8.1.2.

8 Domestic and international actions on PFAS

KEY POINTS ON DOMESTIC AND INTERNATIONAL ACTIONS ON PFAS

- The manufacture, use, sale, offer for sale, and import of certain PFAS (PFOS, PFOA, LC-PFCAs, and their salts and precursors) and products that contain them are prohibited in Canada through the PCTSR under CEPA, with a limited number of exemptions. However, other PFAS are not prohibited and could be used as alternatives to prohibited PFAS.
- New PFAS that are manufactured or imported into Canada are assessed and risks are managed as required through the NSNR.
- The CFIA is working with the provinces and continuing to engage the provinces, municipalities and the biosolids industry on the implementation of an interim standard for PFAS in biosolids imported or sold in Canada as fertilizers.
- The Government of Canada is actively researching the environmental and health impacts of PFAS, including the use of new approach methods to address multiple PFAS simultaneously.
- Environmental and human monitoring and surveillance programs are ongoing, in addition to specific initiatives to address subpopulations who may be more susceptible or highly exposed, including pregnant women and children, First Nation, Metis and Inuit populations, and firefighters.
- Targeted and non-targeted approaches have the potential to contribute to the characterization of environmental profiles, environmental exposures, and health effects.
- Future research will include studies of the effects of single PFAS and real-life mixtures on both ecological and human health endpoints.
- Additional action to address PFAS in Canada is taking place through initiatives such as the Federal Contaminated Sites Action Plan and guidelines for soil and drinking water quality.
- The Stockholm Convention on Persistent Organic Pollutants is an important international agreement that requires that measures be taken to prohibit or restrict a number of PFAS, including PFOA, PFOS, and PFHxS. The listing of LC-PFCAs is also being considered.
- Many other jurisdictions, including the US and the EU, are taking specific action on PFAS.

8.1 Domestic activities

8.1.1 Risk assessment and management under CEPA

In Canada, 3 well-defined subgroups of PFAS have been assessed under CEPA. They have been found to be of concern for the environment and therefore have been added to Schedule 1 of CEPA:

- PFOS and its salts and precursors (EC 2006; HC 2006);
- PFOA and its salts and precursors (EC, HC 2012); and
- LC-PFCAs and their salts and precursors (EC 2012).

These Schedule 1 substances capture entire subgroups based on moieties of concern.

A 2006 Risk Management Strategy for PFOS stated that the ultimate environmental objective was to reduce concentrations of PFOS in the Canadian environment to the lowest level possible (Government of Canada 2006). In 2008, the *Perfluorooctane Sulfonate and Its Salts and Certain Other Compounds Regulations* were published to prohibit the manufacture, import, sale, and use of PFOS, with a limited number of exemptions to allow for the transition to alternatives (Government of Canada 2008).

In 2010, the Government of Canada initiated an Environmental Performance Agreement respecting PFCAs and their Precursors in Perfluorochemical Products Sold in Canada. Over the term of this voluntary 5-year agreement, the 4 participating companies met their commitment to eliminate residual PFOA, residual LC-PFCAs, and residual precursors from their perfluorochemical products sold in Canada.

The manufacture, use, sale, offer for sale, and import of PFOA, LC-PFCAs, their salts and precursors, and products that contain them, have been prohibited since 2016 under the PCTSR, with a limited number of exemptions (Canada 2016). For example, exemptions for PFOA and LC-PFCAs in AFFF for limited uses and in all manufactured items were provided. PFOS was also added to the regulations in 2016, which maintained the regulatory requirements of the *Perfluorooctane Sulfonate and Its Salts and Certain Other Compounds Regulations* and removed certain exemptions. As a result, the *Perfluorooctane Sulfonate and Its Salts and Certain Other Compounds Regulations* were repealed. The PCTSR currently address 94 PFAS identified as being present in Canadian commerce through the DSL, as well as other PFAS for which the presence in Canada is unknown.

In 2018, a consultation document was published on proposed amendments to the PCTSR (Government of Canada 2018a). The proposed regulatory approach was to continue to phase out the use of the toxic substances currently controlled by the regulations. Some exemptions were initially available for PFOS, PFOA, and LC-PFCAs to allow specific market sectors to transition to using alternatives. Comments and information received in response to the consultation document were considered in the development of proposed Regulations, which were published on May 14, 2022, in the *Canada Gazette*, Part I (Canada 2022a). Concurrently, a proposed Order Amending Schedule 3 to CEPA (the Export Control List) was published. In compliance with Canada's obligations under the Rotterdam Convention, this would add PFOA and LC-PFCAs to the Export Control List at the same time, making their exports subject to the *Export of Substances on the Export Control List Regulations,* similar to PFOS, which is already listed on the Export Control List.

New substances (that is, substances not listed on the DSL) that meet trigger quantities which are specified in the NSNR are required to be notified to the government, so that they can be assessed for potential risks to human health and the environment and, if appropriate, control measures can be put in place before they are imported into or manufactured in Canada.

Substances are not grouped when they are assessed under the NSNR; each new substance is notified to the government at a different point in time and is individually evaluated for potential

risks to the environment and the general public originating from industrial and other relevant uses (for example, consumer uses, cosmetics, pharmaceuticals). Over 290 new PFAS have been notified to the New Substances program and have been subject to actions intended to mitigate the risks to human health or the environment. These include 8 Ministerial Conditions (Canada 1996) and, beginning in 2004, 4 Ministerial prohibitions (Canada 2004). A Ministerial Condition is a control measure imposed on a new substance to minimize a suspected risk to human health or the environment, in response to a suspicion that the substance may meet the criteria for “toxic” under CEPA. Substances subject to Ministerial Conditions are not eligible for addition on the DSL and must be notified to the New Substances program whenever a new notifier wishes to import or manufacture the substance.

A new substance assessment takes into consideration potential risks concerning the notified activities as well as any other possible activities involving the substance. When there is suspicion that a significant new activity (SNAc) may result in the substance becoming toxic, the SNAc provisions of CEPA (see section 85 of CEPA) can be applied to a new substance with the publication of a SNAc Notice in the *Canada Gazette*, Part I. A SNAc Notice describes activities that may result in a significantly greater quantity or concentration of the new substance in the environment, or a significantly different manner or circumstance of exposure to the new substance. Under CEPA, a new substance not on the DSL, or an existing substance on the DSL, may be subject to the SNAc provisions of the Act, which applies to anyone using the substance. Any person wishing to engage in a significant new activity in relation to the substance is required to submit a Significant New Activity Notification (SNAN) to the Minister of the Environment containing all the information prescribed in the Notice prior to using the substance for the proposed activity. After the complete information is received, the Minister of the Environment and the Minister of Health will conduct risk assessments of the substance in relation to the proposed SNAc within the timelines set out in the Notice. For new substances not on the DSL, a SNAc Notice may allow the intended use of the substance described in the New Substances Notification. A new substance subject to a SNAc Notice may become eligible for listing on the DSL. Until the new substance is added to the DSL, other persons must continue to notify the manufacture or import of the new substance as specified by the NSNR.

Recent initiatives to gather information to assist the risk management of PFAS include:

- a mandatory notice with respect to certain PFAS was published under section 71 of CEPA on July 27, 2024, with a reporting deadline of January 29, 2025. The purpose of this notice was to collect information on certain PFAS substances, either alone, in mixtures, products, or manufactured items in Canadian commerce for the calendar year 2023.
- a consultation document on the proposed addition of 131 individual PFAS to the National Pollutant Release Inventory (NPRI) was published September 2024. Reporting requirements apply to entities who meet the definition and thresholds listed in the notice. A decision on the final requirements is expected to be published in the Canada Gazette in 2025 with the reporting taking place in the following year for releases of PFAS that occurred during the 2025 calendar year.

8.1.2 Planned and future research, monitoring, and surveillance

8.1.2.1 Ecological

Canadian government research has been ongoing since the early 2000s and has been critical in informing early regulatory action in Canada and internationally. In addition, Canadian research and monitoring have contributed significantly to the understanding of global concentrations and trends of PFAS and are well positioned to support the United Nations Global Monitoring Plan now and in the future. Some recent examples of Government of Canada research projects that have garnered preliminary data include: 1) a research project using targeted analysis (LC-PFCA, PFOS, PFOA, and novel PFAS, including zwitterionic and cationic compounds) and non-targeted methods to investigate bioaccumulation in St. Lawrence River fish; 2) a research project on LC-PFCAs, PFOS, PFOA, and other PFAS (fluorotelomer acids, perfluoropolyether carboxylates, perfluoropolyether sulfonates, chlorine-substituted perfluoroalkyl acids) in wastewater influent, effluent, and Lake Ontario sediment cores; 3) a field-based study on the accumulation of LC-PFCAs, PFOS, and PFOA in freshwater fish and mussels in wastewater effluent-receiving environments; and 4) a field-based study on the accumulation and chronic effects of PFAS in freshwater snails exposed to surface water downstream of Hamilton International Airport. A study to examine the toxicity and bioaccumulation of 4 short-chain (C4 and C6) perfluoroalkyl substances (2 PFCAs and 2 PFSAs) in 3 freshwater species (snail [*Planorbella pilsbryi*], amphipod [*Hyalella azteca*], and frog [*Rana pipiens*]) has also been completed, with data analysis currently in its final stages. The main objective of this study was to determine if the size (chain length) or the carboxylic or sulfonic acid moiety of these compounds affected toxicity and bioaccumulation in aquatic organisms. Future research is building from these single life-stage/generation and single compound exposures to include multi-generational effects and mixture assessments. Research on the acute and chronic toxicity of short-chain (PFBS, PFBA) and ultra-short chain PFAS (trifluoromethane sulfonic acid, TFMS, C1 and trifluoroacetic acid, TFA, C2) is also being conducted on invertebrates (*Daphnia magna* and *Hydra vulgaris*). In addition, several effects-based projects initiated in 2019 are ongoing projects that encompass bioaccumulation, biomagnification, acute and chronic toxicity, multi-generational effects, and fish and snail metabolism.

In addition to discrete research projects, the Government of Canada conducts extensive monitoring in various ecosystems and biota as described in section 4.2. Ongoing monitoring programs include air monitoring in Alert, Nunavut, the Great Lakes Basin, and at various sites through the GAPS network; water quality monitoring at 26 sites including transboundary waters and collection of fish tissues from water bodies throughout Canada; collection of seawater and animal tissues (polar bears, ringed seals, and Arctic char) or eggs (seabirds) in Arctic and Subarctic locations as part of the NCP core EMR projects; monitoring of fish and wildlife across Canada as part of research and monitoring programs under the CMP; and monitoring of influent, effluent, and solids residuals from municipal WWTPs.

Government of Canada researchers have also published numerous review papers on PFAS in relation to ecotoxicology (summarized in Ankley et al. 2021), research priorities to achieve sustainable environmental quality (Fairbrother et al. 2019), oceans (Muir and Miaz 2021), the

Arctic (Muir et al. 2019; Muir and de Wit 2010), marine mammals (Fair and Houde 2018; Barrett et al. 2021), and wildlife (De Silva et al. 2021; Houde et al. 2006, 2011).

Future Government of Canada work is planned to generate transcriptomic, as well as proteomic and lipidomic, dose-response data for zebrafish embryos and adults and northern leopard frog embryos and tadpoles exposed to single PFAS, simple mixtures, and real-world mixtures. This proposed research is relevant to other ecological species and to human health; Government of Canada researchers have shown how transcriptomic data from zebrafish embryo assays can be linked to adverse outcome pathways to make inferences about cross-species apical effects that could result from exposure (Xia et al. 2021). Furthermore, improvements in both targeted and non-targeted chemical analyses (reviewed in De Silva et al. 2021), paired with passive sampling techniques and NAM assays, have the potential to contribute to the characterization of PFAS mixtures that may be found in the environment. Finally, several PFAS have been included in Version 2 of the Ecological Risk Classification of organic substances (ERC2; ECCC 2022a). ERC2 is a high-throughput prioritization method that uses many sources of NAM data, including *in silico*, *in chemico*, and *in vitro* data, to complement traditional *in vivo* sources.

8.1.2.2 Human health

The Government of Canada has been actively carrying out research on the effect of PFAS exposure on the health of Canadians since 2008. This includes laboratory-based research evaluating the health effects posed by PFAS, including PFCAs, PFSAs, fluorotelomers, and sulfonamides (Curran et al. 2008; Lefebvre et al. 2008; Dong et al. 2016; Reardon et al. 2021; Rowan-Carroll et al. 2021), and epidemiological research evaluating the potential effects of PFAS (for example, PFOA, PFOS, PFHxS) exposure during pregnancy on both maternal and child health, such as gestational weight gain, gestational hypertension, pre-eclampsia, gestational diabetes, infertility, pro-inflammatory cytokines, low birth weight, child IQ, neurodevelopment, and newborn markers of immune system development, androgenic endocrine disruption, and metabolic function (Ashley-Martin et al. 2015, 2016, 2017; Vélez et al. 2015; Shapiro et al. 2016; Arbuckle et al. 2020; Borghese et al. 2020; Goodman et al. 2023; Palaniyandi et al. 2023). This research also includes epidemiological studies on the association between different PFAS (for example, PFOA, PFNA, PFDA, PFUnDA, PFHxS, PFOS) as individual chemicals or mixtures and several biochemical markers of thyroid, liver and kidney function and glucose metabolism in the general Canadian population (Borghese et al. 2022; Cakmak et al. 2022). Additionally, toxicological research to advance hazard characterizations for PFAS congeners that are not well studied (that is, PFUnDA) is being planned to increase knowledge on structure-activity relationships between short- and long-chain PFAS.

To continue to improve the understanding of PFAS, Health Canada is leading a collaborative case study (working with other jurisdictions and academics including the United States, Singapore, University of Ottawa, and the University of Birmingham) under the international governmental initiative APCRA. In this case study, transcriptomic points of departure were derived from human liver microtissues exposed to PFAS in order to characterize potency and additivity. Secondly, the analyses correlated chemical potency in subcategorized PFAS with carbon chain-length or based on PFAS mixture composition (Reardon et al. 2021; Rowan-Caroll et al. 2021; Addicks et al. 2023). This enabled ranking based on potency (that is, potential to

induce liver effects) using gene expression data. *In vitro* derived estimates for PFOS and PFOA were found to be more protective when compared to traditional apical points of departure, and common underlying mechanisms of PFAS-induced liver perturbations were identified through altered cholesterol biosynthesis and lipid metabolism, as well as PPARα activation (Rowan-Carroll et al. 2021). Further investigations under this initiative are underway to further refine toxicokinetic models (Lin et al. 2023) and evaluate key endpoints used as categorization targets for future PFAS screening, including the development and validation of NAMs such as 3D liver spheroid model and zebrafish embryo model.

In addition, the Government of Canada is conducting laboratory research on PFOA and PFOS to reveal the mechanisms underlying the suppression of antibody production using mouse models. Research is also ongoing to model the dose-response behaviour of various PFAS in the Canadian population. The research efforts between the Government of Canada and international partners are generating high-throughput toxicokinetic data to extrapolate animal dose responses and *in vitro* biological concentrations response into daily population exposure levels. In parallel, laboratory activities have been initiated to investigate potential markers of immune suppression from animal studies that can be identified in humans. This knowledge gathering will support the development of toxicokinetic models, providing both regulators and scientists with tools to predict exposure across different PFAS and identify potential markers of altered immune functions.

Government of Canada research laboratories have also been focused on improving analytical detection methods for measuring PFAS in different exposure media. Analytical methods were developed to characterize a broad range of PFAS using standard analytical or suspect screening approaches. These methods are being applied for various environments and media such as blood, human milk, umbilical cord blood, drinking water, food, and house dust (Kubwabo et al. 2004, 2005, 2013; Monroy et al. 2008; Rawn et al. 2022a, 2022b). These methods have proven to be important for standardizing the measurement of PFAS within environment and population surveys.

There is also research to help characterize and understand PFAS exposure and effects on subpopulations who may be more susceptible or highly exposed. Many of the studies leverage the MIREC Research Platform. Using interview data and plasma PFAS concentrations, Hall et al. (2024) reported associations between more frequent use of certain personal care products during pregnancy (for example, nail care products, fragrances, makeup, hair products) and higher first trimester plasma concentrations of PFOS and PFOA in MIREC participants (2008-2011). Similar results were observed between prenatal and postnatal personal care product use with certain PFAS measured in human milk. Research is in progress to examine links between diet quality and PFAS concentrations in MIREC youth participants. Given that PFAS may alter immune function, research is also underway to characterize PFAS concentrations during pregnancy and the resulting maternal and child antibody response to common vaccines (that is, measles, mumps, rubella, and varicella). PFAS may also impair liver function during pregnancy and throughout the life-course, and research on the potential hepatotoxic effects of PFAS concentrations during pregnancy is underway. MIREC researchers recently completed analysis of an additional suite of 40 PFAS (including legacy, alternative and precursor compounds) in

women 10 years postpartum (Borghese et al. 2024), and research into the health effects of exposure to these PFAS is forthcoming. Additionally, an analysis of 40 PFAS (including legacy, alternative, and precursor compounds) is underway in a sample of women from the CARTaGENE cohort in Quebec and a sample of pregnant people from the P3 cohort in Alberta. Related research will examine associations with longitudinal health indicators, starting with the age at onset of menopause. Using data from the CHMS, future work could also explore exposure to PFAS, health outcomes, and several factors of vulnerability (for example, age, socioeconomic status, racial/cultural origin). Using data from the Plastics and Personal Care Products Use in Pregnancy (P4) study, the extent to which infants are exposed to PFAS in human milk and formula as well as whether maternal personal care product and food consumption in the early postpartum period affects PFAS concentrations in human milk will be studied.

Monitoring and surveillance activities, such as those conducted through the CHMS and the MIREC longitudinal study, are continuing to collect and analyze biospecimens for historical and replacement PFAS and their precursors and metabolites. Legacy, alternative and precursor PFAS (approximately 40 PFAS analytes) are planned to be assessed in CHMS cycle 6 (2018–2019) biobank samples covering population aged 3 to 79 years. The analysis to be conducted in 2,500 samples will ensure that the results (expected to be available in 2026) are representative of the Canadian population. The same set of PFAS will also be measured in CHMS cycle 8 (2025-2027) enabling an assessment of potential changes in exposure in the Canadian population over time for several PFAS previously not measured in the population of Canada.

Environmental exposures to PFAS have been monitored through the Canadian TDS and the Canadian Drinking Water Survey. Analysis of PFAS in dust samples collected as part of the Canadian House Dust Study (HC 2015) is also underway. Similarly, research funded by the Northern Contaminants Program is also providing information on PFAS exposures in Northern First Nations, Metis, and Inuit communities. More details can be found in section 5.

In support of characterizing the exposure to PFAS of a potentially highly exposed occupational group, the Government of Canada is implementing an action plan to help protect firefighters from harmful chemicals (Helping to protect firefighters from harmful chemicals - Canada.ca). Preliminary work has investigated PFAS in turnout gear and in dust collected at fire stations.

Ongoing priorities for research related to PFAS under Canada’s CMP include characterizing immunotoxicity, hepatotoxicity, and neurotoxicity (including using NAMs) associated with exposure to 23 priority PFAS as well as environmentally relevant PFAS mixtures. Further chemical identification using targeted, suspect screening, and non-targeted analytical methods, as well as additional analysis of biomonitoring data, will contribute to better characterizing environmental exposure and effects.

8.1.3 Guidelines for protection of human health and the environment

A number of guidelines for the protection of human health and the environment have been developed by the Government of Canada (for example, Federal Environmental Quality

Guidelines) or through the Canadian Council of Ministers of the Environment (CCME; that is, Canadian Environmental Quality Guidelines).

Federal Environmental Quality Guidelines are available for PFOS in surface water for the protection of aquatic life as well as for fish tissue, wildlife diet for mammalian and avian consumers of aquatic biota, and bird eggs (ECCC 2018). Canadian Soil and Groundwater Quality Guidelines (SQGs and GWQGs) are also available for PFOS for the protection of human health and the environment (CCME 2021b).

In 2024, Health Canada published the Objective for Canadian drinking water quality: Per- and polyfluoroalkyl substances that recommends a single treatment-based value for a group of PFAS in Canadian drinking water (HC 2024). The objective of 30 ng/L applies to the sum of 25 specific PFAS and serves to reduce potential exposure to PFAS through drinking water while the formal guidelines are being revised.

In the absence of Canadian SQGs for other PFAS at this time, HC has developed soil screening values (SSVs) on the basis of human direct contact with soil for other PFAS[10]. These SSVs are based on readily available scientific studies. They are not subject to the extensive review completed for the CCME SQGs, which undergo internal peer review and public consultation prior to CCME approval. These SSVs for PFAS are used to assess soil at federal contaminated sites. In addition, given the uncertainties associated with the assessment of PFAS contamination, a precautionary approach is warranted. Further work is ongoing to investigate the feasibility of assessing PFAS at contaminated sites as a class or group using environmental guidelines.

The development of Canadian environmental quality guidelines for PFOA for the protection of ecological receptors for surface water, soil, and groundwater is currently underway by the CCME. A draft PFOA surface water guideline was posted by the CCME for public review on October 19, 2023 and comments are being considered. In addition, federal environmental quality guidelines for PFOA for wildlife diet and bird eggs are currently being developed by the Government of Canada.

Provinces and territories develop guidelines/standards that respond to needs within their jurisdictions to address sites on provincial/territorial lands and sites on private properties, including industrial facilities. Through the *Contaminated Sites Regulation*, British Columbia has developed the following standards: 1) soil standards for PFOS and PFBS for the protection of human and ecological health; 2) water standards for the protection of drinking water for PFOS, PFBS, and PFOA; and 3) water standards for the protection of aquatic life for PFOS (Government of British Columbia 1996). British Columbia has also developed water quality guidelines for PFOA (protection of drinking water) and PFOS (protection of freshwater aquatic life and drinking water) (B.C. Ministry of Environment and Climate Change Strategy 2020, 2021). The Government of Alberta has Tier 1 groundwater remediation guidelines for PFOS and

[10] Available upon request to cs-sc@hc-sc.gc.ca.

PFOA and Tier 1 soil remediation guidelines for PFOS for different land uses (AEP 2024a). Additionally, PFOS and PFOA are included in Alberta's Tier 2 soil and groundwater remediation guidelines (AEP 2024b). Quebec has adopted surface water criteria for PFOS and PFOA for the protection of drinking water and aquatic food consumption from the Michigan Department of Environment, Great Lakes, and Energy (MELCCFP 2024). Further, the Institut National de Santé Publique du Québec (INSPQ) has developed a decision-support flowchart for PFAS in drinking water (INSPQ 2023).

In addition, Ontario has published Toxicity Reference Values for PFOS and PFOA in its May 2021 publication of Human Health Toxicity Reference Values (TRVs) Selected for Use at Contaminated sites in Ontario (OMECP 2022). For the assessment and remediation of potentially contaminated sites in the 4 Atlantic Provinces, the governments of these provinces have adopted the Atlantic RBCA Environmental Quality Standards, which address several PFAS in groundwater and soil (APIRI 2022).

8.1.4 Contaminated sites

Federal contaminated sites are located on land owned or leased by the federal government or on land where the federal government has accepted responsibility for the contamination. The Federal Contaminated Sites Inventory shows more than 24 000 suspected, active, and closed federal contaminated sites (as of November 2024[11]), of which there are over 100 sites with confirmed or suspected PFAS contamination (see Figure 3 in section 2.3). Each contaminated site record includes information such as the location of the site, the severity of contamination, the contaminated medium, the nature of the contaminant, and progress made to date in identifying and addressing contamination. Prior to 2023-24, federal sites contaminated with PFAS were not easily identified on the FCSI. As part of an update to the Federal Contaminated Sites Inventory during 2023-24, a contaminant category was added that allows users to search easily for federal sites contaminated with PFAS. The most common source of PFAS at federal contaminated sites is the use of AFFF which includes activities such as firefighting training and the maintenance of firefighting equipment. The Government of Canada continues to take action through the Federal Contaminated Sites Action Plan (FCSAP) to reduce environmental and human health risks from known federal contaminated sites.

ECCC, Fisheries and Oceans Canada, and HC are science-based expert support departments in the FCSAP program, providing guidance, training, and advice for the assessment of ecological and human health risks at federal contaminated sites relevant to their mandates. The FCSAP Secretariat and Expert Support Departments have developed various guidance that provide relevant information on select PFAS, including the Interim Advice to Federal Custodian Departments for the Management of Federal Contaminated Sites Containing Perfluorooctane Sulfonate (PFOS) and other Per- and Polyfluoroalkyl Substances (PFAS) V 1.4.1 (Government of Canada 2018b). HC has prepared a Human Health Risk Assessment (HHRA) Framework for Federal Sites Impacted with Per- and Polyfluoroalkylated Substances (HC 2019) to provide

[11] Up-to-date statistics can be found here: Contaminated Sites by Reporting Organization (tbs-sct).

direction in conducting human health risk assessments at federal sites that have been impacted by PFAS associated with past and/or current use of AFFF. These reports are considered “evergreen” and will be updated on the basis of the evolving science in this area to remain current. The FCSAP Secretariat and all Expert Support Departments are continuing work on guidance that will support the management of their PFAS-contaminated sites.

Available guidelines and screening values (see section 8.1.3) can be used for contaminated sites to evaluate risks to human health and the environment and to establish remediation objectives (CCME 2021b). Guidelines and screening values may be updated as new data become available. Guidelines and screening values are only available for a small number of PFAS and for specific pathways, and thus are not necessarily protective of all human exposure or ecological pathways for all PFAS that may be detected at a site. This presents challenges for the management of contaminated sites. For example, existing environmental guidelines and Health Canada’s drinking water objective were not developed to be protective of the pathway for fish consumption by humans; thus, additional media-specific investigation (that is, analysis of fish tissue) may be needed to assess the risks associated with fish consumption.

There are numerous technical challenges associated with assessment, remediation (refer to section 3.2.6), and risk management activities at PFAS contaminated sites. The disposal of PFAS-impacted waste from PFAS-contaminated sites requires special consideration given the long-term (“forever”) presence of this class of contaminants. The current analytical suite for environmental samples at commercial laboratories includes a small percentage of the known PFAS overall and the current analytical capacity only captures a small number of PFAS found at sites impacted by AFFF. The current approach that considers a small number of PFAS individually has its limitations and results in uncertainty with respect to the assessment, remediation, and management of contaminated sites. Accordingly, taking a precautionary approach to address PFAS as a class allows for the consideration of these uncertainties in the management of contaminated sites.

Where potential ecological or human health risks are identified at PFAS-contaminated sites, action may be necessary to eliminate or reduce exposure to PFAS. Such actions may include: the provision of alternative drinking water sources (for example, bottled water), installation of water treatment systems, implementation of food consumption advisories, and remediation of specific areas of the site to remove PFAS hot spots/source areas. Long-term monitoring and management of PFAS-impacted sites is essential as environmental conditions affecting the migration or transformation of PFAS precursors may change, the analytical suite of PFAS may expand, and environmental guidelines may be revised. Moreover, there is need to verify that mitigation measures are indeed reducing exposure as planned.

In October 2024, Innovation Science and Economic Development Canada (ISED) launched a challenge under the Innovation Solutions Canada Program, focused on advancing the destruction of PFAS compounds in contaminated media (Canada 2024). This initiative seeks to identify innovative, cost-effective, safe, and scalable solutions that lead to the destruction of PFAS across various contaminated solid or aqueous media.

8.1.5 Waste management

In Canada, waste management operations are most often dealt with at the provincial and territorial level. These jurisdictions can regulate the approval, licensing, and monitoring of waste treatment and disposal facilities, including municipal solid waste and hazardous waste. The collection, recycling, composting, and disposal of waste is managed by municipal authorities.[12] The Government of Canada authorities include the control of waste management activities on federal lands and the international and interprovincial movement of hazardous waste and hazardous recyclable materials. The Government of Canada can also apply its authorities under CEPA and other applicable laws to waste management when there is a potential for release of toxic substances (based on their inclusion on Schedule 1 of CEPA) to the air, land, or water (CCME 2014).

Most provinces and territories have regulations in place to control waste management operations and/or facilities. Some jurisdictions choose to have all of their requirements outlined in a regulation, while others prefer to refer to a standard or guidance document in the regulations. However, the level of detail, or depth and stringency of the requirements vary significantly across Canada.

The Basel Convention has adopted the General technical guidelines on the environmentally sound management of wastes consisting of, containing or contaminated with persistent organic pollutants (UNEP 2023b). These guidelines outline environmentally sound management practices for the disposal of wastes containing persistent organic pollutants such as PFAS, including landfilling and thermal treatment. Guidance and studies on the incineration of wastes containing PFAS are also available from a number of subject matter experts including the US EPA (2020a). These experts have identified hazardous waste combustion technologies as having a high potential to control migration of PFAS to the environment if used to destroy or dispose of PFAS-containing materials.

The CFIA regulates the sale and import of biosolids fertilizer products. In October 2024, the CFIA implemented an interim standard of 50 parts per billion (ppb) of PFOS, on a dry weight basis, for biosolids. This interim standard requires that biosolids contain less than 50 ppb (μg/kg) of PFOS on a dry weight basis, before they can be imported or sold in Canada as commercial fertilizer. Preliminary analysis of Canadian biosolids (based on results from both government monitoring and voluntary testing performed by industry) indicated that over 90% of Canadian-produced biosolids contain PFOS concentrations less than 50 ppb, based on dry weight. The CFIA has been working with the provinces, municipalities, and the biosolids industry in implementing the interim standard and began enforcing the standard in October 2024. In Quebec, as of July 20, 2023, section 29.2 of the *Agricultural Operations Regulation* prohibits the agricultural application of imported biosolids and biosolids products.

[12] MSW is regulated by the provinces and territories and managed by the waste management industry under contract to municipal or regional authorities, or managed by municipal authorities directly. In addition, the waste management industry provides services under contract to industrial, commercial and/or institutional waste generators.

8.1.6 Great Lakes Water Quality Agreement

Under the Great Lakes Water Quality Agreement (GLWQA), Canada and the US have agreed to protect human health and the environment through cooperative and coordinated measures to reduce the anthropogenic release of chemicals of mutual concern (CMCs) into the waters of the Great Lakes. Under the GLWQA, the Parties have agreed to adopt, as appropriate, the principles of virtual elimination and zero discharge for releases and control of CMCs. The Government of Canada published Canada's Great Lakes Strategy for PFOS, PFOA, and LC-PFCAs in 2022 (ECCC 2022b). The document outlines risk mitigation and management actions to further protect the Great Lakes from these substances.

Through the Great Lakes Freshwater Ecosystem Initiative, the Government of Canada takes action to address the most significant environmental challenges affecting Great Lakes water quality and ecosystem health by delivering on Canada's commitments under the GLWQA. To support the goal of reducing releases of harmful chemicals, the Government provides funding to projects seeking to increase participation in the application of measures that go beyond regulatory compliance to reduce releases of CMCs (including PFOS, PFOA, and LC-PFCAs) by developing, implementing, assessing, and promoting the use of innovative approaches.

8.1.7 Ozone-depleting Substances and Halocarbon Alternatives Regulations

The *Ozone-depleting Substances and Halocarbon Alternatives Regulations* (ODSHAR) under CEPA set out rules on the import, export, and manufacture of certain ozone-depleting substances (ODS) and products containing, or designed to contain, ozone-depleting substances. The regulations also set out rules concerning halocarbon alternatives. HFCs, HCFCs, and CFCs are substances covered by the ODSHAR that are in most cases also considered PFAS under the OECD definition.

HFCs are replacements for ODS and are potent greenhouse gases, with some having global warming potentials hundreds to thousands of times greater than that of carbon dioxide. The ODSHAR mandates a reduction of domestic HFC consumption by 85% from baseline[13] by 2036.

HFCs are imported into Canada in bulk for use in the manufacture, servicing, and maintenance of refrigeration and air-conditioning equipment, as blowing agents in the manufacture of foam products, and as a propellant in aerosol products. As an alternative to HFCs, the industries have been transitioning to HFOs and HCFOs for some applications as they have a much lower global warming potential. Many HFOs and HCFOs are considered PFAS under the definition of the OECD, but are not regulated under the ODSHAR.

[13] In accordance with the Kigali Amendment, Canada's HFC consumption baseline was calculated by determining the average HFC consumption for the years 2011 to 2013 and adding 15% of Canada's HCFC consumption baseline (expressed in CO2 equivalents).

Tables 3 and 4 of the ODSHAR include some PFAS (HCFCs and HFCs) that were regulated under the NSNR but for which risk management was rescinded when they became subject to the ODSHAR.

8.2 International activities

A growing number of jurisdictions, including the EU and some states in the US, are addressing or proposing to address PFAS as a class. The Government of Canada works with other governments through a number of initiatives including the Stockholm Convention on Persistent Organic Pollutants, the OECD, and tri-laterally with the US EPA and ECHA on the APCRA initiative to collaborate and discuss scientific and regulatory needs. Information about certain key international actions is provided below for context.

8.2.1 Stockholm Convention on Persistent Organic Pollutants (POPs)

The Stockholm Convention on Persistent Organic Pollutants (POPs) aims to protect human health and the environment from substances that are of global concern. POPs listed to the Convention are persistent, bioaccumulative, undergo long-range transport, and lead to significant adverse human health and/or environmental effects. The Stockholm Convention requires Parties to eliminate or severely restrict the production, use, import, and export of intentionally produced POPs and to implement measures to reduce unintentionally produced POPs. In addition, stockpiles and wastes containing POPs must be managed and disposed of in a safe, efficient, and environmentally sound manner. The Stockholm Convention has assessed and listed PFOS, its salts, and perfluorooctane sulfonyl fluoride (PFOSF) in 2009; PFOA, its salts, and PFOA-related compounds in 2019; and PFHxS, its salts, and PFHxS-related compounds in 2022.

In 2021, the Government of Canada nominated LC-PFCAs, their salts and related compounds to the Stockholm Convention. At the 19th meeting of the POPs Review Committee (October 2023), the Committee recommended that the Conference of the Parties consider listing these substances to the Convention at its next meeting in 2025 (POPRC 2023).

8.2.2 Convention on the Prior Informed Consent Procedure for Certain Hazardous Chemicals and Pesticides in International Trade

The Rotterdam Convention on the Prior Informed Consent Procedure for Certain Hazardous Chemicals and Pesticides in International Trade provides an early warning to countries on various hazardous chemicals in international trade that have been banned or severely restricted in other countries to protect human health or the environment. The information shared under this Convention enables governments to assess the risks posed by these hazardous chemicals and to make informed decisions on their future import.

PFOS, perfluorooctane sulfonates, perfluorooctane sulfonamides, and perfluorooctane sulfonyls; and PFOA, its salts, and PFOA-related compounds are listed to Annex III of the Rotterdam Convention, making their trade subject to the prior informed consent procedure.

8.2.3 The Montreal Protocol on Substances that Deplete the Ozone Layer

The Montreal Protocol on Substances that Deplete the Ozone Layer (Montreal Protocol) is an international treaty that controls the production and consumption of ODS, including CFCs and HCFCs, as well as their HFC alternatives. Most CFCs, HCFCs, and HFCs controlled by the Montreal Protocol meet the OECD definition of PFAS.

Under the Montreal Protocol, all Parties have specific responsibilities related to the stepwise phasedown of ODS and HFCs, controls on trade, annual reporting of data, and the development of national licensing systems to control the import and export of ODS and HFCs. The ODSHAR implement Canada's international obligations as set out in the Montreal Protocol.

The pathway to implementation of the HFC phasedown under the Montreal Protocol is to reduce dependency on high-global warming potential (GWP) alternatives and increase the adoption of low-GWP, energy-efficient technologies. In this regard, many of the alternatives to ODS and HFCs adopted for use in refrigeration, foams, and fire-fighting applications (for example, HFOs and HCFOs) also meet the OECD definition of PFAS.

8.2.4 OECD Global Perfluorinated Chemicals Group

The OECD Global Perfluorinated Chemicals Group considers the development, facilitation, and promotion of international stewardship programs and regulatory approaches to reduce emissions of PFAS that are present in products.

The OECD facilitates information exchange and supports the global transition towards safer alternatives. Regulatory and stewardship efforts of various countries on PFAS as well as key reports and support materials are housed on the OECD website "Risk management, risk reduction and sustainability chemistry". In 2017, the OECD developed a non-exhaustive list of 4730 PFAS, including Chemical Abstract Service Registry Numbers, as part of a new Comprehensive Global Database on PFAS. The compilation of the list utilized publicly accessible information sources, including lists from national or international regulatory bodies, public national/regional inventories of chemicals and chemicals in specific uses, national/regional inventories of chemicals subject to specific regulations, and scientific databases. Canada, the US, and the EU were major contributing sources of PFAS data to the database (OECD 2018a). As indicated in section 1.1 (Chemical Scope), this organization also authored the reference and guidance document Reconciling Terminology of the Universe of Per- and Polyfluoroalkyl Substances: Recommendations and Practical Guidance (OECD 2021).

8.2.5 United States of America

In October 2021, a government-wide approach[14] to address current and future PFAS contamination was announced, which included the US EPA PFAS Strategic Roadmap (US EPA 2021c), designed to guide the agency's activities on PFAS. Under the roadmap, the US EPA has proposed to take a number of actions including measures under their new chemicals

[14] FACT SHEET: Biden-Harris Administration Launches Plan to Combat PFAS Pollution

program, adding certain PFAS to their Toxics Release Inventory, and proposing a data gathering rule. As part of the Strategic Roadmap, the US EPA published its National PFAS Testing Strategy, which uses a stepwise testing approach to identify and select candidate PFAS for further testing by developing categories of PFAS on the basis of similarities in structure, physicochemical properties, existing toxicity data, and current manufacturing implications (US EPA 2021d). The information from these candidates may be extrapolated to characterize the hazard potential of their broader corresponding group. In addition, the US EPA has designated PFOA and PFOS as 'hazardous substances' under the Comprehensive Environmental Response, Compensation and Liability Act (CERCLA), which results in reporting requirements and aids in recovering remediation costs.

The US approach also includes actions by the Department of Defense to address their PFAS-contaminated sites, by the US FDA to expand testing of the food supply, by the Department of Agriculture to support research, and by the Department of Homeland Security to inventory their PFAS uses and releases and to consider actions related to emergency responders. Research by a number of other US agencies was announced. These agencies have also established the Interagency Policy Committee on PFAS, which will work to coordinate and help develop new policy strategies to support research, remediation, and removal of PFAS in communities across the country.

The US also has a number of actions that address PFAS in drinking water, such as the Fifth Unregulated Contaminant Monitoring Rule to collect new data on 29 PFAS in drinking water (US EPA 2021e). In April 2024 the US EPA established a *National Primary Drinking Water Regulation* under the *Safe Drinking Water Act* for 6 PFAS with legally enforceable maximum contaminant levels (MCLs). The MCLs for PFOA and PFOS are set at 4 ng/L each, while PFHxS, PFNA, and HFPO-DA are set at 10 ng/L each. In addition, the Regulation includes a hazard index level for mixtures containing 2 or more of PFNA, PFHxS, HFPO-DA and PFBS (US EPA 2024).

In 2016, the US FDA revoked a number of authorizations for LC-PFAS in food packaging materials and in 2020 announced a voluntary phase-out of 6:2 FTOH-containing PFAS. Beginning in 2019, one manufacturer agreed to a phase-out of sales of compounds containing 6:2 FTOH as a food contact substance. In 2020, the remaining 3 manufacturers agreed to a 3-year phase-out of US sales of food contact materials that contain 6:2 FTOH. In 2024, the US FDA announced that manufacturers of the remaining PFAS-containing 'grease-proofers' (that is, PFAS applied to fast food wrappers, microwave popcorn bags, take-out paperboard containers, and pet food bags) authorized for food-contact use in the US have voluntarily stopped selling them for business reasons unrelated to safety (US FDA 2024). Subsequently, in January 2025, the US FDA announced that 35 PFAS-related food contact notifications (FCNs) are no longer effective, following confirmation that these substances are no longer in use in paper-based food packaging in the US (US FDA 2025). The Kigali Amendment to the Montreal Protocol on ODS, which is an international agreement to phase down the production and consumption of HFCs by 80 – 85% by 2047, was ratified by the US in 2022. The American Innovation and Manufacturing (AIM) Act authorizes the US EPA to phase down the production and consumption of a number of listed HFCs, and to manage substitutes and facilitate the transition to new, improved

technologies through sector-based restrictions[15]. Through the US EPA's Significant New Alternatives Policy (SNAP) program, which carries out comparative assessments, a number of specific HFOs were found to be "acceptable" replacements for HFCs in a variety of uses, included as blowing agents and refrigerants[16]. The US EPA SNAP assessment aligns with both the Montreal Protocol on ODS and the US AIM Act.

At the state level, many states including Alaska, Arizona, Arkansas, California, Colorado, Connecticut, Georgia, Hawaii, Illinois, Indiana, Kentucky, Louisiana, Maine, Maryland, Michigan, Minnesota, Nevada, New Hampshire, New Jersey, New York, Rhode Island, Ohio, Vermont, Virginia, Washington, West Virginia, and Wisconsin have prohibitions on the use of firefighting foams (AFFF) containing any type of PFAS (Safer States 2024; Arkansas 2021; Ohio 2022; Virginia 2019; West Virginia 2021). Many states have also taken action to prohibit the use of PFAS in food packaging materials including California, Colorado, Connecticut, Hawaii, Maine, Maryland, Minnesota, New York, Vermont, and Washington; and to prohibit the use of PFAS in cosmetics including California, Colorado, Connecticut, Maryland, New Hampshire, New York, Oregon and Washington (Safer States 2024; State of California 2022b; State of Colorado 2024; State of Maryland 2021). A number of states, including California, Colorado, Connecticut, Massachusetts and Washington have taken action to require the disclosure of PFAS intentionally added to firefighter turnout gear. While Massachusetts and Connecticut have also taken action to prohibit the PFAS in that gear a couple of years following the coming into effect of the disclosure requirement. Some states have taken a variety of other measures on PFAS, for example:

- California
  - Prohibition of the use of all PFAS in products for juveniles (under 12 years old) by 2023 (State of California 2021)
  - Prohibition of the use of all PFAS in textile articles by 2025 (State of California 2022a)
- Colorado
  - Prohibition of the use of PFAS in a wide range of products ranging from dental floss to menstruation products and artificial turf with effective dates ranging from 2025 to 2028 (State of Colorado 2024)
- Maine
  - Reporting and removal of most PFAS in products will start in 2025 with a complete ban of all non-essential uses by 2030 (State of Maine 2021)
- Vermont
  - Prohibition of PFAS from consumer products (carpets, rugs, aftermarket treatments, and ski waxes) (State of Vermont 2021)

[15] American Innovation and Manufacturing Act, 2020
[16] US EPA Significant New Alternatives Policy

8.2.6 European Union

Like Canada, the EU and its member States are Parties to the Stockholm Convention on POPs.

Restrictions are currently in place in the EU for PFOS, PFOA and PFHxS, while restrictions on LC-PFCAs (European Commission 2021) are coming into force in phases from 2023 through 2025. In addition, the EU has restricted the use of PFHxA[17] under the REACH Regulation.

Certain PFAS are listed on the EU's REACH list of Substances of Very High Concern (SVHCs), including PFBS[18] and HFPO-DA.[19]

In October 2020, the European Commission published a plan entitled Chemical Strategy for Sustainability Towards a Toxic-Free Environment (European Commission 2020b), which outlines their intent to ban the class of PFAS in firefighting foams as well as in other uses, allowing their use only where they are essential for society. This objective is based upon the large number of cases of contamination of soil and water, including drinking water, the unacceptable risks to both the environment and human health, and the related societal and economic costs. Other measures to which the EU has committed include working on PFAS through international fora and under other legislation on water, sustainable products, food, industrial emissions, and waste; supporting research and innovation for remediating PFAS contamination; and developing safe substitutes to PFAS.

The European Commission published a draft regulation in November 2024 (European Commission 2024) to restrict firefighting foams containing PFAS following the recommendations provided in ECHA's restriction dossier and the opinions of its scientific committees.[20] If approved, the regulation would ban the placing on the market, use and export of PFAS in firefighting foams after use/sector-specific transitional periods.

In addition, the council of the European Union has adopted a directive for PFAS in drinking water. This includes limits of 100 ng/L for the sum of 20 PFAS and 500 ng/L for the sum of all PFAS. Member states have until January 2026 to comply with the limits (EU 2020).

The EU has also published a broad PFAS restriction proposal that aims to reduce PFAS emissions into the environment. The substances in the scope of the proposed restriction are aligned with the OECD definition of PFAS. The 2 options considered in the proposal are:

(i) a full ban with an 18-month transition period; and
(ii) a ban with use-specific and predominantly time-limited derogations.

If approved, this regulation would prohibit the manufacture, use and placing on the market of PFAS substances on their own, in mixtures or in articles for the vast majority of uses. The proposal underwent a 6-month consultation period that ended on September 25, 2023. Due to the

[17] Press Release - Commission restricts use of a sub-group of PFAS chemicals
[18] Registry of SVHC intentions until outcome - Perfluorobutane sulfonic acid (PFBS) and its salts
[19] MSC unanimously agrees that HFPO-DA is a substance of very high concern
[20] Registry of restriction intentions until outcome - Per- and polyfluoroalkyl substances (PFAS)

significant volume of comments received, the Risk Assessment Committee and the Committee for Socio-Economic Analysis underwent meetings on a sector-by-sector basis. In 2024, sectors analyzed included textiles, food contact materials and packaging, petroleum and mining, and construction products while fluoropolymers, fluorinated gases, energy and transport are planned for 2025. (ECHA 2023e).

8.2.7 Australia and New Zealand

Like Canada, Australia and New Zealand are Parties to the Stockholm Convention on POPs.

Australia does not generally ban or restrict industrial chemicals at the federal level; rather, these risk management actions fall under the jurisdiction of the state or territory. In 2018, South Australia banned fluorinated firefighting foams with a transition period, which ended in January 2020. The Australian government has developed drinking water quality and recreational water guidance values for PFOS, PFOA, and PFHxS. The PFAS National Environmental Management Plan (Heads of EPA Australia and New Zealand 2020) provides the federal, state, and territory governments with a risk-based framework for the regulation of PFAS-contaminated sites and materials, and an intergovernmental agreement provides further specific guidance on actions as PFAS-contaminated sites (Council of Australian Governments 2020). The Australian government is also supporting research into PFAS exposure, health effects, and new remediation treatments.

In New Zealand, both PFOS and PFOA were banned in 2006, with an exemption for use in firefighting foams. However, since 2020, the import, manufacture, and use of PFOS and PFOA have been banned without any exemptions. New Zealand prohibited the class of PFAS for use in cosmetics, with a ban on importing or manufacturing taking effect at the end of 2025 and the sale of PFAS-containing cosmetics prohibited at the end of 2026 (NZ EPA 2024).

8.2.8 International scientific statements

Various groups of academic and government scientists and international bodies have issued statements proposing recommendations related to the current state of science, regulation, and environmental release of PFAS. The Helsingør, Madrid, and Zürich Statements are short publications resulting from expert meetings regarding PFAS (Scheringer et al. 2014; Blum et al. 2015; Ritscher et al. 2018; DeWitt et al. 2024). Signatories to these statements consist of a significant number of scientists, largely from international academic institutions.

The Helsingør Statement on poly- and perfluorinated alkyl substances (PFASs) (Scheringer et al. 2014) described the ubiquity of PFAS in the environment, lack of information on them, potential risks of the transition from regulated PFAS to fluorinated alternatives, lack of current regulatory oversight for fluorinated alternatives, and potential risks resulting from increasing exposure due to the stability of PFAS and perfluorinated transformation products in the environment. The Statement also called for the restriction of PFAS to essential applications only. The Madrid Statement on Poly- and Perfluoroalkyl Substances (PFASs) (Blum et al. 2015) built upon the concerns outlined in the Helsingør Statement, calling on the international community to limit PFAS production and use, and made specific recommendations to scientists, governments, chemical and product manufacturers, businesses and organizations, and

consumers. The Zürich Statement on Future Actions on Per- and Polyfluoroalkyl Substances (PFASs) (Ritscher et al. 2018) is a result of a 2017 workshop held between international scientists and regulators. The Statement echoed the concerns of the 2 aforementioned statements, making a series of recommendations to help reduce and restrict the use of PFAS. The Zürich II Statement on Per- and Polyfluoroalkyl Substances (PFASs) (DeWitt et al. 2024) reflects the insights gained following a second Zürich workshop, 5 years after the previous workshop (that is, Ritscher et al. 2018). The Zürich II Statement highlights possible next steps on the regulatory side as well as non-regulatory actions, incentives, and measures. Workshop participants also supported the idea that continued workshops and multistakeholder exchanges facilitate critical discussions on PFAS.

Taken as a whole, the statements describe challenges related to assessing and managing human and ecological exposure to the extensive class of PFAS and concerns about replacements for regulated PFAS. Recommendations have been issued on cooperative actions and strengthening the science-policy approaches regarding PFAS. Many of these elements speak to taking a preventative and precautionary approach for this class of substances.

9 Findings

KEY POINTS ON FINDINGS

- PFAS have extreme environmental persistence and long-range transport properties, which are resulting in widespread long-term exposure.
- Multiple PFAS are widely present and co-occur in the environment, in wildlife, and in humans across Canada, including in remote regions such as the Arctic and Subarctic.
- Several well-studied PFAS have been shown to bioaccumulate and are associated with negative effects in various organisms, including humans.
- Due to the poorly reversible contamination of most environmental compartments, accumulation of PFAS in biota and the environment will continue in the absence of intervention. PFAS are challenging to remediate from contaminated sites and are impossible to remove from the broader environment.
- While a small number of PFAS have been the focus of a majority of studies, there is a growing body of evidence suggesting that concerns identified for these well-studied substances are more broadly applicable to other PFAS than previously believed.
- The potential for cumulative effects from co-exposure to unknown mixtures of PFAS is an important consideration.
- Chemicals management of PFAS is difficult due to the large number of substances implicated and the exceptionally wide range of associated uses.
- Due to issues as outlined in key findings above, a precautionary, class-based approach to addressing PFAS is needed to protect the environment and people from anticipated adverse effects.

The large number of substances (section 1) and wide spectrum of associated uses (section 2.1) within the class of PFAS present a challenge from a chemicals management standpoint. The extensive use of PFAS in a wide range of applications, including but not limited to certain firefighting foams, food packaging materials, surfactants, lubricants, drugs (including natural health products and non-prescription drugs), medical devices, cosmetics, pesticides, textiles, vehicles, repellents and electronics, continues to contribute to environmental loading and human exposure. In combination with their extreme stability or transformation to other stable PFAS, the net effect of continued environmental release is the long-term occurrence of both direct human and environmental exposure. As a result of this irreversible, or at best poorly reversible, contamination (ECHA 2023b), presence in the environment and uptake by biota and humans will continue and potentially increase in the absence of intervention.

Exposure to PFAS is further magnified by these substances' mobility (section 3.2.4) and long-range transport potential (section 3.2.5). Given that certain neutral PFAS are highly mobile in air (for example, fluorotelomer alcohols) and that ionized forms are mobile in water (for example, PFAAs), PFAS can be transported over long distances and dispersed over large areas, resulting in global distribution. Additionally, some shorter-chain PFAS adopted in place of prohibited long-chain PFAS have proven to be even more mobile on a local scale, potentially implicating transfer to food crops and drinking water.

The combination of the extreme persistence, mobility (allowing local migration), and long-range transport potential of PFAS in the environment has resulted in widespread exposure to PFAS in ecosystems across Canada, as well as in biota and humans - a finding that is supported by available monitoring data (sections 4 and 5). Environmental concentrations are highest in proximity to sources of release but are also of concern in remote regions far removed from areas of production and use, including the Canadian Arctic and Subarctic, because of long-range transport (section 4.1). Over time, Canadian human biomonitoring surveys have consistently noted the near ubiquity of PFOS and PFOA in human plasma (section 5.4). Additionally, certain PFAS have been found in higher concentrations in certain Indigenous or northern communities compared with the rest of the Canadian population; however, other PFAS (for example, PFOA) have been noted to be lower. Certain shorter-chain PFAS with relatively rapid elimination in humans have been shown to be detected in biomonitoring samples in humans in some international data sets (for example, Poothong et al. 2017), which also suggests ongoing exposure. Although monitoring continues to be focused on a relatively small fraction of PFAS, certain biomonitoring efforts in Canada continue to expand and are generating data on a number of previously unmeasured precursor and alternative PFAS. Challenges associated with biomonitoring have also been discussed in this report, including optimization of methods for various biomarkers and complexities in selection of appropriate biological matrices.

Although data have largely been generated for a limited suite of well-studied substances, there is a growing body of evidence linking certain PFAS to negative effects in both wildlife and humans. The ITRC (2021b) notes that, although a few PFAS are well-studied toxicologically, those that have been studied have been found to be capable of causing adverse effects in animals and/or humans. Data for wildlife are largely focused on a small group of species (for example, fish, aquatic invertebrates; see section 6); however, PFAS have been shown to bioaccumulate and cause toxicological effects in various organisms. Apical (for example, growth, reproduction, development) and mechanistic (for example, immunotoxicity, neurotoxicity) endpoint effects have been reported in the literature, with some species being more susceptible to harm. For instance, certain PFAS have been reported to possess a high potential for biomagnification in air-breathing organisms (for example, mammals, birds), which can increase the likelihood of adverse effects. Some PFAS have also been shown to be readily absorbed in humans and can accumulate due to slow elimination and/or ongoing exposure. Similarly to patterns of toxicity observed in wildlife, effects have been noted in multiple human systems and organs including the liver, immune system, kidney, reproduction, development, endocrine disruption (thyroid), and metabolism (lipids, glucose homeostasis, body weight) (section 7).

Concerns surrounding well-studied PFAS have frequently led to regulatory attention (section 8). For example, in Canada, PFOS, PFOA, and LC-PFCAs, their precursors and salts, have all been concluded to be toxic under CEPA and have been prohibited (with a limited number of exemptions). Internationally, LC-PFCAs have been recommended for listing, and PFOS and PFOA have been listed (along with their salts and related compounds) as persistent organic pollutants under the Stockholm Convention. Due in part to various regulatory actions worldwide on PFOA and PFOS, other PFAS (for example, SC-PFCAs, SC-PFSAs) have been introduced as replacements. Initially, shorter-chain replacement substances were thought to have an

overall lower bioaccumulation and toxicity potential on the basis of standard toxicity test results for freshwater aquatic test species such as fish, daphnia, and algae. However, concerns are increasingly being identified for a number of individual or subgroups of short-chain PFAS as they become more data rich and as data for other species, including mammals, become available. PFHxS (used in some cases as a substitute for PFOS, as well as in other applications) along with its salts and related compounds has been accepted for addition to the Stockholm Convention. Another replacement, PFBS, has been identified as a Substance of Very High Concern under REACH, as have HFPO-DA, its salts (HFPO-DA and its ammonium salt are commonly known as GenX), and its acyl halides. In certain applications, PFBS and HFPO-DA are used as replacements for PFOS and PFOA, respectively. Despite these developments, significant gaps in information remain for the majority of PFAS.

Additionally, while laboratory studies have typically involved individual PFAS, environmental sampling and biomonitoring results indicate concurrent exposure of humans and biota to multiple PFAS. Many commercial precursors can transform to stable acids, further contributing to this combined exposure. Currently, the hazards of exposure to multiple PFAS are largely unknown, and the limited studies that have examined interactive effects have yielded complex results, including synergism, antagonism, and additivity, depending on the experimental conditions. Given the likelihood of concurrent exposure to multiple PFAS and the potential for cumulative effects, management of these substances as a class has received much attention (for example, HBM4EU 2019; EFSA 2020; Bil et al. 2021; ECHA 2023b, 2023d). Addressing PFAS as a class would also reduce the chance of regrettable substitution.

The most efficient method to reduce PFAS concentrations in many receiving media, and the only method to reduce PFAS concentrations in ambient environmental media, continues to be upstream management and minimization. Accordingly, scientists, regulators, and other international organizations have increasingly advocated or undertaken new approaches to addressing PFAS (section 8.2). Debates on how to best define the scope of PFAS are appearing in the scientific literature (for example, Kwiatkowski et al. 2020, 2021; Singh and Papanastasiou 2021). Recognizing the current state of the available science and the ongoing environmental release of PFAS, various groups of academic and government scientists have also issued statements (for example, Helsingør [Scheringer et al. 2014]; Madrid [Blum et al. 2015]; Zürich [Ritscher et al. 2018; DeWitt et al. 2024]) proposing approaches that include calls for the use of precaution and restrictions on the uses of PFAS. Among the international community, the US has announced a government-wide approach to address current and future PFAS contamination. In support of this initiative, a group of 67 experts issued a letter to the US EPA advocating a class-based approach to the regulation of PFAS and the elimination of new and non-essential uses (Birnbaum et al. 2021). Further, the EU published a PFAS restriction proposal on March 22nd, 2023. The proposal and comments received during the 6-month consultation period continue to undergo evaluation by ECHA scientific committees. Once evaluation of the entire proposal is finalized, the committees will adopt their opinions which are then delivered to the European Commission; the context underlying the proposal to restrict PFAS is the application of precaution due to the scale of current scientific uncertainty surrounding lesser-studied PFAS (ECHA 2023b). The EU emphasizes that PFAS have structural similarities that trigger hazards and risks among the class of PFAS (ECHA 2023b),

and that combined exposure to multiple PFAS affecting the same target organs could result in cumulative effects that exceed effects thresholds in comparison to single substances (ECHA 2023c).

As a result of the extreme persistence of PFAS (increasingly referred to as “forever chemicals”), their potential for bioaccumulation in organisms and for biomagnification through the food chain, their ability to move locally and over long ranges, challenges encountered in their remediation from contaminated sites, and the impossibility of their removal from the broader environment, presence in the environment and uptake by humans and other biota will continue and potentially increase in the absence of intervention. While there are considerable challenges to understanding the characteristics of substances across the range of PFAS structures, there is a growing body of evidence suggesting that concerns identified for well-studied PFAS are more broadly applicable to other PFAS than previously believed. Additionally, recent studies suggesting the widespread environmental presence of and combined exposure to multiple PFAS, the detection of novel PFAS in the environment, and possible cumulative effects suggest that the potential for adverse effects indicated by studies focusing on individual or limited suites of PFAS may be underestimated.

The following is known on the basis of current information:

- The broad use of PFAS, their transport in the environment, and their ubiquitous presence have resulted in continuous environmental and human exposure to multiple PFAS, a finding that is supported by both environmental monitoring and human biomonitoring studies, including higher exposures in certain human subpopulations.
- Given that PFAS are extremely persistent and have a broad range of uses leading to continued releases to the environment, the amount of PFAS in the environment is expected to increase.
- Exposure to well-studied PFAS can affect multiple systems and organs in both humans and wildlife. Recent information demonstrates that effects on human health occur at lower levels than indicated by previous studies.
- Some well-studied PFAS have demonstrated the potential to bioaccumulate and biomagnify in food webs to an extent that can cause adverse effects in biota, even at low environmental concentrations.
- Potential for cumulative exposure and effects are important considerations as most humans and wildlife exposures occur to unknown mixtures of PFAS.

Despite uncertainties associated with understanding the characteristics of substances across the range of PFAS structures from toxicological, epidemiological and monitoring datasets that are focused on a limited number of PFAS, there is a growing body of evidence suggesting that concerns identified for well-studied PFAS are more broadly applicable to other PFAS than previously believed. Similarly, while the specific hazards associated with mixtures of PFAS are largely unknown, there are many potential sources of PFAS that can lead to exposure and it is reasonable to expect that cumulative effects may occur from exposure to multiple PFAS.

To be protective of the environment and human health, and to apply precaution when addressing gaps in information, it is reasonable to anticipate that the concerns identified for PFAS that have been well studied may also be inherent in other substances in the class.

Owing to the extreme persistence of PFAS and their potential to cause adverse effects, impacts on the environment are expected to increase if entry to the environment continues. On the basis of what is known about well-studied PFAS and the potential for other PFAS to behave similarly, and on the expectation that combined exposures to multiple PFAS increase the likelihood of detrimental impacts, it is concluded that the class of PFAS, excluding fluoropolymers as defined in this report, meets the criteria under paragraph 64(*a*) of CEPA as these substances are entering or may enter the environment in a quantity or concentration or under conditions that have or may have immediate or long-term harmful effects on the environment or its biological diversity. However, it is concluded that the class of PFAS, excluding fluoropolymers as defined in this report, does not meet the criteria under paragraph 64(*b*) of CEPA as these substances are not entering the environment in a quantity or concentration or under conditions that constitute or may constitute a danger to the environment on which life depends.

Owing to the widespread use of PFAS, combined with their ubiquitous presence in the environment, humans are continuously exposed to multiple PFAS, which has the potential to cause effects of concern. On the basis of what is known about well-studied PFAS and the potential for other PFAS to behave similarly, and on the expectation that combined exposures to multiple PFAS increase the likelihood of detrimental impacts, it is concluded that the class of PFAS, excluding fluoropolymers as defined in this report, meets the criteria under paragraph 64(*c*) of CEPA as these substances are entering or may enter the environment in a quantity or concentration or under conditions that constitute or may constitute a danger in Canada to human life or health.

Therefore, it is concluded that the class of PFAS, excluding fluoropolymers as defined in this report, meets 1 or more of the criteria set out in section 64 of CEPA.

Well-studied PFAS meet the persistence criteria as set out in the Persistence and Bioaccumulation Regulations of CEPA. Based on available information and structural similarities, it is expected that other substances within the class of PFAS are also highly persistent or transform to persistent PFAS. It is therefore determined that the class of PFAS meets the persistence criteria as set out in the Persistence and Bioaccumulation Regulations of CEPA. Given that fluoropolymers have been excluded from this assessment, they are also excluded from this determination with regard to the *Persistence and Bioaccumulation Regulations* of CEPA.

There is a high concern identified for the biomagnification (BMF) and trophic magnification (TMF) potential of well-studied PFAS in air-breathing organisms; however, the numeric criteria for bioaccumulation, outlined in the *Persistence and Bioaccumulation Regulations*, are based on bioaccumulation data for freshwater aquatic species which do not account for biomagnification potential. Therefore, application of the criteria would not reflect the concern for dietary-based biomagnification, the primary route of food web exposure identified for well-studied PFAS. Therefore, the bioaccumulation potential of PFAS cannot reasonably be determined according to the regulatory criteria set out in the *Persistence and Bioaccumulation Regulations* of CEPA.

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11 Appendix A: PFAS acronyms

Table A-1. PFAS acronyms in the State of PFAS Report

Substance acronym[a]	CAS RN	Name	Group
7H-PFHpA	1546-95-8	7H-Perfluoroheptanoic acid	Perfluorocarboxylic acid (PFCA)
9Cl-PF3ONS	756426-58-1	Perfluoro(2-((6-chlorohexyl)oxy)ethanesulfonic acid)	Per- and polyfluoroalkyl ether sulfonic acid (PFESA)
11Cl-PF3OUdS	763051-92-9	11-chloroeicosafluoro-3-oxaundecane-1-sulfonic acid	Per- and polyfluoroalkyl ether sulfonic acid (PFESA)
ADONA	958445-44-8	Ammonium 4,8-dioxa-3H-perfluorononanoate	Per- and polyfluoroalkyl ether carboxylic acid (PFECA)
C6O4	1190931-27-1	Acetic acid, 2,2-difluoro-2-[[2,2,4,5-tetrafluoro-5-(trifluoromethoxy)-1,3-dioxolan-4-yl]oxy]-, ammonium salt	Per- and polyfluoroalkyl ether carboxylic acid (PFECA)
Cl-PFESA (6:2) (F-53B)	73606-19-6	6:2 Chlorinated polyfluorinated ether sulfonic acid	Per- and polyfluoroalkyl ether sulfonic acid (PFESA)
Cl-PFECAs	220207-15-8	1-Propene, 1,1,2,3,3,3-hexafluoro-, telomer with chlorotrifluoroethene, oxidized, reduced, Et ester, hydrolyzed, sodium salt	Per- and polyfluoroalkyl ether carboxylic acid (PFECA)
Cl-PFECAs	330809-92-2	1-Propene, 1,1,2,3,3,3-hexafluoro-, telomer with chlorotrifluoroethene, oxidized, reduced, hydrolyzed, ammonium salts	Per- and polyfluoroalkyl ether carboxylic acid (PFECA)
Cl-PFECAs	329238-24-6	Perfluoro acetic acid, α-substituted with the copolymer of perfluoro-1,2-propylene glycol and perfluoro-1,1-ethylene glycol, terminated with chlorohexafluoropropyloxy groups	Per- and polyfluoroalkyl ether carboxylic acid (PFECA)
diPAP (4:2)	135098-69-0	4:2 Fluorotelomer phosphate diester	Polyfluoroalkyl phosphate ester (PAP)
diPAP (6:2)	57677-95-9	6:2 Fluorotelomer phosphate diester	Polyfluoroalkyl phosphate ester (PAP)
diPAP (6:2/8:2)	943913-15-3	6:2/8:2 Fluorotelomer phosphate diester	Polyfluoroalkyl phosphate ester (PAP)

Substance acronym[a]	CAS RN	Name	Group
diPAP (8:2)	678-41-1	8:2 Fluorotelomer phosphate diester	Polyfluoroalkyl phosphate ester (PAP)
diPAP (10:2)	1895-26-7	10:2 Fluorotelomer phosphate diester	Polyfluoroalkyl phosphate ester (PAP)
EEA-NH4	908020-52-0	Ammonium difluoro[1,1,2,2-tetrafluoro-2-(pentafluoroethoxy)ethoxy]acetate	Per- and polyfluoroalkyl ether carboxylic acid (PFECA)
EtFOSE	1691-99-2	N-ethyl perfluorooctane sulfonamido ethanol	Perfluoroalkane sulfonamide (FASA)
EtPFOSA-AcOH	2991-50-6	2-(N-ethyl-perfluorooctane sulfonamido) acetic acid	Perfluoroalkane sulfonamide (FASA)
FBSA	30334-69-1	Perfluorobutane sulfonamide	Perfluoroalkane sulfonamide (FASA)
FOSAA	2806-24-8	Perfluorooctane sulfonamido acetic acid	Perfluoroalkane sulfonamide (FASA)
FTB (5:1:2)	171184-02-4	5:1:2 Fluorotelomer betaine	Fluorotelomer betaine (FTB)
FTCA (5:3)	914637-49-3	5:3 Fluorotelomer carboxylic acid	Fluorotelomer carboxylic acid (FTCA)
FTCA (6:2)	53826-12-3	6:2 Fluorotelomer carboxylic acid	Fluorotelomer carboxylic acid (FTCA)
FTCA (7:3)	812-70-4	7:3 Fluorotelomer carboxylic acid	Fluorotelomer carboxylic acid (FTCA)
FTCA (8:2)	27854-31-5	8:2 Fluorotelomer carboxylic acid	Fluorotelomer carboxylic acid (FTCA)
FTOH (6:2)	647-42-7	6:2 Fluorotelomer alcohol	n:2 Fluorotelomer alcohol (FTOH)
FTOH (8:2)	678-39-7	8:2 Fluorotelomer alcohol	n:2 Fluorotelomer alcohol (FTOH)
FTOH (10:2)	865-86-1	10:2 Fluorotelomer alcohol	n:2 Fluorotelomer alcohol (FTOH)
FTSA (4:2)	757124-72-4	4:2 Fluorotelomer sulfonic acid	n:2 Fluorotelomer sulfonic acid (FTSA)
FTSA (6:2)	27619-97-2	6:2 Fluorotelomer sulfonic acid	n:2 Fluorotelomer sulfonic acid (FTSA)
FTSA (8:2)	39108-34-4	8:2 Fluorotelomer sulfonic acid	n:2 Fluorotelomer sulfonic acid (FTSA)

Substance acronym[a]	CAS RN	Name	Group
FtSOAoS (6:2)	1513864-10-2	6:2 Fluorotelomer sulfinyl amido sulfonic acid	n:2 Fluorotelomer sulfonic acid (FTSA)
FTUCA (6:2)	70887-88-6	6:2 Fluorotelomer unsaturated carboxylic acid	Fluorotelomer unsaturated carboxylic acid (FTUCA)
FTUCA (8:2)	70887-84-2	8:2 Fluorotelomer unsaturated carboxylic acid	Fluorotelomer unsaturated carboxylic acid (FTUCA)
HFPO-DA (Ammonium Salt)	62037-80-3	Ammonium, 2,3,3,3-tetrafluoro-2-(heptafluoropropoxy)propanoate	Per- and polyfluoroalkyl ether carboxylic acid (PFECA)
HFPO-DA	13252-13-6	Hexafluoropropylene oxide dimer acid	Per- and polyfluoroalkyl ether carboxylic acid (PFECA)
HFPO-TA	13252-14-7	Hexafluoropropylene oxide trimer acid	Per- and polyfluoroalkyl ether carboxylic acid (PFECA)
HQ-115	90076-65-6	Bis(trifluoromethane)sulphonimide lithium salt	Perfluoroalkane sulfonamide (FASA)
MeFBSE	34454-97-2	2-(N-methylperfluoro-1-butanesulfonamido) ethanol	Perfluoroalkane sulfonamide (FASA)
MeFOSE	24448-09-7	N-methyl perfluorooctane sulfonamide ethanol	Perfluoroalkane sulfonamide (FASA)
MePFOSA-AcOH	2355-31-9	2-(N-methyl-perfluorooctane sulfonamide) acetic acid	Perfluoroalkane sulfonamide (FASA)
monoPAP (6:2)	57678-01-0	6:2 Fluorotelomer phosphate monoester	Polyfluoroalkyl phosphate ester (PAP)
monoPAP (8:2)	57678-03-2	8:2 Fluorotelomer phosphate monoester	Polyfluoroalkyl phosphate ester (PAP)
Nafion by-product 1	29311-67-9	Perfluoro-3,6-dioxa-4-methyl-7-octenesulfonic acid	Per- and polyfluoroalkyl ether sulfonic acid (PFESA)
N-EtFOSA	4151-50-2	N-ethylperfluorooctane sulfonamide	Perfluoroalkane sulfonamide (FASA)
N-EtFOSAA	2991-50-6	N-ethylperfluorooctane sulfonamido acetic acid	Perfluoroalkane sulfonamide (FASA)
N-MeFOSA	31506-32-8	N-methylperfluorooctane sulfonamide	Perfluoroalkane sulfonamide (FASA)

Substance acronym[a]	CAS RN	Name	Group
N-MeFOSAA	2355-31-9	N-methylperfluorooctane sulfonamido acetic acid	Perfluoroalkane sulfonamide (FASA)
NVHOS	801209-99-4	Perfluoroethoxysulfonic acid	Per- and polyfluoroalkyl ether sulfonic acid (PFESA)
OBS	70829–87–7	Sodium p-perfluorous nonenoxybenzene sulfonate	Perfluoroalkene derivatives
PEPA	267239-61-2	Perfluoro-2-ethoxypropanoic acid	Per- and polyfluoroalkyl ether carboxylic acid (PFECA)
PFBA (C4)	375-22-4	Perfluorobutanoic acid	Perfluorocarboxylic acid (PFCA)
PFBS (C4)	375-73-5	Perfluorobutane sulfonic acid	Perfluorosulfonic acid (PFSA)
PFDA (C10)	335-76-2	Perfluorodecanoic acid	Perfluorocarboxylic acid (PFCA)
PFDoDA (C12)	307-55-1	Perfluorododecanoic acid	Perfluorocarboxylic acid (PFCA)
PFDoS (C12)	79780-39-5	Perfluorododecane sulfonic acid	Perfluorosulfonic acid (PFSA)
PFDS (C10)	335-77-3	Perfluorodecane sulfonic acid	Perfluorosulfonic acid (PFSA)
PFECHS (C8)	335-24-0	Perfluoroethylcyclohexane sulfonic acid	Perfluorosulfonic acid (PFSA)
PFEtS (C2)	354-88-1	Perfluoroethane sulfonic acid	Perfluorosulfonic acid (PFSA)
PFHpA (C7)	375-85-9	Perfluoroheptanoic acid	Perfluorocarboxylic acid (PFCA)
PFHpS (C7)	375-92-8	Perfluoroheptane sulfonic acid	Perfluorosulfonic acid (PFSA)
PFHxA (C6)	307-24-4	Perfluorohexanoic acid	Perfluorocarboxylic acid (PFCA)
PFHxDA (C16)	67905-19-5	Perfluorohexadecanoic acid	Perfluorocarboxylic acid (PFCA)
PFHxS (C6)	355-46-4	Perfluorohexane sulfonic acid	Perfluorosulfonic acid (PFSA)
PFNA (C9)	375-95-1	Perfluorononanoic acid	Perfluorocarboxylic acid (PFCA)
PFNS (C9)	68259-12-1	Perfluorononane sulfonic acid	Perfluorosulfonic acid (PFSA)

Substance acronym[a]	CAS RN	Name	Group
PFO2HxA	39492-88-1	Perfluoro-3,5-dioxahexanoic acid	Per- and polyfluoroalkyl ether carboxylic acid (PFECA)
PFO3OA	39492-89-2	Perfluoro-3,5,7-trioxaoctanoic acid	Per- and polyfluoroalkyl ether carboxylic acid (PFECA)
PFO4DA	39492-90-5	Perfluoro-3,5,7,9-butaoxadecanoic acid	Per- and polyfluoroalkyl ether carboxylic acid (PFECA)
PFO5DoDA	39492-91-6	Perfluoro-3,5,7,9,11-pentaoxadodecanoic acid	Per- and polyfluoroalkyl ether carboxylic acid (PFECA)
PFOA (C8)	335-67-1	Perfluorooctanoic acid	Perfluorocarboxylic acid (PFCA)
PFOcDA (C18)	16517-11-6	Perfluorooctadecanoic acid	Perfluorocarboxylic acid (PFCA)
PFOS (C8)	1763-23-1	Perfluorooctane sulfonic acid	Perfluorosulfonic acid (PFSA)
PFOSA or FOSA	754-91-6	Perfluorooctane sulfonamide	Perfluoroalkane sulfonamide (FASA)
PFOSF	307-35-7	Perfluorooctane sulfonyl fluoride	Perfluoroalkyl sulfonyl fluoride (PASF)
PFPA (C6)	40143-76-8	Perfluorohexyl phosphonic acid	Perfluoroalkyl phosphonic acid (PFPA)
PFPA (C8)	40143-78-0	Perfluorooctyl phosphonic acid	Perfluoroalkyl phosphonic acid (PFPA)
PFPA (C10)	52299-26-0	Perfluorodecyl phosphonic acid	Perfluoroalkyl phosphonic acid (PFPA)
PFPeA (C5)	2706-90-3	Perfluoropentanoic acid	Perfluorocarboxylic acid (PFCA)
PFPeS (C5)	2706-91-4	Perfluoropentane sulfonic acid	Perfluorosulfonic acid (PFSA)
PFPiA (C6/C10)	1240600-40-1	Perfluorohexylperfluorodecyl phosphinic acid	Perfluoroalkyl phosphinic acid (PFPiA)

Substance acronym[a]	CAS RN	Name	Group
PFPiA (C6/C12)	68412-69-1	Perfluorohexylperfluorododecyl phosphinic acid	Perfluoroalkyl phosphinic acid (PFPiA)
PFPiA (C6/C6)	40143-77-9	Bis(tridecafluorohexyl)phosphinic acid	Perfluoroalkyl phosphinic acid (PFPiA)
PFPiA (C6/C8)	610800-34-5	(Heptadecafluorooctyl)(tridecafluorohexyl) phosphinic acid	Perfluoroalkyl phosphinic acid (PFPiA)
PFPiA (C8/C10)	500776-81-8	Perfluorooctylperfluorodecylphosphinic acid	Perfluoroalkyl phosphinic acid (PFPiA)
PFPiA (C8/C8)	40143-79-1	Bis(heptadecafluorooctyl)phosphinic acid	Perfluoroalkyl phosphinic acid (PFPiA)
PFPrA (C3)	422-64-0	Perfluoropropanoic acid	Perfluorocarboxylic acid (PFCA)
PFPrS (C3)	423-41-6	Perfluoropropane sulfonic acid	Perfluorosulfonic acid (PFSA)
PFTeDA (C14)	376-06-7	Perfluorotetradecanoic acid	Perfluorocarboxylic acid (PFCA)
PFTrDA (C13)	72629-94-8	Perfluorotridecanoic acid	Perfluorocarboxylic acid (PFCA)
PFUnDA (C11)	2058-94-8	Perfluoroundecanoic acid	Perfluorocarboxylic acid (PFCA)
PMPA (C3)	13140-29-9	Perfluoro-2-methoxypropanoic acid	Perfluorocarboxylic acid (PFCA)
TFA (C2)	76-05-1	Trifluoroacetic acid	Perfluorocarboxylic acid (PFCA)

[a] The acronyms for the PFCAs and PFSAs could represent either the acid or anionic forms of the chemicals.

12 Appendix B: Biomonitoring data - tables

Table B-1. Detection frequency (%) of PFAS in human blood from national, regional, or small-scale and birth-cohort studies (part 1)

Substance[a]	Canada[b]	Canada[c]	US[d]	France[e]	Sweden[f]	US[g]	US[h]
TFA	-	-	-	-	-	-	-
PFPrA	-	-	-	-	-	-	-
PFBA	5.4	0	-	1.1	-	-	67.7
PFHxA	1	0	-	0	-	-	98
PFHpA	-	-	-	2.8	4.4	43.3	20.2
PFOA	100	99.6	99	100	99.3	98.6	100
PFNA	98.5	96.2	93	99.5	100	92.2	99
PFDA	67.6	60.8	89	89.2	100	65.9	87.9
PFUnDA	36.3	62.4	66	99.5	97.8	58.4	98
PFDoDA	-	-	-	22.3	23	0.3	52.5
PFTrDA	-	-	-	-	-	-	-
PFTeDA	-	-	-	-	-	0	-
PFBS	0.3[i]	0	-	0	-	10.9	3
PFHxS	99.6	94.3	99	99.6	100	99.7	100
PFHpS	-	-	-	53.4	-	-	-
PFOS	99.3	98.9	100	100	100	98.3	100
PFDS	-	-	-	0	-	-	59.6
PFOSA	-	-	-	0.4	-	19.8	3
EtPFOSAA	-	-	-	2.2	-	19.3	3
MePFOSAA	-	-	59	24.6	-	78.8	97
6:2 diPAP	-	-	-	-	-	-	2
6:2 monoPAP	-	-	-	-	-	-	-
PFHxPA	-	-	-	-	-	-	0

[a] Note that other PFAS were measured in the studies listed in this table, but detection frequencies were below 10%. These PFAS include PFPeA, C8 PFPA, PFHxDA, PFODA, FOSAA, 5:3 FTCA, 6:2 FTCA, 7:3 FTCA, 8:2 FTCA, 6:2 FTUCA, 8:2 FTUCA, ADONA, GenX, 4:2 Cl-PFESA, 8:2 diPAP, 8:2 diPAP, 8:2 monoPAP, 4:2 FTSA, 6:2 FTSA, 8:2 FTSA, 9Cl-PF3ONS, 11Cl-PF3OUdS, HFPO-DA, 7H-PFHpA, 6:6 PFPiA, 6:8 PFPiA, NVHOS, PMPA, PEPA, Nafion by-product 1, PFO2HxA, and PFO3OA. Certain other PFAS precursors detected in studies conducted near industrial sources or contaminated sites were not included in this table as they do not represent general population exposure.
[b] Detection frequencies. CHMS cycle 6 2018–2019, Canadian total population (plasma, 3–79 years, n=2354–2514).
[c] % >LOD (limit of detection). Indigenous on-reserve and crown land populations in Canada 2011, Canadian adults (plasma, 20+ years, n=473) (AFN 2013).
[d] Detection frequencies. National Health and Nutrition Examination Survey (NHANES) 2017–2018, US total population (serum, n=1929).
[e] % >LOQ. France 2014–2016, Esteban Study (nationwide), adults (serum, 18–74 years, n=744) (Fillol et al. 2021).
[f] % >LOD. Sweden 2010–2011, subgroup of Riksmaten (Swedish national survey of dietary habits among adults), adults (serum, 18–80 years, n=270) (Bjermo et al. 2013).
[g] Detection frequencies. Biomontoring California (2019). California regional exposure study, Region 2 (CARE-2) adults (serum, 18+ years, n=359) (Biomonitoring California 2019).
[h] Detection frequencies. Biomonitoring California (2019), Asian/Pacific Islander Community exposures (ACE) Project –ACE 2, regional Asian-Pacific islander community adults (serum, 18+ years, n=99) (Biomonitoring California 2019).
[i] CHMS advises to use data with caution.

Table B-1: Detection frequency (%) of PFAS in human blood from national, regional, or small-scale and birth-cohort studies (part 2)

Substance[a]	S. Korea[b]	Germany[c]	Germany[d]	Norway[e]	Greenland[f]	Faroe Islands[g]	Japan[h]	US[i]
TFA	-	-	-	-	-	-	-	74
PFPrA	-	-	-	-	-	-	-	99
PFBA	-	-	-	-	-	4	-	84
PFHxA	-	0	-	0	0	0	38	83
PFHpA	-	5	-	-	0	18	32.8	79
PFOA	91.5	100	100	100	99.8	100	99.9	99
PFNA	94	100	56	100	100	100	99.5	98
PFDA	-	26	1.9	100	99.9	100	99.1	93
PFUnDA	-	1	-	100	99.3	98	99.6	79
PFDoDA	-	0	0	98	0	0	88.4	42
PFTrDA	-	0	-	89	0	-	96.6	37
PFTeDA	-	-	-	10	0	-	13.1	36
PFBS	-	0	0	51	0	0	-	85
PFHxS	99	100	98	100	99.8	100	80.9	99
PFHpS	-	6	-	100	74.7	92	-	96
PFOS	99.7	100	100	100	100	100	100	99
PFDS	-	0	-	77	0	33	-	7.4
PFOSA	88.3	0	-	97	0	6	-	-
EtPFOSAA	-	0	-	-	-	24	-	-
MePFOSAA	-	2	-	-	-	78	-	-
6:2 diPAP	-	0	-	49	-	-	-	-
6:2 monoPAP	-	-	-	41	-	-	-	-
PFHxPA	-	-	-	62	-	-	-	-

[a] Note that other PFAS were measured in the studies listed in this table, but detection frequencies were below 10%. These PFAS include PFPeA, C8 PFPA, PFHxDA, PFODA, FOSAA, 5:3 FTCA, 6:2 FTCA, 7:3 FTCA, 8:2 FTCA, 6:2 FTUCA, 8:2 FTUCA, ADONA, GenX, 4:2 Cl-PFESA, 8:2 diPAP, 8:2 diPAP, 8:2 monoPAP, 4:2 FTSA, 6:2 FTSA, 8:2 FTSA, 9Cl-PF3ONS, 11Cl-PF3OUdS, HFPO-DA, 7H-PFHpA, 6:6 PFPiA, 6:8 PFPiA, NVHOS, PMPA, PEPA, Nafion by-product 1, PFO2HxA, and PFO3OA. Certain other PFAS precursors detected in studies conducted near industrial sources or contaminated sites were not included in this table as they do not represent general population exposure.
[b] Detection frequencies. South Korea 2006–2007, 3 regions (whole blood, 8–82 years, n=319) (Cho et al. 2015).
[c] Detection frequencies. Germany 2019, adults (students of Münster University) (plasma, 20–29 years, n=20) (Göckener et al. 2020).
[d] % >LOQ. Germany 2016, Munich (Site C, control area), adults (plasma, 18–67 years, n=158) (Fromme et al. 2017).
[e] % >MDL (median detection limit). Norway 2013–2014, adults living in Oslo, Norway (serum, 20–66 years, n= 61) (Poothong et al. 2017).
[f] % >DL (detection limit). Denmark (Greenland) 2010–2011, 2013, 2015, ACCEPT (Adapting to Climate Change, Environmental Pollution and Dietary Transition) birth cohort, pregnant Greenlandic Inuit women (serum, 18+ years, n=504) (Hjermitslev et al. 2020).
[g] Detection frequencies. Faroe Islands, 2012, children from birth Cohort 5 study (serum, 5 years old, n=51) (Dassuncao et al. 2018).
[h] % >MDL. Japan, Hokkaido study birth cohort, mother-child pairs (maternal plasma, 31 [mean], n=2206) (Bamai et al. 2020).
[i] % > MDL. Indiana, US, adults (serum, 25–88 years, n=81) (Zheng et al. 2023).

Table B-2. Summary of PFAS monitored in the CHMS

Cycle	Collection years	Age (years)	Biomarkers in plasma
Cycle 1[a]	2007 to 2009	20 to 79	PFCAs: PFOA PFSAs: PFHxS, PFOS
Cycle 2[a]	2009 to 2011	12 to 79	PFCAs: PFBA, PFHxA, PFOA, PFNA, PFDA, PFUnDA PFSAs: PFBS, PFHxS, PFOS
Cycle 5[b]	2016 to 2017	3 to 79	PFCAs: PFBA, PFHxA, PFOA, PFNA, PFDA, PFUnDA PFSAs: PFBS, PFHxS, PFOS
Cycle 6[b]	2018 to 2019	3 to 79	PFCAs: PFBA, PFHxA, PFOA, PFNA, PFDA, PFUnDA PFSAs: PFBS, PFHxS, PFOS

[a] Included persons living in the 10 provinces and 3 territories

[b] Included persons living in the 10 provinces

Table B-3. PFAS plasma concentrations (geometric means and 95th percentiles) and detection frequencies in CHMS cycles 1, 2, 5, and 6

Substance/ population	CHMS Cycle[a]	Year	LOD (µg/L)	Population weighted Detection Frequencies	GM (µg/L) (95% CI)[b]	95th (95% CI)	n
PFOA 3 to 79 years	Cycle 6	2018 to 2019	0.066	100	1.2 (1.1 to 1.3)	2.9 (2.6 to 3.3)	2,513
PFOA 3 to 79 years	Cycle 5	2016 to 2017	0.066	100	1.3 (1.2 to 1.4)	3.1 (2.6 to 3.6)	2,593
PFOA 20 to 79 years	Cycle 6	2018 to 2019	0.066	100	1.2 (1.1 to 1.3)	2.9 (2.6 to 3.3)	1,019
PFOA 20 to 79 years	Cycle 5	2016 to 2017	0.066	100	1.3 (1.2 to 1.5)	3.2 (2.5 to 3.8)	1,055
PFOA 20 to 79 years	Cycle 2	2009 to 2011	0.1	100	2.3 (2.1 to 2.5)	5.3 (3.9 to 6.7)	1,017
PFOA 20 to 79 years	Cycle 1	2007 to 2009	0.3	99 (97.7 to 99.6)	2.5 (2.4 to 2.7)	5.5 (5.1 to 5.8)	2,880
PFOS 3 to 79 years	Cycle 6	2018 to 2019	0.43	99.3 (98.6 to 99.7)	2.5 (2.3 to 2.8)	8.3 (7.2 to 9.4)	2,514
PFOS 3 to 79 years	Cycle 5	2016 to 2017	0.43	99.9 (99.8 to 99.9)	3.0 (2.7 to 3.4)	11 (7.1 to 15)	2,594
PFOS 20 to 79 years	Cycle 6	2018 to 2019	0.43	99.3 (98.3 to 99.7)	2.9 (2.7 to 3.1)	8.6 (6.9 to 10)	1,020

Substance/ population	CHMS Cycle[a]	Year	LOD (µg/L)	Population weighted Detection Frequencies	GM (µg/L) (95% CI)[b]	95th (95% CI)	n
PFOS 20 to 79 years	Cycle 5	2016 to 2017	0.43	99.9 (99.8 to 100)	3.4 (3.0 to 3.9)	13 (8.0 to 17)	1,057
PFOS 20 to 79 years	Cycle 2	2009 to 2011	0.3	99.8 (99.1 to 99.9)	6.9 (6.2 to 7.6)	19 (13 to 25)	1,017
PFOS 20 to 79 years	Cycle 1	2007 to 2009	0.3	99.9 (99.9 to 100)	8.9 (8.0 to 9.8)	27 (22 to 32)	2,880
PFHxS 3 to 79 years	Cycle 6	2018 to 2019	0.063	99.6 (99.1 to 99.9)	0.76 (0.69 to 0.85)	4.0 (2.9 to 5.2)	2,514
PFHxS 3 to 79 years	Cycle 5	2016 to 2017	0.063	99.7 (98.9 to 99.9)	0.90 (0.78 to 1.0)	5.3[d] (1.8 to 8.7)	2,595
PFHxS 20 to 79 years	Cycle 6	2018 to 2019	0.063	99.6 (98.9 to 99.9)	0.83 (0.75 to 0.93)	4.1 (3.2 to 5.1)	1,020
PFHxS 20 to 79 years	Cycle 5	2016 to 2017	0.063	99.6 (98.6 to 99.9)	0.98 (0.85 to 1.1)	5.8[d] (0.39 to 11)	1,057
PFHxS 20 to 79 years	Cycle 2	2009 to 2011	0.2	98.4 (96.4 to 99.3)	1.7 (1.6 to 2.0)	8.9[d] (4.6 to 13)	1,015
PFHxS 20 to 79 years	Cycle 1	2007 to 2009	0.3	97.8 (96.2 to 98.8)	2.3 (2.0 to 2.6)	12 (9.2 to 15)	2,880
PFNA 3 to 79 years	Cycle 6	2018 to 2019	0.13	98.5 (97.3 to 99.1)	0.44 (0.41 to 0.47)	1.2 (1.1 to 1.3)	2,396
PFNA 3 to 79 years	Cycle 5	2016 to 2017	0.13	98.8 (97.1 to 99.5)	0.51 (0.45 to 0.57)	1.5 (1.2 to 1.8)	2,442
PFNA 12 to 79 years	Cycle 6	2018 to 2019	0.13	98.4 (97.1 to 99.1)	0.44 (0.41 to 0.47)	1.2 (1.1 to 1.3)	1,457
PFNA 12 to 79 years	Cycle 5	2016 to 2017	0.13	98.8 (96.9 to 99.6)	0.51 (0.45 to 0.58)	1.5 (1.2 to 1.8)	1,497
PFNA 12 to 79 years	Cycle 2	2009 to 2011	0.2	99.4 (98.6 to 99.8)	0.82 (0.75 to 0.90)	1.9[d] (1.1 to 2.7)	1,524
PFDA 3 to 79 years	Cycle 6	2018 to 2019	0.092	67.6 (61.4 to 73.2)	0.12 (0.11 to 0.14)	0.51 (0.44 to 0.57)	2,354

Substance/ population	CHMS Cycle[a]	Year	LOD (µg/L)	Population weighted Detection Frequencies	GM (µg/L) (95% CI)[b]	95th (95% CI)	n
PFDA 3 to 79 years	Cycle 5	2016 to 2017	0.092	91.4 (86.0 to 94.8)	0.18 (0.16 to 0.20)	0.64 (0.47 to 0.81)	2,360
PFDA 12 to 79 years	Cycle 6	2018 to 2019	0.092	69.0 (63.1 to 74.4)	0.12 (0.11 to 0.14)	0.51 (0.45 to 0.58)	1,427
PFDA 12 to 79 years	Cycle 5	2016 to 2017	0.092	91.4 (85.9 to 94.9)	0.18 (0.16 to 0.21)	0.65 (0.45 to 0.84)	1,450
PFDA 12 to 79 years	Cycle 2	2009 to 2011	0.1	79.3 (72.6 to 847)	0.20 (0.17 to 0.22)	0.66 (0.45 to 0.87)	1,524
PFUnDA 3 to 79 years	Cycle 6	2018 to 2019	0.12	36.3 (29.2 to 44.0)	-	0.43 (0.34 to 0.53)	2508
PFUnDA 3 to 79 years	Cycle 5	2016 to 2017	0.12	35.8 (26.9 to 45.8)	-	0.46 (0.30 to 0.63)	2583
PFUnDA 12 to 79 years	Cycle 6	2018 to 2019	0.12	39.0 (31.3 to 47.2)	-	0.47 (0.35 to 0.60)	1,527
PFUnDA 12 to 79 years	Cycle 5	2016 to 2017	0.12	38.5 (29.1 to 48.9)	-	0.50 (0.34 to 0.67)	1,576
PFUnDA 12 to 79 years	Cycle 2	2009 to 2011	0.09	59.3 (47.5 to 70.0)	0.12 (0.098 to 0.14)	0.56[d] (0.30 to 0.82)	1,522
PFBA 3 to 79 years	Cycle 6	2018 to 2019	0.075	5.4[c] (3.3 to 8.6)	-	0.078 (<LOD to 0.091)	2,509
PFBA 3 to 79 years	Cycle 5	2016 to 2017	0.075	4.2[c] (2.3 to 7.7)	-	<LOD	2,590
PFBA 12 to 79 years	Cycle 6	2018 to 2019	0.075	5.4[c] (3.3 to 8.8)	-	<LOD	1,525
PFBA 12 to 79 years	Cycle 5	2016 to 2017	0.075	3.8[c] (1.8 to 7.8)	-	<LOD	1,583
PFBA 12 to 79 years	Cycle 2	2009 to 2011	0.5	0.40[c] (0.10 to 1.6)	-	<LOD	1,524
PFHxA 3 to 79 years	Cycle 6	2018 to 2019	0.084	1.0[c] (0.30 to 2.9)	-	<LOD	2,512

Substance/ population	CHMS Cycle[a]	Year	LOD (µg/L)	Population weighted Detection Frequencies	GM (µg/L) (95% CI)[b]	95th (95% CI)	n
PFHxA 3 to 79 years	Cycle 5	2016 to 2017	0.084	9.2[c] (5.0 to 16.2)	-	0.13[d] (<LOD to 0.18)	2,593
PFHxA 12 to 79 years	Cycle 6	2018 to 2019	0.084	1.0[c] (0.30 to 3.0)	-	<LOD	1,526
PFHxA 12 to 79 years	Cycle 5	2016 to 2017	0.084	9.2[c] (4.9 to 16.4)	-	0.13[d] (<LOD to 0.18)	1,583
PFHxA 12 to 79 years	Cycle 2	2009 to 2011	0.1	1.6[c] (0.50 to 4.9)	-	<LOD	1,524
PFBS 3 to 79 years	Cycle 6	2018 to 2019	0.066	0.30[c] (0.10 to 0.80)	-	<LOD	2,514
PFBS 3 to 79 years	Cycle 5	2016 to 2017	0.066	0.1[c] (0.10 to 0.30)	-	<LOD	2,584
PFBS 12 to 79 years	Cycle 6	2018 to 2019	0.066	0.20[c] (0.10 to 0.70)	-	<LOD	1,528
PFBS 12 to 79 years	Cycle 5	2016 to 2017	0.066	0.10[c] (0 to 0.30)	-	<LOD	1,577
PFBS 12 to 79 years	Cycle 2	2009 to 2011	0.4	0	-	<LOD	1,524

LOD: limit of detection; DF: detection frequency; GM: geometric mean; n: number of samples/participants

[a] For the purpose of total population comparisons between cycles 1, 2, 5, and 6 for PFOA, PFOS, and PFHxS, estimates were also calculated using data from participants aged 20 to 79 years as participants under the age of 20 years were not included in cycle 1 and participants under the age of 12 years were not included in cycle 2. For total population comparison between cycles 2 ,5, and 6 for PFNA,PFDA, PFUnDA, PFBA, PFHxA, and PFBS, estimates were also calculated using data from participants aged 12 to 79 years as participants under the age of 12 years were not included in cycle 2.

[b] If >40% of samples were below the LOD, the percentile distribution was reported but means were not calculated.

[c] Value must be used with caution due to high variability.

Table B-4. PFAS levels in plasma/serum: females in CHMS, pregnant women from Nunavik, and pregnant women in MIREC

Substance	Source	Year	Age (years)	LOD (µg/L)	DF or % >LOD*	GM (µg/L)	n
PFHxS	Women: CHMS Cycle 5 (plasma)[a]	2016 to 2017	18 to 40	0.063	99	0.44	243
PFHxS	Pregnant women: Nunavik (serum)[a]	2016 to 2017	16 to 40	0.04	100	0.27	97
PFHxS	Pregnant women: Nunavik (serum)[a]	2012	16 to 40	0.2	91.6	0.35	111
PFHxS	Pregnant women: MIREC (plasma)[b]	2008 to 2011	18 to 48	0.3	95	1.03	1,940
PFOS	Women: CHMS Cycle 5 (plasma)[a]	2016 to 2017	18 to 40	0.43	100	1.80	243
PFOS	Pregnant women: Nunavik (serum)[a]	2016 to 2017	16 to 40	0.2	100	3.3	97
PFOS	Pregnant women: Nunavik (serum)[a]	2012	16 to 40	0.3	100	3.8	111
PFOS	Pregnant women: MIREC (plasma)[b]	2008 to 2011	18 to 48	0.3	100	4.56	1,940
PFOA	Women: CHMS Cycle 5 (plasma)[a]	2016 to 2017	18 to 40	0.066	100	0.84	243
PFOA	Pregnant women: Nunavik (serum)[a]	2016 to 2017	16 to 40	0.03	100	0.54	97
PFOA	Pregnant women: Nunavik (serum)[a]	2012	16 to 40	0.07	100	0.67	111
PFOA	Pregnant women: MIREC (plasma)[b]	2008 to 2011	18 to 48	0.1	100	1.65	1,940
PFNA	Women: CHMS Cycle 5 (plasma)[a]	2016 to 2017	18 to 40	0.13	98	0.38	220
PFNA	Pregnant women: Nunavik (serum)[a]	2016 to 2017	16 to 40	0.07	100	2.3	97
PFNA	Pregnant women: Nunavik (serum)[a]	2012	16 to 40	0.24	100	2.0	111
PFDA	Women: CHMS Cycle 5 (plasma)[a]	2016 to 2017	18 to 40	0.092	NR	0.16	222
PFDA	Pregnant women: Nunavik (serum)[a]	2016 to 2017	16 to 40	0.07	100	0.51	97
PFDA	Pregnant women: Nunavik (serum)[a]	2012	16 to 40	0.1	98.1	0.45	111
PFUnDA	Women: CHMS Cycle 5 (plasma)[a]	2016 to 2017	18 to 40	0.12	NR	NR	241
PFUnDA	Pregnant women: Nunavik (serum)[a]	2016 to 2017	16 to 40	0.05	100	0.54	97
PFUnDA	Pregnant women: Nunavik (serum)[a]	2012	16 to 40	0.1	91.8	0.44	111

LOD: limit of detection; DF: detection frequency; GM: geometric mean; n: number of samples/participants; NR: not reported

[*] % >LODs were presented for the Nunavik study in Caron-Beaudoin et al. (2020) and for the MIREC study in Fisher et al. (2016). DFs were presented from CHMS cycle 5 (HC 2023b; personal communication, email Population Studies Division, HC, to Existing Substance Risk Assessment Bureau, HC, May 2022; unreferenced). These values cannot be directly compared as DFs are weighted to be representative of population level detection.
[a] Caron-Beaudoin et al. 2020
[b] Fisher et al. 2016

Table B-5. PFNA levels in CHMS adults and children, Indigenous on-reserve populations, Anishinabe children and youth, pregnant women from Nunavik, and adults from Dene communities (Dehcho region) in the Northwest Territories and a Gwich'in community in the Yukon

Group	Specific Group	Year	Age (years)	LOD (µg/L)	DF or % >LOD [a]	GM (µg/L)	n
Adults	CHMS Cycle 2 (plasma) (HC 2023b)	2009 to 2011	12 to 79	0.2	99.4	0.82	1,524
Adults	Indigenous on to reserve (plasma) (AFN 2013)	2011	20+	0.2	96.2	0.72	473
Youth	CHMS Cycle 5 (plasma) (HC 2023b)	2016 to 2017	12 to 19	0.13	99.4	0.41	494
Youth	CHMS Cycle 2 (plasma) (HC 2023b)	2009 to 2011	12 to 19	0.2	99.1	0.71	507
Youth	Anishinabe (serum) Caron-Beaudoin et al. 2019)	2015	12 to 19	0.07	100	3.01	38
Children	CHMS Cycle 5 (plasma) (HC 2023b)	2016 to 2017	6 to 11	0.13	98.7	0.45	492
Children	Anishinabe (serum) (Caron-Beaudoin et al. 2019)	2015	6 to 11	0.07	100	9.44	45
Children	CHMS Cycle 5 (plasma) (HC 2023b)	2016 to 2017	3 to 5	0.13	99.3	0.45	453
Children	Anishinabe (serum) (Caron-Beaudoin et al. 2019)	2015	3 to 5	0.07	100	3.8	23
Women	CHMS Cycle 5 (plasma) (Caron-Beaudoin et al. 2020)	2016 to 2017	18 to 40	0.13	NR	0.38	243
Pregnant women	Nunavik (serum) (Caron-Beaudoin et al. 2020)	2016 to 2017	16 to 40	0.07	100	2.3	97
Pregnant women	Nunavik (serum) (Caron-Beaudoin et al. 2020)	2012	16 to 40	NR	100	2.0	111
Adults	CHMS Cycle 5 (plasma) (HC 2023b)	2016 to 2017	12 to 79	0.13	98.8	0.51	1,497
Adults	Dene communities in Dehcho region, NWT (plasma) (Garcia-Barrios et al. 2021)	2017	20 to 79	0.01	100	1.42	109
Adults	Gwich'in community, Yukon (serum) (Garcia-Barrios et al. 2021)	2019	20 to 79	0.01	100	0.94	54
Adults	Nunavik, Quebec (plasma) (Aker et al. 2021)	2017	18+	0.10	100	3.7	500

LOD: limit of detection; DF: detection frequency; GM: geometric mean; n: number of samples/ participants; NR: not reported

[a] % >LODs were presented for AFN 2013, Caron-Beaudoin et al. (2019), and Caron-Beaudoin et al. (2020) studies. DFs were presented for CHMS Cycle 1, 2, and 5, and the Garcia-Barrios et al. (2021) study. These values cannot be directly compared as DFs are weighted to be representative of population level detection.

13 Appendix C: Interpretation of biomonitoring data - tables

This Appendix presents data tables for Figures 8 to 10 presented in the Interpretation of HBM data section.

Table C-1. Geometric mean, 25th, 75th, and 95th percentile of the sums of concentrations (in µg/L) of 4 PFAS in the serum/plasma of the general population of Canada based on the CHMS (3 to 79), females of reproductive age from CHMS, pregnant women and adults in Nunavik, and adults from Dene communities in the Dehcho region and a Gwich'in community

Study	n	GM[a]	P25	P75	P95
CHMS: females 18 to 40 (2018 to 2019)[b]	204	3.5	2.4	4.7	8.9[c]
CHMS: all ages (3 to 79) (2018 to 2019)	2,396	5.4	3.4	8.3	16
Nunavik: pregnant women (2016 to 2017)[d]	97	6.8	4.4	9.7	20.6
Nunavik: adults (2017)[e]	500	11	6.5	17.1	37.3
Dehcho NWT: adults (2017)[f]	125	5.06	2.95	8.03	25.56
Old Crow Yukon: adults (2019)[f]	54	3.64	2.28	5.76	9.02

n: number of samples/participants; GM: geometric mean; P25: 25th percentile; P75: 75th percentile; P95: 95th percentile

[a] Estimated from the sum of concentrations of PFOA, PFOS, PFHxS, and PFNA calculated for each participant in the studies (calculations are not shown)

[b] CHMS cycle 6 (2018 to 2019), plasma, females, 18 to 40 years (the sum of PFAS concentrations was estimated using individual data from CHMS [personal communication, email from Population Health Division, HC, to Existing Substances Risk Assessment Bureau, HC, May 2022; unreferenced])

[c] Value must be used with caution due to high variability.

[d] Pregnant women, serum, 16 to 40 years (Caron-Beaudoin et al. 2020)

[e] Adults, serum (18 to 80 years) (Aker et al. 2021)

[f] Adults (20 to 79 years) (Garcia-Barrios et al. 2021)

Table C-2. Geometric mean, 25th, 75th, and 95th percentile of PFOA and PFOS serum/plasma concentrations (in µg/L) in the CHMS total population (3 to 79 years), Nunavik pregnant women (Caron-Beaudoin et al. 2020), Indigenous on-reserve across Canada (AFN 2013), adults from Dene communities in the Dehcho region (Northwest Territories) and Gwich'in community in Yukon (Garcia-Barrios et al. 2021), and Inuit adults of Nunavik, Quebec (Aker at al. 2021).

Study	n PFOA	P25 PFOA	GM PFOA	P75 PFOA	P95 PFOA	n PFOS	P25 PFOS	GM PFOS	P75 PFOS	P95 PFOS
CHMS 2018 to 2019[a]	2,513	0.85	1.2	1.7	2.9	2514	1.5	2.5	4.1	8.3
Nunavik 2016 to 2017 (QC, pregnant women)[b]	97	0.41	0.53	0.74	1.1	97	2	3.3	5.5	12.3
FNBI 2011 (adults, 20+ years)[c]	473	0.89	1.4	2.2	4.1	473	1.6	3.1	6.4	16
Dene communities in Dehcho region 2017 (NWT, 20 to 79 years)[d]	109	0.58	0.88	1.2	3.1	109	1	2	3.4	8.6
Gwich'in community in Yukon 2019 (20 to 79 years)[e]	54	0.65	0.89	1.3	1.9	54	0.6	1.1	1.9	4.1
Nunavik 2017 (18+ years)[f]	500	0.7	1.0	1.5	2.4	500	2.8	5.1	8.9	20.5

n: number of samples/participants; P25: 25th percentile; GM: geometric mean; P75: 75th percentile; P95: 95th percentile

[a] CHMS cycle 6 2018 to 2019, plasma, total population, 3 to 79 years, n=2513 for PFOA, and n=2514 for PFOS (HC 2023b); for P25 and P75 estimates for PFOA and PFOS: personal communication, email from Population Studies Division, HC, to Existing Substance Risk Assessment Bureau, HC, May 2022; unreferenced

[b] Pregnant women, Nunavik, serum, 16–40 years, n=97 (Caron-Beaudoin et al. 2020)

[c] Adults, Indigenous on-reserve and crown land populations, plasma, 20+ years, n= 473 (AFN 2013)

[d] Adults, Dene communities in Dehcho region, Northwest Territories, plasma, 20 to 79 years, n=109 (Garcia-Barrios et al. 2021)

[e] Adults, Gwich'in community, Yukon, serum, 20 to 79 years, n=54 (Garcia-Barrios et al. 2021)

[f] Adults, Inuit of Nunavik from 14 villages (Hudson and Ungava coast) in Quebec, plasma, 18+ years, n=500

14 Appendix D: Biomonitoring data in firefighters – tables

Table D-1. Firefighter serum levels (µg/L) for commonly measured PFAS (geometric means with confidence interval, if available) and comparison population information,[a] including GM and upper CI of GM

Study	PFHxA	PFHpA	PFOA	PFNA	PFDA	PFUnDA	PFBS	PFHxS	PFHpS	PFOS
1) Barton et al. 2020 gender NR; age >18	NR	NR	3.1 (2.2-4.3)	0.47 (0.38-0.58)	NM	NR	NR	16 (9.9-25.8)	0.25 (0.17-0.38)	14 (10.4-19)
Ref. pop.: NHANES 2017–2018; male 20–60 years	-	-	1.6 (1.7)	0.41 (0.47)	-	-	-	1 (1.1)	0.25 (0.2-0.33)	5.5 (5.8)
Ratio of lower CI of GM from FF study / Upper CI of GM in ref. pop.	-	-	1.3	1.0	-	-	-	9.0	0.5	1.8
2) Burgess et al. 2022 Station A; **male,** mean age 42	NM	NM	1.77	0.42	0.25	0.11	NM	3.24	NM	4.30
Ref. pop.: NHANES 2017–2018; male 20–60 years	-	-	1.6 (1.7)	0.41 (0.47)	0.18 (0.2)	0.11 (0.12)	-	1.5 (1.7)	-	5.2 (5.8)
Ratio of lower CI of GM from FF study / Upper CI of GM in ref. pop.	-	-	1.0	1.0	1.3	0.9	-	1.9	-	0.7
3) Burgess et al. 2022 Station B; male, mean age 43	NM	NM	1.92	0.57	0.22	0.14	NM	1.90	NM	5.41
Ref. pop.: NHANES 2017–2018; male 20–60 years	-	-	1.6 (1.7)	0.41 (0.47)	0.18 (0.2)	0.11 (0.12)	-	1.5 (1.7)	-	5.2 (5.8)
Ratio of lower CI of GM from FF study / Upper CI of GM in ref. pop.	-	-	1.1	1.2	1.1	1.2	-	1.1	-	0.9
4) Burgess et al. 2022 Station C; male, mean age 42	NM	NM	2.04	0.60	0.18	0.11	NM	3.78	NM	6.62
Ref. pop.: NHANES 2017–2018; male 20–60 years	-	-	1.6 (1.7)	0.41 (0.47)	0.18 (0.2)	0.11 (0.12)	-	1.5 (1.7)	-	5.2 (5.8)
Ratio of lower CI of GM from FF study / Upper CI of GM in ref. pop.	-	-	1.2	1.3	0.9	0.9	-	2.2	-	1.1
5) Burgess et al. 2022 Station D; male, mean age 43	NM	NM	1.82	0.64	0.19	0.14	NM	1.77	NM	3.69
Ref. pop.: NHANES 2017–2018; male 20–60 years	-	-	1.6 (1.7)	0.41 (0.47)	0.18 (0.2)	0.11 (0.12)	-	1.5 (1.7)	-	5.2 (5.8)
Ratio of lower CI of GM from FF study / Upper CI of GM in ref. pop.	-	-	1.1	1.4	0.95	1.2	-	1.0	-	0.6
6) Burgess et al. 2022 Station A; female, mean age 42	NM	NM	1.35	0.32	0.21	0.12	NM	1.42	NM	2.36
Ref. pop.: NHANES 2017-2018; female 20-60 years	-	-	1.1 (1.2)	0.33 (0.4)	0.19 (0.21)	0.11 (0.13)	-	0.68 (0.75)	-	2.9 (3.3)
Ratio of lower CI of GM from FF study / Upper CI of GM in ref. pop.	-	-	1.1	0.8	1.0	0.9	-	1.9	-	0.7
7) Dobraca et al. 2015 99% male; 2% female; mean age 42.8	NM	0.13 (0.11–0.15)	3.75 (3.37–4.17)	1.15 (1.06–1.25)	0.9 (0.78–1.03)	0.24 (0.21–0.27)	NR	2.26 (2–2.54)	NM	12.5 (11.3–13.8)
Ref. pop.: NHANES 2011–2012; male 20–60 years	-	-	2.4 (2.6)	1.4 (1.6)	0.21 (0.23)	0.12 (0.14)	-	1.7 (1.9)	-	8 (8.9)

Study	PFHxA	PFHpA	PFOA	PFNA	PFDA	PFUnDA	PFBS	PFHxS	PFHpS	PFOS
Ratio of lower CI of GM from FF study / Upper CI of GM in ref. pop.	-	-	1.3	0.7	3.4	1.5	-	1.1	-	1.3
8) Goodrich et al. 2021 89% male; mean age 39 2016-2019	NM	NM	1.79 (1.68-1.89)	0.44 (0.41-0.48)	0.23 (0.22-0.25)	0.12 (0.11-0.13)	NM	2.5 (2.29-2.74)	NM	4.02 (3.74-4.32)
Ref. pop.: NHANES 2017–2018; male 20–60 years	-	-	1.6 (1.7)	0.41 (0.47)	0.18 (0.2)	0.11 (0.12)	-	1.5 (1.7)	-	5.2 (5.8)
Ratio of lower CI of GM from FF study / Upper CI of GM in ref. pop.	-	-	1.0	0.9	1.2	1	-	1.4	-	0.7
9) Graber et al. 2021 male; mean age 47	NM	NM	2.07 (1.89–2.26)	0.97 (0.89–1.05)	0.31 (0.29–0.33)	0.11 (0.1–0.12)	NM	1.83 (1.61–2.09)	NM	4.25 (3.76–4.8)
Ref. pop.: NHANES 2017–2018; male 20–60 years	-	-	1.6 (1.7)	0.41 (0.47)	0.18 (0.2)	0.11 (0.12)	-	1.5 (1.7)	-	5.2 (5.8)
Ratio of lower CI of GM from FF study / Upper CI of GM in ref. pop.	-	-	1.1	1.9	1.5	0.9	-	0.94	-	0.6
10) Jin et al. 2011 male; mean age 40	NR	NR	37.7	1.56	NR	NR	NM	4.77	NM	24.37
Ref. pop.: NHANES 2005–2006; male 20–60 years	-	-	4.8 (5.3)	1.2 (1.5)	NR	NR	-	2.1 (2.5)	-	20 (22)
Ratio of GM from FF study / Upper CI of GM in ref. pop.	-	-	7.1	1	NR	NR	-	1.9	-	1.1
11) Khalil et al. 2020 male; mean age 51	NM	NR	3.33 (2.89–3.84)	0.93 (0.81–1.06)	0.25 (0.22–0.29)	0.12 (0.1–0.14)	NR	3.07 (2.66–3.55)	NM	13.36 (11.64–15.34)
Ref. pop.: NHANES 2009–2010; male 30–55 years	-	-	3.5 (4.0)	1.4 (1.6)	0.3 (0.33)	0.17 (0.2)	-	2.1 (2.4)	-	12 (14)
Ratio of lower CI of GM from FF study / Upper CI of GM in ref. pop.	-	-	0.8	0.6	0.8	0.6	-	1.1	-	0.8
12) Laitinen et al. 2014 male; mean age 44.4	NR	NR	2.94	1.22	NR	NR	NM	2.19	NR	11.1
Ref. pop.: CHMS 2009–2011; male 20–60 years	-	-	2.6 (2.9)	0.81 (0.91)	NR	NR	-	2.3 (2.8)	-	7.9 (9)
Ratio of GM from FF study / Upper CI of GM in ref. pop.	-	-	1.0	1.3	NR	NR	-	0.8	-	1.2
13) Leary et al. 2020 male; mean age 41	NM	NM	2.17[b]	0.45[b]	NM	NM	NM	6.45[b]	NM	10.69[b]
Ref. pop.: NHANES 2017–2018; male 20–60 years	-	-	1.8 (2)	0.51 (0.56)	--	--	-	2 (2.4)	-	6.2 (6.9)
Ratio of GM from FF study / Upper CI of GM in ref. pop.	-	-	1.1	0.8	--	--	-	2.7	-	1.5
14) Nilsson et al. 2022a 98% male; mean age 52; medians	NM	<0.07	1.5	0.32	0.16	<0.08	<0.05	6.5	0.85	14
Ref. pop.: NHANES 2017–2018; male 20–60 years	-	-	1.6 (1.7)	0.41 (0.47)	0.18 (0.2)	0.11 (0.12)	-	1.5 (1.7)	-	5.2 (5.8)
Ratio of lower CI of GM from FF study / Upper CI of GM in ref. pop.	-	-	0.9	0.7	0.8	-	-	3.8	-	2.4
15) Rotander et al. 2015 97% male, 3% female; mean age 50	NR	0.07	4.2	0.69	0.27	0.14	NR	25	NM	66

Study	PFHxA	PFHpA	PFOA	PFNA	PFDA	PFUnDA	PFBS	PFHxS	PFHpS	PFOS
Ref. pop.: CHMS 2016–2017; male 20–60 years	-	-	1.5 (1.8)	0.53 (0.63)	0.19 (0.24)	NR	-	1.5 (1.9)	-	4.2 (5.1)
Ratio of GM from FF study / Upper CI of GM in ref. pop.	-	-	2.3	1.1	1.1	NR	-	13.2	-	12.9
16) Shaw et al. 2013 male; mean age 41.3	NM	0.3	6	2	1	0.2	NR	1	NM	9
Ref. pop.: NHANES 2009–2010; male 30–55 years	-	-	3.5 (4)	1.4 (1.6)	0.3 (0.33)	0.17 (0.2)	-	2.1 (2.4)	-	12 (14)
Ratio of GM from FF study / Upper CI of GM in ref. pop.	-	-	1.5	1.3	3	1	-	0.4	-	0.6
17) Trowbridge et al. 2020 female; mean age 47.5	NR	NR	1.13 (1.05–1.25)	0.77 (0.61–0.74)	0.27 (0.23–0.28)	0.23 (0.14–0.22)	0.13 (0.1–0.16)	4.55 (3.24–4.43)	NM	4.33 (3.68–4.59)
Ref. pop.: NHANES 2014–2015; female 20–60 years	-	-	1.2 (1.3)	0.47 (0.53)	0.13 (0.15)	NR	NM	0.71 (0.81)	-	3.1 (3.4)
Ratio of lower CI of GM from FF study / Upper CI of GM in ref. pop.	-	-	0.8	1.2	1.5	NR	-	4.0	-	1.1
Average of Ratios across studies	**-**	**-**	**1.5**	**1.1**	**1.4**	**1.0**	**-**	**2.8**	**-**	**1.8**

NR: not reported (for example, if a large number of samples is below detection); NM: not monitored (substance not monitored in study); GM: geometric mean; CI: confidence interval; Ref. Pop: reference population

[a] Values for specific populations subsets and upper confidence intervals of geometric means from subpopulations from NHANES and CHMS obtained through personal communication from Population Studies Division, HC, to Existing Substances Risk Assessment Bureau, HC, June 2021; unreferenced.

[b] Median

15 Appendix E: References consulted for health effects information in sections 7.2.1 to 7.2.8

Endpoint	Study type	Reports/ Reviews	Abstracts
Liver	Epidemiological studies	ATSDR 2021	Salihovic et al. 2018; Seo et al. 2018; Attanasio 2019; Bassler et al. 2019; Donat-Vargas et al. 2019a; Dong et al. 2019; Graber et al. 2019; Jain 2019, 2019d; Lin et al. 2019; Nian et al. 2019; Jin et al. 2020; Yao et al. 2020; Averina et al. 2021; Blomberg et al. 2021; Canova et al. 2021; Lee et al. 2021; Han et al. 2021; Yang et al. 2021; Borghese et al. 2022; Cakmak et al. 2022; Choi et al. 2022; Costello et al. 2022; Dunder et al. 2022; Maranhao Neto et al. 2022; Nilsson et al. 2022b; NJ DEP 2021; Haug et al. 2023; Kim OJ et al. 2023; Liao et al. 2023; Limei et al. 2023; Zhang X et al. 2023
Liver	Animal studies	HC 2006; NTP 2019a; NTP 2019b; EFSA CONTAM Panel 2020; NTP 2020Rice et al. 2020; ATSDR 2021; NJ DEP 2021; Rice et al. 2021; Polcher et al. 2023; US EPA 2023a; US EPA 2023b	Ladics et al. 2008; Loveless et al. 2009; Xie et al. 2009; Gordon 2011; Hirata-Koizumi et al. 2012; Serex et al. 2014; Caverly Rae et al. 2015; Hirata-Koizumi et al. 2015; Mukerji et al. 2015; Beekman 2016; Rushing et al. 2017; Sheng et al. 2017; Wang J et al. 2017, 2019c, 2021; Han et al. 2018a, 2018b, 2020; Huck et al. 2018; Lai et al. 2018; Li D et al. 2018; Lv et al. 2018; Sheng et al. 2018; Wu et al. 2018; Zhang H et al. 2018; Conley et al. 2019; Guo et al. 2019, 2021a, 2021b; Li D et al. 2019; Li X et al. 2019; Liang et al. 2019; Singh and Singh 2019a; Su et al. 2019; Huang et al. 2020; Zhou et al. 2020; Chen et al. 2021; Owumi et al. 2021; Shao et al. 2021; Wang C et al. 2021; Wang G et al. 2021; Woodlief et al. 2021; Chen et al. 2022; Conley et al. 2022; Costello et al. 2022; He et al. 2022; Narizzano et al. 2022; Qin et al. 2022a; Shi et al. 2022; Wang Z et al. 2022a; Wang C et al. 2023; Conley et al. 2024; Jackson et al. 2024
Kidney	Epidemiological studies	Stanifer et al. 2018; Ferrari et al. 2019; ATSDR 2021	Blake et al. 2018; Conway et al. 2018; Wang J et al. 2019; Zeng X-W et al. 2019; Jain et al. 2019a, 2019b, 2019c; Scinicariello et al. 2020; Yao et al. 2020; Lin et al. 2021; Moon 2021; Shearer et al. 2021; Erdal et al. 2021; Feng et al. 2022; Li Z et al. 2022d; Nilsson et al. 2022b; Xie LN et al. 2022; Jain 2023; Yang et al. 2023
Kidney	Animal studies	HC 2006; Stanifer	Ladics et al. 2008; Loveless et al. 2009; Gordon 2011; Hirata-Koizumi et al. 2012, 2015; Serex et al. 2014;

		et al. 2018; Ferrari et al. 2019; NTP 2019a; NTP 2019b; NTP 2020; Rice et al. 2020; ATSDR 2021; NJ DEP 2021; Rice et al. 2021; US EPA 2023a	Caverly Rae et al. 2015; Kato et al. 2015; Mukerji et al. 2015; Beekman 2016; Han et al. 2020; Rashid et al. 2020; ECHA 2021b; Owumi et al. 2021; Crute et al. 2023
Immune system	Epidemiological studies	ATSDR 2021; NJ DEP 2021	Averina et al. 2018; Chen Q et al. 2018; Impinen et al. 2018; Pilkerton et al. 2018; Beck et al. 2019; Manzano-Salgado et al. 2019; Wen et al. 2019; Zeng X et al. 2019; Abraham et al. 2020; Ait Bamai et al. 2020; Kvalem et al. 2020; Timmermann et al. 2020; Bulka et al. 2021; Dalsager et al. 2021; Lopez-Espinosa et al. 2021; Shih et al. 2021; Jones et al. 2022; Porter et al. 2022; Qu et al. 2022; Shen et al. 2022; Timmermann et al. 2022; Wang Z et al. 2022b; Zhang Y et al. 2022a; Crawford et al. 2023; Kaur et al. 2023; Pan et al. 2023; Zhang Y et al. 2023
Immune system	Animal studies	NTP 2019a; NTP 2019b; EFSA CONTAM Panel 2020; Rice et al. 2020; ATSDR 2021; NJ DEP 2021; Rice et al. 2021	Ladics et al. 2008; Xie et al. 2009; Gordon 2011; Hirata-Koizumi et al. 2012, 2015; Kato et al. 2015; Bodin et al. 2016; Rushing et al. 2017; Berntsen et al. 2018; Lee et al. 2018; Wang X et al. 2019; McDonough et al. 2020; Shane et al. 2020; Woodlief et al. 2021; Wang M et al. 2021; Wang C et al. 2023
Reproduction	Epidemiological studies	ATSDR 2021; NJ DEP 2021	Joensen et al. 2013; Louis et al. 2015; Jaacks et al. 2016; Zhou et al. 2017; Heffernan et al. 2018; Song X et al. 2018; Zhang S et al. 2018b; Liu et al. 2020; Mitro et al. 2020; Harlow et al. 2021; Luo K et al. 2021; Wang Y et al. 2021; Hærvig et al. 2022; Petersen et al. 2022;

			Yang J et al. 2022; Cohen et al. 2023; Guo et al. 2023; Wang H et al. 2023a; Zeng et al. 2023
Reproduction	Animal studies	HC 2006; Ding et al. 2020; NTP 2019a; NTP 2019b; Rice et al. 2020; ATSDR 2021; NJ DEP 2021; Rice et al. 2021; Polcher et al. 2023; US EPA 2023a; ECHA 2024a	Austin et al. 2003; Miyata 2007; O'Connor et al. 2014; Serex et al. 2014; Kato et al. 2015; Mukerji et al. 2015; Wang X et al. 2018; Zhou et al. 2018, 2020; Conley et al. 2019; Blake et al. 2020; Cao et al. 2020; Li H et al. 2021; Mao et al. 2021; Wang C et al. 2021; Wang Z et al. 2021; Yan et al. 2021; Zhang S et al. 2021; Zou et al. 2021; Huang J et al. 2022b; Li Z et al. 2022b; Xin et al. 2022
Development	Epidemiological studies	ATSDR 2021; Erinc et al. 2021	Meng et al. 2018; Sagiv et al. 2018; Ernst et al. 2019; Huang R et al. 2019; Marks et al. 2019; Wikström et al. 2019, 2020; Xu et al. 2019; Arbuckle et al. 2020; Borghese et al. 2020; Chu et al. 2020; Di Nisio et al. 2020; Huo et al. 2020; Jensen et al. 2020; Liew et al. 2020; Rylander et al. 2020; Xiao et al. 2020; Birukov et al. 2021; Bommarito et al. 2021; Cao et al. 2021; Carwile et al. 2021; Christensen et al. 2021; Deji et al. 2021; Gao et al. 2021; Liu H et al. 2021; Ou et al. 2021; Wang B et al. 2021; Yao et al. 2021; Chang et al. 2022; Cui et al. 2022; Engström et al. 2022; Fan et al. 2022; Hall et al. 2022; Liao et al. 2022a, 2022b; Lin M et al. 2022; Liu B et al. 2022; Mi et al. 2022; Romano et al. 2022; Wang J et al. 2022 Yang L et al. 2022; Yang Z et al. 2022; Yu et al. 2022; Zhang Y et al. 2022b; Zhu et al. 2022; Hirke et al. 2023; Jia et al. 2023; Mwapasa et al. 2023; Padula et al. 2023; Song et al. 2023; Wang H et al. 2023b; Wright et al. 2023
Development	Animal studies	HC 2006; Abbott 2015; Ali et al. 2019; Rice et al. 2020; ATSDR 2021; Rice et al. 2021;	Case et al. 2001; Gordon 2011; Hirata-Koizumi et al. 2012, 2015; O'Connor et al. 2014; Mukerji et al. 2015; Chang et al. 2018; Ramhøj et al. 2018; Song P et al. 2018; Chen et al. 2019; Conley et al. 2019; Du et al. 2019; Singh and Singh 2019b; Zhang et al. 2020; Bao et al. 2021; Li C et al. 2021; Li H et al. 2021; ; Li Z et al. 2021; Luo D et al. 2021; Wang C et al. 2021; Zhang Y et al. 2021; Conley et al. 2022; Dangudubiyyam et al. 2022; Li et al. 2022b; Narizzano et al. 2022; Crute et al. 2023

		Tarapore et al. 2021; Polcher et al. 2023; US EPA 2023a	
Endocrine function (thyroid)	Epidemiological studies	Boesen et al. 2020; ATSDR 2021; Coperchini et al. 2021; NJ DEP 2021	Inoue et al. 2019; Itoh et al. 2019; Reardon et al. 2019; Aimuzi et al. 2020; Kim et al. 2020; Lebeaux et al. 2020; Liang et al. 2020; Liu et al. 2020; Preston et al. 2020; Xiao et al. 2020; Sarzo et al. 2021; Jensen et al. 2022; Nilsson et al. 2022b; Tillaut et al. 2022; Li QQ et al. 2023; Zhang L et al. 2023
Endocrine function (thyroid)	Animal studies	HC 2006; Rice et al. 2020; ATSDR 2021; NJ DEP 2021; Rice et al. 2021; Polcher et al. 2023; US EPA 2023a	Austin et al. 2003; Ladics et al. 2008; Gordon 2011; Hirata-Koizumi et al. 2015; Li et al. 2017; Ramhøj et al. 2018; Conley et al. 2019; Hong et al. 2020; Wang C et al. 2021; Davidsen et al. 2022; Narizzano et al. 2022
Nervous system	Epidemiological studies	EFSA CONTAM Panel 2020; ATSDR 2021	Gump et al. 2011; Niu et al. 2019b; Luo et al. 2020; Shin et al. 2020; Harris et al. 2021; Jedynak et al. 2021; Oh et al. 2021a,2021b; Skogheim et al. 2021; Vuong et al. 2021a, 2021b; Yu et al. 2021a; Bach et al. 2022; Huang Y et al. 2022; Itoh et al. 2022; Luo et al. 2022; Oh et al. 2022a, 2022b; Starnes et al. 2022; Xie Z et al. 2022; Yao et al. 2022; Kim JI et al. 2023; Li QQ et al. 2023; Reardon et al. 2023; Wang H et al. 2023c; Yao et al. 2023; Zhang B et al. 2023
Nervous system	Animal studies	Wang Y et al. 2019b; EFSA CONTAM Panel 2020; Piekarski et al. 2020; ATSDR 2021; US	Austin et al. 2003; Miyata 2007; Johansson et al. 2008; Lee and Viberg 2013; Hirata-Koizumi et al. 2015; Hallgren and Viberg 2016; Salgado et al. 2016; Zhang Q et al. 2016; Kawabata et al. 2017b; Mshaty et al. 2020; Merrill et al, 2022; Ninomiya et al, 2022; Shi et al. 2022; Sim and Lee 2022

		EPA 2023a	
Metabolism and body weight	Epidemiological studies	Qi et al. 2020; ATSDR 2021	Matilla-Santander et al. 2017; Lauritzen et al. 2018; Mancini et al. 2018; Wang Y et al. 2018; Alderete et al. 2019; Christensen et al. 2019; Donat-Vargas et al. 2019b; Fassler et al. 2019; Liu X et al. 2019; Marks et al. 2019; Rahman et al. 2019; Tian et al. 2019; Valvi et al. 2019; Xu et al. 2019; Chen Z et al. 2020; Duan et al. 2020; Li J et al. 2020b; Mitro et al. 2020; Preston et al. 2020; Ren et al. 2020; Wikström et al. 2020; Xiao et al. 2020; Xu H et al. 2020; Averina et al. 2021; Canova et al. 2021; Cao et al. 2021; Ding et al. 2021; Duan et al. 2021; Geiger et al. 2021; Goodrich et al. 2021a; Han et al. 2021; Horikoshi et al. 2021; Janis et al. 2021; Mitro et al. 2021; Thomsen et al. 2021; Valvi et al. 2021; Yu et al. 2021b; Zeeshan et al. 2021; Bloom et al. 2022; Chung et al. 2022; Fan et al. 2022; Hall et al. 2022; Lind et al. 2022; Maranhao Neto et al. 2022; Park et al. 2022; Romano et al. 2022; Wang J et al. 2022; Yang Z et al. 2022; Zhang S et al. 2022; Zhang Y et al. 2022b; Brosset and Ngueta, 2023; Jia et al. 2023; Mwapasa et al. 2023; Padula et al. 2023; Song et al. 2023; Valvi et al. 2023; Wright et al. 2023
Metabolism and body weight	Animal studies	HC 2006; NTP 2019a; NTP 2019b; NTP 2020; Rice et al. 2020; ATSDR 2021; Rice et al. 2021; Polcher et al. 2023; US EPA 2023a	Case et al. 2001; Ladics et al. 2008; Ding et al. 2009; Hines et al. 2009; Xie et al. 2009; Gordon 2011; Fang et al. 2012a; Hirata-Koizumi et al. 2012, 2015; Lv et al. 2013; O'Connor et al. 2014; Serex et al. 2014; Wan et al. 2014; Wang L et al. 2014; Caverly Rae et al. 2015; Mukerji et al. 2015; Yan et al. 2015; Bodin et al. 2016; Zheng et al. 2017; Du et al. 2018; Huck et al. 2018; Lai et al. 2018; Sheng et al. 2018; Zhang H et al. 2018; Conley et al. 2019, 2021; Blake at al. 2020; Zhou et al. 2020; Chen et al. 2021; Li C et al. 2021Shao et al. 2021; Conley et al. 2022; He et al. 2022; Qin et al. 2022b; Shi et al. 2022