# September 2017 DRAFT Per- and Poly-Fluorinated Alkyl Substances Chemical Action Plan (PFAS CAP)

The Washington State departments of Ecology and Health prepared a draft of several PFAS CAP chapters for external review. This document is one chapter to a planned multi-chapter PFAS CAP. This material may be modified in response to comments and the content re-organized for the final Action Plan.

The September 2017 Draft PFAS CAP includes: Health, Environment, Chemistry, Regulations, Uses/Sources, Intro/Scope. This draft may include cross-references to other sections/chapters in the Draft PFAS CAP or notes where additional information will be provided in a later draft.

An updated draft of the PFAS CAP will be provided in November/December 2017 for additional review and comment. The PFAS CAP Advisory Committee will discuss comments on these draft chapters at the November 1, 2017 meeting.

Ecology and Health are asking interested parties to provide feedback. Comments on these draft documents are due to Ecology by **October 20, 2017.**

**Submit comments, suggestions, and questions to Kara Steward at kara.steward@ecy.wa.gov.**

The Draft PFAS CAP documents are posted at https://www.ezview.wa.gov/?alias=1962&pageid=37105 (at the bottom of the webpage).

## *Introduction - Health Concerns*

Public health concern about the presence of PFAS in the environment and humans is increasing. ~~There are reported to be more than 3,000 PFAS on the global market.~~ A recent survey by the Swedish Chemical Agency suggests that there may be more than 3,000 PFAS on the world market (KEMI, 2015). ~~There are more than 3,000 PFAS on the global market, and w~~We know very little about the environmental fate, transport, distribution and toxicity of most of them. Most research and regulation focus on two long-chain ~~PFAS~~perfluoroalkyl acids (PFAAs~~S~~) ~~(i.e.~~ perfluoro-octane sulfonate [PFOS] and perfluoro octanoic acid [PFOA]~~)~~ and their potential precursors. These compounds have been found to cause liver toxicity and tumors, alter hormones and timing of sexual maturation, suppress immune response, and cause reproductive and developmental effects in laboratory animals. Some but not all, epidemiological studies evidence suggest that exposure to PFOA and PFOS in humans: increases cholesterol levels, reduces birth weight, reduces immune antibody response to childhood vaccines and may increase rates of some types of cancers such as kidney and testicular cancer.

~~PFAS~~ PFAAs such as PFOS, PFOA, perfluorohexane sulfonate (PFHxS), perfluorononanoic acid (PFNA) and perfluorodecanoic acid (PFDA) have been detected in serum of pregnant women, amniotic fluid, placental tissue, umbilical cord blood, and breast milk. They have also been measured in infant's blood serum shortly after birth. At birth, infants have roughly the same serum levels of PFOA as their mother, but these serum levels will surpass maternal levels during infancy due to consumption of ~~breastmilk~~breast milk or formula made with contaminated water.

People can be exposed to ~~PFAS~~ PFAAs from a number of sources. These include contaminated drinking water, food grown in contaminated soils or in contact with PFAS coatings on food wrappers, fish caught from contaminated waters, and indoor air and dust that accumulate PFAS from carpets, textiles~~floor polish~~ and other household items. As a result of exposures, some ~~PFAS~~PFAAs, such as PFOA, PFOS, PFHxS, and PFNA, have been found to bioaccumulate in people, fish, and some wildlife. Humans excrete PFAS slowly such that years are required to reduce body burden levels.

Levels of long-chain[1] ~~PFAS~~ PFAAs in humans are declining slowly as industry is phasing-out use of ~~these~~ long-chain PFAAs and their potential precursors globally~~chemicals in the United States~~. Industry is transitioning to shorter-chain ~~PFAS~~ PFAS alternatives and non-fluorinated alternative chemicals. The difference between long-chain and short-chain is the length of the ~~fully fluorinated chain.~~perfluoroalkyl chain (Reference OECD Web portal here http://www.oecd.org/chemicalsafety/portal-perfluorinated-chemicals/ ). Although the toxicity and bioaccumulation potential of short chain ~~PFAS~~ PFAAs that are the potential degradation products from the short-chain PFAS alternatives ~~appear to~~is ~~be~~ lower, there are

[1] According to the Organization for Economic Cooperation and Development: "Long-chain perfluorinated compounds" refers to: Perfluorocarboxylic acids with carbon chain lengths C8 and higher, including perfluorooctanoic acid (PFOA); Perfluoroalkyl sulfonates with carbon chain lengths C6 and higher, including perfluorohexane sulfonic acid (PFHxS) and perfluorooctane sulfonate (PFOS); and precursors of these substances that may be produced or present in products.

**Commented [A1]:** Clarify this as there are likely not 3000 products. This list includes intermediates, discontinued and historical products, as well as current items of commerce. The suggested sentence is more accurate.

**Commented [A2]:** The term bioaccumulation is used loosely and, as presented, could be misinterpreted as being synonymous with detections of selected PFAS in people, fish, and wildlife, rather than evidence of concentrations increasing over time, or biomagnifying through a food web.

**Commented [A3]:** The following statement is made without qualification, "Humans excrete PFAS slowly such that years are required to reduce body burden levels". Is this indicative of all PFAS, or long-chain only? Is the term "slowly" implying that relative to other compounds, PFAS is retained in the body for a long time – or is it relative to animals used in toxicity testing? And isn't it true that once exposure via drinking water stops, elimination rates will cause the body burden levels to decline – so the more important question becomes one of the rate of change in risk? For example, what is the typical period of time needed for a community that has been exposed via drinking water to experience acceptable body burdens after the drinking water pathway has been mitigated?

some preliminary concerns with these chemicals. Study findings indicate that they are extremely persistent, highly soluble in water and mobile in soil. Compared to long-chain ~~PFAS~~ PFAAs they are more challenging to remove from drinking water with current filtration technology, able to migrate more efficiently from paper to food (please provide references for this statement),~~.~~ and more easily taken up from soil by certain food crops. The implications of these replacements on human and environmental health require further elucidation.

~~PFAS~~ PFAAs in ~~your~~ water can contribute significantly to body burden levels. It is well established that serum ~~PFAS~~ PFAAs concentrations are elevated in communities with PFAS in drinking water compared to the general population. The levels of PFOA, PFOS and PFHxS in drinking water for millions of Americans exceed health-advisory levels[2]; this includes residents of Washington State. The sheer number of existing ~~PFAS~~ PFAAs along with our lack of health and environmental effects data on the majority of these compounds has resulted in significant uncertainty that limit our understanding of the potential for human health effects from environmental exposures to ~~PFAS~~ PFAAs ~~-~~mixtures and the levels of exposure required to induce these effects.

Public health agencies have focused on identifying and reducing exposure to long-chain ~~PFAS~~ PFAAs as the key approach to reducing health risk. A number of governments, including the EPA, have developed science-based health advisories for PFOA and PFOA in drinking water. Currently the Washington Department of Health is recommending that people follow the EPA lifetime health advisory of 0.07 µg/L (70 ng/L) combined for PFOS and PFOA in drinking water. The Department may develop state drinking water standards in response to a petition including guidelines for other PFAS detected in Washington State drinking water.



[2] The U.S. E~~e~~nvironmental Protection Agency (EPA) health advisory levels are 0.07 µg/L for PFOA, PFOS or both combined.

## II. How people are exposed to ~~PFAS~~ PFAAs

Available data on how ~~PFAS~~ PFAAs are absorbed from the environment were recently reviewed by ATSDR [2]. Generally, ~~PFAS~~ PFAAs are well absorbed orally. In animal studies absorption rate of orally administered PFOA, PFOS, PFBA, and PFHxS, ranged from greater than 50~~than50~~ percent for PFHxS to greater than 95 percent for PFOA and PFBA. Absorption across the lung has not been well studied, but has been demonstrated in rats for ammonium perfluorooctanate (APFO). Studies of manufacturing workers also support that ~~PFAS~~ PFAAs are absorbed in humans following inhalation exposure [2]. Dermal absorption is less efficient and depends on whether the compound is present as an acid or disassociated anion. When PFOS and PFOA are contaminants in drinking water, dermal absorption from bathing, showering, or washing dishes is expected to be minimal [3]. Once absorbed by humans, long chain ~~PFAS~~ PFAAs bind to proteins, serum albumin, enzymes, and cell surface receptors, and can remain in the body for years. The long retention time in human is in marked contrast to their shorter retention in all other animals tested. Table 1 shows the estimated half-life for long chain PFAS in human serum. Animal studies and human autopsy studies have shown that ~~PFAS~~ PFAAs are primarily stored in the blood, liver, and kidneys. They may also distribute to the lungs, bones, brain, and other tissues [2].

**Table 1.** Serum/plasma elimination half-lives of PFOA, PFOS, and PFHxS from Lau 2015 [4].

| Species | PFOS | | PFOA | | PFHxS | |
|---|---|---|---|---|---|---|
| | Female | Male | Female | Male | Female | Male |
| **Rat** | 62-71 days | 38-41 days | 2-4 hours | 6-7 days | | 29.1 days |
| **Mouse** | 31-38 days | 36-43 days | 17 days | 19 days | 25-27 days | 28-30 days |
| **Monkey** | 110 days | 132 days | 30 days | 21 days | 87 days | 141 days |
| **Rabbit** | | | 7 hours | 5.5 hours | | |
| **Dog** | | | 8-13 days | 20-30 days | | |
| **Cattle** | 56 days | | | 19.2 hours | | |
| **Chicken** | 15-17 days | | | 3.9 days | | |
| **Pig** | 1.7 years | | 236 days | | 2 years | |
| **Humans** | 5.4-5.8 years | | 2.3-3.8 years | | 8.5 years | |

PFOS, PFOA, PFHxS, PFNA are not metabolized in the human body and are considered terminal compounds. However, other PFAS such as fluorotelomer-based compounds, ~~perfluoralkyl~~ perfluoralkane sulfonamides, and sulfonamidoethanols may be metabolized to these terminal compounds in the human body and may be a source of serum PFOA and PFOS [5]. Excretion from the human body occurs primarily through the urine.

### Pathways of human exposure

Pathway(s) of environmental exposure to ~~PFAS~~ PFAAs in humans include:

- Ingestion of contaminated drinking water.
- Ingestion of ~~PFAS that~~PFAAs that have entered or concentrated in the food chain, like fish.
- Ingestion of ~~PFAS~~ PFAAs that have migrated into food from food packaging and food contact surfaces.

**Commented [A4]:** The discussion of absorption, pathways, and kinetics are mixed in the first pages. The authors appear to be thinking about kinetics properties (i.e., absorption, distribution, metabolism, and elimination) while at the same time conveying the key exposure pathways. It would be clearer to begin with exposure pathways and then transition to kinetics.

**Formatted Table**

**Commented [A5]:** This text distinguishes between terminal compounds that are not metabolized, and other PFAS that may be metabolized. Suggest including Buck et al. (2011) along with Egeghy and Lorber (2011; citation 5). Note that Buck et al. (2011, p. 515) also provide specific examples of polyfluoroalkyl substances that have the potential to be transformed abiotically or biotically into terminal PFAS.

**Commented [A6]:** The bulleted list of exposure pathways, while technically accurate, is misleading. For example, the contact pathways (implying dermal exposure) are not expected to be major contributors to body burden levels. As noted above, it would be clearer to first list the potential exposure pathways – perhaps separately grouped in order of expected contribution to body burden. Then follow that with qualifiers that included relative absorption and kinetics information.

- Ingestion of PFAS that have migrated into food crops or food animals from contaminated water and soils
- Ingestion or inhalation of indoor dust and air that have been contaminated by consumer products.
- Contact with treated consumer products such as carpet and textiles.
- Contact with liquid consumer products that contain ~~PFAS ingredients~~PFAAs ingredients such as car wash products and spray-on waterproofing or stain treatments for carpets and textiles.
- Hand-to-mouth transfer from surfaces among infants and toddlers engaged in age-specific activity patterns.
- Ingestion by infants through breast milk or formula mixed with contaminated water.
- Maternal transfer of ~~PFAS~~ PFAAs through the placenta to the developing baby *in utero*.

**Commented [A7]:** These bulleted statements are not true for PFAS as a group of substances. The statements are true for PFAAs and their potential PFAS precursors.

Among these, dietary intake is considered the primary pathway of exposure for most people, particularly through consumption of fish and seafood contaminated with PFAS substances [6, 7]. For people with ~~PFAS~~ PFAAs in drinking water, water consumption can predominate. Sources and pathways of exposure to ~~PFAS~~ PFAAs for children differs from adults. For example, infants rely solely on breast milk or baby formula for their nutrition, so ~~PFAS~~ PFAAs in either of these sources will be the primary pathway for infant exposure. The pathways of exposures are described in more detail below.

### Drinking water

~~Many PFAS~~Many Some PFAS, for example perfluoroalkyl acids (PFAAs) and fluorinated surfactants, are highly soluble in water and when released to the environment can contaminate surface water and groundwater. These PFAS substances has been detected in private drinking water wells, source water, and drinking water across the United States.

A nationwide survey of drinking water conducted under EPA's Unregulated Contaminant Monitoring Rule (UCMR3) tested for PFOS, PFOA, PFNA, PFHxS, PFHpA and PFBS in 4,920 mostly large public water systems between 2013 and 2015 [8]. Testing found that 2.3 percent of the drinking water systems sampled had PFOA at or above the laboratory reporting value of 0.02 µg/L and 0.3 percent had detections above 0.07 µg/L. In this same survey, 1.9 percent of drinking water systems sampled had PFOS at or above the laboratory reporting value of 0.04 µg/L and 0.9 percent had detections above 0.07 µg/L. The other PFAS were detected at even lower percentages of public water systems tested – PFNA (0.28%), PFHxS (1.1%), PFHpA (1.7%), and PFBS (0.16%). In Washington, only three out of 132 water systems sampled reported detections. For information, see section IV, PFAS in Drinking Water in Washington State.

An analysis by Hu et al., 2016 of UCMR3 data estimated that water supplies for six million U.S. residents exceed EPA's lifetime health advisory level (0.07 µg/L ) for PFOS and PFOA [9]. Since this estimate, the Department of Defense has been active in surveying drinking water near military bases that conducted firefighting or training with PFAS-containing foams. Additional locations with contaminated drinking water have been discovered by state investigations of UCMR3 results. Detections of PFAS in U.S.

drinking water are being compiled and tracked by the Social Science Environmental Health Research Institute at Northeastern University in Boston [10].

Drinking water has been a significant source of human exposure in areas where contamination has occurred. The New Jersey Drinking Water Quality Institute Health Effects Subcommittee and others indicate that ongoing human exposure to PFOA in drinking water increases serum levels, on average, by at least 100 times the drinking water concentration (i.e., serum: drinking water ratio of 100:1) [11, 12]. PFOS in drinking water is estimated to result in average serum concentrations 172 times the concentration in drinking water [5]. These approximate ratios were observed in a recent study of California teachers who lived in zip codes with detectable but modest drinking water levels of PFOS and PFOA as measured in the UCMR3 study [13]. Water concentrations in this study ranged from 0.020 to 0.053 µg/L for PFOA and 0.041 to 0.156 µg/L for PFOS. On the other hand, these ratios have not been observed in other communities with elevated drinking water levels. The variability may be related to how long the exposure occurred, how long after the exposure stopped serum sampling was conducted, individual consumption and use patterns of drinking water, and other unknown factors.

Highlighted examples of average serum levels in communities with PFAS in their drinking water are presented in Table 2 and Figure 1. The sources and scenarios of PFAS contamination in the drinking water of these communities varied and included: leaching of industrial wastes from manufacturing plants or nearby waste disposal sites (e.g., Little Hocking, Ohio; Washington County, Minnesota), military bases that used firefighting foam (e.g., Pease Tradesport, New Hampshire), and leaching from land-applied biosolids (Decatur, Alabama) [13-19].



**Commented [A8]:** The New Jersey DWQI reported is cited as support for a serum:water ratio of 100:1. While this is an accurate citation, it perpetuates a misleading summary of the available empirical data. Washington has an opportunity to provide a more complete and accurate perspective. The following information is relevant to this factor since it is used by NJDEP to support a proposed MCL for PFOA. The key is that by failing to account for the incremental contribution of the drinking water pathway, the use of a relative source contribution (RSC) term to also allow for non-drinking water pathways essentially double counts the non-drinking water (baseline) sources of exposure. Since most agencies (including EPA) include an RSC term in the calculation of an MCL, it is more appropriate to use a serum:water ratio that reflects the incremental contribution of drinking water to the body burden.
To extrapolate from internal to external (administered) dose, DWQI relies largely on summary statistics for serum and water measurements in the Little Hocking community, as reported by Emmett et al. (2006). Specifically, DWQI observes that Emmett et al. reported a ratio of summary statistics (median serum and mean water) of 105:1 (see below). Although Emmett et al. also use the term "serum:water", it is clear that they are intentionally including all non-water exposures. Their research answers the question – what would we expect for the median serum PFOA concentration in a community if the average water concentration is X? So it makes sense in this context to include all potential sources in addition to the drinking water ingestion pathway. It would be more accurate to refer to their ratio as a "serum:exposure" ratio. However, it is possible to isolate the drinking water pathway because Emmett et al. also provide summary statistics for a subset of n=20 individuals who reported not drinking tap water as noted below.
Tables 4 and 5 from Emmett et al. (2006) is reproduced below and shows that the median serum PFOA for the "0 drinks per day" group is 301 ng/mL:
Serum:water summary statistics based on Tables 4 and 5 from Emmett et al. (2006).

| Tap Water | Serum (ng/mL) | | | Averag |
|---|---|---|---|---|
| Drinks per Day | median | 25th | 75th | Wate |
| 0 (n=20) | 301 | 233 | 423 | : |
| 1-2 (n=40) | 265 | 176 | 438 | : |
| 3-4 (n=66) | 370 | 206 | 550 | : |
| 5-6 (n=90) | 373 | 242 | 373 | : |
| >8 (n=55) | 486 | 294 | 486 | : |
| All (n=291) | 374 | 221 | 576 | : |

Therefore, 301 ng/mL is the median serum PFOA from *non-drinking water sources* from this study cohort. This can be subtracted from the serum measurements for the drinking water exposure groups to yield estimates of serum levels attributed to drinking water alone, and the corresponding serum:water ratios based on these values:
Serum:water summary statistics based on Tables 4 and 5 from Emmett et al. (2006), after subtracting 301 ng/mL – the median serum PFOA for the "0 drinks per day" group. ...

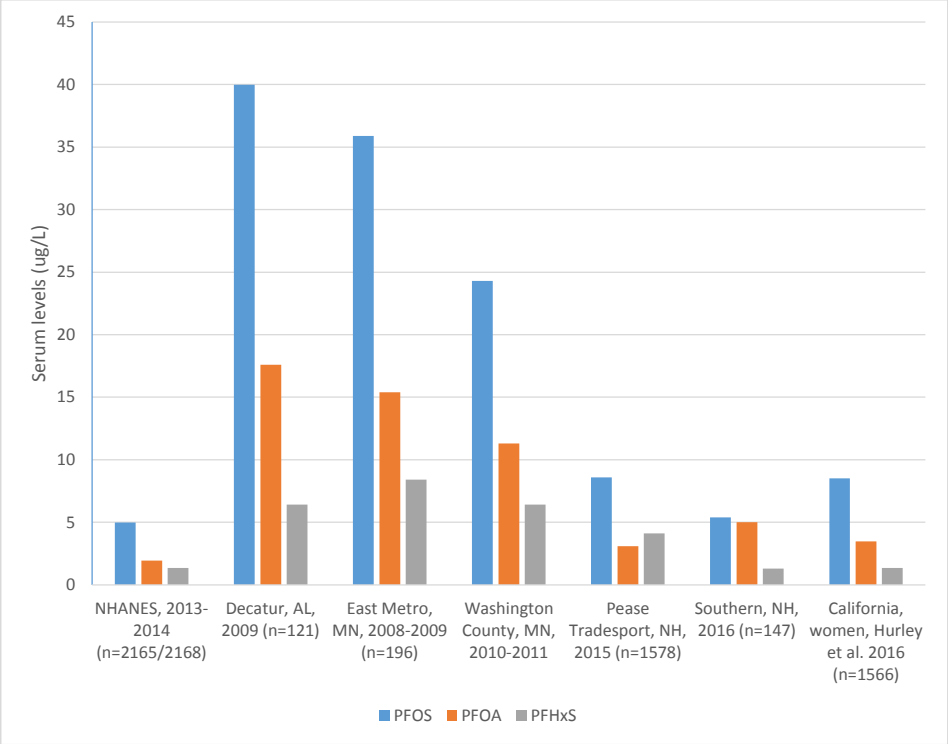


Figure 1. Geometric mean serum levels (µg/L) in various community studies impacted by PFAS in their drinking water compared to current data from NHANES for the general U.S. population [13-19].

Serum ~~PFAS~~ PFAA levels in residents with impacted drinking water were generally much higher than average levels in the U.S. population, as measured by the Centers for Disease Control (CDC) and Prevention, National Health and Nutrition Examination Survey (NHANES) [14]. Table 2 also includes serum levels of manufacturing workers with more direct exposure to PFAS compounds. The serum levels of those exposed occupationally were much higher (100 – 1,000 times higher) than the serum levels in the general U.S. population as measured by CDC's NHANES survey.

When ~~PFAS~~ PFAAs are~~is~~ in drinking water, serum levels in infants are expected to increase faster than adults regardless of whether they breastfeed or formula feed. This is because maternal PFAS shows up in breast milk, and infants drink more water relative to their body weight than adults. Nursing mothers also have higher consumption of water to support milk production.

**How PFAS get into drinking water**

According to Hu et al (ref), aqueous film foaming foam (AFFF) has been a major source of drinking water contamination in the U.S. in locations where AFFF was used for training or where large scale Class B fires occurred.. Emissions and waste from manufacturing plants, leachate from landfills, and land applications of biosolids have also contaminated drinking water. PFAS compounds were not manufactured in Washington, but they may have been used in production of other products at Washington sites. For example, in another state, a company that applied a side-chain fluorinated polymer PFAS coating to textiles released PFAS into the air where the compounds settled on soil and eventually leached into groundwater. [REFERENCE PLEASE] We have little information about where PFAS may have been used or released in the Washington because PFAS compounds are not regulated by existing air or water pollution regulations and are not reported under discharge permits.

**Commented [A9]:** Others have indicated that industrial emissions are the major source globally, and in the U.S. broadly.

Sources, fate and transport of perfluorocarboxylates. *Environmental Science and Technology* **2006,** *40*, (1), 32-44.

Global emission inventories for C4–C14 perfluoroalkyl carboxylic acid (PFCA) homologues from 1951 to 2030, Part I: production and emissions from quantifiable sources. *Environment International* **2014,** *70*, 62-75.

WWTP effluent has been identified as a major contributor of PFAS PFAAs to the aquatic environment [20], as PFAS some PFAAs are not effectively removed during treatment and therefore enter the environment through the discharged effluent [20, 21]. Some PFASPFAAs, particularly the long-chain PFAAs, will partition to sludge in WWTPs and may be released to the environment through land applications of biosolids [22, 23].

PFAS may collect in landfill leachate when disposed items like carpets and coated paper breakdown in landfills. In old unlined landfills, this leachate can contaminate groundwater. In modern landfills, the leachate is collected and transferred to waste water treatment plants. This may lead to the release of PFAS into water that is used downstream for drinking water.

**Food**

The majority (need a better qualifying term here) of the United States population is not exposed to PFAS in their drinking water (I would suggest this is not a true statement as PFASs can be detected at ppt background levels nearly everywhere that is sampled).. [reference please] For the general population, food is considered to be athe primary source of exposure to PFAS. [reference please]

PFAS PFAAs are have been found in the United States food supply in some snack foods, vegetables, meat, dairy products, and wild and farmed fish. In North America, snack foods, beef, shellfish, and potatoes are estimated to be the most common food items that contribute to exposure to PFOA [24]. Also, in Canadian food surveys, PFOA and PFOS were also frequently detected in meat, fish and shellfish, fast food, and microwave popcorn [25].

No acceptable daily dietary intakes have been developed in the United States or Canada for what?. However, Europe developed tolerable daily intakes (TDIs) of 1.5 µg/kg body weight per day for PFOA, and 0.15 µg/kg body weight per day for PFOS [26, 27]. Dietary intakes were calculated for adults and toddlers in Europe. For PFOA, the levels resulted in a daily dietary intake of 4.3 ng/kg for an adult and 16.5 ng/kg for a toddler [28]. Dietary intakes were also calculated by the United States Department of Agriculture. This resulted in an estimated daily exposure of 0.75 ng/kg/day or 60 ng/day for an average 80 kilogram (kg) adult [29]. Meat products contributed to about 40 ng/g day, followed by fish, vegetable

products, cereal, apples, potatoes, peanut butter, dairy, and egg products [29]. Dietary exposure estimates are uncertain. Since there is lack of data of levels of PFOA in food, analytical methods for food lack sufficient sensitivity, detection limits vary greatly among food types, and PFOA levels differ by types of food, sources, and locations [12]. Recently, human daily intake reference doses have been proposed for PFBA, PFBS, PFHxA and PFHxS (Anses 2017: www.anses.rf; https://www.anses.fr/fr/system/files/SUBSTANCES2015SA0127Ra.pdf )

**How PFAS get into food**

Long chain ~~PFAS~~ PFAAs released into the environment can bioaccumulate and concentrate in animals at higher trophic levels such as meat-eating animals and fish. PFOA has been detected in fish and other seafood, although PFOA is much less bioaccumulative in fish than PFOS and other long-chain PFAS substances. Consumption of fish and aquatic organisms may represent a significant contribution of total dietary exposure among recreational and subsistence fishers [12].

PFOA also migrates into food from food packaging, from non-stick pans (although, migration from non-stick PTFE-coated cookware is not considered to be a significant exposure source [12]), microwave popcorn bags, and other food contact surfaces. In 2011 some manufacturers voluntarily stopped distributing long-chain PFAS used in food packaging. In 2016, the U.S. Food and Drug Administration (FDA) amended the food additive regulations to no longer allow use of three specific perfluoroalkyl-ethyl containing food-contact substances[3] as oil and water repellants for paper and paperboard for use in contact with aqueous and fatty foods [30].

**Ambient air**

PFOA and PFOS have been measured in both the gas and particulate phase of ambient air, including in remote areas such as the Arctic [31] and Antarctic [32]. A 2006 study of ambient air in Albany, New York reported mean air concentrations of PFOA at 2.0 and 3.2 pg/m$^3$ in the particulate and gas phase, respectively. PFOS in the same study was reported to be at 0.6 and 1.7 pg/m$^3$ in the particulate and gas phase, respectively [33]. Precursors such as FTOHs, N-EetFOSE, and N-MmeFOSE are more volatile and their atmospheric transport and eventual degradation to terminal PFAS may explain some of the PFOS and PFOA measured in remote areas. Air concentrations of PFAS measured in Western countries were reviewed by Fromme et al., 2009 [33]. Mean background concentrations of PFOA in rural areas were less than 10 pg/m$^3$, while urban areas often had several hundred pg/m$^3$. PFOS levels were low, less than 6 pg/m$^3$ in rural areas and up to 50 pg/m$^3$ in cities [33]. High concentrations were observed along the fence line of an industrial area in the United States where a fluoropolymer processing factory is situated.

[3] The three food contact substances are: 1) Diethanolamine salts of mono- and bis (1 H, 1 H, 2 H, 2 H perfluoroalkyl) phosphates; 2) Pentanoic acid, 4,4-bis [(gamma-omega-perfluoro-C8-20-alkyl)thio] derivatives, compounds with diethanolamine; and 3) Perfluoroalkyl substituted phosphate ester acids, ammonium salts formed by the reaction of 2,2-bis[([gamma], [omega]-perfluoro C4-20 alkylthio) methyl]-1,3-propanediol, polyphosphoric acid and ammonium hydroxide.

The PFOA concentration measured at this site over the 10-week sampling period ranged from 120,000 to 900,000 pg/m$^3$ [34].

### Indoor air and dust

Materials made or treated with side-chain fluorinated polymers ~~fluoropolymers~~ such as carpets, upholstery, and clothing, degrade with normal wear and tear and contribute to PFAS in indoor dust and air. Indoor air and dust are an important source of exposure of PFAS for young children who ingest relatively higher levels of dust via hand-to-mouth activity. PFAS have been detected in indoor dust from homes, offices, vehicles, stores and other indoor spaces. Increased exposure among young children may result from increased contact with carpeted floors and upholstered furniture coupled with hand-to-mouth activity. See Table 5 for a summary of reviewed studies and results.

In 2000-2001, indoor dust samples were collected from 112 homes and 10 day-care centers in North Carolina and Ohio and a number of ~~PFAS~~ PFAAs were measured. PFOA, PFOS, and PFHxS were detected at the highest concentrations [35]. Mean levels detected were greater than 3,000 ng/g for PFOA and greater than 8,000 ng/g for PFOS and PFHxS. Much lower levels of PFOA, PFOS, and PFHxS were detected in house dust, offices, and vehicles in Boston, Massachusetts in 2009. Mean dust levels of PFOS were highest in homes (26.9 ng/g) followed by vehicles (15.8 ng/g), and offices (14.6 ng/g) [36]. This Boston study also measured a range of ~~newer~~ fluorotelomer alcohols~~PFAS~~ in the indoor air of offices and reported maximum levels of 70 ng/m$^3$ for 8:2 FTOH, 12.6 ng/m$^3$ for 10:2 FTOH, 11 ng/m$^3$ for 6:2 FTOH. The compounds 8:2 FTOH and 10:2 FTOH are potential precursors to PFOA and represent a potential inhalation pathway. In another study conducted in Vancouver Canada in 2007 to 2008; PFOA, PFOS and PFNA measured in serum of pregnant women correlated with precursors measured in the indoor air of participants' homes. Specifically, positive associations were discovered between airborne 10:2 FTOH and serum PFOA and PFNA and between airborne MeFOSE and serum PFOS [37]. The median PFOA levels in dust observed in the United States and Canada are higher than the levels found in European countries [38]. This may be due to differences in PFAS use and sources.

Short-chain ~~PFAS~~ alternative surfactants and side-chain polymers have largely replaced long-chain surfactants and polymers that are potential precursors to long-chain PFAAs ~~PFAS~~ in ~~these~~ household items. PFOA and PFOS are still produced in other countries and may be imported into the United States in consumer goods. ~~They~~They Long-chain surfactants and side-chain polymers may also be released from older carpets, floor wax, leather, apparel, upholstered furniture, paper and packaging, coatings, rubber, and plastics.

### Soil

There are several pathways by which PFAS may contaminate soil. PFAS in industrial emissions settle onto surrounding lands. Biosolids impacted by PFAS may also introduce them into agricultural soil. PFAS in contaminated irrigation water will result in transfer from water to soil. For more information on Biosolids, see section X – WWTP residuals (biosolids and Sewage sludge) Analysis and Concentrations.

**Commented [A10]:** Summary statistics from the study by Strynar and Lindstrom (2008) are reported. This statement, "Mean levels detected were greater than 3,000 ng/g for PFOA and greater than 8,000 ng/g for PFOS and PFHxS", should be clarified – what was the sample size and frequency of detection? Is this the arithmetic mean of detects only, or the mean including nondetects?

PFOA has been detected in soils near manufacturing facilities, disposal sites [39], and military bases where certain firefighting foams were used [40]. A Minnesota study conducted in a metropolitan area, measured levels of PFOA and PFOS in surface and subsurface soils; the median levels in surface soils were 8.0 ng/g PFOA dry weight and 12.2 ng/g PFOS dry weight. This study provides evidence of migration through soil into the groundwater table and the aquifer [39].

PFAS in soil may be a direct pathway of exposure for children playing in dirt and for people digging or gardening in the soil. PFAS in soil may also be taken up into edible plants and contribute to dietary exposure [41, 42].

**Commented [A11]:** It would be worth qualifying just how large a source this may be given that it is likely very small unless near a point source.

### Consumer products

Contact with consumer products is a potential source of human exposure to PFAS. PFAS may also be released directly during the use of protective sprays and ski waxes. According to EPA, the latest monitoring data in articles of commerce suggest that commercial carpet-care liquids, treated floor waxes, treated food contact paper, and thread-sealant tapes are likely the most significant sources of human exposure to nine ~~PFAS~~PFAAs, including PFOA in the United States [43]. A Danish survey examined the content of PFAS in carpets and assessed the potential impact on children of PFAS that volatilize into indoor air. The survey determined that rugs emit many different kinds of volatile compounds to the indoor air (e.g., phthalates and ~~PFAS).~~ polyfluoroalkyl susbtances such as fluorotelomer alcohols). PFOA and PFOS were found in all rugs tested; other PFAS such as iso-PFOS and 4H-polyfluorooctanesulfonic acid/6:2 fluorotelomer sulfonate (6:2 FTSA) were also detected. A health risk assessment analysis (based on inhalation only) concluded that rugs in the study were not a health hazard for children [44].

### Child-specific exposure pathways to PFAS

Developmental outcomes have been reported for long-chain PFAS at low exposure levels (references please), ~~,~~ bringing special concern to exposures of the developing fetus and young child. Children's age-specific diet and behaviors create pathways of exposure unique to children. The main routes of childhood exposure include *in utero* exposure, house dust and air, breast milk, and formula prepared with contaminated water.

The presence of PFAS in carpets and other flooring materials and coatings may result in higher exposures to young children because of their age-specific behaviors, increased inhalation rates, and higher dermal contact with the floor [3].

A number of studies demonstrate that PFAS can reach the human fetus during pregnancy and are present in breast milk. For example, PFOA has been measured in placenta, amniotic fluid, maternal serum, umbilical cord blood, and breast milk. PFOS has been detected in the serum of pregnant women and at delivery [45-51], in umbilical cord blood, in breast milk [52-68], and in infants shortly after birth

[69-73]. Table 4, summarizes concentrations of PFAS in women during pregnancy or at delivery, and infants shortly after birth from select studies in the United States and other countries. These studies indicate that PFAS are widely detectable in pregnant women and newborns and that exposures in children may be similar or differ from adults.

Serum PFOA concentrations in infants at birth are similar to those in maternal serum [74]. Transfer from maternal serum to fetus is less efficient for PFOS and PFHxS; ratios of umbilical cord serum/maternal serum of 30 to 60 percent for PFOS and 72 percent for PFHxS have been reported [75]. PFAS are also transferred from mother to infant via breast milk [76]. PFAS levels in breast milk are typically much lower than maternal serum concentrations: PFOS (1-3%), PFOA (<1-4%) and PFHxS (2%) [75]. While low, several studies show that nursing transfers significant amounts of PFOS and PFOA to infants; and was associated with a 30 percent increase in infant serum level per month [76, 77]. Infants who are exposed through breast milk from mothers who use contaminated water and/or from formula prepared with water that contains PFAS are also expected to rapidly exceed their mother's serum concentration due to the higher ingestion of water per body weight [12].

Department of Health and the American Academy of Pediatrics encourages women to breast feed their babies despite the presence of a number of environmental chemicals in breast milk. In nearly all cases the benefits of breast feeding to the baby and mother far outweigh the risks of the contaminant. For PFAS, the long-term health consequences are uncertain at the levels encountered by people with environmental exposures. The significant benefits of breastfeeding are well demonstrated. These benefits include increased protection from childhood infections and diarrheal diseases, improved cognitive development of the child, and lower obesity rates in later life [78, 79].

### Relative contribution from different pathways of exposure

EPA scientists estimated the relative contributions of exposure pathways for typical U.S. exposures and for people exposed to high levels of PFAS in drinking water [5]. For the typical scenario, authors assumed PFOS concentrations were 0.02 µg/L in drinking water (the laboratory reporting limit for PFOS in water at the time of the estimate). For the contaminated scenario, they assumed drinking water levels were 15 µg/L for PFOS. Their estimates are presented graphically below in Figure 2. The fraction of indoor dust ingestion (using median dust and food concentrations) by young children exceeds adults because of age specific behaviors. At 95$^{th}$ percentile assumptions of indoor dust, this fraction is even higher for young children - roughly double their food intake (not shown). For adults with typical exposures, food ingestion is the major contributor. Total daily intake for these typical scenarios was assumed to be 3.85 ng/kg/day for a child and 2.22 ng/kg/day for adult. Both are below the reference level of 20 ng/kg/day set by EPA for lifetime exposure. ~~Modelled~~Modeled exposures in the contaminated water scenario (49.2 ng/kg/d for children and 30.5 ng/kg/d for adults) significantly exceed the EPA RfD [5].

**Commented [A12]:** This summary is informative, particularly the information presented in Figure 2. Additional discussion is warranted on the plausibility of the default 20% RSC term that is used in the EPA Health Advisory for PFOA and PFOS. These data would support a much higher RSC for situations when a community is exposed to elevated levels of PFAS in drinking water, which is cited throughout the chapter as the primary exposure pathway of concern (e.g., p. 16 – Communities living near PFAS sources).

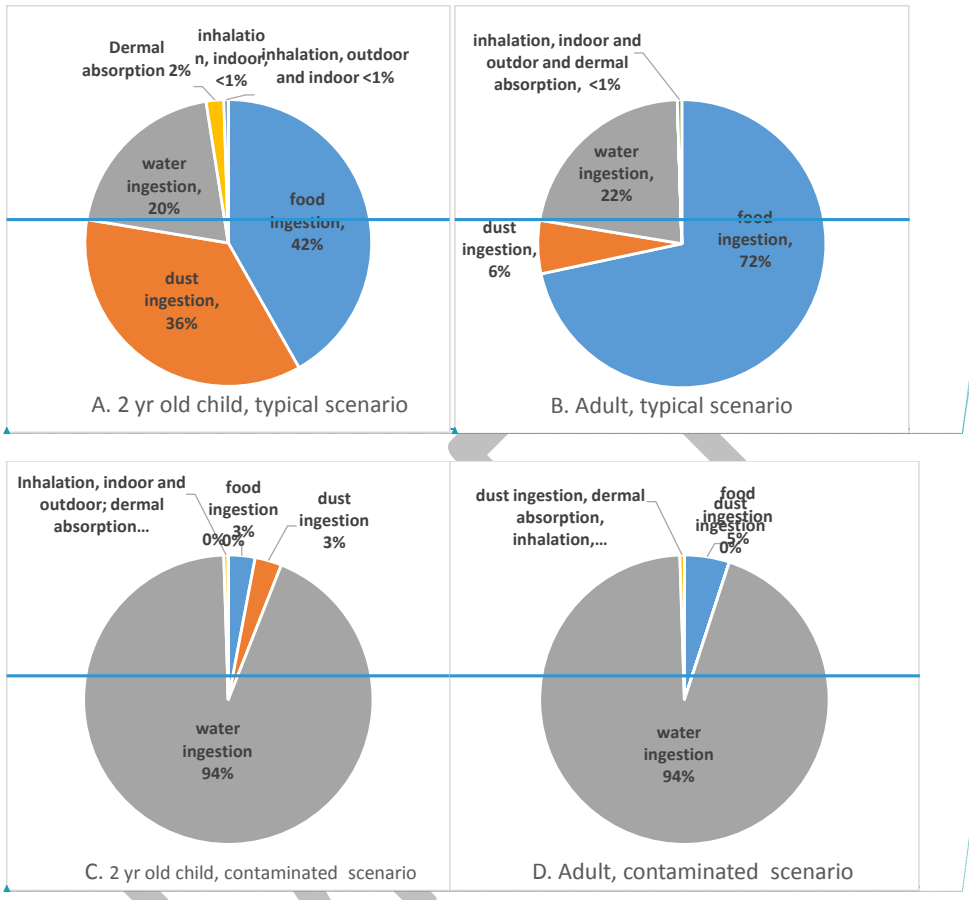


**Figure 2.** Percentage of daily PFOS intake by each exposure pathway for people with 20 ppt vs. 15,000 ppt PFOS in their drinking water, based on median estimates of intake by Egeghy and Lorber 2010 [5]. 5A represents a typical scenario of a 2 year old child (13 kg) who spends more time on the floor, and ingests house dust through normal toddler behavior patterns. 5B represents a typical scenario of an adult (72 kg) for PFOS. For these two scenarios, drinking water concentration was 20 ppt. 5C represents median estimates of pathways of exposure for a young child with high levels of PFOS in drinking water (15,000 ppt) and 5D represents an adult drinking the same water. [REFERENCE(S) PLEASE]

## III. Likely exposure levels in Washington State



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PFAS compounds are expected to be widely detected in the serum of Washington State residents. In exposure investigations, biomonitoring in human blood serum has been useful for measuring aggregate exposure to specific PFAS from multiple sources of exposure (i.e., food, water, consumer products, and indoor dust). Because long chain PFAS have long residence times in humans, biomonitoring has also provided a useful indication of cumulative exposure over time.

Below we discuss the data relevant to likely general population exposure as well as to subgroups that may differ because of their age, diet, occupational exposures, or drinking water contamination.

### General population

Numerous studies have detected certain PFAS in the serum of Americans (Table 2). Only limited evidence of exposures in Washington State exist. A 2004 study by Olsen et al., measured for seven PFAS compounds in stored blood serum of 238 men and women in an elderly Seattle population [80]. Levels measured in this population were comparable to levels measured across the nation [14] (NHANES general population [1999 to 2000]) and in an American Red Cross study from 2000 to 2001 suggesting that this elderly Seattle population was not different than that observed for the rest of the nation.

Serum levels of twelve PFAS have been measured by the CDC every two years since 1999 in a representative United States population. Data from the NHANES is shown in Figure 3 [14, 81]. PFOA, PFOS, PFNA, and PFHxS are routinely detected in nearly all people tested. Figure 3 showed serum levels of the four most highly detected PFAS in human serum in NHANES. Between 1999 and 2014, the geometric mean PFOA and PFOS blood serum concentration decreased from 5.2 to 1.9 µg/L, and 30.4 to 4.99 µg/L, respectively [14]. The reasons for this decline are due to a reduction in environmental emissions by the manufacturers and the phase out in production for C8 compounds in the United States. Serum concentrations were similar in all age groups (12 and older), and were higher in males (geometric mean, 4.80 µg/L) than females (geometric mean, 3.56 µg/L). Mexican-Americans had lower concentrations than non-Hispanic whites or non-Hispanic blacks.

**Commented [A13]:** See Olsen et al. Per- and polyfluoroalkyl substances (PFAS) in American Red Cross adult blood donors, 2000-2015.Environ Res. 2017 Aug;157:87-95. doi: 10.1016/j.envres.2017.05.013.

**Commented [A14]:** Notably, CDC stopped including PFHxA in NHANES because it was not detected.

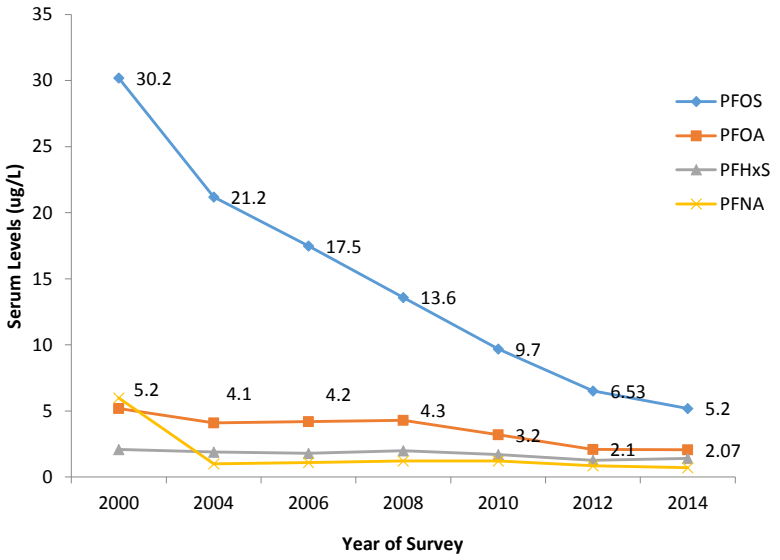



**Figure 3**. Median levels of PFAS in blood serum of a representative biomonitoring survey of the U.S. population [14]. PFOS manufacturing phase-out occurred in 2002. PFOA manufacturing phase-out began in 2008 and was complete for major U.S. manufacturers by 2015.

Two other large biomonitoring surveys have yielded similar results. The Canadian Health Measures Survey is a large government survey of a representative sample of Canadian residents. In 2007 to 2009, and 2009 to 2011, this survey measured PFOA, PFOS, and PFHxS in the plasma of all Canadian participants aged 20 to 79 years, and 12 to 79 years, respectively. The survey in 2009 to 2011 also measured for PFBA, PFHxA, PFBS, PFNA, PFDA, and PFUnDA. The most frequently detected PFAS were PFOS, PFOA and PFHxS with detection frequencies ranging from 98 to 100 percent [82]. Plasma levels of PFOA were similar in both cycles. PFOA levels in children and the elderly were comparable with those in adults [83]. Blood donated to the American Red Cross has also been studied. Olsen et al., 2003, (also 2017) collected 645 serum samples from blood donated in 2000-2001 to the American Red Cross from six different cities. In each city, they collected approximately 10 samples from men and women across five different 10-yr age groups (20-29 through 60-69) and tested these samples for seven different PFAS [84]. A follow-up study, returned to the same six cities and collected an additional 600 plasma samples from blood donated in 2006 [85]. A second follow-up study collected 600 plasma samples from people who donated blood in 2010 from the same six cities [86]. All of these samples were similarly distributed by sex and age group. Beyond sex and age, however, no additional demographic characteristics were recorded for these samples. Overall, geometric mean serum levels were lower than levels found in the U.S. NHANES general population.

### Children

In the general population, average serum levels in children are similar to adults. Table 3 presents results from selected studies of PFAS in serum of United States children. A study of 598 children aged 2 to 12 years old in 1994 to 1995, by Olsen et al., reported that children were comparable to adults in their PFOS and PFOA levels, however children had substantially higher 95$^{th}$ percentile values of PFHxS and perfluorooctanesulfonamidoacetate [87]. The higher levels in this subset of children may have been related to child-specific patterns of exposure to household items such as treated carpet and textiles. In a more recent study children's median serum levels of PFOA, PFOS and PFHxS were all lower than adults in NHANES from the same years [88]. This study, based on serum from 300 Texas children, ages less than 1 to 12 years old in 2009, reported no differences between genders, and that serum concentrations increased with age [88]. Children (less than 12 years old) in the C8 study, with elevated exposures to PFAS in drinking water, especially PFOA, had higher PFOA, PFHxS and PFNA serum levels than adults. This may reflect age-specific consumption of drinking water rates or age-specific behaviors that increase exposure to environmental PFAS [89].

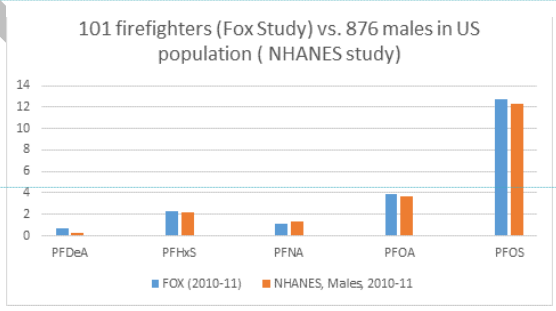
## Communities living near PFAS sources.

It is well established that serum PFAS concentrations are elevated in communities with PFAS in drinking water, see Figure 1 and Table 2. Unlike the general U.S. population, these communities have been exposed by specific identifiable sources of environmental PFAS that have contaminated private and public drinking water systems. As discussed earlier, levels in serum in these communities depend on the levels in water.

## Firefighters

Biomonitoring studies that measured PFAS in serum of fire fighters have been published in the United States and other countries. AFFF has been used by fire departments routinely to extinguish vehicle fires and other fires involving burning petroleum. PFOS, PFOA, PFHxS, and PFNA were the most common detected PFAS in the FOX study of 101 California firefighters [1] . The median serum levels of California firefighters were slightly higher compared to levels of the United States general population (see Figure 4). Higher levels of PFOS and PFHxS were reported in firefighters exposed to older AFFF formulations at AFFF training centers in Australia. In this study, the subset of firefighters who had been exposed for ten years or less had levels of PFOS that were similar to or only slightly above those of the general population [90].

*Figure 4: from the Fox Study [1]*

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**Commented [A15]:** Note the AFFF is most often used to fight high hazard Class B solvent/alcohol and hydrocarbon liquid fires.

**Commented [A16]:** Were any of the data statistically higher – nor clear this is the case from Figure 4; also need units on left scale – ppb's?

This finding suggested that elevated levels were associated with older formulations of AFFF used at the center. In another study, PFOS, PFHxS, perfluoropenanesulfonic acid (PFPeS), perfluoroheptanesulfonic acid (PFHpS), and perfluorononanesulfonic acid (PFNS), and four unknown sulfonic acids (Cl-PFOS, ketone-PFOS, ether-PFHxS, and Cl-PFHxS) were more frequently detected at higher levels in firefighters compared to controls [91]. PFAS were found at slightly higher levels in firefighters from the mid-Ohio River Valley who participated in the C8 health project in 2005 and 2006. Firefighters median PFHxS level was 4.6 ng/mL compared to those who reported other employment (3.6 ng/mL) or no job reported (3.5 ng/mL). Similarly, the PFOS serum levels were 27.9 ng/mL, 23.0 ng/mL, and 20.9 ng/mL, respectively [92]. Eight firefighters in Finland had their serum measured for PFAS before and after they used 3% AFFF in three training sessions. The serum levels of PFHxS and PFNA increased during these sessions, although they were not the main PFAS listed as ingredients used in AFFF [93]. Overall, average PFAS levels in U.S. firefighters appear to be slightly above the general population, and this is an area that needs more detailed studies. Firefighters engaged in more extensive exposure with AFFF during training operations, especially older formulations, may have higher levels of PFAS in their serum than the general population.

### Consumers of fish from contaminated waters

PFOS has been detected by Ecology surveys in Washington freshwater fish at levels up to 87 ng/g in fillets (see Chapter IV, environmental section). Recreational and subsistence fishers who consume fish from urban waters and areas downstream of WWTP discharges may have a higher exposures to PFAs that accumulate in fish.

International studies indicate that PFAS can reach very high levels of contamination in fish and fishermen. In a biomonitoring study of fishery employees at Tangxun Lake, China [19] the median serum levels in 37 fishermen were 10,400 µg/L for PFOS, 542 µg/L for PFHxS and 41 µg/L PFOA. The maximum detection of PFOS was 31,400 µg/L which is higher than the highest recorded PFOS serum level in an employee at an industrial POSF production facility. Lake waters received effluent from fluoropolymer industry facilities and a waste water treatment plant. Since Washington does not have any fluoropolymer manufacturing facilities, exposures this high are unlikely here.

**Table 2. Mean, geometric mean (GM) and/or range of PFOA and or PFOS levels in blood from communities with PFAS contamination in drinking water, and people who worked with PFAS.**

| Study | Drinking water levels (µg/L) | Serum levels (µg/L) | Exposure duration |
|---|---|---|---|
| **PFOA, Lubeck, West Virginia (C8 study) [19]** [a] | 520 [a] | 92 [a] | At least 1 year |
| **PFOA, Tuppers Plain, OH (C8 study) [19]** [a] | 310 [a] | 42 [a] | At least 1 year |
| **PFOA, Little Hocking, Ohio, (2002-2005) [94]** | 3.55 [a] | 298-370 [c] (n=371) | At least 1 year |
| **PFOA, mid-Ohio Valley residents, (2005-2006) [95]** | NA | 28.2 [c] | At least 1 year |
| **PFOA, Arnsberg, Germany, men[96]** | 500-640 [b] | 25.3 [b] (n=101) | Unknown |
| **PFOA, Minnesota, 2009 [15]** | 0.07-0.7 | 17.3 [b] (n=98) | 34 months after exposure that ended in 2009 |
| **PFOA, Washington County, Minnesota, 2010-2011** | NA | 11.3 [b] | Unknown |
| **PFOA, California women, Hurley et al. 2016 [13]** | 0.028 [a] | 4.06 [a] (n=70) | Unknown |
| **PFOA, Hoosick Falls, municipal water, New York, 2016 [97]** | 595 [b] | 23.5 [b] (n=2081) | Unknown |
| **PFOA, Decatur, Alabama, 2009-2010 [15]** | 2.2-78.8 | 17.6 [b] (n=121) | Unknown |
| **PFOA, New Hampshire, Pease Tradesport, 2015 [18]** | 0.35-0.32 [e] | 3.09 [a] (n=1,578) | From January 2008 through May 2014 [c] |
| **PFOS** | | | |
| **PFOS, California women, Hurley et al. 2016 (n=93) [13]** | 0.058 [a] | 11.02 [a] | Unknown |
| **PFOS, Decatur, Alabama, 2009-2010 [15]** | 5.6-248 | 39.98 [b] (n=121) | Unknown |
| **PFOS, Minnesota, 2009 [15]** | ND-1.04 | 39.3 [b] (n=98) | 34 months after exposure that ended in 2009 |
| **PFOS, Arnsberg, Germany, men [96]** | 500-640 | 10.5 [b] (n=101) | Unknown |
| **PFOS, New Hampshire, Pease Tradesport, 2015 [18]** | 2.4-2.5 [d] | 8.59 [a] (n=1,578) | From January 2008 through May 2014 [cd] |

**Commented [A17]:** Table 2 presents a summary of the paired serum and water summary statistics for various communities. The column for Serum Levels (µg/L) should be divided into two columns: 1) Including drinking water; and 2) Excluding drinking water. See Comment #6 above for a discussion of the relevance of this information, and the specific data available for Little Hocking (citation 94). Similar information from other studies should be reported, where available.

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| Study | Drinking water levels (µg/L) | Serum levels (µg/L) | Exposure duration |
|---|---|---|---|
| **For comparison, workers with occupational exposure** | | | |
| **PFOA, 3M workers, Decatur, Alabama (2000) [19]** [a] | NA | 40 – 12,700 (1,130 [b]) (n=263) | Unknown |
| **PFOA, DuPont workers, Parkersbug, West Virginia (2004) [19]** [a] | NA | 494 – 3,210 [a] | Unknown |
| **PFOS, 3M workers, Decatur, Alabama (2000) [19]** [a] | NA | 60 – 10,060 (910 [a]) (n=263) | Unknown |

[a] – Mean or average level
[b] - Geometric mean
[c] – Median
[d] – This population may include adults that work at the Pease Tradeport during 2008-2014
[e] – PFAS samples were collected from Haven well in April and May 2014
NA – not available

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**Table 3. Geometric mean (GM) and range (if available) for serum concentrations of PFOS, PFOA, PFHxS, and PFNA (µg/L) in non-occupationally exposed U.S. populations.**

| Location | Sample Size | Age (yr) | Year | PFOS GM (range) | PFOA GM (range) | PFHxS GM (range) | PFNA GM (range) | Source |
|---|---|---|---|---|---|---|---|---|
| **United States (NHANES)** | 1,562 | ≥12 | 1999-2000 | 30.4 | 5.21- | 2.13 | 0.551 | [98] |
| **United States (NHANES)** | 2,094 | ≥12 | 2003-2004 | 20.7 | 3.95 | 1.93 | 0.966 | [98] |
| **United States (NHANES)** | 2,120 | ≥12 | 2005-2006 | 17.1 | 3.92 | 1.67 | 1.09 | [98] |
| **United States (NHANES)** | 2,100 | ≥12 | 2007-2008 | 13.2 | 4.12 | 1.95 | 1.22 | [98] |
| **United States (NHANES)** | 2,233 | ≥12 | 2009-2010 | 9.32 | 3.07 | 1.66 | 1.26 | [98] |
| **United States (NHANES)** | 1,904 | ≥12 | 2011-2012 | 6.31 | 2.08 | 1.28 | 0.881 | [98] |
| **Canada, CHMS** | 1,376[a] | 20-79 | 2007-2009 | 11.13 | 2.94 | -- | -- | [99] |
| **Canada, CHMS** | 1,504[b] | 20-79 | 2007-2009 | 7.07 | 2.17 | -- | -- | [99] |
| **Canada, CHMS** | 511[a] | 20-79 | 2009-2011 | 8.3 | 2.6 | 2.4[d] | 0.84[e] | [82] |
| **Canada, CHMS** | 506[b] | 20-79 | 2009-2011 | 5.7 | 2.0 | 1.3[d] | 0.81[f] | [82] |
| **23 U.S. States & Washington, D.C.** | 598 | 2-12 | 1994-1995 | 37.5 (6.7-515.0) | 4.9 (<1.9-56.1) | 4.5 (<1.4-711.7) | -- | [100] |
| **6 U.S. Cities (Red Cross)** | 645 | 20-69 | 2000-2001 | 34.9 (<4.3-1656.0) | 4.6 (<1.9-52.3) | 1.9 (<1.4-66.3) | 0.57[¶] (0.1-2.7) | [101] |
| **6 U.S. Cities (Red Cross)** | 600 | 20-69 | 2006 | 14.5[†] (<2.5-77.9) | 3.4[†] (<1.0-28.1) | 1.5[†] (<0.5-56.5) | 0.97[†¶] (0.1-5.1) | [85] |
| **6 U.S. Cities (Red Cross)** | 600 | 20-69 | 2010 | 8.3[†] (<0.4-102) | 2.44[†] (0.4-22.2) | 1.34[†] (<0.05-19.2) | 0.83[†] (0.04-10.8) | [86] |
| **Decatur, AL** | 153 | ≥12 | 2010 | 39.8 (5.4-472) | 16.3 (2.2-144) | 6.4 (0.6-59.1) | 1.7 (0.3-5.5) | [102] |
| **Washington County, MN** | 196 | 20-86 | 2008-2009 | 35.9 (3.2-448) | 15.4 (1.6-177) | 8.4 (0.32-316) | -- | [103] |
| **Washington County, MN** | 164 | n.r. | 2010-2011 | 24.3 | 11.3 | 6.4 | -- | [104] |
| **Ohio/West Virginia** | 69,030 | 1.5->100 | 2005-2006 | 19.2 | 32.9 | 3.3 | 1.4 | [105] |
| **Mid-Ohio River Valley** | 6,536 | 0-12 | 2005-2006 | 20.7[c] | 32.6[c] | -- | -- | [106] |
| **Mid-Ohio River Valley** | 5,934 | 12-18 | 2005-2006 | 19.3[c] | 26.3[c] | -- | -- | [106] |
| **Dallas, TX** | 300 | 0-12 | 2009 | 4.10[‡] (<0.2-93.30) | 2.85[‡] (<0.1-13.50) | 1.20[‡] (<0.1-31.20) | 1.20[‡] (<0.1-55.80) | [88] |
| **Cincinnati, OH** | 353 | 6-8 | 2005-2007 | 13.2 (<LOD[§]-96.0) | 7.8 (<LOD-55.9) | 5.1 (<LOD-185.0) | 1.4 (<LOD-6.8) | [107] |
| **San Francisco, CA** | 351 | 6-8 | 2005-2009 | 13.2 (3.8-104.0) | 5.7 (2.4-18.2) | 3.0 (0.3-192.0) | 1.7 (0.6-15.5) | [107] |

**[†]plasma concentration (µg/L)**

**Table 3. Geometric mean (GM) and range (if available) for serum concentrations of PFOS, PFOA, PFHxS, and PFNA (µg/L) in non-occupationally exposed U.S. populations.**

| Location | Sample Size | Age (yr) | Year | PFOS GM (range) | PFOA GM (range) | PFHxS GM (range) | PFNA GM (range) | Source |
|---|---|---|---|---|---|---|---|---|

[‡]Median
[§]LOD = Limit of detection
[¶]Reported in Olsen, Lange [86]
[a] only males
[b] only females
[c] Median concentration
d –Sample size for males n=510 and females n=505
[e] –Males 12-79 years of age
[f] – Females 12-79 years of age

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**Table 4. Median/geometric mean concentrations of PFOS, PFOA, PFHxS, ~~and~~ PFNA, and PFDA in vulnerable populations from select studies (*n*>30) in the United States, Canada and other countries.**

| | | Concentration (µg/L) | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Year (s)** | **n** | **PFOS** | **PFOA** | **PFHxS** | **PFNA** | **PFDA** | **Sample type** | **Location** | **Ref** |
| **2003-2004** | 76 | 12/ 12.3 | 2.6/ 2.39 | | | | Serum, pregnant women | NHANES | [51] |
| **2003-2006** | 242, 241, 225 [c] | 13.2 | 5.4 | 1.5 | 0.9 | 0.2 | Maternal serum measured at 16 ± 3 weeks gestation | HOME study, Cincinnati, Ohio | [50] |
| **2005-2006** | 252 | 7.8 | 1.5 | 0.97 | | | Maternal serum at 15 weeks | Alberta, Canada | [46] |
| **2008-2011** | 1743 | 4.7/ 4.59 | 1.7/ 1.66 | 1/ 1.01 | | | Maternal plasma, 14 weeks of gestation | Canada, MIREC study (10 cities across Canada) | [49] |
| **2003-2006** | 71 | 12.7 (100) | 4.8 (100) | 1.2 (98.6) | 0.82 (100) | 0.2 (97.2) | Maternal serum, 16 weeks, (Fd, %) | Cohort of women, Cincinnati, Ohio | [47] |
| | | 8.5 (100) | 3.3 (100) | 1.2 (93) | 0.66 (100) | 0.2 (90.1) | Maternal serum, delivery, (Fd, %) | | |
| | | 3.5 (98.6) | 3.1 (100) | 0.6 (97.2) | 0.41 (98.6) | <LOD (16.9) | Infant's cord serum, (Fd, %) | | |
| **2004-2005** | 101 | 16.6 | 2.13 | 1.82 | 0.73 | | Maternal serum at 24-28 weeks | Canada | [48] |
| | 101 | 14.54 | 1.81 | 1.62 | 0.69 | | Maternal serum at delivery | | |
| | 105 | 6.08 | 1.58 | 2.07 | 0.72 | | Umbilical cord serum | | |
| **2007** | 98 | 2.1[a] | 0.9[a] | 0.4[a] | 0.3[a] | | Dried blood spot, infant | Texas | [71] |
| **2004-2005** | 299 | 4.9[a] | 1.6[a] | - | - | | Umbilical cord serum | Maryland | [52] |
| **2003-2004** | 20[b] | 1.59 | 0.73 | 1.64 | 0.35 | | Dried blood spot, infant (newborn | New York | [72] |

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| | | Concentration (µg/L) | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Year (s)** | **n** | **PFOS** | **PFOA** | **PFHxS** | **PFNA** | **PFDA** | **Sample type** | **Location** | **Ref** |
| | | | | | | | screening program) | | |
| **2008-2009** | 67 | 6.15 | 4.5 | 1.25 | 1.7 | 0.35 | Serum, 2-8 years old | California | [73] |
| **2012-2015** | 200 | 4.47/ 4.20 | 1.29/ 1.24 | 0.861/ 0.904 | 0.644/ 0.647 | 0.212/ 0.198 | Maternal serum, Pregnant women (MAMAS study) | California | [108] |
| **2005-2008** | 100 | 4.44 | 1.47 | 0.58 | 0.36 | | Umbilical cord serum | Ottawa, Canada | [69] |
| **2007** | 98 | 2.1 | 0.9 | 0.4 | 0.3 | | Dried blood spot, infant | Texas | [71] |
| **2011-2013** | 64 | 1.6 | 0.885 | | | | Cord plasma (umbilical cord blood) | Netherlands | [70] |
| **2007-2009** | 391 | 4.66 † | 1.53 | 0.44 | 0.56 | 0.23 | Serum, pregnant women | Norway, Mother-and-child contaminant Cohort study (MISA) | [45] |
| **2002-2005** | 185 | 5.2 | 1.4 | | | | Maternal blood | Sapporo, Japan (Hokkaido Study) | [109] |
| **2005-2006** | 12,476 | 22.7 | 69.2 | | | | Blood serum | Children 1-17.9 years (Frisbee et al. 2010) | [106] |

[a] Geometric mean
[b] Pooled samples
[c] Sample size of 242 corresponds to PFOA, PFOS, and PFHxS; sample size of 241 corresponds to PFNA, and sample size of 225 corresponds to PFDA.
HOME - Health Outcomes and Measures of the Environment Study
MAMAS – Measuring Analytes in Maternal Archived Samples
n = sample size
Fd = frequency of detection
† = Corresponds to median linear PFOS.

**Table 5. PFAS detected in residential dust, office dust and indoor air from selected studies in the U.S, and other countries**

| Chemical name | Exposure related information | Units/ matrix | n | mean/ GM | 50th percentile | 95th percentile | Range/ min/ max | % with detectable levels/ % > LOQ/ LOD | Sour |
|---|---|---|---|---|---|---|---|---|---|
| **PFNA, PFOA, PFHpA, PFHxA, PFOS, and 8:2 FTOH** | Measured in dust of offices, homes and vehicles | ng/g | | | | | | >50% (detected in offices, homes & vehicles) | |
| **PFTeDA** | Office dust, Jan and March 2009, Boston, MA | ng/g | 31 | 18.6 | | | 9.35-367 | 71 | |
| **PFTrDA** | Office dust, Jan and March 2009, Boston, MA | ng/g | 31 | 21.6 | | | 8.67-768 | 58 | |
| **PFDoA** | Office dust, Jan and March 2009, Boston, MA | ng/g | 31 | 40 | | | 6.56-481 | 87 | |
| **PFUnA** | Office dust, Jan and March 2009, Boston, MA | ng/g | 31 | 19 | | | 9.22-373 | 52 | |
| **PFDA** | Office dust, Jan and March 2009, Boston, MA | ng/g | 31 | 46.5 | | | 5.3-492 | 97 | |
| **PFNA** | Office dust, Jan and March 2009, Boston, MA | ng/g | 31 | 63 | | | 10.9-639 | 94 | [36] Fraser AJ. et al. 2013 |
| **PFOA** | Office dust, Jan and March 2009, Boston, MA | ng/g | 31 | 32 | | | 15.8-336 | 74 | |
| **PFHpA** | Office dust, Jan and March 2009, Boston, MA | ng/g | 31 | 27.6 | | | 6.5-388 | 97 | |
| **PFHxA** | Office dust, Jan and March 2009, Boston, MA | ng/g | 31 | 10.8 | | | 5.06-102 | 68 | |
| **PFPeA** | Office dust, Jan and March 2009, Boston, MA | ng/g | 31 | †† | | | 5.95-27.5 | 39 | |
| **PFBA** | Office dust, Jan and March 2009, Boston, MA | ng/g | 31 | †† | | | 5.06-148 | 48 | |
| **PFOS** | Office dust, Jan and March 2009, Boston, MA | ng/g | 31 | 14.6 | | | 6.8-98.2 | 55 | |
| **PFHxS** | Office dust, Jan and March 2009, Boston, MA | ng/g | 31 | †† | | | 5.24-18.5 | 23 | |
| **PFBS** | Office dust, Jan and March 2009, Boston, MA | ng/g | 31 | †† | | | 8.25-12 | 10 | |
| **6:2 FTOH** | Office dust, Jan and March 2009, Boston, MA | ng/g | 31 | †† | | | 90.6-2,390 | 35 | |
| **8:2 FTOH** | Office dust, Jan and March 2009, Boston, MA | ng/g | 31 | 309 | | | 15.7-3,390 | 100 | |
| **10:2 FTOH** | Office dust, Jan and March 2009, Boston, MA | ng/g | 31 | 210 | | | 12.2-2050 | 90 | |

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| Chemical name | Exposure related information | Units/ matrix | n | mean/ GM | 50th percentile | 95th percentile | Range/ min/ max | % with detectable levels/ % > LOQ/ LOD | Sour |
|---|---|---|---|---|---|---|---|---|---|
| **MeFOSE** | Office dust, Jan and March 2009, Boston, MA | ng/g | 31 | †† | | | 11.0-113 | 19 | |
| **6:2 FTOH** | Indoor air in offices in Boston, MA. † | pg/m$^3$ | 30 | 1,320 | | | <LOD (19.5)-11,000 | 93 | |
| **8:2 FTOH** | Indoor air in offices in Boston, MA. † | pg/m$^3$ | 30 | 9,920 | | | 283-70,600 | 100 | |
| **10:2 FTOH** | Indoor air in offices in Boston, MA. † | pg/m$^3$ | 30 | 2,850 | | | 138-12,600 | 100 | |
| **EtFOSA** | Indoor air in offices in Boston, MA. † | pg/m$^3$ | 30 | 17 | | | <LOD (1.26) - 115 | 97 | |
| **MeFOSA** | Indoor air in offices in Boston, MA. † | pg/m$^3$ | 30 | 29.1 | | | 5.93-162 | 100 | [110] Fraser AJ et al. 2012 |
| **EtFOSE** | Indoor air in offices in Boston, MA. † | pg/m$^3$ | 30 | 18.1 | | | <LOD (0.03)-216 | 90 | |
| **MeFOSE** | Indoor air in offices in Boston, MA. † | pg/m$^3$ | 30 | 289 | | | 48.5-3,880 | 100 | |
| **Σ PFCs (PFBS, PFHxS, PFOS, PFBA, PFHxA, PFOA, PFNA and PFDA)** | House dust in 2008, Flanders, Belgium | ng/g | 43 | 19.3 | 2.9 | 34.9 | 0.1-406 | | |
| **PFOS** | House dust in 2008, Flanders, Belgium | ng/g | 43 | 9.4 | 0.5 | | <0.1-211 | 15 | |
| **PFOA** | House dust in 2008, Flanders, Belgium | ng/g | 43 | 6.4 | 0.7 | | <0.05-109 | 24 | [38] D'Hollander W. et al. 2010 |
| **Σ PFCs (PFBS, PFHxS, PFOS, PFBA, PFHxA, PFOA, PFNA and PFDA)** | Office dust in 2008, Flanders, Belgium | ng/g | 10 | 100 | 10 | 449 | 2.2-647 | | |
| **PFOS** | Office dust in 2008, Flanders, Belgium | ng/g | 10 | 55 | 2.2 | | 0.4-526 | 21 | [38] D'Hollander W. et al. 2010 |
| **PFOA** | Office dust in 2008, Flanders, Belgium | ng/g | 10 | 14 | 2.9 | | 0.7-61 | 29 | |
| **PFNA** | House dust, Jan and March 2009, Boston, MA | ng/g | 30 | 10.9 | | | 6.21 - 1,420 | 67 | |
| **PFOA** | House dust, Jan and March 2009, Boston, MA | ng/g | 30 | 23.7 | | | 5.71-894 | 77 | |
| **PFHpA** | House dust, Jan and March 2009, Boston, MA | ng/g | 30 | 12 | | | 4.93-586 | 80 | |
| **PFHxA** | House dust, Jan and March 2009, Boston, MA | ng/g | 30 | 8.65 | | | 4.85-1,380 | 57 | |
| **PFBA** | House dust, Jan and March 2009, Boston, MA | ng/g | 30 | 13.9 | | | 4.89-999 | 90 | [36] Fraser AJ. et al. 2013 |

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| Chemical name | Exposure related information | Units/ matrix | n | mean/ GM | 50th percentile | 95th percentile | Range/ min/ max | % with detectable levels/ % > LOQ/ LOD | Sour |
|---|---|---|---|---|---|---|---|---|---|
| **PFOS** | House dust, Jan and March 2009, Boston, MA | ng/g | 30 | 26.9 | | | 14.1-280 | 73 | |
| **8:2 FTOH** | House dust, Jan and March 2009, Boston, MA | ng/g | 30 | 10.8 | | | 9.19-136 | 57 | |
| **PFBS** | House dust in 2011, Canada | ng/g | 18 | 6.1/0.7 | <0.5 | | <0.5-5.1 | 28 | |
| **PFHxS** | House dust in 2011, Canada | ng/g | 18 | 140/21 | 14 | | 2.9-1,300 | 100 | |
| **PFHpS** | House dust in 2011, Canada | ng/g | 18 | 4.1/0.6 | <0.5 | | <0.5-46 | 22 | |
| **PFOS** | House dust in 2011, Canada | ng/g | 18 | 180/39 | 37 | | <0.5-1,300 | 94 | |
| **PFDS** | House dust in 2011, Canada | ng/g | 18 | 2.2/1.8 | 2.1 | | <0.5-5.1 | 94 | |
| **PFBA** | House dust in 2011, Canada | ng/g | 18 | 9.2/3.6 | 2.6 | | <0.5-42 | 94 | |
| **PFPeA** | House dust in 2011, Canada | ng/g | 18 | 17/4.9 | 5.2 | | <0.5-93 | 83 | [111] Beeson, S et al. 2011 |
| **PFHxA** | House dust in 2011, Canada | ng/g | 18 | 77/33 | 35 | | 2.3-390 | 100 | |
| **PFHpA** | House dust in 2011, Canada | ng/g | 18 | 55/19 | 21 | | 1.4-320 | 100 | |
| **PFOA** | House dust in 2011, Canada | ng/g | 18 | 120/50 | 38 | | 4.3-820 | 100 | |
| **PFNA** | House dust in 2011, Canada | ng/g | 18 | 44/18 | 15 | | 1.4-220 | 100 | |
| **PFDA** | House dust in 2011, Canada | ng/g | 18 | 44/16 | 15 | | 1.7-250 | 100 | |
| **PFUA** | House dust in 2011, Canada | ng/g | 18 | 31/8 | 6.1 | | <0.5-240 | 94 | |
| **PFDoA** | House dust in 2011, Canada | ng/g | 18 | 36 | 10 | | 1.4-160 | 100 | |
| **PFTrA** | House dust in 2011, Canada | ng/g | 18 | 9.9/2.3 | 2.4 | | <0.5-67 | 78 | |
| **PFTA** | House dust in 2011, Canada | ng/g | 18 | 6.5/3.3 | 3.3 | | <0.5-24 | 94 | |
| **PFOSA** | House dust in 2011, Canada | ng/g | 18 | <0.5-0.3 | <0.5 | | <0.5-<0.5 | 0 | |
| **NMeFOSA** | House dust in 2011, Canada | ng/g | 16 | 3/2.5 | 2.3 | | 1.2-13.8 | 100 | |
| **NEtFOSA** | House dust in 2011, Canada | ng/g | 16 | 0.55-0.14 | 0.15 | | <0.06-2.8 | 50 | |
| **NMeFOSAA** | House dust in 2011, Canada | ng/g | 18 | 36/2.3 | 1.2 | | <0.5-440 | 50 | |
| **NEtFOSAA** | House dust in 2011, Canada | ng/g | 18 | 58/32 | 27 | | 3.2-240 | 100 | |
| **NMeFOSE** | House dust in 2011, Canada | ng/g | 16 | 152/65 | 49 | | 15-910 | 100 | |

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| Chemical name | Exposure related information | Units/ matrix | n | mean/ GM | 50th percentile | 95th percentile | Range/ min/ max | % with detectable levels/ % > LOQ/ LOD | Sour |
|---|---|---|---|---|---|---|---|---|---|
| **NEtFOSE** | House dust in 2011, Canada | ng/g | 16 | 14/5.3 | 10 | | <0.02-190 | 88 | |
| **6:2 FTOH** | House dust, 2000-2001, Ohio and North Carolina | ng/g | 26/ 23 a | 501/355 a | | | | | [35, 112] |
| **8:2 FTOH** | House dust, 2000-2001, Ohio, and North Carolina | ng/g | 28/ 32 a | 1,043/ 747 a | | | | | |
| **10:2 FTOH** | House dust, 2000-2001, Ohio, and North Carolina | ng/g | 28/ 28 a | 555/459 | | | | | |
| **PFHxA** | House dust, 2000-2001, Ohio, and North Carolina | ng/g | 54/ 50 a | 1,049 /1,486 a | | | | | |
| **PFHpA** | House dust, 2000-2001, Ohio, and North Carolina | ng/g | 40/ 43 a | 1,312 /1,550 a | | | | | |
| **PFOA** | House dust, 2000-2001, Ohio, and North Carolina | ng/g | 56/ 52 a | 3,155/ 2,977 a | | | | | |
| **PFNA** | House dust, 2000-2001, Ohio, and North Carolina | ng/g | 22/ 25 a | 393/438 a | | | | | |
| **PFDA** | House dust, 2000-2001, Ohio, and North Carolina | ng/g | 17/ 17 a | 291/ 423 a | | | | | |
| **PFUA** | House dust, 2000-2001, Ohio, and North Carolina | ng/g | 21/ 20 a | 704/ 694 a | | | | | |
| **PFDoA** | House dust, 2000-2001, Ohio, and North Carolina | ng/g | 11/ 10 a | 804/ 425 a | | | | | |
| **PFOS** | House dust, 2000-2001, Ohio, and North Carolina | ng/g | 56/ 50 a | 8,353 /7,688 a | | | | | |
| **PFHxS** | House dust, 2000-2001, Ohio, and North Carolina | ng/g | 48/ 39 a | 8,828/14,187 a | | | | | |
| **PFBS** | House dust, 2000-2001, Ohio, and North Carolina | ng/g | 20/ 17 a | 1,560/ 510 a | | | | | |

LOQ – Limit of Quantitation.
LOD – Limit of Detection
a – Sample size (n) and mean values correspond to Ohio, and North Carolina.
† Participants ranged in age from 25 to 64 years, consisted of 26 females and 5 males, and worked at least 18 hours per week in offices,
†† Values no reported due to low percentage of detection (less than 50 percent),
PFBS -Perfluorobutane sulfonate [PFBS],
PFHxS - Perfluorohexane sulfonate,
PFOS – Perfluorooctane sulfonate,
9 perfluorinated carboxylates (C4 –C12: perfluorobutyrate [PFBA], perfluoropentanoate [PFPeA], perfluorohexanoate [PFHxA], perfluoroheptanoate [PFHpA], PFOA, PFNA, perfluorodecanoate [PFDA], perfluoroundecanoate [PFUnA], and perfluorododecanoate [PFDoA]), Fluorotelomer alcohols (6:2, 8:2 and 10:2 FTOH), FOSE alcohols (N-MeFOSE and N-Et FOSE), and C13 (perfluorotridecanoate [PFTrDA]) and C14 (perfluorotetradecanoate [PFTeDA])

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## IV PFAS in drinking water in Washington State

Between January 2013 and December 2015, 132 public water systems in Washington participated in the EPA's third Unregulated Contaminant Monitoring Rule (UCMR3). Together the tested systems serve the majority (94 percent) of Washington residents served by public water systems. All 113 large Group A systems that serve more than 10,000 people and 19 smaller systems tested their water for six PFAS: PFOA, PFOS, PFBS, PFNA, PFHxS, and PFHpA. Laboratory analysis used EPA method 537 Rev 1.1. PFAS levels above the laboratory reporting limits were found in three public water systems (Figure 6). PFOS was detected in one public water system (City of Issaquah) above what EPA would establish in May 2016 as the lifetime health advisory level (LHAL) of 0.07 µg/L.

**Commented [A18]:** Were PFPeA and PFHxA included in the testing?

The reporting limits in the UCMR3 were somewhat higher than what laboratories are routinely reporting in 2017, so it is possible that more systems would have low but detectable levels if the UCMR3 survey were run today. Still, the survey showed that these six PFAS were not widespread in public water systems in Washington State.

Since the UCMR3 sampling, a number of local investigations have occurred in the state. These include efforts by the City of Issaquah to explore sources of PFAS responsible for contamination detected in one production well in the UCMR3. Investigations have also been initiated by military bases that were identified by the Department of Defense (DOD) as having used or trained with AFFF fire-fighting foams. And other water systems in the vicinity of the military facilities have also conducted monitoring for PFAS.

So far, all detections in Washington State drinking water have been in groundwater wells and are believed to have resulted from historical use of firefighting foam, specifically AFFF. This may be partly because additional investigations at military bases have specifically looked in areas where firefighting foam was used. Other non-military sites where this firefighting foam was likely used include: fire training centers, airports that conducted or hosted fire training, crash sites of planes, oil trains, trucks, or other vehicles where foam was used to extinguish the fire, and fire stations that conducted on-site training with AFFF. Details of these localized investigations are described below.

**Commented [A19]:** Is it known that AFFF was used in these areas proximate to all these GW wells? HAS DOE ruled out all other sources of potential contamination?

### Community specific drinking water data

**City of Issaquah**

The City of Issaquah discovered PFOS, PFHxS, and smaller amounts of PFOA, PFNA, PFHpA in one production well in their public water system as part of UCMR3 testing. PFOS concentration in the affected well ranged from 0.4 to 0.6 µg/L and PFHxS ranged from 0.201 to 0.241 µg/L. Other PFAS were less than 0.03 µg/L. The well blended water in a ratio of 1:4 with a deeper PFAS-free adjacent well before it entered the distribution system. After blending, the water level did not exceed the provisional EPA health advisory at that time (0.4 µg/L for PFOA; 0.2 µg/L for PFOS). Additional sampling in November 2015 across the Issaquah system found PFOS was at 0.106 µg/L at the entry point of the two

blended wells and at levels ranging from 0.068 to 0.038 µg/L in the western portion of the distribution system. At each site, PFHxS was present at about ½ the PFOS concentration. When news coverage in January 2016 sparked public concern about the contamination, the city shut down the well and eventually invested over $1 million in a granular activated carbon treatment system. The treatment system has been effective at removing PFAS and is routinely tested for performance. The city also began investigating the source of contamination. Their investigation concluded that the likely source of contamination was the Eastside Fire and Rescue headquarters. Soil samples in a fire-fighting training area at the headquarters contained PFAS from fire-fighting foam. Additionally, one monitoring well and two drinking water production wells operated by nearby Sammamish Plateau Water system were found to contain PFOA and PFOS at levels well below the 2016 EPA health advisory of 0.07 µg/L. These wells continue to be monitored.

**City of Dupont**

As part of UCMR3 testing, the City of DuPont detected levels of PFOA (≤ 0.030 µg/L) in two wells in the southwest area of the distribution system. PFAS were not detected in the three wells serving the north and east areas of the distribution system. The City of DuPont is considering conducting some follow-up monitoring for PFAS (but that has not occurred as of July 2017).

**Joint Base Lewis- McChord -** The Army's Fort Lewis facility and the Air Force's McChord Field facility are currently operated as a joint military base, but have separate water systems. Only Fort Lewis's water system was included in the UCMR3 testing in 2014. Testing at McChord was conducted under a DOD policy directive.

**Fort Lewis -** As part of the UCMR3 testing at Fort Lewis, PFOA was detected at 0.051 µg/L in one well and PFHpA at 0.013 µg/L in another. Subsequent testing in November 2016 confirmed the previous detections in those two wells and showed PFOA at just above the EPA LHAL in one well which was then taken offline. The November 2016 testing also revealed additional drinking water sources with PFAS. The well that serves the military golf course in DuPont had levels just above the LHAL, and bottled water was supplied at that facility. And the primary source of drinking water for the main base (Sequalitchew Springs and infiltration gallery) has around 0.013 µg/L PFOS + 0.006 µg/L PFOA.

**McChord Field -** In March 2017, the base announced it had shut down three drinking water wells that contained PFAS above the EPA LHAL. Levels in these wells from the November 2016 sampling were reported to be 0.25, 0.216, and 0.071 µg/L. A few other wells have levels of PFAS below the EPA LHAL. As a result of the detections in these wells affiliated with McChord Field, a large water system immediately west of McChord Field (Lakewood Water District) is planning to conduct PFAS monitoring in the latter half of 2017 and in 2018.

JBLM ~~staff believe~~staff believes the contamination came from foam used through the early 1990s for firefighter training at several locations on the east side of McChord Field's runway and on Fort Lewis' Gray Army Airfield. According to the base, use of foams containing the chemicals was discontinued at JBLM more than 20 years ago. As of July 2017 JBLM staff is developing plans to install GAC treatment at drinking water sources contaminated with PFAS to reduce levels to below the LHAL.

Another military site managed by JBLM with potential for PFAS use, the Yakima Training Center, tested drinking water in November 2016, and there were no detections.

**Naval Air Station (NAS), Whidbey Island**

In 2015, the Naval Air Station Whidbey Island detected PFAS in groundwater at locations around Ault Field on the main base north of Oak Harbor and in a well at the Outlying Landing Field (OLF) southwest of Coupeville. In October 2016, the Navy announced it would begin voluntarily testing drinking water wells for two specific PFAS (i.e., PFOA and PFOS) around those two areas.


Consistent with Navy policy, the base targeted their testing in offsite wells within 1 mile downgradient from potential sources such as firefighting training areas and airfields where firefighting foam may have been used. The testing area has expanded over time to include wells within one mile down gradient of wells with detections.

As of July 2017, the Navy has tested 113 well water samples from properties near OLF; seven private wells contained levels of PFOA ranging from 0.13 to 0.66 µg/L, and another two wells had levels of PFOA below the EPA LHAL, one of which supplies water to the town of Coupeville. This well contains PFOA at around 0.06 µg/L but blends with three other wells with no PFAS detections [113]. Thus water entering Coupeville's distribution system has 0.025 to 0.03 µg/L PFOA.

Near Ault Field, of 105 well water samples, one well east of Ault Field detected PFOA just above the EPA LHAL, and another well south of Ault Field contained levels of PFOS at 2.5 to 3.8 µg/L. This is the only well so far affiliated with the Naval Air Station's PFAS sampling that has detections of PFOS. Two other wells near Ault Field had detections of PFOA less than the EPA LHAL.

The Navy is providing bottled water when results show PFOA and PFOS exceed the EPA LHAL. The Navy is also moving forward on their source investigation. Results from 27 new groundwater monitoring wells at OLF showed that three contained PFOS and/or PFOA above the EPA LHAL. Based on the local hydrogeology the groundwater direction is generally to the south at OLF. The Navy also released a policy regarding removal, disposal, and replacement of legacy AFFF that contains PFOS and/or PFOA, including prohibitions on using this type of foam for future training exercises.

At least twelve small public water systems on Whidbey Island have tested their wells for PFAS as of June 2017, and none of them had any detections.

**Fairchild Airforce Base (AFB) and surrounding areas, Spokane County (2017)**

In monitoring conducted per the DOD directive, Fairchild AFB tested groundwater on the base at five locations including fire-training areas andtwo2 sites of previous plane crashes. The results of this testing were not made public except to acknowledge that PFAS were detected. Drinking water on the base is supplied by the base's wells near the Spokane River several miles north of the base and is not contaminated with PFOS or PFOA. However, based on other groundwater monitoring results, Fairchild conducted off-base testing for PFOA and PFOS in residential wells east of the base and municipal wells for the City of Airway Heights northeast of the base. Sampling is continuing with current expansions out to the North and Northeast of the base.

Results for private wells were not provided to the public but preliminary results provided to DOH for Airway Heights municipal system showed 1.1- 1.2 µg/L PFOS and 0.3 -0.32 µg/L PFOA in the affected wells. These levels are approximately 17 times higher than the EPA LHAL for PFOS and PFOA. A third phase was just announced (7/11/17) and will include about 50 residential wells just North of the base.

The Airforce policy is to notify and provide bottled water immediately if levels for PFOS and PFOA in drinking water exceed the EPA health advisory level. This included customers of the City of Airway Heights (population 6,200) public water system.

The public water system of Airway Heights shut down their three contaminated wells and used an emergency intertie with the City of Spokane water system to flush their system with clean water. Flushing included draining reservoirs and water towers and continued until measurements taken at over 20 points in their distribution system were well below the 0.070 µg/L health advisory for PFOS and PFOA. During the flushing, the city warned residents located West of Hayford Road to not drink or cook with water from city pipes and people were provided bottled water by Fairchild AFB. The city has since added another connection to the City of Spokane to supply drinking water while they consider treatment options for the contaminated wells.

According to Fairchild AFB, the base has transitioned to an alternative AFFF, called Phoscheck 3, that is PFOS-free and has only trace amounts of PFOA, yet still provides adequate fire protection for critical assets and infrastructure. Additionally, AFFF is no longer used during live-fire training and the fire trucks on base are being outfitted with a test system that prevents any foam discharge during equipment testing.

### Drinking water remediation options

PFAS (which ones?) cannot be removed from drinking water by boiling or with standard treatment process, but can be removed by reverse osmosis, ion exchange, nanofiltration and granular activated carbon (GAC) treatment systems.

In 2016, the Water Research Foundation released a study of 15 full-scale PFAS water treatment systems throughout the country [114]. The study included a wide spectrum of treatment techniques and collected objective measurements of 23 PFAS in source water, finished drinking water or potable reuse product water, and at various steps along the treatment train. It also compared performance of GAC and a new technology using nanofiltration in a laboratory setting.

The study found that traditional water treatment systems: aeration, chlorine dioxide, dissolved air flotation, coagulation, flocculation, sedimentation, granular filtration, and microfiltration were all ineffective for removing PFAS including PFOA and PFOS. Anion exchange was moderately effective in treating PFOA, highly effective for PFOS and PFHxS, and failed to remove several PFAS that were C7 in length or shorter. Granular activated carbon (GAC) removed over 90% of long chain PFAS but was ineffective at removing shorter chain PFAS. Nanofiltration and reverse osmosis filtration removed even the smallest PFAS [114].

Recently, the Calgon Corporation conducted a study and researched several GAC subtypes (e.g., bituminous re-agglomerated coal (filtrasorb-virgin), direct activated coconut, and reactivated bituminous re-agglomerated coal (filtrasorb-react)). They concluded that bituminous and reactivated bituminous are effective GAC materials at removing long and short chain PFAS [115].

Besides performance in removing PFAS, large system treatment options differ in installation cost, required maintenance, and water and energy requirements. Reverse osmosis also removes beneficial minerals from the water.

For private well owners, NSF International recently developed a certification for home filters that remove PFOA and PFOS from drinking water. To make a PFOA/PFOS reduction claim, a certified water filter must be able to reduce these chemicals to below the EPA healthy advisory limit of 0.07 µg/L. NSF certified filter systems have also been verified to meet the contaminant reduction claims on the label, to not contain misleading advertising on their labels, to not add anything harmful to the water, and to be structurally sound in their engineering and construction.

The Minnesota Health Department has also sponsored independent performance testing of commercially available point-of-use water filter devices in 2008. They identified eleven devices that sufficiently removed PFOS, PFOA and PFBS contaminants. More information is at their website [116].

**Next steps - identifying and testing other drinking water sources that may have PFAS contamination.**

DOH advises residents in Washington to follow the EPA health advisory when PFAS are found in drinking water. In order to identify other drinking water sources that may be impacted, DOH is working to map areas where drinking water sources (both private and public) may be at increased risk of PFAS contamination. DOH is also developing a funding program to assist public water systems who have not yet tested for PFAS.

DOH used risk factors for PFAS in water reported by Hu et al. 2016 [9] to generate a map of potential point sources across Washington State. We focused on locations where AFFF was potentially released for this preliminary analysis. Specifically, we generated a map of military land, airports with personnel certified in the use of AFFF, known fire training facilities, and records of AFFF releases obtained from the Washington State Department of Ecology spills program. Data on the location of fire training facilities are incomplete, as there is not a comprehensive list of fire training centers, and trainings using AFFF are not formally documented and take place at a range of facility types under multiple jurisdictions. Additionally, reporting AFFF spills to DOE is voluntary and not comprehensive. Despite the limitations, the map provides useful information for the preliminary evaluation of risk.

We used our map of potential point sources to identify drinking water sources with an increased risk of PFAS contamination that should be prioritized for testing. We calculated the number of community and transient non-community Group A [4] sources within a mile of an identified point source. We calculated the percentage of those water sources that were tested as part of UCMR3 data collection. We found that potential sources of PFAS contamination related to AFFF were distributed across Washington State (Figure 7). We also identified many public water systems within a mile of potential point sources that were not tested for PFAS contamination as part of UCMR3 (Figure 8).

A number of the areas in red on panel B identified as high priorities for testing have already been tested as part of military site testing such as areas around Whidbey Island Naval Air Station, JBLM in Pierce County, and Fairchild Airforce Base near Spokane. Additional water testing results and potential sources can be incorporated to refine the mapping. This preliminary map of potential point sources also provides a useful resource to private well owners and Group B water systems [5] for identifying water sources that should be tested.



[4] Group A Transient Non-Community water systems serve: twenty-five or more different people each day for sixty or more days within a calendar year; twenty-five or more of the same people each day for sixty or more days, but less than one hundred eighty days within a calendar year; or one thousand or more people for two or more consecutive days within a calendar year.
http://www.doh.wa.gov/CommunityandEnvironment/DrinkingWater/WaterSystemAssistance/TNCWaterSystems

[5] Group B public water systems serve fewer than 15 connections and fewer than 25 people per day.

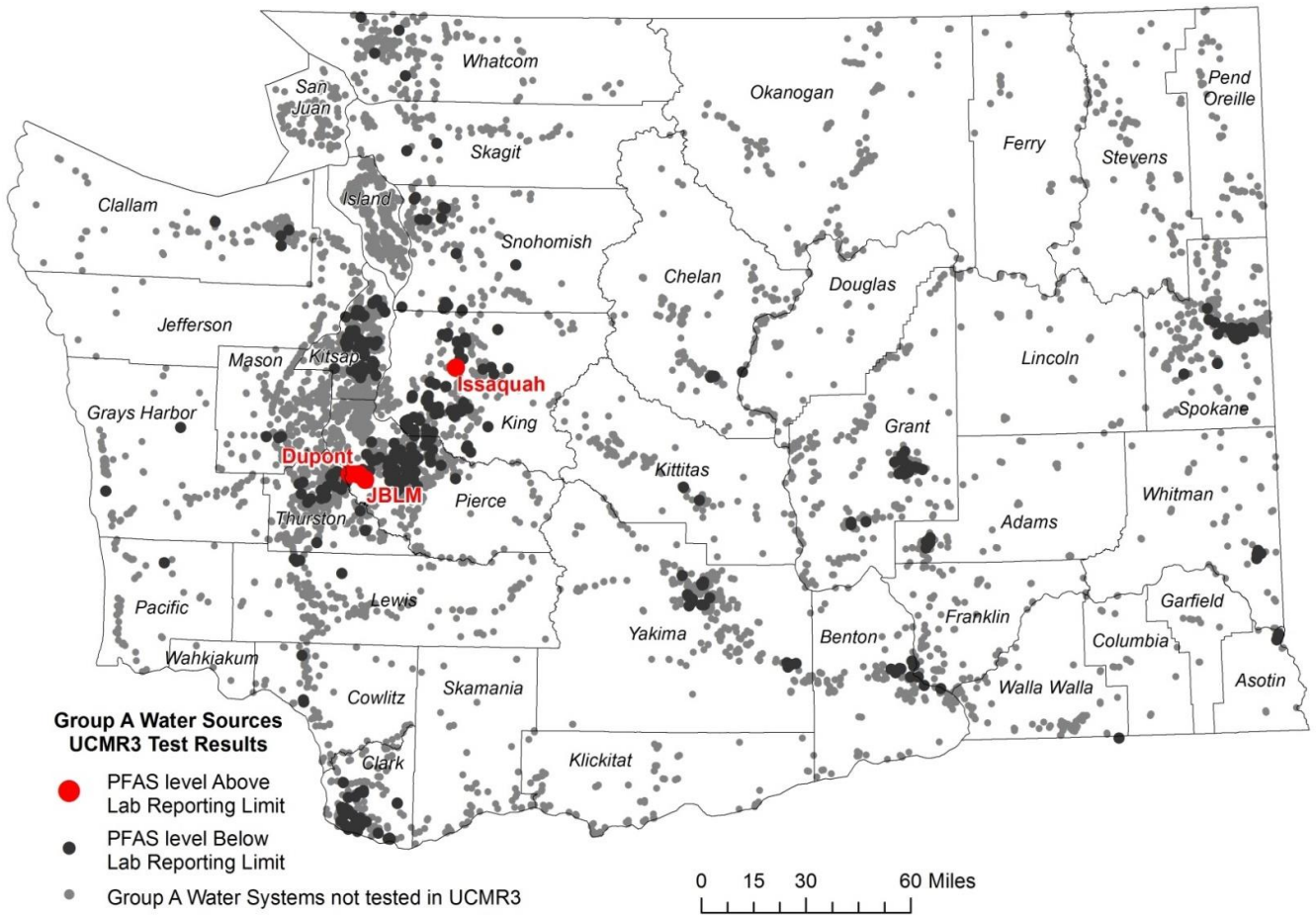


Figure 6. Results of UCMR3 drinking water testing for PFAS in Washington State.

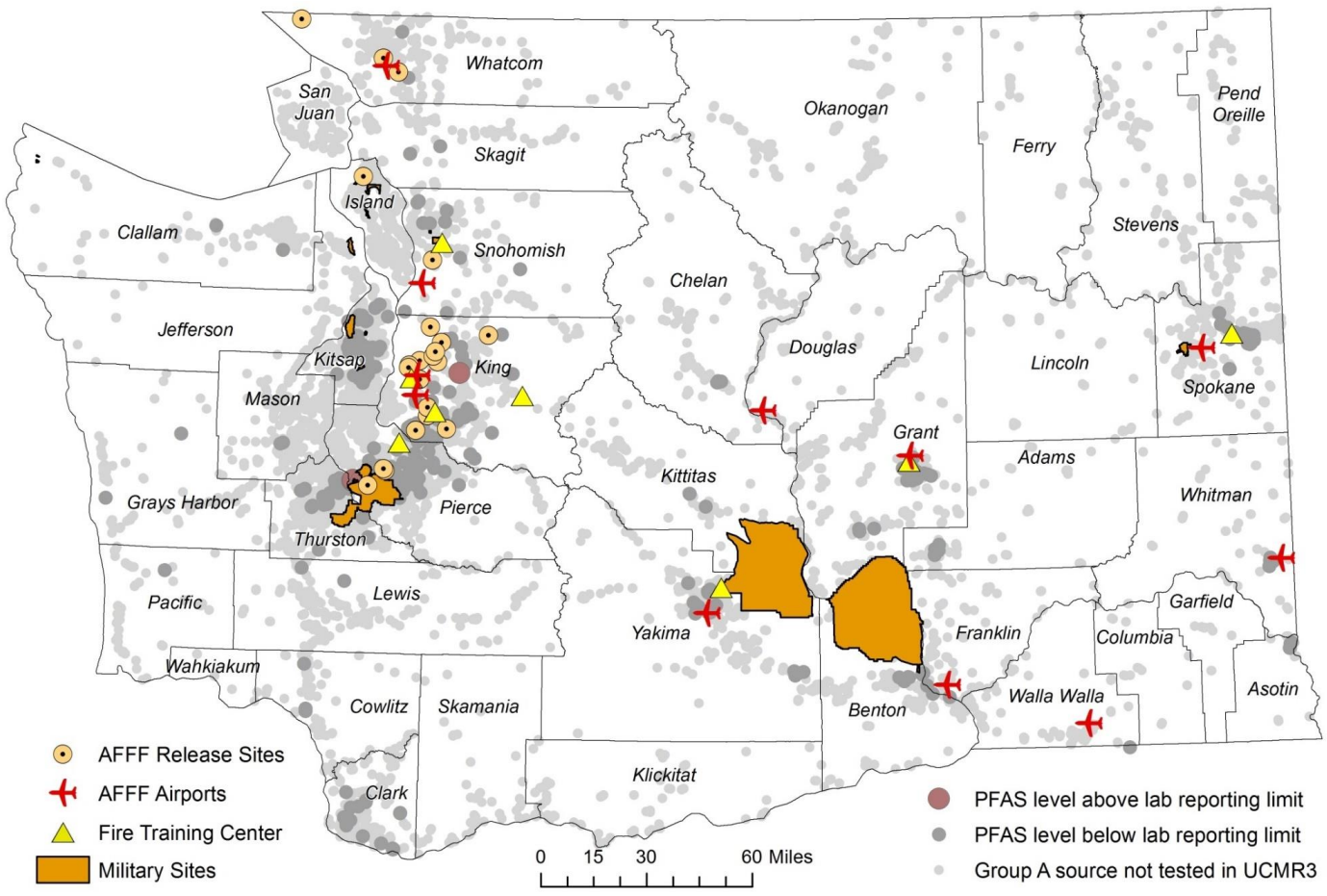


Figure 7. Potential PFAS sources related to the use of AFFF in Washington State

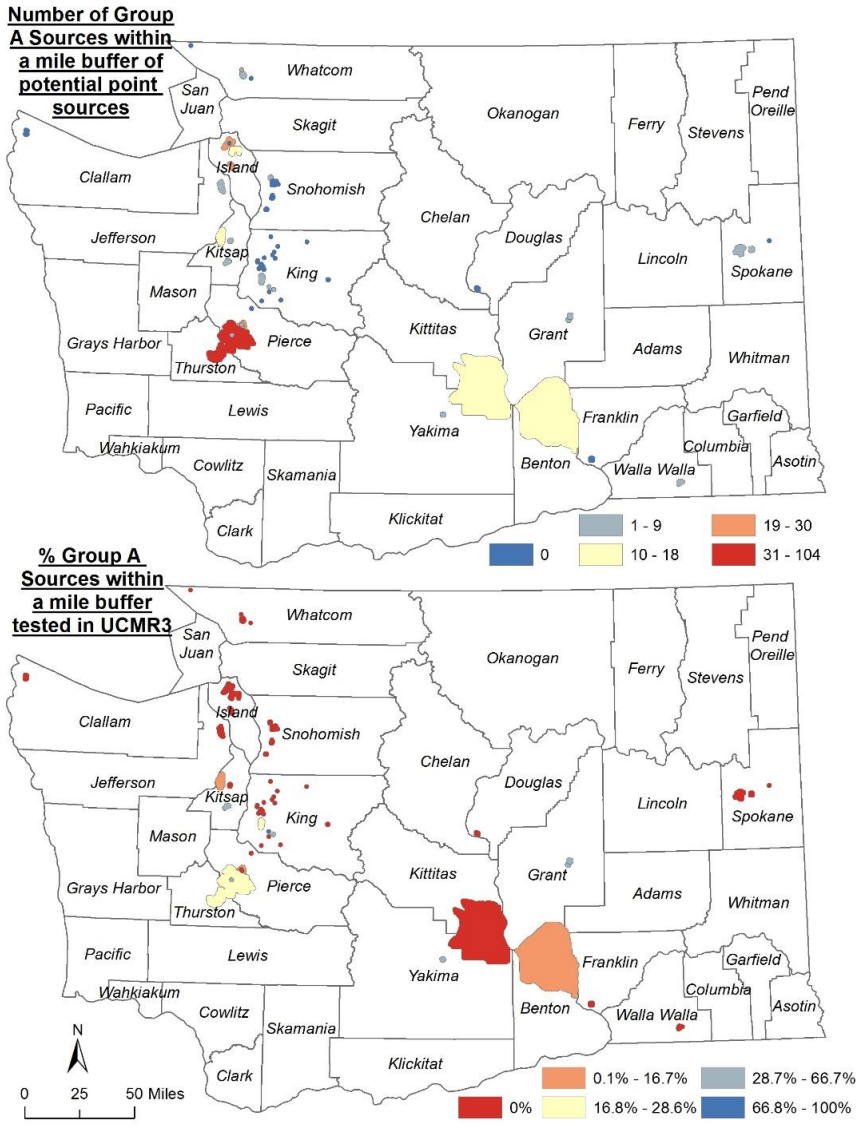


Figure 8. The number of Group A community and non-transient, non-community public water systems within a mile of a potential point source (Panel A) and the percentage of those sources tested for PFAS as part of UCMR3 (Panel B).

## V. Toxicology of long-chain ~~PFAS~~Perfluoroalkyl Acids~~PFAS~~(PFAAs)

Commented [A20]: Clear, specific, descriptive terms.

The toxicology and health research on PFOA and PFOS ~~PFAS compounds~~ have been recently reviewed by the Environmental Protection Agency [117, 118], the CDC Agency for Toxic Substances and Disease Registry [2], the International Agency for Research on Cancer [119], the National Toxicology Program [120], and Health Canada [121].

Adverse effects reported in laboratory animals fed ~~PFAS~~ PFOA and PFOS may include: liver toxicity, immune suppression, altered hormone levels, tumors, and reproductive and developmental problems. In animals, the developing fetus and nursing offspring are particularly vulnerable to PFAS exposure during their development. Developmental effects in animals include reduced fetal growth and altered bone development, altered behavior, and altered timing of sexual maturation in adolescence.

Some, but not all, studies of people exposed to ~~PFAS~~ PFOA and PFOS substances over a long period of time indicate that PFAS exposure may:

- Increase cholesterol levels.
- Alter thyroid hormones.
- Affect the developing fetus and childhood learning and behavior.
- Increase some types of cancers, including prostate, kidney, and testicular cancer.
- Affect the immune system and reduce immune response to vaccines in children.

Information specific to individual long-chain ~~PFAS~~ perfluoroalkyl acids (PFOA, PFOS, PFHxS, and PFNA) ~~compounds~~ is summarized below ~~followed by a discussion and review of available information on short-chain PFAS~~.

### PFOA (CAS No. 335-67-1)

**Toxicology**

In animal testing PFOA causes liver effects (hypertrophy, necrosis, effects on the metabolism and deposition of dietary lipids, and adenomas) [122-126], kidney toxicity [125, 127], and immune effects [128-130]. PFOA is also a reproductive and developmental toxicant. PFOA is not genotoxic or mutagenic but it causes nonmalignant lesions including testicular Leydig cell adenomas [126, 131], pancreatic acinar cell tumors [126], and ovarian tubular hyperplasia in animal studies [24].

Numerous health effects are associated with PFOA exposure in humans. Epidemiological studies have been conducted in workers from chemical plants that produced or used PFOA, in communities with high levels of PFOA in drinking water, and in the general population. These studies report associations between PFOA exposure and high cholesterol [94, 106, 132-138], increased liver enzymes [132, 139-142], decreased vaccination response [143-145], thyroid disorders [146-151], pregnancy-induced hypertension and preeclampsia [152-155], and cancer (testicular and kidney) [24]. From these epidemiological investigations, the strongest and most consistent associations between PFOA exposure and adverse health effects in humans are elevated serum cholesterol, low density lipoproteins (LDL) and

uric acid, suggesting metabolic disorders [4, 74]. Analysis by the New Jersey Drinking Water Quality Institute concluded that epidemiological findings provide some evidence of a causal relationship between PFOA and both cholesterol and alanine aminotransferase [74].

**Absorption, metabolism, distribution, excretion:**

Based on animal data, PFOA is expected to be readily absorbed via oral ingestion and inhalation in people. The acid can be absorbed dermally but the anionic form of PFOA found in drinking water is not absorbed across skin. PFOA is highly persistent in the human body, because it is not readily eliminated and is not metabolized[6]. When PFOA enters the body it accumulates mainly in blood serum, the kidneys, and the liver, although it can accumulate in the lungs, heart, muscle, testes and uterus [156]. The half-life[7] of PFOA in humans is 2.3 – 3.8 years with very little difference between sexes. In contrast, the half-life values for the monkey, rat, and mouse are 20.8 days, 4 to 6 days, and 17 to 19 days, respectively (Table 1). The long half-life of PFOA in humans is attributed to resorption of PFOA following filtration by the kidney. Instead of being eliminated in urine, 99.94% is reabsorbed and returned to the blood in the renal tubules. [157]. This is achieved by active transport and is a saturable process. Branched-chain PFOAs are less likely to be reabsorbed in the kidney than the linear molecules based on half-life information in humans [117].

PFOA binds preferentially to proteins, enzymes, and cell surface receptors (e.g. PPARα, constitutive androstane receptor (CAR), pregnane X receptor (PXR), farnesoid receptor (FXR), triiodothyronine (T3) receptor, estrogen receptor), but it has also high affinity for binding with serum albumin (greater than 90 percent), β-lipoproteins and liver fatty acid binding proteins [2, 156].

**Effects on liver, kidney and blood lipids:**

A common indicator of PFOA exposure in most animals studies is changes in liver weight (e.g., increased liver weight). In animals PFOA is an agonist for PPARα, although it can also bind to PPAR gamma receptor (PPARγ) [158]. These are nuclear receptors that play key roles during fetal development and in fatty acid storage and metabolism of lipids and glucose in adults.

Studies conducted in rats, and mice have shown that exposure to PFOA can lead to liver effects such as hypertrophy, necrosis, effects on the metabolism and deposition of dietary lipids, and adenomas [122-126]. Decreased body weight, increase liver weight, and decreased serum cholesterol are endpoints well demonstrated in subchronic studies in monkeys and rats. The most prominent lesion of the liver in monkeys and rats was centrilobular hepatocellular hypertrophy.

[6] PFOA is not metabolized, thus, any effects observed in toxicological studies are the result of parent compound, not metabolites.
[7] There is a broad range of half-lives in human epidemiology studies, suggesting a variability in human transport and binding capabilities resulting from genetic variations in transporter structures and, consequently, in function (EPA, 2016 – Health Effects support document for PFOA).

In contrast with animal findings, epidemiologic evidence in humans suggest that exposure to PFOA and PFOS increases cholesterol levels. Significant associations were observed in occupational and community studies between higher plasma PFOA and serum cholesterol levels. Other studies report no associations. Positive associations have also been reported with lipids, including low density lipoprotein (LDL) and increase in total cholesterol and PFOA exposure. No associations have been reported with high density lipoprotein (HDL), and triglycerides. Others studies report no association between PFOA exposure and LDL and increased triglycerides [117].

**Immune toxicity:**

In 2016, the National Toxicology Program (NTP) published a systematic review of animal and human data which concluded that PFOA is a presumed [8] immune hazard to humans based on evidence that PFOA and PFOS suppress the body's production of antibodies. Mice exposed to higher levels of PFOA or PFOS produced fewer antibodies when challenged with antigen. Similarly, humans with high levels of either chemical had lower antibody levels to common childhood vaccines. NTP also concluded that there was a high level of evidence that PFOA increased hypersensitivity-related outcomes from animal studies, and low level of evidence from human studies [120].

**Reproductive and Developmental effects:**

PFOA is a known developmental toxicant in animals. It has been evaluated in several animal species, including fish, rats, mice, and monkeys [159]. Developmental effects include: decreased neonatal survival (rat, mouse), body weight changes, reduced ossification, delays in eye opening, and body hair growth (mouse) [160], altered puberty, [125, 160, 161], reduced fetal growth [162], retarded mammary gland[9] development (mouse dam and offspring) [160, 163-168], and delayed vaginal opening (mouse) [159]). Recent studies show that developmental exposure to low doses of PFOA in mice causes cellular changes indicative of liver toxicity that persists until adulthood [74]. Overall, toxicity studies available for PFOA demonstrate that the developing fetus is particularly sensitive to PFOA-induced toxicity [117]. Developmental toxicity of PFOA depends on timing and level of exposure to the developing fetus and newborn and is influenced by sex and species differences in elimination rate of PFOA [159].

There are only a few studies which have looked for evidence of these developmental effects in people. These studies evaluated the effect of PFOA on human sexual development and onset of puberty with inconsistent findings. Other few human studies found no association between PFOA exposure and delayed onset of puberty [117]. There has been no evidence of bone or skeletal abnormalities in infants or children exposed to PFAS. There has also been no consistent evidence of increased miscarriages or birth defects in humans due to PFOA exposure.

[8] Presumed hazards are considered to be one step below a known hazard, on the five-step scale NTP uses for hazard identification, from not identified to known to be a hazard.
[9] The mode of action for PFOA-induced delayed mammary gland development is unknown and requires further investigation (EPA, 2016 – Drinking Health Advisory for PFOA).

A recent systematic review using the Program on Reproductive Health and the Environment's Navigation Guide systematic review methodology, found sufficient evidence that PFOA reduces fetal growth in humans. Their meta-analysis of nine epidemiological studies showed a 18.9 gram reduction in birth weight for every 1 ng/mL increase in maternal sera or cord PFOA level [169]. Follow-up studies have suggested that these children with lower birth weights grow normally. Low birth weight (<2500 g) is a known risk factor for diseases later in life but the weight difference observed to correlate with higher PFOA exposure were generally small and of unknown clinical significance [162]. Recent analysis of the Flemish Environmental Health Survey suggested that PFOA may amplify effects of other environmental pollutants on low birth weight [170]. It has been suggested that low glomerular filtration (GFR) rate may explain some of the association observed in epidemiological studies, as individuals with low GFR have higher serum levels of PFOA as well as lower birth weight [171].

**Hormone effects:**

Experimental studies in rats and monkeys have shown that PFOA impairs thyroid hormone homeostasis by reducing T3 and T4 levels. Occupational studies found no association between thyroid hormone and PFOA levels (i.e. T3, T4, or TSH) [158]. Results from NHANES study found higher concentrations of serum PFOA and PFOS associated with thyroid disease in the United States [172]. Overall, it is difficult to draw a solid conclusion from these studies regarding levels of PFOA and evidence of thyroid disease in humans.

Increased estradiol levels and decreased testosterone levels have been observed in experimental animal studies. In humans, some occupational studies have reported association of serum PFOA levels with sex hormones (estradiol and testosterone). Other studies found no association. Given the sex differences and longer half-life in rats, more studies are needed to address the effects of PFAS exposure on sex hormones [158].

A study by researchers from Hokkaido University (Japan) found a link between levels of PFOA and PFOS in mother's blood and hormone levels in their offspring. High blood PFOA levels in mothers were linked to lower dihydroepiandrosterone (DHEA) levels in cord blood [109].

**Cancer:**

The mode of tumorigenic action of PFOA in rodents is not clearly understood, but available data suggest that the induction of tumors is likely due to non-genotoxic mechanisms involving membrane receptor activation and perturbations of the endocrine system [117]. There is evidence that PFOA is a potent peroxisome[10] proliferator that induces peroxisome formation in the livers of rats and mice [130, 173-176]. There is also evidence to indicate that liver tumors and toxicity in rodents are mediated by binding

[10] Peroxisomes are single-membrane organelles found in a number of plant and animal cells that have the capacity to carry out beta oxidation of long-chain fatty acids and other substrates through hydrogen peroxide-generating pathways and without the generation of adenosine triphosphate (ATP), cited in EPA, 2016.

to the PPARα receptor in the liver. It is uncertain whether the presence of liver tumors in rats treated with PFOA, and its interaction of PFOA with PPARα is relevant to humans, since there are differences in the mode-of-action and in downstream response in humans compared to rodents [177].

In occupationally exposed workers, associations between exposure to PFOS or PFOA and male reproductive, kidney and bladder cancers have been reported. However, associations are generally weak and are not consistent across studies [3, 178]. In addition, the sample sizes for many of these studies are small, and caution is needed in interpreting the results. Studies in populations exposed to low levels of PFOA and PFOS have shown equivocal results for a variety of cancers with no consistent associations [178].

**Commented [A21]:** Add a second citation to Chang et al. 2014 to support this statement on p.42, "Studies in populations exposed to low levels of PFOA and PFOS have shown equivocal results for a variety of cancers with no consistent associations [178].", and the similar statement on p. 45 for PFOS. Note that this additional citations covers in detail many of the same studies that are discussed in the Health chapter, and can be cited in multiple places. Note specifically the important points made regarding the lack of coherence in cancer findings between the animal toxicity studies and epidemiologic studies.

Two studies conducted by members of the C8 Health Project, Science Panel showed a positive association between PFOA serum levels (mean serum level at enrollment of 0.024 µg/mL) and kidney and testicular cancers [179, 180]. The Science Panel concluded that a "probable link" existed between PFOA exposure and testicular and kidney cancer, but no other types of cancer. On the other hand, two occupational studies in Minnesota and West Virginia found no associations of increased risk of kidney and testicular cancer [181, 182]. General population studies found no associations between mean serum PFOA levels up to 0.0866 µg/mL and colorectal, breast, prostate, bladder, or liver cancer [183-186], (cited in [117]).

According to ATSDR "there is no conclusive evidence that perfluoroalkyls cause cancer in humans. Some increases in prostate, kidney, and testicular cancers have been seen in individuals exposed to high levels. These results should be interpreted cautiously because the effects were not consistently found and most studies did not control for other potential factors such as smoking [2]." In non-occupational exposed members of the general population, cancers linked with PFOS or PFOA exposure include testicular, kidney, and breast cancer, though results remained inconclusive. Additionally, no associations have been observed between PFOS or PFOA exposure and a variety of other cancers [3].

In a report on the evaluation of the carcinogenicity and genotoxicity of PFOA and its salts, the Health Council of the Netherlands concluded that the available data on PFOA and its salts are insufficient to evaluate the carcinogenic properties. After reviewing the epidemiology studies, they concluded that available studies were of varying quality with several having significant weaknesses. Several studies report elevated risks for certain types of cancer but overall there is no cancer type that is consistently elevated in these studies. According to the Health Council, the cancer type of highest concern is kidney cancer. With regard to carcinogenicity studies in animals, the Health Council concluded that the animal studies show development of benign tumors in rodents, but are negative with respect to malignant tumors. The occurrence of liver, pancreatic acinar cell tumors and Leydig cell tumors in animal studies may be explained in large part by peroxisome proliferation. These tumors are species-specific and are unlikely to have relevance for liver, pancreatic, and testicular cancer in humans [187]. The European Chemicals Agency (ECHA) concluded that there is insufficient data for the tumors observed in rats on the mode of action of PFOA to conclude that tumors are not relevant for humans [188].

Lastly, EPA found "suggestive evidence" of carcinogenic potential of PFOA in humans based primarily on the C8 Health Study [117]. EPA also concluded that the PPARα mode of action for the liver tumors observed in rats have no relevance to humans [117]. The International Agency for Research on Cancer (IARC) has classified PFOA as possibly carcinogenic to humans (Group 2B) [119].

### Key epidemiological studies

Numerous epidemiological studies have examined the relationship between serum PFOA levels and potential health effects in occupational populations, highly-exposed residential communities and general population studies in the United States. Overall, the approximate range in serum PFOA concentrations in PFOA-exposed workers is 0.010 to about > 2.0 µg/mL, in high exposure communities is 0.010 to 0.100 µg/mL and in the general population is below limit of detection (LOD) to about < 0.010 µg/mL [117].

Below, we summarize brief reviews of three communities affected by releases of PFAS in drinking water.

#### Mid-Ohio River Valley (West Virginia)

DuPont's Washington Works Plant in southwest Parkersburg, West Virginia released PFOA into the air and Ohio River from the 1950s until the early 2000s. Subsequently, drinking water for communities in the mid-Ohio Valley became contaminated. PFOA reached drinking water supplies by entering the groundwater and was detected in six public water systems in 2002. Exposures to the communities started in 1951 and peaked in the early 1990s.

Between 2005 and 2013, the C8 Health Project, Science Panel carried out exposure and health studies in the mid-Ohio Valley communities affected by water contamination. The Science Panel assessed the links between PFOA and a number of diseases and concluded that a "probable link" existed between PFOA and high cholesterol, ulcerative colitis, thyroid disease, testicular cancer, kidney cancer, and pregnancy-induced hypertension among the population evaluated [189]. They found no probable link to many other conditions including: heart disease, chronic liver or kidney disease, stroke, several autoimmune disease, occurrence of common infectious diseases or respiratory disease, asthma, or birth defects.

Serum levels of PFOA in communities exposed to contaminated drinking water were elevated compared to the general population. The mean PFOA serum concentration of residents living near this fluoropolymer production facility had much higher than the geometric mean serum concentration in the NHANES general population during the same time period [190]. In all, the C8 Health Project recruited over 69,000 residents living in this community who had consumed drinking water for at least one year from the Lubeck and Mason County water districts in West Virginia, the Belpre, Little Hocking, Tuppers Plains-Chester, and Pomeroy water districts in Ohio, or private water source within the geographical boundaries of the public water sources [117].

**Commented [A22]:** The following statement regarding the "probable link" findings from the C8 Health Project is made, "They found no probable link to many other conditions, including: heart disease, chronic liver or kidney disease, stroke, several autoimmune disease, occurrence of common infectious diseases or respiratory disease, asthma, or birth defects." Be sure to include the follow-on studies that are available, and actually cited elsewhere in this report. For example, Looker et al. (2014), citation #145, is important for the reassessment of immunotoxicity. The C8 Health Project published probable link reports did not link PFOA exposure to reduced antibody titer rise, and in fact found no probable link between PFOA exposures and autoimmune dysfunction or incidences of infectious disease. Looker et al. (2014) is a follow-up study from the C8 Health Project that is not associated with the "Probable Link" reports. See: http://www.c8sciencepanel.org/prob_link.html. Moreover, Looker et al. (2014) only found an association with PFOA exposure in adults and reduced A/H3N2 titer; none of the other viral antibodies assessed were reduced, and no association between PFOA exposure and increase in cold or influenza or any disease was found.

The highest PFOA drinking water concentration was found at the Lubeck, West Virginia, Ohio followed by Tuppers Plain, Ohio. The average PFOA water concentration at these locations were 520 µg/L and 310 µg/L, respectively (Table 2) [19]. Levels were approximately over 7,000 and 4,000 times higher than the current EPA lifetime health advisory for PFOA and PFOS of 0.07 µg/L, respectively. Emmett et al. 2006 suggested that residential water was the likely pathway of exposure of PFOA [94].

The overall geometric mean serum PFOA concentration was 32.9 µg/L compared to 3.9 µg/L for NHANES (2003 to 2004) [19, 89]. In the C8 Health Project, serum PFOA concentrations were higher in males compared to females. The overall geometric mean was 39.4 µg/L for males and 27.9 µg/L for females [19]. Women have additional pathways to clear PFAS through their menstrual cycle [191], childbirth [45, 47, 192] and breastfeeding [58, 192, 193]. In comparison, mean serum PFOA levels in groups of workers at DuPont's facilities were much higher and ranged from 494 µg/L to 3,210 µg/L [3].

The Science Panel considered drinking water contaminated with PFOA coming from the DuPont plant as the principal route of exposure for this population. Other investigators also concluded that the increased PFOA concentration was associated with consumption of drinking water contaminated with PFOA [94, 95, 194-199]. Following the 2005 to 2006 study by the C8 Health Project, carbon filters were installed to remove PFOA from public drinking water systems. As a result, PFOA serum concentrations declined 26 percent between November to December 2007 and May to June 2008 in the groups from Little Hocking and Lubeck water districts indicating a serum elimination half-life of 2.3 years [199].

**3M PFAS manufacturing facility in Minnesota ("East Metro" Study of Minneapolis-St Paul)**

The Minnesota Department of Health conducted a community exposure assessment of PFAS released from the 3M Cottage Grove manufacturing facility as well as several local landfills where the plant had legally disposed of wastes in the 1950s, 1960s, and 1970s. Several PFAS were detected in public and private wells in the East Metro communities in the metropolitan area of Minneapolis-St Paul. PFOA and PFOS levels in municipal wells ranged from non-detect to 0.9 µg/L. In private wells the levels ranged from non-detect to 2.2 µg/L for PFOA and non-detect to 3.5 µg/L for PFOS [200]. Drinking water contamination was discovered in 2004 and water filtration to remove PFAS was installed in 2006. Biomonitoring was conducted to assess community exposure in 2008 [201]. In 2014, follow-up biomonitoring was conducted to assess water filtration as a public health intervention. Eight PFAS were tested in 149 long-term residents of Oakdale, Lake Elmo, and Cottage Grove who drank contaminated drinking water before the intervention and had participated in past studies, and 156 new Oakdale residents who moved to the area after the intervention. PFOS, PFOA, and PFHxS were found in the blood of almost all long-term residents tested. Levels of these PFAS decreased between 2008 and 2014 in most people. On average, individual levels of PFOS went down by 45 percent, PFOA by 59 percent, and PFHxS by 34 percent over six years. PFAS blood levels in long-term residents are still higher than levels seen in the U.S. population [17]. Sex and age were related to PFAS levels, and older people and men had higher PFAS levels.

**Decatur Alabama (in the Vicinity of Decatur, Alabama and Morgan, Lawrence, and Limestone Counties)**

In 2007, a manufacturer of PFAS in Decatur, Alabama, notified EPA that perfluorocarboxylic acids (PFCA) were discharged into the Decatur Utilities Dry Creek Wastewater Treatment Plant. From 1996 to 2008 treated sewage sludge (biosolids) from Decatur Utilities was used as a soil amendment on about 5,000 acres of privately owned agricultural fields in Lawrence, Morgan, and Limestone Counties in Alabama [15]. As a result, PFAS chemicals were found in the Decatur Utilities biosolids, surface water, groundwater, and drinking water. PFOA was detected in 57 percent of surface waters near the fields. Four out of 19 (22 percent) private wells had PFOA concentrations above the EPA's Health Advisory level of 0.07 µg/L [19].

PFAS were measured in the serum of people that lived and worked in the affected public water system. The levels were higher compared to the levels found in the 2007-2008 NHANES United States general population data. Serum PFOA concentrations in 121 residents with affected public drinking water ranged from 2.2 to78.8 µg/L. The range of serum PFOA concentrations in the private drinking water wells with detectable levels (n=9) were 7.6 to 144 µg/L [19]. Workers from the 3M manufacturing plant in Decatur were also tested for exposure. Mean blood serum concentrations of PFAS in occupationally exposed workers of both sexes ranged from 1,290 µg/L to 2,440 µg/L for PFOS and from 1,460 µg/L to 1,780 µg/L for PFOA [3].

## PFOS CAS No. 1763-23-1

**Toxicology**

PFOS is a developmental toxicant in animal studies. PFOS also produced liver toxicity (liver weight co-occurring with decreased cholesterol, hepatic steatosis[11]), developmental neurotoxicity (altered spatial learning and memory), immune effects, and tumors (thyroid and liver). Overall, the fetus is particularly sensitive to PFOS-induced toxicity.

Human epidemiology data report associations between PFOS exposure and high cholesterol [106, 133, 137, 138, 147, 202-211], thyroid hormone levels and/or thyroid disease [150, 172, 212], immune suppression [143, 144], and some reproductive and developmental parameters, including reduced fertility and fecundity [213]. Some studies show an association between PFOS and chronic kidney disease [214, 215]. EPA's 2016 review recognized that while some human studies suggest an association with bladder, colon, and prostate cancer, the literature is inconsistent and some studies are confounded by failure to control for risk factors such as smoking [118].

**Absorption, metabolism, distribution, excretion:**

[11] Steatosis means fat accumulation in the liver.

PFOS is well absorbed from the gastrointestinal tract but there is little information about absorption across skin or lung surfaces. Because of its chemical properties, absorption across tissues likely involves active transport rather than simple diffusion [118]. PFOS accumulates in the liver, kidney, and blood plasma. PFOS is resistant to metabolic break down. It binds to nuclear receptors (e.g., PPARα), proteins in blood (e.g., serum, transferrin, immunoglobulins, transthyretin, fatty acid binding proteins), and enzymes [176, 216-221]. PFOS is eliminated in feces and urine in rats [75].

The average half-life of PFOS in humans is 5.4 years in males, and 6.7 years in females [146]. The serum elimination half-lives in other species are listed in Table 1. The long half-life of PFOS in humans is attributed to resorption of PFOS in the kidney. PFOS that would normally be eliminated in urine is resorbed from the renal tubules and returned to the blood [75]. This resorption is believed to be accomplished by membrane transporters with saturable kinetics [118]. A study shows that linear PFOS bind stronger to albumin and other serum proteins than branched chains [222], and highly branched PFOS content in serum is a biomarker of exposure to PFOS-precursors [223].

**Effects on liver, kidney and blood lipids:**

Increased liver weight is the most sensitive outcome in animal testing of PFOS exposure. Some studies observed effects on liver weight at low doses [224, 225]. PFOS induces decreased serum cholesterol levels and high density lipoproteins in rats [226-228], decreased very low density lipoproteins in mice [229], and liver retention of triglycerides in mice [218, 230].

The main observations from human studies are increased cholesterol levels and increased biomarkers of liver damage [158]. Results of many human studies have linked PFOS levels with total cholesterol, low density lipoproteins, and triglycerides [106, 133, 137, 138, 147, 202-207, 209-211, 231, 232].

Epidemiological evidence supports an association between PFOS and increased total cholesterol, triglycerides, and uric acid in the general population [118, 233]. PFOS was also significantly associated with increased total cholesterol, HDL-cholesterol, and LDL-cholesterol in children enrolled in the C8 Health Study [106].

Results from some occupational population studies have found positive associations between PFOS exposure and serum lipids. The most comprehensive epidemiological data linking health outcomes and PFOS and PFOA exposure was reported from the Mid-Ohio Valley communities whose drinking water was contaminated by PFOA emissions from the Washington Works plant in Parkersburg, West Virginia. Two studies reported elevation of alanine transaminase levels and increase in cholesterol levels following PFOS and PFOA exposure [106, 140].

**Immune Toxicity**

The National Toxicology Program (NTP) concludes that there is evidence of suppressed disease response and suppressed natural killer cell activity by PFOS. Both are hallmarks of adverse immune effects [120].

The NTP concluded that "PFOS is presumed to be an immune hazard to humans based on a high level of evidence that PFOS suppressed the antibody response from animal studies and a moderate level of evidence from studies in humans [120]." Among mouse studies that examined males and females, males had health impacts at lower doses than females [234-236].

**Reproductive and Developmental effects:**

Studies in laboratory animals show that PFOS ingestion produces developmental effects including: decreased body weight [237, 238], increased serum glucose levels and insulin resistance in adult offspring [239, 240], developmental delays [241] and increased pup mortality [242-244]. Neonatal mortality occurred when dams were given gestational doses greater than 1 mg/kg/day. Lowered pup body weight occurred at maternal doses of 0.4 mg/kg/day. Death in newborn pups is thought to result from an interaction between PFOS and natural lung surfactant that disrupts lung function [118].

A large number of epidemiological studies in humans have been conducted on reproductive outcomes for both men and women, and on developmental outcomes. These were reviewed by EPA in 2016 [118]. Higher PFOS in serum has been associated with reduced fertility and fecundity measures, reduced birth weight, low birth weight (defined as less than 2,500 g), and fetuses small for gestation age. Evidence for each of these outcomes also includes well designed studies that looked for and did not find an association with serum PFOS level. Most studies of semen quality parameters have not seen an association between serum PFOS and sperm quality.

Regarding pregnancy-related outcomes in women, a study found an association between PFOS levels and preeclampsia, but no association with miscarriages [155]. A study of miscarriage in a population exposed to background levels of PFOS, found limited evidence of association with serum levels of PFOS [245]. An increased risk of pregnancy-induced hypertension was associated with PFOS exposure [152]. A few studies have reported an positive association with gestational diabetes (preconception serum PFOS) [246], pre-eclampsia [155] and pregnancy-induced hypertension [152] in some populations with a range of PFOS serum concentrations of 13.1 to 14.1 µg/L.

**Hormone effects:**

A number of animal studies have examined thyroid hormones following oral dosing with PFOS. Results are mixed [118]. PFOS frequently reduced T4 with slight to no changes in T3 or TSH, although a 26-week study of adult monkeys by Seacat et al., did show decreased T3 and increased TSH. Decreased T3 or T4 were observed in rodent and monkey studies at serum concentrations in the 70 to 90 µg/mL range for PFOS. Pregnant rats and neonatal rats appeared to be more sensitive, exhibiting total T4 depression when serum PFOS reached about 20 and 40 µg/mL, respectively [118].

Epidemiological studies show limited evidence that serum PFOS levels are associated with altered thyroid hormone levels and thyroid disease. Thyroid hormone measured in mostly male occupational cohorts have not correlated with serum PFOS levels [147]. In the general United States population, NHANES data reported that males but not females were more likely to report having a currently treated

thyroid disease if they were in the top 25 percent of PFOS serum levels ( greater than 36.8 µg/L) [172]. PFOS in serum was associated with increased TSH among those with risk factors for thyroid disease (low iodine status or certain antibodies). Participants with both risk factors appeared to be more susceptible to PFOS associated disruption of thyroid hormone concentrations than were people without these two risk factors [247]. In the Norwegian Mother and Child Cohort Study, pregnant women showed a trend of increasing serum TSH levels with increasing PFOS serum levels. [248].

A study by researchers from Hokkaido University (Japan) found a link between levels of PFOA and PFOS in mother's blood and hormone levels in their offspring. High blood perfluorooctanyl sulphonate (PFOS) levels in mothers were linked to lower levels in babies' blood of the glucocorticoid hormones cortisol and cortisone. These regulate glucose metabolism and the immune system. High PFOS levels were also linked to higher levels of the androgenic hormone dihydroepiandrosterone (DHEA). This helps control the development of male characteristics [109]. Another study found an inverse association between PFOS and serum estradiol in women age 42 to 65 years old [249].

**Nervous system effects**

Studies on neurotoxicity of PFOS are limited but the prenatal period appears to be a sensitive period for PFOS impact on the brain and behavioral function after birth. One study found significantly increased motor activity and decreased habituation of male offspring at one time point (PND 17) following gestational and lactational dosing of dams with 1.0 mg/kg/day of PFOS [241]. In another study, mice exposed to 0.75 mg/kg of PFOS when they were 10 days old displayed abnormal habituation responses in motor activity testing [250]. Rats exposed prenatally and through lactation performed worse in a test of spatial memory and learning [251].

**Cancer**

A chronic study of PFOS exposed rats showed increased incidence of hepatocellular adenomas/ carcinomas in female rats (10% at the highest dose) and liver tumors in males at all doses. Thyroid follicular cell adenomas and carcinomas were observed in both the male and female rats. EPA evaluators concluded that clear dose-response relationships were lacking in these observations [118]. Mammary gland tumors in female rats were observed but lacked a dose-response pattern [213].

Several human epidemiology studies evaluated the association between PFOS and cancers in occupationally exposed groups [252-254]. No association was found between PFOS levels and colorectal cancer in the C8 Health Project. No association was found between PFOS levels and breast cancer [255], bladder, pancreatic, liver or prostate cancer in the general Danish population [184]. Incidence of prostate cancer was found for a group with PFOS serum levels above the median (0.009 µg/mL) and a first-degree relative with prostate cancer indicating a potential genetic risk factor [185]. While some epidemiology studies of PFOS exposure report elevated risk of bladder and prostate cancer, limitations in design and analysis make it difficult to draw definitive conclusions[118].

The International Agency for Research on Cancer (IARC) working group has not classified PFOS. The EPA under its Guidelines for Carcinogen Risk Assessment (USEPA 2005a), concluded there is "suggestive evidence for carcinogenic potential" in humans based on the liver and thyroid adenomas observed in a chronic rat study [225].

## **Perfluorohexane sulfonate (PFHxS)** CAS # 355-46-4

PFHxS is a common ingredient in AFFF foam, and is frequently a co-contaminant with PFOS in water impacted by military firefighting activities. In 2016, EPA concluded that it had insufficient information to establish a health advisory for PFHxS in drinking water. PFHxS is routinely measured as part of the CDC NHANES survey, and is declining in serum of the U.S. population. In the 2013 to2014 survey, the median serum level of PFHxS was 1.4 µg/L with 95 percent of the population below 5.6 µg/L. PFHxS and its salts were recently added to the REACH candidate list for Substances of Very High Concern in recognition of its high degree of persistence and bioaccumulation.

**Toxicology:**

**Absorption, metabolism, distribution, excretion:**

Although PFHxS is structurally very similar to PFOS, it may differ in uptake and storage in human tissues. Autopsy investigations in 20 Spanish adults reported that PFHxS was most frequently detected in the lung (32%). Kidney and lung tissue had the highest mean concentration 20.8 and 8.1 ng/g wet weight, respectively (Perez et al. 2013). PFHXS is not metabolized in the body and urine is the main route of elimination [256]. Elimination in humans is much slower than in laboratory animals (see Table 1).

**Commented [A23]:** Please see Appendix C of our comments for a critical review of this study.

**Effects on Liver, kidney and blood lipids:**

PFAS, including PFHxS, are known to activate a hormone receptor, called $PPAR_{\alpha}$, involved with regulation of lipid and glucose metabolism. Butenoff et al., 2009, studied PFHxS in rats dosed by gavage at 0.3, 1, 3, and 10 mg/kg/d for 14 days prior to, during, and following pregnancy. Offspring were not dosed directly but were exposed by placental transfer *in utero* and via nursing. At all doses, reductions in serum total cholesterol were observed indicating that PFHxS is a potent agonist for PPARα. At 3 and 10 mg/kg, the study reported increased liver-to-body weight and liver-to-brain weight ratios, centrilobular hepatocellular hypertrophy, hyperplasia of thyroid follicular cells and decreased hematocrit [257].

In a mouse study, PFHxS (6 mg/kg/day) was administered in the diet for 4–6 weeks. PFHxS markedly reduced plasma triglycerides, total cholesterol and very low- and high-density lipoproteins, mainly by impairing lipoprotein production. In addition, PFHxS increased liver weight and hepatic triglyceride content [229].

PPARα is more highly expressed in rodent liver than in human liver. In humans, activation of PPARα generally leads to reduced plasma lipids. However, PFAS are more typically associated with increased lipids in human studies. For PFHxS specifically, the results appear to be mixed.

- Nelson et al., analyzed NHANES 2003 to 2004 data on adult participants and reported that increasing levels of PFHxS in serum were associated with lower total cholesterol, and specifically, low density (LDL) cholesterol. In contrast, increasing serum levels of PFOS, PFOA and PFNA in this population were associated with increased total cholesterol and LDL [138].
- A 2007 to 2009 Canadian health measures survey found a significant positive association between PFHxS serum levels and total cholesterol (TC), low-density lipoprotein cholesterol (LDL), total cholesterol/high density lipoprotein cholesterol ratio (TC/HDL), and non-HDL cholesterol as well as an elevated odds of high cholesterol [207]. The concentration of PFHxS in this study was relatively high for a reference population.
- No association between levels of PFHxS and total cholesterol, LDL or triglycerides were observed in the Norwegian Mother and Child Cohort Study which measured maternal PFAS levels and plasma lipids mid-pregnancy in 2003 to 2004 [210].

**Immune toxicity:**

An investigation of children aged 5 and 7 years old from the Faroe Islands in the North Atlantic showed that common exposures to PFOS, PFOA, PFHxS, PFNA and PFDA measured in blood serum were associated with lower anti-body responses to childhood immunizations (vaccinations) and an increased risk of antibody concentrations below the level needed to provide long-term protection against diphtheria and tetanus [143].

In a study from Taiwan PFAS serum levels including PFHxS were reported to be significantly higher in children with asthma compared to children without asthma [258].

No association was found between prenatal exposure to five PFAS, including PFHxS, and symptoms of infections at age 1 to 4 years old among 359 children in the Odense Child cohort [259].

**Reproductive and Developmental effects:**

One reproductive and developmental toxicity test specific to PFHxS was identified. In a modified OECD 422 guideline-based test, rats were treated by gavage with potassium PFHxS (control, 0.3, 1, 3, and 10 mg/kg body weight and day) 14 days prior to cohabitation, during cohabitation and until day of sacrifice (21 days of lactation). Males were treated for a minimum of 42 days. No reproductive or developmental effects were reported although the short duration of offspring observation does not provide definitive evidence of no reproductive or developmental effects [257].

Human evidence of an effect of PFHxS on reproduction or development is limited, and considered in the context of a broader PFAS assessment.

- After adjusting for age, race/ethnicity, education, ever smoking, and parity, women with higher levels of PFAS had earlier menopause than did women with the lowest PFAS levels [191]. The association with PFHxS in serum was monotonic.
- No association was found between PFHxS exposure and miscarriage in Danish pregnant women [260].

- After adjustment for potential confounders, PFOA and PFHxS were associated with a reduction in fecundity in the Canadian Maternal-Infant Research on Environmental Chemicals study.[49].
- Plasma concentrations of PFHxS, perfluoroheptanoic acid (PFHpA), and perfluorononanoic acid (PFNA) were inversely associated with endometriosis-related infertility, but the associations were attenuated in the sensitivity analyses [261].
- Another Danish study found that high levels of perfluorinated acids including PFHxS in blood serum were associated with fewer normal sperm cells in normal young men [262].
- A study of a large cohort from Avon in the UK with prenatal blood concentration (medians) of 19.2 ng/mL PFOS, 3.7 ng/mL PFOA and 1.6 ng/mL PFHxS showed that the most exposed mothers from the upper tertile gave birth to girls weighing 140 gram less than for the less exposed but at 20 months the girls with high PFOS exposure weighed 580 gram more [263].
- In a study from Canada there was no significant effect of PFAS on birth weight. Median blood levels were 7.8, 1.5 and 0.97 ng/mL for PFOS, PFOA and PFHxS, respectively [46].

**Hormone effects**

Data from NHANES for 2007 to 2008 were used to evaluate the effect of PFOS, PFOA, PFNA, PFDA, PFHxS, and 2-(N-methyl-perfluorooctane sulfonamide) acetic acid on the levels of six thyroid function variables [151]. Total thyroxine levels were found to increase with increase in PFHxS serum levels ($p<0.01$) [151].

A study investigated exposure levels of PFAS in infant serum and correlated these levels with thyroid hormones (THs). Total PFAS exposure level was 2.63-44.7ng/mL in the case group and 2.44-22.4ng/mL in the control group. Levels of certain PFASs (PFOA, perfluorotridecanoic acid [PFTrDA], and perfluorohexane sulfonate [PFHxS]) showed a moderate to weak correlation with relevant antibodies [264].

In a systematic review of ten epidemiological studies, some consistency in positive association was reported between TSH level in maternal sera during pregnancy and exposure to PFHxS and PFOS [265].

**Neurobehavioral effects:**

Studies in mice have shown that PFHxS given orally at a critical period in brain development can alter adult spontaneous behavior and cognitive function in both male and female mice, effects that are both dose-response related and long-lasting/irreversible. Doses were 0, 0.61, 6.1 or 9.2 mg/kg. [266, 267]. The authors reported concomitant alterations in neuroprotein levels that may help explain the findings and that indicate that PFHxS may act as a developmental neurotoxicant [266]. Similar findings have been observed for PFOS and PFOA.

Data from the NHANES 1999-2004 and the C8-Health Project showed positive association with attention deficit-hyperactivity disorder (ADHD) and PFHxS blood levels [268, 269]. The later study found a specific association with ADHD and PFHxS blood levels. The prevalence of ADHD plus medication increased with PFHxS serum levels, with an adjusted odds ratio of 1.59 (95 percent confidence interval, 1.21 to 2.08) comparing the highest quartile of exposure to the lowest.

Higher blood levels of PFOS, PFNA, PFDA, PFHxS and PFOSA (but not PFOA) were associated with significantly shorter "Impaired Response Inhibition" (IRT) during the "differential reinforcement of low rates of responding" (DRL) tasks measuring children's impulsivity [270].

No associations were observed between prenatal PFAS concentrations and SDQ scores. However, a two-fold increase in 5-year serum-PFOA, PFNA, and PFDA concentrations was associated with increases in total SDQ scores by 1.03 (95 percent CI: 0.11, 1.95), 0.72 (95 percent CI: 0.07, 1.38) and 0.78 points (95 percent CI: 0.01, 1.55), respectively. In conclusion, higher serum PFAS concentrations in children ages 5- and 7-years, but not prenatally, were associated with parent-reported behavioral problems at age 7 [271].

**Cancer:**

Few studies have looked specifically at the association between PFHxS and cancer. No rodent bioassays for carcinogenicity were located.

An association between certain PFAAs and hereditary prostate cancer was reported in a case -control study of people with prostate cancer, and a statistically significant interaction was seen for PFHxS [185].

**Other**

**Bone Mineral Density, and Osteoporosis**

In a representative sample of the U.S. adult population, serum PFAS concentrations were associated with lower bone mineral density, which varied according to the specific PFAS and bone site assessed. Most associations were limited to women. Osteoporosis in women was also associated with PFAS exposure, but was based on a small number of cases. In women, the prevalence of osteoporosis was significantly higher in the highest versus the lowest quartiles of PFOA, PFHxS, and PFNA, with odd ratios of 2.59 (95 percent CI: 1.01, 6.67), 13.20 (95 percent CI: 2.72, 64.15), and 3.23 (95 percent CI: 1.44, 7.21), respectively, based on 77 cases in the study sample [272].

**Adiposity**

Several studies have investigated but not found evidence that PFHxS exposure in early life is associated with body fat or body weight. In a study of 444 Faroese children born between 2007 to 2009, no clear association was found for maternal serum-PCBs, p,p'-DDE, PFHxS, PFNA and PFDA and body mass index (BMI [273]. A recent study evaluated associations of prenatal PFAS levels including PFHxS with body fat in girls. No effects were associated with percent body fat ( percent BF) regarding levels of PFHxS [274]. Similar studies also found no associations for PFHxS exposure and adiposity in early and mid-childhood among girls [275] and other PFAS measured related to body mass index (BMI), waist circumference (WC), and percent BF [276].

## Perfluorononanoic acid (PFNA) and its sodium and ammonium salts:

CAS #: 375-95-1, 21049-39-8, and 4149-60-4

PFNA and its sodium and ammonium salts are identified as SVHC by the European Chemicals Agency (ECHA) because they are toxic for reproduction, and a Persistent, Bioaccumulative and Toxic (PBT) substance. PFNA meets the criteria of Article 57 (d) of REACH set out in Annex XIII of Regulation (EC) 1907/2006 [277]. Data on bioaccumulation indicates that PFNA accumulates in humans and other mammals, and magnification occurs in certain food webs in the environment.

**Toxicology**

Similar to PFOA, PFNA activates peroxisome proliferator activated receptor (PPARα), as well as other nuclear receptors (e.g. constitutive androstane receptor (CAR) and pregnane X receptor (PXR), in rodents) [278, 279].

**Absorption, metabolism, distribution, excretion:**

According to ECHA, the toxicokinetics of PFNA and PFOA are similar in rats, mice and in humans [280]. Based on toxicokinetics data for other PFAS, PFNA is readily absorbed following oral and inhalation exposure in laboratory animals, and there is no indication that PFNA is metabolized. Several studies in rats, mice, rainbow trout, seals, whales and gulls indicate that PFNA accumulates mainly in the blood and liver [277]. Although the distribution of PFAS differs in species, PFAS can also distribute in the kidney and bladder [281]. In humans, PFNA is distributed in a similar way as PFOA, with the highest concentrations in the liver, blood, lungs and kidneys. Urine is the primary route of excretion of PFNA. Elimination half-lives of PFNA vary among species and there are also major differences between sexes. In general, the serum and hepatic half-lives of PFNA are longer than those of PFOA [282]. PFNA half-lives are 2.3 days in female rats and 29.6 days in male rats. The rate of elimination in male and female rats is 30.6 days and 1.4 days, respectively [282]. It is recognized that organic anion transporters play a key role in PFAS renal elimination, a process that is sex, species, and chain-length dependent.

No studies were identified on absorption of PFNA in humans. Based on animal studies it is expected that PFNA is well absorbed through oral and inhalation routes [277].

The half-lives of PFNA in serum in the general population are estimated to be between 1.7 and 3.2 years, depending on sex and age. Age is positively associated with serum PFNA levels, and men have higher serum levels than women. [277].

**Effects on liver, kidney and blood lipids:**

NHANES data from the 2003 to 2004 participants 12 to 80 years of age show that total cholesterol (TC) and non-high density cholesterol (non-HDL) were positively associated with PFOS, PFOA, and PFNA [138]. Other studies also showed positive association with PFNA and TC [283, 284]. No significant association of PFNA exposure with TC was found in a study of pregnant women [210]. A positive association was observed between PFNA and total bilirubin levels [141].

In animals, increased liver weight was observed in mice at 0.45 mg/kg/day dosed for 21 days [285]. Increased serum glucose and other effects were observed at 1 mg/kg/day, and related biochemical effects at 0.2 mg/kg/day, in mice dosed for 14 days [286].

**Immune toxicity:**

Studies on the effects of PFNA on the immune system and human outcomes are limited. A large cross-sectional study of the general U.S. population found no association between PFNA and immune response [287]. Two studies assessed the relationship between exposure to PFNA and wheezing and found no association [144, 287]. An association with decreased vaccine response was greater for PFNA than other PFAS [144].

In animal studies, PFNA and other PFAS caused immunotoxicity in mice dosed at 1 mg/kg/day for 14 days [288].

**Reproductive and Developmental effects:**

There is limited information regarding PFNA developmental effects and reproduction. There was a positive association between higher serum levels of PFNA and early menopause and hysterectomy in a cross-sectional study of the U.S. population [191] and minimal and inconsistent evidence of an association with endometriosis in a case-control study in two U.S. cities [289].

ECHA concluded that PFNA is a developmental toxicant. Although, PFNA is not listed in the Annex VI of Classification Labelling and Packaging (CLP) regulation there is evidence that PFNA and its sodium and ammonium salts meet the criteria for classification as toxic for reproduction [277].

In animals, PFNA causes developmental effects in mice including postnatal mortality, decreased pup weight gain, and delays in reaching markers of development [278, 290]. The wild type (WT) and knockout (KO) mice were exposed to PFNA at oral doses that ranged from 0.83 to 2 mg/kg/day. In WT litters, PFNA reduced the number of live pups at birth and decreased survival at weaning in the 1.1 and 2 mg/kg/day groups. Delayed eye opening and decreased pup weights were also seen at 2 mg/kg/day. KO litters did not have reduced survival, effects on pup weight, or developmental delay [290]. Both studies concluded that PFNA is more potent than PFOA as a developmental toxicant, based on studies of PFOA in similar strains of mice used in other PFNA studies [161, 291]. This toxicity is most likely related to both its intrinsic potency and longer persistence in the body compared to PFOA [292]. At higher dose (5 mg/kg/day) PFNA caused decreased maternal weight gain and decreased pup weight at birth in rats [293].

The New Jersey Drinking Water Quality Institute Health Effects Subcommittee concluded that PFNA causes adverse effects on developmental endpoints, including neonatal mortality and postnatal growth and development in animals [292].

**Hormone effects:**

Some studies in the U.S. general population evaluated the association of PFNA with an increase of thyroid stimulating hormone (TSH). None of these studies found a positive association between PFNA

and thyroid hormones [150, 151, 294]. Epidemiological results from other studies generally do not provide evidence of associations with PFNA and thyroid hormones [292].

**Neurobehavioral effects:**

A study looked at the long-term impacts of PFAS in adult zebrafish. Zebrafish were exposed to PFOS, PFOA, and PFNA (Control 0µM, 2.0µM) for the first five days post fertilization. At six months post fertilization, no PFAS treatment resulted in a significant change in total body length or weight. In terms of behavior, PFNA males showed a reduction in total distance traveled and time of immobility, and an increase in thigmotaxis behavior, aggressive attacks, and preference for the bright section of the tank. A significant decrease was also observed in the expression of slco2b1 gene in both sexes for PFNA and PFOS exposure groups. This study demonstrates that acute exposure to PFNA and other PFAS result in significant biochemical and behavioral changes in young adult zebrafish six months after exposure [295]. Prenatal exposure to PFAS, including PFNA, was not associated with an increased risk of attention deficit hyperactivity disorder (ADHD) or childhood autism in the Danish National Birth Cohort [296].

**Cancer:**

There is a data gap in animal testing as no lifetime rodent study was identified. A single case-control study in humans found no association between serum levels of PFNA and prostate cancer [185].

**Other**

*In vitro* and *In vivo* studies showed that PFNA was acutely toxic in human macrophage cell lines (TLT cells) and produced higher levels of oxidative stress, in zebrafish and TLT cells than PFOA and PFOS [297]. In the human placental choriocarcinoma cell line JEG-3, longchain perfluorinated chemicals (PFCs) including PFOS, perfluorododecanoic acid (PFDoA), PFNA and PFOA showed significant cytotoxicity [298]. The dose-response was observed with PFAS in Xenopus laevis A6 kidney epithelial cells. PFNA and PFBS did not significantly change cell population levels, while PFOS and PFOA caused a decrease in cell numbers compared to controls [299].

## VI. Existing health advice and health-based guidance values

Public Health Advice

Identifying and removing preventable sources of exposure is the only known way to reduce PFAS exposure and body burden. Data collected by Minnesota Department of Health (Figure 5) demonstrates that installing water treatment to remove long-chain PFAS compounds from contaminated drinking water reduced blood serum levels of PFAS in impacted residents.

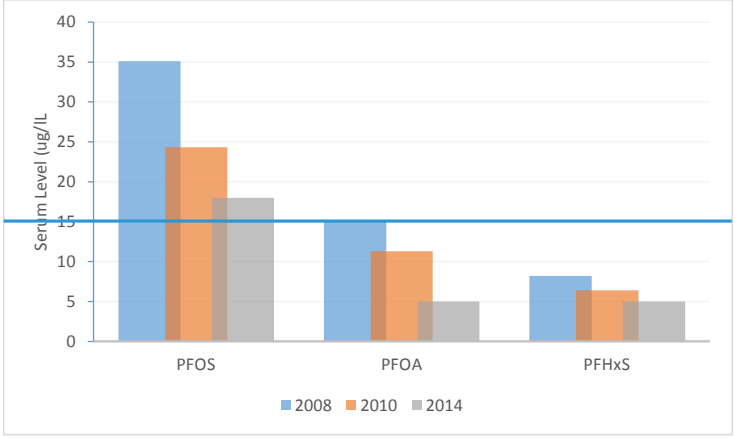


**Figure 5.** Median serum levels at three time points in Minnesota residents after water filtration was installed to remove PFAS from contaminated drinking water [300].

If drinking water contains PFOS and PFOA combined above 70 ppt, the EPA health advisory level, people are advised to use an alternate water source for drinking, food preparation, brushing teeth, and any activity that might result in ingesting water.

There are currently no fish consumption advisories for PFOS in Washington State. Department of Health reviewed fish data collected by Ecology in 2008 and 2016 and found that some fillet tissue levels exceeded provisional health-based screening levels (i.e., 23 µg/g and 8 µg/g for both the general population and high consumers, respectively). The current dataset for any given fish species for waterbody is too small to provide an adequate basis for a fish consumption advisory but the agencies will work together to identify and collect the needed additional data to support the fish advisory program.

### Drinking water Advisories

Currently there are no enforceable federal drinking water standards for PFAS substances. The EPA and some states, including New Jersey, Maine, Michigan Minnesota, North Carolina, and Vermont, - have established state health advisory levels. Some European countries have also developed drinking water

**Commented [A24]:** The introduction that precedes the state-by-state summaries is missing a short description of what a health advisory is, and is not. Sometimes advisories are misinterpreted as indicating a level of health concern. Similar to the Clarification Statement issued by USEPA (2016) regarding the PFOA and PFOS advisories, Washington should clarify that the advisories calculated by USEPA and the states represent levels that risk managers can use as a guide for public health decisions. Per EPA Office of Water's own documentation, the PFOA and PFOS health advisories are designed to provide even "the most sensitive populations, with a margin of protection from a lifetime of exposure" and identify concentrations "at which adverse health effects are not anticipated to occur over a lifetime."

health-based guidance values (HBGV)[12] for PFOA, PFOS and related substances. These are described below and in Table 7.

Washington State Department of Health (DOH) has not developed an independent state health advisory level for drinking water. We reviewed and support EPA's May 2016 health advisory level for drinking water of 0.07 µg/L for PFOA and PFOS combined. EPA's methods are reasonable and appear to be sufficiently protective for pregnant women, nursing women, and children [301].

In response to a recent petition, the State Board of Health will consider whether to set a state standard for PFOS and PFOA and address other PFAS detected in state drinking water.

**EPA Life-time health advisory levels for PFOA and PFOS, 2016**

In May 2016, EPA Office of Water (OW) replaced the 2009 provisional health advisory levels with new, lifetime health advisories for PFOS and PFOA. The advisory also applies to shorter-term consumption during critical life-stages such as pregnancy and infancy. The advisory level of 0.07 µg/L for both PFOA and PFOS is intended to provide margin of health protection, including for the most sensitive groups, from a lifetime of exposure to these contaminants from drinking water [24]. This level is based on peer-reviewed toxicological studies of exposure of animals to PFOA and PFOS, applying scientifically appropriate uncertainty factors.

In deriving the lifetime HA for exposure to PFOA from drinking water, EPA considered two critical endpoints observed in male and female mice: decreased pup ossification in male and female pups, and accelerated puberty in male pups following exposure during gestation and lactation [117, 161]. Species and sex differences in the rate of PFOA clearance from serum following exposure vary by several orders of magnitude. In addition, the kinetics for PFOA are dose-dependent. To address this, EPA developed a pharmacokinetic model to convert internal dose (serum level) measured in animal studies into a human equivalent dose (HED). The HED is the estimated external intake required to reach the same internal dose in humans. Specifically, the RfD for PFOA of 0.00002 mg/kg/day was based on a LOAEL of 1.0 mg/kg-d in mice (average serum concentration in mice was 38 mg/L), an estimated human equivalent dose of 0.0053 mg/kg/day, and an uncertainty factor of 300. The uncertainty factor was comprised of a 10-fold safety factor for intra-individual uncertainty, an additional 3-fold safety factor for uncertainty in extrapolating from animals to humans, and a 10-fold safety factor for use of a LOAEL rather than a NOAEL [24].

An RfD of 0.00002 mg/kg/day was also selected for PFOS [213]. This value is based on a NOAEL of 0.1 mg/kg-day for developmental effects (decreased pup body weight) in a two-generation study in rats Luebker et al., 2005) [237]. The internal doses associated with no adverse effects on developmental and liver endpoints (NOAELs) from a number of animal studies that EPA considered were all very similar: average serum concentrations ranged 6.26–38 mg/L. EPA applied a pharmacokinetic model to calculate

[12] A HBGV is a level of a chemical that a person can consume without adverse effects over a given time period.

a human equivalent dose of 0.00051 mg/kg-day and applied a 30-fold safety factor to account for variability in individual human response to exposure (10x) and uncertainty in extrapolating from animals to humans, particularly toxicodynamic differences (3x) [118].

EPA classified both PFOA and PFOS as having "Suggestive Evidence of Carcinogenic Potential." For cancer risk, EPA concluded that only PFOA had sufficient data to calculate a quantitative cancer risk .The resulting drinking water level associated with a one-in-a-million cancer risk was 0.5 µg/L - higher than the RfD based on developmental effects. EPA chose to base its drinking water advisory level on the latter to protect against all outcomes.

To calculate drinking water health advisory levels for PFOA and PFOS, EPA used 90th percentile drinking water consumption rates for nursing women, 54 mL/kg-day. This is approximately 3. 8 L/day for a 70 kg person. This is in contrast to most other risk assessments which have used standard (less conservative) assumptions 2 L/day drinking water intake for a 70 kg person. EPA also used a conservative assumption of 20% relative source contribution for the percentage of intake at the RfD that could come from drinking water. This is the recommended default when other sources are known to be significant and but intake from other sources is not well quantified. Given their similar observed toxicity and identical RfD, EPA recommends that PFOA and PFOS combined do not exceed the 2016 health advisory level [301].

**State action levels**

Based on the detection of PFAS in drinking water, eight states established independent health advisory levels for PFOA and/or PFOS. Since EPA published their final health advisory for PFOA and PFOS in 2016, most states are using the EPA guidance. Three states Vermont (PFOA, PFOS - 0.02 µg/L), New Jersey (PFOA - 0.04 µg/L; proposed 0.014 µg/L), and Minnesota (PFOA, 0.035 µg/L, and PFOS, 0.027 µg/L) have adopted levels lower than EPA's health guidance values.

The State of Minnesota also established health risk limits for PFBS, PFBA, and PFNA of 9, 7, and 0.013 µg/L, respectively. Minnesota has not developed a health risk level for PFHxS, but it recommends to use the health based value for PFOS of 0.027 µg/L as a surrogate for PFHxS until more toxicological research is available. New Jersey is planning to initiate rule-making to adopt a proposal of 0.013 µg/L for PFNA. The State of Connecticut opted to include PFHxS, PFNA, and PFHpA into the total PFAS concentration not to exceed 0.07 µg/L in a water sample. These are described below and in Table 7.

**Connecticut**

The Connecticut Department of Public Health (DPH) considers EPA's Health Advisory of 0.07 µg/L for PFOA and PFOS to be health protective and adopts this as their action level for drinking water. DPH includes PFHxS, PFNA, and PFHpA in the total PFAS concentration not exceed 0.07 µg/L. These were added out of consideration of their similar chemical structures, toxicity in rodents, potential to bioaccumulate, and frequent co-exposure with PFOS and PFOA in water sampling. DPH acknowledged

that much less was known about PFHpA, but they included it along with the other two as a precautionary approach.

Connecticut also applied their default guidance for semi-volatile organics to the scenario of showering and bathing with water that contains PFAS. They advise that when the level of five PFAS in water is 3-30 times higher than 0.070 µg/L, bathing and showering should be discontinued within three months. If the concentration is more than 30 times the action level, showing and bathing should cease immediately. [302].

**New Jersey, 2015 for PFNA**

In 2015, the New Jersey Drinking Water Quality Institute recommended 0.013 µg/L as a health-based maximum contaminant level (MCL) for PFNA in drinking water. In 2017, the State of New Jersey Department of Environmental Protection accepted this proposal and initiated rule-making to adopt this as a state standard. The proposed MCL is based on a study of developmental effects in which pregnant mice were exposed to PFNA for 16 days. The health-based MCL is further supported by data on effects in the offspring in the same study, and on increased liver weight and other effects in additional rodent studies from the same and other laboratories [303].

**New Jersey, 2017 for PFOA**

In 2017, the same New Jersey panel recommended a health-based MCL for PFOA of 0.014 µg/L based on increased relative liver weight in mice. An RfD of 0.000002 mg/kg-day was selected based on increased relative liver weight in male mice (Loveless et al., 2006) [304] and a 300-fold safety factor. New Jersey added an extra 10-fold safety factor to account for another endpoint, delayed mammary development, which was seen at lower levels in certain mouse studies. The health-based MCL based on a lifetime cancer risk of $1 \times 10^{-6}$ was calculated to be 0.014 µg/L – the same advisory level derived from the most sensitive non-cancer endpoint. For the development of a health-based MCL, the panel considered higher internal dose in humans compared to animals, due to longer human half-life. For non-cancer effects, the dose-response modeling was based on serum PFOA data from end of dosing period. For cancer effects, serum PFOA data was not available, so animal-to-human internal dose comparison was based on half-life differences [305]. This recommendation has not been accepted by the State of New Jersey Department of Environmental Protection or adopted by the state in rule.

**Maine CDC, 2016**

The Maine CDC adopted the U.S. EPA lifetime health advisory for PFOA and PFOS (Drinking Water Health Advisories for PFOA and PFOS) of 0.07 µg/L as Maximum Exposure Guidelines (MEGs). Previously, the Maine CDC developed a MEG for PFOA of 0.1 µg/L or 100 ng/L, but had not developed a MEG specific for PFOS. The lifetime health advisory includes a value for each chemical individually, and when both PFOA and PFOS are present, the summed concentration should not exceed the 0.07 µg/L or 70 ng/L advisory level [306, 307].

**Minnesota Department of Health (MDH) 2008 for PFOS and PFOA and Minnesota 2011 PFBA and PFBS**

In 2011, the MDH developed a subchronic reference dose for PFBS of 0.0042 mg/kg body weight per day based on a NOAEL of 60 mg/kg body weight (bw) per day in a 90 days rat study [308]. The mean human half-life was estimated at 28 days. A half-life adjustment factor of 142 was used for extrapolation to a human equivalent dose of 0.42 mg/kg bw per day. They also developed a subchronic health based guidance for groundwater of 9 µg PFBS/L [309].

For drinking water exposure to PFBA, the MDH chose liver weight changes, morphological changes in liver and thyroid gland, decreased TT4, and decreased red blood cells, hematocrit and hemoglobin as the critical effect in a 90-day dose study of PFBA in rats. MDH calculated a HED of 0.86 mg/kg/day (factor of 8 adjusts for half-life duration of 3 days in humans versus 9.22 hours in male rats), and an uncertainty factor of 300 to derive an RfD 0.0029 mg/kg-day. MDH used a chronic intake rate 0.043 L/Kg-day, and a RSC of 20 percent to yield a HRL of 7 µg/L.

MDH has not developed a HRL for PFHxS. The MDH recommends using the health based value for PFOS (0.027 µg/L) as a surrogate for PFHxS until more toxicological research is available. The basis for this rational is that PFHxS remains in the body longer than PFOS and appears to be similar in toxicity.

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**Minnesota 2017 for PFOA and PFOS**

The MDH recently revised their state health advisory level for PFOA and PFOS. The guidance values apply to short periods of time (i.e., weeks to months) during pregnancy and breastfeeding, as well as over a lifetime of exposure [310].

For drinking water exposure to PFOA, the MDH chose delayed ossification, accelerated preputial separation in male offspring, trend for decreased pup body weight, and increased maternal liver weight as the critical effects in a 17-day dose study of ammonium PFOA in mice. MDH calculated a HED of 0.0053 mg/kg/day, and an uncertainty factor of 300 to derive an RfD of 0.000018 mg/kg-day. MDH modelled 95th percentile daily water and breast milk intake by infants [13], and a RSC of 50 percent to yield a health based value of 0.035 µg/L [311].

For PFOS, MDH used the same endpoint and study as EPA for their point of departure: decreased pup body weight from a 12-week two-generation study of ammonium PFOS in rats (Luebker et al., 2005) [237]. A HED was calculated (0.00051 mg/kg-day) and multiplied by an uncertainty factor of 100 to derive an RfD of 0.0000051 mg/kg/day. MDH modelled 95th percentile daily water and breastmilk

[13] Two exposure scenarios were examined: 1) an infant fed formula reconstituted with contaminated water starting at birth and continuing ingestion of contaminated water through life; and 2) an infant exclusively breast-fed for 12 months, followed by drinking contaminated water through life.

consumption rates for infants[14], and a RSC of 50 percent to derive the health based value of 0.027 µg/L [312].

**Vermont for PFOA**

In 2016, the Vermont Department of Health's adopted a drinking water health advisory level and an Interim Ground Water Enforcement Standard for PFOA of 0.02 µg/L. These Vermont values are based on the RfD in the 2016 EPA PFOA health advisory, drinking water exposure assumptions for a child less than 1 year of age (instead of default adult exposure assumptions), and the default RSC factor of 20 percent [313].

**International action levels**

Several countries have established drinking water health guidance levels for PFAS.

**Australia**

In 2016, the Australian Department of Health commissioned Food Standards Australia New Zealand (FSANZ) to develop health based guidance values for perfluorooctane sulfonate (PFOS), perfluorooctanoic acid (PFOA) and perfluorohexane sulfonate (PFHxS) [314].

The Department of Health has published FSANZ's report on Perfluorinated Chemicals in Food (the report) which includes the derivation of the final health based guidance values for site investigations in Australia, a dietary exposure assessment and risk management advice for authorities investigating PFAS contamination.

FSANZ looked at comprehensive international assessments on the health effects of PFAS and recommended TDIs of 0.02 µg/kg bw/day for PFOS and PFHxS, and 0.16 µg/kg bw/day for PFOA. The drinking water values recommended by FSANZ were 0.07 µg/L for PFOS and PFHxS, and 0.56 µg/L for PFOA. Recreational water quality values were set at 0.7 µg/L for PFOS and PFHxS, and 5.6 µg/L for PFOA [315]. While there are insufficient data to recommend a regulatory approach and set maximum limits in the Food Standards Code, FSANZ proposed trigger points for investigation for PFOS + PFHxS combined and PFOA.

**Health Canada**

The Canadian Drinking Water Quality Guideline (CDWQG) has developed Drinking Water Guidance Values (DWGVs) for PFOS and PFOA. **The DWGV for PFOS of 0.3 µg/L (300 ng/L)** was based on a study

[14] Two exposure scenarios were examined: 1) and infant fed formula reconstituted with contaminated water starting at birth and continuing ingestion of contaminated water through life; and 2) an infant exclusively breast-fed for 12 months, followed by drinking contaminated water through life.

with monkeys that assessed serum level changes of thyroid hormones, decreases in high density lipids and cholesterol, decrease in bilirubin levels in males, and thymus atrophy in females.
**The DWGV for PFOA of 0.7 µg/L (700 ng/L)** was based on a study with monkeys that assessed liver weight and body weight as a function of dose [316]. More recently, the Federal-Provincial-Territorial Committee on Drinking Water has assessed PFOA in drinking water. The CDWQG proposes a maximum acceptable concentration (MAC) of 0.0002 mg/L (0.2 µg/L) for PFOA in drinking water, based on liver effects in rats [121].

**United Kingdom Drinking Water Inspectorate (DWI) Guidance, 2009**

The United Kingdom Drinking Water Inspectorate (DWI) issued guidance for concentrations of PFOA and PFOS in drinking water in 2007, and revised the guidance in 2009. DWI developed different tiers for guidance. Tier 2 included a health guidance value of 0.3 µg/L for PFOA and PFOS. This value was based on a range of effects on the liver, kidneys, and the hematological and immune systems. It considered that the TDI was adequate to protect against other potential effects such as cancer. Tier 3 considered a PFOA and PFOS concentration of 1.0 µg/L in water. This value will be protective for the entire population. Tier 4 requires notification by water companies of any event which has or may adversely impact the quality of water. For PFOA, the level was set at greater than 45 µg/L. This value is based on a TDI of 0.15 µg/kg/day, 2 L/day of drinking water consumed by a 60 Kg adult [317].

**German Drinking Water Commission (GDWC)**

The German Drinking Water Commission (GDWC) developed a precautionary action **value of 5.0 µg/L for adults and 0.5 µg/L for infants for combined PFOA and PFOS in drinking water**. These action levels indicate when immediate action is required to reduce exposure to PFOA and PFOS from drinking water. For pregnant women and infants GDWC recommends that water containing a composite of PFOS and PFOA concentration exceeding 0.5 µg/L should not be used to prepare baby food. In addition, pregnant women should avoid regular intake of water or other beverage products with more than 0.5 µg/L. A specific health-based value of 0.3 µg/L in drinking water for life long exposure was derived based on toxicological data. TDI value of 0.1 µg/kg-day was developed based on a 2-year dietary study and two-generation reproduction and developmental study of ammonium PFOA, both in rats, and the NOAEL from the 2-year dietary study in rats of potassium PFOS. This value is protective for both infants and pregnant women [317, 318].

Recently, the German Human Biomonitoring Commission (HBM Commission) established a level for PFOA and PFOS in blood plasma at 2 ng/ml for PFOA and 5 ng/ml for PFOS. The Commission used human data that indicates that PFOA can cause problems in humans with pregnancy, birth weight, cholesterol and hormones levels, and reduced the effectiveness of vaccines. The values represent the upper bound in the range of human serum concentrations that were without a significant association with these health effects in epidemiological studies. They indicate a level in serum where no adverse effects are expected [319].

**Sweden**

There is an action limit for the sum of 11 PFAS compounds in drinking water of 0.09 µg/L in Sweden, provided by the National Food Agency. The compounds included are: perfluorobutane sulfonate (PFBS), perfluorohexane sulfonate (PFHxS), PFOS, 6:2 fluorotelomer sulfonic acid (6:2 FTSA), perfluorobutanoic acid (PFBA), perfluoro-n-pentanoic acid (PFPeA), perfluorohexanoic acid (PFHxA), perfluoroheptanoic acid (PFHpA), PFOA, perfluorononanoic acid (PFNA), and perfluorodecanoic acid (PFDA) [320]. This action limit is based on a potential risk for human health from PFAS in drinking water. If concentrations of these 11 compounds are higher than the action limit, the National Food Agency recommends to reduce exposure.

**Netherlands, 2011**

Netherlands developed a maximum tolerable level of PFOS in drinking water of 0.53 µg/L, based on the EFSA (2008) TDI 0.15 µg /kg bw/day (the calculation was not further specified). A negligible level of 0.0053 µg/L was derived by the further use of a factor of 100 [321].

**Other recommendations**

**Recommendations from Grandjean et al. 2013**

Using data from an immunotoxicity assessment in the Faroe Islands in children ages 5 and 7 years, and assuming a linear dose-response, Grandjean et al. 2013 calculated a $BMDL_5$ serum concentration of 1.3 µg/L for PFOS and 0. 3 µg/L for PFOA [322]. Applying an uncertainty factor of ten to take into account individual susceptibility, the BMDLs resulted in a reference serum concentration of about or below 0. 1 µg/L for PFOA and PFOS combined. Assuming no other sources of exposure, a serum concentration of 0.1 µg/L would correspond to a water concentration of approximately 0.001 µg/L [323]. According to the study authors, this set of calculations don't represent a formal risk evaluation.

**Commented [A25]:** Why is this included? This section is a summary of regulatory health-based standards. Presumably those regulators have considered the available science on these chemistries in establishing their risk-based policies.

**Fish Advisories**

Several states with localized surface water contamination (e.g., near manufacturing plants) have developed fish advisories for PFAS, including Alabama, Michigan, Minnesota, and Wisconsin. Other states are considering fish advisories for PFAS, including Washington State.

In Minnesota fish tissue with more than 800 ng/g PFOS in edible parts are listed as do not eat, fish with 40-800 ng/g have various recommended consumption restrictions, and fish with less than 40 ng/g have no suggested consumption limits.

The Dutch National Institute for Public Health and the Environment has calculated a maximum permissible concentration[15] for PFOS of 0.65 ng/g for fresh water (based on consumption of fish by humans as the most critical route). This value is based on a consumption of 115 grams of fish per day [324].

### Advisories for total daily intake or dietary intake

**ATSDR intermediate-duration oral Minimal Risk Levels (MRL) for PFOS and PFOA**

In their 2015 Draft Toxicological Profile for PFAS, ATSDR proposed an intermediate-duration oral MRL of 0.00002 ($2x10^{-5}$) mg/kg/day for PFOA based on a BMDL of $1.54x10^{-3}$ mg/kg/day for increased absolute liver weight in monkeys administered PFOA via a capsule for 26 weeks [2]. ATSDR derived an intermediate-duration oral MRL of 0.00003 ($3x10^{-5}$) mg/kg/day for PFOS based on a NOAEL of $2.52x10^{-3}$ mg/kg/day for increased absolute liver weight in monkeys administered PFOS via a capsule for 6 months [2]. ATSDR has not established chronic MRLs for PFOS or PFOA, and they have not calculated MRLs for other PFAS.

**European Food Safety Authority (EFSA), 2008 for PFOS and PFOA**

In 2008 the EFSA reviewed and evaluated the available PFOA and PFOS toxicity studies and derived a TDI for both chemicals. TDIs are expressed on a per body weight basis and represent levels of a substance that can be ingested over a lifetime without significant health risk [26] .

For PFOS, the NOAEL of 0.03 mg/kg bw per day was identified from a sub-chronic study with Cynomolgus monkeys showing changes in lipids and thyroid hormones at the next higher dose level. The Environment Food Safety Administration identified a TDI for PFOS of 150 ng/kg body weight per day. An uncertainty factor of 200 was applied to the NOAEL of 0.03 mg/kg bw per day (100 for inter- and intra-species differences and 2 to compensate for uncertainties related to the duration of the key study and the elimination kinetics of PFOS [26].

For PFOA, EFSA identified a NOAEL, 0.06 mg/kg bw-d based on hepatocellular hypertrophy and increased in liver weight in male rats. EFSA identified a bench mark dose level $(BMDL)_{10}$ of 0.3 mg/kg-d as the POD to derive a TDI. EFSA derived a TDI for PFOA of 1.5 µg/kg- bw per day. An uncertainty factor of 200 was applied to the $BMDL_{10}$ of 0.3 mg/kg bw per day (100 for inter- and intra-species differences and 2 to compensate for uncertainties related to the duration of the key study and the elimination kinetics of PFOS) [26].

**Regulation in Europe**

[15] Maximum Permissible Concentration is the level at which no harmful effects are expected, based on annual average concentrations.

In Europe, provisional drinking water standards range from 0.1 to 0.5 µg/L for PFOS. The Directive on "Environmental Quality Standards" (EQSD) set an annual average environmental quality standard (AA-EQS) for PFOS in surface freshwater at 0.00065 µg/L, based on the potential for secondary poisoning in humans due to fish consumption [325].

**Table 7 Summary of U.S. Health advisory guidelines for Per- and Polyfluoroalkyls**

| Agency | Description | Chemical | Health limit (µg/L) | Basis for decision/ endpoint |
|---|---|---|---|---|
| **EPA 2016** | Drinking water health advisory - lifetime | PFOA | 0.07 | RfD of 0.00002 mg/kg/day based on a LOAEL from a developmental toxicity study in mice Lau et al. (2006) [161]. This value is based on the HED for Dev effects. |
| **EPA 2016** | Drinking water health advisory - lifetime | PFOS | 0.07 | Based on an RfD derived from a NOAEL for developmental toxicity study in rats (Luebker et al., 2005) [237]; the critical effects included reduced pup weight. The RfD of 0.00002 mg/kg/day calculated from HED |
| **Connecticut, 2016** | Drinking water health advisory | PFOA/PFOS, and PFHxS, PFNA, andPFHpA | 0.07 | Based on EPA's RfD for PFOA and PFOS of 0.00002 mg/kg/day. |
| **Minnesota, 2011** | Health risk limit for drinking water | PFBS | 7.0 | Decreased hemoglobin and hematocrit, histological changes in kidney; RfD of 0.0014 mg/kg-d (Rats, males) |
| **Minnesota, 2011** | Health risk limit for drinking water | PFBA | 7.0 | liver weight changes, morphological changes in liver and thyroid gland, decreased TT4, and decreased red blood cells, hematocrit and hemoglobin; RFD of 0.0029 mg/kg-d. |
| **Minnesota, 2017** | Health risk limit for drinking water | PFOA | 0.035 | Delayed ossification, accelerated PPS in male offspring, ↓ pup body weight, ↑ maternal liver weight. |
| **Minnesota, 2017** | Health risk limit for drinking water | PFOS | 0.027 | An RfD of 0.0051 µg/Kg/day was calculated based on decreased pup body weight. |
| **New Jersey, 2017** | Proposed state MCL for drinking water | PFNA | 0.013 | Developmental effects in which pregnant mice were exposed to PFNA for 16 days. |
| **New Jersey, 2017** | Recommended by technical committee as a MCL for drinking water | PFOA | 0.014 | An RfD of 0.000002 mg/kg-day was selected based on BMD modeling of increased liver weight in mice. |
| **Vermont, 2016** | Interim Ground Water Enforcement Standard | PFOA | 0.02 | Reference Dose (RfD) of 2 x $10^{-5}$ mg/kg/day based on 2016 EPA's health advisory study. |

PFBS – Perfluorobutane sulfonate
PFBA – Perfluorobutyrate
PFHxS – perfluorohexane sulfonate
PFNA - perfluorononanoic acid
PFHpA - perfluoroheptanoic acid

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## VI. Short chain fluorinated alternatives – ~~Are the fluorinated alternatives to long-chain PFAS Safer?~~

As a result of industry and EPA actions, industry is transitioning away from long-chain[16] ~~PFAS~~ PFAAs and their potential precursors to ~~shorter~~short-~~er~~ chain alternatives (fluorosurfactants and side-chain fluorinated polymers) ~~PFAS~~ and non-fluorinated chemicals. The ~~PFAS~~ PFAAs that are potential terminal degradation products from the short-chain alternative chemistries ~~in this group~~ contain ~~short~~ perfluoroalkyl chains of three to five fully fluorinated carbons, with a carboxylate or sulfonate group on one end (e.g., PFHxA, PFPeA, PFBA, PFBS). The short-chain alternatives have ~~hundreds~~ numerous potential ~~of~~ derivatives ~~as more complex molecules~~ such as: *N*-Methyl perfluorobutane sulfonamidoethanol (MeFBSE) and *N*-methyl perfluorohexane sulfonamidoethyl acrylate [326]. Short chain ~~PFAS~~ alternatives generally have a perfluoroalkyl moiety as a key functional component and they are similar in structure to the long-chain ~~PFAS~~ substances which they are replacing~~PFAS~~. Biomonitoring studies indicate that unlike long-chain ~~PFAS~~ PFAAs (e.g., PFOA, PFOS, PFHxS), short-chain PFAAs (e.g., PFBA, PFBS, PFHxA) ~~they~~ do not persist in human serum. They have been measured in other tissues in both animals and human autopsy studies (e.g., liver, bone, brain, lung and kidney) but the extent of tissue storage in humans is not known. Short-chain ~~PFAS~~ PFAAs still contain fluorine-carbon bonds and are expected to be persistent in the environment. ~~They~~ Short-chain PFAAs are also soluble in water and can be taken up into plants from soil. Therefore, accumulation in the environment, groundwater, and the food supply may still occur [327]. More information on specific short-chain compounds ~~are~~ is discussed in the environment section. There is limited information on the exposure and toxicity of these compounds including body burden, toxicity of different routes of exposure, mechanisms of action, and mixture effects. Therefore, it is challenging to fully assess their potential impact in humans and the environment.

~~Fluorinated short-chains~~Fluorinated ~~s~~Short-chain fluorosurfactants and side-chain polymers may be used in a wide array of application including ~~s are used in~~ textiles, paper, food contact materials, aqueous film-forming foam (AFFF), surfactants~~, in aerospace materials, hydraulic tubing, chemical processing, semiconductor manufacture, transportation, etc.~~. The most important short-chain perfluoroalkyl acids ~~PFAS~~ include PFBA and PFHxA, their salts and precursors, and potential precursor substances that can degrade to form them such as ~~including the~~ short-chain ~~fluorotelomers~~fluorotelomer-based products~~s (FTOH) such as 4:2 FTOH and 6:2 FTOH~~ and short-chain ECF-based products [326]. Common examples of short-chain alternatives include: fluorotelomer-based products (e.g., $C_6F_{13}$, 6:2 fluorotelomer alcohol, 6:2 FTOH; 6:2 fluorotelomer methacrylate, 6:2 FTMAC, and 6:2 fluorotelomer sulfonyl chloride), short-chain perfluorobutane sulfonyl products ~~(e.g., CF, n=4)~~, Per- and Poly- fluoroalkyl ether carboxylic acids (PFECAs), perfluoropolyether (PFPE) products, fluorinated oxetane products~~, and short-chain perfluoroalkyl acids (PFAAs) (CF, n≤7)~~ [328].

**Commented [A26]:** Note: while this is correct nomenclature of the acids and sulfonates noted above, short-chain fluorotelomer intermediates such as 6:2 fluorotelomer alcohol contains 6 fully fluorinated carbons: $CF_3(CH_2)_5CH_2CH_2$-OH. Please see the next paragraph.

**Commented [A27]:** State specifically what "they" are here

**Commented [A28]:** REFERENCE PLEASE. Please see Appendix C of our comments for a critical review of Pérez F, Nadal M, Navarro-Ortega A, Fàbrega F, Domingo JL, Barceló D, Farréa M, "Accumulation of Perfluoralkyl Substances In Human Tissues" Environment International 59 (2013) 354–362.

**Commented [A29]:** Be specific here. This broad statement is inaccurate. There is a substantial amount of information available for PFBA, PFBS and PFHxA.

**Commented [A30]:** This is not true for PFHxA, PFBS and PFBA. A human reference dose has been determined for them based on the extensive data available. See: https://www.anses.fr/fr/system/files/SUBSTANCES2015SA0127Ra.pdf

[16] According to OECD: "Long-chain perfluorinated compounds" refers to: Perfluorocarboxylic acids with carbon chain lengths C8 and higher, including perfluorooctanoic acid (PFOA); Perfluoroalkyl sulfonates with carbon chain lengths C6 and higher, including perfluorohexane sulfonic acid (PFHxS) and perfluorooctane sulfonate (PFOS); and Precursors of these substances that may be produced or present in products.

Dominant sources of fluorotelomers found in AFFFs include 6:2 fluorotelomermercaptoalkylamido sulfonate (FTAS) and 6:2 fluorotelomersulfonamide alkylbetaine (FTAB). D'Agostino and Mabury et al. 2014 identified PFAS classes in AFFFs with fluorinated chain lengths ranging from $C_3$ to $C_{15}$ [329]. The Fire Fighter Foam Coalition notes that C6-based AFFF fluorosurfactants and their likely break down products are low in toxicity and not considered to be bioaccumulative or biopersistent [330].

~~These compounds have become long-chain replacements as processing aids in fluoropolymer manufacturing. While the environmental risk and toxicity of long-chain PFAS has been widely recognized, for most short-chain replacements and their precursors, there is limited information on the hazard, exposure, or toxicity.~~

Short-chain fluorinated products can also degrade into the environment to other forms. For example, perfluorohexanoic acid (PFHxA) is both a degradation product and potential impurity ~~of C6~~in short-chain fluorotelomer-based ~~, which is used to make C6 fluorotelomer~~ acrylate polymers [328]. ~~PFHxA is used to produce stain- and grease-proof coatings on food packaging and household products.~~ A degradation product of fluorotelomer thiol and fluorotelomer sulfonyl products is 6:2 fluorotelomer sulfonate (6:2 FTSA), which has some potential use ~~is used~~ as a polymer processing aid in the synthesis of fluoropolymers [331].

EPA has reviewed ~~substitutes~~ alternative products that are intended to meet the commitment to cease manufacture and use of ~~for PFOAP~~PFOA and PFOS~~,~~, their long-chain homologues and potential precursors since 2000. According to EPA, ~~shorter~~short-~~er~~ chain ~~-length perfluorinated telomeric~~alternative substances have been received and reviewed as alternatives for a variety of uses including, textile, carpet and paper additive uses and tile surface treatments. To date, over 75 (need an updated value please) pre-manufacture notices have been received for telomers based on short~~er~~ chain alternatives. According to EPA, degradation products from telomers are currently being tested for developmental and reproductive effects, subchronic toxicity (e.g. liver toxicity), pharmacokinetics, carcinogenicity, avian reproductive effects and chronic aquatic toxicity [332]. EPA safety reviews are not available for public inspection, but much of the supporting data has been published.

Some preliminary concerns about ~~shorter~~some short-~~er~~ chain ~~PFASP~~ alternatives ~~FAS~~ compared to long-chain substances~~PFAS~~ include [333]:

- Higher volatility may increase potential inhalation exposure~~s~~. (e.g., short-chain fluorotelomer alcohols and perfluorobutane sulfonamide alcohols)
- Highly solubility in water make ~~them~~ short-chain PFAAs such as PFBA and PFBS more mobile in soil and sediment than long chain PFOA and PFOA.
- Some drinking water treatments, such as activated carbon systems, are less efficient at removing ~~them~~short-chain PFAAs.
- ~~They~~ Short-chain PFAAs are more easily leached from biosolids (produced during wastewater treatment).

**Commented [A31]:** These two compounds cited are the basic fluorotelomers used to manufacture AFFF surfactants from the telomer process. They are not sources of fluorotelomers - they are the fluorotelomers used.

**Commented [A32]:** This is not true

**Commented [A33]:** This sentence is not a true statement.

- ~~Smaller chain lengths~~Short-chain PFAAs are more easily taken up from soil by certain food crops [334].
- Upon absorption, they may have increased or differential uptake into certain biological tissues [335].
- Increased transfer of short-chain PFAAs across the placenta to fetus [336].
- ~~Short-chain perfluoroalkyl sulfonates and carboxylates and their polyfluorinated homologues are highly resistant to microbial degradation [337].~~ Long chains have same characteristics
- Perfluoroether carboxylic acids and perfluoroether sulfonic acids are environmentally stable and mobile, and have a high global contamination potential.
- ~~Many PFAS, such as 6:2 fluorotelomer- and perfluorobutane sulfonyl fluoride-based (PBSF) substances, break down to short-chain PFCAs and PFSAs.~~ Long chains have same characteristics
- Although available toxicity shows ~~they~~ short-chain PFAAs are less toxic and more rapidly excreted, their greater exposure potential needs to be considered in health risk analysis.

**Commented [A34]:** This study is highly questionable. First, it is a single determination. Many scientists would argue that this study is an analytical artifact, not a reproducible, scientifically rational finding and therefore should not be given significant weight or merit

**Commented [A35]:** Greater than what? The exposure potential is no greater than the long-chain substances they are replacing. Moreover, there is a strong argument to be made that the exposure to short-chain alternatives it must be LESS because many applications are not using these chemistries any more.

**Sources and pathways of human exposure**

**Sources of exposure**

Short chain alternatives can enter the environment at manufacturing sites where they are produced ~~and used to produce fluoropolymers as well as during use and disposal of fluoropolymer resins~~ [338]. The serum half-life elimination of short-chain fluorinated alternatives in humans and mammals are shorter than their longer-chain homologues.

**Commented [A36]:** This is not a common use of the short-chains discussed.

**Commented [A37]:** The more common sources of exposure would be from treated products.

**Indoor air and dust**

U.S. studies of PFAS, including short chain PFAS, in indoor dust were recently reviewed by Mitro et al 2016 [339]. The results of their meta-analysis, which relied primarily on four studies [35, 36, 340, 341], are shown in Table 8.

**Table 8.** Pooled geometric means and 95% confidence intervals for PFAS detected in indoor dust in the United States by Mitro et al., 2016 [339]. The results indicate that long-chain and short-chain PFAS are prevalent in indoor air dust. Long-chain had much higher levels compared to the short-chain.

| | No. datasets Pooled | Geometric mean (ng/g) | 95% Confidence Interval (CI) |
|---|---|---|---|
| **8:2 FTOH** | 4 | 39.48 | (8.29, 187.99) |
| **PFOS** | 9 | 38.91 | (17.47, 86.69) |
| **PFOA** | 9 | 37.34 | (20.26, 68.81) |
| **PFHxS** | 6 | 16.97 | (4.17, 69.02) |
| **PFNA** | 8 | 14.97 | (9.98, 22.46) |
| **PFHpA*** | 5 | 14.37 | (6.21, 33.28) |
| **PFDoA** | 3 | 13.72 | (4.91, 38.32) |

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| | | | |
|---|---|---|---|
| **PFHxA *** | 5 | 11.4 | (4.82, 26.96) |
| **PFDA** | 6 | 10.92 | (6.23, 19.14) |
| **PFBA *** | 3 | 8.3 | (3.72, 18.54) |
| **PFBS *** | 3 | 5.1 | (1.66, 15.66) |

* Indicates short chain ~~PFAS~~PFAAs.
8:2 FTOH - 1H,1H,2H,2H-perfluorodecanol; 2-(perfluorooctyl)ethanol; 1-Decanol, 3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluoro-
PFOS – Perfluorooctanesulfonate; perfluorooctanesulfonic acid (C8)
PFOA – Perfluorooctanoic acid; perfluorooctanoate (C8)
PFHxS – Perfluorohexanesulfonate, perfluorohexanesulfonic acid (C6)
PFNA – Perfluorononanoic acid, perfluorononanoate (C9)
PFHpA – Perfluoroheptanoic acid (C7)
PFDoA – Perfluoro-n-dodecanoic acid, perfluorododecanoate (C10)
PFHxA – Perfluorohexanoic acid; PFHA (C6)
PFDA - Perfluoro-n-decanoic acid; perfluorodecanoic acid; perfluorodecanoate; PfDeA (C10)
PFBA - Perfluorobutyric acid; heptafluorobutyric acid; perfluorobutanoic acid (C4)
PFBS - perfluorobutanesulfonate; perfluorbutanesulfonic acid; nonafluorobutanesulfonic acid; nonafluorobutanesulfonic acid; PFBuS (C4)

In a study from Vancouver, Canada, FTOHs were the predominant PFAS of those measured in indoor air in homes. Median levels of 8:2 FTOH and 6:2 FTOH pg/m$^3$ were 2.7 ng/m$^3$ and 1 ng/m$^3$, respectively [342]. 8:2 FTOH (geometric mean >45 ng/m$^3$) was detected in indoor air in an office building built in 2008 with new carpeting and furniture [110].

**Commented [A38]:** Please check on the correct units here

Polyfluroalkyl phosphate diesters (diPAPs) were detected in dust from households sampled in Vancouver Canada in 2007 and 2008. Levels of total diPAPs were 7,637 ng/g (mean) and 2,214 ng/g (median). Perfluoroalkyl phosphonates (PFPAs) and perfluoroalkyl phosphinates (PFPIAs) were also detected at low levels in a group of households [343].

**Food**

Short-chain ~~PFAS~~PFAAs, perfluoropentanoic acid (PFPeA) and perflurobutane sulfonic acid (PFBS) have been found in whole fish (striped mullet, anchovies, and young hake), swordfish fillets and hake roe taken from fish markets in Spain [344]. In addition, 6:2 fluorotelomer-based side-chain fluorinated polymers and perfluoropolyethers (PFPEs) are used in food contact applications [338].

The uptake of PFBA was observed in lettuce grown in an industrially impacted biosolids-amended soil. The levels of PFBA were 266.1 ng/g. Lettuce grown in the control soil also accumulated low levels of PFBA (6.9 ng/g). PFBA also accumulated to a lesser extend in tomatoes grown in an industrially impacted soil. The levels of PFBA were 56.1 ng/g. This study shows that PFBA has the potential to accumulate in lettuce grown in contaminated soils. In both the field and greenhouse studies, bioconcentration factors for shorter chain perfluoroalkyl acids (PFAAs) were greater than one, indicating accumulation in the plant tissues [345].

**Drinking and surface water**

~~PFAS~~ PFAAs with shorter carbon chains, such as PFBS, perfluorobutanoic acid (PFBA), PFPeA, and perfluorohexanoic acid (PFHxA) have been detected in drinking water [346]. Shorter chain PFAS (PFBS, PFPeA and PFHxA) were detected in the low ng/L range in finished drinking water. PFHxA was detected at 62 ng/L in finished water at a single site [347]. In an European study, PFBS and PFPeA were the predominant PFAS in both tap and bottled water [348].

Twelve previously undiscovered PFECAs and PFESAs were identified in surface water in North Carolina [349]. In addition, in a 2014 study of effluents from municipal and industrial waste water treatment plants in San Francisco Bay, the levels of short-chain PFAS (PFBA, PFHxA) significantly increased compared to a study conducted in 2009. Elevated concentrations of 6:2 fluorotelomer sulfonate (FtS) (as well as PFOS) were apparent in some treatment plants from firefighting foam contamination [350].

**Commented [A39]:** Long chains or short chains?

**Commented [A40]:** Quantify

**Consumer products**

Side-chain fluorinated~~Fluorinated~~ polymer products, such as ones derived from N-methyl-perfluorooctanesulfonamido ethanol (N-MeFOSE) have been used in carpets and textiles for stain resistance [331, 351]. Fluorotelomer-based side-chain fluorinated polymer products have been used in surface treatment products, with increasing use of shorter chain chemicals. PFPEs are used in these applications as well [338]. Shorter chain PFCAs (e.g., four carbon atoms) and PFBS are reported in household products [352]. FTOHs were also found in household products purchased during 2011 to 2013. The highest levels found were in the group of treated floor waxes and stone and wood sealants. One sample contained 331 µg/g of 6:2 FTOH and 92.4 µg/g 8:2 FTOH [353].

**Toxicity**

Toxicity information on three common short chain ~~PFAS~~ PFAAs are reviewed below: PFHxA, PFBS, and PFBA.

## Perfluorohexanoic acid (PFHxA)

PFHxA is a six carbon (C6) perfluorinated carboxylic acid that is a potential manufacturing impurity in the fluorotelomer process and degradation product of short-chain fluorosurfactants and side-chain fluorinated polymers that are ~~and fluorosurfactant that functions as a precursor and component of surfactants and surface protectors~~ used in industrial settings and consumer products, such as stain resistance in clothing and textiles, as paper and packaging coatings, in waxes and cleaning agents, in pesticides, and in hydraulic fluids in airplanes [354]. ~~PFHxA is a degradation product of 6:2 fluorotelomer compounds used to manufacture fluorinated polymers and other fluorotelomer-based products~~ [355]. PFHxA is a strong acid in its acid form. However, in the environment it readily dissociates ~~and in water it will dissociate~~ into the conjugate base anion~~.~~ which is the form relevant for human and environmental exposure assessment. ~~This~~ The Perfluorohexanoate anion will be the predominant species in water under typical environmental conditions.

**Commented [A41]:** These two sentences as originally written are false and make statements that are factually incorrect. Text edited to be factually correct

PFHxA is stable and will be persistent in the environment. Potential precursors of PFHxA include: polyfluorinated polymer ELN101570-2 in Capstone® ST-100/ST-110/ST-100HS/FS-82, which is a chemical use in components of stone and tile sealants, and polyfluorinated polymer in Capstone® FS-81 and Capstone® TR, which is used in component of paints and coatings and presale textile and fabric protection products [356].

**Commented [A42]:** Specific company products should not be singled out. If product names are included, then all companies in this space should be included.

**Toxicology**

**Absorption, metabolism, distribution, excretion:**

Available data indicates that PFHxA is rapidly absorbed via oral absorption in rats and mice, is not metabolized, and is readily eliminated (within 24 hours). In mice, rats and monkeys, NaPFHx was mainly excreted via the urine, with a small percentage (about 10 percent) excreted in feces [357].

Serum elimination half-lives were estimated to be 1.6 hours in males and 0.6 hours in female rats [358]. After long-term oral administration of PFHxA in rats, the blood half-life elimination was 2.2-2.8 hours, and the urinary excretion were 1.9 to 3.1 hours. After a single intravenous injection of 10 mg PFHxA per kilogram of body weight in monkeys, the serum half-life elimination was 2 to 5 hours in both males and females. The half-lives were longer at 14 to 47 hours after long-term oral exposure in monkeys [359].

The serum half-life elimination in humans exposed to high concentrations of PFHxA was estimated to be within 14 to 49 days [360]. The levels of PFHxA in ski waxers increased during ski season, then decreased to below the detection limit after exposure ceased. These data suggest that PFHxA is cleared from blood more rapidly than PFOA and shortly after exposure ceases [361].

**Effects on liver, kidney and blood lipids:**

The target organ of toxicity for PFHxA is the liver [117]. Effects observed in the liver in studies with PFHxA were generally mild and reversible.

PFHxA showed low toxicity following repeated oral exposure. In two sub-chronic (90-day) studies in rats with PFHxA, the NOAEL of 20 and 50 mg/kg bw/day were based on mild effects observed at the 100 and 200 mg/kg bw/day doses, respectively. Effects included microscopic lesions in nasal tissue, changes in serum chemistry parameters and relative kidney weights [357].

In a 90 days gavage study in rats, rats fed with sodium salt of PFHxA at 0, 20, 100 or 500 mg/kg bw/day, relative liver weights were significantly increased at the highest dose. Mild reversible increase in aspartate transaminase, alanine transaminase and alkaline phosphatase activities were noted at the 100 and 500 mg/kg bw/day doses. There was also pale discoloration of the liver at this dose, but no other treatment-related gross observations. Relative thyroid weight was also significantly increased in female rats at the 500 mg/kg bw/day dose [362, 363].

In another study in rats fed by oral gavage 0, 50 or 200 mg/kg bw/day of PFHxA for 90 days, a slight but significant decrease (10 percent) in mean red blood cell parameters (red blood cell count, hemoglobin and hematocrit) was observed at the 200 mg/kg bw/day dose [364]. Levels of alanine transaminase and alkaline phosphatase increased at the highest dose, and the levels of cholesterol decreased at the 50 and 200 mg/kg bw/day doses. Liver weight increased at the highest dose and, in all treatment groups,

increases in kidney weight were reported. Minimal centrilobular hepatocellular hypertrophy was observed in 7 out of 10 animals. All of the observed effects related to treatment with PFHxA were mild, and many were reversible during the recovery period. The NOAEL of 50 mg/kg bw/day was established based on effects on bodyweight, serum chemistry parameters and relative kidney weights at the 200 mg/kg bw/day dose.

A more recent two-year oral chronic study in rats fed PFHxA at 2.5, 15 or 100 mg/kg bw/day (males) and 5, 30 or 200 mg/kg bw/day (females) by gavage for up to 104 consecutive weeks showed some deaths in rats. However, deaths were not attributed to the exposures. The most relevant treatment-related effect was a slight histological changes in the kidney and tubular degeneration. A NOAEL of 15 mg/kg bw/day for males and 30 mg/kg bw/day for females, was established based on the pathological effects in the kidney [365].

**Immune toxicity:** No information was found for this outcome.

**Reproductive and Developmental effects:**

PFHxA has low developmental toxicity [2]. No treatment-related effects were noted in a developmental perinatal, and postnatal reproduction study conducted in pregnant mice given 0, 7, 35, or 175 mg/kg bw/day ammonium PFHx from gestation days 6 to 18. Male and female offspring (F1 generation) of these mice were administered the same doses from days 20 to 41 after birth. In the initial generation, a NOAEL for maternal toxicity of 175 mg/kg/day was derived. A NOAEL of 35 mg/kg/day was derived for fetal toxicity based on an increased number of stillborn pups and pups dying on postnatal day (PND 1) at the 175 mg/kg/day dose [357].

In a second developmental study, the NOAEL for maternal and fetal toxicity was derived as 100 mg/kg bw/day, based on reduced maternal bodyweight and decreased fetal weight at the 500 mg/kg bw/day. There was no clear evidence of developmental toxicity [366].

The National Industrial Chemicals Notification and Assessment Scheme (NICNAS) Australia concluded that PFHxA should be classified as developmental toxicant based on still births, increased postnatal pup mortality, decreased pup body weight, corneal opacity and microphthalmia observed in mice with ammonium salt of PFHxA [357]. The relevance of these developmental effects is unknown to humans.

**Hormone effects:**

In a 90 day gavage study in rats, rats fed with sodium salt of PFHxA at 0, 20, 100 or 500 mg/kg bw/day, experienced minimal hypertrophy of the thyroid follicular epithelium in the 500 mg/kg dose group. The effect was reversible and consistent with the induction of hepatic microsomal enzymes that led to increased biliary excretion of the thyroid hormone T4 (thyroxine), subsequent elevation of thyroid-stimulating hormone (TSH), and the consequent follicular hypertrophy [362, 363].

**Neurobehavioral effects:** No information was found for this outcome.

**Cancer:**

There was no evidence of carcinogenicity in either male or female rats treated daily with PFHxA for 104 weeks during a two-year chronic toxicity study [365]. Overall, there is no evidence of carcinogenicity associated with PFHxA treatment in rats.

**Other**

Rabbits exposed to high levels of PFHxA (single doses of 0.1 mL) had severe eye irritation [367].

**Exposure:**

The Centers for Disease Control and Prevention does not include this metabolite in its biomonitoring surveys of the U.S. population. PFHxA was detected in approximately 50 percent of the samples (n=66,899) (mean level of about 1 ng/mL in serum/plasma) in communities living near industrial sources in the C8 Health Project [89]. PFHxA was detected in whole blood (up to 12 ng/L) (approximately half of the serum/plasma levels) from ski waxers during peak ski season [361, 368].

PFHxA may be rapidly eliminated from the serum, however, some body burden may remain in organs and other tissues. This aspect of body burden has not been well characterized [326]. In a human autopsy study in Spain, PFHxA was detected at the highest concentration in the lung tissue (50.1 µg/L), followed by the bone (30.6 µg/L). PFHxA was also detected in the brain, liver and kidney [369].

**Risk Assessment and advisories:** No information was found.

**Commented [A43]:** We again refer to our critical review of the referenced study (Perez et al) in Appendix C of our comment letter and note the Gannon 2011 study (reference 358), which showed full clearance from rats and mice in 24 hours.

## Perfluorobutane sulfonate and its precursors (PFBS), CAS # 375-73-5

Perfluorobutane sulfonyl fluoride (FBSF) and N-methyl perfluorobutane sulfonamide ethyl acrylate (C4-acrylate, CAS # 67584-55-8) are important derivatives or precursors of PFBS. For instance, FBSF is more reactive than PFBS, and is classified in REACH as acutely toxic and as a skin and eye irritant. C4- acrylate is also an eye irritant and may cause skin sensitization [326].

PFBS has the potential to become a globally distributed pollutant, and is classified as a persistent chemical. PFBS is water soluble and highly resistant to degradation, but is not bioaccumulative or toxic to aquatic organisms [370]. The perfluorobutanesulfonate anion is highly persistent and environmental levels may continue to increase over time due to indirect release pathways [370].

**Toxicology**

**Absorption, metabolism, distribution, excretion:**

PFBS is almost completely absorbed orally and by inhalation, and to a lesser degree by skin absorption. The primary route of elimination of PFBS from the body is in urine. PFBS does not bioaccumulate in organisms. Estimates of serum elimination half-lives are as follows: less than 5 hours in rats, approximately 4 days in monkeys, and 28 days in humans. In some workers, the mean serum elimination half-life of PFBS was determined to be 25.8 days.

**Effects on liver, kidney and blood lipids:**

In animals, PFBS is less toxic to the liver than PFOS, but at large doses has the potential to damage the liver, kidneys and blood [326]. PFBS activated the mouse and human PPARα in *in vitro* assays. Its activation was weaker than PFHxA, PFOA, PFNA, and PFHxS. Compared to PFOS, PFBS had comparable activity on the human receptor and less activity on the mouse receptor [176].

In an oral study with mice, PFBS reduced plasma triglycerides (TG) to a lesser degree than PFHxS or PFOS, which markedly reduced TG and total cholesterol by impairing lipoprotein production [229]. In a two generation reproduction study with the potassium salt of PFBS in rats exposed to 0, 30, 100 300 and 1000 mg PFBS kg/body weight per day for 10 weeks showed increased liver weight and some effect in the kidneys (minimal to mild microscopic findings in the medulla and papilla) in the 300 and 1000 mg/Kg/day doses. A NOAEL for the parental generations was 100 mg/kg/day [371].

**Immune toxicity:**

No epidemiological studies or *in vivo* testing in animals for immune toxicity of PFBS were identified. Limited *in vitro* testing using human cell lines, suggests that PFBS can act similarly to PFOS in inhibiting NF-kB activation and reducing cytokine production, specifically the cytokines interleukin 10 and tumor necrosis factorα [372, 373]. NF-κB is a nuclear factor involved in early cellular response to a number of harmful cellular stimuli such as stress, free radicals, antigens, and bacterial lipopolysaccharides. This effect was independent of PPARα activation in the cell line tested.

PFBS inhibited the release of tumor necrosis factor-α (TNF-α) and interleukin (IL) IL-10 in human cell lines, but IL-6 and interferon-γ (IFN-γ) were unaffected. In THP-1 cells, PFBS also inhibited the protein

NF-κB activation by inhibiting LPS-induced phosphorylation of P65, necessary for NF-κB transcription, and prevented I-κB kinase degradation [326]. PPAR-α was not activated [373].

**Reproductive and Developmental effects:**

In rodents, no adverse health effects were observed in a study of fetal development and no significant alterations on fertility or reproduction in the parental or offspring generations were observed in a two-generation follow up study using doses from 30 to 1,000 mg/kg [371, 374]. In addition, there were no changes in male or female organs in both generations, in sperm parameters, mating, estrous cycles, pregnancy, or natural delivery. The reproductive NOAEL was >1,000 mg/kg/day in both generations. Postnatal survival, developmental and growth of pup was unaffected in F1 and F2 generations except for slight delay in onset of puberty and weight gain in F1 males in the highest dose (1,000 mg/kg-day). Thus, it was concluded that PFBS was not a developmental toxicant in fish [370].

**Hormone effects:** No information was found for this outcome.

**Neurobehavioral effects:** No information was found for this outcome.

**Cancer:** No information was found for this outcome.

**Other**

In a 90 day oral gavage study, male rats exposed to PFBS at doses of 200 and 600 mg/kg/day, showed increased adverse clinical observations and reductions in red blood cells, hemoglobin concentration and hematocrit [308]. This study identified a NOAEL value of 60 and 600 mg/kg/day for changes in blood chemistry for male and female rats respectively. [375].

**Most sensitive effect**

Changes in blood chemistry in male rats were found at a concentration of 200 mg/kg-day. Sixty mg/kg-day was identified as the NOAEL [308].

**Exposure in the general population**

In a 2010 study from 600 American Red Cross U.S. adult blood donors, PFBS serum levels were below the quantification limit [86]. Low levels of PFBS (<0.02 – 0.04 ng/mL) were found in seven samples of ski wax technicians [361]. NHANES data from 2003 to 2010, including over 2,000 serum samples showed that the levels of PFBS were mostly below the quantification limit [81].

In a human autopsy tissue study, PFBS had the highest concentration in the lung tissue. It was also found in the liver, kidneys and bones [369].

**Populations with higher exposure**

The serum concentrations of PFBS in workers employed by 3M Company ranged from less than 5 to 25 ng/mL [376]. In Sweden the levels of PFBS in blood serum from women living in an area where drinking water was contaminated with firefighting foam increased 11% per year from 1996 to 2010 [377].

**Risk Assessment and advisories:**

In 2008, the Minnesota Department of Health derived a health risk limit for PFBS. The MDH developed a subchronic reference dose for PFBS of 0.0042 mg/Kg body weight per day based on a NOAEL of 60 mg/kg bw per day in a 90 days rat study [308]. The mean human half-life was estimated to 28 days. A half-life adjustment factor of 142 was used for extrapolation to a human equivalent dose of 0.42 mg/kg b. w. per day. Based on that they also developed a subchronic health based guidance for groundwater of 9 µg PFBS/L [309].

## **Perflurobutanoic acid (PFBA),** CAS # 3794-64-7

PFBA is a perfluoroalkyl carboxylate that is used in photographical film and as a chromatography additive for use in high performance liquid chromatography (HPLC) and liquid chromatography mass spectrometry (LCMS) applications. PFBA could be formed by the degradation of indirect precursors of perfluoro carboxylic acids (PFCAs) that have four perfluorinated carbon atoms.

**Toxicology**

**Absorption, metabolism, distribution, excretion:**

The serum elimination half-life of PFBA in humans, was estimated to be 72 hours for males and 87 hours for females. PFBA is excreted faster (approximately within 24 hours) in rats and mice [326]. On average, the cumulative excretion of PFBA 24 hours after an oral dose was approximately 35 percent in urine and 4 to 11 percent in feces in male mice. In female mice, excretion was 65 to 69 percent in urine, and 5 to 7 percent in feces [378].

**Effects on liver, kidney and blood lipids:**

PFBA appears to activate the peroxisome proliferator-activated receptor alpha (PPAR-α) in mice and humans [379]. PFBA has a higher PPAR-α activity in the liver than PFBS, PFHxS, and PFOS [176]. PFBA is less active than PFOA [159].

In a 90 day rat study, 30 mg/kg body weight/ day resulted in increased liver weight and reduced thyroid hormone in males [380]. In 28-day and 90-day oral toxicity studies in rats, male rats had an increased liver weight, slight to minimal hepatocellular hypertrophy; decreased total serum cholesterol; and reduced serum thyroxin. The NOAEL for male rats was 6 mg PFBA/kg/day in both the one-month and the three-month studies. A NOAEL of greater than 150 mg/kg/day in the 28-day study and greater than 30 mg/kg/day in the 90-day study were observed in female rats [381].

Pregnant mice exposed to PFBA at doses of 35, 175, and 350 mg/kg/day showed maternal liver effects at doses above 175 mg/kg/day [382].

**Immune toxicity:** No information was found for this outcome.

**Reproductive and Developmental effects:**

Exposure to high doses of PFBA during pregnancy (up to 350 mg/kg) did not adversely altered neonatal survival or growth in mice, although some developmental delays were noted [383]. The relative lack of

adverse developmental effects of PFBA (compared to PFOA) is in part, due to the rapid elimination of this chemical.

**Hormone effects:** No information was found for this outcome.

**Neurobehavioral effects:** No information was found for this outcome.

**Cancer:** No information was found for this outcome.

**Most sensitive effect**

The most sensitive effect seen is altered liver and thyroid hormones. Animal studies identified a NOAEL value of six and 30 mg/kg/day for male and female rats, respectively [326]. Another study observed a NOAEL in female rats at doses greater than 150 mg/kg/day in a 28 days study, and greater than 30 mg/kg/day in a 90 day study [381].

**Exposure:**

Limited monitoring data are available for PFBA. PFBA has been detected in groundwater in Minnesota near the 3M Cottage Grove facility, and in municipal drinking water in Washington County, Minnesota [378].

PFBA was detected in 98 percent of backyard garden produce tested in a small study of 20 gardens in an area of Minnesota impacted by contaminated water. The median PFBA produce concentration was 0.68 µg/kg. The amount of PFBA in the water, the amount of garden watering, and the type of produce grown were found to contribute the most to the amount of PFBA in produce [384].

**General population**

In a study of autopsy tissues PFBA was found in the kidneys, lungs, liver, and brain of humans. Relatively high concentrations of PFBA were found in the kidney (464 ng/g wet weight) and lung (304 ng/g wet weight) [369].

**Populations with higher exposure**

Serum PFBA concentrations were detected only in 4 percent of the serum of former and current employees of the 3M Cottage Grove Facility in Minnesota. Serum concentrations were above 2 ng/mL, with maximum concentrations of 6.2 ng/mL for the former employees and 2.2 ng/mL for the current employees [378].

Low levels of PFBA ( less than 0.08 to 0.068 ng/mL) were found in seven samples of ski wax technicians [361]. A follow up study of 11 male ski wax technicians showed average levels of 1.8 ng/mL PFBA [368].

**Risk Assessment and advisories:**

The Minnesota Department of Health has developed a health advisory level of 7 µg/L for PFBA based on liver weight changes, morphological changes in liver and thyroid gland, decreased TT4, and decreased red blood cells, hematocrit, and hemoglobin in rats. The MDH developed an RfD of 0.0029 mg/kg-day [385].

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