Per- and Poly-Fluorinated Alkyl Substances Chemical Action Plan (PFAS CAP) – 2019 Updates

Updated Health Chapter

In 2017, the Washington State departments of Ecology and Health shared draft PFAS CAP chapters with external parties for review and comment. Comments received are available online. This document is either an update of a 2017 draft or a new 'chapter.' Ecology and Health are sharing chapters with interested parties prior to the April 2019 PFAS CAP webinar (*previously planned for March*). Updates will be discussed during the April webinar. We expect to publish the entire Draft PFAS CAP around June 2019 followed by a 60-day comment period.

In April 2019, Ecology and Health will host a PFAS CAP webinar (*date not yet set*) to:

- Briefly review activities underway: firefighting foam, food packaging, drinking water.
- Review updated/new chapters – comments will be accepted on the updated chapters. Responses will be provided after the 2019 public comment period (summer 2019).
- Discuss preliminary recommendations – requesting comments and suggestions from interested parties – due a week after the webinar.
- Submit comments online.

Quick summary of PFAS CAP efforts:

- PFAS CAP Advisory Committee and interested parties met in 2016, 2017 and 2018.
- September 2017 Draft PFAS CAP chapters posted:

Intro/Scope	Environment
Biosolids	Health
Chemistry	Regulations
Ecological Toxicology	Uses/Sources

- March of 2018, Ecology and Health published the Interim PFAS CAP.
- The 2019 updated PFAS CAP "chapters" to be posted (in the order we expect to post on the PFAS CAP website):

Biosolids	*Analytical methods (new)*
Ecological Toxicology	Chemistry
Environment	*Fate and Transport (new)*
Regulations	*Economic analysis (new)*
Uses/Sources	*Preliminary Recommendations (new)*
Health	

Questions - contact Kara Steward at kara.steward@ecy.wa.gov.

This document is posted on the PFAS CAP Website - https://www.ezview.wa.gov/?alias=1962&pageid=37105

Appendix #: Health

Abstract

Public health concern about per- and polyfluoroalkyl substances (PFAS) has grown as an increasing number of these chemicals are detected in drinking water, food samples, house dust, indoor air, and in wildlife and human biomonitoring studies. In Washington, perfluoroalkyl acids (PFAAs) have been identified in drinking water in Issaquah and in and around three military bases: Joint Base Lewis-McChord, Naval Air Station Whidbey Island, and Fairchild Air Force Base. In each area, drinking water samples exceeded the lifetime health advisory level of 0.07 µg/L (ppb), set by the U.S. Environmental Protection Agency (EPA) in 2016. PFAS-based firefighting foam is believed to be the primary source of contamination at all of these areas.

People can be exposed to PFAS from a number of sources. These include contaminated drinking water, food grown in contaminated soils or in contact with food wrappers that contain PFAS, fish caught from contaminated waters, and indoor air and dust that accumulate PFAS from carpets, textiles and other household items. Although, it has been difficult to assess which sources contribute the most to human exposure, studies identify food and drinking water as the likely main routes of human exposure.

Exposure to PFAS is widespread. The PFAAs most commonly detected in people's serum[1] - perfluorooctane sulfonic acid (PFOS), perfluorooctanoic acid (PFOA), perfluorononanoic acid (PFNA), and perfluorohexane sulfonic acid (PFHxS) - are well absorbed when ingested. Because it takes a long time for our bodies to excrete these perfluoroalkyl acids (PFAAs), they accumulate over time in our blood and tissues. PFOA, PFOS, PFNA, and PFHxS are routinely detected in serum of nearly all people tested. The National Health and Nutrition Examination Survey (NHANES) data shows declines in blood concentrations of PFOA and PFOS-related compounds following phase-outs in U.S. production and use.

Animal studies provide strong evidence of developmental toxicity and other health effects for a number of perfluoroalkyl compounds. At low doses, PFOA and PFOS cause malformations, low birth weight, delayed mammary gland development, and altered neurodevelopment. PFOA and PFOS can cause liver toxicity and tumors, alter hormones and timing of sexual maturation and suppress immune response in laboratory animals. The available epidemiologic studies suggest links between PFAAs exposure and several health outcomes including increases in cholesterol levels, reduction in birth weight, reduction in immune antibody response to childhood vaccines and increases in rates of some cancers such as kidney and testicular.

The Washington Department of Health offers voluntary PFAS sampling in drinking water to certain public water systems to understand occurrence of these chemicals in our state, and to know if the water is safe to drink. DOH recommends that public water systems and other drinking water systems follow the 2016 EPA drinking water advisory for PFOA and PFOS. DOH also supports the State Board of Health (SBOH) in developing state drinking water standards for PFAAs.

[1] Serum is the part of our blood left when red blood cells, white blood cells and clotting factors are removed.

1.0 PFAS contamination of drinking water in Washington state

Per- and polyfluoroalkyl substances (PFAS) contamination has been found in drinking water in several areas of the state. In all cases where drinking water exceeded the lifetime health advisory level (LHAL) of 0.07 µg/L set by EPA in 2016, water systems took action to meet the health advisory. Available state data are presented below with a summary of actions taken in each area.

1.1 PFAS monitoring under EPA's Unregulated Contaminant Monitoring Rule (UCMR3)

During 2013-2015, 132 public water systems in Washington conducted monitoring for six perfluoroalkyl acids (PFAAs) under EPA's UCMR3. The systems included all 113 large Group A[2] systems that serve more than 10,000 people and 19 smaller systems. The systems tested cover the majority (94 percent) of Washington residents served by public water systems. Six PFAAs (perfluorooctane sulfonic acid (PFOS), perfluorooctanoic acid (PFOA), perfluorononanoic acid (PFNA), perfluorobutane sulfonic acid (PFBS) and perfluorohexane sulfonic acid (PFHxS), and perfluoroheptanoic acid (PFHpA)) were measured using EPA Method 537 with reporting limits between 0.02 and 0.04 parts per billion (ppb). PFOA and PFOS levels above the laboratory reporting limits were detected in three Washington public water systems (Table 1). Only one, the City of Issaquah, had a source that exceeded the LHAL for PFOA and PFOS.

Table 1. Washington State PFAAs detections 2013-2015, EPA Unregulated Contaminant Monitoring Rule compared to the 2016 EPA lifetime health advisory level.

Public Water System	Combined PFOA & PFOS (ppb)	Total PFAS measured (ppb) [a]	2016 EPA lifetime health advisory PFOA and PFOS (ppb)
Issaquah Water System (one well)	**0.490**[b]	**0.796**[b]	**0.07**
City of DuPont Water System (two wells)	0.030	0.030	
JBLM - Lewis (two wells)	0.013 – 0.051	0.051	

[a] Issaquah detected six PFAAs, City of DuPont detected only PFOA, and Fort Lewis detected PFOA and PFHpA.

[b]This well was blended 1:4 with an uncontaminated well before distribution, so the concentration of PFOA and PFOS combined at the nearest homes was closer to 0.10 ppb. Levels were lower still in other parts of the Issaquah water system.

1.2 PFAS monitoring post-UCMR3

Since the UCMR3 sampling, several military bases have tested drinking water sources in response to a directive from the Department of Defense [1-3]. This voluntary testing effort found PFAAs in drinking water sources at or near McChord Airfield, Fort Lewis, NAS Whidbey and

[2] Group A water systems have 15 or more service connections or serve 25 or more people 60 or more days per year.

Fairchild AFB (Table 2). The primary source suspected at each base is firefighting foam. Each of these military installations has conducted additional monitoring to determine the extent of PFAAs contamination in drinking water wells both on and off base. The military has also provided treatment assistance to nearby private well owners and public water systems to reduce exposure to PFAAs.

Table 2. Military detections of PFOS and PFOA in public and private drinking water wells near U.S. military bases in Washington compared to the 2016 EPA lifetime health advisory level.

Area (date of latest update)	**# of Wells monitored**	**Wells above the LHAL**	**Combined PFOA & PFOS (ppb)**	**EPA lifetime health advisory PFOA & PFOS (ppb)**
Naval Air Station Whidbey Island (Nov, 2016- Jun, 2017)	234	15	0.003 – **3.8 PFOS** 0.001 – **0.66 PFOA**	**0.07**
Fairchild AFB Includes City of Airway Heights (January, 2019)	369	89	**0.073 – 5.7**	
JBLM	21	5	Lewis Golf Course: 0.059-**0.078** Lewis well 17: **0.071-0.088** McChord Field (3 wells): **0.076-0.250**	

City of Issaquah

As part of the EPA's UCMR3 testing (2013-2015), the City of Issaquah discovered PFOS, PFHxS, and smaller amounts of PFOA, PFNA, and PFHpA in one production well in their public water system. 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. Water from the well was blended in a ratio of 1:4 with a deeper adjacent well that was PFAS-free before it entered the distribution system. After blending, the water level did not exceed the 2009 provisional EPA health advisory, which was 0.4 µg/L for PFOA and 0.2 µg/L for PFOS [4]. In November 2015, additional sampling across the Issaquah system found PFOS was at 0.106 µg/L at the entry point of the two blended wells, and levels ranging from 0.068 to 0.038 µg/L in more distant areas of the distribution system. At each site, PFHxS was present at about half the PFOS concentration. PFBS was also detected in the contaminated well in the 2015 sampling. In January 2016, the city shut down the well and eventually invested over $1 million in a granular activated carbon (GAC) treatment system installed in May 2016. Since June 2016, the treatment system has been effective at removing PFOA and PFOS, and is routinely tested for performance. The city investigated the potential sources of contamination, and concluded that the likely source was the Eastside Fire and Rescue headquarters about a mile up gradient. Soil samples in a firefighting training area at the headquarters contained PFOA and PFOS from firefighting foam. One

monitoring well and two drinking water production wells operated by nearby Sammamish Plateau Water system were also found to contain PFOA and PFOS at trace levels [5, 6]. These wells continue to be monitored.

Naval Air Station (NAS), Whidbey Island

In 2016, the Naval Air Station Whidbey Island detected PFAAs in off-base drinking water wells near Ault Field in Oak Harbor and at the Outlying Landing Field (OLF) southeast of the town of Coupeville. In October 2016, the Navy announced it would begin voluntarily testing drinking water wells for two specific PFAAs (i.e., PFOA and PFOS) around those two areas. Consistent with Navy policy, the base targeted their testing in off-base drinking water wells located within one mile downgradient from potential or known sources of Aqueous Film Forming Foam (AFFF). The Navy continues to test drinking water wells in these areas with PFAAs detections and wells adjacent to properties with exceedances of the LHAL.

As of December 2018, the Navy has tested 234 drinking water wells (112 from properties near OLF, and 122 near Ault Field, including Area 6 [3]). Fifteen drinking water wells exceeded the LHAL for PFOS and/or PFOA (eight near OLF, and seven near Ault Field, including Area 6) (Table 2). The Navy continues to provide bottled water to residents whose results for PFOA and/or PFOS exceed the LHAL.

The Town of Coupeville (referred to as the Town) has detected PFAAs in public water wells near OLF. The Town of Coupeville's water is a blend of water between multiple wells. As such, the Town is able to keep the levels of PFOA and PFOS below the LHAL [7]. The Town continues to monitor their wells and are working with the Navy to install a GAC treatment system to keep the Town's water below the LHAL.

The Navy has conducted a number of public meetings where they have presented health information and answered people's questions about the potential health effects of PFAS. The Navy continues to work on its source investigation and has a policy regarding removal, disposal, and replacement of legacy AFFF [2].

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

In December 2017, the Navy detected PFAAs in nine on-base groundwater wells at the Area 6 landfill; one well was above the LHAL. As of December 2018, the Navy has sampled 17 drinking water wells and 16 groundwater wells (used for irrigation or non-potable water) off-base near the Area 6 Landfill. Five drinking water wells exceeded the LHAL. No exceedances for PFOS and/or PFOA were identified for the groundwater wells [8].

[3] Area 6 was a Navy disposal site from the 1960s to 1990s for industrial (Former Industrial Waste Disposal Area) and household wastes (Navy Municipal Landfill).

Fairchild Air Force Base (AFB) and surrounding areas, Spokane County

Fairchild AFB detected PFAAs in groundwater monitoring wells on the base, in monitoring required by the Department of Defense. Drinking water on the base comes from wells several miles north of the base near the Spokane River, and a well located on the southern tip of the base (S01, Well 2). These wells are not contaminated with PFOS or PFOA. Based on groundwater monitoring results, Fairchild conducted off-base testing for PFAS in public and private drinking water wells in several phases. They detected PFAAs in private wells east of the base, municipal wells for the City of Airway Heights northeast of the base, and other community and private wells to the north and northeast of the base.

As of January 2019, the Air Force has tested 369 drinking water wells. Eighty nine residential wells exceeded the LHAL, the levels ranged from 73 parts per trillion (ppt) to 5,700 ppt total for both PFOS and PFOA combined. Four municipal wells were sampled for PFOA and PFOS and two exceeded the LHAL (Table 2). 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 about 17 times higher than the LHAL for PFOS and PFOA. The Fairchild AFB policy is to notify well owners and immediately provide bottled water, if levels for PFOS and PFOA in drinking water exceed the health advisory level.

In response to PFAAs detection in April 2017, the public water system of Airway Heights shut down their 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. During the flushing, the city warned residents west of Hayford Road to not drink or cook with water from city pipes, and Fairchild AFB provided bottled water to them. The city has since added another connection to the City of Spokane to supply drinking water while they pursue treatment options for the contaminated wells. The time critical removal action (TCRA) initiated treatment for PFOS/PFOA in Airway Heights municipal well #9 [9]. Fairchild AFB has designed and installed a temporary treatment system on municipal well #9 to provide water from the City of Spokane during high-demand summer and fall months. The system is designed to operate for three summer and fall seasons, while a long-term solution is identified. Fairchild AFB continues monitoring locations and developing regional geologic settings, geologic cross sections, and groundwater surface maps to understand the movement of contaminants in the water, and identify data gaps.

According to a November 2018 progress report [9], Fairchild AFB has installed 68 GAC residential treatment systems out of 81 impacted residential wells. The seasonal treatment system at Airway Heights municipal well #9 has been operating since August 2018. The system was drained and sealed for winter weather in October 2018, and is anticipated to restart in the spring of 2019.

According to Fairchild AFB, the base has transitioned to a safer foam that is PFOS-free and has only trace amounts of PFOA. The substitute foam is based on C6 fluorochemistry. Fairchild no longer uses AFFF during live fire training. Fire trucks on base are being outfitted with a test system that prevents any foam discharge during equipment testing. AFFF use is limited to emergency responses with immediate containment requirements. The Strategic Environmental Research and Development Program (SERDP), Environmental Security Technology Certification Program (ESTCP) is funding research on new fluorine-free firefighting foam

formulations that can meet the military's performance requirements (Mil-Spec), and are readily biodegradable [10-12].

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.

Fort Lewis

Fort Lewis monitored seven drinking water sources as part of the UCMR3 monitoring. 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 LHAL in one well. This well has been offline since then, and is likely to remain offline. The November 2016 testing also revealed additional wells with PFAAs contamination. A well that serves the military golf course near DuPont had levels just above the LHAL. Bottled water was supplied at that facility, and point-of-use treatment devices are now used to reduce exposure to PFAAs. The primary source of drinking water (Sequalitchew Springs and infiltration gallery) for the vast majority of the main base generally has around 0.02 µg/L of PFOS and PFOA combined.

McChord Field

McChord Field was not involved in UCMR3 monitoring because the population served by McChord's water system at that time was below 10,000. In the November 2016 monitoring conducted at JBLM facilities, PFOS and small amounts of PFOA were reported in three drinking water wells serving McChord Field totaling 0.25, 0.216, and 0.071 µg/L respectively. A few other wells have levels of PFOS and PFOA below the LHAL. In March 2017 the Air Force announced it had shut down the three wells that contained PFOS and PFOA above the LHAL.

JBLM staff believes contamination in both areas came from firefighting foam used through the early 1990s for firefighter training at several locations associated with McChord Field's runway and Fort Lewis's Gray Army Airfield, as well as other potential sources such as landfills. According to JBLM staff, use of foams containing PFAS was discontinued more than 20 years ago. In January 2019, DOH's Office of Drinking Water approved plans to install GAC treatment at the four drinking water wells with the highest levels of PFAAs that serve McChord Field.

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

City of Lakewood, Lakewood Water District

The Lakewood Water District tested five of its drinking water wells as part of the UCMR3 monitoring, and no PFAAs were detected at that time. In its most recent monitoring for PFAAs in October 2018, Lakewood sampled seven wells near JBLM. Wells in the shallower and intermediate depth aquifers had detections of PFAAs (primarily PFOS and PFHxS), while wells in the deeper aquifer did not. All results for PFOS plus PFOA are below the LHAL [13]. However, the levels of PFOS plus PFHxS in two wells were slightly above 0.07 ppb. Lakewood Water District has been proactive and evaluated options to remove these PFAS at levels above 0.07 ppb. They have removed the two wells from operation. In early 2019, Lakewood plans to

install GAC treatment at the well closest to McChord Field. Lakewood will continue to test and monitor its system for PFAAs [14].

City of DuPont

As part of UCMR3 testing, the City of DuPont detected levels of PFOA (around 0.03 µg/L) in two wells in the southwest area of its distribution system. PFOA and PFOS were not detected in the three wells serving the north and east areas of the distribution system. In October 2018, DuPont conducted follow-up monitoring for PFAAs, but the results were inconclusive due to detections in the quality control samples.

City of Tacoma, Tacoma Public Utilities

Tacoma tested its South Tacoma Wellfield as part of the UCMR3 monitoring, and no PFAAs were detected at that time. In late summer 2018, Tacoma Public Utilities tested for PFAAs in some of the individual wells at the southern end of its South Tacoma Wellfield. This was a voluntary effort to understand if PFAAs existed in its water sources near JBLM. One of the wells sampled (Well 10C, which supplies a tiny fraction of the drinking water produced by the wellfield, and is in the shallow aquifer) showed PFAAs levels that slightly exceeded the LHAL. Tacoma notified customers and closed the well for additional testing and maintenance. The exposure risk was limited to customers who collected unfluoridated water in their own containers from this well. Tacoma's Green River source, which serves all Tacoma Water customers with the vast majority of their drinking water, showed no detections of PFAAs [15].

2.0 PFAS exposure in people

Exposure to PFAS is widespread. The PFAAs most commonly detected in people's blood serum - PFOS, PFOA, PFNA, and PFHxS - are well absorbed when ingested. Because it takes a long time for our bodies to excrete these PFAAs, they accumulate over time in our blood and tissue. Other PFAAs like perfluorobutanoic acid (PFBA), PFBS, and perfluorohexanoic acid (PFHxA), are more efficiently excreted, and are less likely to accumulate in our bodies overtime. Most other PFAS do not have methods for measurement and have not be included in biomonitoring studies. There are thousands of PFAS compounds and only about 30 have been looked for in human exposure studies.

Since 1999, the Centers for Disease Control and Prevention (CDC) has regularly measured for 12 PFAAs in the U.S. general population using the National Health and Nutrition Examination Survey (NHANES). PFOA, PFOS, PFNA, and PFHxS are routinely detected in serum of nearly all people tested [16, 17]). The data in Figure 1 show declines in blood concentrations following phase-outs in U.S. production, and use of PFOA and PFOS-related compounds [18, 19]. Similar results and trends were reported in a large study of American Red Cross blood donors from 2000 through 2015 [20].

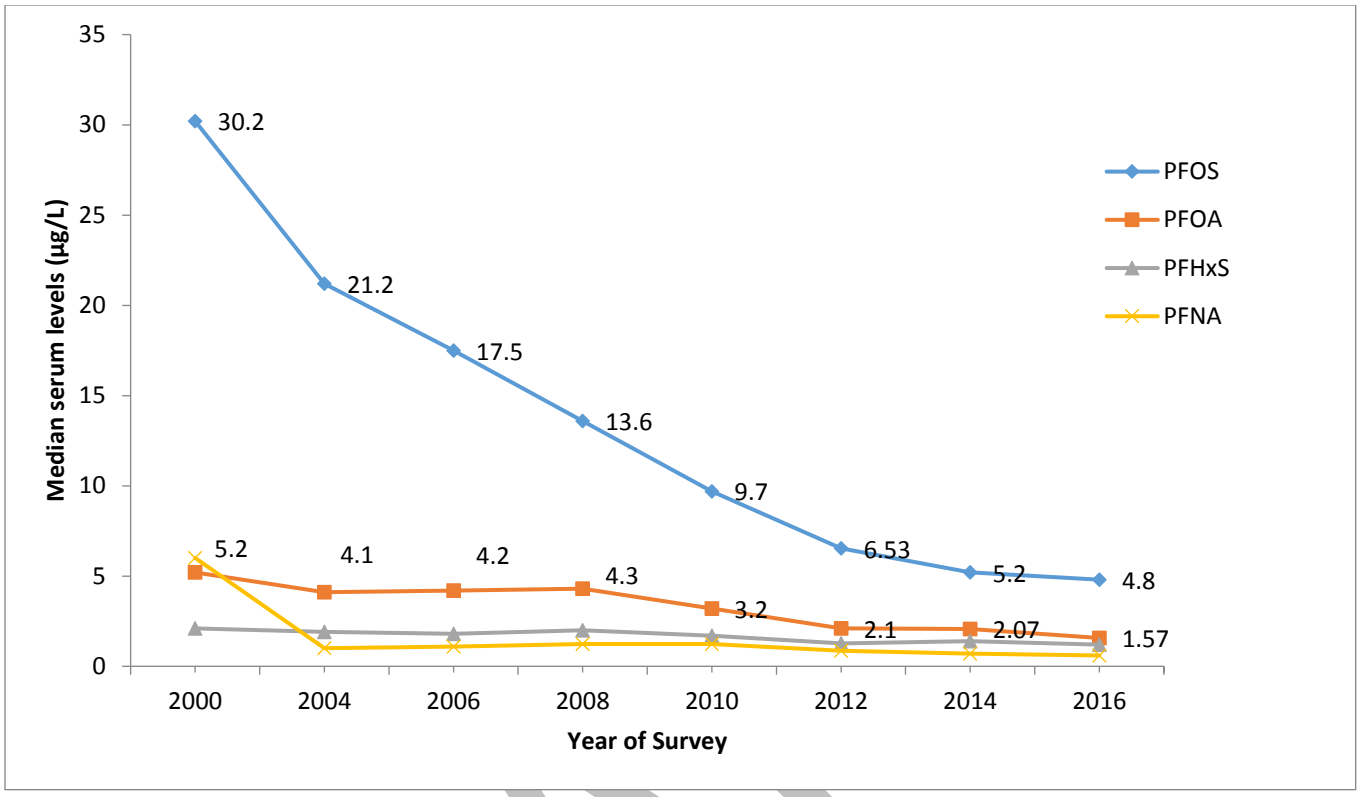

Figure 1. Median levels of PFAAs in serum from a representative U.S. population, National Health and Nutrition Examination Survey. A phase-out of U.S. production and use of PFOS and PFOA occurred between 2002-2015 [17].

Recent exposure estimates for measured PFAAs in the general U.S. population are available in Figure 2 and include adults [17], pregnant women [21]) and children [22]. These studies collected serum samples from U.S. populations with no known industrial source of elevated PFAAs exposure. The levels measured in these studies likely reflect non-occupational exposures to PFAS in our diet, consumer products and homes. Biomonitoring data for the general population of Washington is limited to one study in 2004 by Olsen et al., in which seven PFAAs compounds were measured in stored blood serum of 238 elderly men and women in Seattle [23]. These levels were comparable to national levels in adults at the time [17].

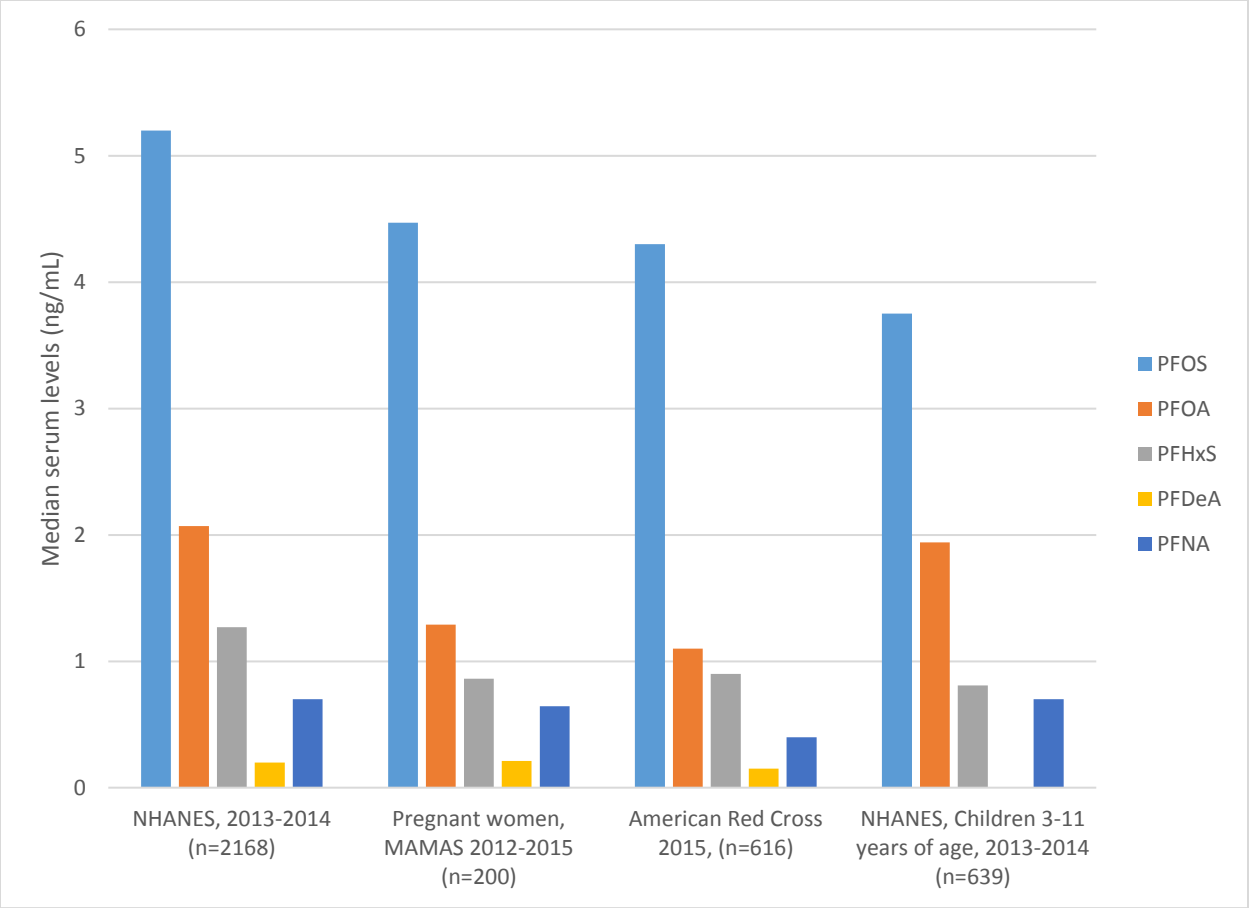

Figure 2. Median PFAAs serum levels in the general U.S. population.

A number of studies have also investigated PFAS concentrations in serum of subpopulations. In the NHANES 2013-2014 study serum concentrations were lower in young people (ages 12 to 19) compared to the total general population, and were higher in males (median PFOA, 2.37 µg/L, PFOS 6.4 µg/L) than females (median PFOA, 1.67 µg/L, and PFOS 4.0 µg/L). Mexican-Americans had lower median serum concentrations than non-Hispanic whites or non-Hispanic blacks [17].

The Asian/Pacific Islander Community Exposures study (this community is part of the biomonitoring program in California) found significant associations between PFAAs serum levels and demographic factors such as age, sex, U.S. residency, birth country, household income, and language. Researchers concluded that California's regional immigration and racial/ethnicity patterns may contribute to differences in PFAAs and other contaminants across the state [24]. The PFAAs serum levels on these communities were similar to the levels found in the NHANES Asian community (Figure 3).

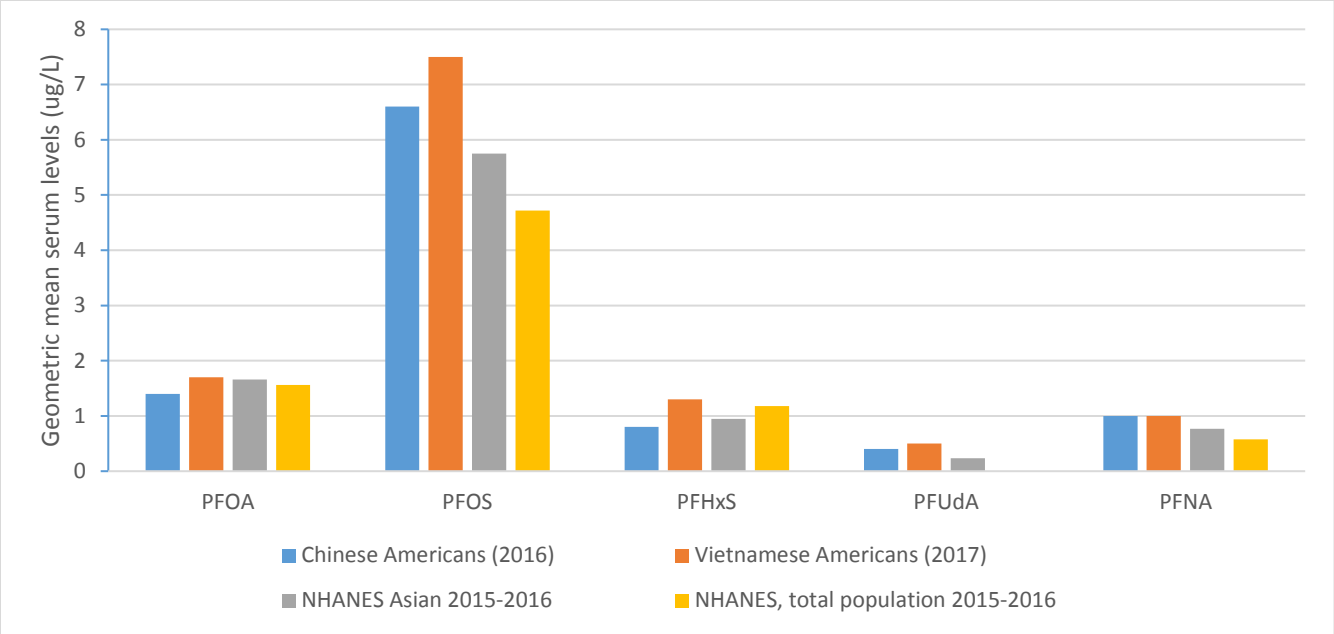

Figure 3. Geometric mean PFAAs serum levels in the Asian and Pacific Islander communities in San Francisco Bay Area [24].

2.1 Communities with elevated PFAAs exposure

It is well established that PFAAs exposure is higher in communities impacted by industrial PFAS emissions and waste. Figure 4 show the higher concentrations of serum PFAAs in several communities impacted by PFAS manufacturing plants in Minnesota and Alabama, and commercial use of PFAS in New York and Vermont. These communities had extended exposure to elevated PFAS in their drinking water.

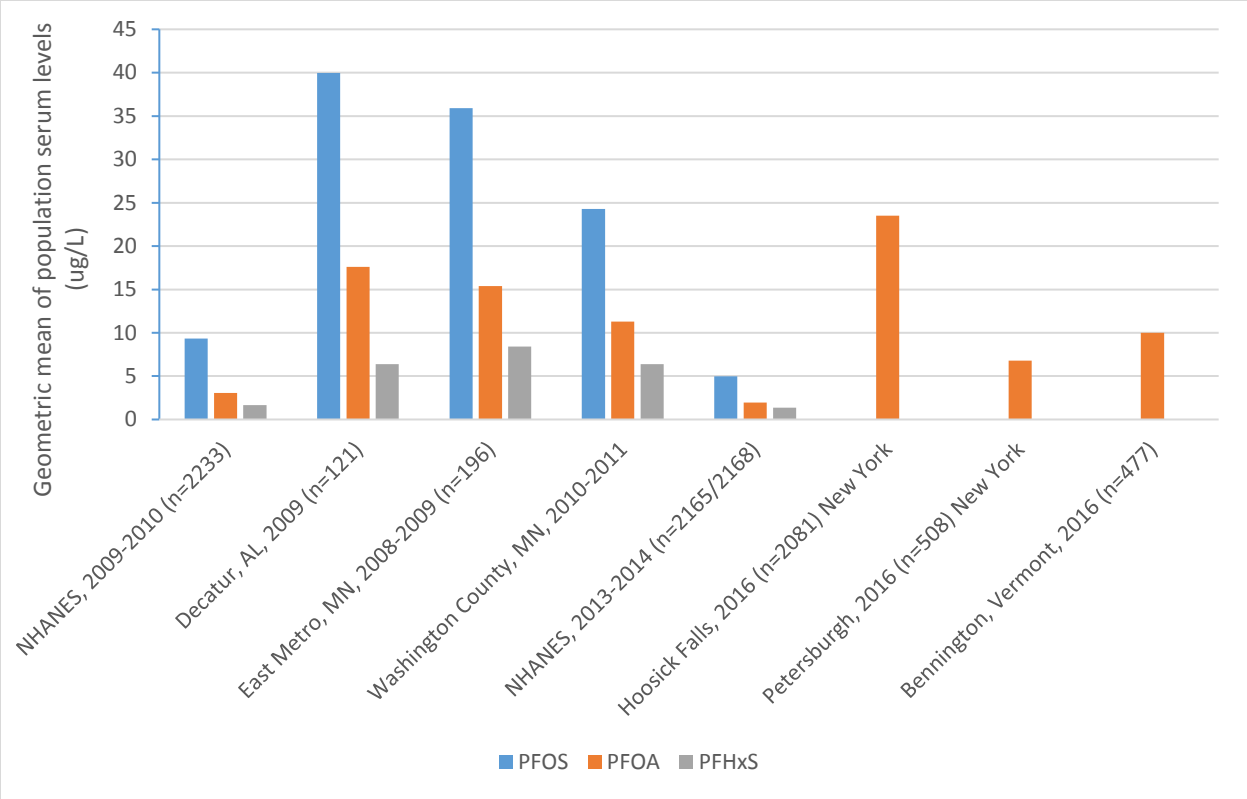

Figure 4. Elevated serum PFAAs levels (µg/L) in communities with drinking water impacted by industrial sources compared to the U.S. general population (NHANES) [17, 25-29].

Decatur, Alabama

In 2007, a manufacturer of PFAS in Decatur, Alabama, notified EPA that perfluorocarboxylic acids (PFCAs) were discharged into the Decatur Utilities Dry Creek Wastewater Treatment Plant. From 1996 to 2008, treated sewage sludge (biosolids) from Decatur Utilities was applied repeatedly as a soil amendment on about 5,000 acres of privately owned agricultural fields in Lawrence, Morgan, and Limestone counties in Alabama [25]. 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 LHAL of 0.07 µg/L [30].

PFAAs were measured in the serum of people who lived and worked in the affected area. Serum PFOA concentrations in 121 residents, with affected public drinking water, ranged from 2.2 to 78.8 µg/L. Serum PFOA concentrations in residents served by nine private drinking water wells, with detectable levels, ranged from 7.6 to 144 µg/L [30]. Workers from the 3M manufacturing plant in Decatur were also tested for exposure. Mean blood serum concentrations of PFAS in occupationally exposed workers 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 [31].

Minnesota- East-Metro Area

The Minnesota Department of Health (MDH) conducted a community exposure assessment of PFAS released from the 3M Cottage Grove manufacturing facility and several local landfills where the plant had disposed of wastes in the 1950s, 1960s, and 1970s. Several PFAAs were detected in public and private wells in the East Metro 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 [32]. Drinking water contamination was discovered in 2004, and water filtration to remove PFAAs was developed and installed in 2006. Biomonitoring was conducted to assess community exposure in 2008 [27]. In 2014, follow-up biomonitoring was conducted to assess water filtration as a public health intervention. Eight PFAAs 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. PFOS, PFOA, and PFHxS were found in the blood of almost all long-term residents tested. Levels of these PFAAs 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 were still higher than those in the U.S. population [27]. Sex and age were related to PFAAs levels, and older people and men had higher PFAAs levels.

Water filtration is effective at lowering exposure to PFAAs to people. Data collected by MDH (Figure 5) demonstrates that installing water filtration systems to remove PFAAs compounds from contaminated drinking water reduced serum levels of PFAAs in exposed residents. Similarly, serum levels of PFOA from two communities in Mid-Ohio Valley (Little Hocking, and Lubeck) residents drinking contaminated water also declined after the water was treated with GAC filtration system in the public water supply [33].

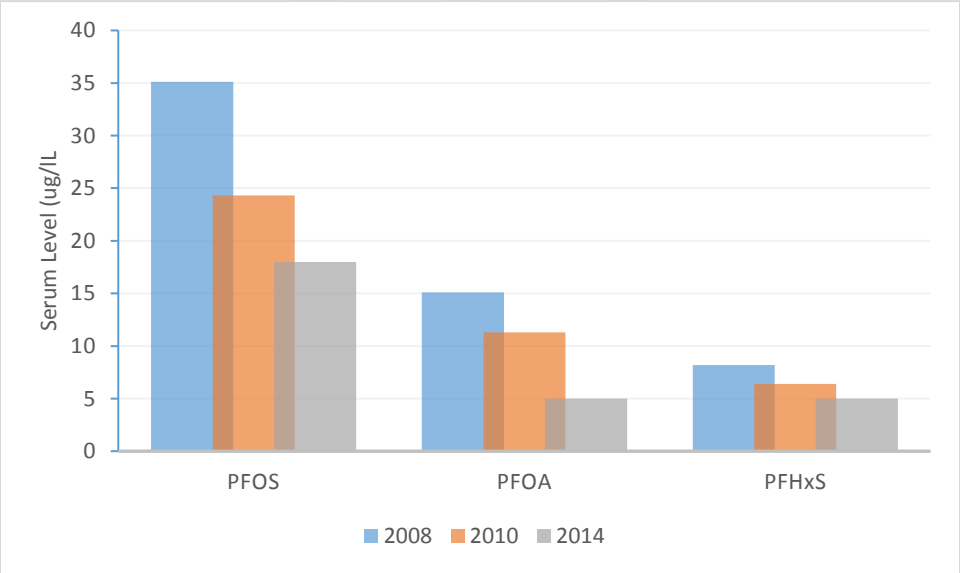

Figure 5. Median serum levels at three time points in Minnesota residents after water filtration was installed to remove PFAAs from contaminated drinking water [34].

New York State Department of Health (NYSDOH)

NYSDOH conducted blood PFAAs testing in four communities served by public water supplies: Hoosick Falls (February – April 2016), Petersburgh (April 2016), Newburgh, and Suffolk County (Westhampton area). These communities were affected by industrial pollution and the main contaminant tested was PFOA [28] [35].

NYSDOH conducted an investigation of cancer incidence in Hoosick Falls from 1995-2014, focusing on cancers that have been associated with PFOA exposure. NYSDOH published the results of the investigation in a report and made it publicly available on the department's website. Higher rates of cancers associated with PFOA exposure were not found in the study area [36].

Vermont

In early 2016, the Vermont Agency of Natural Resources/Department of Environmental Conservation sampled five private drinking water wells and the North Bennington municipal water supply for PFAAs. Five private wells tested showed PFOA concentrations ranging from 40 to 2,880 ppt, above the state's drinking water health advisory level of 20 ppt. Public water testing in Vermont indicated detectable PFOA contamination in public water supplies. This was associated with localized air emissions or discharges. Of the five public water systems that tested positive for PFAAs, three were part of the Bennington PFOA problem, one was the public water supply found to be contaminated in Pownal (Pownal Fire District 2), and the other was the public well serving the Airport Business Park in Clarendon [37].

In April 2016, blood testing was conducted in Vermont as part of the state's response to PFOA contamination of drinking water wells in North Bennington [38]. There were 477 adults and children in the study. PFOA blood levels for the Bennington/North Bennington group ranged from 0.3 to 1,125.6 μg/L. The geometric mean was 10.0 μg/L, higher than 2.1 μg/L for the U.S. population [39].

Figure 6 show serum levels in two communities with drinking water contamination impacted by PFAS-containing firefighting foam, which is also the suspected source of PFAS contamination here in Washington state.

A national study is planned to better understand the specific exposures and health impacts associated with firefighting foam at military bases. The study will be conducted by CDC, and the Agency for Toxic Substances and Disease Registry (CDC/ ATSDR).

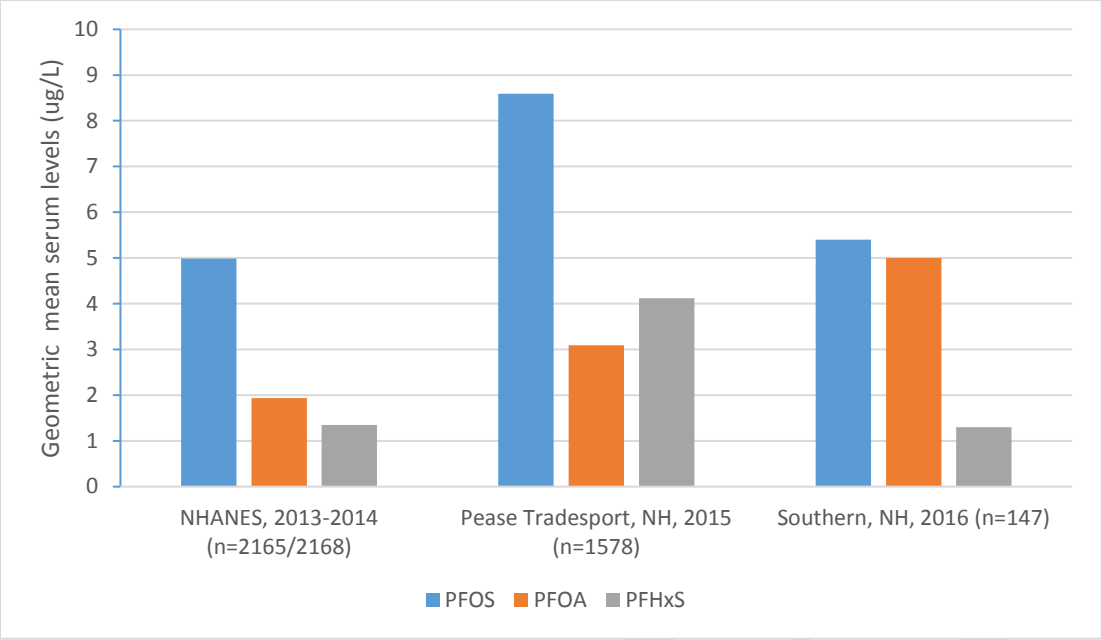

Figure 6. Geometric serum levels (µg/L) in two communities with drinking water impacted by firefighting foam. NHANES is a general population sample used as a reference.

Pease Internationl Tradeport, New Hampshire

In May 2014, PFAAs were detected in public drinking water in one of three wells at the Pease Tradeport in Portsmouth, N.H. The suspected contamination source is firefighting foam used at the former Pease Air Force Base. In the Haven well, PFOS and PFOA were detected at concentrations of 2,500 ppt and 350 ppt, respectively, prompting the City of Portsmouth to shut down the well on May 12, 2014. PFHxS was also found at concentrations of 830 ppt in the Haven well.

Due to concern about PFAAs exposure, the New Hampshire Department of Health and Human Services (DHHS) implemented blood testing for people in communities where PFAAs were found in drinking water above the EPA lifetime health advisory level. These communities were residents from the Pease Tradeport and southern N.H. Starting in April 2015, 1,578 members of the Pease Tradeport community had their blood tested for PFOA, PFOS, PFHxS, and other PFAAs. PFOS, PFOA, and PFHxS, were detected in more than 94 percent of participants' serum samples; PFNA was also detected in the majority of participants' serum samples. Geometric mean serum values of PFOS, PFOA, and PFHxS were 8.6 µg/L, 3.1 µg/L, and 4.1 µg/L, respectively, which were statistically higher than the U.S. population [40, 41].

In 2016, DHHS expanded blood testing for PFAAs to residents of southern New Hampshire affected by firefighting foam contamination. Since 2016 and 2017, 694 residents had their blood tested. Overall, people from these communities had higher blood PFOA, PFOS, and PFHxS levels compared with the general U.S. population [42].

2.2 Children's exposures

In the general population, children's serum levels of the primary PFAAs measured are often similar or lower than adult levels. Table 3 presents results from selected biomonitoring studies of PFAAs in serum of U.S. children. A study of 598 children, ages 2 to 12 years, in 1994 and 1995, by Olsen et al., reported that children were comparable to adults in their PFOS and PFOA levels. However, children had substantially higher 95th percentile values of PFHxS and perfluorooctanesulfonamidoacetate [43]. 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 2009 study, 1-to-2-year old children had median serum levels of PFOA, PFOS and PFHxS lower than adults in NHANES from the same years [44]. This study reported no difference between genders, and increased concentrations with age.

A nationally representative subsample of 639 children, ages 3-11 years, in NHANES 2013-2014 detected PFOA, PFOS, PFHxS, and PFNA in all children at levels similar to those of NHANES 2013-2014 in adolescents and adults (Figure 7) [45].

When drinking water contains elevated PFAAs, children's exposures are frequently higher than adults. This may reflect age-specific consumption of drinking water, breastfeeding, or other age-specific behaviors that increase exposure. Pease Tradeport children had significantly higher median serum PFOS, PFOA and PFHxS, levels compared with adults and children from the general U.S. population (Figure 7) [40]. Children younger than 12 years in the C8 study, with elevated exposures to PFAAs in drinking water, especially PFOA, had higher PFOA, PFHxS, and PFNA serum levels than adults (Figure 8) [46].

A 2018 study investigated maternal transfer of PFAAs to 2-to-4-month-old infants, specifically the influence of maternal serum levels, gestational age, breast-feeding, and contaminated drinking water [47]. Maternal serum levels of PFHxS, PFOS, PFOA, PFNA, PFDA, and PFUnDA during pregnancy, and a few weeks after delivery, significantly contributed to infant PFAA serum levels, reflecting both placental and mother's milk transfer. The efficiency of PFAAs transfer from mother to infant decreased with increasing PFAAs chain length. Compared to their mothers, infants living in an area receiving PFAS-contaminated drinking water had 3-fold higher mean serum PFBS, and PFHxS levels [47]. Other studies suggest that the efficiency of PFAAs transfer from mother to infant decreases with increasing perfluoroalkyl chain length [48-51].

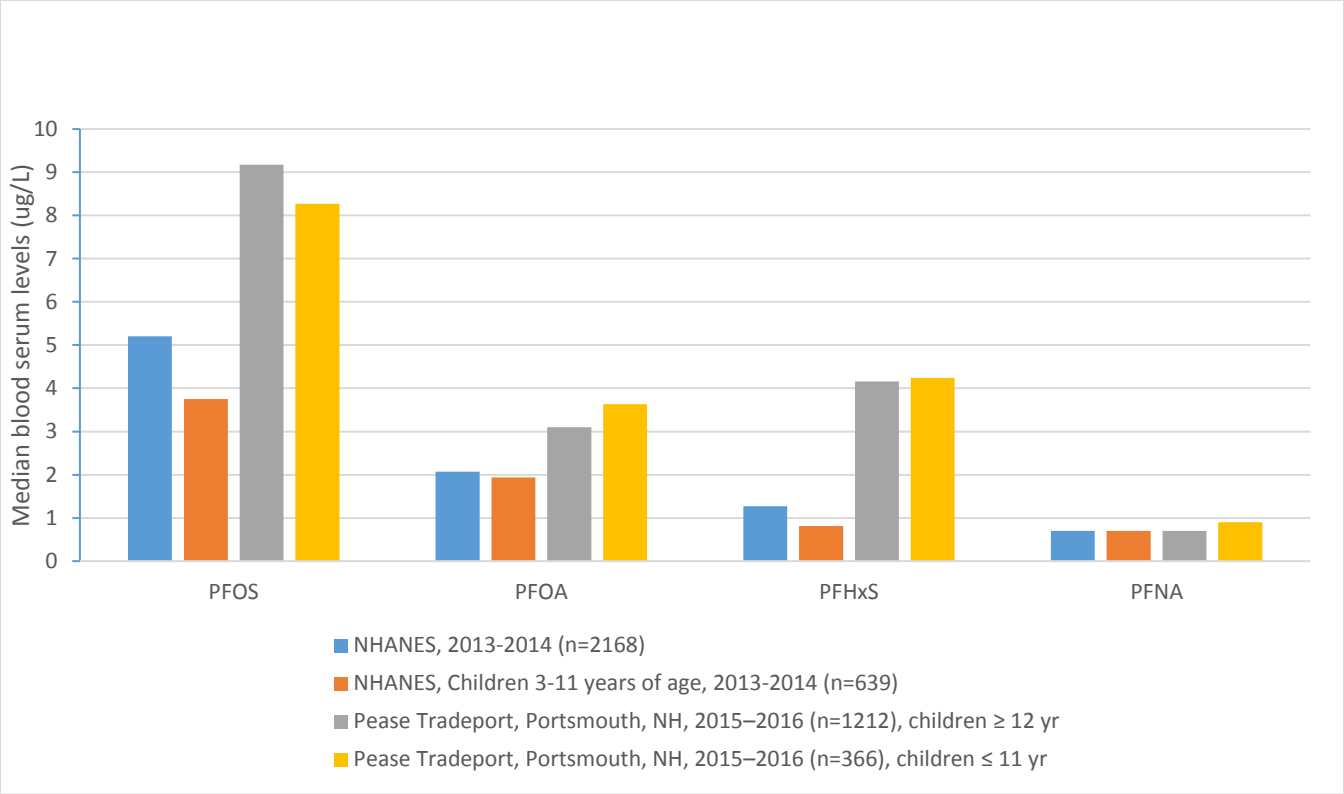

Figure 7. Median serum levels (ug/L) in adults and children NHANES general U.S. population (2013-2014) compared with children from Pease Tradeport, Portsmouth, N.H., 11 years of age and younger, and 12 years of age and older (Pease Tradeport PFC Blood Testing Program:April 2015 – October 2015) [40, 45].

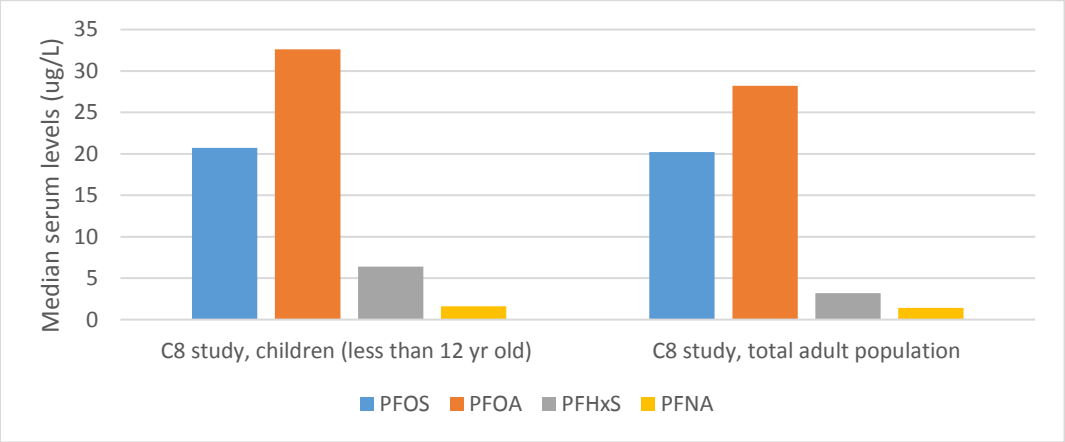

Figure 8. Population median serum levels for the C8 health study, Ohio River Valley. The study enrolled 69,030 participants over a 13-month period in 2005–2006 [46].

2.3 Firefighters

Biomonitoring studies that measured PFAAs in serum of fire fighters have been published in the U.S. and other countries. AFFF Class B foam has been used by firefighters at airports, petroleum

refineries and terminals, large chemical plants, military installations, and along rails and roads to extinguish fires involving burning petroleum and other flammable liquids. PFOS, PFOA, PFHxS, and PFNA were the most commonly detected PFAS in the blood serum of 200 California firefighters (Firefighters Occupational Exposure (FOX) study) [52]. The median serum levels of California firefighters were slightly higher for PFOS, PFOA and PFHxS compared to NHANES levels (Figure 9). In 2013, ABC News Australia reported that PFAAs levels were 20 times higher in aviation firefighters from Australia, according to a study conducted by Airservices Australia. PFOS levels were 10 to 20 times higher than the general population [53].

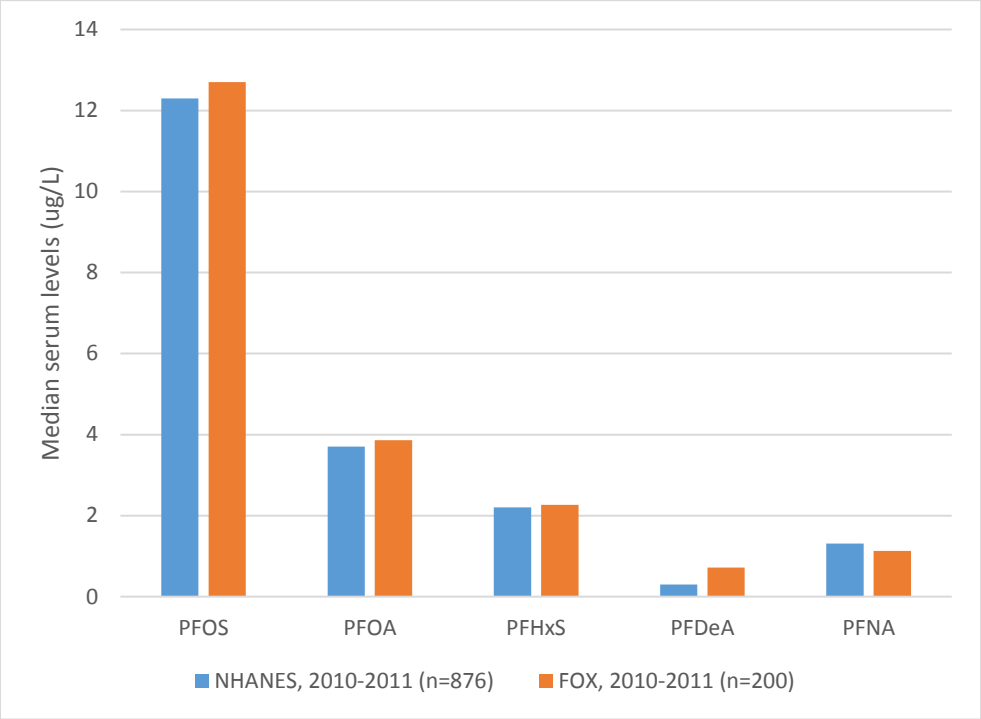

Figure 9. Median blood serum levels in California firefighters (n=200, Firefighter Occupational Exposures (FOX) study) vs. adult men in NHANES 2010-2011 (n=876).

Overall, average PFAAs levels in U.S. firefighters appear to be slightly above the general population, and this is an area that needs more detailed studies. Firefighter PFAS levels depend on the type of AFFF exposure and formulation, years on the job, gender, and the number of blood donations. Firefighters engaged in more extensive exposure with AFFF during training operations, especially older formulations, may have higher levels of PFAAs in their serum than the general population.

3.0 Sources and pathways for human exposure

Most people tested in the U.S. have some PFAS in their blood. This ubiquitous exposure appears to come from:

Non-point or diffuse sources

- Dietary exposure to PFAS in the global environment [54].
- Eating foods that have been in contact with PFAS-coated food papers [55, 56].
- Swallowing or inhaling indoor dust and air in homes, offices, and other buildings with PFAS-containing consumer products, such as treated carpets or furniture [57-62].
- Using consumer products that contain PFAS ingredients such as certain cleaning products, cosmetics, carpet treatments, car washes, water proofing sprays, and dental floss [63-65].

Local sources around a release site.

- Drinking contaminated water [66-68].
- Eating fish and shellfish or wild game from contaminated areas [30].
- Eating animal products (meat, eggs, milk) or crops exposed to contaminated feed, soils or water [69, 70].
- Work exposures: making or processing PFAS-containing materials at your job, using PFAS containing products at your job (e.g., fire fighters) [30].

While dietary intake is the primary pathway of exposure for most people, water consumption may predominate, when drinking water contains elevated levels of PFAS. The primary pathways of exposure are described in more detail below.

3.1 Drinking water

Drinking water has been a significant source of human exposure in areas where contamination has occurred. PFAS that are soluble in water, mobile in soil and persistent in the environment are prone to contaminate surface and ground water when released into the environment.

According to Hu et al, 2016, the two most significant risk factors for U.S. drinking water contamination are proximity to military fire training areas and proximity to industrial sites that make or use PFAS [71]. Leachate from landfills and land applications of biosolids have also contaminated groundwater and drinking water [72-80]. PFAS were found in groundwater monitoring wells located near these landfills. Facilities nearby that accepted industrial wastes impacted private and public wells, and municipal drinking water.

Three Washington military bases have discovered PFAAs contamination of groundwater associated with fire training areas. PFAS compounds were not manufactured in Washington, but industrial sites may have released PFAS through their use of PFAS-containing products. PFAS compounds are not regulated by existing air or water pollution regulations and are not reported under current discharge permits. Consequently, we have little information about commercial or industrial sites where PFAS may have been used or released in Washington (see more information in the uses section).

The New Jersey Drinking Water Quality Institute's Health Effects (NJDWQI) Subcommittee and others indicate that ongoing human exposure to PFOA in drinking water results in serum levels, on average, about 100 times the drinking water concentration (i.e., serum: drinking water ratio of 100:1) [81, 82]. PFOS in drinking water is estimated to result in average serum concentrations 172 times the concentration in drinking water [83, 84]. 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 [84]. 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. These ratios have not been observed in other communities with elevated drinking water levels. Levels in serum are likely to relate to how long the drinking water exposure occurred, the timing of serum sampling relative to when the exposure occurred, individual consumption and use patterns of drinking water, and other unknown factors.

3.2 Food

Food is the primary way most people are exposed to the PFAAs commonly detected in human serum [31, 85]. Only limited direct testing has been conducted for PFAS in North American foods. In the U.S. and Canada, PFOA and PFOS have been detected in snack foods, vegetables, oils and butter, meat, dairy products, wild and farmed fish, shellfish, fast food, and microwave popcorn [86, 87]. Dietary exposure studies reported a positive association between PFAS serum concentrations in California children and adults, and their consumption of butter/margarine, fish, meat products, and microwave popcorn [88]. Another study found an association between higher fish and shellfish consumption and several PFAS in a representative sample of the U.S. population [89].

The European Food Safety (EFSA) Panel on Contaminants in the Food Chain recently assessed over 20,000 PFOA and PFOS tests results from common foods sampled across the European Union. The EFSA panel concluded that fish and other seafood, meat and meat products, and eggs and egg products were important contributors to chronic exposure for PFOS to Europeans. Fish and other seafood were important contributors to chronic exposure for PFOA [90].

Some PFAS, especially shorter-chain PFAAs, may be taken up by food plants growing in contaminated soils, biosolids or water [70, 91]. PFAS that bioaccumulate build up in livestock and fish when present in their food or water [92-96]. PFAS may also migrate into food from coated food wrappers, fast food containers, microwave popcorn, and non-stick baking papers [56, 97, 98].

3.3 Consumer products

Contact with consumer products is a potential source of human exposure to PFAS. Although PFOA and PFOS are not readily absorbed through skin, residues on hands can be absorbed if swallowed. Inhalation of volatile PFAS is another route of exposure. According to EPA, 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 in the U. S. [99]. For example, disproportionately high serum levels of PFHxS, PFOS and PFOA in one family was linked to repeated household carpet treatments conducted with a Scotchgard product [64]. High PFAAs levels were identified in ski waxes, leather samples, outdoor textiles and some baking papers [100]. A large number of other consumer products may also contain PFAS

ingredients including cleaning products, automotive products, stain-resistant carpets and upholstery, water proof clothing and gear, and personal care products including cosmetics and dental floss. Better studies are needed to understand their contribution to exposure.

Carpets

A 2016 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). 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. An analysis of health risk (based on an oral derived no effect level [DNEL] of 0.03 µg/kg day) concluded that rugs in the study were not a health hazard for children [101]. Short-chain PFAS chemistries (e.g., 6-carbon side-chain fluorinated acrylate and methacrylate polymers, and fluorosurfactants) have largely replaced long-chain PFAS in these household items. In February 2018, the California Department of Toxic Substances and Control proposed to list PFAS in carpets and rugs as priorities for action under the Safer Consumer Products regulation. Concerns included the hazard traits and potential for long-term exposure to people and the environment. This proposed action is still under consideration. PFOA, PFHxS and PFOS may still be released from older carpets, floor wax, leather, apparel, upholstered furniture, paper and packaging, coatings, rubber, and plastics.

Cosmetics

Polymeric (e.g., fluoropolymer, perfluoropolyether polymers, and side-chain fluorinated polymers) and non-polymeric (perfluoroalkyl and polyfluoroalkyl) PFAS compounds have been detected in personal care products and cosmetics [97]. Some examples include dental floss and micro powders used in creams and lotions, cosmetics, shampoos, nail polish, eye makeup, and denture cleaners.

PFAAs, including PFOA, have been detected at low levels in personal care products such as cosmetics and sunscreens. The levels ranged from non-detect to 5.9 µg/g for cosmetics and from non-detect to 19 µg/g for sunscreens. High concentrations of PFCAs (35 µg/g) were found in talc treated with polyfluoroalkyl phosphate esters (PAPs) [102] A recent survey on cosmetics was conducted on the Danish market. The results from the survey showed that a variety of fluoroalkyl substances and other fluorinated compounds are present in cosmetic products. With the exception of sunscreens, the highest measured concentrations were found in foundations (2,160 ng/g) for PFOA [103].

3.4 Indoor air and dust

As certain consumer products degrade with normal wear and tear, they may contribute to PFAS levels in indoor dust and air. Indoor air is inhaled by occupants and indoor dust is both inhaled and swallowed, especially by young children who crawl on the floor and engage in hand-to-mouth activity.

In 2000-2001, a number of PFAS were measured in U.S. indoor dust samples collected from 112 homes and 10 day-care centers in North Carolina and Ohio. PFOA, PFOS, and PFHxA were the most commonly detected (median concentrations of 142, 201, and 54.2 ng/g, respectively). Some

dust samples had very high concentrations of PFOS and PFHxS (up to 12,100 and 35,700 ng/g respectively) [104]. Much lower concentrations were also detected in all house dust samples (n = 18) from Vancouver Canada. PFOA, PFOS, and PFHxA had median values of 38, 37, and 35 ng/g, respectively. PFOA, PFOS, and PFHxS were also routinely detected in indoor dust from homes, offices, and vehicles in Boston, Mass. in 2009 [62].

Another Boston study sampled PFAS in air in 30 offices in seven buildings, and compared this to serum levels in 31 office occupants. This Boston study also detected a range of newer PFAS in more than 90 percent of the indoor air samples of offices, and reported maximum levels of 70 ng/m^3 for 8:2 fluorotelomer alcohol (8:2 FTOH), 12.6 ng/m^3 for 10:2 FTOH, and 11 ng/m^3 for 6:2 FTOH [61]. Collectively, FTOHs in air significantly predicted PFOA in serum of office workers ($p < 0.001$) and explained approximately 36 percent of the variation in serum PFOA concentrations. PFOS in serum was not associated with air levels of perfluorooctane sulfonamides (PFOSAs)/perfluorooctane sulfonamido ethanols (N-EtFOSEs). The compounds 8:2 FTOH and 10:2 FTOH are precursors to PFOA, and represent a potential inhalation pathway.

A home where carpets had been treated eight times with Scotchgard formulations over 15 years had elevated serum levels of PFHxS, PFOS and PFOA in house dust (2780, 1090, 550 ng/g dust respectively) and in the serum of family members (PFHxS ranged 27.5-423 ng/mL, PFOS ranged 15.2-108 ng/mL, and PFOA ranged 2.40-9.23 ng/mL). The authors concluded that the ingestion and/or inhalation of household dust was the likely pathway of their elevated exposure [64].

In another exposure study, PFOA, PFOS and PFNA measured in serum of pregnant women in Vancouver, Canada, in 2007 to 2008, correlated with precursor chemicals 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 N-methyl perfluorooctane sulfonamido ethanol (N-MeFOSE) and serum PFOS [105]. The median PFOA levels in dust observed in the U.S. and Canada are higher than the levels found in European countries [106]. This may be due to differences in PFAS use and sources.

4.0 Human health concerns

The toxicology and health research on the most commonly detected PFAAs compounds were recently reviewed and assessed by several authoritative agencies including the Environmental Protection Agency (2016) [107, 108], the Agency for Substances and Disease Registry (2015) [31] and (2018) [109], the National Toxicology Program (NTP) (2016) [110], the International Agency for Research on Cancer (IARC) (2014) [111], Health Canada (2016) [112, 113], and the EFSA 2018 [90]. EPA and the NTP are collaborating on a risk-based approach for conducting additional PFAS toxicity testing and facilitate health assessments [114]. Health-based-values derived in these assessments are in Table 4.

While firm conclusions about the effects of PFAS on human health are not possible due to limitations of animal and epidemiological studies, and inconsistency in findings across different human populations, there is broad agreement in these authoritative reviews that elevated PFOA and PFOS exposure in humans over an extended period may contribute to the following outcomes:

- Increased serum levels of liver enzymes and cholesterol.
- Immune system suppression and reduced immune response to vaccines in children.
- Lower birth weights, and altered growth and development children.
- Altered hormone signaling, especially thyroid hormones and testosterone.
- Increased time to get pregnant, and increased rates of pregnancy-induced hypertension and preeclampsia.
- Increased risk of thyroid disease.
- Increased some types of cancers, including kidney and testicular cancer.

4.1 PFAA concerns

PFOS and PFOA are the best studied and most prevalent PFAAs measured in human serum. The primary human health concerns associated with these two compounds and other closely related PFAAs are discussed below.

Liver toxicity and cholesterol levels

In experimental animals, the liver is a sensitive target for exposures to a number of PFAAs. Specific toxicity observed includes increased liver weight, fat accumulation in liver cells, and decreased serum cholesterol and triglyceride levels. Degenerative changes in the liver have been observed [107, 108].

Humans do not appear to be as sensitive to liver injury as rats, mice, or monkeys. In human observational studies, increased serum levels of total cholesterol and low-density lipoprotein (LDL) cholesterol have been associated with higher serum levels of PFOA, PFOS, and PFNA [115-117]. Altered liver enzyme levels in serum, suggestive of liver damage, have been associated with higher serum levels of PFOA, PFOS, and PFHxS [118-120].

Immune toxicity and hypersensitivity reactions

A 2016 systematic review by the NTP concluded that PFOA and PFOS are "presumed immune hazards" to humans, based on evidence that they suppress the production of antibodies in response to an antigen in experimental animals and people [121]. Mice exposed to higher levels of PFOA or PFOS produced fewer antibodies when challenged with an antigen. Human evidence includes observations of reduced antibody response to childhood vaccines associated with higher serum levels of PFOS, PFOA, PFHxS, and PFDA [122-124]. The NTP review did not find consistent associations between PFOS or PFOA exposure and lowered resistance to infectious disease in people [110].

In addition, PFOA has been associated with a single autoimmune outcome (ulcerative colitis) in two highly exposed populations [125, 126] and with hypersensitivity outcomes such as asthma in some general population studies [127, 128]. Serum PFOA was not associated with asthma in a large occupational study [125]. NTP concluded that there was high level of confidence that PFOA increased hypersensitivity-related outcomes in animals but only low confidence in evidence from human studies [110].

Developmental toxicity

There is strong evidence of developmental effects of PFOA and PFOS in experimental animals including fetal loss, altered fetal bone development, lower birth weight, reduced pup survival, altered behavior in offspring, and altered timing of sexual maturation in offspring at adolescence [129-133]. PFNA produced many similar effects in mouse studies [134, 135].

The most consistent finding in humans of developmental effects for PFOA, PFOS and PFHxS is lower birth weight [108, 136, 137]. A meta-analysis reported that, for every 1 ng/mL increase in maternal serum concentration, there was an associated 14.7 gram decrease in birth weight for PFOA and 2.7 gram decrease in birth weight for PFOS [138]. Slight delays in the age of puberty have been associated with serum PFOA (girls) and with serum PFOS (girls and boys) [139-141].

Reproductive toxicity and pregnancy conditions

In some rodent studies, decreased serum testosterone, and changes in serum estradiol and sperm parameters were observed following exposure to PFOS [142-144] PFNA [145] and perfluorododecanoic acid (PFDoDA) [146]. No declines in fertility were evident in rodent testing for PFOS, PFOA, PFHxS or PFBS [130, 132, 147, 148]. Mammary gland development was delayed in female mice exposed to PFOA during fetal development and lactation [149]. The delays did not impair successful nursing of their young [150].

In a general population study, Vested et al. 2013 found that higher maternal serum PFOA was associated with lower sperm count in boys when they reached young adulthood [151]. In a highly exposed population in Italy (especially to PFOA) young adult men had higher serum PFAAs levels, reduced serum testosterone, and semen quality and shorter penis length and anogenital distance than a comparison population in an uncontaminated area [152]. Some epidemiological studies report reduced fertility associated with higher serum PFOA PFOS, PFHxS [153-155]. Other studies have looked for, and not found, these associations with fertility. Studies of communities with elevated exposure have looked for, and generally not found associations between PFOA and birth defects, miscarriage or pre-term birth. Other PFAAs are not as well studied.

A large study of an exposed community (C8 Health study) found suggestive evidence that PFOA increases the risk of pregnancy-induced hypertension and preeclampsia, both potentially serious conditions for pregnant women [156-159].

Hormone disruption and thyroid disease

Some alterations in thyroid hormone levels have been observed in laboratory animals exposed to PFOA, PFOS, or PFDA. Thyroid toxicity (hyperplasia, hypertrophy) has been observed in laboratory animal studies of PFHxS and PFBA but may be secondary to liver toxicity [147, 160].

There is limited human evidence of increased risk for thyroid disease and hypothyroidism, especially among women, associated with PFOA and PFOS and PFHxS [161-163]. A number of other studies looked for, and did not find, associations. Inconsistent associations have been reported across human studies between serum PFOA and PFOS and serum levels of thyroid stimulating hormone (TSH), triiodothyronine (T3), or thyroxine (T4) [163-170].

Cancer

Chronic exposure studies in rats have found increased tumors in liver (PFOA, PFOS), pancreas and testes (PFOA), and thyroid (PFOS) [144, 171, 172].

In 2016, EPA concluded that there was suggestive evidence of carcinogenic potential of both PFOA and PFOS in humans. For PFOA, EPA relied primarily on findings of the C8 study, and for PFOS, the evidence primary came from observations of liver and thyroid adenomas in chronic rat bioassays [107, 108].

The IARC classified PFOA as possibly carcinogenic to humans (Group 2B) based on limited evidence in animals, and a higher risk of testicular and kidney cancer associated with PFOA exposure in the C8 health Study [111, 173]. PFOS has not been classified by IARC.

4.2 Shorter chain fluorinated alternatives (PFAS)

While the PFAAs mentioned above readily bioacummulate in people, biomonitoring studies indicate that PFAS with shorter carbon chains (e.g., PFBA, PFBS, and PFHxA, 6:2 FTOH) are much less persistent in human serum [174]. Only two short-chain PFAAs have been measured by the CDC since 1999. PFBS and PFHpA have been infrequently detected, and the levels are relatively low compared to other PFAAs [175]. Short-chain PFAS have been detected in breastmilk. For instance, perfluoropentanoic acid (PFPeA), PFHxA, PFHpA, and PFBS were commonly detected in breast milk among Korean women [176]. Polyfluoroalkyl phosphate surfactants (PAPS) (e.g., 4:2 diPAP, 6:2 diPAP, 8:2 diPAP, and 10:2 diPAP) were detected in Canadian breast milk [177].

There is limited information on the exposure and toxicity for most shorter-chain PFAS. There is even less information on their commercial precursors (e.g., perfluoroalkyl phosphinic acid (PFPiA), perfluoroether carboxylic and sulfonic acids (PFECAs and PFESAs) [178-180] and environmental degradates such as 5:3 FTCA and 6:2 FTSA.

Some preliminary concerns about some short-chain alternatives compared to long-chain substances include [179]:

- Higher volatility may increase inhalation exposures (e.g., fluorotelomer alcohols precursors and perfluorobutane sulfonamide alcohols).
- Higher solubility in water makes short-chain PFAAs, such as PFBA and PFBS, more mobile in soil and sediment.
- Short‑chain PFAS still have the potential for long-range transport. They are detected in remote regions and show a wide spread distribution [181].
- Some drinking water treatments, such as activated carbon systems, are less efficient at removing short-chain PFAS [182].
- Short-chain PFAS are more easily leached from biosolids (produced during wastewater treatment) [183].
- Short-chain PFAS are more easily taken up from soil by certain food crops [183].
- Short-chain PFAS may more easily cross the placenta to the fetus [168].
- Short-chain PFAS are still highly resistant to microbial degradation. Perfluoroether carboxylic acids and perfluoroether sulfonic acids are environmentally stable and mobile, and have a high global contamination potential.

- Although short-chain PFAS are more rapidly excreted from the human body, their prevalence in the environment may contribute to chronic exposures.

4.3 Toxicology and health effects of short-chain perfluoroalkyl acids (PFAAs)

Toxicity information on four common short chain PFAAs are reviewed below.

Perfluorobutanoic acid (PFBA)

The serum elimination half-life of PFBA in humans was estimated to be 72 hours for males and 87 hours for females [184]. In laboratory animal studies, exposure to high levels of PFBA resulted in increased liver weight, changes in thyroid hormones, and decreased cholesterol [185, 186]. Other effects of PFBA exposure included delayed development [187].

In a 90-day study of rats, 30 mg/kg body weight per day resulted in increased liver weight and reduced thyroid hormone in males [185]. 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 no observable adverse effect level (NOAEL)[4] for male rats was 6 mg PFBA/kg-day in 28-day and 90-day 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 [186].

Exposure to high doses of PFBA during pregnancy (up to 350 mg/kg-day) did not adversely alter neonatal survival or growth in mice, although some developmental delays were noted [188]. The relative lack of adverse developmental effects of PFBA (compared to PFOA) is in part, due to the rapid elimination of this chemical.

Studies of health effects of PFBA in humans are lacking.

Perfluorobutanesulfonate acid (PFBS)

PFBS has an estimated serum elimination half-life of 25.8 days in humans [189]. In laboratory animals, PFBS is less toxic to the liver than PFOS, but has the potential to damage the liver, kidneys, and alter cholesterol levels and blood chemistry [184, 190]. The most sensitive effect appears to be changes in blood chemistry [148].

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 [190].

In a two-generation reproduction study with the potassium salt of PFBS in rats exposed to 0, 30, 100, 300 and 1,000 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) at the 300- and 1,000-mg/kg-day doses. A NOAEL for the parental generations (F0) was 100 mg/kg-day. Postnatal survival, developmental, and growth of pups was unaffected in F1 and

[4] NOAEL is the dose of a chemical at which there were no statistically or biologically significant increases in frequency or severity of adverse effects seen between the exposed population and its appropriate control. Although effects may be produced at this dose, they are not considered to be adverse.

F2 generations, except for a slight delay in onset of puberty and weight gain in F1 males in the highest dose.[191].

Studies in humans are lacking. Exposure to PFBS was associated with an increased risk of endometriosis-related infertility in a study of Chinese women [192].

Perfluorohexanoic acid (PFHxA)

The serum half-life elimination in humans exposed to high concentrations of PFHxA was estimated to be within 14 to 49 days [193]. In laboratory animals, PFHxA toxicity in the liver was generally mild and reversible. In a 90-day study, rats fed with the sodium salt of PFHxA (at 0, 20, 100 or 500 mg/kg bw-day) had significantly increased relative liver weights at the highest dose. Mild reversible increases 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 [194, 195]. Increased thyroid weight and minimal hypertrophy of the thyroid follicular epithelium were observed in female rats at 500-mg/kg-day dose [194, 195]. Effects on kidney and tubular degeneration was observed in a rodent study [196]. In reproductive and developmental toxicity studies, PFHxA was less toxic than PFOA in mice and rats. [195, 197]. Decreased pup birth weight and pup mortality in mice were seen at the highest doses tested (175 mg/kg body weight) [187, 198]. A cancer study in rodents of PFHxA was negative for tumors or cancer [196].

Studies on potential health effects of PFHxA in people are lacking.

Perfluoroheptanoic acid (PFHpA)

There is very limited data in laboratory animals to assess PFHpA. *In vitro* studies showed that PFHpA is as biologically active as PFOA in activating PPARα, however this activity was not evident *in vivo*, probably because PFHpA was rapidly excreted, and did not concentrate in the rodent liver [199-203]. People do not excrete PFHpA as rapidly as rodents. In a study of 11 professional ski waxers, it took between 31 and 123 days after exposure ceased for their individual serum level of PFHpA to drop by half. A study of Chinese adults reported a longer estimated half-life in human serum (1.5 years) [204, 205].

Studies in humans are lacking. Fu et al. 2014 did not find that PFHpA in serum of adults was associated with increased serum lipids, particularly total cholesterol and LDL cholesterol at environmental exposure levels [57]. Epidemiological studies investigating immuno-toxicity, did not find associations between serum PFHpA levels and diphtheria or tetanus antibody levels in adults [203], or risk of asthma diagnosis, eczema, or wheezing in children [206]. Mattsson et al. 2015 reported that the risk of coronary artery disease was higher in individuals with serum PFHpA levels in the 3rd quartile of exposure, but not the 4th (highest) exposure quartile [207].

5.0 Public health advice

5.1 Washington public health advice for PFAS in drinking water

Since EPA established drinking water health advisories for PFOA and PFOS in 2016, the Washington State Department of Health has recommended that public water systems follow the LHAL for PFOA and PFOS. The EPA advisory is intended to provide a margin of health protection, including for the most sensitive groups, over a lifetime of exposure to these contaminants from drinking water. EPA's advisory levels of 0.070 µg/L (or parts per billion) for PFOA and PFOS combined are based on the best available science at the time. EPA used complex modelling to derive equivalent human doses from animal doses for the most sensitive endpoint thought to be relevant to humans. EPA also used conservative assumptions about drinking water ingestion rates, and relative source contribution to derive drinking water advisories (see Table 4). EPA health advisories are non-regulatory and non-enforceable standards.

There are no enforceable federal drinking water standards for PFAS compounds. EPA is currently in the process of making a regulatory determination about whether to set maximum contaminant levels (MCLs) for PFOA and PFOS. If EPA decides to develop MCLs, the process of establishing MCLs takes years before regulations are adopted.

In the meantime, DOH supports the Washington State Board of Health (SBOH) to develop state drinking water standards for PFAAs. The SBOH, in response to an October 2017 petition, is considering whether to set a state drinking water standard or advisory level for PFAAs detected in state drinking water. DOH is recommending that the board consider the state action level (SAL) process for PFAAs. This will provide a quicker response and allow for the development of new toxicological data on a broad set of PFAS identified from preliminary exposure studies that capture potential occurrence in the environment. The goal is to implement state standards to address the PFAAs of highest concern to Washington drinking water, and support the regulatory framework for drinking water cleanup and mitigation. We expect a proposed rule in 2019 with rule adoption by early 2020.

Until the SBOH completes its rule-making standards, our recommendations for private well owners, community and public drinking water systems are as follows:

- Review the well log, well depth and casing design, and hydrology of the area to assess your risk, if PFAAs contamination has been detected near your water source. We encourage systems to participate in free voluntary water testing for these contaminants, when invited to do so by DOH or the military.
- Use a validated method, such as EPA method 537, rev 1.1., when testing for PFAAs in drinking water.
- If water testing shows that the concentration of PFOA and PFOS combined in drinking water is more than 0.070 µg/L, use another source of water for drinking and cooking, food preparation, brushing teeth, and any activity that might result in ingesting water.
- As an interim measure, when PFHxS, PFNA, PFHpA, PFOA, and PFOS combined are above 0.070 ppb, we recommend that water utilities provide a public notice to their customers. The notice should encourage pregnant and nursing women, women planning

to become pregnant, and parents, guardians, or caregivers of infants to consult with their healthcare provider about drinking the water.

It is important to acknowledge that we are in the midst of a very active research effort to understand the human health impacts of exposure to various PFAS. Health researchers continue to study health outcomes in human populations with elevated exposures. EPA is using rapid toxicity-screening tools to investigate potential biological activities of 75 compounds that are representative of the various classes of PFAS chemistry. Industry and independent scientists are publishing new findings regularly in peer-reviewed scientific literature. The public health advice reflects our best judgement for protecting human health while waiting for a clearer picture from the evolving science. Our scientists are following this research to inform our advice.

5.2 Drinking water health advisories set by other states, EPA, and other countries

Eight states have established independent standards for PFAAs in drinking water. Most are advisory and only New Jersey and Vermont have adopted enforceable drinking water limits, called MCLs. A current listing of state and international standards and guidance values for PFAAs in groundwater, drinking water, and surface water/effluent wastewater is maintained by the Interstate Technology and Regulatory Council (ITRC). We refer readers to this resource as the information is rapidly changing. The ITRC intends to update this as new information is gathered [208] (https://pfas-1.itrcweb.org/fact-sheets/).

In November 2018, EPA released proposed reference doses (RfDs)[5] for Gen X, and PFBS for public review and comment period (Table 4). Although these values have been through peer-review, they are draft values and may change. It is unclear whether EPA health advisories for drinking water will follow. North Carolina worked with EPA to set a state drinking water advisory of 140 ppt for hexafluoropropylene oxide dimer acid (Gen X).

5.3 Assessment and advice for PFAS contaminants in recreational fish

Recreational, subsistence fishers, and low-income or tribal communities that consume fish from urban waters, and areas downstream of wastewater treatment plant discharges, may have higher exposures to PFAS that accumulate in fish. Serum of fish and shellfish consumers who participated in NHANES in 2007-2014 had higher levels of several PFAS [89]. Researchers determined that consumers of fish and shellfish are at higher risk of exposure to certain PFAS than non-consumers. In Washington, PFOS was detected by Ecology surveys in Washington freshwater fish at levels up to 87 ng/g in fillets (see Environmental chapter).

International studies indicate that some PFAAs, such as PFOS, PFHxS and PFOA, can reach very high levels in serum of fishermen who eat fish from industrially impacted areas [30]. A recent study also identified a number of novel PFAS in fish from the Yangtze River and Tandxun Lake, China (including 6 sulfonate classes, 2 amine classes, 1 carboxylate class, and 1 *N*-heterocycle class) [209]. The discovery of these PFAS in fish demonstrates bioavailability and

[5] A reference dose is an estimate of the amount of a chemical a person can ingest daily over a lifetime that is unlikely to lead to adverse health effects.

the potential for bioaccumulation for these compounds or their precursors, whose toxicity and environmental fate has not been studied.

Several states with localized surface water contamination have developed fish advisories for PFAAs, including Alabama, Michigan, Minnesota, New Jersey, Oregon, and Wisconsin (Table 7). Other states are considering fish advisories. 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. New Jersey issued a consumption advisory for 12 species of fish that were found to contain chemicals belonging to the PFAS family [210]. Michigan has developed Eat Safe Fish Guidelines for PFOS across numerous waterbodies [211]. These guidelines are set to be protective for everyone including children, pregnant and breastfeeding women, and people with existing health problems such as cancer or diabetes.

There are currently no fish consumption advisories for PFAAs in Washington. DOH determined provisional health-based screening levels for PFOS and PFOA (23 µg/g and 8 µg/g for both the general population and high consumers, respectively). DOH reviewed fish data collected by Ecology in 2008 and 2016 and found that some fillet tissue levels exceeded these values. PFOS was detected in Washington freshwater fish at levels up to 87 ng/g in fillets (see Environmental chapter). DOH determined that the current dataset for any given fish species for waterbody was too small to provide an adequate basis for a fish consumption advisory, but the agencies are working together to collect and assess additional data to determine whether a fish advisory is necessary.

5.4 Risk-based water sampling – testing drinking water wells

DOH used risk factors for PFAS in water reported by Hu et al. 2016 [71] to generate a map of areas more likely to have drinking water impacted by PFAS. Since there are no PFAS manufacturing plants in Washington, we focused on locations where AFFF was potentially released. Specifically, we mapped military land, airports certified to use AFFF, known fire training facilities, and sites with a record of AFFF releases obtained from the Washington State Department of Ecology spills program. Limitations of this map include: no comprehensive list of fire training centers, lack of records of where fire departments and other users may have trained with AFFF, and voluntary and incomplete reporting of AFFF spills to Ecology. Despite the limitations, the map provides useful information for the preliminary evaluation of risk.

We used the map to identify drinking water sources to prioritize for voluntary testing. Community and transient non-community Group A sources, within two miles of properties identified as a potential point source, were considered potentially at risk. We found that potential point sources of PFAS contamination related to AFFF were distributed across Washington. We also identified numerous public water systems within two miles of potential point sources that were not tested for PFAS contamination as part of UCMR3 (Figure 10).

In 2017 and 2018, DOH offered free voluntary PFAS sampling to these 300 water systems (up to 500 water samples anticpated) to understand occurrence of these chemicals in drinking water in our state, and to know if the water is safe to drink. Costs of sampling are being covered by the EPA state revolving fund. DOH is contracting with the University of Washington Tacoma, for

sample analysis of 14 PFAS chemicals. Sample collection and results reporting are expected in 2019.

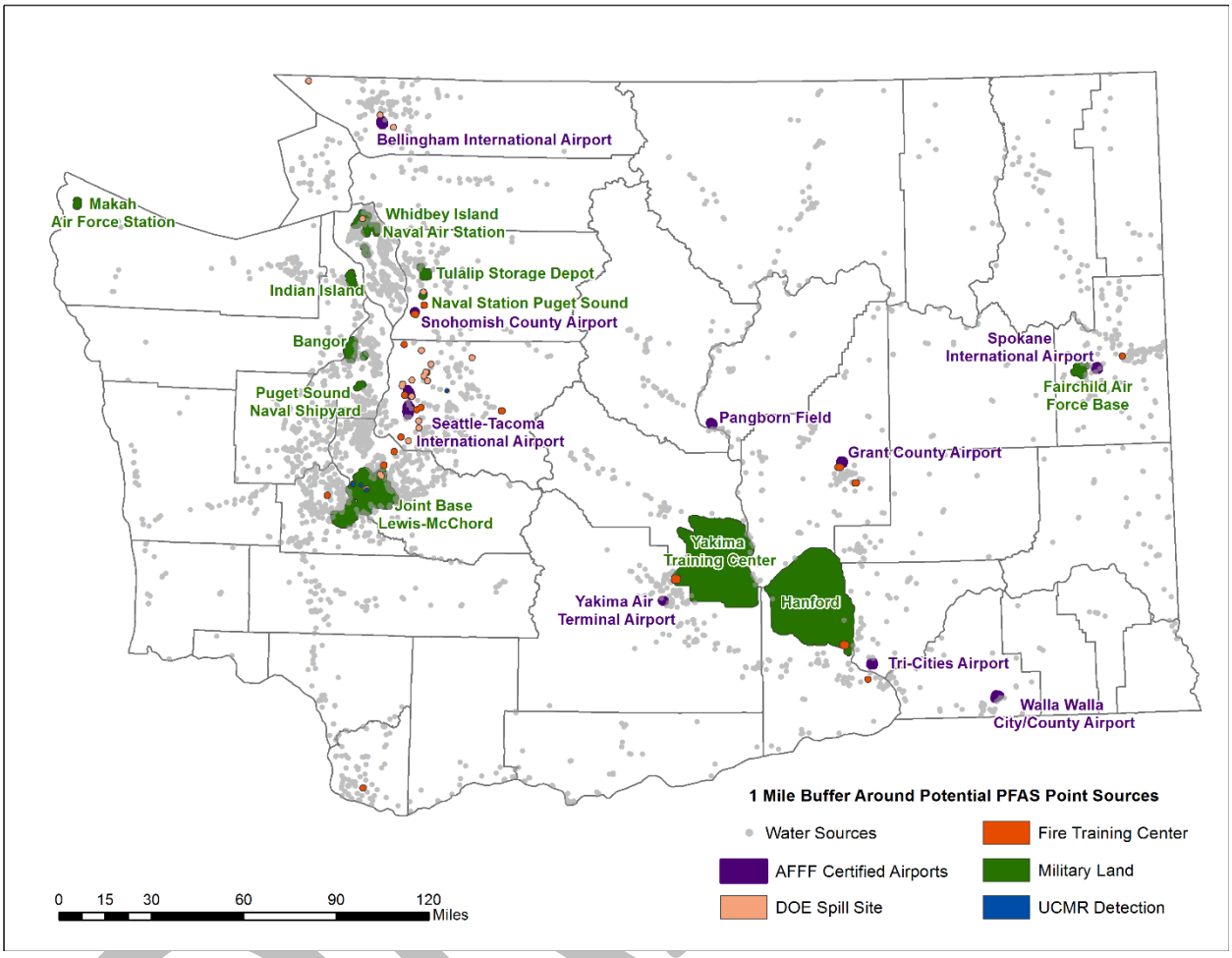

Figure 10. Potential PFAS sources related to the use of AFFF in Washington State.

5.5 Additional tables

Table 3. Median/geometric mean concentrations of PFOS, PFOA, PFHxS, PFNA, and PFDA in vulnerable populations from select studies (*n* > 30 participants) 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	USA NHANES	[212]
2003-2004	20[b]	1.59	0.73	1.64	0.35		Dried blood spot, infant (newborn screening program)	New York	[213]
2002-2005	185	5.2	1.4				Maternal blood	Sapporo, Japan (Hokkaido Study)	[214]
2004-2005	101	16.6	2.13	1.82	0.73		Maternal serum at 24-28 weeks	Canada	[215]
	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		
2004-2005	299	4.9[a]	1.6[a]	-	-		Umbilical cord serum	Maryland	[216]
2003-2006	242, 241, 225[c]	13.2	5.4	1.5	0.9	0.2	Maternal serum measured at 16 ± 3 weeks gestation	Cincinnati, Ohio HOME study	[217]
2003-2006	71	12.7 (100)	4.8 (100)	1.2 (98.6)	0.82 (100)	0.2 (97.2)	Maternal serum, at16 weeks, (Fd, %)	Cincinnati, Ohio Multi-ethnic cohort of women,	[218]
		8.5 (100)	3.3 (100)	1.2 (93)	0.66 (100)	0.2 (90.1)	Maternal serum, at 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, %)		

		Concentration (µg/L)							
Year (s)	**n**	**PFOS**	**PFOA**	**PFHxS**	**PFNA**	**PFDA**	**Sample type**	**Location**	**Ref**
2005-2006	252	7.8	1.5	0.97			Maternal serum at 15 weeks	Alberta, Canada	[219]
2007	98	2.1[a]	0.9[a]	0.4[a]	0.3[a]		Dried blood spot, infant	Texas	[220]
2005-2008	100	4.44	1.47	0.58	0.36		Umbilical cord serum	Ottawa, Canada	[221]
2007-2009	391	4.66 †	1.53	0.44	0.56	0.23	Serum, pregnant women	Norway, Mother-and-child contaminant Cohort study (MISA)	[222]
2008-2009	67	6.15	4.5	1.25	1.7	0.35	Children's Serum, 2-8 years old	California	[88]
2009	300	4.1	2.85	1.2	1.2	<0.2	Children's Serum, boys and girls 0-12 years	Dallas, Texas	[44]
2008-2011	1743	4.7/ 4.59	1.7/ 1.66	1/ 1.01			Maternal plasma, at 14 weeks of gestation	Canada, MIREC study (10 cities across Canada)	[154]
2011-2013	64	1.6	0.885				Cord plasma (umbilical cord blood)	Netherlands	[223]
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	[21]
Populations with higher exposure (C8 health study)									
2005-2006	12,476	22.7	69.2				Blood serum	Add location Children 1-17.9 years (Frisbee et al. 2010)	[116]

[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.

6.0 Health-based guidance values

EPA develops RfDs [6] and health advisory levels to guide human health protection. The reference doses for PFAAs are based on the most sensitive effects observed in animal studies that were deemed relevant to humans (Table 4). Health research and exposure studies were also reviewed and used to support the selection of critical effects and extrapolate from rodents to humans.

Table 4. EPA's reference doses and health advisories levels for drinking water [224, 225].

Chemical	EPA critical effect	Point of departure	Uncertainty factor (UF)	Critical Study	EPA's chronic RfD (mg/kg-d)	Drinking Water Equivalent Level (DWEL)(µg/L)	Lifetime HA for drinking water (µg/L)
PFOA (2016)	Developmental effects (skeletal effects and accelerated puberty in male pups	0.0053 mg/kg-day ($LOAEL_{HED}$)	300	Lau et al. 2006	0.00002	0.37	0.07
PFOS (2016)	Developmental effects (e.g., decreased pup body weight)	0.00051 mg/kg-day ($NOAEL_{HED}$)	30	Luebker et al. (2005b)	0.00002	0.37	0.07
PFBS (2018 draft)	Thyroid effects in offspring (decreased serum T4). Also kidney effects	$BMDL_{20}$ = 4.2 mg/kg-day	300	Gestational exposure study (Feng et al., 2017)	0.01		

[6] A reference dose is an estimate of the amount of a chemical a person can ingest daily over a lifetime that is unlikely to lead to adverse health effects.

Chemical	EPA critical effect	Point of departure	Uncertainty factor (UF)	Critical Study	EPA's chronic RfD (mg/kg-d)	Drinking Water Equivalent Level (DWEL)(µg/L)	Lifetime HA for drinking water (µg/L)
GenX* (2018 draft)	Single cell necrosis in the liver	$BMDL_{10}$ = 0.023 mg/kg-day	300 (chronic) 100 (subchronic)	Reproductive/ developmental toxicity study; DuPont-18405-1037(2010)	0.00008		

* GenX refers to hexafluoropropylene oxide (HFPO) dimer acid and its ammonium salt
BMDL – Benchmark dose level

6.1 Agency for Toxic Substances and Disease Registry (ATSDR) minimal risk levels (MRLs)

On June 20, 2018, ATSDR issued a revised draft Toxicological Profile for Perfluoroalkyls for public comment. In this revision, the agency derives "provisional intermediate Minimal Risk Levels" for PFOA, PFNA, PFOS, and PFHxS (Table 5). The calculated MRLs are seven and 10 times lower than EPA's reference dose level for PFOA and PFOS, respectively. ATSDR states that these provisional MRLs are intended to serve as "screening levels" for identifying contaminants and potential health effects that may be of concern at hazardous waste sites and should not be used for regulatory action, including to define clean-up or action levels.

The four PFAAs MRLs are estimates of the amount of a chemical that a person can eat and drink each day over an intermediate period (2 weeks to 1 year) without detectable risk to health. MRLs are intended to serve as a tool to help public health professionals determine areas and populations potentially at risk for health effects from exposure. MRLs are "screening levels" for identifying contaminants and potential health effects that may be of concern at hazardous waste sites and should not be used for regulatory action, including to define clean-up or action levels [226].

Exposure above the MRL does not mean that health problems will occur. It may instead act as a signal to look more closely for exposures occurring at a particular site. To develop a drinking water screening value, ATSDR uses the Environmental Media Exposure Guidelines (EMEGs) for intermediate exposures (15-364 days). ATSDR has derived EMEGs for these PFAAs [227].

Table 5. ATSDR minimal risk levels and Environmental Media Exposure Guidelines derived for PFAAs [227, 228].

	Critical effect	Point of departure (mg/kg-day)	UF	Critical Study	Oral intermediate ATSDR, MRLs (mg/kg-d)	Drinking water
PFOA	Neurodevelopmental and skeletal effects in mice	0.000821 (LOAEL $_{HED}$)	300	Koskela et al. 2016; Onishchenko et al. 2011	0.000003	78 ppt (adult) 21 ppt (child)
PFOS	Delayed eye opening and decreased pup weight in rats	0.000515 (NOAEL $_{HED}$)	30 & 10	Luebker et al. 2005a	0.000002	53 ppt (adult) 14 ppt (child)
PFNA	Decreased body weight and developmental delays in mice	0.001 (NOAEL $_{HED}$)	30 & 10	Das et al. 2015	0.000003	78 ppt (adult) 21 ppt (child)
PFHxS	Thyroid follicular cell damage in rats	0.0047 (NOAEL $_{HED}$)	30 & 10	Butenhoff et al. 2009a	0.00002	517 ppt (adult) 140 ppt (child)

LOAEL - Lowest-observed-adverse-effect level. The lowest exposure level of chemical in a study, or group of studies, that produces statistically or biologically significant increases in frequency or severity of adverse effects between the exposed population and its appropriate control.
NOAEL - No-observed-adverse-effect level.
HED – Human equivalent dose

6.2 International guidance values

German human biomonitoring commission (HBM Commission)

In 2017, the German Human Biomonitoring Commission (HBM Commission) derived health-related guidance values in blood plasma for PFOA and PFOS. The HBM I value represents the concentration of a substance in human biological material at which, and below, there is no risk of adverse health effects, and no need for action. Based on an assessment of literature on human epidemiological studies, and on animal studies, the HBM commission derived an HBM I value of 2 ng/mL for PFOA and 5 ng/mL for PFOS [229]. In deriving the HBM I, the commission included the fertility and pregnancy, weight of newborns at birth, lipid metabolism, immunity after vaccination, hormonal development, thyroid metabolism, and onset of menopause as relevant, and significantly associated with an exposure to PFOA and/or PFOS.

French Agency for Food, Environmental and Occupational Health and Safety (ANSES)

In 2017, the French Agency for Food, Environmental and Occupational Health and Safety developed human reference doses (toxicity reference values - TRVs) for PFBA, PFHxS, PFBS, and PFHxA based on studies conducted in laboratory animals (Table 6) [230]. TRVs are established for a given critical effect, and are specific to a substance, a duration of exposure (acute, subchronic or chronic), and a route of exposure (oral, inhalation, etc.).

Table 6. Toxicity reference values developed by the French Agency for Food, Environmental and Occupational Health and Safety [230]**.**

	Critical effect and study	Critical concentration	Uncertainty factor (UF)	Toxicity reference value (TRV) (mg/kg-day)
PFBA	Hepatic effects Butenhoff *et al*., 2012	NOAEL = 6 mg/kg-d Adj NOAEL HED = 1.764 mg/kg-d	75	0.024
PFHxS	Hepatic effects Butenhoff *et al*., 2012	NOAEL = 1 mg/kg-d Adj NOAEL HED = 0.289 mg/kg-d	75	0.004
PFBS	Renal effects (Hyperplasia tubular) Lieder *et al*., 2009b	BMD 10% = 24 mg/kg-d Adj BMD 10% = 6.06 mg/kg-d	75	0.08
PFHxA	Renal effects (papillary necrosis & tubular degeneration) Klaunig *et al*., 2015	NOAEL = 30 mg/kg-d Adj: $NOAEL_{HED}$ = 7.91 mg/kg-d	25	0.32

LOAEL - Lowest lowest-observed-adverse-effect level.
NOAEL - No-observed-adverse-effect level.
BMD – Benchmark dose; Adjustment (Adj) BMD
HED – Human equivalent dose

European Food Safety Authority (EFSA)

In 2018, the EFSA issued a provisional scientific opinion on tolerable weekly intakes of PFOA and PFOS [90]. EFSA used a different approach and did not derive their estimates from adverse health outcomes in controlled animal studies. Rather, they used serum measurements in human observational studies to model serum levels associated with 5 percent changes in adverse outcomes. After an extensive review of epidemiological evidence, they selected the outcomes with the strongest evidence for a causal association with PFOS and PFOA. These were increased serum cholesterol, decreased antibody response to vaccines, and lower birthweight for PFOS,

and increased serum cholesterol, elevated liver enzyme (ALT), and decreased birth weight for PFOA. They then used a physiologically based pharmacokinetic modelling (PBPK) to estimate the dietary intake that would produce that serum level over a lifetime of continuous exposure. For children, they used maternal serum levels and models of maternal transfer during gestation and breastfeeding to target children's serum levels at five years old [90].

PFOS

Serum levels associated with a 5 percent change in total cholesterol or birthweight ranged 21-25 ng/mL. The serum level for vaccine response was lower, 10.5 ng/ml. This translated into daily dietary intakes of 1.8-2.0 ng/kg bw- day.

PFOA

Serum levels associated with a 5 percent change in total cholesterol ranged 9.2-9.4 ng/ml, for increase in liver enzyme was 21 ng/mL, and for birth weight ranged 4.4-10.6 ng/mL. This tranlated into daily dietary intakes of 0.4-2.0 ng/kg bw-day.

Table 7. Fish consumption advisories for PFAAs. Source: Wisconsin Department of Natural Resources (DNR) [231].

State	Agency	Date	Category	Units	PFOS	PFOA	PFNA	PFOS+PFHxS
Alabama	DPH	2012	RfD	µg/kg-day	0.077			
			no restriction	µg/kg	0 - 40			
			1 meal/week	µg/kg	41 - 200			
			1 meal/month	µg/kg	201 - 800			
			do not eat	µg/kg	>800			
Michigan	DHHS	2014	RfD	µg/kg-day	0.014			
			16 meals/month	ppb	≤ 9			
			12 meals/month	ppb	>9 - 13			
			8 meals/month	ppb	>13 - 19			
			4 meals/month	ppb	>19 - 38			
			2 meals/month	ppb	>38 - 75			
			1 meal/month	ppb	>75 - 150			
			6 meals/year	ppb	>150 - 300			
			do not eat	ppb	> 300			
Minnesota	MDH	2018	RfD	µg/kg-day	0.0051			
			unrestricted	ppb	≤ 10			
			1 meal/week	ppb	>10 - 50			
			1 meal/month	ppb	>50 - 200			
			do not eat	ppb	>200			
New Jersey	DEP/DOH	2018	RfD**	ng/kg/day	1.8	2	0.74	
****preliminary RfDs & advisories *advice for sensitive populations**			unlimited**	ppb	0.56	0.62	0.23	
			1 meal/week**	ppb	3.9	4.3	1.6	
			1 meal/month**	ppb	17	18.6	6.9	
			1 meal/3 months**	ppb	51, N/A*	57, N/A*	21, N/A*	
			1 meal/year**	ppb	204, N/A*	226, N/A*	84, N/A*	
			do not eat**	ppb	>204, N/A*	>226, N/A*	>84, N/A*	

State	Agency	Date	Category	Units	PFOS	PFOA	PFNA	PFOS+PFHxS
New York	DOH	2017	refers to Michigan and Minnesota advisory levels; PFOS action level determination in progress					
Oregon	OHA	2013	RfD	µg/kg-day	0.08	0.08		
			Fish tissue screening value	mg/kg	0.2	0.2		
Wisconsin	DNR/DHS	2007	RfD	µg/kg/day	0.075			
			unlimited	ng/g	<38			
			1 meal/week	ng/g	38 - 160			
			1 meal/month	ng/g	>160 - 700			
			do not eat	ng/g	>700			

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List of chemical acronyms used in this chapter.

CAS No.	Acronym	Chemical Name
1895-26-7	10:2 diPAP	10:2 fluorotelomer phosphate diester
865-86-1	10:2 FTOH	10:2 fluorotelomer alcohol
135098-69-0	4:2 diPAP	4:2 fluorotelomer phosphate diester
914637-49-3	5:3 FTCA	5:3 fluorotelomer carboxylic acid
57677-95-9	6:2 diPAP	6:2 fluorotelomer phosphate diester
647-42-7	6:2 FTOH	6:2 fluorotelomer alcohol
27619-97-2	6:2 FTSA	6:2 fluorotelomer sulfonic acid
678-41-1	8:2 diPAP	8:2 fluorotelomer phosphate diester
678-39-7	8:2 FTOH	8:2 fluorotelomer alcohol
754-91-6	PFOSA	perfluorooctane sulfonamide
1691-99-2	N-EtFOSE	perfluorooctane sulfonamido ethanol
13252-13-6	Gen X	hexafluoropropylene oxide dimer acid, trade name for ammonium 2,3,3,3-tetrafluoro-2-(heptafluoropropoxy) propanoate; perfluoro-2-propoxypropanoic acid (PFPrOPrA)
24448-09-7	N-MeFOSE	N-methyl perfluorooctane sulfonamido ethanol
	PAPs	Polyfluoroalkyl phosphoric acid esters / Polyfluoroalkyl phosphates / (n:2) Fluorotelomer phosphates
	PFAA	perfluorinated alkyl acid
	PFAS	per- and polyfluorinated alkyl substances
375-22-4	PFBA	perfluorobutanoic acid
375-73-5	PFBS	perfluorobutane sulfonic acid
	PFCA	perfluoroalkyl carboxylic acid
335-76-2	PFDA	perfluorodecanoic acid
307-55-1	PFDoDA	perfluorododecanoic acid
	PFECA	perfluoroether carboxylic acid
	PFESA	perfluoroether sulfonic acid
375-85-9	PFHpA	perfluoroheptanoic acid
307-24-4	PFHxA	perfluorohexanoic acid
355-46-4	PFHxS	perfluorohexane sulfonic acid
375-95-1	PFNA	perfluorononanoic acid
335-67-1	PFOA	perfluorooctanoic acid
1763-23-1	PFOS	perfluorooctane sulfonic acid
2706-90-3	PFPeA	perfluoropentanoic acid
731858-13-2	PFPIA	perfluoroalkyl phosphinic acid
2058-94-8	PFUnDA	perfluoroundecanoic acid