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Maximum Contaminant Level Goal (MCLG) Summary Document for a Mixture of Four Per- and Polyfluoroalkyl Substances (PFAS):

HFPO-DA and its Ammonium Salt (also known as GenX Chemicals), PFBS, PFNA, and PFHxS

CASRN 13252-13-6 and 62037-80-3 (HFPO-DA)
CASRN 375-73-5 and 29420-49-3 (PFBS)
CASRN 375-95-1 (PFNA)
CASRN 355-46-4 (PFHxS)

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Notices

This document has been reviewed in accordance with EPA policy and approved for publication.

This document provides a summary of information used to develop the proposed MCLG for the mixture of HFPO-DA and its ammonium salt (also known as GenX chemicals)[1], PFBS, PFNA, and PFHxS.

Mention of trade names or commercial products does not constitute endorsement or recommendation for use.

[1]EPA notes that the chemical HFPO-DA is used in a processing aid technology developed by DuPont to make fluoropolymers without using PFOA. The chemicals associated with this process are commonly known as GenX Chemicals and the term is often used interchangeably for HFPO-DA along with its ammonium salt.

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Abbreviations and Acronyms

AFFF	aqueous film-forming foam
ATSDR	Agency for Toxic Substances and Disease Registry
BDL	below the detection limit
BMD	benchmark dose
CDC	Centers for Disease Control and Prevention
CTEPP	Children's Total Exposure to Persistent Pesticides and Other Persistent Organic Pollutants
DA	dose addition
DWI-BW	body weight-adjusted drinking water intake
E	duration-relevant exposure
EPA	U.S. Environmental Protection Agency
FAO	Food and Agriculture Organization Area
FDA	U.S. Food and Drug Administration
FIFRA	Federal Insecticide, Fungicide, and Rodenticide Act
GCA	groundwater contamination area
GenX chemicals	hexafluoropropylene oxide (HFPO) dimer acid and HFPO dimer acid ammonium salt
GD	gestational day
HA	health advisory
HBWC	health-based water concentration
HED	human equivalent dose
HDPE	high density polyethylene
HFPO	hexafluoropropylene oxide
HI	hazard index
HQ	hazard quotient
IRIS	Integrated Risk Information System
L/kg/day	liters per kilogram body weight per day
LOAEL	lowest-observed-adverse-effect level
LOD	limit of detection
LOQ	limit of quantitation
MAMA	Methods Advancement for Milk Analysis
MCLG	Maximum Contaminant Level Goal
MDL	method detection limit
MF	modifying factor
mg/kg/day	milligrams per kilogram body weight per day
mg/L	milligrams per liter
MOA	mode of action
MRL	minimal risk level
MW	molecular weight
ng/L	nanograms per liter
NHANES	National Health and Nutrition Examination Survey
NOAA	National Oceanic and Atmospheric Administration
NOAEL	no-observed-adverse-effect level
NPDWR	National Primary Drinking Water Regulation
NRSA	National Rivers and Streams Assessment
NTP	National Toxicology Program
PECO	Population, Exposure, Comparator, and Outcome

PFAS	per- and polyfluoroalkyl substances
PFBS	perfluorobutanesulfonic acid
PFHpA	perfluoroheptanoic acid
PFHxA	perfluorohexanoic acid
PFHxS	perfluorohexanesulfonic acid
PFNA	perfluorononanoic acid
PFOA	perfluorooctanoic acid
PFOS	perfluorooctanesulfonic acid
PND	postnatal day
POD	point of departure
ppt	parts per trillion
PSA	prostate-specific antigen
PVDF	polyvinylidene fluoride
PWS	public water system
RfD	reference dose
RfV	reference value
RSC	relative source contribution
SAB	Science Advisory Board
SDWA	Safe Drinking Water Act
UCMR	Unregulated Contaminant Monitoring Rule
UCMR 3	third Unregulated Contaminant Monitoring Rule
UF	uncertainty factor
UF_A	interspecies uncertainty factor
UF_D	database uncertainty factor
UF_H	human interindividual variability uncertainty factor
UF_S	extrapolation from subchronic to chronic exposure duration uncertainty factor
µg/L	micrograms per liter
WOS	Web of Science
WWTP	wastewater treatment plant

1.0 Introduction and Background

1.1 Purpose

Section 1412(a)(3) of the Safe Drinking Water Act (SDWA) requires the Administrator of the U.S. Environmental Protection Agency (EPA) to propose a Maximum Contaminant Level Goal (MCLG) simultaneously with the National Primary Drinking Water Regulation (NPDWR). The MCLG is set, as defined in Section 1412(b)(4)(A), at "the level at which no known or anticipated adverse effects on the health of persons occur and which allows an adequate margin of safety." Consistent with SDWA 1412(b)(3)(C)(i)(V), in developing the MCLG, EPA considers "the effects of the contaminant on the general population and on groups within the general population such as infants, children, pregnant women, the elderly, individuals with a history of serious illness, or other subpopulations that are identified as likely to be at greater risk of adverse health effects due to exposure to contaminants in drinking water than the general population." Other factors considered in determining MCLGs include health effects data on drinking water contaminants and potential sources of exposure other than drinking water. MCLGs are not regulatory levels and are not enforceable.

The purpose of this document is to provide a summary of the health effects and exposure information and analyses, and to describe the derivation of EPA's proposed MCLG for a mixture of the following per- and polyfluoroalkyl substances (PFAS): hexafluoropropylene oxide (HFPO) dimer acid and its ammonium salt (also known as GenX chemicals)[2], perfluorobutane sulfonic acid and its related compound potassium perfluorobutane sulfonate (PFBS), perfluorononanoic acid (PFNA), and perfluorohexanesulfonic acid (PFHxS).[3] The PFAS mixture MCLG is based on a hazard index (HI) approach, a commonly used component-based mixture risk assessment method (see Section I.D and EPA, 2022c). This document is not intended to be an exhaustive description of all health effects or modeled endpoints (i.e., human health toxicity assessment) nor a drinking water health advisory (HA); rather, this document summarizes key elements (e.g., reference doses (RfDs) from recently published, peer-reviewed, publicly available assessments for HFPO-DA (EPA, 2021a; 2022a), PFBS (EPA, 2021b; 2022b), PFNA (ATSDR, 2021), and PFHxS (ATSDR, 2021) that EPA used to develop health-based water concentrations (HBWCs) that inform the proposed MCLG for HFPO-DA, PFBS, PFNA, and PFHxS.

1.2 Co-Occurrence of PFAS in Drinking Water

Improved analytical monitoring and detection methods have enabled detection of the co-occurrence of multiple PFAS in drinking water, ambient surface waters, aquatic organisms, biosolids (sewage sludge), and other environmental media (EPA, 2022a,b; 2023a,b,c,d,e,f). PFOA and PFOS have historically been target analytes, and the focus of many environmental monitoring studies. More recent monitoring studies, however, have begun to focus on additional PFAS via advanced analytical instruments/methods and non-targeted analysis (De Silva et al., 2020; McCord and Strynar, 2019; McCord et al., 2020).

[2]EPA notes that the chemical HFPO-DA is used in a processing aid technology developed by DuPont to make fluoropolymers without using PFOA. The chemicals associated with this process are commonly known as GenX Chemicals and the term is often used interchangeably for HFPO-DA along with its ammonium salt.

[3] Note: EPA is also proposing individual MCLGs for two PFAS (perfluorooctanoic acid (PFOA) and perfluorooctanesulfonic acid (PFOS); see EPA 2023a,b,c,d.

EPA uses the Unregulated Contaminant Monitoring Rule (UCMR) to collect occurrence data for contaminants that are suspected to be present in drinking water and do not have health-based standards under SDWA. Between 2013 and 2015, EPA's third UCMR (UCMR 3) required all large public water systems (PWSs) (each serving more than 10,000 people) and a statistically representative national sample of 800 small PWSs (each serving 10,000 people or fewer) to monitor for 30 unregulated contaminants in drinking water, including six PFAS: PFOS, PFOA, PFNA, PFHxS, perfluoroheptanoic acid (PFHpA), and PFBS. UCMR 3 data demonstrated that two or more of those six PFAS co-occurred in 48% (285/599) of sampling events with PFAS detected, and PFOA and PFOS co-occurred in 27% (163/599) of sampling events with two or more PFAS detected (EPA, 2019b). EPA found that 4% of PWSs reported results for which one or more of the six UCMR 3 PFAS were measured at or above their respective minimum reporting levels.[4] In addition to the UCMR 3 data collection, many states have undertaken more recent efforts to monitor for PFAS in both source and finished drinking water using newer analytical methods and reflecting lower reporting limits than those in UCMR 3. These results show continued PFAS occurrence and co-occurrence in multiple geographic locations. These data also show certain PFAS, including PFOS, PFOA, PFNA, PFHxS, and PFBS, at lower concentrations and significantly greater frequencies than were measured under UCMR 3. Additionally, these state monitoring data include results for HFPO-DA (which were not included in the suite of PFAS analyzed in UCMR 3) and demonstrate HFPO-DA (and co-occurrence with other PFAS) in drinking water in at least nine states (EPA, 2023f). In 2023–2025, UCMR 5 will collect new monitoring data on 29 PFAS including HFPO dimer acid, PFBS, PFNA, and PFHxS, which will help increase EPA's understanding of PFAS occurrence and co-occurrence in drinking water.

Further discussion of the occurrence of HFPO-DA, PFBS, PFNA, and PFHxS in drinking water (and other environmental media) can be found in EPA's occurrence Technical Support Document (EPA 2023f).

1.3 Dose Additivity for PFAS

PFAS, including HFPO-DA, PFBS, PFNA, and PFHxS, disrupt signaling of multiple biological pathways resulting in common adverse effects on several biological systems and functions, including thyroid hormone levels, lipid synthesis and metabolism, development, and immune and liver function (ATSDR, 2021; EFSA, 2018, 2020; EPA, 2022c). EPA has developed a *Framework for Estimating Noncancer Health Risks Associated with Mixtures of Per- and Polyfluoroalkyl Substances (PFAS)* (hereafter called "PFAS Mixtures Framework") (EPA, 2022c), based on existing EPA mixtures guidelines and guidance (EPA, 1986, 2000a). The PFAS Mixtures Framework describes a flexible, data-driven approach that facilitates practical component-based mixtures evaluation of two or more PFAS based on dose additivity. All of the approaches described in the PFAS Mixtures Framework, including the HI approach (Section III), involve integrating dose-response metrics that have been scaled based on the potency of each PFAS in the mixture.

[4] The 4% figure is based on 198 PWSs reporting measurable PFAS results for one or more sampling events from one or more of their sampling locations. Those 198 PWSs serve an estimated total population of approximately 16 million (EPA, 2019b,c).

Because PFAS are an emerging chemical class of note for toxicological evaluations and human health risk assessment, mode of action (MOA) data may be limited or not available for many PFAS. As such, the component-based approaches for assessing risks of PFAS mixtures are focused on evaluation of similarity of toxicological endpoint/effect rather than similarity in MOA, consistent with EPA mixtures guidance (EPA, 2000a). Precedents of prior research conducted on mixtures of various chemical classes with disparate molecular initiating events, but common key events[5] or adverse outcomes, support the use of dose additive models for estimating mixture-based risks (EPA, 2022c). In particular, Conley et al., 2022 recently investigated *in vivo* effects in maternal rats and offspring from combined exposure to PFOA and PFOS during gestation and early lactation. The study included a series of experiments designed to characterize dose response curves across multiple endpoints for PFOA and PFOS individually, followed by a mixture study of the two chemicals combined. The mixture experiment was designed to test for shifts in the PFOA dose response curves from combined exposure to a fixed dose of PFOS and to compare dose additivity and response additivity model predictions. For nearly all endpoints amenable to mixture model analyses, the dose addition equation produced equivalent or better estimates of observed data than response addition (a detailed discussion of PFAS mixtures research, including dose additive and response additive models can be found in EPA, 2022c). Thus, in the absence of detailed characterization of molecular mechanisms for most PFAS, it is considered a reasonable health-protective assumption that PFAS which can be demonstrated to share one or more key events or adverse outcomes will produce dose-additive effects from co-exposure (EPA, 2022c). EPA received a generally favorable review from EPA's Science Advisory Board (SAB) (EPA SAB, 2022) for its development of approaches based on dose additivity, including the HI approach, to evaluate and manage risk from PFAS mixtures in drinking water and other environmental media.[6] For a detailed description of the evidence supporting dose additivity for PFAS, see EPA (2022c).

1.4 Mixture Approaches Considered

There has been a lot of work evaluating parameters that best inform the combining of PFAS components identified in environmental matrices into mixtures analyses. Indeed, there is currently no consensus on whether or how PFAS should be combined for risk assessment purposes. EPA considered several approaches to account for dose additive noncancer effects associated with HPFO-DA, PFBS, PFNA, and PFHxS in mixtures. PFAS can affect multiple human health endpoints and differ in their impact (i.e., potency of effect) on target organs/systems. For example, one PFAS may be most toxic to the liver, and another may be most toxic to the thyroid but both chemicals affect the liver and the thyroid. Other chemicals regulated as groups operate through a common mode of action and predominately affect one human health endpoint. This supports a flexible data-driven approach that facilitates the evaluation of multiple health endpoints, such as the hazard index.

EPA considered the two main types of HI approaches: 1) the general HI which allows for component chemicals in the mixture to have different health effects or endpoints as the basis for the component chemical reference values (e.g., RfDs), and 2) the target-organ specific HI which

[5] "Key event" is an empirically observable precursor step that is itself a necessary element of the mode of action or is a biologically based marker for such an element (EPA, 2005).

[6] "The SAB supports dose additivity based on a common outcome, instead of a common mode of action as a health protective default assumption and does not propose another default approach." (EPA SAB, 2022)

relies on reference values based on the same organ or organ system (e.g., liver-, thyroid-, or developmental-specific). The general HI approach is based on the overall RfD which is protective of all effects, and thus is a more health protective indicator of risk. The target-organ specific HI approach produces a less health protective estimate of risk than the general HI when a contaminant impacts multiple organs because the range of potential effects has been scoped to a specific target organ, which may be one of the less potent effects or for which there may be significant currently unquantified effects. Additionally, a target-organ specific HI approach relies on toxicity values aggregated by the "same" target organ endpoint/effect, and the absence of information about a specific endpoint may result the contaminant not being adequately considered in a target-organ specific approach, and thus, underestimating potential health risk. A target-organ specific HI can only be performed for those PFAS for which a health effect specific RfD is calculated. For example, for some PFAS a given health effect might be poorly characterized or not studied at all, or, as a function of dose may be one of the less(er) potent effects in the profile of toxicity for that particular PFAS. Another limitation is that so many PFAS lack human epidemiological or experimental animal hazard and dose-response information across a broad(er) effect range thus limiting derivation of target-organ specific values. A similar, effect/endpoint-specific method called the relative potency factor (RPF) approach, which represents the relative difference in potency of an effect/endpoint between an index chemical and other members of the mixture, was also considered. (Further background on all of these approaches, plus illustrative examples, and a discussion of the advantages and challenges associated with each approach can be found in Section 5 and 6 in EPA 2022c).

EPA also considered setting individual MCLGs instead of and in addition to using a mixtures-based approach for HFPO-DA, PFBS, PFNA, and/or PFHxS in mixtures. EPA ultimately selected the general HI approach for establishing an MCLG for these four PFAS, as described in greater detail below, because it provides the most health protective endpoint for multiple PFAS in a mixture to ensure there would be no known or anticipated adverse effects on the health of persons. EPA also considered a target- specific HI or relative potency factor approach but, because of information gaps, EPA may not be able to ensure that the MCLG is sufficiently health protective. If the Agency only established an individual MCLG, the Agency would not provide any protection against dose-additivity from regulated co-occuring PFAS (see Rule Preamble for additional discussion).

1.5 Overview of Mixture Hazard Index (HI) MCLG Approach

For chemicals exhibiting a noncancer threshold for toxic effects (Category II or III; e.g., see EPA, 1985; 1991) and nonlinear carcinogens (e.g., see EPA, 2006), EPA establishes the MCLG based on a toxicity value, typically an RfD, but similar toxicity values may also be used when they represent the best available science (e.g., Agency for Toxic Substances and Disease Registry (ATSDR) Minimal Risk Level[7] (MRL)). The MCLG is designed to be protective of effects over a lifetime of exposure with an adequate margin of safety, including for sensitive populations and life stages consistent with SDWA 1412(b)(3)(C)(i)(V) and 1412(b)(4)(A). The calculation of a MCLG for a chemical exhibiting a noncancer threshold for toxic effects or a nonlinear carcinogen includes an oral toxicity reference value (RfV) such as an RfD (or MRL),

[7] An MRL is an estimate of the daily human exposure to a hazardous substance that is likely to be without appreciable risk of adverse noncancer health effects over a specified duration of exposure (ATSDR, 2021).

body weight-based drinking water intake (DWI-BW), and relative source contribution (RSC) as presented in Equation 1.

$$\boldsymbol{MCLG} = \left(\frac{Oral\ RfD}{DWI\text{-}BW}\right) * RSC \qquad \text{(Eqn. 1)}$$

Where:

RfD = chronic reference dose—an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily oral exposure of the human population to a substance that is likely to be without an appreciable risk of deleterious effects during a lifetime.

DWI-BW = An exposure factor in the form of the 90th percentile body weight-adjusted drinking water intake for the identified population or life stage, in units of liters of water consumed per kilogram body weight per day (L/kg/day). The DWI-BW considers both direct and indirect consumption of drinking water (indirect water consumption encompasses water added in the preparation of foods or beverages, such as tea or coffee). Chapter 3 of EPA's *Exposure Factors Handbook* (EPA, 2019a) provides DWI-BWs for various populations or life stages within the general population based on publicly available, peer-reviewed data such as National Health and Nutrition Examination Survey (NHANES) data.

RSC = relative source contribution—the percentage of the total oral exposure attributed to drinking water sources (EPA, 2000b), with the remainder of the exposure allocated to all other routes or sources.

The approach to select the DWI-BW and RSC for MCLG derivation includes a step to identify sensitive population(s) or life stage(s) (i.e., those that may be more susceptible or sensitive to a chemical exposure) by considering the available data for the contaminant, including the adverse health effects in the toxicity study on which the RfD was based (known as the critical effect within the critical or principal study). Although data gaps can complicate identification of the most sensitive population (e.g., not all windows or life stages of exposure or health outcomes may have been assessed in available studies), the critical effect and point of departure[8] (POD) that form the basis for the RfD (or MRL) can provide some information about sensitive populations because the critical effect is typically observed at the lowest tested dose among the available data. Evaluation of the critical study, including the exposure window, may identify a sensitive population or life stage (e.g., pregnant women, formula-fed infants, lactating women). In such cases, EPA can select the corresponding DWI-BW for that sensitive population or life stage from the Exposure Factors Handbook (EPA, 2019a) to derive the MCLG. In the absence of information indicating a sensitive population or life stage, the DWI-BW corresponding to the general population may be selected for use in MCLG derivation.

To account for potential aggregate risk from exposures and exposure pathways other than oral ingestion of drinking water, EPA applies an RSC when calculating MCLGs to ensure that an

[8] The POD is the dose-response point that marks the starting point for low-dose extrapolation. The POD may be a no-observed-adverse-effect level (NOAEL)/lowest-observed-adverse-effect level (LOAEL), but ideally is established from benchmark dose (BMD) modeling of the experimental data, and generally corresponds to a selected estimated low-level of response (e.g., 1% to 10% incidence for a quantal effect). Depending on the mode of action and other available data, some form of extrapolation below the POD may be employed for estimating low-dose risk or the POD may be divided by a series of UFs to arrive at a reference dose (RfD) (EPA, 2012).

individual's total exposure to a contaminant does not exceed the daily exposure associated with the toxicity value (threshold level), consistent with EPA (2000b) and long-standing EPA methodology for establishing drinking water MCLGs and NPDWRs. The RSC represents the proportion of an individual's total exposure to a contaminant that is attributed to drinking water ingestion (directly or indirectly in beverages like coffee, tea, or soup, as well as from transfer to dietary items prepared with drinking water) relative to other exposure pathways. The remainder of the exposure equal to the RfD (or MRL) is allocated to other potential exposure sources (EPA, 2000b). The purpose of the RSC is to ensure that the level of a contaminant (e.g., MCLG), when combined with other identified potential sources of exposure for the population of concern, will not result in exposures that exceed the RfD (or MRL) (EPA, 2000b).

To determine the RSC, EPA follows the Exposure Decision Tree for Defining Proposed RfD (or POD/UF) Apportionment in EPA's *Methodology for Deriving Ambient Water Quality Criteria for the Protection of Human Health* (EPA, 2000b). EPA considers whether there are significant known or potential uses/sources of the contaminant other than drinking water, the adequacy of data and strength of evidence available for each relevant exposure medium and pathway, and whether adequate information on each exposure source is available to quantitatively characterize the exposure profile. The RSC is developed to reflect the exposure to the general population or a sensitive population within the general population. When exposure data are available for multiple sensitive populations or life stages, the most health-protective RSC is selected. In the absence of adequate data to quantitatively characterize exposure to a contaminant, EPA typically selects an RSC of 20% (0.2). When scientific data demonstrating that sources and routes of exposure other than drinking water are not anticipated for a specific pollutant, the RSC can be raised as high as 80% based on the available data, thereby allocating the remaining 20% to other potential exposure sources (EPA, 2000b).

EPA's protocol for MCLG development for the mixture of HFPO-DA, PFBS, PFNA, and PFHxS follows existing agency guidance, policies, and procedures related to the three key inputs described above (i.e., RfD/MRL, DWI-BW, and RSC) and longstanding agency mixtures guidance (EPA, 1986, 2000a) to address dose additive effects. First, EPA derives a health-based water concentration (HBWC), calculated using the MCLG equation above (Equation 1), for each of the four PFAS (see Sections II A-D). Peer reviewed, publicly available assessments for HFPO-DA (EPA, 2021c), PFBS (EPA, 2021d), PFNA (ATSDR, 2021), and PFHxS (ATSDR, 2021) provide the oral toxicity values (i.e., RfD or MRL) used to calculate the HBWCs for these four PFAS. The DWI-BW for each of the four PFAS is selected from EPA's *Exposure Factors Handbook* (EPA, 2019a), taking into account the relevant sensitive population(s) or life stage(s). RSCs are determined based on a literature review of potential exposure sources of the four PFAS, and analysis using the Exposure Decision Tree approach (EPA, 2000b). Finally, to account for dose additive noncancer effects, the HBWCs for HFPO-DA, PFBS, PFNA, and PFHxS are used in a HI approach, a commonly used component-based mixture risk assessment method (EPA, 2022c).

Following EPA's data-driven approach for component-based mixtures assessment based on dose additivity (i.e., see Figure 4-1 in EPA, 2022c), the agency selected the HI approach for MCLG development because HBWCs for HFPO-DA, PFBS, PFNA, and PFHxS are available or can be calculated. Although a single PFAS may occur in drinking water at concentrations below where EPA might establish an individual MCLG, PFAS tend to co-occur (see Section I.B). Hence,

deriving a MCLG based on the concentration of an individual PFAS without consideration of the dose additive effects that would occur from other PFAS that may be present in water may not result in a sufficiently protective MCLG with an adequate margin of safety. The HI approach is health-protective for development of a mixture MCLG because the HBWCs are based on the most sensitive known adverse health outcome for each mixture component. Thus, the overall HI ensures that the MCLG protects against noncancer health risk associated with exposure to a mixture of PFHxS, HFPO-DA, PFNA, and PFBS.

The HI is based on an assumption of dose addition (DA) among the mixture components (EPA, 2000a; Svendsgaard and Hertzberg, 1994). In the HI approach, an HQ is calculated as the ratio of human exposure (E) to a health-based RfV for each mixture component chemical (i) (EPA, 1986). The HI involves the use of RfVs for each PFAS mixture component (in this case, PFHxS, HFPO-DA, PFNA, and PFBS), which have been selected based on sensitive health outcomes and which are expected to be protective of all other adverse health effects observed after exposure to the individual PFAS. This approach, which protects against all adverse effects and not just a single adverse outcome/effect, is a conservative risk indicator and appropriate for MCLG development. The HI is dimensionless, so in the HI formula, E and the RfV must be in the same units (Equation 2). For example, if E is the oral intake rate (milligrams per kilogram per day (mg/kg/day)), then the RfV could be the RfD or MRL, which have the same units. Alternatively, the exposure metric can be a media-specific metric such as a measured water concentration (e.g., nanograms per liter or ng/L) and the RfV can be an HBWC (e.g., ng/L). The component chemical HQs are then summed across the mixture to yield the HI (Equation 2). A mixture HI exceeding 1.0 indicates potential risk for a given environmental medium or site. The HI provides an indication of: (1) concern for the overall mixture and (2) potential driver PFAS (i.e., those PFAS with high(er) HQs). For a detailed discussion of PFAS dose additivity and the HI approach, see the PFAS Mixtures Framework (EPA, 2022c).

$$HI = \sum_{i=1}^{n} HQ_i = \sum_{i=1}^{n} \frac{E_i}{RfV_i} \qquad \text{(Eqn. 2)}$$

Where:

HI = Hazard Index

HQ_i = Hazard Quotient for chemical i

E_i = Exposure, i.e., dose (mg/kg/day) or occurrence concentration, such as in drinking water (in milligrams per liter or mg/L), for chemical i

RfV_i = Reference value (e.g., oral RfD or MRL) (mg/kg/day), or corresponding HBWC; e.g., such as a MCLG for chemical i (in mg/L)

2.0 Health-Based Water Concentrations

2.1 HFPO-DA

HFPO dimer acid and its ammonium salt are shorter-chain PFAS that were intended to be a replacement for the longer-chained PFOA. Together, they are referred to as "GenX chemicals" because they are associated with the GenX processing aid technology to make fluoropolymers without using PFOA (EPA, 2021c). In water, both HFPO dimer acid and its ammonium salt dissociate to form the HFPO dimer acid anion (HFPO-) as a common analyte.

The HBWC that the agency is using for the HI MCLG was derived from the agency's 2021 human health toxicity assessment, specifically the chronic RfD of 3E-06 mg/kg/day based on liver effects observed following oral exposure of mice to GenX Chemicals (EPA, 2021c). Summaries of key information from the toxicity assessment and health advisory document (EPA, 2022a; i.e., information about the RfD, DWI-BW, and RSC that were used to derive the lifetime noncancer HA value for HFPO-DA) are presented in the following sections. Based on the toxicity assessment, the HBWC value of 10 ng/L for HFPO-DA is used as a component of the HI MCLG for the mixture of HFPO-DA, PFBS, PFNA, and PFHxS (see Section 3.0).

2.1.1 Toxicity

EPA's HBWC for HFPO-DA is derived from a chronic RfD that is based on liver effects observed following oral exposure of mice to HFPO-DA (EPA, 2021c, 2022a).

Oral toxicity studies in rodents exposed to HFPO-DA report a range of toxic effects. Repeated-dose oral exposure of rats and mice resulted in liver toxicity (e.g., increased relative liver weight, hepatocellular hypertrophy, apoptosis, and single-cell/focal necrosis), kidney toxicity (e.g., increased relative kidney weight), immune system effects (e.g., antibody suppression), hematological effects (e.g., decreased red blood cell count, hemoglobin, and hematocrit), reproductive/developmental effects (e.g., increased number of early deliveries, placental lesions, changes in maternal gestational weight gain, and delays in genital development in offspring), and cancer (e.g., liver and pancreatic tumors) (EPA, 2021c).

The most sensitive noncancer effects observed among the available data were the adverse effects on liver, which were observed in both male and female mice and rats across a range of exposure durations and dose levels, including the lowest tested dose levels and shortest exposure durations (EPA, 2021c). Noncancer liver effects formed the basis for the chronic RfD of 3E-06 mg/kg/day, which EPA used to derive the lifetime HA value of 10 ng/L for HFPO-DA (EPA, 2022a). To develop the chronic RfD for HFPO-DA, EPA derived a human equivalent dose (HED) of 0.01 mg/kg/day from a no-observed-adverse-effect level (NOAEL) of 0.1 mg/kg/day for liver effects in the identified critical study (an oral reproductive/developmental toxicity study in mice; Dupont 18405-1037, 2010). EPA then applied a composite uncertainty factor (UF) of 3,000 (i.e., 10X for intraspecies variability (UF_H), 3X for interspecies differences (UF_A), 10X for extrapolation from a subchronic to a chronic dosing duration (UF_S), and 10X for database deficiencies (UF_D)) to yield the chronic RfD (EPA, 2021c).

There is suggestive evidence of carcinogenic potential of oral exposure to HFPO-DA in humans, but the available data are insufficient to derive a cancer risk concentration in water for HFPO-DA (EPA, 2021c, 2022a).

2.1.2 Exposure Factor

To select an appropriate DWI-BW for use in derivation of the noncancer HBWC for HFPO-DA, EPA considered the HFPO-DA exposure interval used in the oral reproductive/developmental toxicity study in mice that was the basis for chronic RfD derivation (the critical study). In this study, parental female mice were dosed from pre-mating through lactation, corresponding to three potentially sensitive human adult life stages that may represent critical windows of exposure for HFPO-DA: women of childbearing age, pregnant women, and lactating women (Table 3-63 in EPA, 2019a). Of these three, the DWI-BW for lactating women (0.0469 L/kg/day) is anticipated to be protective of the other two sensitive life stages. Therefore, EPA used the DWI-BW for lactating women to calculate the noncancer lifetime HA value for HFPO-DA (EPA, 2022a).

2.1.3 Relative Source Contribution

The HBWC for HFPO-DA was calculated using an RSC of 0.20, meaning that 20% of the exposure—equal to the RfD—is allocated to drinking water, and the remaining 80% is attributed to all other potential exposure sources (EPA, 2022a). Selection of this RSC was based on EPA's determination that the available exposure data for HFPO-DA did not enable a quantitative characterization of relative HFPO-DA exposure sources and routes. In such cases, an RSC of 0.20 is typically used (EPA, 2000b).

2.1.4 Derivation of HFPO-DA HBWC

The HBWC for HFPO-DA and is calculated as follows and summarized in Table 1:

$$\textbf{GenX Chemicals HBWC} = \left(\frac{\text{RfD}}{\text{DWI-BW}}\right) * \text{RSC}$$

$$= \left(\frac{0.000003\ \frac{\text{mg}}{\text{kg/day}}}{0.0469\ \frac{\text{L}}{\text{kg/day}}}\right) * 0.2$$

$$= 0.00001\ \frac{\text{mg}}{\text{L}}$$

$$= 0.01\ \frac{\mu\text{g}}{\text{L}}$$

$$= 10\ \frac{\text{ng}}{\text{L}}\ \text{or parts per trillion (ppt)}$$

Table 1. HFPO-DA HBWC – Input Parameters and Value

Parameter	Value	Units	Source
Chronic oral RfD	3E-06	mg/kg/day	Final RfD based on critical liver effects (constellation of liver lesions as defined by the National Toxicology Program (NTP) Pathology Working Group) in parental female mice exposed to HFPO dimer acid ammonium salt by gavage from pre-mating through lactation (53–64 days) (EPA, 2021c; Dupont 18405-1037, 2010).
DWI-BW	0.0469	L/kg/day	90th percentile two-day average, consumer-only estimate of combined direct and indirect community water ingestion for lactating women (age 13 to < 50 years) based on 2005−2010 NHANES data (EPA, 2019a).
RSC	0.2	N/A	Based on a review of the available scientific literature on HFPO-DA potential exposure routes and sources (EPA, 2021c).
HFPO-DA HBWC = 0.00001 mg/L or 10 ppt			

2.2 PFBS

PFBS and its related compound K^+PFBS are shorter-chain PFAS that were developed as "safer" replacements for the longer-chained PFOS. In water, K^+PFBS dissociates to the deprotonated anionic form of PFBS (PFBS-) and the K^+ cation at environmental pH levels (pH 4–9). These three PFBS chemical forms are referred to collectively as PFBS.

The HBWC that the agency is using for the HI MCLG was derived from the agency's 2021 human health toxicity assessment, specifically the chronic RfD of 3E-04 mg/kg/day based on thyroid effects observed seen in newborn mice born to mothers that had been orally exposed to PFBS throughout gestation (EPA, 2021d). Summaries of key information from the toxicity assessment and HA document (i.e., information about the RfD, DWI-BW, and RSC that were used to derive the lifetime noncancer HA value for PFBS) are presented in the following sections. Based on the toxicity assessment, and consistent with the HA analysis, the HBWC of 2,000 ng/L for PFBS is used as a component of the Hazard Index MCLG for the mixture of HFPO-DA, PFBS, PFNA, and PFHxS (see Section 3.0).

2.2.1 Toxicity

EPA's HBWC for PFBS was derived using a chronic oral RfD based on thyroid effects seen in an oral toxicity study in mice (EPA, 2021d, 2022b).

EPA's final toxicity assessment for PFBS (EPA, 2021d) considered all publicly available human, animal, and mechanistic studies of PFBS exposure and effects. The assessment identified associations between PFBS exposure and thyroid, developmental, and kidney effects based on studies in animals. The limited evidence for thyroid or kidney effects in human studies was equivocal, and no studies evaluating developmental effects of PFBS in humans were available. Human and animal studies evaluated other health effects following PFBS exposure including

effects on the reproductive system, liver, and lipid and lipoprotein homeostasis, but the evidence did not support clear associations between exposure and effect (EPA, 2021d).

The most sensitive noncancer effect observed was an adverse effect on the thyroid (i.e., decreased serum total thyroxine) seen in newborn mice (postnatal day (PND) 1) born to mothers that had been orally exposed to K^+PFBS throughout gestation (Feng et al., 2017; EPA, 2021d). This critical effect was the basis for the chronic RfD of 3E-04 mg/kg/day which EPA used to derive the noncancer lifetime HA value for PFBS (EPA, 2021d, 2022b). To develop the chronic RfD for PFBS,[9] EPA derived an HED of 0.095 mg/kg/day from benchmark dose (BMD) modeling of the critical effect in mice. EPA then applied a composite UF of 300 (i.e., 10X for UF_H, 3X for UF_A, and 10X for UF_D) to yield the chronic RfD (EPA, 2021d).

There were no human or animal studies identified that evaluated the potential carcinogenicity of PFBS (EPA, 2021d, 2022b).

2.2.2 Exposure Factor

To select an appropriate DWI-BW for use in deriving the HBWC, EPA considered the PFBS exposure interval used in the developmental toxicity study in mice that was the basis for chronic RfD derivation. In this study, pregnant mice were exposed throughout gestation, which is relevant to two human adult life stages: women of child-bearing age who may be or become pregnant, and pregnant women and their developing embryo or fetus (Table 3-63 in EPA, 2019a). Of these two, EPA selected the DWI-BW for women of child-bearing age (0.0354 L/kg/day) to derive the noncancer lifetime HA for PFBS because it is higher and therefore more health-protective (EPA, 2022b).

2.2.3 Relative Source Contribution

The HBWC for PFBS was calculated using an RSC of 0.20, meaning that 20% of the exposure—equal to the RfD—is allocated to drinking water, and the remaining 80% is attributed to all other potential exposure sources (EPA, 2022b). This was based on EPA's determination that the available data on PFBS exposure routes and sources did not enable a quantitative characterization of PFBS exposure. In such cases, an RSC of 0.20 is typically used (EPA, 2000b).

2.2.4 Derivation of PFBS HBWC

The HBWC for PFBS and is calculated as follows and summarized in Table 2:

$$\textbf{PFBS HBWC} = \left(\frac{\text{RfD}}{\text{DWI-BW}}\right) * \text{RSC}$$

$$= \left(\frac{0.0003 \ \frac{\text{mg}}{\text{kg/day}}}{0.0354 \frac{\text{L}}{\text{kg/day}}}\right) * 0.2$$

[9] Data for K+PFBS were used to derive the chronic RfD for the free acid (PFBS), resulting in the same value (3E-04 mg/kg/day), after adjusting for differences in molecular weight (MW) between K+ PFBS (338.19) and PFBS (300.10) (EPA, 2021d).

$$= 0.0017 \frac{\text{mg}}{\text{L}} \left(\text{rounded to } 0.002 \frac{\text{mg}}{\text{L}}\right)$$

$$= 2 \frac{\mu\text{g}}{\text{L}}$$

$$= 2{,}000 \frac{\text{ng}}{\text{L}} \text{ or ppt}$$

Table 2. PFBS HBWC – Input Parameters and Value

Parameter	Value	Units	Source
Chronic RfD	3E-04	mg/kg/day	Final RfD based on critical effect of decreased serum total thyroxine in newborn (PND 1) mice after gestational exposure to the mother (EPA, 2021d; Feng et al., 2017).
DWI-BW	0.0354	L/kg/day	90th percentile two-day average, consumer-only estimate of combined direct and indirect community water ingestion for women of childbearing age (13 to < 50 years) based on 2005−2010 NHANES data (EPA, 2019a).
RSC	0.2	N/A	Based on a review of the available scientific literature on PFBS potential exposure routes and sources (EPA, 2021d).
PFBS HBWC = 0.002 mg/L or 2,000 ppt			

2.3 PFNA

PFNA has been used as a processing aid in the production of fluoropolymers, primarily polyvinylidene fluoride (PVDF), which is a plastic designed to be temperature resistant and chemically nonreactive (EPA, 2020; NJDWQI, 2017; Prevedouros et al., 2006). PFNA has been used since the 1950s in a wide variety of industrial and consumer products (see RSC Section below). It has also been used in aqueous film-forming foam (AFFF) for fire suppression (EPA, 2020; Laitinen et al., 2014).

PFAS have been measured in human blood samples taken as part of the NHANES. PFNA was measured in serum samples collected in 2013−2014 from more than 2,000 survey participants, with a geometric mean concentration of 0.675 micrograms per liter (µg/L) and 95th percentile concentration of 2.00 µg/L (EPA, 2021e).

ATSDR has published a toxicological profile for a group of PFAS including PFNA and has developed an intermediate-duration oral MRL for PFNA (ATSDR, 2021)[10]. EPA's derived HBWC for PFNA (described below) is based on the ATSDR MRL (ATSDR, 2021), a DWI-BW (selected by EPA) that corresponds to this MRL, and an RSC selected by EPA. There is no published EPA human health toxicity assessment for PFNA; however, EPA's Integrated Risk Information System (IRIS) program is developing a human health toxicity assessment for PFNA,

[10] ATSDR is currently updating their assessment for PFNA, and their perfluoroalkyls assessment is "in development" (https://www.atsdr.cdc.gov/toxprofiledocs/index.html).

which is expected to undergo public comment and external peer review in FY2023 (EPA, 2021e, 2022c). EPA's IRIS assessment will use systematic review methods to evaluate the epidemiological and toxicological literature for PFNA, including consideration of relevant mechanistic evidence (EPA, 2021e).

2.3.1 Toxicity

The HBWC for PFNA is based on an ATSDR intermediate-duration oral MRL that was based on developmental effects seen in mice after oral PFNA exposure (ATSDR, 2021).

Studies of oral PFNA exposure in rodents have reported adverse effects on the liver, development, and reproductive and immune systems (ATSDR, 2021). The most sensitive noncancer effects and basis for the ATSDR intermediate-duration oral MRL (and thus EPA's HBWC) were decreased body weight gain and impaired development (i.e., delayed eye opening, preputial separation, and vaginal opening) in mice born to mothers that were gavaged with PFNA from gestational days (GDs) 1–17 (with presumed continued indirect exposure of offspring via lactation), and monitoring until PND 287 (ATSDR, 2021). The study reporting these effects (Das et al., 2015) was selected by ATSDR as the principal study for MRL derivation. To derive the MRL, an HED of 0.001 mg/kg/day was calculated from the NOAEL of 1 mg/kg/day identified in the study. Then, ATSDR applied a total UF of 30 (i.e., 10X for UF_H and 3X for UF_A) and a modifying factor (MF) of 10X for database deficiencies to account for the small number/limited scope of studies examining PFNA toxicity following intermediate-duration exposure. The resulting intermediate-duration oral MRL was 3E-06 mg/kg/day (ATSDR, 2021). EPA did not apply an additional UF to adjust for subchronic-to-chronic duration (i.e., UF_S) to calculate the HBWC because the critical effects were observed during a developmental life stage[11] (EPA, 2002). Toxicological assessments based on animal studies for PFNA from other sources (e.g., states) are in a similar range as this value, providing additional support (e.g., 4.3×10^{-6} mg/kg/day to 1.2×10^{-5} mg/kg/day; see Addendum A in EPA, 2021e).

The carcinogenic potential of PFNA has been examined in three epidemiological studies. No consistent associations between serum PFNA levels and breast cancer or prostate cancer were found (ATSDR, 2021).

2.3.2 Exposure Factor

Based on the life stages of exposure in the principal study from which the intermediate-duration MRL was derived (i.e., directly to maternal animals during gestation, and indirectly to offspring during gestation and lactation), EPA identified three potentially sensitive life stages that may represent critical windows of exposure for PFNA: women of childbearing age (13 to < 50 years), pregnant women, and lactating women (Table 3-63 in EPA, 2019a). The DWI-BW for lactating women (0.0469 L/kg/day; 90th percentile direct and indirect consumption of community water, consumer-only two-day average) was selected to calculate the HBWC for PFNA because it is the

[11] As stated in EPA (2002), "…This is because it is assumed that most endpoints of developmental toxicity can be caused by a single exposure. If, however, developmental effects are more sensitive than those seen after longer-term exposures, then even the chronic RfD/RfC should be based on such effects to reduce the risk of potential greater sensitivity in children. Because the standard studies currently conducted for developmental toxicity involve repeated exposures, data are not often available on which endpoints may be induced by acute, subacute, subchronic, or chronic dosing regimens and, therefore, on which should be used in setting various duration reference values."

highest of the three DWI-BWs and is anticipated to be protective of the other two sensitive life stages.

2.3.3 Relative Source Contribution

EPA calculated the HBWC for PFNA using an RSC of 0.20, meaning that 20% of the exposure—equal to the MRL—is allocated to drinking water, and the remaining 80% is attributed to all other potential exposure sources. This was based on EPA's determination that the available data on PFNA exposure routes and sources did not permit quantitative characterization of PFNA exposure. In such cases, an RSC of 0.20 is typically used (EPA, 2000b). See Appendix A for complete details on the RSC determination for PFNA.

2.3.4 Derivation of PFNA HBWC

The HBWC for PFNA is calculated as follows and summarized in Table 3:

$$\textbf{PFNA HBWC} = \left(\frac{\text{MRL}}{\text{DWI-BW}}\right) * \text{RSC}$$

$$= \left(\frac{0.000003 \ \frac{\text{mg}}{\text{kg/day}}}{0.0469 \frac{\text{L}}{\text{kg/day}}}\right) * 0.2$$

$$= 0.000014 \ \frac{\text{mg}}{\text{L}} \left(\text{rounded to } 0.00001 \ \frac{\text{mg}}{\text{L}}\right)$$

$$= 0.01 \ \frac{\mu\text{g}}{\text{L}}$$

$$= 10 \ \frac{\text{ng}}{\text{L}} \text{ or ppt}$$

Table 3. PFNA HBWC – Input Parameters and Value

Parameter	Value	Units	Source
Intermediate-Duration Oral MRL	3E-06[a]	mg/kg/day	Based on decreased body weight gain and delayed eye opening, preputial separation, and vaginal opening in mouse offspring after gestational and presumed lactational exposure (ATSDR, 2021; Das et al., 2015).
DWI-BW	0.0469	L/kg/day	90th percentile two-day average, consumer-only estimate of combined direct and indirect community water ingestion for lactating women (13 to < 50 years) based on 2005−2010 NHANES data (EPA, 2019a).
RSC	0.2	N/A	Based on a review of the current scientific literature summarized in this document (see Appendix A).
PFNA HBWC = 0.00001 mg/L or 10 ppt			

Note:

[a] Note that ATSDR MRLs and EPA RfDs are not necessarily equivalent (e.g., intermediate-duration MRL vs. chronic RfD; EPA and ATSDR may apply different uncertainty/modifying factors) and are developed for different purposes. In this case, EPA did not apply an additional UF_S to calculate the HBWC for PFNA because the critical effect is identified in a developmental population (EPA, 2002).

2.4 PFHxS

PFHxS has been used in laboratory applications and as a raw material or a precursor for the manufacture of PFAS/perfluoroalkyl sulfonate-based products, though production of PFHxS in the United States was phased out by its major manufacturer in 2002 (Backe et al., 2013; Buck et al., 2011; OECD, 2011 and Sigma-Aldrich, 2014 as cited in NCBI, 2022). PFHxS has also been used in firefighting foam and carpet treatment solutions, and it has been used as a stain and water repellant (Garcia and Harbison, 2015 as cited in NCBI, 2022).

PFAS have been measured in human blood samples taken as part of the NHANES. PFHxS was measured in serum samples collected in 2013−2014 from more than 2,000 survey participants, with a geometric mean concentration of 1.35 µg/L and 95th percentile concentration of 5.60 µg/L (EPA, 2021e).

ATSDR has published a toxicological profile for a group of PFAS including PFHxS and has calculated an intermediate-duration oral MRL for PFHxS (ATSDR, 2021)[12]. EPA's derived HBWC for PFHxS described below is based on the ATSDR MRL (ATSDR, 2021), a DWI-BW (selected by EPA) that corresponds to the MRL, and an RSC selected by EPA. There is no published EPA human health toxicity assessment for PFHxS; however, EPA's IRIS program is developing a human health toxicity assessment for PFHxS, which is expected to undergo public comment and external peer review in FY2023 (EPA, 2022c). EPA's IRIS assessment will use systematic review methods to evaluate the epidemiological and toxicological literature for PFHxS, including consideration of relevant mechanistic evidence (EPA, 2021e).

2.4.1 Toxicity

The HBWC for PFHxS is derived using an ATSDR intermediate-duration oral MRL based on thyroid effects seen in male rats after oral PFHxS exposure (ATSDR, 2021). Toxicity studies of oral PFHxS exposure to animals also have reported health effects on the liver, thyroid, and development (ATSDR, 2021). The most sensitive noncancer effect observed was thyroid follicular epithelial hypertrophy/hyperplasia in parental male rats that had been exposed for 42–44 days, identified in the principal developmental toxicity study selected by ATSDR (NOAEL of 1 mg/kg/day for this effect) (Butenhoff et al., 2009; ATSDR, 2021). This critical effect was the basis for the ATSDR intermediate-duration oral MRL which EPA used to derive the HBWC for PFHxS. An HED of 0.0047 mg/kg/day was calculated from the NOAEL of 1 mg/kg/day identified in the principal study. ATSDR applied a total UF of 30 (i.e., 10X for UF_H and 3X for UF_A) and a MF of 10X for database deficiencies to yield an intermediate-duration oral MRL of 2E-05 mg/kg/day (ATSDR, 2021). To calculate the HBWC, EPA applied an additional UF of 10 to adjust for subchronic-to-chronic duration (i.e., UF_S), per agency guidance (EPA, 2002), because the effect is not in a developmental population (i.e., thyroid follicular epithelial hypertrophy/hyperplasia in parental male rats). The resulting adjusted chronic reference value is 2E-06 mg/kg/day. Toxicological assessments based on animal studies for PFHxS from other

[12] ATSDR is currently updating their assessment for PFHxS, and their perfluoroalkyls assessment is "in development" (https://www.atsdr.cdc.gov/toxprofiledocs/index.html).

sources (e.g., states) are in a similar range as this value, providing additional support (e.g., 3.8×10^{-6} to 9.7×10^{-6} mg/kg/day; see Addendum A in EPA, 2021e).

The carcinogenic potential of PFHxS has been examined in four epidemiological studies (ATSDR, 2021). Bonefeld-Jorgensen et al. (2014) reported a significant negative correlation between serum PFHxS levels (mean concentration 1.2 ng/mL) and breast cancer risk among Danish women. However, a study in Greenland found a significant, positive association between high serum levels of PFHxS and breast cancer risk (Wielsøe et al., 2017). The median serum PFHxS concentration among cases in that study was 2.52 ng/mL and serum levels ranged from 0.19 ng/mL to 23.40 ng/mL (Wielsøe et al., 2017). Hardell et al. (2014) found a statistically significant interaction between above-median PFHxS concentrations and increased risk for prostate cancer among men with genetics as a risk factor (first-degree relative). Prostate-specific antigen (PSA) levels were not associated with serum PFHxS levels (mean concentration 3.38 ng/mL) in men 20–49 or 50–69 years of age (Ducatman et al., 2015). EPA has not yet completed an evaluation and classification of the carcinogenicity of PFHxS, and thus, the HBWC and MCLG are based on noncancer effects.

2.4.2 Exposure Factor

No sensitive population or life stage was identified for DWI-BW selection for PFHxS because the critical effect on which the ATSDR MRL was based (thyroid alterations) was observed in adult male rats. Since this exposure life stage does not correspond to a sensitive population or life stage, a DWI-BW for adults within the general population (0.034 L/kg/day; 90th percentile direct and indirect consumption of community water, consumer-only two-day average, adults 21 years and older) was selected for HBWC derivation (EPA, 2019a).

2.4.3 Relative Source Contribution

EPA calculated the HBWC for PFHxS using an RSC of 0.20, meaning that 20% of the exposure—equal to the chronic reference value—is allocated to drinking water, and the remaining 80% is attributed to all other potential exposure sources. This was based on EPA's determination that the available data on PFHxS exposure routes and sources did not permit quantitative characterization of PFHxS exposure. In such cases, an RSC of 0.20 is typically used (EPA, 2000b). See Appendix B for complete details on the RSC determination for PFHxS.

2.4.4 Derivation of PFHxS HBWC

The HBWC for PFHxS is calculated as follows and summarized in Table 4:

$$\textbf{PFHxS HBWC} = \left(\frac{\text{Chronic reference value}}{\text{DWI-BW}}\right) * \text{RSC}$$

$$= \left(\frac{0.000002 \ \frac{\text{mg}}{\text{kg/day}}}{0.034 \frac{\text{L}}{\text{kg/day}}}\right) * 0.2$$

$$= 0.0000092 \ \frac{\text{mg}}{\text{L}} \left(\text{rounded to } 0.000009 \ \frac{\text{mg}}{\text{L}}\right)$$

$$= 0.009 \frac{\mu g}{L}$$

$$= 9 \frac{ng}{L} \text{ or ppt}$$

Table 4. PFHxS HBWC – Input Parameters and Value

Parameter	Value	Units	Source
Chronic reference value	2E-06[a]	mg/kg/day	Based on thyroid follicular epithelial hypertrophy/hyperplasia in parental male rats (exposed 42–44 days) (ATSDR, 2021; Butenhoff et al., 2009).
DWI-BW	0.034	L/kg/day	90th percentile two-day average, consumer-only estimate of combined direct and indirect community water ingestion for adults 21 years and older based on 2005−2010 NHANES data (EPA, 2019a).
RSC	0.2	N/A	Based on a review of the current scientific literature summarized in this document (see Appendix B).
PFHxS HBWC = 0.000009 mg/L or 9 ppt			

Note:

[a] Note that MRLs and RfDs are not necessarily equivalent (e.g., intermediate-duration MRL vs. chronic RfD, EPA and ATSDR may apply different uncertainty/modifying factors) and are developed for different purposes. In this case, EPA applied an additional UF of 10 to account for subchronic-to-chronic duration (i.e., UF_S) yielding a chronic reference value of 2E-06 mg/kg/day, which was used to calculate the HBWC for PFHxS (EPA, 2002).

3.0 Derivation of PFAS Mixture Hazard Index MCLG

To account for dose additive noncancer effects associated with HFPO-DA, PFBS, PFHxS, and PFNA, EPA is proposing a MCLG for the mixture of these four PFAS based on the HI approach (EPA, 2022c). As described in Section I.D., a mixture HI can be calculated when HBWCs (e.g., HAs) for a set of PFAS are available or can be calculated. HQs are calculated by dividing the measured component PFAS concentration in water (e.g., expressed as ng/L) by the relevant HBWC (e.g., expressed as ng/L), as shown in the equation below. Component HQs are then summed across the PFAS mixture to yield the PFAS mixture HI MCLG. A PFAS mixture HI MCLG greater than 1.0 indicates an exceedance of the health protective level and indicates potential human health risk for noncancer effects from the PFAS mixture in water. For more details, please see EPA (2022c). The proposed mixture HI MCLG for HFPO-DA, PFBS, PFNA, and PFHxS is as follows:

$$HI\ MCLG = \left(\frac{[GenX_{water}]}{[GenX_{HBWC}]}\right) + \left(\frac{[PFBS_{water}]}{[PFBS_{HBWC}]}\right) + \left(\frac{[PFNA_{water}]}{[PFNA_{HBWC}]}\right) + \left(\frac{[PFHxS_{water}]}{[PFHxS_{HBWC}]}\right) = 1.0$$

$$HI\ MCLG = \left(\frac{[GenX_{water}]}{[10\ ng/L]}\right) + \left(\frac{[PFBS_{water}]}{[2000\ ng/L]}\right) + \left(\frac{[PFNA_{water}]}{[10\ ng/L]}\right) + \left(\frac{[PFHxS_{water}]}{[9\ ng/L]}\right) = 1.0$$

Where

$[PFAS_{water}]$ = the measured component PFAS concentration in water and

$[PFAS_{HBWC}]$ = the HBWC of a component PFAS.

Although current weight of evidence suggests that PFAS vary in their precise structure and function, exposure to different PFAS can result in similar health effects; as a result, PFAS exposures are likely to result in dose-additive effects and therefore the assumption of dose-additivity is reasonable (ATSDR, 2021; EPA, 2022a). While individual PFAS can pose a potential risk to human health if the exposure level exceeds the chemical-specific toxicity value (RfD or MRL) (i.e., individual PFAS HQ > 1.0), mixtures of PFAS can result in dose-additive health effects when lower individual concentrations of PFAS are present in that mixture. For example, if the individual HQs for PFHxS, HFPO-DA, PFNA, and PFBS were each 0.9 that would indicate that the measured concentration of each PFAS in drinking water is below the level of appreciable risk (recall that an RfV, such as an oral RfD, represents an estimate at which no appreciable risk of deleterious effects exists). However, the overall HI for that mixture would be 3.6 (i.e., sum of four HQs of 0.9). A HI of 3.6 means that the total measured concentration of PFAS is 3.6 times the level associated with potential health risks. Thus, setting a MCLG based on the concentration of an individual PFAS without considering the potential dose-additive effects from other PFAS in a mixture would likely not provide a sufficiently protective MCLG with an adequate margin of safety. In order to account for dose additive noncancer effects associated with co-occurring PFAS, to protect against health impacts from likely multi-chemical exposures of PFHxS, HFPO-DA, PFNA, and PFBS, the agency is proposing use of the HI approach, a commonly used component-based mixture risk assessment method, for the MCLG for these four PFAS. Consistent with the statutory requirement under 1412(b)(4)(A) of SDWA, establishing the MCLG for PFHxS, HFPO-DA, PFNA, and PFBS at a HI = 1.0 ensures that the MCLG is set at a level at which there are no known or anticipated adverse effect on the health of persons and which ensures an adequate margin of safety.

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APPENDIX A. PFNA: Summary of Occurrence in Water and Detailed Relative Source Contribution.

Occurrence in Water

The use and production of PFNA could result in its release to the aquatic environment through various waste streams (NCBI, 2022). PFNA has an estimated water solubility of 62.5 µg/L (6.25×10^{-2} mg/L) at 25 °C and when released to surface water, it is expected to adsorb to suspended solids and sediment (NCBI, 2022). Volatilization from water surfaces is not expected to be an important fate process for PFNA (NCBI, 2022).

Drinking Water

Based on results from EPA's UCMR 3 monitoring, PFNA has been detected in 0.28% of drinking water systems in the United States, with mean and median detected concentrations of 36 ng/L and 32 ng/L, respectively. The UCMR 3 maximum concentration detected in drinking water systems was 56 ng/L (EPA, 2017). Drinking water samples collected from public drinking water systems that are impacted by wastewater treatment effluent often contain higher concentrations of perfluoroalkyls than samples collected from systems that are not impacted by wastewater treatment effluent (Schultz et al., 2006a,b, as cited in ATSDR, 2021). For example, PFNA was detected in all samples collected from a public drinking water system in Los Angeles that was highly impacted by wastewater treatment effluent; the mean concentrations of PFNA in influent and effluent samples were 5.5 ng/L and 3.5 ng/L, respectively (Quinones and Snyder, 2009 as cited in ATSDR, 2021). In comparison, no perfluoroalkyl chemicals were detected in influent or finished drinking water in samples collected from a public drinking water system in Aurora, Colorado that was not highly impacted by wastewater treatment effluent (Quinones and Snyder, 2009 as cited in ATSDR, 2021). PFNA was detected in 30% of public drinking water systems tested in New Jersey (Post et al., 2013 as cited in ATSDR, 2021).

A Standard of Quality for PFAS in bottled water is 0.005 µg/L (5 ng/L) for one PFAS (e.g., PFNA) and 0.0010 µg/L (10 ng/L) for more than one PFAS (IBWA, 2022).

For more information about PFNA occurrence in drinking water, please see EPA (2022f).

Groundwater

PFNA was detected at a concentration of 25.7 ng/L (0.0257 µg/L) in one of 19 well water samples collected from farms near Decatur, Alabama that have historically applied fluorochemical industry-impacted biosolids to fields (Lindstrom et al., 2011 as cited in NCBI, 2022). PFNA was also detected in groundwater samples collected in 2010 from the Highland Creek watershed in Canada at concentrations ranging from 0.071 ng/L to 0.54 ng/L (0.000071 µg/L to 0.00054 µg/L) (Meyer et al., 2011, as cited in NCBI, 2022). In this study, the authors reported that none of the sampling sites receive water that is impacted by known PFAS sources (Meyer et al., 2011). Median and maximum groundwater concentrations of 105 ng/L (0.105 µg/L) and 3,000 ng/L (3 µg/L), respectively, were detected at 10 U.S. military installations (Anderson et al., 2016 as cited in ATSDR, 2021).

Surface Water

In a 2016 study, PFNA was detected in each of 37 surface water sampling sites in the northeast United States, with a maximum concentration of 14 ng/L (0.014 µg/L) measured at Mill Cove, Rhode Island (Zhang et al., 2016 as cited in ATSDR, 2021). Concentrations of PFNA in 11 lake water samples and 14 surface water samples collected in Albany, New York ranged from not detected to 3.51 ng/L (0.00351 µg/L) and from < 0.25 ng/L to 5.90 ng/L (< 0.00025 µg/L to 0.00590 µg/L), respectively (Kim and Kannan, 2007 as cited in ATSDR, 2021). Concentrations of PFNA in 12 remote and urban Minnesota surface water samples, including samples collected from Lake Michigan, ranged from < 0.3 ng/L to 3.1 ng/L (< 0.0003 µg/L to 0.0031 µg/L) (Simcik and Dorweiler, 2005 as cited in ATSDR, 2021). PFNA was detected in 38% of 8 surface water samples from U.S. streams in the Great Lakes basin collected during 1994 to 2000 at concentrations between 0.03 ng/L and 0.4 ng/L (0.00003 µg/L and 0.0004 µg/L) (Klecka et al., 2010 as cited in NCBI, 2022).

PFNA was detected in 6 locations in the Delaware River at concentrations ranging from 1.65 ng/L to 976 ng/L (0.00165 µg/L to 0.976 µg/L) in 2007 to 2009 (DRBC, 2013 as cited in ATSDR, 2021). PFNA was detected at concentrations of 2.24 ng/L to 194 ng/L (0.00224 µg/L to 0.194 µg/L) in 11 samples with the highest total PFAS levels out of 100 samples collected from 80 sites in the Cape Fear River Basin, North Carolina in 2006 (Nakayama et al., 2007 as cited in ATSDR, 2021 and NCBI, 2022). Mean and median PFNA concentrations were 33.6 ng/L and 5.70 ng/L (0.0336 µg/L and 0.00570 µg/L), respectively, with PFNA not detected in 10.1% of the samples (Nakayama et al. 2007 as cited in ATSDR, 2021). PFNA was detected at concentrations between 12.4 ng/L and 286 ng/L (0.0124 µg/L to 0.286 µg/L) in 9 of 32 surface water samples collected from ponds and streams near farms near Decatur, Alabama that have historically applied fluorochemical industry-impacted biosolids to fields (Lindstrom et al., 2011 as cited in NCBI, 2022). Median and maximum surface water concentrations of 96 ng/L (0.096 µg/L) and 10,000 ng/L (10 µg/L), respectively, were detected at 10 U.S. military installations (Anderson et al., 2016 as cited in ATSDR, 2021).

Concentrations of PFNA in creek and river samples measured throughout Canada ranged from < 125 pg/L to 3,000 pg/L (< 0.000125 µg/L to 0.003 µg/L) (D'eon et al., 2009 as cited in NCBI, 2022). Also, PFNA concentrations ranged from 0.80 ng/L to 2.4 ng/L (0.0008 µg/L to 0.0024 µg/L) in surface water samples collected from Highland Creek watershed, Canada in 2010 (Meyer et al., 2011 as cited in NCBI, 2022). Concentrations of PFNA in lake water samples collected from four lakes on Cornwallis Island, Canada from 2003 to 2005 ranged from not detected to 6.1 ng/L (0.0061 µg/L) (Stock et al., 2007 as cited in NCBI, 2022).

RSC for PFNA

Literature Search and Screening

In 2020, EPA conducted a broad literature search to evaluate evidence for pathways of human exposure to eight PFAS chemicals (PFOA, PFOS, PFBA, PFBS, PFDA, perfluorohexanoic acid (PFHxA), PFHxS, and PFNA) (Holder et al., in prep). This search was not date limited and spanned the information collected across the Web of Science (WOS), PubMed, and ToxNet/ToxLine (now ProQuest) databases. The results of the PFNA literature search of publicly available sources are available through EPA's Health & Environmental Resource Online website at https://hero.epa.gov/hero/index.cfm/project/page/project_id/2633.

The 2,408 literature search results for PFNA were imported into SWIFT-Review (Sciome, LLC, Research Triangle Park, NC) and filtered through the Evidence Stream tags to identify human studies and non-human (i.e., those not identified as human) studies (Holder et al., in prep). Studies identified as human studies were further categorized into seven major PFAS pathways (Cleaning Products, Clothing, Environmental Media, Food Packaging, Home Products/Articles/Materials, Personal Care Products, and Specialty Products) as well as an additional category for Human Exposure Measures. Non-human studies were grouped into the same seven major PFAS pathway categories, except that the Environmental Media category did not include soil, wastewater, or landfill. Only studies published between 2003 and 2020 were considered. Application of the SWIFT-Review tags identified 1,359 peer-reviewed papers matching these criteria for PFNA.

Holder et al. (in prep) screened the 1,359 papers to identify studies reporting measured occurrence of PFNA in human matrices and media commonly related to human exposure (human blood/serum/urine, drinking water, food, food contact materials, consumer products, indoor dust, indoor and ambient air, and soil). For this synthesis, additional screening was conducted to identify studies relevant to surface water (freshwater only) and groundwater using a keyword[13] search for water terms.

Following the Population, Exposure, Comparator, and Outcome (PECO) criteria outlined in Table A-1, the title and abstract of each study were independently screened for relevance by two screeners using *litstream*^{TM}. A study was included as relevant if it was unclear from the title and abstract whether it met the inclusion criteria. When two screeners did not agree if a study should be included or excluded, a third reviewer was consulted to make a final decision. The title and abstract screening of Holder et al. (in prep) and of this synthesis resulted in 679 unique studies being tagged as relevant (i.e., having data on occurrence of PFNA in exposure media of interest) that were further screened with full-text review using the same inclusion criteria. After additional review of the evidence collected by Holder et al. (in prep), 98 studies originally identified for other PFAS also contained information relevant to PFNA. Based on full-text review, 171 studies were identified as having relevant, extractable data for PFNA from the United States, Canada, or Europe for environmental media, not including studies with only human biomonitoring data. Of these 171 studies, 156 were identified from Holder et al. (in prep), where primary data were extracted into a comprehensive evidence database. Parameters of interest included: sampling dates and locations, numbers of collection sites and participants, analytical methods, limits of detection and detection frequencies, and occurrence statistics. Fifteen of the 171 studies were identified in this synthesis as containing primary data on only surface water and/or groundwater.

The evidence database of Holder et al. (in prep) additionally identified 18 studies for which the main article was not available for review. As part of this synthesis, 17 of the 18 studies could be retrieved. An additional three references were identified through gray literature sources that were included to supplement the search results. The combined 20 studies underwent full-text screening using the inclusion criteria in Table A-1. Based on full-text review, five studies were identified as relevant.

[13] Keyword list: water, aquifer, direct water, freshwater, fresh water, groundwater, ground water, indirect water, lake, meltwater, melt water, natural water, overland flow, recreation water, recreational water, river, riverine water, riverwater, river water, springwater, spring water, stream, surface water, total water, water supply

Table A-1. Populations, Exposures, Comparators, and Outcomes (PECO) Criteria

PECO Element	Inclusion Criteria
Population	Adults and/or children in the general population and populations in the vicinity of PFAS point sources from the United States, Canada, or Europe
Exposure	Primary data from peer-reviewed studies collected in any of the following media: ambient air, consumer products, drinking water, dust, food, food packaging, groundwater[a], human blood/serum/urine, indoor air, landfill, sediment, soil, surface water[a] (freshwater), wastewater/biosolids/sludge
Comparator	Not applicable
Outcome	Measured concentrations of PFNA (or measured emissions from food packaging and consumer products only)

Note:
[a] Surface water and groundwater were not included as relevant media in Holder et al. (in prep). Studies were re-screened for these two media in this synthesis.

Using the screening results from the evidence database and this synthesis, a total of 176 studies were identified as relevant. Forty-seven of these contained information relevant to the U.S. and were summarized for this effort.

Additional Screening

EPA also searched the following gray literature sources for information related to relative exposure of PFNA for all potentially relevant routes of exposure (oral, inhalation, dermal) and exposure pathways relevant to humans:

- ATSDR's *Toxicological Profiles;*
- CDC's national reports on human exposures to environmental chemicals;
- EPA's CompTox Chemicals Dashboard;
- EPA's fish tissue studies;
- EPA's Toxics Release Inventory;
- EPA's UCMR data;
- Relevant documents submitted under the Toxic Substances Control Act and relevant reports from EPA's Office of Chemical Safety and Pollution Prevention;
- U.S. Food and Drug Administration's (FDA's) *Total Diet Studies* and other similar publications from FDA, U.S. Department of Agriculture, and Health Canada;
- National Oceanic and Atmospheric Administration's (NOAA's) National Centers for Coastal Ocean Science data collections;
- National Science Foundation direct and indirect food and/or certified drinking water additives;
- PubChem compound summaries;
- Relevant sources identified in the relative source contribution discussions (Section 5) of EPA's *Proposed Approaches to the Derivation of a Draft Maximum Contaminant Level Goal for Perfluorooctanoic Acid (PFOA)/Perfluorooctane Sulfonic Acid (PFOS) in Drinking Water; and*
- Additional sources, as needed.

EPA has included available information from these gray literature sources for PFNA relevant to its uses, chemical and physical properties, and for occurrence in drinking water (directly or indirectly in beverages like coffee, tea, commercial beverages, or soup), ambient air, foods (including fish and shellfish), incidental soil/dust ingestion, and consumer products. EPA has also included available information specific to PFNA below on any regulations that may restrict PFNA levels in media (e.g., water quality standards, air quality standards, food tolerance levels).

Summary of Potential Sources of PFNA Exposure

EPA presents information below from studies performed in the United States. While studies from non-U.S. countries inform an understanding global exposure sources and trends, the RSC determination is based on the available data for the United States.

Dietary Sources

Seafood

PFNA was detected in 108 of 157 fish tissue composite samples collected during EPA's National Lake Fish Tissue Study, with a maximum concentration of 9.70 ng/g and a 50th percentile concentration of 0.32 ng/g (Stahl et al., 2014). It was detected in one of 162 fish tissue composite samples collected during EPA's 2008–2009 National Rivers and Streams Assessment (NRSA) at a concentration of 2.48 ng/g (Stahl et al., 2014). More recently, PFNA was detected in 135 of 349 fish tissue composite samples at concentrations ranging from 0.100 ng/g to 1.910 ng/g in EPA's 2013–2014 NRSA (EPA, 2020). PFNA was also detected in 119 of 152 fish tissue composite samples at concentrations ranging from 0.12 ng/g to 9.32 ng/g in EPA's 2015 Great Lakes Human Health Fish Fillet Tissue Study (EPA, 2021). In 2001, PFNA was detected at mean concentrations of 1.0 ng/g, 0.57 ng/g, 2.8 ng/g, 2.9 ng/g, and 1.1 ng/g (wet weight) in whole body homogenates of lake trout collected from Lake Superior, Lake Michigan, Lake Huron, Lake Erie and Lake Ontario, respectively (Furdui et al., 2007 as cited in ATSDR, 2021 and NCBI, 2022). In addition, PFNA was detected in lake trout at concentrations of 0.70 ng/g for Lake Superior, 1.4 ng/g for Lake Huron, 2.6 ng/g for eastern Lake Erie, and 0.90 ng/g for Lake Ontario; PFNA was also detected at a concentration of 1.2 ng/g in walleye collected from western Lake Erie (De Silva et al., 2011; ATSDR, 2021). PFNA was detected in mixtures of whole fish from the Missouri River, the Mississippi River, and the Ohio River at concentrations of 0.43 ng/g, 0.78 ng/g, and 1.03 ng/g, respectively (Ye et al., 2008; ATSDR, 2021). Concentrations of PFNA ranged from 0.01 ng/g to 0.73 ng/g in capelin whole body samples, < 0.09 ng/g to 1.3 ng/g in cod muscle samples, and 0.05 ng/g to 8.0 ng/g in salmon muscle samples collected from the Hudson Bay region of northeast Canada in 1999 to 2003 (Kelly, et al. 2009; NCBI, 2022). PFNA was not included in NOAA's National Centers for Coastal Ocean Science, National Status and Trends Data (NOAA, 2022).

Five additional studies were identified that evaluated PFNA levels in seafood (Byrne et al., 2017; Chiesa et al., 2019; Schecter et al., 2010; Young et al., 2013, 2022) (Table A-2). Four of these studies analyzed fish purchased from stores and fish markets. PFNA was detected infrequently in samples reported in Chiesa et al (2019), Schecter et al. (2010) and Young et al. (2013): one of ten samples of striped bass (1.4 ng/g) and in one of nine samples of shrimp (1.2 ng/g), but not in samples of crab meat, catfish, clams, cod, flounder, pangasius, pollock, tuna (including canned), salmon, scallops, tilapia, canned sardines, or frozen fish sticks. No other fish types were sampled in these three studies, and other than canned tuna and sardines, none were analyzed as prepared

for eating. Seafood samples reported in Young et al. (2022) reported detectable PFNA in five out of the eight types of seafood evaluated. These included canned clams, canned tuna, cod, crab meat, and pollock (fish fillets and frozen fish sticks). No PFNA was detected in salmon, tilapia or shrimp. Seafood packaging was also evaluated for PFAS coatings, and it was determined the packaging did not contribute to any PFAS concentrations observed in the study.

One study evaluated fish samples collected directly from rivers and lakes (Byrne et al., 2017). As part of a study to assess exposure to PFNA and other PFAS among residents of two remote Alaska Native villages on St. Lawrence Island, Byrne et al. (2017) measured PFAS concentrations in stickleback and Alaska blackfish, resident fish used as sentinel species to detect accumulation of PFAS in the local environment. Stickleback were collected from three locations—Suqitughneq (Suqi) River watershed (n = 9 composite samples), Tapisaggak (Tapi) River (n = 2 composite samples), and Troutman Lake (n = 3 composite samples). Blackfish were collected from the Suqi River (n = 29) but were not found in the other water bodies. Authors reported that the Suqi River watershed was upstream and downstream of a formerly used defense site and Tapi River was east of a military site, however at the start of the study none of the sites were known to be contaminated with PFAS. The sample dates were not reported. PFNA was not detected in the blackfish samples but was detected in 100%, 56%, and 50% of stickleback samples from Troutman Lake, Suqi River, and Tapi River, respectively, with authors noting that PFNA was the most frequently detected PFAS in stickleback. PFNA concentrations ranged between 2.72 ng/g–4.13 ng/g ww at Troutman Lake, from below the limit of detection (LOD) to 1.52 ng/g ww at Suqi River, and < LOD–0.78 ng/g ww at Tapi River (LOD not reported; limit of quantitation (LOQ) = 0.5–1 ng/g ww). The authors reported that total PFAS levels were "exceptionally high" in Troutman Lake and hypothesized that stickleback were exposed to a local PFAS source and that contaminant may be leaching from village and military landfills.

The remaining four studies purchased seafood from stores and fish markets (Chiesa et al., 2019; Schecter et al., 2010; Young et al., 2013, 2022). Young et al. (2013) assessed fish and shellfish collected in 2010–2012 from retail markets across the continental United States. Retail markets in California, Florida, Illinois, Mississippi, New Jersey, New York, Tennessee, Texas, and Washington, D.C. were represented. Authors selected the ten most consumed fish and shellfish in the United States that were farm raised, wild caught, or had unknown origin. Among the crab meat, shrimp, striped bass, catfish, clams, cod, flounder, pangasius, pollock, tuna, salmon, scallops, and tilapia, PFNA was only detected in one of nine samples of shrimp at a concentration of 1.2 ng/g and one of ten samples of striped bass at a concentration of 1.4 ng/g. Young et al. (2022) evaluated fish and shellfish collected from retail markets in the Washington, D.C. metropolitan area, from March 2021 through May 2022. Some clam samples were also purchased online. Eight seafood products were selected that represented those in the top ten types of seafood consumed in the United States. Seafood products were farm raised, wild-caught or of unknown origin. PFNA was detected in all clam (n=10) and crab (n=11) samples with concentrations ranging up to 796 ng/kg for clams and 350 ng/kg for crabs. Samples of cod (40%, n=10), pollock (20%, n=10) and canned/pouch tuna (30%, n=10) also had detectable PFNA with concentrations of 45-103 ng/kg, 100-106 ng/kg and 44-77 ng/kg, respectively. Salmon, shrimp and tilapia did not have detectable levels of PFNA (MDL=30-39 ng/kg). Schecter et al. (2010) evaluated PFNA and other PFAS in seafood collected from five Dallas, Texas grocery stores in 2009. The origin or source of seafood was not described. Seafood included canned sardines in water, canned tuna, fresh catfish fillet, cod, frozen fish sticks, salmon, and tilapia (n = 1

composite sample for each seafood type). PFNA was not detected in any of the seafood samples. Finally, in a multicontinental study, Chiesa et al. (2019) collected salmon from a wholesale fish market in Milan, Italy; the sampling year was not reported. Wild-caught salmon samples originated from the United States (n = 7), Canada (n = 15), and Scotland (n = 2), while farmed salmon samples originated from Norway (n = 25) and Scotland (n = 17). Among the salmon that originated from the United States – Pacific Ocean (Food and Agriculture Organization Area (FAO) 67 and 77), two species—*Oncorhynchus kisutch* and *Oncorhynchus keta*—were analyzed, with PFNA not detected in either species (LOQ = 0.005 ng/g). PFNA was also not detected in wild-caught salmon from Canada and Scotland.

Table A-2. Summary of PFNA Data in Seafood

Study	Location and Source	Seafood Type	Results
		United States	
Byrne et al. (2017)	United States (Alaska) Stickleback collected from three locations on St. Lawrence Island: Suqitughneq (Suqi) River watershed (upstream and downstream of a formerly used defense site), Tapisaggak (Tapi) River (located approximately 5 km east of military site), and Troutman Lake, a coastal lake situated adjacent to the village of Gambell. Alaska blackfish collected from the Suqi River but were absent from the other water bodies. Sampling year not reported. No sites were known to be contaminated with PFAS at the initiation of the study.	Stickleback and Alaska blackfish	**Stickleback:** **Troutman Lake: n = 3*, DF[a] 100%, mean[a] (range) = 3.43 (2.72–4.13) ng/g ww** **Suqi River: n = 9*, DF[a] 56%, range = < LOD–1.52] ng/g ww** **Tapi River: n = 2*, DF[a] 50%, range = < LOD–0.78 ng/g ww** Blackfish: n = 29, DF 0% (LOQ = 0.5–1 ng/g ww for all PFAS) *Number of composite samples, each composed of ~10 stickleback fish

Study	Location and Source	Seafood Type	Results
United States			
Young et al. (2013)	United States (California; Illinois; Mississippi; Tennessee; Florida; New Jersey; New York; Texas; Washington, D.C.) Fish and shellfish collected from retail markets in 11 areas across the continental United States from 2010–2012. The fish and shellfish included farm raised, wild caught, and unknown origin, as well as freshwater fish, saltwater fish, and euryhaline fish. Crab meat, clams, cod, flounder, pangasius, salmon, scallops, and tilapia purchased from Washington, D.C. Shrimp purchased from Orlando, Florida; Memphis, Tennessee; and Nashville, Tennessee. Striped bass purchased from New York, New York and Cherry Hill, New Jersey. Catfish purchased from Indianola, Mississippi; Dallas, Texas; Tampa, Florida; and Orlando, Florida. Pollock purchased from Huntington Beach, California. Tuna purchased from Chicago, Illinois.	Crab, shrimp, striped bass, catfish, clams, cod, flounder, pangasius, pollock, tuna (can and pouch), salmon, scallops (bay and sea), tilapia	**Shrimp: n = 9, DF[a] 11%, range = ND–1.2* ng/g** **Striped bass: n = 10, DF[a] 10%, range = ND–1.4* ng/g** Crab meat: n = 1, DF 0% Catfish: n = 13, DF 0% Clams: n = 1, DF 0% Cod: n = 1, DF 0% Flounder: n = 1, DF 0% Pangasius: n = 1, DF 0% Pollock: n = 1, DF 0% Tuna: n = 3, DF 0% Salmon: n = 2, DF 0% Scallops: n = 2, DF 0% Tilapia: n = 1, DF 0% (MDL = 0.60 ng/g for all seafood) *This value was above the MDL but below the LOQ; LOQ is estimated as 3x the MDL

Study	Location and Source	Seafood Type	Results
	United States		
Young et al. (2022)	United States (Washington, D.C.) Fish and shellfish collected from retail markets in the Washington, D.C. metropolitan area from 2021-2022. Fish and shellfish samples included farm raised, wild-caught and unknown origin. Country of origin was provided, if known. Ten samples of each seafood type, except for crab, which included 11 samples.	Crab, clams (can), shrimp, cod, pollock (fish sticks, fillet), salmon, tuna (can and pouch), tilapia	**Clam meat: n=10, DF 100% range=333-796 ng/kg** **Crab: n=11, DF 100%, range=54-350 ng/kg** **Cod: n=10, DF 40%, range= <MDL-103 ng/kg** **Tuna: n=10, DF 30%, range=<MDL-77 ng/kg** **Pollock: n=10, DF 20%, range=<MDL-106 ng/kg** Salmon: n=10, DF 0% Shrimp: n=10, DF 0% Tilapia: n=10, DF 0% MDL=30 ng/kg (instrument 1) MDL=39 ng/kg (instrument 2)
Schecter et al. (2010)	United States (Texas) Seafood samples from five different grocery stores in Dallas, Texas were collected in 2009. Ten individual samples were collected for each food type and combined to form composite samples. The origin/source of the food samples were not reported.	Salmon, canned tuna, fresh catfish fillet, tilapia, cod, canned sardines, frozen fish sticks	Salmon: n = 1, DF 0% Canned tuna: n = 1, DF 0% Fresh catfish fillet: n = 1, DF 0% Tilapia: n = 1, DF 0% Cod: n = 1, DF 0% Canned sardines: n = 1, DF 0% Frozen fish sticks: n = 1, DF 0% (LOD not reported for any seafood type) *n reflects number of composite samples, each composed of ~10 individual samples

Study	Location and Source	Seafood Type	Results
	United States		
Chiesa et al. (2019)	United States (Pacific Ocean) Wild-caught fish were collected at a wholesale fish market in Milan, Italy. Sampling year was not reported. The wild-caught salmon were from USA-Pacific Ocean (Food and Agriculture Organization Area 67 and 77).	Wild-caught salmon (*Oncorhynchus kisutch* and *Oncorhynchus keta*)	*Oncorhynchus kisutch:* n = 5, DF 0% *Oncorhynchus keta*: n = 2, DF 0% (LOQ = 0.005 ng/g)

Notes: DF = detection frequency; ww = wet weight, LOD = limit of detection; LOQ = limit of quantitation; MDL = method detection limit; ND = not detected.

[a] The DF and/or mean was not reported in the study and was calculated in this synthesis. Means were calculated only when DF = 100%.

Other Food Types

PFNA was included in a suite of PFAS evaluated in FDA's 2019, 2021, and 2022 Total Diet Study Sampling (U.S. FDA, 2020a,b, 2021a,b, 2023a,b,c,d); it was detected at concentrations of 233 ng/kg (0.233 ng/g) in baked cod and 50 ng/kg (0.050 ng/g) in frozen (oven-cooked) fish sticks or patties in 2021, but it was not detected in any of the other food samples tested. It should be noted that FDA indicated that the sample sizes used in the PFAS 2019, 2021, and 2022 Total Diet Study Sampling were limited and that the results should not be used to draw definitive conclusions about PFAS levels in the general food supply (U.S. FDA, 2022c). PFNA was not detected in milk samples collected from a farm with groundwater known to be contaminated with PFAS; however, it was detected in produce (corn) collected from an area near a PFAS production plant in FDA studies of the potential PFAS exposure to the U.S. population (U.S. FDA 2018, 2021c). PFNA was detected in beef steak in the Canadian Total Diet studies from 1992 to 2004, but it was not detected in any of the other food samples tested (ATSDR, 2021; Tittlemier et al., 2007).

Seven U.S. studies were identified that examined PFNA in breastmilk or food types other than breastmilk (Blaine et al., 2013, 2014; Kuklenyik et al., 2004; Schecter et al., 2010; Tipton et al., 2017; von Ehrenstein et al., 2009; Young et al., 2012) (Table A-3). Few U.S. studies analyzed foods from any one origin—only two studies sampled from store- or market-bought meats, eggs, produce, and dairy, one studied wild alligator meat, two sampled from crops (produce and corn grain and stover) grown in biosolids-amended soils (and also control and municipal soils) as part of greenhouse and field studies, and two studied breastmilk.

Two studies purchased food items from stores and markets for evaluation (Schecter et al., 2010; Young et al., 2012). Schecter et al. (2010) assessed PFNA and other PFAS in food samples collected from five Dallas, Texas grocery stores in 2009. The origin or source of each food was not described. Food items included meat products (bacon, canned chili, chicken breast, ground beef, roast beef, ham, sausage, and turkey), dairy (butter, cheeses, frozen yogurt, ice cream, milk, and yogurt), eggs, and grains (cereal), fruits and vegetables (apples, potatoes), and fats/other (canola oil, margarine, olive oil, peanut butter). PFNA was not detected in any of the food samples. In Young et al. (2012), cow milk was purchased from retail markets across the continental United States representing 17 states; the sampling year was not reported. Cow milk samples included organic milk, vitamin D added milk, and ultra-pasteurized milk. PFNA was not detected in any of the 49 retail milk samples (method detection limit (MDL) = 0.28 ng/g).

One study investigated PFAS levels from wild meat (Tipton et al., 2017). Tipton et al. (2017) assessed alligator tail meat that was collected during the South Carolina recreational hunting season between September to October 2015. Tail meat samples were collected from four different public hunt units—Southern Coastal, Middle Coastal, Midlands, and Pee Dee. PFNA was detected in samples from all hunt units with the exception of the Midlands (n = 2), where PFNA was not detected. Median concentrations from Southern Coastal (n = 19), Middle Coastal (n = 17), and Pee Dee (n = 2) were 0.107 ng/g, 0.102 ng/g, and 0.117 ng/g wet mass, respectively.

Two studies by Blaine et al. (2013, 2014) evaluated PFNA in crops grown in greenhouse and field studies. In Blaine et al. (2014), PFAS levels were measured in celery root, pea fruit, and radish root grown in a greenhouse study with control (unamended) soil, industrially impacted soil, and municipal soil (n = 3–5). PFNA was detected in radish root and celery shoot from all three soils and pea fruit from only industrially impacted soil. Mean concentrations of PFNA in radish root for the control, industrially impacted, and municipal soil were 4.79 ng/g, 26.88 ng/g, and 5.99 ng/g, respectively. Mean concentrations of PFNA in celery shoot for the control, industrially impacted, and municipal soil were 1.89 ng/g, 13.81 ng/g, and 1.62 ng/g, respectively. The mean concentration of PFNA in pea fruit in the industrially impacted soil was 1.45 ng/g. Authors noted minor cross-contamination of the control soil due to the proximity of the unamended soil to biosolids-amended soil. In Blaine et al. (2013), authors studied the uptake of PFAS into edible crops in both field and greenhouse studies. In the field study, PFAS levels were measured in corn grain and corn stover grown with control (unamended), urban biosolids-amended, and rural biosolids-amended soil (n = 3–7). Mean PFNA concentrations were below the LOQ in both corn grain and corn stover grown in any field study plots (< 0.10 ng/g for corn grain; < 0.29 ng/g for corn stover). In the greenhouse study, lettuce and tomato plants were grown in control soil, industrially impacted soil, or municipal soil (n = 3–5). Mean PFNA concentrations were below the LOQ (2.96 ng/g) in any tomato plants but was detected in lettuce grown in industrially impacted soil and municipal soil at mean concentrations of 57.39 ng/g and 4.73 ng/g, respectively. PFNA was not detected above the LOQ (0.04 ng/g) in lettuce grown in control soil. Sampling year was not reported.

The remaining two studies evaluated the occurrence of PFNA in breastmilk (Kuklenyik et al., 2004; von Ehrenstein et al., 2009). von Ehrenstein et al. (2009) collected breastmilk samples between December 2004 and July 2005 from women between the ages of 18 and 38 at the time of recruitment as part of the pilot study Methods Advancement for Milk Analysis (MAMA). Women provided milk samples at two visits—the first visit was 2–7 weeks postpartum, and the second visit was 3–4 months postpartum. PFNA was not detected in any of the samples from the first visit (n = 18) or second visit (n = 20). Similarly, PFNA was below the LOD (1.0 ng/mL) in the samples reported by Kuklenyik et al. (2004). Kuklenyik et al. (2004) did not report information on the breastmilk donors or the sampling procedure as it was unavailable; PFNA was not detected in either of the two samples.

Table A-3. Summary of PFNA Data in Other Food

Study	Location and Source	Food Types	PFNA Results
		United States	
Schecter et al. (2010)	United States (Texas) Food samples from five different grocery stores in Dallas, Texas were collected in 2009. Ten individual samples were collected for each food type and combined to form composite samples. The origin/source of the food samples were not reported.	Dairy; fruits and vegetables; grains; meat; fats/other	Meat Hamburger: n = 1, DF 0% Bacon: n = 1, DF 0% Sliced turkey: n = 1, DF 0% Sausages: n = 1, DF 0% Ham: n = 1, DF 0% Sliced chicken breast: n = 1, DF 0% Roast beef: n = 1, DF 0% Canned chili: n = 1, DF 0% Dairy and Eggs Butter: n = 1, DF 0% American cheese: n = 1, DF 0% Other cheese: n = 1, DF 0% Whole milk: n = 1, DF 0% Ice cream: n = 1, DF 0% Frozen yogurt: n = 1, DF 0% Whole milk yogurt: n = 1, DF 0% Cream cheese: n = 1, DF 0% Eggs: n = 1, DF 0% Grains Cereals: n = 1, DF 0% Fruits and Vegetables Apples: n = 1, DF 0% Potatoes: n = 1, DF 0% Fats and Other Olive oil: n = 1, DF 0% Canola oil: n = 1, DF 0% Margarine: n = 1, DF 0% Peanut butter: n = 1, DF 0% (LOD not reported for any food item) *n reflects number of composite samples, each composed of ~10 individual samples

Study	Location and Source	Food Types	PFNA Results
		United States	
Young et al. (2012)	United States (17 states) Retail cow's milk samples were all pasteurized whole milk, commercially available, and purchased at retail markets across the continental United States representing 17 states. Samples were organic milk, vitamin D added milk, or ultra-pasteurized milk. Sampling year not reported.	Dairy	n = 49, DF 0% (MDL = 0.28 ng/g)
Tipton et al. (2017)	United States (South Carolina) Alligator tail meat samples were collected from a local wild game meat processer during the South Carolina recreational hunt season between September to October 2015. Samples were from four different public hunt units—Southern Coastal, Middle Coast, Midlands, and Pee Dee.	Meat	**Alligator tail:** **Southern coastal: n = 19, DF[a] 74%, median (range) = 0.107 (< 0.088–0.551) ng/g wet mass** **Middle coastal: n = 17, DF[a] 65%, median (range) = 0.102 (< 0.073–0.553) ng/g wet mass** **Pee Dee: n = 2, DF[a] 100%, median (range) = 0.117 (0.100–0.135) ng/g wet mass** Midlands: n = 5, DF 0% (RL not reported)

Study	Location and Source	Food Types	PFNA Results
		United States	
Blaine et al. (2014)	United States (Midwest) Crops grown in in greenhouse study with control (unamended), industrially impacted soil, or municipal soil. Control soil had minor cross-contamination due to proximity to biosolids-amended fields. Industrially impacted soil was amended with industrially impacted biosolids, and municipal soil was amended with municipal biosolids for over 20 years. Crops grown in the greenhouse study were grown from seed in pots, which were randomly arranged within the greenhouse. Sampling year not reported.	Fruits and vegetables	**Radish root:** **Control: n = 3–5, DF NR, mean = 4.79 ng/g** **Industrially impacted; n = 3–5, DF NR, mean = 26.68 ng/g** **Municipal: n = 3–5, DF NR, mean = 5.99 ng/g** **Celery shoot:** **Control: n = 3–5, DF NR, mean = 1.89 ng/g** **Industrially impacted: n = 3–5, DF NR, mean = 13.81 ng/g** **Municipal: n = 3–5, DF NR, mean = 1.62 ng/g** Pea fruit: Control: n = 3–5, DF 0% **Industrially impacted: n = 3–5, DF NR, mean = 1.45 ng/g** Municipal: n = 3–5, DF 0% (LOQ = 0.07 ng/g)

Study	Location and Source	Food Types	PFNA Results
		United States	
Blaine et al. (2013)	United States (Midwest) Crops grown in urban and rural full-scale field study with control (unamended) and biosolids-amended soil. Three agricultural fields were amended (0.5×, 1×, or 2×) with municipal biosolids. Urban biosolids (1× and 2×) were from a WWTP receiving both domestic and industrial waste. Rural biosolids (0.5×) were from a WWTP receiving domestic waste only. Control plots were proximal to the rural and urban amended corn grain and corn stover field sites; sampling year not provided. Crops grown in greenhouse study with control (nonamended) and biosolids-amended soil. Nonamended soil obtained from a field that received commercial fertilizers and had a similar cropping system as the nearby municipal soil site. Municipal soil was obtained from a reclamation site in Illinois where municipal biosolids were applied at reclamation rates for 20 years, reaching the cumulative biosolids application rate of 1,654 Mg/ha. Industrially impacted soil was created by mixing composted biosolids from a small municipal (but impacted by PFAA manufacturing) WWTP with control soil on a 10% mass basis. Sampling year not provided.	Fruits and vegetables; grains	Field study: Corn grain: Urban nonamended: n = 3–7, DF NR, mean = < 0.10 ng/g Urban 1×: n = 3–7, DF NR, mean = < 0.10 ng/g Urban 2×: n = 3–7, DF NR, mean = < 0.10 ng/g Rural nonamended: n = 3–7, DF NR, mean = < 0.10 ng/g Rural 0.5×: n = 3–7, DF NR, mean = < 0.10 ng/g Corn stover: Urban nonamended: n = 3–7, DF NR, mean = < 0.29 ng/g Urban 1×: n = 3–7, DF NR, mean = < 0.29 ng/g Urban 2×: n = 3–7, DF NR, mean = < 0.29 ng/g Rural nonamended: n = 3–7, DF NR, mean = < 0.29 ng/g Rural 0.5×: n = 3–7, DF NR, mean = < 0.29 ng/g (LOQ = 0.10 ng/g for corn grain; LOQ = 0.29 ng/g for corn stover) Greenhouse study: Lettuce: Nonamended: n = 3–5, DF NR, mean = < 0.04 ng/g **Industrially impacted: n = 3–5, DF NR, mean = 57.39 ng/g** **Municipal: n = 3–5, DF NR, mean = 4.73 ng/g** Tomato: Nonamended: n = 3–5, DF NR, mean = < 2.86 ng/g Industrially impacted: n = 3–5, DF NR, mean = < 2.86 ng/g Municipal: n = 3–5, DF NR, mean = < 2.86 ng/g (LOQ = 0.04 ng/g for lettuce; LOQ = 2.86 ng/g for tomato)

Study	Location and Source	Food Types	PFNA Results
	United States		
von Ehrenstein et al. (2009)	United States (North Carolina) As part of the Methods Advancement for Milk Analysis (MAMA) pilot study, 34 breastfeeding women aged 18 to 38 years at recruitment provided breastmilk samples at two visits. The first visit occurred 2–7 weeks postpartum, and the second visit occurred 3–4 months postpartum. Both visits were between December 2004 and July 2005.	Breastmilk	Visit #1: = 18, DF 0% Visit #2: n = 20, DF 0% (LOQ = 0.30 ng/mL)
Kuklenyik et al. (2004)	United States (Georgia) Authors reported that no information was provided on the human milk donors or the sampling procedure.	Breastmilk	n = 2, DF 0% (LOD = 1.0 ng/mL)

Notes: DF = detection frequency; LOD = limit of detection; LOQ = limit of quantitation; 0.5×, 1×, or 2× = ½, 1, or 2 times the agronomic rate of biosolids application to meet nitrogen requirements of the crop; MDL = method detection limit; NR = not reported; RL = reporting limit; WWTP = wastewater treatment plant.
Bold indicates detected levels of PFNA in food.
[a] The DF and/or mean was not reported in the study and was calculated in this synthesis. Means were calculated only when DF = 100%.

Food Contact Materials

PFNA has been detected in the packaging paper of one of three brands of microwave popcorn bags (uncooked and cooked) (Sinclair et al., 2007; ATSDR, 2021). One other study analyzed the occurrence of PFAS in treated food contact paper and other consumer products purchased from local retailers and online stores in the United States between March 2007 and September 2011 (Liu et al., 2014). All treated food contact paper was manufactured in the United States. PFNA was detected in 33% of samples (n = 9), with two of the detects below 10 ng/g and the third detect at 212 ng/g.

In 2011, FDA reached a voluntary agreement with industry to remove from the market certain PFAS greaseproofing agents used in fast food packaging. As such, the reported detection of PFNA in fast food packaging in the above cited studies may be an overestimation of the occurrence and levels of PFNA in current food packaging paper.

Consumer Products

Since the 1950s, PFNA has been used in industrial and consumer products, including fabric and carpet protective coatings, paper coatings, insecticide formulations, and surfactants (NCBI, 2022). PFNA and other long-chain PFAS are found in aqueous film forming foams, cosmetics, dental floss, floor polish, leather, food packaging materials, lithium batteries, ski wax, treated apparel, work apparel for medical staff, pilots, and firefighters, and in hair treatment products (NCBI, 2022).

Based on limited testing, PFNA has been detected in rinsates from fluorinated high-density polyethylene (HDPE) containers used by one pesticide product supplier (EPA, 2022a). PFNA is not a registered pesticide under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), and EPA does not set a 40 CFR Part 180 pesticide tolerance in food and feed commodities for PFNA (U.S. GPO, 2022). Maximum residue levels for PFNA were not found in the Global Maximum Residue Level Database (Bryant Christie Inc., 2022).

Two studies were identified that analyzed PFNA concentrations in a range of consumer products, including children's nap mats, household carpet/fabric-care liquids, and textiles (Liu et al., 2014; Zheng et al., 2020) (Table A-4). Of the two U.S. studies, the consumer products evaluated are likely used by adults (e.g., floor waxes), can come into contact with both adults and children (e.g., treated upholstery), or the user was not specified (e.g., clothing).

Zheng et al. (2020) determined the occurrence of ionic and neutral PFAS in the childcare environment (dust and nap mats). Samples of children's nap mats were collected from seven Seattle childcare centers (n = 26; 20 polyurethane foam, 6 vinyl cover samples). PFNA was detected in 36% of nap mat samples with a mean concentration of 0.19 ng/g. Half of the analyzed mats were purchased as new products and the other half were used. The authors reported that total PFAS levels in the new vs. used mats were not significantly different. Total PFAS levels in mat foam vs. mat covers were also similar. Based on these results, the authors suggested that indoor air was not the major source of PFAS in mats and that PFAS in mats could be associated with the manufacturing process. Liu et al. (2014) analyzed the occurrence of PFAS in consumer products (including pre-treated carpeting, commercial carpet-care liquids, household carpet/fabric-care liquids, treated apparel, treated home textiles and upholstery, treated non-woven medical garments, treated floor waxes and stone-wood sealants, membranes

for apparel, and thread-sealant tapes and pastes) purchased between March 2007 and September 2001 from local retailers and online stores in the United States. The consumer products originated from the United States, England, Vietnam, China, Thailand, El Salvador, Bangladesh, Dominican Republic, Malaysia, and Indonesia. PFNA was detected in 44% of 9 pre-treated carpeting samples (ranging from below the detection limit (BDL) to 236 ng/g); in 58% of 12 commercial carpet/fabric-care liquid samples (BDL–8,860 ng/g); in 15% of 13 household carpet/fabric-care liquid and foam samples (BDL–37.3 ng/g); in 60% of 15 treated apparel samples (BDL–235 ng/g); in 100% of 6 treated home textile and upholstery samples with a mean of 42.6 ng/g; in 56% of 9 treated non-woven medical garment samples (BDL–334 ng/g); in 88% of 8 treated floor wax and stone/wood sealant samples (BDL–2,740 ng/g); and in 75% of 8 membranes for apparel samples (BDL–12.8 ng/g). PFNA was not detected in thread-sealant tapes and pastes (n = 6). Detection limits were not reported in the study.

Table A-4. Summary of PFNA Consumer Product Data

Study	Location	Site Details	Results
		United States	
Zheng et al. (2020)	United States (Seattle, Washington)	Children's nap mat samples (n = 26, finely cut) from seven Seattle childcare centers, including polyurethane foam (n = 20) and vinyl cover (n = 6) samples. Sampling year not reported.	N = 26, DF 36%, mean, median (range) = 0.19, 0.11 (ND–0.65) ng/g (MDL = 0.08 ng/g)
Liu et al. (2014)	United States (unspecified)	Consumer products commonly used indoors were purchased between March 2007 and September 2011 from local retailers and online stores in the United States. The samples analyzed for PFCAs included pre-treated carpeting, commercial carpet/fabric-care liquids, household carpet/fabric-care liquids and foams, treated apparel, treated home textile and upholstery (i.e., mattress pads), treated non-woven medical garments, treated floor waxes and stone-wood sealants, membranes for apparel, and thread-sealant tapes and pastes. The products originated from the United States, England, Vietnam, China, Thailand, El Salvador, Bangladesh, Dominican Republic, Malaysia, and Indonesia.	Pre-treated carpeting: n = 9, DF[a] 44%, range = BDL–236 ng/g Commercial carpet/fabric-care liquids: n = 12, DF[a] 58%, range = BDL–8,860 ng/g Household carpet/fabric-care liquids and foams: n = 13, DF[a] 15%, range = BDL–37.3 ng/g Treated apparel: n = 15, DF[a] 60%, range = BDL–235 ng/g Treated home textile and upholstery: n = 6, DF[a] 100%, mean[a] (range) = 42.6 (3.80–213) ng/g Treated non-woven medical garments: n = 9, DF[a] 56%, range = BDL–334 ng/g Treated floor waxes and stone-wood sealants: n = 8, DF 88%, range = BDL–2,740 ng/g Membranes for apparel: n = 8, DF[a] 75%, range = BDL–12.8 ng/g Thread-sealant tapes and pastes: n = 6, DF[a] 0% (DL not reported)

Notes: BDL = below detection limit; DF = detection frequency; DL = detection limit; MDL = method detection limit; ND = not detected.
[a] The DF and/or mean was not reported in the study and was calculated in this synthesis. Means were calculated only when DF = 100%.

Indoor Dust

In a Wisconsin Department of Health Services study, Knobeloch et al. (2012) examined levels of 16 perfluoroalkyl chemicals in vacuum cleaner dust from 39 Wisconsin homes across 16 counties in March and April 2008 (Table A-5). Samples from these homes built between 1890 and 2005 were collected during a pilot study to assess residential exposure to persistent contaminants found in the Great Lakes Basin. PFNA was found in all samples at a median concentration of 12 ng/g. The number of rooms with synthetic, wall-to-wall carpeting and the square footage of the homes were both significantly positively correlated with dust concentrations of PFNA. Based on the results of this study, the authors suggested that perfluoroalkyl chemicals may be ubiquitous contaminants in U.S. homes. In an EPA study of 112 indoor dust samples collected from vacuum cleaner bags from homes and daycare centers in North Carolina and Ohio in 2000–2001 (EPA's Children's Total Exposure to Persistent Pesticides and Other Persistent Organic Pollutants (CTEPP) study), samples were collected from 102 homes and 10 daycare centers in North Carolina (49 homes, 5 daycare centers) and Ohio (53 homes, 5 daycare centers) (Strynar and Lindstrom, 2008). Results were not reported separately for homes and daycares. Overall, PFNA was detected in 42.9% of all samples (n = 112) with mean and median concentrations of 22.1 ng/g and 7.99 ng/g, respectively. The authors concluded that the study measured perfluorinated compounds in house dust at levels that may represent an important pathway for human exposure.

Additional peer-reviewed studies were identified that evaluated the occurrence of PFNA and other PFAS in dust of indoor environments, primarily in homes, as well as in schools, childcare facilities, offices, and vehicles (Byrne et al., 2017; Fraser et al., 2013; Karásková et al., 2016; Kato et al., 2009; Scher et al., 2019; Wu et al., 2014; Zheng et al., 2020;) (Table A-5). For those studies with results stratified for U.S. homes, PFNA levels and detection frequencies were lowest in a study of remote Alaska Native villages (35% detection, median below 0.2 ng/g), while in other U.S. locations, PFNA was detected in at least 65% of samples (some studies reporting 100% detection) at widely varying mean and median levels across the studies (from approximately 4 ng/g to 70 ng/g). Few studies sampled childcare centers, vehicles, and offices, and none of the reviewed studies reported measurements in other microenvironments (e.g., public libraries, universities).

Several studies reported results from dust samples collected only from homes (Byrne et al., 2017; Scher et al., 2019; Wu et al., 2014), with one study sampling from locations near a PFAS production facility. Scher et al. (2019) evaluated indoor dust in 19 homes in Minnesota within a groundwater contamination area (GCA) in the vicinity of a former 3M PFAS production facility. Homes within the GCA had previous or ongoing PFAS contamination in drinking water and were served by the Oakdale, Minnesota PWS or a private well previously tested and shown to have detectable levels of PFOA or PFOS. In the house dust samples, collected from July to September 2010, the detection frequencies for PFNA were 68% and 95% for entryways to the yard and interior living spaces such as the family or living rooms, respectively (n = 19 each), with median concentrations of 9.7 ng/g and 26 ng/g, respectively. PFAS concentrations in both sampling locations were higher than corresponding soil concentrations, suggesting that interior sources were the main contributors to PFAS in house dust.

Byrne et al. (2017) assessed exposure to PFNA and other PFAS among residents of two remote Alaska Native villages on St. Lawrence Island. PFAS concentrations were measured in dust collected from the surfaces of floors and furniture of 49 homes on St. Lawrence Island during February–April of 2013 and 2014. Residents were asked not to sweep or dust for one week prior to sampling. The authors described the overall PFAS levels in dust samples as "on the lower end of those reported worldwide in other studies." PFNA was detected in 35% of all samples (n = 49) with a median value below the LOD (0.1 ng/g–0.2 ng/g). Wu et al. (2014) measured concentrations of five PFCs in residential dust in California in 2008–2009. Dust samples were collected from the carpet or area rug in the main living area of the home. Homes of parents with young children and homes with older adults were differentiated to characterize the relationship between serum concentrations of PFCs and several other factors, including PFC concentrations in residential dust. PFNA was detected in 65% of samples from households with young children in Northern California (n = 82), with mean and median concentrations of 67.4 ng/g and 9.70 ng/g, respectively. PFNA was detected in 72% of samples from households of older adults in central California (n = 42), with mean and median concentrations of 58.5 ng/g and 11.85 ng/g, respectively.

Apart from the information reported by Strynar and Lindstrom (2008), one other study included childcare centers in the locations sampled (Zheng et al., 2020). Zheng et al. (2020) collected dust samples from seven childcare centers in Seattle, Washington (n = 14) and one childcare facility in West Lafayette, Indiana (n = 6 across six rooms); the sampling year was not reported. The included childcare facilities consisted of several building types, including multiple classrooms, a former church, and a former home. Because centers were vacuumed and mopped daily, dust samples were obtained from elevated surfaces (shelving, tops of bookcases/storage cubbies) along with floor dust. PFNA was detected in all samples at mean and median concentrations of 3.2 ng/g and 1.7 ng/g, respectively.

One study evaluated PFNA levels in vehicles and offices, in addition to homes. Fraser et al. (2013) collected dust samples between January and March 2009 from 3 microenvironments of 31 individuals in Boston, Massachusetts (offices (n = 31), homes (n = 30), and vehicles with sufficient dust for analysis (n = 13)). Study participants worked in separate offices located across seven buildings, which were categorized as Building A (n = 6), Building B (n = 17), or Other (n = 8). Building A was a newly constructed (approximately one year prior to study initiation) building with new carpeting and new upholstered furniture in each office; Building B was a partially renovated (approximately one year prior to study initiation) building with new carpeting throughout hallways and in about 10% of offices. The other buildings had no known recent renovation occurred. Study offices were not vacuumed during the sampling week and participants were asked not to dust or vacuum their homes and vehicles for at least one week prior to home sampling. PFNA was detected in 94%, 67%, and 85% of office, home, and vehicle dust samples, respectively, with geometric mean concentrations of 63.0 ng/g, 10.9 ng/g, and 14.7 ng/g, respectively. Geometric mean PFNA concentrations were statistically significantly higher in offices compared to homes and vehicles. The study also observed that PFNA concentration in house dust was significantly predictive of PFNA serum concentration.

Two studies evaluated dust samples collected across multiple continents (Karásková et al., 2016; Kato et al., 2009). Karásková et al. (2016) examined PFAS levels in house dust collected between April and August 2013 from the living rooms and bedrooms of 14 homes in the United

States, 15 homes in Canada, and 12 homes in the Czech Republic (locations unspecified). PFNA was detected in all U.S. samples (n = 20) at mean and median concentrations of 10.9 ng/g and 3.9 ng/g, respectively. The authors reported PFNA concentrations were significantly higher in North America compared to the Czech Republic, which they indicated may suggest a faster shift from long chain PFAS to their shorter chain homologues in Europe than in North America. Overall, no significant differences in total PFAS concentrations were found between the bedroom and living room in the same household although significant relationships were found based on type of floors, number of residents, and age of the house. A second multicontinental study (Kato et al., 2009) measured PFC concentrations in 39 household dust samples collected in 2004 from homes in the United States (Atlanta, GA) (n = 10), United Kingdom (n = 9), Germany (n = 10), and Australia (n = 10). Across all 39 homes, PFNA was detected in 25.6% of samples with a median concentration below the LOQ (2.6 ng/g). The authors did not report stratified PFNA data by country.

Table A-5. Summary of PFNA Indoor Dust Data

Study	Location	Site Details	Results
		United States	
Scher et al. (2019)	United States (Twin Cities metropolitan region, Minnesota)	Nineteen homes in three cities within a GCA near former 3M PFAS production facility as well as from three homes in the Twin Cities Metro outside the GCA. Dust samples collected from an entryway to the yard and from an interior living space (e.g., family room, living room) in each home in July–September 2010. Homes within the GCA had previous or ongoing PFAS contamination in drinking water and were served by the Oakdale, Minnesota public water system or a private well previously tested and shown to have detectable levels of PFOA or PFOS. Results were not reported for homes outside the GCA.	Entryway: n = 19, DF 68%, median (range) = 9.7 (< RL–1,000) ng/g Living room: n = 19, DF 95%, median (range) = 26 (< RL–450) ng/g (RL = 5 ng/g)
Byrne et al. (2017)	United States (St. Lawrence Island, Alaska)	Dust samples collected from the surfaces of floors and furniture from 49 homes during February–April of 2013 and 2014. Participants were asked not to sweep or dust for one week prior to sampling.	n = 49, DF 35%, median (95th percentile) = < LOD (1.93) ng/g (MDL = 0.1–0.2 ng/g for all PFAS)
Wu et al. (2014)	United States (Central Valley area, California)	Distributions of PFC dust concentrations were determined for households with young children in Northern California (n = 82) and households of older adults in central California (n = 42). Dust samples were collected in 2008–2009 from the carpet or area rug in the main living area of the homes. Homes of parents with young children and homes with older adults were differentiated to characterize the relationship between serum concentrations of PFCs and PFC concentrations measured in residential dust.	Parents of young children: n = 82, DF 65%, mean, median (range) = 67.4, 9.70 (ND–1,910) ng/g Older adults: n = 42, DF 72%, mean, median (range) = 58.5, 11.85 (ND–883) ng/g (LOD = 0.10 ng/mL) *Data below LOQ replaced by LOD/√2

Study	Location	Site Details	Results
		United States	
Knobeloch et al. (2012)	United States (Great Lakes Basin, Wisconsin)	Dust samples were collected by the Wisconsin Department of Health Services from 39 Wisconsin homes across 16 counties in March–April 2008. Vacuum bags were collected or bagless vacuums were emptied into sterilized glass jars. Homes were built between 1890 and 2005.	n = 39, DF 100%, median (range) = 12 (1.3–280) ng/g (RL = 1 ng/g)
Zheng et al. (2020)	United States (Seattle, Washington; West Lafayette, Indiana)	Seven childcare centers in Seattle (14 samples) and one center in Lafayette (6 samples); sampling year not reported. Since all centers were vacuumed and mopped daily, dust samples from elevated surfaces (shelving, tops of bookcases/storage cubbies) were collected along with floor dust in the same sample.	n = 20; DF 100%, mean, median (range) = 3.2, 1.7 (0.11–13) ng/g (MDL = 0.08)
Strynar and Lindstrom (2008)	United States (North Carolina; Ohio)	Dust samples from vacuum cleaner bags were obtained in 2000–2001 during the EPA's Children's Total Exposure to Persistent Pesticides and Other Persistent Organic Pollutants (CTEPP) study from North Carolina (49 homes, 5 daycare centers) and Ohio (53 homes, 5 daycare centers). Vacuum cleaner bags were only collected if available at each site.	n = 112; DF 42.9%, mean, median (maximum) = 22.1, 7.99 (263) ng/g (LOQ = 11.3 ng/g) *Values below the LOQ assigned a value of LOQ/√2

Study	Location	Site Details	Results
		United States	
Fraser et al. (2013)	United States (Boston, Massachusetts)	Dust samples were collected in January–March 2009 from offices (n = 31), homes (n = 30), and vehicles (n = 13) of 31 individuals. Study participants worked in separate offices located across seven buildings, which were categorized into Building A, Building B, and Other. Six samples were collected from Building A, a newly constructed (approximately one year prior to study initiation) building with new carpeting and new upholstered furniture in each office. Seventeen samples were collected from Building B, a partially renovated (approximately one year prior to study initiation) building with new carpeting throughout hallways and in about 10% of offices. Eight samples were collected from the other five remaining buildings where no known recent renovation occurred. Study offices were not vacuumed during the sampling week and homes and vehicles were not vacuumed for at least one week prior to sampling. Entire accessible floor surface areas and tops of immovable furniture were vacuumed in offices and the main living area of homes. Entire surface areas of the front and back seats of vehicles were vacuumed. Number of home dust samples was reduced to 30 because 1 participant lived in a boarding house with no main living area. Sufficient mass of dust for analysis was available from only 13 vehicles.	Homes: n = 30, DF 67%, GM (range) = 10.9 (6.21–1,420 ng/g) Offices: n = 31, DF 94%, GM (range) = 63.0 (10.9–639) ng/g Vehicles: n = 13, DF 85%, GM (range) = 14.7 (4.95–101 ng/g) (LOQ = 5 ng/g) *GM calculated by replacing values < LOQ with LOQ/√2 *Range of detected values reported

Study	Location	Site Details	Results
		United States	
Karásková et al. (2016)	United States (unspecified), Canada (unspecified), Czech Republic (unspecified)	Fifty-six dust samples from 14 homes in the United States, 15 homes in Canada, and 12 homes in the Czech Republic were collected between April and August 2013. Samples were collected in living rooms and bedrooms.	United States: n = 20, DF 100%, mean, median (range) = 10.9, 3.9 (1.1–62.9) ng/g Canada: n = 20, DF 95.0%, mean, median (range) = 19.4, 4.4 (< MQL–195) ng/g Czech Republic: n = 16, DF 50.0%, mean, median (range) = 3.0, < MQL (ND–11.0) ng/g (MDL = 0.27–1.33 ng/g; MQL = 0.72–3.48 ng/g; ranges represent lower bound and upper bound which were calculated by dividing the MDL/MQL by the biggest and smallest dust sample weight, respectively) *Mean calculated only from values > MQL *Median calculated by replacing values < MQL with √2/2*MQL
Kato et al. (2009)	United States (Atlanta, Georgia), Germany (unspecified), United Kingdom (unspecified), Australia (unspecified)	Thirty-nine household dust samples from the United States (n = 10), Germany (n = 10), United Kingdom (n = 9), and Australia (n = 10) collected in 2004 for method validation. Dust sampling procedures not described.	n = 39, DF 25.6%, median (range) = < LOQ (< LOQ–832) ng/g (LOQ = 2.6 ng/g)

Notes:
GCA = groundwater contamination area; DF = detection frequency; RL = reporting limit; LOD = limit of detection; MDL = method detection limit; ND = not detected; LOQ = limit of quantitation; GM = geometric mean; MQL = method quantification limit.

Air

Perfluoroalkyl chemicals have been released to air from wastewater treatment plants, waste incinerators, and landfills (EPA, 2016), though there is limited information on the detection levels or frequencies of PFNA in either indoor or ambient air. ATSDR (2021) notes perfluoroalkyl chemicals have been detected in air and they can be transported long distances via the atmosphere. For example, in a study performed from April 2007 to January 2009, PFNA was detected at an average concentration of 0.3 pg/m^3 in 8% of 141 atmospheric samples from Atlantic and Southern Oceans and coastal areas of the Baltic Sea (Dreyer et al, 2009; NCBI, 2022). PFNA is not expected to be broken down directly by photolysis (NCBI, 2022). PFNA can undergo hydroxylation in the atmosphere, with a (predicted average) atmospheric hydroxylation rate of 8.41 x 10^{-13} cm^3/molecule – second to a (derived) rate of 5.2 x 10^{-11} cm^3/molecule – second (with corresponding estimated half-life of 31 days for this reaction in air) (NCBI, 2022, EPA, 2022b). With a vapor pressure of 4.83 x 10^{-3} mm Hg at 20 °C (extrapolated), 8.3 x 10^{-2} mm Hg at 25 °C (estimated), 8.4 mm Hg at 99.63 °C (measured), and a (measured) range of 4.80 x 10^{-3} mm Hg to 9.77 x 10^{-3} mm Hg, volatilization is not expected to be an important fate process for this chemical (ATSDR, 2021, NCBI, 2022, EPA, 2022b). EPA's Toxics Release Inventory reported release data for PFNA in 2020, with a total on-site disposal, off-site disposal, and other releases concentration of 0 pounds from one facility (EPA, 2022c). PFNA is not listed as a hazardous air pollutant (EPA, 2022d).

Indoor Air

No studies from the U.S. reporting levels of PFNA in indoor air were identified from the primary or gray literature.

Ambient Air

A single U.S. study measured levels of PFNA in ambient air (Kim and Kannan, 2007). Kim and Kannan (2007) analyzed particle phase (n = 8) and gas phase (n = 8) concentrations of perfluorinated acids in ambient air samples collected in and around Albany, New York in May and July 2006 to examine the relative importance of certain media pathways to the contamination of urban lakes. PFNA was detected in all gas phase samples with mean and median concentrations of 0.21 pg/m^3 and 0.20 pg/m^3, respectively. PFNA was also detected in the particulate phase, but the detection frequency was not reported. Authors reported particulate phase mean and median concentrations of 0.13 pg/m^3 and below the LOQ (0.12 pg/m^3), respectively.

Soil

The use and production of PFNA could result in its release to soils through various waste streams (NCBI, 2022). When released to soil, PFNA is expected to have no mobility (NCBI, 2022). PFNA has been measured in grass samples grown in soil containing PFNA and other PFAS near Decatur, Alabama (ATSDR, 2021; Yoo et al., 2011). In addition, PFNA has been found to accumulate in the roots of maize plants grown in soil containing PFNA and other PFAS (Krippner et al., 2014; ATSDR, 2021).

Seven U.S. studies were identified that evaluated the occurrence of PFNA and other PFAS in soil (Anderson et al., 2016; Blaine et al., 2013; Eberle et al., 2017; Galloway et al., 2020; Nickerson et al., 2020; Venkatesan and Halden, 2014; Zhu and Kannan, 2019) (Table A-6). Among these

studies, three analyzed soils potentially impacted by past AFFF use. The PFNA detection frequencies varied widely (from less than 20% to over 90%) but mean concentrations tended to be below 5 ng/g. Few studies analyzed soils in the vicinity of fluoropolymer manufacturing facilities or by contaminated soil amendments. Other than control soils in two greenhouse and field studies and one reference site, the U.S. studies did not evaluate soils without amendments or without a nearby current or historical PFAS source.

Two studies analyzed soils in the vicinity of fluoropolymer manufacturing facilities (Galloway et al., 2020; Zhu and Kannan, 2019). Galloway et al. (2020) collected soil samples in December 2016 and March 2018 near a fluoropolymer production facility outside Parkersburg, West Virginia. The 2016 sampling included sites 4.0 km–48.1 km downwind to the north and northeast of the facility and the 2018 sampling included sites 1.3 km–45.4 km north of the facility. PFNA was detected in six of eight of the 2016 samples, however only one was above the LOQ with a concentration of 1.63 ng/g. PFNA was also detected in six of seven of the 2018 samples, however only one was above the LOQ with a concentration of 1.92 ng/g at a distance of 1.3 km. Both the 2016 and 2018 samples that were above the LOQ were reported at the site closest to the facility. In Zhu and Kannan (2019), authors studied PFAS concentrations in soil contaminated by a nearby fluoropolymer manufacturing facility in Little Hocking, Ohio, that had been manufacturing fluorochemicals for over five decades. The 45-acre well field located in a floodplain meadowland was divided into quadrants and surface soil samples were collected from multiple locations within each quadrant in October 2009. PFNA was detected in all 19 samples with mean and median concentrations of 2.7 ng/g and 2.5 ng/g, respectively.

Three studies analyzed soils potentially impacted by AFFF use (Anderson et al., 2016; Eberle et al., 2017; Nickerson et al., 2020). Anderson et al. (2016) assessed 40 sites across 10 active Air Force installations throughout the continental United States and Alaska between March and September 2014. Installations were included if there was known historic AFFF release in the period 1970–1990. It is assumed that the measured PFAS profiles at these sites reflect the net effect of several decades of all applicable environmental processes. The selected sites were not related to former fire training areas and were characterized according to volume of AFFF release—low, medium, and high. Across all sites, the PFNA detection frequency was 71.43% in 100 surface soil samples (median concentration of detects was 1.3 ng/g) and 14.42% in 112 subsurface soil samples (median concentration of detects was 1.5 ng/g). PFNA was detected more frequently at high-volume release sites (50.8% in 32 surface soil samples with mean concentration of 2.5 ng/g; 84.4% in 31 subsurface soil samples with mean concentration of 2.4 ng/g) than at low-volume sites (50.0% in 12 surface soil samples with mean concentration of 2.7 ng/g; 17.6% in 17 subsurface soil samples with mean concentration of 1.0 ng/g) and medium-volume sites (38.3% in 56 surface soil samples with mean concentration of 2.2 ng/g; 67.9% in 64 subsurface soil samples with mean concentration of 2.1 ng/g). Authors noted that given PFNA is not present in 3M AFFF formulations, there may be some degree of telomer-based AFFF contamination. Nickerson et al. (2020) developed a method to quantify anionic, cationic, and zwitterionic PFAS from AFFF-impacted soils. The method was applied to two soil cores collected from two different AFFF-impacted former fire training areas; the sampling year and geographic location were not provided. Eleven soil samples, corresponding to 11 depths ranging from 0.46 m to 15.1 m, were evaluated from Core E, and 12 soil samples, at depths ranging from 0.30 to 14.2 m, were evaluated from Core F. In Core E, PFNA was detected in 5 of 11 samples at depths both at the surface and further below ground with PFNA concentrations ranging from

below the LOQ to 1.96 ng/g dw. In Core F, PFNA was detected in 5 of 12 samples at the 5 depths closest to the surface, with concentrations ranging from below the LOQ to 4.17 ng/g dw (LOQ not reported). Eberle et al. (2017) investigated the effects of an in situ chemical oxidation treatment for remediation of chlorinated volatile organic compounds and PFAAs co-contaminants. Soil samples were collected in 2012–2013 before and after a pilot scale field test at a former fire training site at Joint Base Langley-Eustis, Virginia. Monthly fire training activities were conducted at the site from 1968 to 1980 and irregular fire training activities continued until 1990. Impacted soil was excavated in 1982 but details were not provided. PFNA was detected in 1 of 5 pre-treatment samples and in 13 of 14 post-treatment samples. Of the available three paired pre- and post-treatment soil samples, PFNA was not detected pre-treatment in two pairings but detected post-treatment at 0.07 ng/g and 0.05 ng/g post-treatment. For the third pairing, PFNA was detected at 1.1 ng/g pre-treatment and below the LOQ (0.06 ng/g) post-treatment.

Of the remaining two studies conducted in the United States, Venkatesan and Halden (2014) conducted outdoor mesocosm studies to examine the fate of PFAS in biosolids-amended soil collected during 2005–2008. Biosolids were obtained from a wastewater treatment plant (WWTP) in Baltimore that primarily treated wastewater from domestic sources with only minor contribution (1.9%) from industry. The number of samples was not provided but PFNA was detected in the control (nonamended) soil at levels below 0.5 ng/g dw and in the biosolids-amended soil at a level not reported by the authors. In a field and greenhouse study, Blaine et al. (2013) studied the uptake of PFAS into edible crops grown in control and biosolids-amended soil. In the field study, urban biosolids were obtained from a WWTP receiving both domestic and industrial waste while rural solids were obtained from a WWTP receiving domestic waste only. PFNA was detected in soils from urban (mean = 0.20 ng/g, 0.28 n/g, and 0.40 ng/g in control, 1×[14] and 2× amended fields, respectively) and rural fields (mean = 0.06 ng/g and 0.75 ng/g in control and 0.5× amended fields, respectively). In the greenhouse study, three soils (nonamended control, industrially impacted, and municipal) were investigated. Industrially impacted soils contained composted biosolids from a small municipal WWTP that was impacted by PFAA manufacturing while municipal soils were obtained from a reclamation site in Illinois where municipal biosolids were applied for 20 years. PFNA was detected in all three soils at an average concentration of 0.30 ng/g, 20.15 ng/g, and 6.11 ng/g in control, industrially impacted, and municipal soil, respectively. Authors noted that the trace levels of PFAS detected in the control soil may be due to minor cross-contamination from plowing, planting, or atmospheric deposition from the surrounding area where biosolids have been applied.

[14] 0.5×, 1×, or 2× is defined as ½, 1, or 2 times the agronomic rate of biosolids application to meet nitrogen requirements of the crop.

Table A-6. Summary of PFNA Data in Soil

Study	Location	Site Details	Results
		United States	
Galloway et al. (2020)	United States (Parkersburg, West Virginia)	Soil samples collected near a fluoropolymer facility in two sampling trips in December 2016 and March 2018. The 2016 sampling trip included a collection radius 4.0–48.1 km downwind to the north and northeast of the facility. The 2018 sampling trip focused on samples collected to the north of the facility with a radius of 1.3–45.4 km.	2016 sampling: Drag Strip Road (4.0 km) = 1.63 ng/g Veto Lake (8.0 km) = <LOQ Veto Road (13.0 km) = ND Veto Road, dup. (13.0) = ND Strouds Run (15.3 km) = < LOQ Lookout Park (24.0 km) = < LOQ Archers Fork #1 (35.3 km) = < LOQ Archers Fork #2 (48.1 km) = < LOQ 2018 sampling: LHWA (1.3 km) = 1.92 ng/g Veto Lake (8.0 km) = < LOQ Veto Lake, dup. (8.0 km) = < LOQ Watertown (24.3 km) = ND Beverly (32.1 km) = < LOQ L. Olive Green Creek (39.9 km) = < LOQ Reinersville (45.4 km) = < LOQ (LOQ = 1 ng/g)
Zhu and Kannan (2019)	United States (Washington County, Ohio)	Surface soil (0–6 cm) samples collected in October 2009 from a 45-acre field located within a 1-mile radius of a fluoropolymer manufacturing facility in Little Hocking that had been manufacturing fluorochemicals for over five decades. The site was divided into quadrants and soil samples were collected from multiple locations within each quadrant.	n = 19, DF 100%, mean, median (range) = 2.7, 2.5 (1.6–6.3) ng/g dw (LOD = 0.1356 ng/g dw; LOQ = 0.452 ng/g dw)

Study	Location	Site Details	Results
		United States	
Anderson et al. (2016)	United States (national)	Forty AFFF-impacted sites from ten active U.S. Air Force installations with historic AFFF release between 1970 and 1990 that were not related to former fire training areas. It is assumed that the measured PFAS profiles at these sites reflect the net effect of several decades of all applicable environmental processes. AFFF-impacted sites included emergency response locations, hangers and buildings, and testing and maintenance related to regular maintenance and equipment performance testing of emergency vehicles and performance testing of AFFF solution. Previous remedial activities for co-occurring contaminants were not specifically controlled for in the site selection process; active remedies had not been applied at any of the sites selected. Approximately ten samples were collected between March and September 2014 at each site for surface and subsurface soil; sites were grouped according to volume of AFFF release—low-volume typically had a single AFFF release, medium-volume had one to five releases, and high-volume had multiple releases.	Surface soil: Overall: n = 100, DF 71.43%, median (maximum) = 1.3 (23.0) ng/g *Breakdown by site:* Emergency Response (low-volume release): n = 12, DF 50.0%, mean (range) = 2.7 (1.5–4.1) ng/g Hangars and Buildings (medium-volume release): n = 56, DF 38.3%, mean (range) = 2.2 (0.21–12) ng/g Testing and Maintenance (high-volume release): n = 32, DF 50.8%, mean (range) = 2.5 (0.24–23) ng/g (RL = 0.23 ng/g) Subsurface soil: Overall: n = 112, DF 14.42%, median (maximum) = 1.5 (6.49) ng/g *Breakdown by site:* Emergency Response (low-volume release): n = 17, DF 17.6%, mean (range) = 1.0 (0.5–1.5) ng/g Hangars and Buildings (medium-volume release): n = 64, DF 67.9%, mean (range) = 2.1 (0.21–12) ng/g Testing and Maintenance (high-volume release): n = 31, DF 84.4%, mean (range) = 2.4 (0.24–23) ng/g (RL = 0.24 ng/g) *Median calculated using quantified detections *Non-detects were substituted with ½ the reporting limit

Study	Location	Site Details	Results
		United States	
Nickerson et al. (2020)	United States (unspecified)	Soil cores E and F from two different AFFF-impacted fire training areas; sampling year and geographic location not provided. Soil core E contained 11- 0.3 m increment samples from 0.3–15.2 m below ground surface and was collected in an area where the surficial soils were likely disturbed due to regrading and other soil redistribution activities. Soil core F contained 12- 0.61 m increment samples from 0–14.2 m below ground surface and was collected in an area where the surficial soils were highly permeable only within the upper 0.5 to 1 m, and the underlying impermeable clay layer exhibited a relatively high cation exchange capacity and organic carbon content. The water table was relatively shallow (depth < 3 m) at both sites.	Core E: 0.46 m = 1.96 ng/g dw 2.9 m = < LOQ 3.66 m = < LOQ 3.96 m = < LOQ 4.27 m = < LOQ 4.57 m = < LOQ 4.88 m = 0.22 ng/g dw 7.01 m = 0.26 ng/g dw 8.38 m = 0.73 ng/g dw 10.5 m = 1.09 ng/g dw 15.1 m = < LOQ Core F: 0.30 m = 0.70 ng/g dw 1.22 m = 4.17 ng/g dw 1.83 m = 3.23 ng/g dw 2.44 m = 1.04 ng/g dw 3.05 m = 0.64 ng/g dw 4.11 m = < LOQ 7.62 m = < LOQ 8.84 m = < LOQ 9.45 m = < LOQ 10.5 m = < LOQ 11.9 m = < LOQ 14.2 m = < LOQ (LOQ not reported)

Study	Location	Site Details	Results
		United States	
Eberle et al. (2017)	United States (Joint Base Langley-Eustis, Virginia)	Pilot testing area in former fire training area (Training Site 15) at Joint Base Langley-Eustis where monthly fire training activities were conducted from 1968 to 1980 in a zigzag pattern burn pit. Facility was abandoned in 1980 but irregular fire training activities using an above-ground germed burn pit continued until 1990. Impacted soil was removed in 1982 but additional details of the excavation are not well known. Soil samples collected for pre- (April and September 2012) and post- (December 2013) in situ chemical oxidation treatment using a peroxone activated persulfate (OxyZone) technology. Treatment was conducted in Test Cell 1 over 113 days (April–August 2013). Soil samples were collected adjacent to wells; wells outside Test Cell 1 were used as sentry wells. Well IDs for pre- and post-sampling were not provided but the following three pairings were assumed based on Table 2 in the paper: U-20 with SB-106; U-16 with SB-112; and I-1 with SB-109.	Pre-treatment: I-1 (1.2–4.3 m) = 1.1 ng/g I-2 (1.2–4.3 m) = ND U-12 (2.1 m) = ND U-16 (3.0 m) = ND U-20 (1.8 m) = ND (LOQ = 0.68–0.72 ng/g) Post-treatment: SB-101 (4.3 m) = 0.07 ng/g SB-105 (1.8 m) = 0.02 ng/g SB-106/U-20 (1.8 m) = 0.07 ng/g SB-106 (4.3 m) = 0.14 ng/g SB-107 (1.8 m) = 0.03 ng/g SB-107 (4.3 m) = 0.2 ng/g SB-108 (1.8 m) = 0.03 ng/g SB-108 (4.3 m) = 0.15 ng/g SB-109/I-1 (3 m) = <LOQ SB-111 (4.3 m) = 0.29 ng/g SB-112 (1.8 m) = 0.06 ng/g SB-112/U-16 (3 m) = 0.05 ng/g SB-114 (1.8 m) = 0.3 ng/g SB-114 (4.3 m) = 0.33 ng/g (LOQ = 0.06 ng/g)

Study	Location	Site Details	Results
		United States	
Venkatesan and Halden (2014)	United States (Baltimore, Maryland)	Archived agricultural soil (nonamended) collected during 2005–2008 at a depth of 0–20 cm from the United States Department of Agriculture-Agricultural Research Service Beltsville Agricultural Research Center; number of sampling sites and number of samples not provided. Biosolids-amended soil obtained by mixing biosolids and soil at a volumetric ratio of 1:2. Biosolids were from Back River WWTP in Baltimore, a full-scale activated sludge treatment plant. Raw wastewater was primarily from domestic sources with only minor contribution (1.9%) from industry.	Nonamended: n = NR, DF NR, authors noted PFNA concentration was between 0.1–0.5 ng/g dw Amended: n = NR, DF NR, authors noted the detected levels of PFNA, along with PFOA, PFNA, PFDA, and PFUnA in the control soil accounted for 0.3–3% of their initial levels in the amended soil mix (MDL = 0.08 ng/g)

Study	Location	Site Details	Results
		United States	
Blaine et al. (2013)	United States (Midwest)	Urban and rural full-scale field study with control (nonamended) and biosolids-amended plots. Three agricultural fields were amended (0.5×, 1×, or 2×) with municipal biosolids. Urban biosolids (1× and 2×) were from a WWTP receiving both domestic and industrial waste. Rural biosolids (0.5×) were from a WWTP receiving domestic waste only. Control plots were proximal to the rural and urban amended corn grain and corn stover field sites; sampling year not provided. Greenhouse study with control (nonamended) and biosolids-amended soil. Nonamended soil obtained from a field that received commercial fertilizers and had a similar cropping system as the nearby municipal soil site. Municipal soil was obtained from a reclamation site in Illinois where municipal biosolids were applied at reclamation rates for 20 years, reaching the cumulative biosolids application rate of 1,654 Mg/ha. Industrially impacted soil was created by mixing composted biosolids from a small municipal (but impacted by PFAA manufacturing) WWTP with control soil on a 10% mass basis. Sampling year not provided.	Field study: Urban non-amended: n = 3–7, DF NR, mean = 0.20 ng/g Urban 1×: n = 3–7, DF NR, mean = 0.28 ng/g Urban 2×: n = 3–7, DF NR, mean = 0.40 ng/g Rural non-amended: n = 3–7, DF NR, mean = .06 ng/g Rural 0.5×: n = 3–7, DF NR, mean = 0.75 ng/g (LOQ not reported) Greenhouse study: Nonamended: n = 3–5, DF NR, mean = 0.30 ng/g Industrially impacted: n = 3–5, DF NR, mean = 20.15 ng/g Municipal: n = 3–5, DF NR, mean = 6.11 ng/g (LOQ not reported)

Notes: AFFF = aqueous film-forming foam; DF = detection frequency; dw = dry weight; LOQ = limit of quantitation; LHWA = Little Hocking Water Association; LOD = limit of detection; MDL = method detection limit; 0.5×, 1×, or 2× = ½, 1, or 2 times the agronomic rate of biosolids application to meet nitrogen requirements of the crop; ND = not detected; NR = not reported; RL = reporting limit; WWTP = wastewater treatment plant.

Sediment

When released into water, PFNA is expected to adsorb to suspended solids and sediments (NCBI, 2022). Concentrations of PFNA in sediment samples collected from the Hudson Bay region of northeast Canada ranged from < 0.06 ng/g to 0.14 ng/g (dry weight) (Kelly et al., 2009; NCBI, 2022).

Biomonitoring in the U.S. Population

CDC's NHANES results show that PFNA has been detected in > 95% of blood samples from NHANES participants for most years evaluated (CDC, 2019, 2021a,b, 2022). Whole-weight serum levels of PFNA in the 50th percentile of the U.S. population for all years evaluated since 1999 were 0.600 µg/L in 1999–2000 (detected in 96% of samples), 1.00 µg/L in 2003–2004 (detected in 98.2% of samples), 1.10 µg/L in 2005–2006 (detected in 99% of samples), 1.23 µg/L in 2007–2008 (detected in 99.5% of samples), 1.23 µg/L in 2009–2010 (detected in 99.8% of samples), 0.860 µg/L in 2011–2012 (detected in 99.2% of samples), 0.700 µg/L in 2013–2014 (detected in 98.7% of samples), 0.600 µg/L in 2015–2016 (detected in 98.7% of samples), and 0.400 µg/L in 2017–2018 (detected in 92% of samples) (CDC, 2019, 2021a,b, 2022).

Recommended RSC

In summary, based on the physical properties, detected levels, and available exposure information for PFNA, multiple non-drinking water sources (fish and shellfish, non-fish food, some consumer products, indoor dust, and air) are potentially significant exposure sources. Following the Exposure Decision Tree in EPA's 2000 Methodology (EPA, 2000), significant potential sources other than drinking water ingestion were identified (Box 8A in the Decision Tree); however, information is not available to quantitatively characterize exposure from these different sources (Box 8B in the Decision Tree). Therefore, EPA recommends an RSC of 20% (0.20) for PFNA.

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APPENDIX B. PFHxS: Summary of Occurrence in Water and Detailed Relative Source Contribution.

Occurrence in Water

The production of PFHxS and its use as a raw material or precursor for manufacturing PFAS-based products, as well as its previous use in firefighting foam and carpet treatment solutions, could result in its release to the aquatic environment through various waste streams (NCBI, 2022). PFHxS has an estimated water solubility of 6,200 µg/L (6.2 mg/L) at 25 °C and when released to surface water, it is not expected to adsorb to suspended solids and sediment (NCBI, 2022). Volatilization from water surfaces is not expected to be an important fate process for PFHxS (NCBI, 2022).

Drinking Water

Based on results from EPA's UCMR 3 monitoring, PFHxS has been detected in 1.12% of drinking water systems in the United States, with mean and median concentrations of 140 ng/L and 73 ng/L, respectively. The maximum concentration detected in drinking water systems was 1,600 ng/L (EPA, 2017). Drinking water samples collected from public drinking water systems that are impacted by wastewater treatment effluent often contain higher concentrations of perfluoroalkyls than samples collected from systems that are not impacted by wastewater treatment effluent (Schultz et al., 2006a,b, as cited in ATSDR, 2021). For example, PFHxS was detected in all samples collected from a public drinking water system in Los Angeles that was highly impacted by wastewater treatment effluent; the mean concentrations of PFHxS in influent and effluent samples were 5.1 ng/L (0.0051 µg/L) and 6.1 ng/L (0.0061 µg/L), respectively (Quinones and Snyder, 2009 as cited in ATSDR, 2021). PFHxS has also been detected in the municipal drinking water of communities located near a fluorochemical facility in Minnesota (ATSDR, 2008). In comparison, no perfluoroalkyl chemicals were detected in influent or finished drinking water samples collected from a public drinking water system in Aurora, Colorado that was not highly impacted by wastewater treatment effluent (Quinones and Snyder, 2009 as cited in ATSDR, 2021).

For more information about PFHxS occurrence in drinking water, please see EPA (2022f).

A Standard of Quality for PFAS in bottled water is 0.005 µg/L (5 ng/L) for one PFAS (e.g., PFHxS) and 0.0010 µg/L (10 ng/L) for more than one PFAS (IBWA, 2022).

Groundwater

PFHxS was detected in each of the well water samples from a PFAS manufacturing facility in Minnesota at concentrations ranging from 6,470 ng/L to 40,000 ng/L (6.47 µg/L to 40.0 µg/L) (3M, 2007 as cited in ATSDR, 2021, NCBI, 2022). PFHxS was measured in offsite groundwater near a PFAS manufacturing facility in Alabama at concentrations ranging from 12.7 ng/L to 622 ng/L (0.0127 µg/L to 0.622 µg/L) (3M, 2010 and Lindstrom et al., 2011 as cited in ATSDR, 2021). Median and maximum groundwater (i.e., not finished drinking water) concentrations of 870 ng/L and 290,000 ng/L (0.870 µg/L and 290 µg/L), respectively, were detected at 10 U.S. military installations (Anderson et al., 2016 as cited in ATSDR, 2021).

Surface Water

PFHxS in water bodies in New York was measured at concentrations ranging from 4.2 ng/L to 8.5 ng/L (0.0042 µg/L to 0.0085 µg/L) in Onondaga Lake (a Superfund site due to contamination from industrial activity along its banks), from 2.5 ng/L to 5.6 ng/L (0.0025 µg/L to 0.0056 µg/L) in Erie Canal, and from 0.9 ng/L to 2.8 ng/L (0.0009 µg/L to 0.0028 µg/L) in other lakes and rivers (Sinclair et al., 2006 as cited in ATSDR, 2021 and NCBI, 2022). PFHxS concentrations measured in lake water samples collected near Albany, New York ranged from < 0.25 ng/L to 4.05 ng/L (< 0.00025 µg/L to 0.00405 µg/L) (Kim and Kannan, 2007 as cited in ATSDR, 2021 and NCBI, 2022). PFHxS concentrations ranged from < 0.25 ng/L to 0.36 ng/L (< 0.00025 µg/L to 0.00036 µg/L) in rain and snow samples collected in Albany, New York in 2006 to 2007 (Kim and Kannan, 2007 as cited in NCBI, 2022). PFHxS was detected in more than 90% of 37 surface water sites sampled across the northeastern United States in 2014 at a maximum concentration of 43 ng/L (0.043 µg/L) at Mill Cove, Rhode Island, and a median concentration of 0.7 ng/L (0.0007 µg/L) (Zhang et al., 2016 as cited in ATSDR, 2021).

PFHxS concentrations in surface water collected from the Delaware River ranged from less than the detection limit to 4.48 ng/L (0.00448 µg/L) in 2007 to 2009 (DRBC, 2013 as cited in ATSDR, 2021). PFHxS was measured in 100 samples collected from 80 sites from Cape Fear Basin, North Carolina at an average concentration of 7.29 ng/L (0.00729 µg/L), a median concentration of 5.66 ng/L (0.00566 µg/L), and a maximum concentration of 35.1 ng/L (0.0351 µg/L), with PFHxS not detected in 45.6% of the samples (Nakayama et al. 2007, as cited in ATSDR, 2021).

PFHxS concentrations in water samples collected from Resolute Lake and Meretta Lake in 2003 and 2004 in the Canadian Arctic ranged from 1.5 ng/L to 24 ng/L (0.0015 µg/L to 0.024 µg/L) (Stock et al., 2007 as cited in NCBI, 2022). PFHxS measured in surface water near a PFAS manufacturing facility in Minnesota ranged from 93.6 ng/L to 4,580 ng/L (0.0936 µg/L to 4.58 µg/L) (3M, 2007 as cited in ATSDR, 2021). Median and maximum surface water concentrations of 710 ng/L and 815,000 ng/L (0.710 µg/L and 815 µg/L), respectively, were detected at 10 U.S. military installations (Anderson et al., 2016 as cited in ATSDR, 2021).

RSC for PFHxS

Literature Search and Screening

In 2020, EPA conducted a broad literature search to evaluate evidence for pathways of human exposure to eight PFAS chemicals (PFOA, PFOS, PFBA, PFBS, PFDA, PFHxA, PFHxS, and PFNA) (Holder et al., in prep). This search was not date limited and spanned the information collected across the WOS, PubMed, and ToxNet/ToxLine (now ProQuest) databases. The results of the PFHxS literature search of publicly available sources are available through EPA's Health & Environmental Resource Online website at https://hero.epa.gov/hero/index.cfm/project/page/project_id/2630.

The 950 literature search results for PFHxS were imported into SWIFT-Review (Sciome, LLC, Research Triangle Park, NC) and filtered through the Evidence Stream tags to identify human studies and non-human (i.e., those not identified as human) studies (Holder et al., in prep). Studies identified as human studies were further categorized into seven major PFAS pathways (Cleaning Products, Clothing, Environmental Media, Food Packaging, Home

Products/Articles/Materials, Personal Care Products, and Specialty Products) as well as an additional category for Human Exposure Measures. Non-human studies were grouped into the same seven major PFAS pathway categories, except that the Environmental Media category did not include soil, wastewater, or landfill. Only studies published between 2003 and 2020 were considered. Application of the SWIFT-Review tags identified 654 peer-reviewed papers matching these criteria for PFHxS.

Holder et al. (in prep) screened the 654 papers to identify studies reporting measured occurrence of PFHxS in human matrices and media commonly related to human exposure (human blood/serum/urine, drinking water, food, food contact materials, consumer products, indoor dust, indoor and ambient air, and soil). For this synthesis, additional screening was conducted to identify studies relevant to surface water (freshwater only) and groundwater using a keyword[15] search for water terms.

Following the PECO criteria outlined in Table B-1, the title and abstract of each study were independently screened for relevance by two screeners using *litstream*^{TM}. A study was included as relevant if it was unclear from the title and abstract whether it met the inclusion criteria. When two screeners did not agree if a study should be included or excluded, a third reviewer was consulted to make a final decision. The title and abstract screening of Holder et al. (in prep) and of this synthesis resulted in 494 unique studies being tagged as relevant (i.e., having data on occurrence of PFHxS in exposure media of interest) that were further screened with full-text review using the same inclusion criteria. After additional review of the evidence collected by Holder et al. (in prep), 109 studies originally identified for other PFAS also contained information relevant to PFHxS. Based on full-text review, 172 studies were identified as having relevant, extractable data for PFHxS from the United States, Canada, or Europe for environmental media, not including studies with only human biomonitoring data. Of these 172 studies, 161 were identified from Holder et al. (in prep), where primary data were extracted into a comprehensive evidence database. Parameters of interest included: sampling dates and locations, numbers of collection sites and participants, analytical methods, limits of detection and detection frequencies, and occurrence statistics. Eleven of the 172 studies were identified in this synthesis as containing primary data on only surface water and/or groundwater.

[15] Keyword list: water, aquifer, direct water, freshwater, fresh water, groundwater, ground water, indirect water, lake, meltwater, melt water, natural water, overland flow, recreation water, recreational water, river, riverine water, riverwater, river water, springwater, spring water, stream, surface water, total water, water supply

Table B-1. Populations, Exposures, Comparators, and Outcomes (PECO) Criteria

PECO Element	Inclusion Criteria
Population	Adults and/or children in the general population and populations in the vicinity of PFAS point sources from the United States, Canada, or Europe
Exposure	Primary data from peer-reviewed studies collected in any of the following media: ambient air, consumer products, drinking water, dust, food, food packaging, groundwater[a], human blood/serum/urine, indoor air, landfill, sediment, soil, surface water[a] (freshwater), wastewater/biosolids/sludge
Comparator	Not applicable
Outcome	Measured concentrations of PFHxS (or measured emissions from food packaging and consumer products only)

Note:
[a] Surface water and groundwater were not included as relevant media in Holder et al. (in prep). Studies were re-screened for these two media in this synthesis.

The evidence database of Holder et al. (in prep) additionally identified 18 studies for which the main article was not available for review. As part of this synthesis, 17 of the 18 studies could be retrieved. An additional three references were identified through gray literature sources, described below, that were included to supplement the search results. The combined 20 studies underwent full-text screening using the inclusion criteria in Table B-1. Based on full-text review, five studies were identified as relevant.

Using the screening results from the evidence database and this synthesis, a total of 177 peer-reviewed studies were identified as relevant. Fifty of these contained information relevant to the U.S.

Additional Screening

EPA also searched the following gray literature sources for information related to relative exposure of PFHxS for all potentially relevant routes of exposure (oral, inhalation, dermal) and exposure pathways relevant to humans:

- ATSDR's *Toxicological Profiles*;
- CDC's national reports on human exposures to environmental chemicals;
- EPA's CompTox Chemicals Dashboard;
- EPA's fish tissue studies;
- EPA's Toxics Release Inventory;
- EPA's UCMR data;
- Relevant documents submitted under the Toxic Substances Control Act and relevant reports from EPA's Office of Chemical Safety and Pollution Prevention;
- U.S. Food and Drug Administration's (FDA's) *Total Diet Studies* and other similar publications from FDA, U.S. Department of Agriculture, and Health Canada;
- NOAA's National Centers for Coastal Ocean Science data collections;
- National Science Foundation direct and indirect food and/or certified drinking water additives;
- PubChem compound summaries;

- Relevant sources identified in the relative source contribution discussions (Section 5) of EPA's *Proposed Approaches to the Derivation of a Draft Maximum Contaminant Level Goal for Perfluorooctanoic Acid (PFOA)/Perfluorooctane Sulfonic Acid (PFOS) in Drinking Water*; and
- Additional sources, as needed.

EPA has included available information from these gray literature sources for PFHxS relevant to its uses, chemical and physical properties, and for occurrence in drinking water (directly or indirectly in beverages like coffee, tea, commercial beverages, or soup), ambient air, foods (including fish and shellfish), incidental soil/dust ingestion, and consumer products. EPA has included available information specific to PFHxS below on any regulations that may restrict PFHxS levels in media (e.g., water quality standards, air quality standards, food tolerance levels).

Summary of Potential Sources of PFHxS Exposure

EPA presents information below from studies performed in the United States. While studies from non-U.S. countries inform an understanding global exposure sources and trends, the RSC determination is based on the available data for the United States.

Dietary Sources

Seafood

PFHxS was detected in 71 of 157 fish tissue composite samples collected during EPA's National Lake Fish Tissue Study, with a maximum concentration of 3.50 ng/g and a 50th percentile concentration of < 0.12 ng/g (Stahl et al., 2014). It was not detected in the 162 fish tissue composite samples collected during EPA's 2008–2009 National Rivers and Streams Assessment (NRSA) (Stahl et al., 2014). More recently, PFHxS was detected in 32 of 349 fish tissue composite samples at concentrations ranging from 0.121 ng/g to 0.980 ng/g in EPA's 2013–2014 NRSA (EPA, 2020). PFHxS was also detected in 1 of 152 fish tissue composite samples at a concentration of 0.96 ng/g in EPA's 2015 Great Lakes Human Health Fish Fillet Tissue Study (EPA, 2021). PFHxS has been detected in a mixture of fish fillet samples collected from Mississippi River sites in Minnesota at a concentration of 0.47 ng/g (Delinsky et al., 2010; ATSDR, 2021). PFHxS has been detected in Irish pompano (*Diapterus auratus*), silver porgy (*Diplodus argenteus*), and grey snapper (*Lutjanus griseus*) from the St. Lucie Estuary in in NOAA's National Centers for Coastal Ocean Science, National Status and Trends Data (NOAA, 2022).

Five additional U.S. studies were identified that evaluated PFHxS levels in seafood (Byrne et al., 2017; Chiesa et al., 2019; Schecter et al., 2010; Young et al., 2013, 2022) (Table B-2). One study evaluated fish samples collected directly from rivers and lakes (Byrne et al., 2017). As part of a study to assess exposure to PFHxS and other PFAS among residents of two remote Alaska Native villages on St. Lawrence Island, Byrne et al. (2017) measured PFAS concentrations in stickleback and Alaska blackfish, resident fish used as sentinel species to detect accumulation of PFAS in the local environment. Stickleback were collected from three locations—Suqitughneq (Suqi) River watershed (n = 9 composite samples), Tapisaggak (Tapi) River (n = 2 composite samples), and Troutman Lake (n = 3 composite samples). Blackfish were collected from the Suqi River (n = 29) but were not found in the other water bodies. Authors reported that the Suqi River

watershed was upstream and downstream of a formerly used defense site and Tapi River was approximately 5 km east of a military site, however at the start of the study none of the sites were known to be contaminated with PFAS. The sample dates were not reported. PFHxS was not detected in any of the stickleback and blackfish samples, despite the authors noting that stickleback from Troutman Lake had "exceptionally high" total PFAS concentrations.

The remaining four studies purchased seafood from stores and fish markets (Chiesa et al., 2019; Schecter et al., 2010; Young et al., 2013, 2022). Young et al. (2013) assessed fish and shellfish collected in 2010–2012 from retail markets across the continental United States. Retail markets in California, Florida, Illinois, Mississippi, New Jersey, New York, Tennessee, Texas, and Washington, D.C. were represented. Authors selected the ten most consumed fish and shellfish in the United States that were farm raised, wild caught, or had unknown origin. Among the crab meat, shrimp, striped bass, catfish, clams, cod, flounder, pangasius, pollock, tuna, salmon, scallops, and tilapia, PFHxS was only detected in one of ten samples of striped bass at a concentration of 0.66 ng/g. Young et al. (2022) evaluated fish and shellfish purchased from retail markets in the Washington. D.C. metropolitan area and online markets (clams only) from March 2021 through May 2022. Seafood samples represented eight of the top ten consumed fish and shellfish in the United States. Seafood samples were farm raised, wild-caught or of unknown origin, and location of harvest was provided when known. PFHxS was only detected in two seafood types, crab and clam meat. All samples of clam meat (n=10) had detectable concentrations of PFHxS, ranging from 51-605 ng/kg. Only two samples of crabs (n=11) had detectable levels of 112 and 242 ng/kg. Authors also analyzed food packaging for PFAS analytes and did not identify any packaging samples with detectable levels of PFAS. Schecter et al. (2010) evaluated PFHxS and other PFAS in seafood collected from five Dallas, Texas grocery stores in 2009. The origin or source of seafood was not described. Seafood included canned sardines in water, canned tuna, fresh catfish fillet, cod, frozen fish sticks, salmon, and tilapia (n = 1 composite sample for each seafood type). PFHxS was only detected in cod at a concentration of 0.07 ng/g ww. Finally, in a multicontinental study, Chiesa et al. (2019) collected salmon from a wholesale fish market in Milan, Italy; the sampling year was not reported. Wild-caught salmon samples originated from the United States (n = 7), Canada (n = 15), and Scotland (n = 2), while farmed salmon samples originated from Norway (n = 25) and Scotland (n = 17). Among the salmon that originated from the United States Pacific Ocean (FAO 67 and 77), two species—*Oncorhynchus kisutch* and *Oncorhynchus keta*—were analyzed, with PFHxS not detected in either species (LOQ = 0.015 ng/g). PFHxS was also not detected in wild-caught salmon from Canada and Scotland.

Table B-2. Summary of PFHxS Data in Seafood

Study	Location and Source	Seafood Type	Results
		United States	
Byrne et al. (2017)	United States (Alaska) Stickleback collected from three locations on St. Lawrence Island: Suqitughneq (Suqi) River watershed (upstream and downstream of a formerly used defense site), Tapisaggak (Tapi) River (located approximately 5 km east of military site), and Troutman Lake, a coastal lake situated adjacent to the village of Gambell. Alaska blackfish collected from the Suqi River but were absent from the other water bodies. Sampling year not reported. No sites were known to be contaminated with PFASs at the initiation of the study.	Stickleback and Alaska blackfish	Stickleback: Troutman Lake: n = 3*; DF 0% Suqi River: n = 9*; DF 0% Tapi River: n = 2*; DF 0% Blackfish: n = 29; DF 0% (LOQ = 0.5–1 ng/g ww for all PFAS) *Number of composite samples, each composed of ~10 stickleback fish

Study	Location and Source	Seafood Type	Results
		United States	
Young et al. (2013)	United States (California; Illinois; Mississippi; Tennessee; Florida; New Jersey; New York; Texas; Washington, D.C.) Fish and shellfish collected from retail markets in 11 areas across the continental United States from 2010–2012. The fish and shellfish included farm raised, wild caught, and unknown origin, as well as freshwater fish, saltwater fish, and euryhaline fish. Crab meat, clams, cod, flounder, pangasius, salmon, scallops, and tilapia purchased from Washington, D.C. Shrimp purchased from Orlando, Florida; Memphis, Tennessee; and Nashville, Tennessee. Striped bass purchased from New York, New York and Cherry Hill, New Jersey. Catfish purchased from Indianola, Mississippi; Dallas, Texas; Tampa, Florida; and Orlando, Florida. Pollock purchased from Huntington Beach, California. Tuna purchased from Chicago, Illinois.	Crab, shrimp, striped bass, catfish, clams, cod, flounder, pangasius, pollock, tuna (can and pouch), salmon, scallops (bay and sea), tilapia	**Striped bass: n = 10, DF[a] 10%, range = ND–0.66* ng/g** Crab meat: n = 1, DF 0% Shrimp: n = 9, DF 0% Catfish: n = 13, DF 0% Clams: n = 1, DF 0% Cod: n = 1, DF 0% Flounder: n = 1, DF 0% Pangasius: n = 1, DF 0% Pollock: n = 1, DF 0% Tuna: n = 3, DF 0% Salmon: n = 2, DF 0% Scallops: n = 2, DF 0% Tilapia: n = 1, DF 0% (MDL = 0.55 ng/g for all seafood) *This value was above the MDL but below the LOQ; LOQ is estimated as 3x the MDL

Study	Location and Source	Seafood Type	Results
		United States	
Young et al. (2022)	United States (Washington, D.C.) Fish and shellfish collected from retail markets in the Washington, D.C. metropolitan area from 2021-2022. Fish and shellfish samples included farm raised, wild-caught and unknown origin. Country of origin was provided, if known. Ten samples of each seafood type, except for crab, which included 11 samples.	Crab, clams (can), shrimp, cod, pollock (fish sticks, fillet), salmon, tuna (can and pouch), tilapia	**Clams: n=10, DF 100%, range=51-605 ng/kg** **Crab meat: n=11, DF 20%, range= <MDL-242 ng/kg** Shrimp: n=10, DF 0% Cod: n=10, DF 0% Pollock: n=10, DF 0% Tuna: n=10, DF 0% Salmon: n=10, DF 0% Tilapia: n=10, DF 0% (MDL = 20 ng/kg instrument 1; MDL=17 ng/kg instrument 2)
Schecter et al. (2010)	United States (Texas) Seafood samples from five different grocery stores in Dallas, Texas were collected in 2009. Ten individual samples were collected for each food type and combined to form composite samples. The origin/source of the food samples were not reported.	Salmon, canned tuna, fresh catfish fillet, tilapia, cod, canned sardines, frozen fish sticks	**Cod: n = 1, point = 0.07 ng/g ww, LOD = NR** Salmon: n = 1, DF 0%, LOD = 0.07 ng/g ww Canned tuna: n = 1, DF 0%, LOD = 0.05 ng/g ww Fresh catfish fillet: n = 1, DF 0%, LOD = 0.06 ng/g ww Tilapia: n = 1, DF 0%, LOD = 0.04 ng/g ww Canned sardines: n = 1, DF 0%, LOD = 0.06 ng/g ww Frozen fish sticks: n = 1, DF 0%, LOD = 0.09 ng/g ww *Number of composite samples, each composed of ~10 individual samples

Study	Location and Source	Seafood Type	Results
		United States	
Chiesa et al. (2019)	United States (Pacific Ocean) Wild-caught fish were collected at a wholesale fish market in Milan, Italy. Sampling year was not reported. The wild-caught salmon were from USA-Pacific Ocean (Food and Agriculture Organization Area 67 and 77).	Wild-caught salmon (*Oncorhynchus kisutch* and *Oncorhynchus keta*)	*Oncorhynchus kisutch*: n = 5, DF 0% *Oncorhynchus keta*: n = 2, DF 0% (LOQ = 0.015 ng/g)

Notes: DF = detection frequency; LOD = limit of detection; LOQ = limit of quantitation; MDL = method detection limit; ND = not detected; NR = not reported; ww = wet weight. Bold indicates detected levels of PFHxS in food.

[a] The DF and/or mean was not reported in the study and was calculated in this synthesis. Means were calculated only when DF = 100%.

Other Food Sources

PFHxS was included in a suite of PFAS evaluated in FDA's 2019, 2021, and 2022 Total Diet Study Sampling (U.S. FDA, 2020a,b, 2021a,b, 2022a,b); however, it was not detected in any of the food samples tested. It should be noted that FDA indicated that the sample sizes used in the PFAS 2019, 2021, and 2022 Total Diet Study Sampling were limited and that the results should not be used to draw definitive conclusions about PFAS levels in the general food supply (U.S. FDA, 2022c). PFHxS was detected in milk samples collected from a farm with groundwater known to be contaminated with PFAS; however, it was not detected in produce collected from an area near a PFAS production plant, in FDA studies of the potential exposure to the U.S. population to PFAS (U.S. FDA, 2018, 2021c). PFHxS is not a registered pesticide under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), and EPA does not set a 40 CFR Part 180 pesticide tolerance in food and feed commodities for PFHxS (U.S. GPO, 2022). Maximum residue levels for PFHxS were not found in the Global Maximum Residue Level Database (Bryant Christie Inc., 2022).

Nine peer-reviewed studies were identified that examined PFHxS in food sources other than seafood, with 2 in breastmilk and 7 in food types other than breastmilk (Blaine et al., 2013, 2014; Genualdi et al., 2017; Kuklenyik et al., 2004; Schecter et al., 2010; Scher et al., 2018; Tipton et al., 2017; von Ehrenstein et al., 2009; Young et al., 2012) (Table B-3). Few U.S. studies analyzed foods from any one origin—four sampled crops grown in areas with known or suspected PFAS contamination, including biosolids-amended soils, two sampled from crops as part of greenhouse and field studies, one studied wild-caught alligator meat. Only two studies sampled from store- or market-bought meats, eggs, produce, and dairy.

Scher et al. (2018) evaluated garden produce samples from homes in Minnesota within and outside of a GCA in the vicinity of a former 3M PFAS production facility. Twenty homes within the GCA had previous or ongoing PFAS contamination in drinking water and were served by the Oakdale, Minnesota public water system or a private well previously tested and shown to have detectable levels of PFOA or PFOS. A total of 279 produce samples (232 inside GCA, 47 outside GCA) were collected between May and October 2010. PFHxS was detected in 1% of the 232 produce samples from inside the GCA (1 floret sample and 1 leaf sample). The authors suggested that the two detections were associated with PFAS present in irrigation water that had accumulated in produce. They also noted that accumulation of PFAS was particularly high in florets. Three homes that were outside the GCA served as a reference. No PFHxS was detected in produce samples from home gardens outside the GCA. Genualdi et al. (2017) analyzed PFAS contamination in a Massachusetts cranberry bog approximately 10 miles from a military base with a history of AFFF usage. Ten cranberry samples were taken directly from trucks transporting cranberries and 32 cranberry samples were collected directly from the bog water in November 2016. PFHxS was not detected in any samples (MDL = 0.79 ng/g).

Two studies purchased food items from stores and markets for evaluation (Schecter et al., 2010; Young et al., 2012). Schecter et al. (2010) assessed PFHxS and other PFAS in food samples collected from five Dallas, Texas grocery stores in 2009. The origin or source of each food was not described. Food items included meat products (bacon, canned chili, chicken breast, ground beef, roast beef, ham, sausage, and turkey), dairy (butter, cheeses, frozen yogurt, ice cream, milk, and yogurt), eggs, grains (cereal), fruits and vegetables (apples, potatoes), and fats/other (canola oil, margarine, olive oil, peanut butter). PFHxS was not detected in any of the food samples. In

Young et al. (2012), cow milk was purchased from retail markets across the continental United States representing 17 states; the sampling year was not reported. Cow milk samples included organic milk, vitamin D added milk, and ultra-pasteurized milk. PFHxS was not detected in any of the 49 retail milk samples (MDL = 0.15 ng/g).

One study investigated PFAS levels from wild meat (Tipton et al., 2017). Tipton et al. (2017) assessed alligator tail meat that was collected during the South Carolina recreational hunting season between September to October 2015. Tail meat samples were collected from four different public hunt units—Southern Coastal, Middle Coastal, Midlands, and Pee Dee. PFHxS was detected in all samples from all hunt units. Median concentrations from Southern Coastal (n = 19), Middle Coastal (n = 17), Midlands (n = 5), and Pee Dee (n = 2) were 0.087 ng/g, 0.099 ng/g, 0.0816 ng/g, and 0.093 ng/g wet mass, respectively.

Two studies by Blaine et al. (2013, 2014) evaluated PFHxS in crops grown in greenhouse and field studies. In Blaine et al. (2014), PFAS levels were measured in celery root, pea fruit, and radish root grown in a greenhouse with control (unamended) soil, industrially impacted soil, and municipal soil (n = 3–5). PFHxS was detected in radish root from all three soils, celery shoot from the industrially impacted and municipal soil, and pea fruit from only industrially impacted soil. Mean concentrations of PFHxS in radish root for the control, industrially impacted, and municipal soil were 3.81 ng/g, 2.84 ng/g, and 4.33 ng/g, respectively. Mean concentrations of PFHxS in celery shoot for the industrially impacted and municipal soil were 3.19 ng/g and 0.38 ng/g, respectively. The mean concentration of PFHxS in pea fruit in the industrially impacted soil was 0.24 ng/g. Authors noted minor cross-contamination of the control soil due to the proximity of the unamended soil to biosolids-amended soil. In Blaine et al. (2013), authors studied the uptake of PFAS into edible crops in both field and greenhouse studies. In the field study, PFAS levels were measured in corn grain and corn stover grown with control (unamended), urban biosolids-amended, and rural biosolids-amended soil (n = 3–7). Mean PFHxS concentrations were below the LOQ in both corn grain and corn stover grown in any field study plots (< 0.04 ng/g for corn grain; < 0.29 ng/g for corn stover). In the greenhouse study, lettuce and tomato plants were grown in control soil, industrially impacted soil, or municipal soil (n = 3–5). Mean PFHxS concentrations were below the LOQ for lettuce and tomato grown in the control soil and for tomato grown in municipal soil; however, mean PFHxS levels were 10.44 ng/g and 5.54 ng/g for lettuce grown in industrially impacted and municipal soils, respectively, and 0.76 ng/g for tomato grown in industrially impacted soil. Sampling year was not reported.

The remaining two studies evaluated the occurrence of PFHxS in breastmilk (Kuklenyik et al., 2004; von Ehrenstein et al., 2009). von Ehrenstein et al. (2009) collected breastmilk samples between December 2004 and July 2005 from women between the ages of 18 and 38 at the time of recruitment as part of the pilot study Methods Advancement for Milk Analysis (MAMA). Women provided milk samples at two visits—the first visit was 2–7 weeks postpartum, and the second visit was 3–4 months postpartum. PFHxS was not detected in any of the samples from the first visit (n = 18) or second visit (n = 20). Similarly, PFHxS was below the LOD (0.3 ng/mL) in the samples reported by Kuklenyik et al. (2004). Kuklenyik et al. (2004) did not report information on the breastmilk donors or the sampling procedure as it was unavailable; PFHxS was not detected in either of the two samples.

Table B-3. Summary of PFHxS Data in Other Food

Study	Location and Source	Food Types	Results
		United States	
Scher et al. (2018)	United States (Minnesota) Home garden produce samples were collected between May and October 2010 from 20 homes in 3 cities within a GCA as well as 3 homes in the Twin Cities Metro outside the GCA. Homes within the GCA were near a former 3M PFAS production facility, had previous or ongoing PFAS contamination in drinking water, and were served by the Oakdale, Minnesota public water system or were formerly or currently using a private well previously tested and shown to have detectable levels of PFOA or PFOS. 279 produce samples (232 within GCA and 47 outside GCA) consisting of mature, edible portions of plants were analyzed. Plant part categories included floret, fruit, leaf, root, seed, and stem.	Fruits and vegetables	Within GCA: **All:** n = 232, DF 1%, median (range) = ND (ND–0.066) ng/g **Floret: n = 5, DF 20%, median (range) = ND (ND–0.066) ng/g** **Leaf: n = 35, DF 3%, median (range) = ND (ND–0.046) ng/g** Garden fruit (n = 98), yard fruit (n = 13), root (n = 29), seed (n = 29), and stem (n = 23): DF 0% Outside GCA: All: n = 47, DF 0% Floret (n = 1), garden fruit (n = 15), yard fruit (n = 4), leaf (n = 12), root (n = 5), seed (n = 5), and stem (n = 5): DF 0% (MDL = 0.003 to 0.029 ng/g depending on the analyte and type of produce)
Genualdi et al. (2017)	United States (Massachusetts) Samples from cranberry bog with surface water contaminated with PFAS—likely due to proximity to a military base with a history of AFFF usage. The bog was located approximately 10 miles from the military base. Ten cranberry samples taken directly from trucks transporting cranberries (five samples each from two trucks) and 32 cranberry samples taken directly from 12 sections of the bog water. Samples collected in November 2016.	Fruits	n = 42, DF 0% (MDL = 0.79 ng/g)

Study	Location and Source	Food Types	Results
		United States	
Schecter et al. (2010)	United States (Texas) Food samples from five different grocery stores in Dallas, Texas were collected in 2009. Ten individual samples were collected for each food type and combined to form composite samples. The origin/source of the food samples were not reported.	Dairy; fruits and vegetables; grains; meat; fats/other	Meat Hamburger: n = 1, DF 0%, LOD = 0.04 ng/g ww Bacon: n = 1, DF 0%, LOD = 0.05 ng/g ww Sliced turkey: n = 1, DF 0%, LOD = 0.02 ng/g ww Sausages: n = 1, DF 0%, LOD = 0.04 ng/g ww Ham: n = 1, DF 0%, LOD = 0.02 ng/g ww Sliced chicken breast: n = 1, DF 0%, LOD = 0.02 ng/g ww Roast beef: n = 1, DF 0%, LOD = 0.02 ng/g ww Canned chili: n = 1, DF 0%, LOD = 0.01 ng/g ww Dairy and Eggs Butter: n = 1, DF 0%, LOD = 0.09 ng/g ww American cheese: n = 1, DF 0%, LOD = 0.04 ng/g ww Other cheese: n = 1, DF 0%, LOD = 0.04 ng/g ww Whole milk: n = 1, DF 0%, LOD = 0.02 ng/g ww Ice cream: n = 1, DF 0%, LOD = 0.03 ng/g ww Frozen yogurt: n = 1, DF 0%, LOD = 0.02 ng/g ww Whole milk yogurt: n = 1, DF 0%, LOD = 0.03 ng/g ww Cream cheese: n = 1, DF 0%, LOD = 0.02 ng/g ww Eggs: n = 1, DF 0%, LOD = 0.04 ng/g ww Grains Cereals: n = 1, DF 0%, LOD = 0.04 ng/g ww Fruits and Vegetables Apples: n = 1, DF 0%, LOD = 0.02 ng/g ww Potatoes: n = 1, DF 0%, LOD = 0.04 ng/g ww Fats/Other Olive oil: n = 1, DF 0%, LOD = 0.3 ng/g ww Canola oil: n = 1, DF 0%, LOD = 0.5 ng/g ww Margarine: n = 1, DF 0%, LOD = 0.03 ng/g ww Peanut butter: n = 1, DF 0%, LOD = 0.03 ng/g ww *n reflects number of composite samples, each composed of ~10 individual samples

Study	Location and Source	Food Types	Results
		United States	
Young et al. (2012)	United States (17 states) Retail cow's milk samples were all pasteurized whole milk, commercially available, and purchased at retail markets across the continental United States representing 17 states. Samples were organic milk, vitamin D added milk, and ultra-pasteurized milk. Sampling year not reported.	Dairy	n = 49, DF 0%, (MDL = 0.15 ng/g)
Tipton et al. (2017)	United States (South Carolina) Alligator tail meat samples were collected from a local wild game meat processer during the South Carolina recreational hunt season between September to October 2015. Samples were from four different public hunt units—Southern Coastal, Middle Coast, Midlands, and Pee Dee.	Meat	**Alligator tail:** **Southern coastal: n = 19, DF[a] 100%, median (range) = 0.087 (0.051–0.252) ng/g wet mass** **Middle coastal: n = 17, DF[a] 100%, median (range) = 0.099 (0.063–0.272) ng/g wet mass** **Midlands: n = 5, DF[a] 100%, median (range) = 0.0816 (0.054–0.158) ng/g wet mass** **Pee Dee: n = 2, DF[a] 100%, median (range) = 0.093 (0.071–0.115) ng/g wet mass** (RL not reported)

Study	Location and Source	Food Types	Results
		United States	
Blaine et al. (2014)	United States (Midwest) Crops grown in in greenhouse study with control (unamended), industrially impacted soil, or municipal soil. Control soil had minor cross-contamination due to proximity to biosolids-amended fields. Industrially impacted soil was amended with industrially impacted biosolids, and municipal soil was amended with municipal biosolids for over 20 years. Crops grown in the greenhouse study were grown from seed in pots, which were randomly arranged within the greenhouse. Sampling year not reported.	Fruits and vegetables	**Radish root:** **Control: n = 3–5, DF NR, mean = 3.81 ng/g** **Industrially impacted; n = 3–5, DF NR, mean = 2.84 ng/g** **Municipal: n = 3–5, DF NR, mean = 4.33 ng/g** **Celery shoot:** Control: n = 3–5, DF 0% **Industrially impacted: n = 3–5, DF NR, mean = 3.19 ng/g** **Municipal: n = 3–5, DF NR, mean = 0.38 ng/g** **Pea fruit:** Control: n = 3–5, DF 0% **Industrially impacted: n = 3–5, DF NR, mean = 0.24 ng/g** Municipal: n = 3–5, DF 0% (LOQ = 0.03 ng/g)

Study	Location and Source	Food Types	Results
		United States	
Blaine et al. (2013)	United States (Midwest) Crops grown in urban and rural full-scale field study with control (unamended) and biosolids-amended soil. Three agricultural fields were amended (0.5×, 1×, or 2×) with municipal biosolids. Urban biosolids (1× and 2×) were from a WWTP receiving both domestic and industrial waste. Rural biosolids (0.5×) were from a WWTP receiving domestic waste only. Control plots were proximal to the rural and urban amended corn grain and corn stover field sites; sampling year not provided. Crops grown in greenhouse study with control (nonamended) and biosolids-amended soil. Nonamended soil obtained from a field that received commercial fertilizers and had a similar cropping system as the nearby municipal soil site. Municipal soil was obtained from a reclamation site in Illinois where municipal biosolids were applied at reclamation rates for 20 years, reaching the cumulative biosolids application rate of 1,654 Mg/ha. Industrially impacted soil was created by mixing composted biosolids from a small municipal (but impacted by PFAA manufacturing) WWTP with control soil on a 10% mass basis. Sampling year not provided.	Fruits and vegetables; grains	Field study: Corn grain: Urban nonamended: n = 3–7, DF NR, mean = < 0.04 ng/g Urban 1×: n = 3–7, DF NR, mean = < 0.04 ng/g Urban 2×: n = 3–7, DF NR, mean = < 0.04 ng/g Rural nonamended: n = 3–7, DF NR, mean = < 0.04 ng/g Rural 0.5×: n = 3–7, DF NR, mean = < 0.04 ng/g Corn stover: Urban nonamended: n = 3–7, DF NR, mean = < 0.29 ng/g Urban 1×: n = 3–7, DF NR, mean = < 0.29 ng/g Urban 2×: n = 3–7, DF NR, mean = < 0.29 ng/g Rural nonamended: n = 3–7, DF NR, mean = < 0.29 ng/g Rural 0.5×: n = 3–7, DF NR, mean = < 0.29 ng/g (LOQ = 0.04 ng/g for corn grain; LOQ = 0.29 ng/g for corn stover) Greenhouse study: Lettuce: Nonamended: n = 3–5, DF NR, mean = <0.01 ng/g **Industrially impacted: n = 3–5, DF NR, mean = 10.44 ng/g** **Municipal: n = 3–5, DF NR, mean = 5.54 ng/g** Tomato: Nonamended: n = 3–5, DF NR, mean = < 0.03 ng/g **Industrially impacted: n = 3–5, DF NR, mean = 0.76 ng/g** Municipal: n = 3–5, DF NR, mean = < 0.03 ng/g (LOQ = 0.01 ng/g for lettuce; LOQ = 0.03 ng/g for tomato)

Study	Location and Source	Food Types	Results
	United States		
von Ehrenstein et al. (2009)	United States (North Carolina) As part of the Methods Advancement for Milk Analysis (MAMA) pilot study, 34 breastfeeding women aged 18 to 38 years at recruitment provided breastmilk samples at two visits. The first visit occurred 2–7 weeks postpartum, and the second visit occurred 3–4 months postpartum. Both visits were between December 2004 and July 2005.	Breastmilk	Visit #1: n = 18, DF 0% Visit #2: n = 20, DF 0% (LOQ = 0.30 ng/mL)
Kuklenyik et al. (2004)	United States (Georgia) Authors reported that no information was provided on the human milk donors or the sampling procedure.	Breastmilk	n = 2, DF 0% (LOD = 0.3 ng/mL)

Notes: AFFF = aqueous film-forming foam;DF = detection frequency; GCA = groundwater contamination area; LOD = limit of detection; LOQ = limit of quantitation; MDL = method detection limit; ND = not detected; NR = not reported; RL = reporting limit; ww = wet weight; WWTP = wastewater treatment plant.
Bold indicates detected levels of PFHxS in food.
[a] The DF and/or mean was not reported in the study and was calculated in this synthesis. Means were calculated only when DF = 100%.

Consumer Products

PFHxS has been used in laboratory applications and as a raw material or a precursor for the manufacture of PFAS/perfluoroalkyl sulfonate-based products, though production of PFHxS in the United States was phased out by its major manufacturer in 2002 (Backe et al., 2013, Buck et al., 2011; OECD, 2011 and Sigma-Aldrich, 2014; NCBI, 2022). PFHxS has also been used in firefighting foam and carpet treatment solutions, and it has been used as a stain and water repellant (Garcia and Harbison, 2015; NCBI, 2022). PFHxS has been detected in aqueous film forming foam, aftermarket carpet protection products, chipboards, leather, membranes for apparel, treated apparel, and photoprint ink and laser ink (Backe et al., 2013; Bečanová, et al., 2016; Buck et al., 2011; Glüge et al., 2021; Herzke et al., 2009; Kotthoff et al., 2015; Liu et al., 2014; NCBI, 2022; Norwegian Environment Agency, 2018).

Two studies were identified that analyzed PFHxS concentrations in a range of consumer products, including children's nap mats, household carpet/fabric-care liquids, and textiles (Liu et al., 2014; Zheng et al., 2020) (Table B-4). Few U.S. studies analyzed children's products, fabric treatments, treated fabrics, sealants, and similar products, and none of the U.S. studies reviewed sampled for PFAS in other household products and articles such as cosmetics, cleaners, paints, upholstered furniture, etc. Of the U.S. studies, the majority of the consumer products evaluated are likely used by adults (e.g., floor waxes), can come into contact with both adults and children (e.g., treated upholstery), or the user was not specified (e.g., clothing).

Zheng et al. (2020) determined the occurrence of ionic and neutral PFAS in the childcare environment (dust and nap mats). Samples of children's nap mats were collected from seven Seattle childcare centers (n = 26; 20 polyurethane foam, 6 vinyl cover samples). PFHxS was detected in 73% of nap mat samples with a mean concentration of 0.32 ng/g. Half of the analyzed mats were purchased as new products and the other half were used. The authors reported that total PFAS levels in the new vs. used mats were not significantly different. Total PFAS levels in mat foam vs. mat covers were also similar. Based on these results, the authors suggested that indoor air was not the major source of PFAS in mats and that PFAS in mats could be associated with the manufacturing process.

Liu et al. (2014) analyzed the occurrence of PFAS in consumer products (including commercial carpet/fabric-care liquids, household carpet/fabric-care liquids, treated apparel, treated home textile and upholstery, treated floor waxes and stone-wood sealants, membranes for apparel, and thread-sealant tapes and pastes) purchased between March 2007 and September 2011 from local retailers and online stores in the United States. PFHxS was analyzed in a subset of these consumer products, originating from the United States, England, Dominican Republic, Vietnam, and China, and was detected in one out of two commercial carpet/fabric-care liquids samples at 194 ng/g, in two out of four household carpet/fabric-care liquids and foams samples at 88.8 ng/g and 155 ng/g, in one out of two treated children's apparel samples at 1.70 ng/g (in boy's uniform pants), in one out of two treated home textile and upholstery samples at 12.1 ng/g, in one apparel membrane sample at 7.10 ng/g, and in one out of two thread-sealant tapes and pastes samples at 60.3 ng/g. PFHxS was not detected in one treated floor wax and stone/wood sealant sample. Detection limits were not reported in the study.

Table B-4. Summary of PFHxS Consumer Product Data

Study	Location	Site Details	Results
		United States	
Zheng et al. (2020)	United States (Seattle, Washington)	Children's nap mat samples (n = 26, finely cut) from seven Seattle childcare centers, including polyurethane foam (n = 20) and vinyl cover (n = 6) samples. Sampling year not reported.	n = 26, DF 73%, mean, median (range) = 0.32, 0.30 (< ND–0.73) ng/g (MDL = 0.05 ng/g)
Liu et al. (2014)	United States (unspecified)	Consumer products commonly used indoors were purchased between March 2007 and September 2011 from local retailers and online stores in the United States. A subset of samples were analyzed for PFSAs and included commercial carpet/fabric-care liquids, household carpet/fabric-care liquids and foams, treated apparel (i.e., one girl's uniform pants and one boy's uniform pants), treated home textile and upholstery (i.e., mattress pads), treated floor waxes and stone-wood sealants, membranes for apparel, and thread-sealant tapes and pastes. The subset of products originated from the United States, England, Dominican Republic, Vietnam, and China.	Commercial carpet/fabric-care liquids: n = 2, DF[a] = 50%, range = BDL–194 ng/g Household carpet/fabric-care liquids and foams: n = 4, DF[a] = 50%, range = BDL–155 ng/g Treated apparel: n = 2, DF[a] = 50%, range = BDL–1.70 ng/g Treated home textile and upholstery: n = 2, DF[a] = 50%, range = BDL–12.1 ng/g Treated floor waxes and stone-wood sealants: n = 1, DF 0% Membranes for apparel: n = 1, point = 7.10 ng/g Thread-sealant tapes and pastes: n = 2, DF[a] = 50%, range = BDL–60.3 ng/g (DL not reported)

Notes: BDL = below detection limit; DF = detection frequency; DL = detection limit; MDL = method detection limit ND = not detected.
[a] The DF and/or mean was not reported in the study and was calculated in this synthesis. Means were calculated only when DF = 100%.

Indoor Dust

In a Wisconsin Department of Health Services study, Knobeloch et al. (2012) examined levels of 16 perfluoroalkyl chemicals in vacuum cleaner dust from 39 Wisconsin homes across 16 counties in March and April 2008 (Table B-5). Samples from these homes built between 1890 and 2005 were collected during a pilot study to assess residential exposure to persistent contaminants found in the Great Lakes Basin. PFHxS was found in all samples at a median concentration of 16 ng/g. Mean levels of PFHxS in dust were significantly higher in homes built between 1968 and 1995 (219 ng/g vs. 57 ng/g in homes constructed in other years). Based on the results of this study, the authors suggested that perfluoroalkyl chemicals may be ubiquitous contaminants in U.S. homes. In an EPA study of 112 indoor dust samples collected from vacuum cleaner bags from homes and daycare centers in North Carolina and Ohio in 2000–2001 (EPA's CTEPP study), samples were collected from 102 homes and 10 daycare centers in North Carolina (49 homes, 5 daycare centers) and Ohio (53 homes, 5 daycare centers) (Strynar and Lindstrom, 2008). Results were not reported separately for homes and daycares. Overall, PFHxS was detected in 77.7% of all samples (n = 112) at mean and median concentrations of 874 and 45.5 ng/g, respectively. The authors concluded that the study measured perfluorinated compounds in house dust at levels that may represent an important pathway for human exposure.

Additional peer-reviewed studies were identified that evaluated the occurrence of PFHxS and other PFAS in dust of indoor environments, primarily in homes, as well as in schools, childcare facilities, offices, and vehicles (Byrne et al., 2017; Fraser et al., 2013; Karásková et al., 2016; Kato et al., 2009; Knobeloch et al., 2012; Scher et al., 2019; Wu et al., 2014; Zheng et al., 2020) (Table B-5). For those studies with results stratified for U.S. homes, PFHxS levels and detection frequencies were lowest in a study of remote Alaska Native villages (27% detection, median below 0.2 ng/g), while in other U.S. locations, PFHxS was detected in at least 40% of samples (some studies reporting 100% detection) at widely varying mean and median levels across the studies (from on the order of 10 ng/g to on the order of 200 ng/g) with one study reporting the highest mean value (219 ng/g) from homes built between 1968 and 1995. The two studies also reporting home measurements from other countries differed in how PFHxS levels in the U.S. ranked relative to other countries, with one study ranking the U.S. highest and the other second lowest. Few studies sampled childcare centers, vehicles, and offices, and none of the reviewed studies reported measurements in other microenvironments (e.g., public libraries, universities).

Several studies reported results from dust samples collected only from homes (Byrne et al., 2017; Scher et al., 2019; Wu et al., 2014), with one study sampling from locations near a PFAS production facility. Scher et al. (2019) evaluated indoor dust in 19 homes in Minnesota within a GCA in the vicinity of a former 3M PFAS production facility. Homes within the GCA had previous or ongoing PFAS contamination in drinking water and were served by the Oakdale, Minnesota public water system or a private well previously tested and shown to have detectable levels of PFOA or PFOS. In the house dust samples, collected from July to September 2010, the detection frequencies for PFHxS were 68% and 84% for entryways to the yard and interior living spaces such as the family or living rooms, respectively (n = 19 each), with median concentrations of 8.2 ng/g and 18 ng/g, respectively. PFAS concentrations in both sampling locations were higher than corresponding soil concentrations, suggesting that interior sources were the main contributors to PFAS in house dust.

Byrne et al. (2017) assessed exposure to PFHxS and other PFAS among residents of two remote Alaska Native villages on St. Lawrence Island. PFAS concentrations were measured in dust collected from the surfaces of floors and furniture of 49 homes on St. Lawrence Island during February–April of 2013 and 2014. Residents were asked not to sweep or dust for one week prior to sampling. The authors described the overall PFAS levels in dust samples as "on the lower end of those reported worldwide in other studies." PFHxS was found in 27% of all samples (n = 49) with a median value below the LOD (0.1 ng/g–0.2 ng/g). Wu et al. (2014) measured concentrations of five PFAS in residential dust in California in 2008–2009. Dust samples were collected from the carpet or area rug in the main living area of the home. Homes of parents with young children and homes with older adults were differentiated to characterize the relationship between serum concentrations of PFAS and several other factors, including PFAS concentrations in residential dust. PFHxS was detected in 51% of samples from households with young children in Northern California (n = 82), with mean and median concentrations of 142 ng/g and 5.30 ng/g, respectively. PFHxS was detected in 52% of samples from households of older adults in central California (n = 42), with mean and median concentrations of 55 ng/g and 5.55 ng/g, respectively.

Apart from the information reported by Strynar and Lindstrom (2008), one other study included childcare centers in the locations sampled, (Zheng et al., 2020). Zheng et al. (2020) collected dust samples from seven childcare centers in Seattle, Washington (n = 14) and one childcare facility in West Lafayette, Indiana (n = 6 across six rooms); the sampling year was not reported. The included childcare facilities consisted of several building types, including multiple classrooms, a former church, and a former home. Because centers were vacuumed and mopped daily, dust samples were obtained from elevated surfaces (shelving, tops of bookcases/storage cubbies) along with floor dust. PFHxS was detected in 95% of samples at mean and median concentrations of 0.34 ng/g and 0.25 ng/g, respectively.

One study evaluated PFHxS levels in vehicles and offices, in addition to homes. Fraser et al. (2013) collected dust samples between January and March 2009 from 3 microenvironments of 31 individuals in Boston, Massachusetts (offices (n = 31), homes (n = 30), and vehicles with sufficient dust for analysis (n = 13)). Study participants worked in separate offices located across seven buildings, which were categorized as Building A (n = 6), Building B (n = 17), or Other (n = 8). Building A was a newly constructed (approximately one year prior to study initiation) building with new carpeting and new upholstered furniture in each office. Building B was a partially renovated (approximately one year prior to study initiation) building with new carpeting throughout hallways and in about 10% of offices. The Other buildings had no known recent renovation occurred. Study offices were not vacuumed during the sampling week and participants were asked not to dust or vacuum their homes and vehicles for at least one week prior to home sampling. Because PFHxS was detected in less than 50% of samples in all three microenvironments, geometric means were not reported. The detection frequencies for PFHxS were 23%, 40%, and 46% for offices, homes, and vehicles, respectively, with the range of detected values reported as 5.24 ng/g–18.5 ng/g, 6.05 ng/g–430 ng/g, and 5.22 ng/g–108 ng/g, respectively.

Two studies evaluated dust samples collected across multiple continents (Karásková et al., 2016; Kato et al., 2009). Karásková et al. (2016) examined PFAS levels in house dust collected between April and August 2013 from the living rooms and bedrooms of 14 homes in the United States, 15 homes in Canada, and 12 homes in the Czech Republic (locations unspecified). PFHxS

was detected in all U.S. samples (n = 20) at mean and median concentrations of 13.8 ng/g and 8.7 ng/g, respectively. The authors reported significant differences between countries for PFHxS concentrations, with a trend of U.S. > Canada ~ Czech Republic and suggested that the differences may be explained by differences in the market, import history, and usage of these substances. (Note: As stated previously, while studies from non-U.S. countries inform an understanding global exposure sources and trends, the RSC determination is based on the available data for the United States). Overall, no significant differences in total PFAS concentrations were found between the bedroom and living room in the same household although significant relationships were found based on type of floors, number of residents, and age of the house. A second multicontinental study (Kato et al., 2009) measured PFC concentrations in 39 household dust samples collected in 2004 from homes in the United States (Atlanta, GA) (n = 10), United Kingdom (n = 9), Germany (n = 10), and Australia (n = 10). Across all 39 homes, PFHxS was detected in 79.5% of samples with a median concentration of 185.5 ng/g. Authors presented the median and maximum PFHxS concentrations by country in a bar chart, which showed that PFHxS was detected in all countries. The median and maximum PFHxS concentrations for the 10 United States (Atlanta, GA) house dust samples were approximately 96.4 ng/g and 231.3 ng/g, respectively. The highest median was found in Australia, followed by the United Kingdom, the United States, and Germany in decreasing order; statistical significance on the comparison of median PFHxS concentrations by country was not reported.

Table B-5. Summary of PFHxS Indoor Dust Data

Study	Location	Site Details	Results
		United States	
Scher et al. (2019)	United States (Twin Cities metropolitan region, Minnesota)	Nineteen homes in three cities within a GCA near former 3M PFAS production facility as well as from three homes in the Twin Cities Metro outside the GCA. Dust samples collected from an entryway to the yard and from an interior living space (e.g., family room, living room) in each home in July–September 2010. Homes within the GCA had previous or ongoing PFAS contamination in drinking water and were served by the Oakdale, Minnesota public water system or a private well previously tested and shown to have detectable levels of PFOA or PFOS. Results were not reported for homes outside the GCA.	Entryway: n = 19, DF 68%, median (range) = 8.2 (< RL–94) ng/g Living room: n = 19, DF 84%, median (range) = 18 (< RL–790) ng/g (RL = 5 ng/g)
Byrne et al. (2017)	United States (St. Lawrence Island, Alaska)	Dust samples collected from the surfaces of floors and furniture from 49 homes during February–April of 2013 and 2014. Participants were asked not to sweep or dust for one week prior to sampling.	n = 49; DF 27%, median (95th percentile) = < LOD (3.13) ng/g (MDL = 0.1–0.2 ng/g for all PFAS)
Wu et al. (2014)	United States (Central Valley area, California)	Distributions of PFC dust concentrations were determined for households with young children in Northern California (n = 82) and households of older adults in central California (n = 42). Dust samples were collected in 2008–2009 from the carpet or area rug in the main living area of the homes. Homes of parents with young children and homes with older adults were differentiated to characterize the relationship between serum concentrations of PFCs and PFC concentrations measured in residential dust.	Parents of young children: n = 82, DF 51%, mean, median (range) = 142, 5.30 (ND–7,490) ng/g Older adults: n = 42, DF 52%, mean, median (range) = 55, 5.55 (ND–1,050) ng/g (LOD = 0.10 ng/ml) *Data below LOQ replaced by LOD/√2

Study	Location	Site Details	Results
		United States	
Knobeloch et al. (2012)	United States (Great Lakes Basin, Wisconsin)	Dust samples were collected by the Wisconsin Department of Health Services from 39 Wisconsin homes across 16 counties in March–April 2008. Vacuum bags were collected or bagless vacuums were emptied into sterilized glass jars. Homes were built between 1890 and 2005.	n = 39, DF 100%, median (range) = 16 (2.1–1,000) ng/g (RL = 1 ng/g)
Zheng et al. (2020)	United States (Seattle, Washington; West Lafayette, Indiana)	Seven childcare centers in Seattle (14 samples) and one center in Lafayette (6 samples); sampling year not reported. Since all centers were vacuumed and mopped daily, dust samples from elevated surfaces (shelving, tops of bookcases/storage cubbies) were collected along with floor dust in the same sample.	n = 20; DF 95%, mean, median (range) = 0.34, 0.25 (< ND–0.89) ng/g (MDL = 0.05 ng/g)
Strynar and Lindstrom (2008)	United States (North Carolina; Ohio)	Dust samples from vacuum cleaner bags were obtained in 2000–2001 during EPA's Children's Total Exposure to Persistent Pesticides and Other Persistent Organic Pollutants (CTEPP) study from North Carolina (49 homes, 5 daycare centers) and Ohio (53 homes, 5 daycare centers). Vacuum cleaner bags were only collected if available at each site.	n = 112, DF 77.7%, mean, median (maximum) = 874, 45.5 (35,700) ng/g (LOQ = 12.9 ng/g) *Values below the LOQ assigned a value of LOQ/√2

Study	Location	Site Details	Results
		United States	
Fraser et al. (2013)	United States (Boston, Massachusetts)	Dust samples were collected between January–March 2009 from offices (n = 31), homes (n = 30), and vehicles (n = 13) of 31 individuals. Study participants worked in separate offices located across seven buildings, which were categorized into Building A, Building B, and Other. Six samples were collected from Building A, a newly constructed (approximately one year prior to study initiation) building with new carpeting and new upholstered furniture in each office. Seventeen samples were collected from Building B, a partially renovated (approximately one year prior to study initiation) building with new carpeting throughout hallways and in about 10% of offices. Eight samples were collected from the other five remaining buildings where no known recent renovation occurred. Study offices were not vacuumed during the sampling week and homes and vehicles were not vacuumed for at least one week prior to sampling. Entire accessible floor surface areas and tops of immovable furniture were vacuumed in offices and the main living area of homes. Entire surface areas of the front and back seats of vehicles were vacuumed. Number of home dust samples was reduced to 30 because 1 participant lived in a boarding house with no main living area. Sufficient mass of dust for analysis was available from only 13 vehicles.	Homes: n = 30, DF 40%, range = 6.05–430 ng/g Offices: n = 31, DF 23%, range = 5.24–18.5 ng/g Vehicles: n = 13, DF 46%, range = 5.22–108 ng/g (LOQ = 5 ng/g) *Range of detected values reported

Notes: DF = detection frequency; GCA = groundwater contamination area; LOD = limit of detection; LOQ = limit of quantitation; MDL = method detection limit; MQL = method quantification limit; ND = not detected; RL = reporting limit.

Air

Perfluoroalkyl chemicals have been released to air from wastewater treatment plants, waste incinerators, and landfills (EPA, 2016), though there is limited information on the detection levels or frequencies of PFHxS in either indoor or ambient air. NCBI (2022) notes that PFHxS has been detected in particulates and in the vapor phase in air and it can be transported long distances via the atmosphere; it has been detected at low concentrations in areas as remote as the Arctic and ocean waters. For example, PFHxS was detected in particle-phase air samples collected in 2007 and 2008 from the Atlantic Ocean, Southern Ocean, and Baltic Sea (Dreyer et al., 2009; NCBI, 2022). PFHxS is not expected to be broken down directly by photolysis (NCBI, 2022). PFHxS in the particle-phase can be removed from the atmosphere through wet and dry deposition (NCBI, 2022). PFHxS in the vapor phase can undergo hydroxylation in the atmosphere, with a (predicted average) atmospheric hydroxylation rate of 2.16×10^{-15} cm^3/molecule – second to a (derived) rate of 1.4×10^{-13} cm^3/molecule – second at 25 °C (with corresponding estimated half-life of 115 days for this reaction in air) (NCBI, 2022; EPA, 2022a). With a vapor pressure of 0.0046 mm Hg at 25 °C (estimated), 8.10×10^{-9} mm Hg (measured average), and 8.19×10^{-9} mm Hg (predicted average), volatilization is not expected to be an important fate process for this chemical (NCBI, 2022, EPA, 2022a). EPA's Toxics Release Inventory reported release data for PFHxS in 2020, with total on-site disposal, off-site disposal, and other releases concentrations of 1 pound at an individual facility and 122 pounds at a second facility (EPA, 2022b). PFHxS is not listed as a hazardous air pollutant (EPA, 2022c).

Indoor Air

No studies from the U.S. reporting levels of PFHxS in indoor air were identified from the primary or gray literature.

Ambient Air

Kim and Kannan (2007) analyzed particle phase (n = 8) and gas phase (n = 8) concentrations of perfluorinated acids in ambient air samples collected in and around Albany, New York in May and July 2006 to examine the relative importance of certain media pathways to the contamination of urban lakes. PFHxS was detected in all gas phase samples with mean, and median concentrations of 0.31 pg/m^3 and 0.34 pg/m^3, respectively, but was not detected in the particle phase (LOQ = 0.12 pg/m^3).

Soil

The production of PFHxS and its use as a raw material or precursor for manufacturing PFAS based products, as well as its previous use in firefighting foam and carpet treatment solutions, could result in its release to soils through various waste streams (NCBI, 2022). When released to soil, PFHxS is expected to have very high mobility (NCBI, 2022). The maximum concentration of PFHxS in soil samples collected from a PFAS production facility in Minnesota was 3,470 ng/g, with PFHxS detected in 90% of the samples collected (3M, 2007; ATSDR, 2021; NCBI, 2022). The maximum concentration of PFHxS in soil samples collected at a fire training area at a PFAS production facility in Minnesota was 62.2 ng/g, with PFHxS detected in 100% of samples (3M, 2007; ATSDR, 2021). PFHxS was also detected in soil samples collected from a former sludge incorporation area at a PFAS production facility in Decatur, Alabama, with average levels ranging from 3.56 ng/g to 270 ng/g, with PFHxS detected in 86% of the samples

collected (3M, 2012; ATSDR, 2021). PFHxS has been found to accumulate in the roots of maize plants grown in soil containing PFHxS and other PFAS (Krippner et al., 2015; ATSDR, 2021).

Seven additional peer-reviewed studies were identified that evaluated the occurrence of PFHxS and other PFAS in soil (Anderson et al., 2016; Blaine et al., 2013; Eberle et al., 2017; Nickerson et al., 2020; Scher et al., 2018, 2019; Venkatesan and Halden, 2014) (Table B-6). Among the studies conducted in the United States, three analyzed soils potentially impacted by past AFFF use. At all such sites, PFHxS was detected in at least 50% of samples, typically at levels less than 100 ng/g, but some values were higher and, in some cases, the subsurface PFHxS levels were higher than in the surface soil. Other than control soils in two greenhouse and field studies and one reference site, the U.S. studies did not evaluate soils without amendments or without a nearby current or historical PFAS source.

Two studies by Scher et al. (2018; 2019) evaluated soils collected in 2010 from the garden planting area of 20 homes in Minnesota within a GCA impacted by the former 3M PFAS production facility. Homes within the GCA had previous or ongoing PFAS contamination in drinking water and were served by the Oakdale, Minnesota public water system or a private well previously tested and shown to have detectable levels of PFOA or PFOS. Both studies reported similar median PFHxS levels of 0.08 ng/g and 0.057 ng/g (n = 20–34) from the 2019 and 2018 publications, respectively. Scher et al. (2018) also reported a median PFHxS concentration of 0.078 ng/g from six samples collected outside the GCA.

Three studies analyzed soils potentially impacted by AFFF use (Anderson et al., 2016; Eberle et al., 2017; Nickerson et al., 2020). Anderson et al. (2016) examined surface and subsurface soil from 40 sites across 10 active Air Force installations throughout the continental United States and Alaska between March and September 2014. Installations were included if there was known historic AFFF release in the period 1970–1990. It is assumed that the measured PFAS profiles at these sites reflect the net effect of several decades of all applicable environmental processes. The selected sites were not related to former fire training areas and were characterized according to volume of AFFF release—low, medium, and high. Across all sites, the PFHxS detection frequency was 76.92% in 100 surface soil samples (median concentration of detects was 5.7 ng/g) and 59.62% in 112 subsurface soil samples (median concentration of detects was 4.4 ng/g). PFHxS was detected more frequently at high-volume release sites (82.5% in 32 surface soil samples with mean concentration of 19.7 ng/g; 87.5% in 31 subsurface soil samples with mean concentration of 9.3 ng/g) than at low-volume sites (75.0% in 12 surface soil samples with mean concentration of 13.9 ng/g; 58.8% in 17 subsurface soil samples with mean concentration of 57.9 ng/g) and medium-volume sites (59.2% in 56 surface soil samples with mean concentration of 39.4 ng/g; 71.4% in 64 subsurface soil samples with mean concentration of 55.4 ng/g). Nickerson et al. (2020) developed a method to quantify anionic, cationic, and zwitterionic PFAS from AFFF-impacted soils. The method was applied to two soil cores collected from two different AFFF-impacted former fire training areas; the sampling year and geographic location were not provided. Eleven soil samples, corresponding to 11 depths ranging from 0.46 m to 15.1 m, were evaluated from Core E, and 12 soil samples, at depths ranging from 0.30 m to 14.2 m, were evaluated from Core F. PFHxS was detected at all depths analyzed for both cores, with concentrations ranging from 1.17 ng/g dw to 160.6 ng/g dw for Core E and 0.66 ng/g dw to 296.4 ng/g dw for Core F. Eberle et al. (2017) investigated the effects of an in situ chemical oxidation treatment for remediation of chlorinated volatile organic compounds and

PFAAs co-contaminants. Soil samples were collected in 2012–2013 before and after a pilot scale field test at a former fire training site at Joint Base Langley-Eustis, Virginia. Monthly fire training activities were conducted at the site from 1968 to 1980 and irregular fire training activities continued until 1990. Impacted soil was excavated in 1982 but details were not provided. PFHxS was detected in 4 of 5 pre-treatment samples and in all 14 post-treatment samples. In the available three paired pre- and post-treatment soil samples, two pairings showed a decrease in PFHxS concentration after treatment, from 6.7 ng/g to 1.40 ng/g in one pairing and from 12 ng/g to 1.44 ng/g in the other pairing. In the third pairing, PFHxS was not detected pre-treatment and was found at 0.31 ng/g post-treatment.

Of the remaining two studies conducted in the United States, Venkatesan and Halden (2014) conducted outdoor mesocosm studies to examine the fate of PFAS in biosolids-amended soil collected during 2005–2008. Biosolids were obtained from a WWTP in Baltimore that primarily treated wastewater from domestic sources with only minor contribution (1.9%) from industry. PFHxS was not detected in the control (nonamended) soil and not consistently detected in the biosolids-amended soil (MDL = 0.03–0.14 ng/g dw). In a field and greenhouse study, Blaine et al. (2013) studied the uptake of PFAS into edible crops grown in control and biosolids-amended soil. In the field study, urban biosolids were obtained from a WWTP receiving both domestic and industrial waste while rural solids were obtained from a WWTP receiving domestic waste only. Mean PFHxS concentrations were below the LOQ (0.01 ng/g) in the urban control and biosolids-amended soils and in the rural control soil. In the rural biosolids-amended soil, the mean PFHxS concentration was 0.016 ng/g. In the greenhouse study, three soils (nonamended control, industrially impacted, and municipal) were investigated. Industrially impacted soils contained composted biosolids from a small municipal WWTP that was impacted by PFAA manufacturing while municipal soils were obtained from a reclamation site in Illinois where municipal biosolids were applied for 20 years. PFHxS was detected in all three soils at an average concentration of 0.44 ng/g, 1.38 ng/g, and 5.11 ng/g in control, industrially impacted, and municipal soil, respectively. Authors noted that the trace levels of PFAS detected in the control soil may be due to minor cross-contamination from plowing, planting, or atmospheric deposition from the surrounding area where biosolids have been applied.

Table B-6. Summary of PFHxS Data in Soil

Study	Location	Site Details	Results
		United States	
Scher et al. (2019)	United States (Twin Cities metropolitan region, Minnesota)	Area near former 3M PFAS production facility. Soil composite samples (200–500 g) collected in 2010 from the garden planting area of 20 homes in 3 cities within a GCA as well as from 3 homes in the Twin Cities Metro outside the GCA. Homes within the GCA had previous or ongoing PFAS contamination in drinking water and were served by the Oakdale, Minnesota public water system or a private well previously tested and shown to have detectable levels of PFOA or PFOS. Results were not reported for homes outside the GCA.	n = 20, DF 85%, median (90th percentile) = 0.08 (0.16) ng/g (RL = 0.0008–0.033 ng/g for all PFAS)
Scher et al. (2018)	United States (Twin Cities metropolitan region, Minnesota)	Area near former 3M PFAS production facility. Soil samples collected in 2010 at a sample depth of 0–6 inches from the garden planting area of 20 homes in 3 cities within a GCA as well as from 3 homes in the Twin Cities Metro outside the GCA. Homes within the GCA had previous or ongoing PFAS contamination in drinking water and were served by the Oakdale, Minnesota public water system or was formerly or currently using a private well previously tested and shown to have detectable levels of PFOA or PFOS. At 14 homes, soil samples were collected on two separate days.	Within GCA: n = 34, DF 71%, median (range) = 0.057 (ND–0.24) ng/g Outside GCA: n = 6, DF 100%, median (range) = 0.078 (0.028–0.11) ng/g (MDL = 0.008–0.033 ng/g for all PFAS) *Values below the method reporting limit but above the lowest calibration limit (estimated values) were included in all analyses as quantitative results *Values below the lowest calibration limit were replaced with ½ of the limit

Study	Location	Site Details	Results
		United States	
Anderson et al. (2016)	United States (national)	Forty AFFF-impacted sites from ten active U.S. Air Force installations with historic AFFF release between 1970 and 1990 that were not related to former fire training areas. It is assumed that the measured PFAS profiles at these sites reflect the net effect of several decades of all applicable environmental processes. AFFF-impacted sites included emergency response locations, hangers and buildings, and testing and maintenance related to regular maintenance and equipment performance testing of emergency vehicles and performance testing of AFFF solution. Previous remedial activities for co-occurring contaminants were not specifically controlled for in the site selection process; active remedies had not been applied at any of the sites selected. Approximately ten samples were collected between March and September 2014 at each site for surface and subsurface soil; sites were grouped according to volume of AFFF release—low-volume typically had a single AFFF release, medium-volume had one to five releases, and high-volume had multiple releases.	Surface soil: Overall: n = 100, DF 76.92%, median (maximum) = 5.7 (1,300) ng/g *Breakdown by site:* Emergency Response (low-volume release): n = 12, DF 75.0%, mean (range) = 13.9 (0.38–64) ng/g Hangars and Buildings (medium-volume release): n = 56, DF 59.2%, mean (range) = 39.4 (0.34–1,300) ng/g Testing and Maintenance (high-volume release): n = 32, DF 82.5%, mean (range) = 19.7 (0.29–180) ng/g (RL = 0.29 ng/g) Subsurface soil: Overall: n = 112, DF 59.62%, median (maximum) = 4.4 (520) ng/g *Breakdown by site:* Emergency Response (low-volume release): n = 17, DF 58.8%, mean (range) = 57.9 (0.37–520) ng/g Hangars and Buildings (medium-volume release): n = 64, DF 71.4%, mean (range) = 55.4 (0.35–1,300) ng/g Testing and Maintenance (high-volume release): n = 31, DF 87.5%, mean (range) = 9.3 (1.1–40) ng/g (RL = 0.31 ng/g) *Median calculated using quantified detections *Non-detects were substituted with ½ the reporting limit

Study	Location	Site Details	Results
		United States	
Nickerson et al. (2020)	United States (unspecified)	Soil cores E and F from two different AFFF-impacted fire training areas; sampling year and geographic location not provided. Soil core E contained 11- 0.3 m increment samples from 0.3–15.2 m below ground surface and was collected in an area where the surficial soils were likely disturbed due to regrading and other soil redistribution activities. Soil core F contained 12- 0.61 m increment samples from 0–14.2 m below ground surface and was collected in an area where the surficial soils were highly permeable only within the upper 0.5 to 1 m, and the underlying impermeable clay layer exhibited a relatively high cation exchange capacity and organic carbon content. The water table was relatively shallow (depth < 3 m) at both sites.	Core E: 0.46 m = 1.44 ng/g dw 2.9 m = 2.12 ng/g dw 3.66 m = 4.17 ng/g dw 3.96 m = 15.21 ng/g dw 4.27 m = 28.68 ng/g dw 4.57 m = 4.13 ng/g dw 4.88 m = 5.73 ng/g dw 7.01 m = 13.86 ng/g dw 8.38 m = 160.6 ng/g dw 10.5 m = 139.0 ng/g dw 15.1 m = 1.17 ng/g dw Core F: 0.30 m = 11.07 ng/g dw 1.22 m = 296.4 ng/g dw 1.83 m = 276.2 ng/g dw 2.44 m = 106.2 ng/g dw 3.05 m = 42.69 ng/g dw 4.11 m = 28.78 ng/g dw 7.62 m = 14.19 ng/g dw 8.84 m = 6.26 ng/g dw 9.45 m = 3.25 ng/g dw 10.5 m = 0.66 ng/g dw 11.9 m = 3.06 ng/g dw 14.2 m = 7.96 ng/g dw (LOD/LOQ not reported)

Study	Location	Site Details	Results
		United States	
Eberle et al. (2017)	United States (Joint Base Langley-Eustis, Virginia)	Pilot testing area in former fire training area (Training Site 15) at Joint Base Langley-Eustis where monthly fire training activities were conducted from 1968 to 1980 in a zigzag pattern burn pit. Facility was abandoned in 1980 but irregular fire training activities using an above-ground germed burn pit continued until 1990. Impacted soil was removed in 1982 but additional details of the excavation are not well known. Soil samples collected for pre- (April and September 2012) and post- (December 2013) in situ chemical oxidation treatment using a peroxone activated persulfate (OxyZone) technology. Treatment was conducted in Test Cell 1 over 113 days (April–August 2013). Soil samples were collected adjacent to wells; wells outside Test Cell 1 were used as sentry wells. Well IDs for pre- and post-sampling were not provided but the following three pairings were assumed based on Table 2 in the paper: U-20 with SB-106; U-16 with SB-112; and I-1 with SB-109.	Pre-treatment: I-1 (1.2–4.3 m) = 12 ng/g I-2 (1.2–4.3 m) = 83 ng/g U-12 (2.1 m) = 1.2 ng/g U-16 (3.0 m) = 6.7 ng/g U-20 (1.8 m) = ND (LOQ = 0.68–0.72 ng/g) Post-treatment: SB-101 (4.3 m) = 8.08 ng/g SB-105 (1.8 m) = 0.83 ng/g SB-106/U-20 (1.8 m) = 0.31 ng/g SB-106 (4.3 m) = 5.08 ng/g SB-107 (1.8 m) = 2.11 ng/g SB-107 (4.3 m) = 3.99 ng/g SB-108 (1.8 m) = 1.48 ng/g SB-108 (4.3 m) = 4.83 ng/g SB-109/I-1 (3 m) = 1.44 ng/g SB-111 (4.3 m) = 11.85 ng/g SB-112 (1.8 m) = 2.57 ng/g SB-112/U-16 (3 m) = 1.4 ng/g SB-114 (1.8 m) = 3.63 ng/g SB-114 (4.3 m) = 16.17 ng/g (LOQ = 0.12 ng/g)

Study	Location	Site Details	Results
		United States	
Venkatesan and Halden (2014)	United States (Baltimore, Maryland)	Archived agricultural soil (nonamended) collected during 2005–2008 at a depth of 0–20 cm from the United States Department of Agriculture-Agricultural Research Service Beltsville Agricultural Research Center; number of sampling sites and number of samples not provided. Biosolids-amended soil obtained by mixing biosolids and soil at a volumetric ratio of 1:2. Biosolids were from Back River WWTP in Baltimore, a full-scale activated sludge treatment plant. Raw wastewater was primarily from domestic sources with only minor contribution (1.9%) from industry.	Nonamended: n = NR, DF 0% Amended: n = NR, DF[a] 0% (MDL = 0.03–0.14 ng/g dw for all PFAS)

Study	Location	Site Details	Results
		United States	
Blaine et al. (2013)	United States (Midwest)	Urban and rural full-scale field study with control (nonamended) and biosolids-amended plots. Three agricultural fields were amended (0.5×, 1×, or 2×) with municipal biosolids. Urban biosolids (1× and 2×) were from a WWTP receiving both domestic and industrial waste. Rural biosolids (0.5×) were from a WWTP receiving domestic waste only. Control plots were proximal to the rural and urban amended corn grain and corn stover field sites; sampling year not provided. Greenhouse study with control (nonamended) and biosolids-amended soil. Nonamended soil obtained from a field that received commercial fertilizers and had a similar cropping system as the nearby municipal soil site. Municipal soil was obtained from a reclamation site in Illinois where municipal biosolids were applied at reclamation rates for 20 years, reaching the cumulative biosolids application rate of 1,654 Mg/ha. Industrially impacted soil was created by mixing composted biosolids from a small municipal (but impacted by PFAA manufacturing) WWTP with control soil on a 10% mass basis. Sampling year not provided.	Field study: Urban non-amended: n = 3–7, DF NR, mean < 0.01 ng/g Urban 1×: n = 3–7, DF NR, mean < 0.01 ng/g Urban 2×: n = 3–7, DF NR, mean < 0.01 ng/g Rural non-amended: n = 3–7, DF NR, mean < 0.01 ng/g Rural 0.5×: n = 3–7, DF NR, mean = 0.16 ng/g (LOQ = 0.01 ng/g) Greenhouse study: Nonamended: n = 3–5, DF NR, mean = 0.44 ng/g Industrially impacted: n = 3–5, DF NR, mean = 1.38 ng/g Municipal: n = 3–5, DF NR, mean = 5.11 ng/g (LOQ not reported)

Notes: AFFF = aqueous film-forming foam; DF = detection frequency; dw = dry weight; GCA = groundwater contamination area; LOD = limit of detection; LOQ = limit of quantitation; MDL = method detection limit; 0.5×, 1×, or 2× = ½, 1, or 2 times the agronomic rate of biosolids application to meet nitrogen requirements of the crop; ND = not detected; NR = not reported; RL = reporting limit; WWTP = wastewater treatment plant.

[a] Venkatesan and Halden (2014) reported that PFHxS was not consistently detected in biosolids-amended mesocosms.

Sediment

When released into water, PFHxS is not expected to adsorb to suspended solids and sediments (NCBI, 2022). However, PFHxS was detected in 28% of sediment samples collected along the Mississippi River shoreline in the vicinity of a PFAS production facility in Minnesota, at a maximum concentration of 11.5 ng/g (3M, 2007; ATSDR, 2021; NCBI, 2022). PFHxS was also detected in 96% of sediment samples collected from two coves of the Mississippi River (East and West coves) located at the eastern and western ends of the PFAS production facility, at a maximum concentration of 126 ng/g (3M, 2007; ATSDR, 2021). PFHxS was not detected in any Mississippi River transect sediment samples (collected at points crossing the river near the PFAS facility) (3M, 2007; ATSDR, 2021). PFHxS has been detected in sediment core samples collected from three Canadian Arctic lakes in 2003 and 2005 at concentrations ranging from approximately 1 ng/g to 10 ng/g (NCBI, 2022; Stock et al., 2007).

Biomonitoring in the U.S. Population

As indicated by CDC's NHANES results, PFHxS was detected in the blood of > 97% of NHANES participants for most of the years in which it was evaluated (CDC, 2019, 2021a, b, 2022). Whole-weight serum levels of PFHxS in the 50th percentile of the U.S. population for all years evaluated since 1999 were 2.10 µg/L in 1999–2000 (detected in 99.7% of samples), 1.90 µg/L in 2003–2004 (detected in 97.7% of samples), 1.80 µg/L in 2005–2006 (detected in 95.9% of samples), 2.00 µg/L in 2007–2008 (detected in 99.2% of samples), 1.70 µg/L in 2009–2010 (detected in 99.4% of samples), 1.27 µg/L in 2011–2012 (detected in 98.4% of samples), 1.40 µg/L in 2013–2014 (detected in 98.8% of samples), 1.20 µg/L in 2015–2016 (detected in 98.4% of samples), and 1.10 µg/L in 2017–2018 (detected in 99% of samples) (CDC, 2019, 2021a,b, 2022).

Recommended RSC

In summary, based on the physical properties, detected levels, and available exposure information for PFHxS, multiple non-drinking water sources (fish and shellfish, non-fish food, some consumer products, indoor dust, and soil) are potentially significant exposure sources. Following the Exposure Decision Tree in EPA's 2000 Methodology (EPA, 2000), significant potential sources other than drinking water ingestion were identified (Box 8A in the Decision Tree); however, information is not available to quantitatively characterize exposure from these different sources (Box 8B in the Decision Tree). Therefore, EPA recommends an RSC of 20% (0.20) for PFHxS.

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