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Bioaccumulation of Perfluoroalkyl Sulfonamides (FASA)

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Abstract

Hundreds of sites across the United States have high concentrations of perfluoroalkyl sulfonamides (FASA), but little is known about their propensity to accumulate in fish. FASA are precursors to terminal per- and polyfluoroalkyl substances (PFAS) that are abundant in diverse consumer products and aqueous film-forming foams manufactured using electrochemical fluorination (ECF AFFF). In this study, FASA with C3–C8 carbon chain lengths were detected in all fish samples from surface waters up to 8 km downstream of source zones with ECF AFFF contamination. Short-chain FASA ≤ C6 have rarely been included in routine screening for PFAS, but availability of new standards makes such analyses more feasible. Bioaccumulation factors (BAF) for FASA were between 1 and 3 orders of magnitude greater than their terminal perfluoroalkyl sulfonates. Across fish species, BAF for FASA were greater than for perfluorooctanesulfonate (PFOS), which is presently the focus of national advisory programs. Similar concentrations of the C6 FASA (<0.36–175 ng g^{-1}) and PFOS (0.65–222 ng g^{-1}) were detected in all fish species. No safety thresholds have been established for FASA. However, high concentrations in fish next to contaminated sites and preliminary findings on toxicity suggest an urgent need for consideration by fish advisory programs.

Graphical Abstract

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The authors declare no competing financial interest.

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.estlett.4c00143.
Sample information; supporting descriptions of extraction methods, analyses, and quality assurance/quality control; and tables and figures of peak areas, concentrations, and bioaccumulation factor data(PDF) Concentrations (Table S13) XLSX)

Complete contact information is available at: https://pubs.acs.org/doi/10.1021/acs.estlett.4c00143

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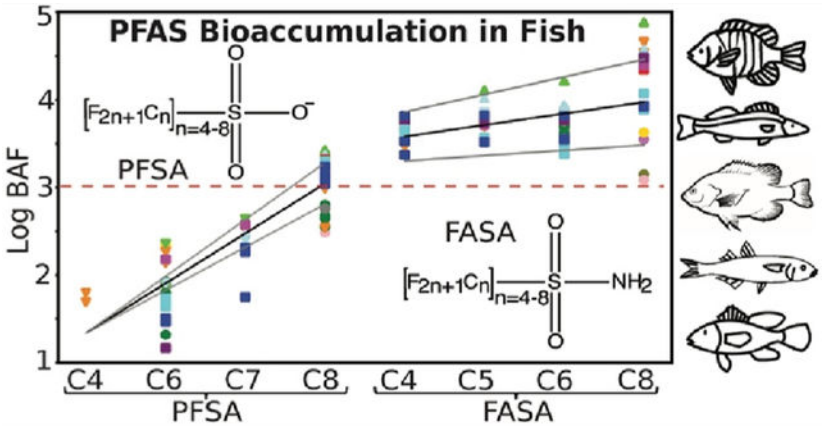

Keywords

Perfluoroalkyl sulfonamides (FASA); perfluorooctanesulfonate (PFOS); precursors; bioaccumulation; fish

INTRODUCTION

Perfluoroalkyl acids (PFAA) with longer perfluorinated carbon chains (C > 7) bioaccumulate in aquatic food webs, posing risks to local fish consumers.[1,2] Many states are urgently developing fish consumption advisories for per- and polyfluoroalkyl substances (PFAS) to mitigate exposure risks for human populations.[3] However, these advisories predominantly focus on perfluorooctanesulfonate (PFOS) and have not yet considered the diverse mixture of potentially bioaccumulative PFAS in aquatic ecosystems.[4,5] Major PFAS contamination sources such as aqueous film-forming foams (AFFF) and consumer products contain large quantities of precursors that transform into terminal PFAA.[6–9] The transformation pathway for precursors into terminal PFAA includes the formation of stable intermediate compounds, such as perfluoroalkyl sulfonamides (FASA; $C_nF_{2n+1}SO_2NH_2$), that persist in the environment.[10–12] High concentrations of FASA have been reported in aquatic ecosystems next to contaminated sites, but their bioaccumulation potential is relatively unknown.[13–15] Here, we compare the bioaccumulation potential of diverse FASA in recreational fish species to that of their terminal PFAA.

Prior work on the bioaccumulation potential of FASA has focused on perfluorooctane sulfonamide (FOSA), the eight-carbon (C8) precursor to PFOS.[16–19] Data on other FASA in biological samples are limited since they have rarely been included in targeted PFAS measurements.[20,21] However, analytical standards have recently become available, making them amenable to standard detection methods. Between 2000 and 2002, production of the parent chemical to PFOS and its precursors was phased out in North America.[20,22] Much of the chemistry then shifted to perfluorobutane sulfonyl fluoride derivatives,[23] with reported uses in semiconductor manufacturing.[24] This has resulted in detection of perfluorobutane sulfonamide (FBSA), the C4 precursor, in products[25] and environmental samples.[18,26,27] Perfluorohexane sulfonamide (FHxSA), the C6 precursor, is frequently detected at airports and military fire-training areas due to historical use of AFFF manufactured by 3M using

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electrochemical fluorination (ECF AFFF).[28–30] Recent studies have detected FBSA and FHxSA in fish[1,14,26,31] and other species,[18,32–34] suggesting short-chain FASA (≤C6) may bioaccumulate.

The main objective of this work is to better understand the propensity of diverse FASA to bioaccumulate in recreational fish. To do this, we present new measurements of C3–C8 FASA in fish and surface waters from a coastal watershed contaminated by ECF AFFF.[10,29] This work presents some of the first field-measured bioaccumulation factors (BAF) for short-chain FASA in recreational fish. We use the results to highlight gaps in ongoing biomonitoring programs, toxicity assessments, and fish consumption advisories for PFAS.

METHODS AND MATERIALS

Field Sampling.

Between May and September 2021, we collected paired surface water and fish samples from nine sites within three waterbodies in a groundwater-dominated coastal watershed that is described in prior work.[29] Field sampling regions are commonly used for recreational and subsistence fishing. An upgradient military base on Cape Cod, Massachusetts, U.S.A., that historically used ECF AFFF is the predominant PFAS source to these regions.[35] We sampled several sites based on proximity to known AFFF source zones, including a groundwater-fed seepage pond (Moody Pond), followed by a groundwater-fed river (Quashnet River) and the downstream estuary (Waquoit Bay) (Figure S1).

We collected surface water grab samples at each site in duplicate ($n = 20$) along with field blanks ($n = 5$) in 1 L bottles (Table S1). Collaborators at the Massachusetts Division of Fisheries and Wildlife and the Division of Marine Fisheries collected 17 common fish species concurrently with water sampling (Table S2). All field samples were stored frozen at −20 °C prior to analysis. Additional details on field sampling are provided in the Supporting Information(SI Sections 1.1–1.2).

Sample Extraction.

Water samples (300 mL) were extracted by weak anion exchange (WAX) solid phase extraction (SPE) with dispersive Envi-Carb cleanup, following established methods.[21,36] For fish samples with fork length >14 cm, we extracted PFAS from muscle fillets to best capture the fraction consumed by recreational fishers. For individual and composite fish samples <14 cm fork length, we measured whole-body concentrations. Homogenized tissues (0.5 g wet-weight) were extracted using acetonitrile and a bead blender, followed by WAX SPE cleanup, modified from established methods (SI Sections 1.3–1.4; Table S3).[17,21,37]

Instrumental Analysis.

Sample extracts were analyzed for targeted PFAA ($n = 18$) and FASA ($n = 4$) using an Agilent (Santa Clara, CA) 6460 triple quadrupole liquid chromatography tandem mass spectrometer in negative electrospray ionization (ESI−) mode, following previously published methods (SI Section 1.5).[1,36] Targeted PFAS were quantified using isotopic dilution and extracted internal standards (Table S4). FASA were quantified using the internal

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standard for FOSA. Linear and branched isomers of perfluorohexanesulfonate (PFHxS) and PFOS were quantified separately using available isomeric standards. FASA were quantified as the sum of isomers using linear isomer calibration curves (SI Section 1.6; Figures S2–S3). All results are discussed as the sum of the isomers.

We used suspect screening to analyze water and fish tissue extracts for additional PFAS using a Vanquish Flex ultrahighperformance liquid chromatograph coupled with a quadrupole Orbitrap Exploris 120 MS (ThermoFisher, U.S.) in ESI–mode (UHPLC-HRMS). Details of the analysis are provided in SI Section 1.7 (Table S5). Confidence levels of 2a or 3 were assigned accordingly.[38,39] Identification of perfluoropentane sulfonamide (FPeSA) with a newly available reference standard led to quantification of this compound on the UHPLC-HRMS.

Quality Assurance/Quality Control and Statistical Analyses.

Details on blanks (Table S6), duplicates, procedural and matrix spike recoveries (Table S7), and internal standard recoveries (Table S8) are provided in SI Section 1.8. Method detection limits (MDLs) were calculated based on the average concentration at which the sample signal-to-noise ratio was three, multiplied by the sample dilution volumes or weights. Only values > MDLs are reported (SI Section 1.9; Table S9). Method trueness was assessed using NIST SRM 1947 (SI Section 1.10; Table S10).

All statistical analyses were performed in Python version 3.7.4 using *SciPy*[40] and *statsmodels*.[41] Targeted PFAS with <70% detection frequency were excluded from statistical summaries. We imputed values <MDL for analytes with ≥70% detection frequency using MDL/√2. Detectable PFAS concentrations in both surface water and fish tissue samples were used to calculate field-measured bioaccumulation factors (BAF) (μg of PFAS kg^{-1} wet-weight fish tissue/μg of PFAS L^{-1} water). Statistically significant differences among PFAS concentrations by location and species were assessed using one-way ANOVA followed by Tukey's HSD test for surface water samples and Kruskal−Wallis followed by the Dunn−Bonferroni post hoc test for fish samples and BAF data (SI Section 1.11, Table S11A–B).

RESULTS AND DISCUSSION

Diverse FASA Detected in Surface Water and Fish.

In surface waters, PFAA and FASA of varying chain lengths were detected downgradient from an ECF AFFF-contaminated military base (Table S12A–C). FASA accounted for 2–7% of the sum of targeted PFAS (Σ_{23}PFAS) in surface water samples. C3–C6 and C8 FASA were detected in all samples from Moody Pond (closest to the AFFF source zones) and the downgradient Quashnet River (Table S12B). FASA concentrations in Moody Pond were significantly higher than the downgradient sites (Tukey HSD, $p < 0.05$) (Table S11A). Perfluorosulfonates (PFSA) were detected at the highest concentrations in surface waters (Figure 1A, Table S13A–B). PFSA concentrations differed significantly among sites (Tukey HSD, $p < 0.05$) with Moody Pond > Quashnet River > Waquoit Bay (Table S11A). Most of

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Σ_{23}PFAS in surface water consisted of PFHxS (25–51%) and PFOS (13–41%), followed by various perfluorocarboxylates (ΣPFCA = 25–34%) (Figure S4.

In fish tissue, FASA accounted for a much greater proportion (up to 86%) of Σ_{23}PFAS compared to surface waters (Figure 1B, Figures S5–S6). The predominant FASA detected was FHxSA. FHxSA is a stable intermediate transformation product of C6 sulfonamido precursors that make up a large fraction of the PFAS in ECF AFFF manufactured by 3M and can eventually transform into PFHxS as the terminal product.[10,12,28] In tissue samples, FHxSA accounted for 7–64% (mean ± SD = 33 ± 18%) of Σ_{23}PFAS from Moody Pond and 4–42% (16 ± 9%) at the downgradient sites. FBSA accounted for 2–24% of Σ_{23}PFAS across fish samples and FPeSA accounted for <1–8%. FOSA accounted for only 1–5% of Σ_{23}PFAS in fish from Moody Pond but up to 44% in fish from Waquoit Bay. Even-chain length FASA have recently been detected in fish from other AFFF-impacted sites, confirming their widespread presence in biological tissues.[14,42]

Suspect screening analysis of fish tissue detected C3 (perfluoropropane sulfonamide: FPrSA) and C7 (perfluoroheptane sulfonamide: FHpSA) FASA in samples from all three waterbodies (Table S14, Figure S7). Only FPrSA was detected in the surface water samples. Odd-chain length FASA have rarely been measured in fish.[1,43] Other PFAS identified by suspect screening in water and fish samples are presented in Table S15.

High Concentrations of FASA in Fish Tissue.

Concentrations of FHxSA in fish (<0.36–175 ng g^{-1}) were comparable to PFOS (0.65–222 ng g^{-1}) (Table S13A, Figures S5–S6). Other FASA in fish (FBSA: <0.19–40 ng g^{-1}, FPeSA: <0.01–23 ng g^{-1}, FOSA: <0.20–29 ng g^{-1}) were present at similar concentrations to PFHxS (<0.14–40 ng g^{-1}) (Table S13A). Concentrations of FASA, PFHxS, and PFOS were significantly lower in fish from Waquoit Bay compared to fish from Moody Pond and the Quashnet River (Dunn, $p < 0.05$) (Table S11A, Figures S5–S6).

Substantial peak areas for FPrSA were detected by suspect screening analysis in fish samples (Table S14). Lower peak areas for FPrSA in fish further from the AFFF source zones suggest a similar spatial pattern in accumulation as the other FASA that were quantified using targeted methods (Figure S7). Several past studies have used suspect screening to identify odd-chain length FASA in fish[1,43] and marine mammals.[44,45] This is the first study to quantify FPeSA using an available reference standard. Measured FPeSA concentrations reported here are greater than semiquantified values reported elsewhere.[1,18,43]

Despite widespread detection at high concentrations in aquatic biota, no safety thresholds have been established for FASA. Fish consumption advisories have focused predominantly on PFOS.[4] The state of Massachusetts allows unlimited fish consumption when PFOS ≤ 0.50 ng g^{-1} for the general population.[46] All fish samples from all sites exceeded these concentrations for PFOS. Fish (both muscle and whole-body samples) from Moody Pond and the Quashnet River additionally exceeded the 1 meal/month limit of 15 ng g^{-1} for the general population (Figure 1B). For sensitive populations, all whole-body fish from Moody

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Pond and the Quashnet River exceeded the do not consume limit of 81 ng g^{-1}, while only muscle tissue for yellow perch from Moody Pond exceeded this limit.

FASA Bioaccumulate to a Greater Extent than PFSA of Equivalent Chain Length.

Field-measured bioaccumulation factors (BAF, L kg^{-1} wet-weight) were higher for FASA than their terminal PFSA of equivalent chain length (Figure 2, Table S16). For FASA (C4–C6, C8), log BAF ranged between 3.1 and 4.9 in whole-body fish and 2.2–4.3 in muscle tissue samples (Table S17). For PFSA (C4, C6–C8), we found lower ranges of log BAF in whole-body (1.2–3.4) and muscle tissue samples (0.1–3.2) (Table S17). BAF for FASA were between 1 to 3 orders of magnitude greater than their terminal PFSA. Higher BAF for FOSA relative to PFOS in fish have been reported previously.[47,48] No reference standards were available for quantification of FPrSA and FHpSA, so BAF values were not determined.

Limited data on FASA bioaccumulation other than FOSA are available for comparison with prior work. Log BAF for FOSA in whole-body fish and muscle tissue reported here (2.8–4.9) fall within the same ranges as prior work (1.9–5.2).[1,31,47–49] A prior study[1] estimated potential BAF for FOSA in fish using MDLs for water samples that were below detection, and values in this study are similar. This is the first study to report log BAF for FPeSA in fish tissues (2.5–4.1). Whole-body log BAF for FHxSA in fish species reported here (3.4–4.2) are similar to the one prior field-based BAF study by Munoz et al. (3.0–4.1).[31] Bioconcentration factors (log BCF) measured in fathead minnow organ tissues from a mobile fish lab experiment produced comparable values to field-based BAF measured here for FHxSA (3.3–3.6) and FOSA (3.6–4.6) (Table S18).[50,51]

For FBSA, whole-body fish BAF reported in this work (3.4–3.8) are higher than the only other reported field-measured BAF by Munoz et al. (2.0–3.2)[31] and log BCF measured in the mobile fish lab experiment (2.8–3.2).[51] Since the mobile fish lab study[51] did not consider potential dietary uptake and focused on organ tissues, a low bias is plausible. In the Munoz et al.[31] study, concentrations of FBSA in water were close to the reported MDL, and whole-body fish concentrations were much lower than those reported in this work. Some of the observed differences in BAF therefore likely reflect analytical uncertainty. Different tissue extraction methods and instruments for quantification were used across studies, and there is no commercially available matched internal standard for FBSA.[31] Observed variability in BAF/BCF for FBSA indicates additional fish tissue data, and interlaboratory assessments of analytical uncertainty are needed.

FASA BAF Show Weaker Chain-Length Dependence than PFSA.

Figure 2 shows a statistically significant linear relationship ($p < 0.05$) between BAF and PFAS chain length with a strong relationship for PFSA ($R^2 = 0.76$) and a weaker relationship for FASA ($R^2 = 0.16$) (Figure S8). Similarly, Fischer et al.[52] recently showed a strong relationship between binding of PFAA to blood proteins and molecular weight, but weaker relationships for FASA. At close to neutral pH, a greater fraction of FASA compared to PFAA will be present in solution, allowing greater membrane permeability and accumulation in lipid rich tissues.[53,54] In contrast to PFAA, prior studies have also measured more FOSA in whole blood than in serum or plasma.[55,56] It is unclear why FASA

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partitioning to tissues does not follow the same patterns with molecular weight as PFAA and other persistent organic pollutants. Further mechanistic studies on the tissue-specific uptake and partitioning of FASA are needed to resolve this uncertainty.

Role of Precursor Biotransformation.

Precursor biotransformation has the potential to confound field-measured BAF and chain-length-dependent relationships.[57,58] Metabolism of FASA into terminal compounds would enhance BAF for PFSA of equivalent chain length relative to true values.[20] Field-measured BAF therefore represent an upper bound of potential BAF for terminal PFSA. For PFSA in this study, strong chain-length dependence of BAF suggests limited contributions from precursor biotransformation to observed concentrations in tissues.

For FASA, potential metabolism of other intermediate precursors with the same carbon chain length could elevate BAF and explain a weaker chain-length dependence. However, suspect screening analysis did not identify other C4, C5, or C8 precursors in water, which would be expected if such precursor transformation was important. No additional precursors were identified in fish samples, only different variations of the sulfonic acids (Table S15). Additional C6 ECF-based sulfonamido precursors (Table S15) were detected in Moody Pond surface water closest to the AFFF source zones and could contribute to FHxSA and PFHxS accumulation.[57] However, BAF for C6 PFAS were not enhanced relative to other PFAS, suggesting they are unlikely to be driven by precursor metabolism. Biotransformation experiments are needed to better understand the impacts of precursor metabolism on tissue concentrations in biota. For example, biological mechanisms for metabolism of the sulfonamide headgroup are not well understood.[20,59]

Implications.

Results of this study emphasize that FASA are an important class of precursors that have an enhanced propensity for bioaccumulation compared to their terminal degradation products. Our field-measured BAF suggest even short-chain FASA ≤ C6 bioaccumulate. BAF for FASA were up to 3 orders of magnitude higher than their terminal PFSA, including PFOS, in this study.

Estimated pK_a values of 6.2–9.7 for the C3–C8 sulfonamide congeners compared to <4.0 for PFAA[60] suggest surface waters will contain comparatively greater fractions of neutral FASA species that can penetrate cell membranes and accumulate at higher intracellular levels due to hydrophobic interactions.[54,61] Toxicological studies have suggested that adverse effects of FASA exposure reflect the less hydrophilic nature of the sulfonamide headgroup.[53,61–63] Preliminary data show even the shortest-chain FASA have high bioactivity and elicit developmental toxicity.[53,61–63] Additional physicochemical and toxicological data on diverse FASA precursors are needed to better understand their bioaccumulation potential and toxicity.

This study highlights the environmental persistence of FASA with varying chain lengths in surface waters and fish species. Detection of short-chain FASA such as FBSA in biota in this work and elsewhere suggests widespread contamination by these compounds.[1,14,26,31] However, FASA of varying chain lengths are infrequently included in biomonitoring efforts,

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and regulatory limits on concentrations in fish tissue or surface waters have yet to be established. Fish consumption advisory programs in the U.S.A are mainly focusing on PFOS as the PFAS of concern, and in 2024, advisories were in place in 17 states. These programs have yet to consider the broad mixture of environmentally relevant PFAS.[3,4,46] Our results suggest that additional work is needed to assess how consuming fish affects FASA exposures and risks. New commercially available analytical standards can help to facilitate routine measurements of FASA with diverse chain lengths. Inclusion of FASA in standardized analytical methods recommended by the U.S. Environmental Protection Agency would help ensure their inclusion in national drinking water monitoring and fish consumption guidance.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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REFERENCES

(1). Pickard HM; Ruyle BJ; Thackray CP; Chovancova A; Dassuncao C; Becanova J; Vojta S; Lohmann R; Sunderland EM PFAS and Precursor Bioaccumulation in Freshwater Recreational Fish: Implications for Fish Advisories. Environ. Sci. Technol 2022, 56, 15573. [PubMed: 36280234]

(2). Conder JM; Hoke RA; Wolf W. de; Russell MH; Buck RC Are PFCAs Bioaccumulative? A Critical Review and Comparison with Regulatory Criteria and Persistent Lipophilic Compounds. Environ. Sci. Technol 2008, 42 (4), 995–1003. [PubMed: 18351063]

(3). Great Lakes Consortium for Fish Consumption Advisories: Best Practice for Perfluorooctane Sulfonate (PFOS) Guidelines; Minnesota Department of Health, 2019.

(4). Barbo N; Stoiber T; Naidenko OV; Andrews DQ Locally Caught Freshwater Fish across the United States Are Likely a Significant Source of Exposure to PFOS and Other Perfluorinated Compounds. Environ. Res 2023, 220, No. 115165.

(5). Freshwater Fish Consumption Advisory List, 2021. Massachusetts Department of Public Health. https://www.mass.gov/doc/publichealth-freshwater-fish-consumption-advisories-2021/download (accessed 2023-12-05).

(6). Harris KJ; Munoz G; Woo V; Sauvé S; Rand AA Targeted and Suspect Screening of Per- and Polyfluoroalkyl Substances in Cosmetics and Personal Care Products. Environ. Sci. Technol 2022, 56, 14594. [PubMed: 36178710]

(7). Ruyle BJ; Thackray CP; McCord JP; Strynar MJ; Mauge-Lewis KA; Fenton SE; Sunderland EM Reconstructing the Composition of Per- and Polyfluoroalkyl Substances in Contemporary Aqueous Film-Forming Foams. Environ. Sci. Technol. Lett 2021, 8 (1), 59–65. [PubMed: 33628855]

(8). Barzen-Hanson KA; Roberts SC; Choyke S; Oetjen K; McAlees A; Riddell N; McCrindle R; Ferguson PL; Higgins CP; Field JA Discovery of 40 Classes of Per- and Polyfluoroalkyl Substances in Historical Aqueous Film-Forming Foams (AFFFs) and AFFF-Impacted Groundwater. Environ. Sci. Technol 2017, 51 (4), 2047–2057. [PubMed: 28098989]

(9). Schwartz-Narbonne H; Xia C; Shalin A; Whitehead HD; Yang D; Peaslee GF; Wang Z; Wu Y; Peng H; Blum A; Venier M; Diamond ML Per- and Polyfluoroalkyl Substances in Canadian Fast Food Packaging. Environ. Sci. Technol. Lett 2023, 10, 343. [PubMed: 37970096]

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

(10). Ruyle BJ; Thackray CP; Butt CM; LeBlanc DR; Tokranov AK; Vecitis CD; Sunderland EM Centurial Persistence of Forever Chemicals at Military Fire Training Sites. Environ. Sci. Technol 2023, 57 (21), 8096–8106. [PubMed: 37184088]

(11). Zhang W; Pang S; Lin Z; Mishra S; Bhatt P; Chen S Biotransformation of Perfluoroalkyl Acid Precursors from Various Environmental Systems: Advances and Perspectives. Environ. Pollut 2021, 272, No. 115908.

(12). Ruyle BJ; Schultes L; Akob DM; Harris CR; Lorah MM; Vojta S; Becanova J; McCann S; Pickard HM; Pearson A; Lohmann R; Vecitis CD; Sunderland EM Nitrifying Microorganisms Linked to Biotransformation of Perfluoroalkyl Sulfonamido Precursors from Legacy Aqueous Film-Forming Foams. Environ. Sci. Technol 2023, 57, 5592. [PubMed: 36972708]

(13). Liu M; Munoz G; Vo Duy S; Sauvé S; Liu J Per- and Polyfluoroalkyl Substances in Contaminated Soil and Groundwater at Airports: A Canadian Case Study. Environ. Sci. Technol 2022, 56 (2), 885–895. [PubMed: 34967613]

(14). Carrizo JC; Munoz G; Vo Duy S; Liu M; Houde M; Amé MV; Liu J; Sauvé S PFAS in Fish from AFFF-Impacted Environments: Analytical Method Development and Field Application at a Canadian International Civilian Airport. Sci. Total Environ 2023, 879, No. 163103.

(15). Maizel AC; Shea S; Nickerson A; Schaefer C; Higgins CP Release of Per- and Polyfluoroalkyl Substances from Aqueous Film-Forming Foam Impacted Soils. Environ. Sci. Technol 2021, 55 (21), 14617–14627. [PubMed: 34665614]

(16). Gebbink WA; Glynn A; Darnerud PO; Berger U Perfluoroalkyl Acids and Their Precursors in Swedish Food: The Relative Importance of Direct and Indirect Dietary Exposure. Environ. Pollut 2015, 198, 108–115. [PubMed: 25590128]

(17). Dassuncao C; Hu XC; Zhang X; Bossi R; Dam M; Mikkelsen B; Sunderland EM Temporal Shifts in Poly- and Perfluoroalkyl Substances (PFASs) in North Atlantic Pilot Whales Indicate Large Contribution of Atmospheric Precursors. Environ. Sci. Technol 2017, 51 (8), 4512–4521. [PubMed: 28350446]

(18). Barrett H; Du X; Houde M; Lair S; Verreault J; Peng H Suspect and Nontarget Screening Revealed Class-Specific Temporal Trends (2000–2017) of Poly- and Perfluoroalkyl Substances in St. Lawrence Beluga Whales. Environ. Sci. Technol 2021, 55 (3), 1659–1671. [PubMed: 33444015]

(19). Gebbink WA; Bignert A; Berger U Perfluoroalkyl Acids (PFAAs) and Selected Precursors in the Baltic Sea Environment: Do Precursors Play a Role in Food Web Accumulation of PFAAs? Environ. Sci. Technol 2016, 50 (12), 6354–6362. [PubMed: 27192404]

(20). Martin JW; Asher BJ; Beesoon S; Benskin JP; Ross MS PFOS or PreFOS? Are Perfluorooctane Sulfonate Precursors (PreFOS) Important Determinants of Human and Environmental Perfluorooctane Sulfonate (PFOS) Exposure? J. Environ. Monit 2010, 12 (11), 1979. [PubMed: 20944836]

(21). Method 1633 Analysis of Per- and Polyfluoroalkyl Substances (PFAS) in Aqueous, Solid, Biosolids, and Tissue Samples by LC-MS/MS; USEPA, 2024.

(22). Pickard HM; Criscitiello AS; Spencer C; Sharp MJ; Muir DCG; De Silva AO; Young CJ Continuous Non-Marine Inputs of per- and Polyfluoroalkyl Substances to the High Arctic: A Multi-Decadal Temporal Record. Atmospheric Chem. Phys 2018, 18 (7), 5045–5058.

(23). Wang Z; Cousins IT; Scheringer M; Buck RC; Hungerbuühler K Global Emission Inventories for C4–C14 Perfluoroalkyl Carboxylic Acid (PFCA) Homologues from 1951 to 2030, Part II: The Remaining Pieces of the Puzzle. Environ. Int 2014, 69, 166–176. [PubMed: 24861268]

(24). Chen Y-J; Wang R-D; Shih Y-L; Chin H-Y; Lin AY-C Emerging Perfluorobutane Sulfonamido Derivatives as a New Trend of Surfactants Used in the Semiconductor Industry. Environ. Sci. Technol 2024, 58, 1648–1658. [PubMed: 38175212]

(25). Chu S; Letcher RJ In Vitro Metabolic Formation of Perfluoroalkyl Sulfonamides from Copolymer Surfactants of Pre- and Post-2002 Scotchgard Fabric Protector Products. Environ. Sci. Technol 2014, 48 (11), 6184–6191. [PubMed: 24784168]

(26). Chu S; Letcher RJ; McGoldrick DJ; Backus SM A New Fluorinated Surfactant Contaminant in Biota: Perfluorobutane Sulfonamide in Several Fish Species. Environ. Sci. Technol 2016, 50 (2), 669–675. [PubMed: 26649981]

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

(27). Kaboré HA; Vo Duy S; Munoz G; Méité L; Desrosiers M; Liu J; Sory TK; Sauvé S Worldwide Drinking Water Occurrence and Levels of Newly-Identified Perfluoroalkyl and Polyfluoroalkyl Substances. Sci. Total Environ 2018, 616–617, 1089–1100.

(28). Nickerson A; Rodowa AE; Adamson DT; Field JA; Kulkarni PR; Kornuc JJ; Higgins CP Spatial Trends of Anionic, Zwitterionic, and Cationic PFASs at an AFFF-Impacted Site. Environ. Sci. Technol 2021, 55 (1), 313–323. [PubMed: 33351591]

(29). Ruyle BJ; Pickard HM; LeBlanc DR; Tokranov AK; Thackray CP; Hu XC; Vecitis CD; Sunderland EM Isolating the AFFF Signature in Coastal Watersheds Using Oxidizable PFAS Precursors and Unexplained Organofluorine. Environ. Sci. Technol 2021, 55 (6), 3686–3695. [PubMed: 33667081]

(30). McDonough CA; Choyke S; Barton KE; Mass S; Starling AP; Adgate JL; Higgins CP Unsaturated PFOS and Other PFASs in Human Serum and Drinking Water from an AFFF-Impacted Community. Environ. Sci. Technol 2021, 55 (12), 8139–8148. [PubMed: 34029073]

(31). Munoz G; Mercier L; Duy SV; Liu J; Sauvé S; Houde M Bioaccumulation and Trophic Magnification of Emerging and Legacy Per- and Polyfluoroalkyl Substances (PFAS) in a St. Lawrence River Food Web. Environ. Pollut 2022, 309, No. 119739.

(32). Beale DJ; Hillyer K; Nilsson S; Limpus D; Bose U; Broadbent JA; Vardy S Bioaccumulation and Metabolic Response of PFAS Mixtures in Wild-Caught Freshwater Turtles (Emydura Macquarii Macquarii) Using Omics-Based Ecosurveillance Techniques. Sci. Total Environ 2022, 806, No. 151264.

(33). Dewapriya P; Nilsson S; Ghorbani Gorji S; O'Brien JW; Bräunig J; Gómez Ramos MJ; Donaldson E; Samanipour S; Martin JW; Mueller JF; Kaserzon SL; Thomas KV Novel Per- and Polyfluoroalkyl Substances Discovered in Cattle Exposed to AFFF-Impacted Groundwater. Environ. Sci. Technol 2023, 57, 13635. [PubMed: 37648245]

(34). Guckert M; Rupp J; Nuürenberg G; Nödler K; Koschorreck J; Berger U; Drost W; Siebert U; Wibbelt G; Reemtsma T Differences in the Internal PFAS Patterns of Herbivores, Omnivores and Carnivores - Lessons Learned from Target Screening and the Total Oxidizable Precursor Assay. Sci. Total Environ 2023, 875, No. 162361.

(35). Tokranov AK; LeBlanc DR; Pickard HM; Ruyle BJ; Barber LB; Hull RB; Sunderland EM; Vecitis CD SurfaceWater/Groundwater Boundaries Affect Seasonal PFAS Concentrations and PFAA Precursor Transformations. Environ. Sci. Process. Impacts 2021, 23, 1893. [PubMed: 34779453]

(36). Weber AK; Barber LB; LeBlanc DR; Sunderland EM; Vecitis CD Geochemical and Hydrologic Factors Controlling Subsurface Transport of Poly- and Perfluoroalkyl Substances, Cape Cod, Massachusetts. Environ. Sci. Technol 2017, 51 (8), 4269–4279. [PubMed: 28285525]

(37). Schultes L; Sandblom O; Broeg K; Bignert A; Benskin JP Temporal Trends (1981–2013) of Per- and Polyfluoroalkyl Substances and Total Fluorine in Baltic Cod (Gadus Morhua). Environ. Toxicol. Chem 2020, 39 (2), 300–309. [PubMed: 31610607]

(38). Charbonnet JA; McDonough CA; Xiao F; Schwichtenberg T; Cao D; Kaserzon S; Thomas KV; Dewapriya P; Place BJ; Schymanski EL; Field JA; Helbling DE; Higgins CP Communicating Confidence of Per- and Polyfluoroalkyl Substance Identification via High-Resolution Mass Spectrometry. Environ. Sci. Technol. Lett 2022, 9 (6), 473–481. [PubMed: 35719859]

(39). Schymanski EL; Jeon J; Gulde R; Fenner K; Ruff M; Singer HP; Hollender J Identifying Small Molecules via High Resolution Mass Spectrometry: Communicating Confidence. Environ. Sci. Technol 2014, 48 (4), 2097–2098. [PubMed: 24476540]

(40). Virtanen P; Gommers R; Oliphant TE; Haberland M; Reddy T; Cournapeau D; Burovski E; Peterson P; Weckesser W; Bright J; van der Walt SJ; Brett M; Wilson J; Millman KJ; Mayorov N; Nelson ARJ; Jones E; Kern R; Larson E; Carey CJ; Polat İ; Feng Y; Moore EW; VanderPlas J; Laxalde D; Perktold J; Cimrman R; Henriksen I; Quintero EA; Harris CR; Archibald AM; Ribeiro AH; Pedregosa F; van Mulbregt P; et al. SciPy 1.0: Fundamental Algorithms for Scientific Computing in Python. Nat. Methods 2020, 17 (3), 261–272. [PubMed: 32015543]

(41). Seabold S; Perktold J Statsmodels: Econometric and Statistical Modeling with Python. In Proc. of the 9th Python in Science Conference, 2010; pp 92–96.

(42). Kaboré HA; Goeury K; Desrosiers M; Vo Duy S; Liu J; Cabana G; Munoz G; Sauvé S Novel and Legacy Per- and Polyfluoroalkyl Substances (PFAS) in Freshwater Sporting Fish from

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Background and Firefighting Foam Impacted Ecosystems in Eastern Canada. Sci. Total Environ 2022, 816, No. 151563.

(43). Nilsen E; Muensterman D; Carini L; Waite I; Payne S; Field JA; Peterson J; Hafley D; Farrer D; Jones GD Target and Suspect Per- and Polyfluoroalkyl Substances in Fish from an AFFF-Impacted Waterway. Sci. Total Environ 2024, 906, No. 167798.

(44). Wang Q; Ruan Y; Jin L; Zhang X; Li J; He Y; Wei S; Lam JCW; Lam PKS Target, Nontarget, and Suspect Screening and Temporal Trends of Per- and Polyfluoroalkyl Substances in Marine Mammals from the South China Sea. Environ. Sci. Technol 2021, 55, 1045. [PubMed: 33395277]

(45). Spaan KM; van Noordenburg C; Plassmann MM; Schultes L; Shaw S; Berger M; Heide-Jørgensen MP; Rosing-Asvid A; Granquist SM; Dietz R; Sonne C; Rigét F; Roos A; Benskin JP Fluorine Mass Balance and Suspect Screening in Marine Mammals from the Northern Hemisphere. Environ. Sci. Technol 2020, 54 (7), 4046–4058. [PubMed: 32160740]

(46). Evaluation of PFAS in Recreational Waterbodies in Massachusetts, 2021. Massachusetts Department of Public Health. https://www.mass.gov/doc/technical-basis-for-issuing-fish-advisories0/download (accessed 2023–12–05).

(47). Burkhard LP Evaluation of Published Bioconcentration Factor (BCF) and Bioaccumulation Factor (BAF) Data for Per- and Polyfluoroalkyl Substances Across Aquatic Species. Environ. Toxicol. Chem 2021, 40 (6), 1530–1543. [PubMed: 33605484]

(48). Munoz G; Budzinski H; Babut M; Drouineau H; Lauzent M; Menach KL; Lobry J; Selleslagh J; Simonnet-Laprade C; Labadie P Evidence for the Trophic Transfer of Perfluoroalkylated Substances in a Temperate Macrotidal Estuary. Environ. Sci. Technol 2017, 51 (15), 8450–8459. [PubMed: 28679050]

(49). Furdui VI; Stock NL; Ellis DA; Butt CM; Whittle DM; Crozier PW; Reiner EJ; Muir DCG; Mabury SA Spatial Distribution of Perfluoroalkyl Contaminants in Lake Trout from the Great Lakes. Environ. Sci. Technol 2007, 41 (5), 1554–1559. [PubMed: 17396640]

(50). Barber LB; Pickard HM; Alvarez DA; Becanova J; Keefe SH; LeBlanc DR; Lohmann R; Steevens JA; Vajda AM Uptake of Per- and Polyfluoroalkyl Substances by Fish, Mussel, and Passive Samplers in Mobile-Laboratory Exposures Using Groundwater from a Contamination Plume at a Historical Fire Training Area, Cape Cod, Massachusetts. Environ. Sci. Technol 2023, 57, 5544. [PubMed: 36972291]

(51). Vajda A; Hill N; Barber L; Lohmann R; Becanova J; Vojta S; Pickard H; Bertolatus D; LeBlanc D Tissue-Specific Bioconcentration of per- and Polyfluoroalkyl Substances by Fathead Minnows from Contaminated Groundwater at a Fire-Training Area, Cape Cod, Massachusetts from 2019; U.S. Geological Survey Data Release, 2024. DOI: 10.5066/P9TGHQWB.

(52). Fischer FC; Ludtke S; Thackray C; Pickard HM; Haque F; Dassuncao C; Endo S; Schaider L; Sunderland EM Binding of Per- and Polyfluoroalkyl Substances (PFAS) to Serum Proteins: Implications for Toxicokinetics in Humans. Environ. Sci. Technol 2024, 58, 1055. [PubMed: 38166384]

(53). Rericha Y; Cao D; Truong L; Simonich MT; Field JA; Tanguay RL Sulfonamide Functional Head on Short-Chain Perfluorinated Substance Drives Developmental Toxicity. iScience 2022, 25 (2), No. 103789.

(54). Nouhi S; Ahrens L; Campos Pereira H; Hughes AV; Campana M; Gutfreund P; Palsson GK; Vorobiev A; Hellsing MS Interactions of Perfluoroalkyl Substances with a Phospholipid Bilayer Studied by Neutron Reflectometry. J. Colloid Interface Sci 2018, 511, 474–481. [PubMed: 29073553]

(55). Poothong S; Thomsen C; Padilla-Sanchez JA; Papadopoulou E; Haug LS Distribution of Novel and Well-Known Poly- and Perfluoroalkyl Substances (PFASs) in Human Serum, Plasma, and Whole Blood. Environ. Sci. Technol 2017, 51 (22), 13388–13396. [PubMed: 29056041]

(56). Kärrman A; Van Bavel B; Järnberg U; Hardell L; Lindström G Perfluorinated Chemicals in Relation to Other Persistent Organic Pollutants in Human Blood. Chemosphere 2006, 64 (9), 1582–1591. [PubMed: 16403420]

(57). McDonough CA; Choyke S; Ferguson PL; DeWitt JC; Higgins CP Bioaccumulation of Novel Per- and Polyfluoroalkyl Substances in Mice Dosed with an Aqueous Film-Forming Foam. Environ. Sci. Technol 2020, 54 (9), 5700–5709. [PubMed: 32248687]

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(58). Zhang X; Lohmann R; Sunderland EM Poly- and Perfluoroalkyl Substances in Seawater and Plankton from the Northwestern Atlantic Margin. Environ. Sci. Technol 2019, 53 (21), 12348–12356. [PubMed: 31565932]

(59). Chen M; Qiang L; Pan X; Fang S; Han Y; Zhu L In Vivo and in Vitro Isomer-Specific Biotransformation of Perfluorooctane Sulfonamide in Common Carp (Cyprinus Carpio). Environ. Sci. Technol 2015, 49 (23), 13817–13824. [PubMed: 26053759]

(60). Rayne S; Forest K A New Class of Perfluorinated Acid Contaminants: Primary and Secondary Substituted Perfluoroalkyl Sulfonamides Are Acidic at Environmentally and Toxicologically Relevant pH Values. J. Environ. Sci. Health Part A 2009, 44 (13), 1388–1399.

(61). Slotkin TA; MacKillop EA; Melnick RL; Thayer KA; Seidler FJ Developmental Neurotoxicity of Perfluorinated Chemicals Modeled in Vitro. Environ. Health Perspect 2008, 116 (6), 716–722. [PubMed: 18560525]

(62). Dasgupta S; Reddam A; Liu Z; Liu J; Volz DC High-Content Screening in Zebrafish Identifies Perfluorooctanesulfonamide as a Potent Developmental Toxicant. Environ. Pollut 2020, 256, No. 113550.

(63). Truong L; Rericha Y; Thunga P; Marvel S; Wallis D; Simonich MT; Field JA; Cao D; Reif DM; Tanguay RL Systematic Developmental Toxicity Assessment of a Structurally Diverse Library of PFAS in Zebrafish. J. Hazard. Mater 2022, 431, No. 128615.

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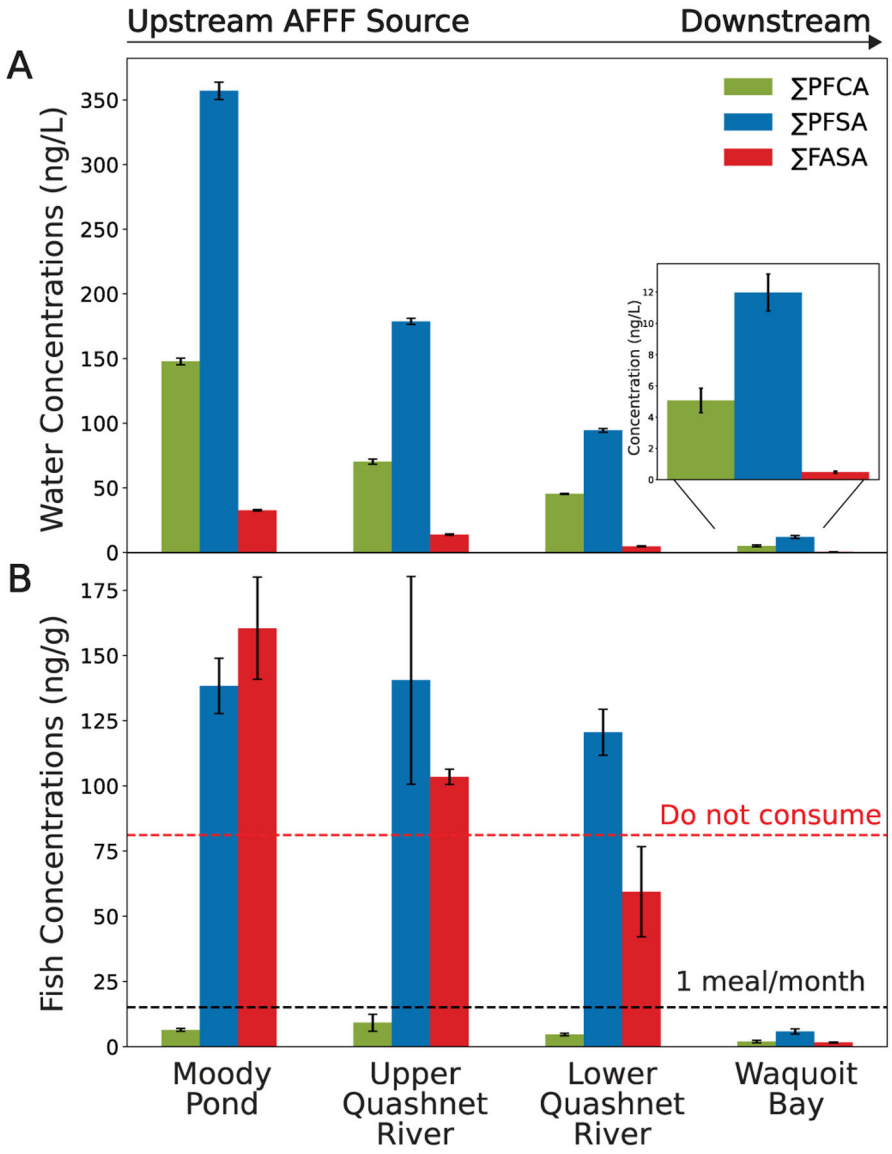

Figure 1.

Concentrations of targeted PFAS in water and recreational fish are shown as means with standard errors. PFAS concentrations (ng L^{-1} water or ng g^{-1} wet-weight tissue) in surface water samples in panel (A) are based on $n = 2$ to $n = 8$ field replicates per site (Table S1). Panel (B) shows results for whole-body fish samples ($n = 2$–11 samples per site; Table S2), grouped by site, for the sum of C3–C13 perfluorocarboxylates (ΣPFCA), sum of C4–C10 perfluorosulfonates (ΣPFSA), and sum of C4–C6, and C8 perfluoroalkyl sulfonamides (ΣFASA). Field sites represent a hydrological gradient moving away from the AFFF source zones (Figure S1). The black dotted line corresponds to the fish consumption guidelines set by the state of Massachusetts, U.S.A., of 1 meal/month (15 ng g^{-1} PFOS) for the general population. The red dotted line corresponds to the do not consume limit (81 ng g^{-1} PFOS) for sensitive populations.

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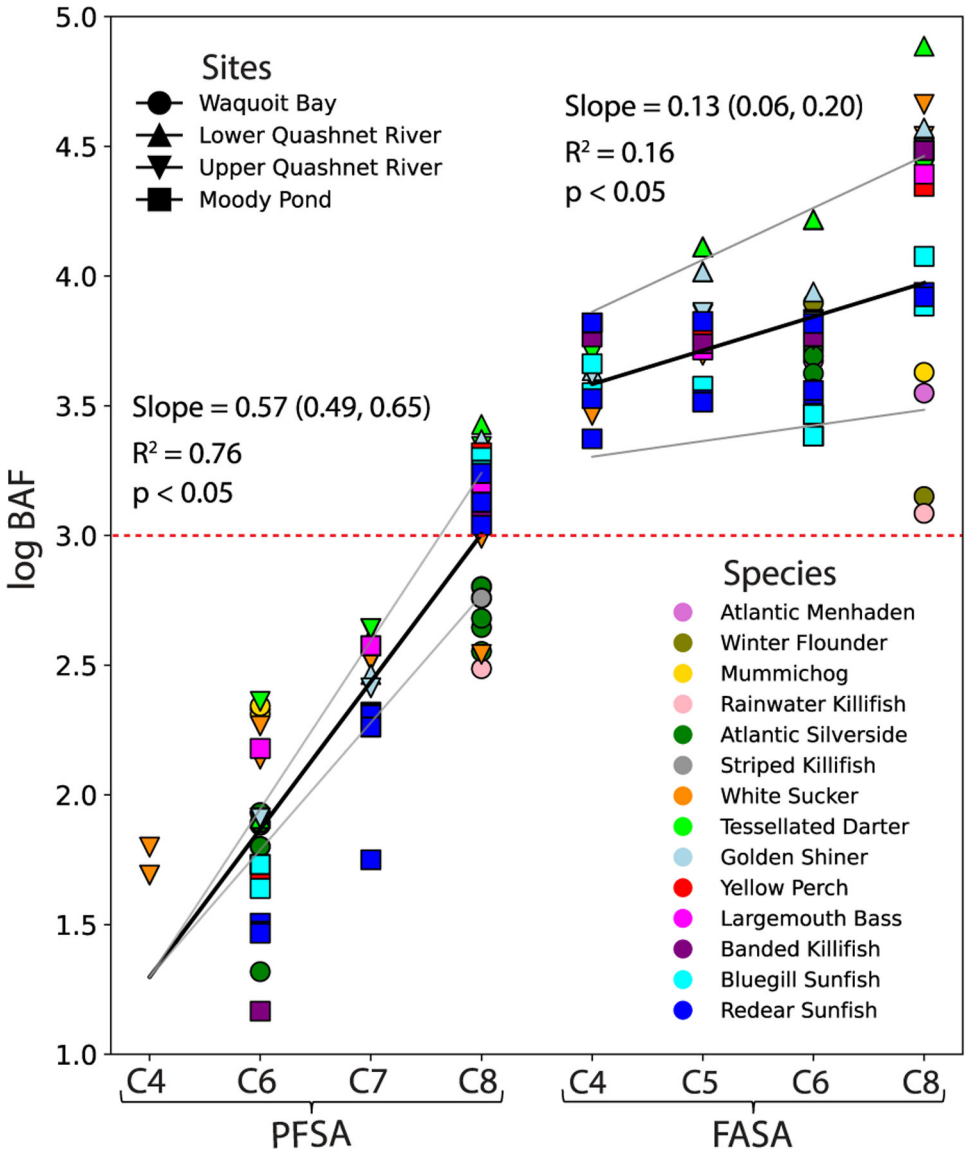

Figure 2.

Field-measured bioaccumulation factors (BAF, L kg^{-1}) for perfluorosulfonates (PFSA) and perfluoroalkyl sulfonamides (FASA) in whole-body fish species from sites within the three waterbodies downstream of ECF AFFF-contaminated sites on Cape Cod, Massachusetts, U.S.A. Each marker indicates an individual measurement. Marker type denotes sample site collection, and marker color denotes species. R^2 values and p-values are based on linear regression (shown as solid lines with 95% confidence interval) of BAF data for C4 (PFBS), C6 (PFHxS), C7 (PFHpS), and C8 (PFOS) PFSA and C4 (FBSA), C5 (FPeSA), C6 (FHxSA), and C8 (FOSA) FASA for whole-body fish samples. The red dotted line indicates the threshold of log BAF ≥ 3.0 at which PFAS have a tendency to bioaccumulate. Figure S8 shows BAF results for muscle tissue.