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CRITICAL REVIEW

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Monitoring of Perfluorinated Compounds in Aquatic Biota: An Updated Review

PFCs in Aquatic Biota

Magali Houde,*[,†] Amila O. De Silva,[‡] Derek C. G. Muir,[‡] and Robert J. Letcher[§]

[†]Environment Canada, Centre Saint-Laurent, 105 McGill Street, Montréal, Québec, Canada, H2Y 2E7

[‡]Environment Canada, National Water Research Institute, 867 Lakeshore Road, Burlington, Ontario, Canada, L7R 4A6

[§]Environment Canada, Wildlife and Landscape Science Directorate, National Wildlife Research Centre, Carleton University, 1125 Raven Road, Ottawa, Ontario, Canada, K1A 0H3

Supporting Information

ABSTRACT: The goal of this article is to summarize new biological monitoring information on perfluorinated compounds (PFCs) in aquatic ecosystems (post-2005) as a followup to our critical review published in 2006. A wider range of geographical locations (e.g., South America, Russia, Antarctica) and habitats (e.g., high-mountain lakes, deep-ocean, and offshore waters) have been investigated in recent years enabling a better understanding of the global distribution of PFCs in aquatic organisms. High concentrations of PFCs continue to be detected in invertebrates, fish, reptiles, and marine mammals worldwide. Perfluorooctane sulfonate (PFOS) is still the predominant PFC detected (mean concentrations up to 1900 ng/g ww) in addition to important concentrations of long-chain perfluoroalkyl carboxylates (PFCAs; sum PFCAs up to 400 ng/g ww). More studies have evaluated the bioaccumulation and biomagnification of these compounds in both freshwater and marine food webs. Several reports have indicated a decrease in PFOS levels over time in contrast to PFCA concentrations that have tended to increase in tissues of aquatic organisms at many locations. The detection of precursor metabolites and isomers has become more frequently reported in environmental assessments yielding important information on the sources and distribution of these contaminants. The integration of environmental/ecological characteristics (e.g., latitude/longitude, salinity, and/or trophic status at sampling locations) and biological variables (e.g., age, gender, life cycle, migration, diet composition, growth rate, food chain length, metabolism, and elimination) are essential elements in order to adequately study the environmental fate and distribution of PFCs and should be more frequently considered in study design.

Perfluorinated compounds (PFCs) and their precursors have been at the center of an increasing number of environmental monitoring studies mainly because of their persistence, bioaccumulative potential, and global distribution, particularly in aquatic biological samples. This special issue on PFCs reflects the scientific research interest for these chemical pollutants in the aquatic environment. Our first review on the biological monitoring of polyfluoroalkyl substances, published in 2006, covered the literature up to early 2006[1] and demonstrated that measurements of PFCs and their precursors in biota were critical to the assessment of their sources, fate, temporal trends, and distribution in the environment. The purpose of the present review is to summarize new information on PFCs in aquatic ecosystems post-2005. This article covers the biological monitoring of PFCs in aquatic environments, the geographical and temporal trends, the contamination profiles in organisms, and the assessments of precursors and isomers, as well as the bioaccumulation and the biomagnification in aquatic food webs. The review highlights actual knowledge gaps and possible future research perspectives.

PFCS IN AQUATIC BIOTA

Since 2006, more than 40 studies have reported concentrations of PFCs in aquatic biological samples. Interestingly, the study sites found in the literature have covered a wider range of regions and habitats than in the past. Therefore, a clearer picture of the global PFC contamination in aquatic biota can be drawn from these concentration data for invertebrates, fish, reptiles, aquatic birds, and marine mammals. The majority of recent PFC biological assessment studies were located in Asia, Europe, North America, and the Arctic, although other regions of the world, such as South America, Antarctica, and Russia are now being investigated. A larger breadth of perfluoroalkyl sulfonates (PFSAs) and perfluoroalkyl carboxylates (PFCAs) of various chain lengths and configurations

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Table 1. List and Description of Acronyms for PFCs, Precursors, and Isomers Used in the Review

PFCs	Perfluorinated Compounds
Perfluoroalkyl sulfonate: PFSA	
PFBS	Perfluorobutane sulfonate
PFHxS	Perfluorohexane sulfonate
PFHS	Perfluoroheptane sulfonate
PFOS	Perfluorooctane sulfonate
PFDS	Perfluorodecane sulfonate
Perfluoroalkyl carboxylate: PFCA	
PFHxA	Perfluorohexanoic acid
PFHpA	Perfluoroheptanoic acid
PFOA	Perfluorooctanoic acid
PFNA	Perfluorononanoic acid
PFDA	Perfluorodecanoic acid
PFUnA	Perfluoroundecanoic acid
PFDoA	Perfluorododecanoic acid
PFTrA	Perfluorotridecanoic acid
PFTA	Perfluorotetradecanoic acid
PFPA	Perfluoropentadecanoic acid
Isomers	
n-PFOS	Linear PFOS
mono(trifluoromethyl) PFOS = monomethyl-PFOS	
bis(trifluoromethyl) PFOS = dimethyl-PFOS	
Precursors	
Fluorotelomer saturated and unsaturated carboxylic acids	
8:2 FTUCA	2H-hexadecafluoro-2-decenoic acid
10:2 FTUCA	2H-octadecafluoro-2-dodecenoic acid
7:3 FTCA	2H,2H,3H,3H-pentadecafluorodecanoic acid
8:2 FTCA	2H,2H-heptadecafluorodecanoic acid
10:2 FTCA	2H,2H-nonadecafluorododecanoic acid
Perfluorosulfonamides	
PFOSA	Perfluorooctane sulfonamide
NEtFOSA	*N*-ethyl perfluorooctane sulfonamide
NEtFOSAA	2-(*N*-ethylperfluorooctane sulfonamido) acetic acid
FOSAA	2-(perfluorooctanesulfonamido) acetic acid
NMeFOSA	*N*-methylperfluoro-1-octanesulfonamide
Sulfonamide ethanols	
MeFBSE	*N*-methyl perfluorobutane sulfonamide ethanol
NEtFOSE	*N*-ethyl perfluorooctane sulfonamide ethanol
NMeFOSE	*N*-methyl perfluorooctane sulfonamide ethanol
Fluorotelomer alcohols	
6:2 FTOH	1H,1H,2H,2H-perfluorooctanol
8:2 FTOH	1H,1H,2H2H-perfluorodecanol
10:2 FTOH	1H,1H,2H,2H-perfluorododecanol

have been monitored in biotic samples in addition to an increasing list of precursors and new categories of PFCs (Table 1). Nevertheless, perfluorooctane sulfonate (PFOS) remains the predominant PFC found in all species, tissues, and locations analyzed around the world (Figure 1). PFOA and PFOS accumulation in marine mammals (e.g., >1200 ng/g ww in liver) is common in the Arctic, Europe, and Asia, while levels are much lower in the southern hemisphere. These contamination trends are likely due to continued use of PFOA and PFOS precursors ("PreFOS"), such as fluorotelomer alcohols and polyfluoroalkyl phosphate and/or continued oceanic and atmospheric inputs of sources resulting in exposure and bioavailability of these PFCs in the northern hemisphere.

Fish, bird, and marine mammal have been studied at various locations around the world while most invertebrate work has been limited to East Asia (Tables S1 and S2). A few extensive monitoring studies have been conducted such as the assessment of PFCs in fish from 59 lakes and the Mississippi River in Minnesota, USA[2] and PFCs and precursors (as well as structural isomers of PFOS) in herring gull eggs from 15 colonies in the Laurentian Great Lakes, Canada/USA.[3,4] Recently, Gebbink et al.[5] reported on PFCAs and PFSAs, as well as precursors such as perfluorooctane sulfonamide (PFOSA; main PFOS precursor), *N*-methyl perfluorooctanesulfonamide (NMeFOSA), fluorotelomer unsaturated carboxylic acids (FTUCAs), and fluorotelomer alcohols (FTOHs), in the eggs of four different gull species (*Larids*) collected in 2008 from 15 freshwater and marine colony sites across eight Canadian provinces. These extensive monitoring studies yielded highly valuable information on the distribution and the potential sources of these chemicals over large but specific territories.

More than a dozen studies have reported PFC concentrations from regions or in species for which very little or no data existed before, providing additional information on the environmental distribution of these chemicals. For example, PFCs were analyzed for the first time in liver of marine mammals sampled around Korea,[6] India,[7] and Russia,[8] indicating levels lower than those previously reported from other regions of the world. Low but detectable concentrations of PFOS (<0.1−9.4 ng/g ww) and perfluorooctanoate (PFOA; <0.2−2.5 ng/g ww) were measured in birds and seals from Antarctica and the Southern Hemisphere.[9,10] PFCs were also quantified in mullet and pelicans from North Columbia, South America,[11] as well as in mussels, fish, fur seals, and Franciscana and tucuxi dolphins from South Brazil.[12,13] Generally, levels of PFCs were lower in aquatic wildlife from South America compared to North America.[12]

Additional information on the exposure of aquatic wildlife to PFCs within aquatic organisms was provided by studies of tissue distribution. For example, analyses of ten harbor seal organs showed that PFCs tend to accumulate primarily in blood (38% of the total PFC burden) > liver (36%) > muscle (13%) > lung (8%) > kidney (2%) > blubber (2%) > heart (1%) > brain (1%) > thymus (<0.01%) and thyroid (<0.01%).[14] PFOS was additionally detected in the brain of harbor porpoises from the Black Sea (range: 3.5−100 ng/g ww).[15] The tissue distribution of these chemicals in Chinese sturgeons from the Yangtze River[16] and brown pelicans from Columbia[11] indicated widespread contamination of organs. The profile of contamination also varied according to tissue.

Species from remote locations, such as high-altitude lakes, offshore waters, and deep-sea ocean, were also contaminated with low concentrations of PFCs.[17−20] PFOS was the predominant PFC detected in fish muscle collected from mountain lakes and rivers at 4000 m elevation in China.[18] PFCAs and PFOS were detected in fish collected from high-mountain lakes from the French Alps with perfluoroundecanoate (PFUnA), perfluorodecanoate (PFDA), and PFOS being predominant in liver.[20] PFOS was found as the primary PFC in liver of deep-diving melon-headed whales stranded along the

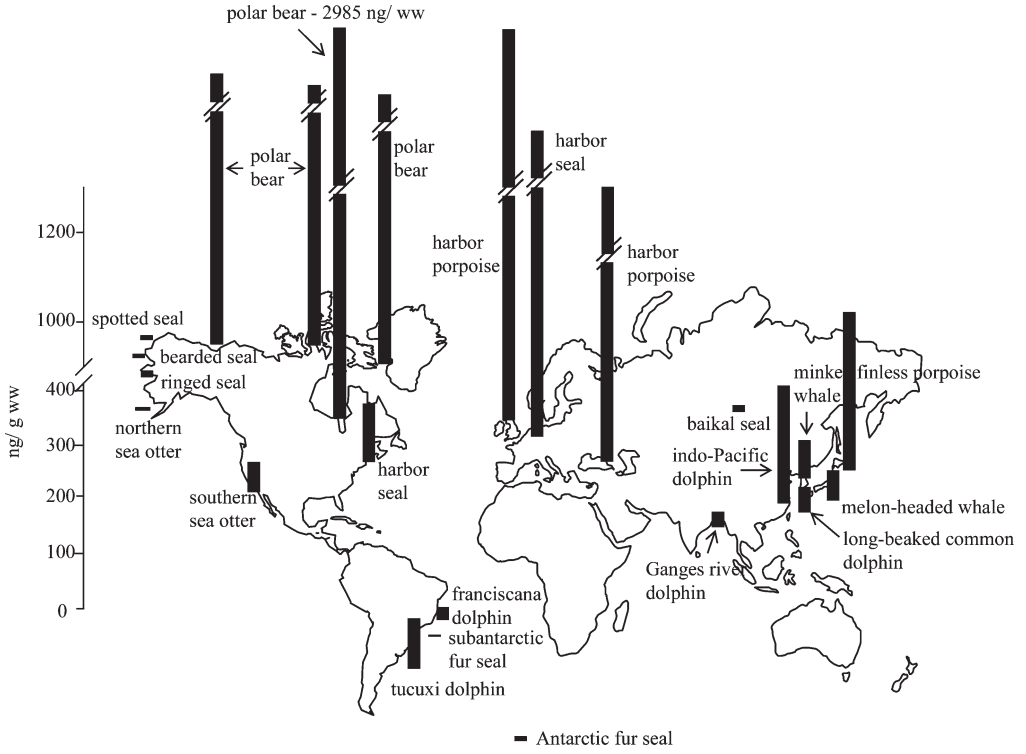

Figure 1. Recently reported (2006−2010) PFOS concentrations in liver of marine mammals worldwide.[6−8,10,12,13,15,19,21,30,36,65−67,102−104]

Japanese coasts (1982, $n = 12$, mean of 7.1 ng/g ww; 2006, $n = 2$, 56.6 ng/g ww) in addition to its precursor PFOSA (1982, 8.8 ng/g ww; 2006, 36.1 ng/g ww).[19] Tuna sampled in off-shore waters and open-ocean sites from the Pacific rim indicated PFOS and PFUnA as predominant congeners in liver tissue.[17] The presence of these contaminants in organisms from the "roof of the world" and remote open-water locations support the hypothesis that atmospheric deposition may be a contamination source for these aquatic environments.[18,20]

In nearshore coastal environments, PFOS was the predominant PFC measured in shallow water fish of Japan compared to a dominance of PFOA in tidal flat invertebrates and mudskipper fish possibly indicating differences in exposure patterns and bioavailability of the chemicals in this region.[21] Additionally PFC assessments in edible fish from different locations were used to evaluate the possible risk intake by humans. At several locations, fish was established as a significant source of dietary PFOS exposure; a substance for which guidelines of fish consumption exist in some regions.[22−25] The presence of long-chain PFCAs in fish from a few Asian and North American locations, at levels similar to PFOS, indicate that consumption advisories for these chemicals may need to be considered.[23]

PFCs in Arctic biota have been the subject of two recent reviews as part of the Arctic Monitoring Assessment Program.[26] In 2010 Letcher et al.[27] published a detailed review of the exposure and effects of persistent organohalogen contaminants, including PFCs, in arctic wildlife. Also in 2010, Butt et al.[28] conducted a comprehensive review of levels and trends of PFCs in the arctic environment, including organisms from marine and freshwater ecosystems. Consequently, only articles on PFCs in the Arctic environment published after the review period covered by Butt et al. 2010 (late 2008) are included in the present review. In brief, PFOS was generally predominant in Arctic wildlife followed by perfluorononanoic acid (PFNA) and PFUnA.[28] Relatively high PFOSA levels were also found in Arctic cetaceans. A recent spatiotemporal trends study of PFCs in polar bears from eleven subpopulations in Alaska, Canada, and East Greenland reported PFSA, PFCA, and PFOSA concentrations (in liver) to be the highest in bears from southern Hudson Bay, and lower but comparable among the Beaufort Sea, Gulf of Boothia/Lancaster Sound, Baffin Bay, and Davis Strait bears.[29]

Overall, the assessment of PFCs in aquatic environments clearly indicates the widespread distribution of perfluorinated chemicals and exposure of important wildlife species. Nevertheless, there is still a lot to learn about the presence and the distribution of PFCs, particularly in Africa and Australia. Butt et al.[28] have also underlined the lack of information about PFC levels in the Russian region of the Arctic, which compromises two-thirds of the circumpolar Arctic.

CONTAMINATION PROFILE

The most notable observation made during the course of this review was the preponderance of long-chain PFCAs found in organisms, particularly from East Asia and northern latitudes (Figure 2). PFCs detected in livers of tuna collected from the Pacific rim were predominantly PFOS and PFUnA whereas PFDA and perfluorododecanoate (PFDoA) were also commonly identified.[17] The predominace of PFUnA was also observed in livers of dolphins and porpoises,[30] fish,[31] and waterbird eggs[32] from China, and in fish and egg yolks collected around Lake Shihwa, Korea.[33,34] Significant correlations between PFUnA and PFDoA in the egg yolks were found suggesting common source of emission for these PFCAs.[33] A specific accumulation of C_7-C_{12} PFCAs, in particular PFNA, was also observed in Baikal seals, Russia.[8] In addition to Asian sites, the long-chain PFCA profile was also observed in Arctic regions. Indeed, high proportion of $C_{11}-C_{15}$ PFCAs were quantified in Arctic seabirds[28,35] and PFCA concentrations in polar bear liver (Alaska, Canada, and East Greenland; 2006−2008) were composed largely

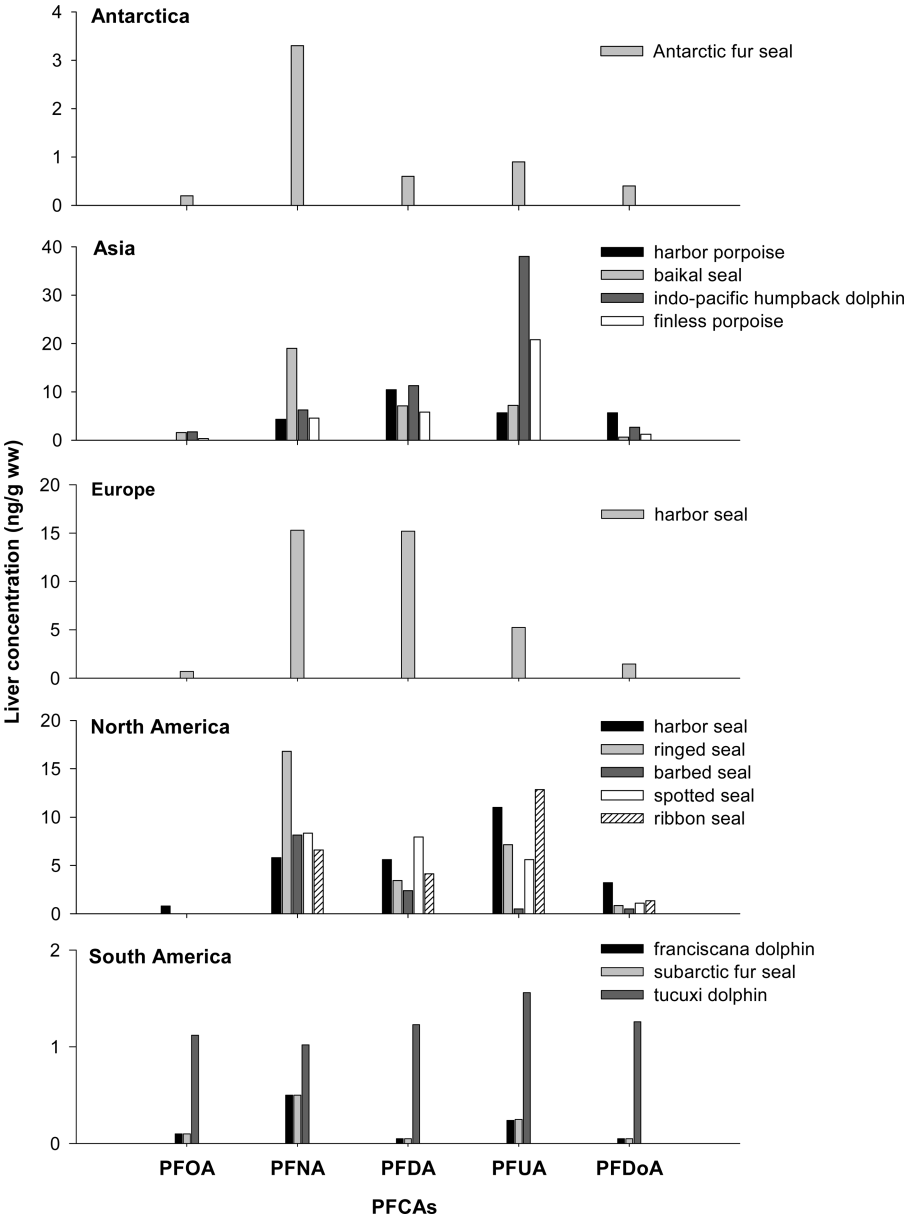

Figure 2. Contamination profile of PFCAs in marine mammal livers by continent, based on available data.[6,8,10,12−15,19,30,36,103] North America data are from Arctic populations.

of C_9−C_{11} with much lesser amounts of PFOA, PFDoA, and perfluorotridecanoate (PFTrA).[29] Analyses of Northwest Atlantic harbor seal livers also indicated the presence of C_7−C_{12} PFCAs, with C_{11} accounting for 47−63% of PFCA.[36] Short-chain PFCAs (PFHpA and PFOA) were present in seal pup but not adults indicating a possible difference in the metabolism and/or elimination of PFCs by immature seals.[36] These data indicate the importance of age and/or development of organisms in biotransformation and bioaccumulation processes. The contamination profile may suggest specific sources of emission in East Asia dominated by long-chain PFCAs[17] followed by long-range transport via ocean and atmospheric pathways to Northern regions of the globe.[37−39]

PFC PRECURSORS AND ISOMERS

Our previous review[1] underlined the need for more data on the propensity for accumulation of PFCA and PFSA precursors as well as the identification of new classes of PFCs in biological samples. These knowledge gaps are slowly being investigated in field-based studies. Much of the research pertaining to fluorotelomer acid biomonitoring has focused on chemicals with an even number of perfluorocarbons and two hydrocarbons due to purified standard availability including 6:2, 8:2, 10:2 FTCA, and their α, β-unsaturated analogs (6:2 FTUCA, 8:2 FTUCA, and 10:2 FTUCA). Despite some limited investigation of these chemicals, there are very few detected concentrations. Recently, the biotransformation pathway of fluorotelomer precursors has been further scrutinized and some fluorotelomer metabolites, that may have longer half-lives than the x:2 FTCAs and x:2 FTUCAs and therefore better candidates for biomonitoring, have been highlighted.[40,41]

In the Great Lakes region, fluorotelomer acids and fluorotelomer alcohols were analyzed but not detected in herring gull

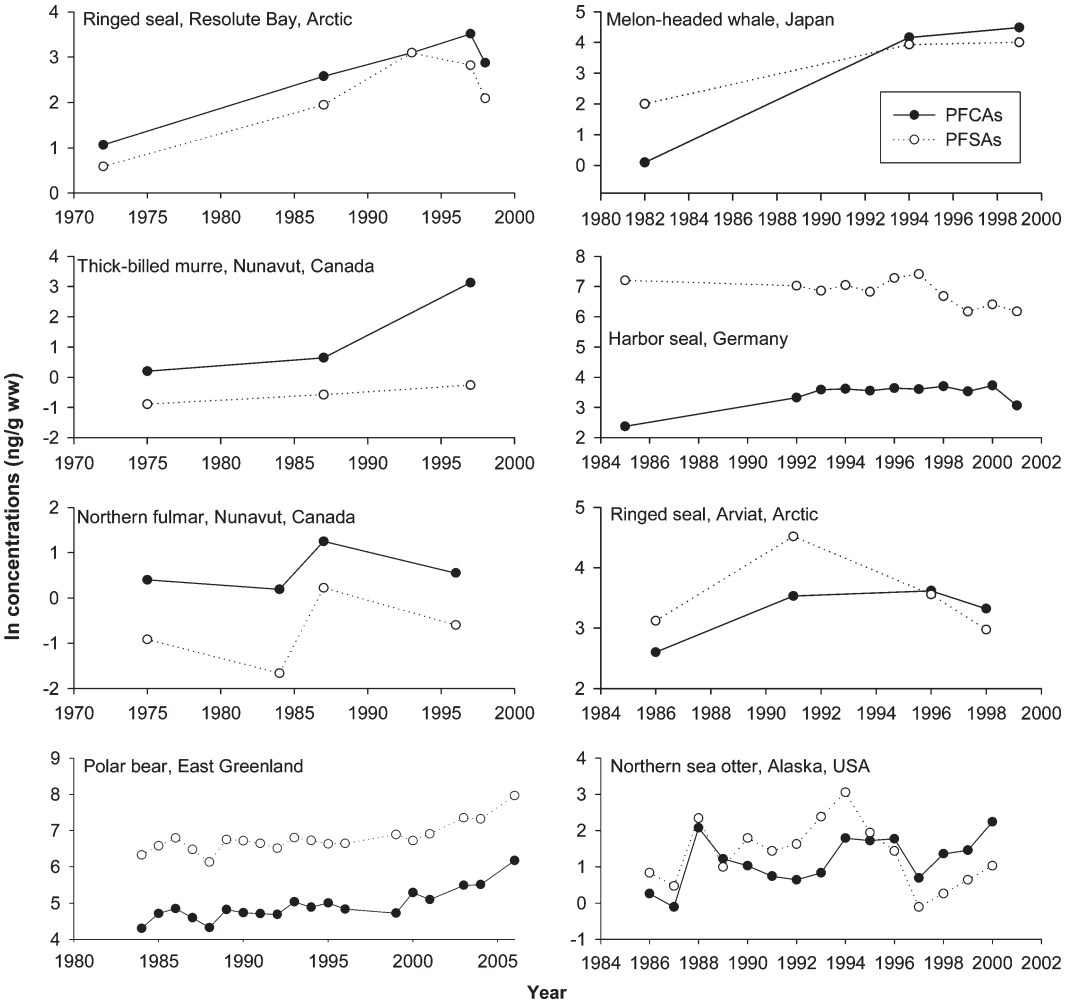

Figure 3. Temporal trends of PFCAs and PFSAs in liver of organisms for which data were reported in studies. Concentrations (ng/g ww) have been ln transformed for comparison.[19,63,65,67,68,71] The totals are the sum of C_4-C_{15} for PFCAs and the sum of C_4, C_6, C_8 and C_{10} for PFSAs.

eggs from 15 colonies[3] while 8:2 and 10:2 FTUCAs were detected in lake trout homogenates.[42] In polar bear liver samples (2006−2008; n = 165 animals), 10:2 FTUCA was barely quantifiable in all but one Beaufort Sea bear.[29] FTOHs were not detectable in any bear sample, and levels of PFOSA were in the low ng/g ww range but quantifiable with very high frequency in samples.[29] An extensive suite of PFC precursors, including perfluorosulfonamides, FTCAs, and FTUCAs were assessed in nine organs and eggs of Chinese sturgeons from China.[16] The authors reported for the first time FOSAA in wildlife in addition to 7:3 FTCA and NEtFOSAA.[16] A wide series of PFSA and PFCA precursors, including a suite of ethanoic acids (e.g., FTCA/FTUCA), sulfonamides, and sulfonamide were also analyzed in ten different harbor seal organs; only MeFBSE could be quantified in thyroid and blubber (up to 2.0 ng/g ww).[14] Concentrations of NEtFOSA in Indo-Pacific humpback dolphins from China ranged from <0.25 to 3.37 ng/g ww and from <0.25 to 0.5 ng/g ww in finless porpoise; 8:2 FTCA/FTUCA could be identified but were under limit of quantification for both species.[30] Additionally, NMeFOSE was detected in bile of dabs captured in Iceland and the North Sea (n = 60, range: <0.08−2.90 ng/g ww),[43] and NEtFOSA was quantified in guillemot eggs from Iceland (n = 3; mean: 0.77 ng/g ww), Norway (n = 4; range: nd−9.9 ng/g ww), and Sweden (n = 3; mean: 1.1 ng/g ww).[44] According to these authors, the presence of PFOSA in these samples may suggest the possible biotransformation of NEtFOSA in guillemot.[44] Finally, 6:2 fluorotelomer sulfonate was analyzed, but not detected, in bird blood collected from Norway[45] and NEtFOSAA was identified in fish blood (<0.30−5.3 ng/g ww) and liver (range: 0.30−20 ng/g ww) from Lake Shihwa, Korea but not in invertebrates sampled from the same location.[34]

The two most common industrial syntheses of PFCs have differing isomeric purities whereby telomerization typically consists of linear perfluoroalkyl isomer and electrochemical fluorination (ECF) consists of a mixture of linear and branched perfluoroalkyl isomers. Thus, isomer determination of PFOA is particularly interesting because this compound has experienced large-scale production with both methods. Tracking enantiomers of PFCs may also prove useful for source tracking.[46] Some measurements of PFCs in biota have focused on isomer-specific analyses. Benskin et al. recently (2010) reviewed PFC isomer findings in the abiotic and biotic environment.[47]

Technical PFOS is typically 30% branched PFOS isomers; however, the PFOS isomer profile in fish and wildlife is typically enriched in the linear isomer (n-PFOS). For example, Houde et al. observed a predominance of the linear PFOS isomer in whole body homogenate of top predator lake trout (n-PFOS: 88−93% of the

total PFOS) and its prey organisms from Lake Ontario.[48] Similarly, in clam, shrimp, and fish collected in Georgia, USA, PFOS isomer profiles in soft tissue, muscle, and liver ranged from 77 to 89% linear PFOS.[25] Powley et al. reported that PFOS isomer profiles in seals from the Canadian Arctic were composed of 96% linear isomer.[49] However, Powley et al. also observed that linear PFOS comprised 50% of the total PFOS in Arctic cod, which represents a unique finding wherein the PFOS isomer pattern in wildlife is depleted in the linear isomer relative to the technical mixture (around 70% of linear PFOS).

Chu and Letcher examined the porportion of ten branched PFOS and linear PFOS structural isomers in herring gull egg and polar bear liver and plasma samples.[50] Linear PFOS accounted for >90% of the ΣPFOS in bird egg and bear liver samples and >80% for the bear plasma samples while the percentage of linear PFOS in commercial PFOS product has been reported to be <80%. In an large-scale spatial study on polar bear from Alaska, Canada, and East Greenland, PFOS comprised consistently ∼99% of the linear PFOS isomer.[29] Linear and branched (six mono(trifluoromethyl) and four bis(trifluoromethyl)) branched isomers of PFOS were also analyzed and reported in eggs of herring gull across the Laurentian Great Lakes of North America.[4] Linear PFOS consistently dominated the isomer pattern in all eggs, comprising between 95.0% and 98.3% of the ΣPFOS concentration. Overall, results of these wildlife (gulls and polar bears) studies suggested that bis(trifluoromethyl) branched isomers are selectively degraded, metabolized, or less accumulated in animal tissues, and that linear PFOS is selectively enriched via preferential bioconcentration, uptake, and accumulation in their respective food webs. This finding is consistent with the absence of bis(trifluoromethyl) PFOS isomers recently reported for zooplankton and lake trout in the Lake Ontario aquatic food web.[48]

There are some currently proposed mechanisms for PFC accumulation but further research is warranted. It is apparent that some mechanisms involved in PFOS accumulation are not as effective for perfluorocarboxylates and vice versa. For example, PFOS undergoes enterohepatic recirculation to a greater extent than the perfluorocarboxylates. Differences in elimination rates between sexes of certain species are pronounced for perfluorocarboxylates but less so for PFOS, likely due to binding to organic anion transporters. Some research has examined differential PFC isomer accumulation in lab-based exposures. Preferential accumulation of linear PFCs occurred in tissues of rats dosed with ECF PFOA and PFOS[51,52] and preferential elimination of branched isomers was observed in their urine. This is suggestive that branched isomers have a lower capacity to bind to organic anion transporters and undergo saturable renal resorption (i.e., active transport from proximal tubular filtrate in kidney to venous blood) compared to linear isomers. This effect was more pronounced for perfluorocarboxylates compared to PFOS. In fact, in a subchronic exposure, elimination rates of branched PFOS isomers were not statistically different from the linear PFOS isomer.[52] Sharpe et al.[53] also noted some preferential accumulation of linear PFOS in fish following a two week exposure to technical PFOS. More recently, O'Brien et al.[54] observed enrichment of linear PFOS isomer in livers of chicken embryos exposed to technical PFOS in ovo. Binding to other proteins such as serum and liver proteins may also be a factor.

Unlike PFOS, historical production of PFOA, realized by both telomerization and ECF, led several researchers to propose that isomer signatures of PFOA could be used for ECF versus telomerization source tracking.[55] In all biological samples, including humans, PFOA isomer profiles are predominantly (>95%) linear PFOA.[47] This was confirmed by analyses of Lake Ontario food web samples,[56,57] dolphin plasma from the Gulf of Mexico,[58] and Arctic biota consisting of cod, seals, and polar bears.[49,59] The hypothesis that PFOA isomer signatures may be used to discern source inputs is confounded by pharmacokinetics revealing preferential retention of linear PFC isomer retention in lab-based exposures to ECF technical mixtures in rodents, fish, and chicken embryos.[51,52,54,60,61] Despite this, enantioselective PFOS isomer determination demonstrates promise for elucidating PFOS precursor exposure.[46] Furthermore, isomer profiling of longer chain perfluorocarboxylates revealed an unknown source of perfluorocarboxylates isomers with terminal isopropyl perfluoroalkyl branching as noted in polar bears, dolphins, ringed seals, and Lake Ontario trout;[56,57,59] these analyses are, however, limited to Canada.

TEMPORAL TRENDS

The number of PFC temporal trend studies in aquatic biota has increased over the past 5 years. (Figure 3). The observed trends vary among locations or species but general tendencies can nonetheless be drawn. The analyses of Baikal seal archived liver samples indicated that PFOS, PFNA, and PFDA levels were significantly higher in animals collected in 2005 than 1992, suggesting active sources of these chemicals in Russia.[8] Temporal trend of PFSAs in lake trout from Lake Ontario indicated an increase from 1979 to 2004 with peak concentrations noted in 1993.[57] A similar pattern was observed for PFCAs with a peak of concentrations in 1988.[57] Perfluorodecane sulfonate (PFDS) and PFOSA levels exhibited a declining trend after peak levels were reached in 1993.[57] Marginal PFOS and PFCA increases in adult harbor seal livers of the N.W. Atlantic were observed between 2000 and 2007, also indicating continuous sources of PFOS in this environment.[36]

Since the manufacturing phase-out of PFOS by the 3M Co. between 2000 and 2002, minor PFOS production continued in Europe and in China (<42−82 t in Europe and <50 t in China in 2003), although China had increased perfluorooctanesulfonylfluoride (PFOSF) production to 200 t by 2006.[62] In their 2010 Arctic environment review, Butt et al.[28] reported a general increase in PFC levels since the 1970s, but indicated some cases from the Canadian Arctic where a decrease in PFOS concentrations was observed. In contrast, a recent temporal trend study (1972−2006) on PFCs was completed for East Greenland polar bear[63] indicating that, as of 2006, levels of PFOS and PFCAs continued to increase exponentially over time.

Decrease in PFOS concentrations in biota of different locations were also reported following the phase-out of PFOSF-based fluorooctanesulfonylfluoride-based chemicals in 2000−2002 (with a different pattern for PFCAs). For example, historical eel samples from The Netherlands have shown a PFOS increase, by a factor of 2 to 4, from 1978 to the mid-1990s, followed by a return to initial level by 2008.[64] A 48% decrease in PFOS concentrations (although not statistically significant) was found between 1999 and 2008 in harbor seal liver samples collected in German Bight simultaneous to a 95% decline in PFOSA. PFOA and C_5−C_7 PFSA concentrations also decreased significantly.[65] However, PFOS concentrations in seal were still high (2008, n = 3, mean of 480 ng/g ww) and levels of C_9−C_{13} PFCAs were constant.[65] A significant increase of PFDS was reported during the same period.[65] For marine mammals,

PFOA levels increased significantly between 1992 and 2002 in southern sea otter livers and PFOS increased from 1992 and 1998 then decreased after 2000.[66] A similar diminution in PFOS levels was observable in northern sea otters from Alaska between 2001 and 2007[67] and decreases in PFOSA were noticed in melon-headed whales from Japan,[19] lake trout from Lake Ontario,[57] and ringed seals from the Canadian Arctic.[68] PFOS and PFNA significantly decreased between 2000 and 2008 in plasma/serum of loggerhead sea turtles sampled in South Carolina.[69] Comparison of modeled PFOS concentrations to biomonitoring data indicated that a rapid decrease in PFOS concentrations (in response to production phase-out) in marine biota is possible only if the major exposure route in marine food webs is by the uptake of precursors followed by in vivo biotransformation to PFOS.[69] The continuous increase in PFOS body burdens observed in marine organisms from other regions may reflect exposure primarily to PFOS itself.[69] The apparent discrepancy between PFOS and PFCA trends is likely due to continued use of PFOA and precursors and/or continued oceanic and atmospheric inputs of sources, and thus exposure and bioavailability of this PFC in the northern hemisphere. The differential inputs of PFOA and PFOS precursors, such as fluorotelomer alcohols and polyfluoroalkyl phosphate may also contribute to these trend differences.

Commenting on the study design considerations for determining significant increasing or decreasing trends of persistent organic pollutants in wildlife, Rigét et al. concluded that annual sampling is essential if the goal is to detect 5% annual change with a significance level of 5% at a power (probability of a false positive or negative trend) of 80% within a 10-year period.[70] By this criteria, only a few temporal trend studies on PFCs are able to approach this level, e.g., those with > $n = 10$ years of data and low within-year variation. Extending the time series by 5 or more years would improve the statistical power of all studies shown in Figure 3.

In melon-headed whales, the proportion of PFSAs in total PFC concentrations decreased from 75% in 1982 to 51% in 2006 compared to an increase in PFCAs from 25% in 1982 to 49% in 2006; PFUnA was the major PFCA detected in Japanese whale livers after 2000.[19] In Alaskan sea otter livers, PFNA concentration increased by a factor of 10 between 2004 and 2007, an observation also verified for PFUnA.[67] PFC profiles of contamination in northern and southern American sea otters are similar but vary considerably from profiles detected in sea otters from Asia/Russia suggesting different emission sources.[67] An increase of long-chain PFCA prevalence in livers of seabirds from the Canadian Arctic was also noted.[71] Overall, observations made in aquatic wildlife worldwide seem to indicate that PFCAs levels may surpass those of PFSAs in the future. However, this prediction also depends on trends in use and emissions. For example, the USEPA PFOA stewardship program (http://www.epa.gov/opptintr/pfoa/pubs/stewardship/) could result in declining emissions of PFCAs to the atmosphere and oceans.[37,72]

BIOMAGNIFICATION

In all ecosystems, food web structures regulate the pathways and flow rates of energy and nutrients to top predators. They also regulate the transfer of chemical contaminants to apex organisms, a phenomenon known as biomagnification. Understanding biomagnification (biomagnification factor = BMF; concentration in predator/concentration in prey) is a crucial criteria in the regulatory frameworks for the evaluation of commercial chemicals.[73] A BMF > 1 indicates the biomagnification of the substance between prey and predator. Another interesting way of studying the fate of pollutants in ecosystems, and conceptualizing predator−prey interactions, is to compare their accumulation through trophic levels of food webs by the determination of the trophic magnification factor (TMF). TMF estimation provides the most conclusive evidence of the ability of chemicals to biomagnify in food webs (TMF > 1).[73] These TMF analyses allow comparison among freshwater, marine water, temperate, tropical, or arctic systems.[74]

The ecological, biological, and chemical parameters involved in the transfer and accumulation of contaminants in food webs are complex and intertwined. Models are useful tools to quantify and evaluate the importance of these variables in the biomagnification of substances at specific locations. Bioaccumulation models generally use the equilibrium partition coefficient of octanol−water (log K_{ow}) as a tool to express the tendency of chemicals to migrate from water to lipids of organisms.[73] The different chemical properties of PFCs, compared to hydrophobic organic contaminants, necessitate the use of different models to estimate their accumulation profile. De Vos et al.[75] used the bioaccumulation model OMEGA and compared their results with field-based food chain data. Results suggested that the uptake of PFOS was comparable to that of moderately hydrophobic compounds and that the elimination of PFOS was best described by the kinetics of metals, which makes PFOS accumulation behavior similar to that of short- and medium-chained fatty acids. Pharmacokinetic and environmental assessment studies can be revealing of the driving forces behind accumulation for PFCs. For example, gender differences in accumulation of carboxylates and sulfonates have been observed and could be explained by their binding to organic anion transporter proteins.[76,77] Faster depuration rates of PFOA in female fish were also observed compared to male.[78] The uptake of the neutral species (e.g., PFOSA, perfluorooctane sulfonamide alcohols, fluorotelomer acrylates) is also an issue.[79] High PFOA in some wildlife could be due to this exposure route which results in nonsteady state conditions, i.e., PFOA may be detectable only when animals are near wastewater outfalls. Environmental studies can also inform on the specific accumulation of some precursors in species, such as PFOSA in cetaceans. Current models do not have means of predicting these phenomena.

Field-based studies have shown biomagnification of PFCs in birds and marine mammals.[1,28,80−83] Most BMFs and TMFs reported in this review, primarily from marine ecosystems, were indeed above 1 (Table S3). Butt et al.[28] have reviewed the biomagnification of PFCs in Arctic food webs indicating trophic biomagnification especially for PFOS and long-chain PFCAs (including post-2006 references by Haukås et al. in 2007 and Powley et al. in 2008[49,84]). Only marine food webs have been studied in the Arctic and data from these food web studies generally included samples collected over several years or at different locations.[28] Tomy et al.[83] conducted a western Canadian Arctic food web study and reported TMFs, calculated from liver and whole-body estimate concentrations in marine mammals and fish, exceeding 1 for C_8−C_{11}, PFOS, and PFOSA with TMF increasing with increasing chain length for PFCAs. Similar positive trophic biomagnification (TMFs range between 2 and 11) was observed for PFOSA, PFOS, and C_8−C_{14} in another Canadian Arctic food web based on wet weight and protein weight concentrations (lipid weight concentration for PFOSA).[82]

PFOS and C_8-C_{11} PFCA concentrations biomagnified in bottlenose dolphin food webs from southern locations in the United States, using whole-body burden estimate.[80] For zooplankton and serum of five fish species collected in Beijing, China, there were significant relationships between trophic levels and concentrations of PFOS, PFDA, and PFNA.[31] Relative to their diet, PFOS biomagnified by a factor of 9 in waterfowl birds from the United States.[81] In a Lake Ontario food web, differences were found in the pharmacokinetic of PFOS isomers.[48] Bis-(trifluoromethyl)-PFOS did not bioaccumulate in wildlife as opposed to linear-PFOS and mono(trifluoromethyl)-PFOS which did bioaccumulate but at different degrees. These results emphasize the importance of molecular structure of isomers in the bioaccumulation of PFCs[48] indicating the need for more research on the bioaccumulation potential of PFC isomers. Overall, PFSAs may be more bioaccumulative than PFCAs of the same fluorinated carbon chain length.[85] PFOS seems to have the highest accumulation potential in food webs whereas bioaccumulation of long-chain PFCAs appears to increase with the chain length. PFCAs with seven fluorinated carbons or less seem do not readily bioaccumulate as previously observed in an experimental fish study.[86]

■ ENVIRONMENTAL/ECOLOGICAL PARAMETERS

Multiple environmental/ecological parameters may influence the biomagnification of PFCs in food webs. Environmental characteristics of sampling locations such as latitude/longitude, depth, volume, or trophic status (i.e., plankton biomass, phosphorus and organic carbon content) are important variables.[74] A study on the effects of water salinity on the bioaccumulation of PFCs in oysters has indicated that salinity not only can affect the chemistry of PFCs but also the physiology of oyster, consequently contributing to sorption and bioaccumulation of PFCAs in these organisms.[87] In brief, an increase of salinity induced an increase in PFC uptake and depuration by oysters; the fact that the increase in uptake rate was greater than that of depuration rate led to enhanced bioaccumulation with increasing salinity.[87]

Feeding ecology may influence the bioaccumulation of PFCs as homeotherms have higher feeding rates than poikilotherms which may result in higher levels of contaminants in birds and mammal compared to fish and invertebrates.[84,88] A study reporting PFCs in four different gull species from 15 freshwater and marine colony sites across eight Canadian provinces indicated that all the freshwater colonies had higher PFSA concentrations in their eggs compared to the marine colonies with the exception of one colony in Atlantic Canada. Dietary tracers ($\delta^{15}N$ and $\delta^{13}C$ stable isotopes) suggested that gulls from most marine colonies were exposed to PFCs via marine prey. For freshwater colonies, stable isotopes suggested both aquatic as well as terrestrial prey consumption were sources for PFC exposure depending on the colony.[5] Seasonal changes in food intake during fattening, growth, or reproduction periods and food web (length, structure/composition, or the introduction of invasive species) may all influence the distribution and fate of contaminants.[27] Migration or temporary residency to more northern and more industrialized areas may also be an important factor in the exposure to PFCs.[84]

Biological variables such as size, sex, age, physical condition, life cycle, and metabolic activity are also important when analyzing contaminant levels in biological samples. The lipid and protein content of tissue, which vary according to season, reproduction, migration, feeding rate, diet composition, growth rate, and food chain length,[89] should be taken into account in PFC analyses (specifically proteins for PFCs). Results from experimental studies have noted the importance of neutral precursors in wildlife,[28,90,91] because of their rapid biodegradation in organisms and the formation of more bioaccumulative products, highlighting the importance of considering biotransformation in analyses. Contaminants analyzed in fish, marine mammals, and bird egg suggest oviparous and viviparous transfer of PFCs to offspring.[9,10,16,36,45,92,93] Additionally, the lack of correlation found in some environmental studies between PFC concentrations and sex or age of organisms[6,15,17,65] is different from the sex-related differences in accumulation and elimination observable in pharmacokinetic studies. These results of maternal transfer and age/sex association suggest that future environmental work should consider large data sets enabling age class and gender comparison.

Changes in the distribution and bioaccumulation of contaminants are expected to occur as a result of climate change. Climate change can affect transport volumes and pathways of different air and water masses, modifying sea-ice conditions and consequently affecting Arctic wildlife and food webs. Although very limited, some studies have linked Arctic warming climate change to region-specific shifts in food web structure and thus dietary influences on the level and pattern of contaminant exposure in mammals and birds.[94,95] For polar bears in Hudson Bay, studies have shown that shifts in diet (and their food webs) have a contaminant-specific effects on spatial or temporal trends of chlorinated and brominated contaminants.[94,95] This may also be true for PFCs, but has yet to be shown. Changes in water mass distribution may also result in changes in temperature, salinity, species composition, and food web structures.[96] Modifications in temperature may also alter partitioning of organic compounds between dissolved and particulate phase in water and air and therefore affect the bioavailability of contaminants in aquatic ecosystems.[96] Ultimately, annual changes in contaminants biomagnification could be indicative of climate change disturbance.

■ RESEARCH NEEDS AND FUTURE PERSPECTIVES

As reported in our review in 2006,[1] the majority of biomonitoring data has been generated by a small number of laboratories, although the number has increased. There is some overlap among the species and locations analyzed, and data have shown good agreement among studies. Data produced by individual laboratories for temporal trend analyses were considered acceptable because of consistent intralaboratory analytical bias over time. Studies have used similar ion-pairing liquid extraction methods, although free-acid analysis approaches are being used as well and incorporate solid-phase extraction, liquid extraction (without an ion-pairing agent), or direct LC-MS injection. Systems and materials have become more specialized for PFC determination, and this appears to have translated into better interlaboratory precision and accuracy, and quantification limits that are consistently in the sub-ppb range. Even greater sensitivity for PFCs is being achieved with LC-MS/MS systems that can quantify at levels approaching the parts-per-trillion level. Challenges to PFSA analyses, such as matrix effects on ionization enhancement/suppression in the LC-MS, are also factors that can significantly affect results and may be addressed by use of isotope-labeled standards and standard addition techniques. The stability of PFSAs and PFCAs gives

confidence that sample storage conditions are not a major factor that would influence data quality, and lends justification and confidence to the use of archived samples. In recent years, analyses for major PFSAs and PFCAs have been based on individual isotope-enriched surrogates.

Recent interlaboratory studies on perfluorinated compounds in environmental samples have indicated improvement in the quality of the analyses of PFCAs and PFSAs.[97−99] The use of well-defined native standards and mass-labeled internal standards and better clean up of extracts have been identified as keystones in the accuracy and precision of sample analyses.[98] Reference values for PFCs have been reported for the first time in Standard Reference Materials (human serum and milk) by the National Institute of Standards and Technology[99] improving the quality control practice of PFC measurements. However, interferences in PFC analyses, especially with PFSAs, are still more common than one would think[99,100] which highlights the need for quality control practices such as the monitoring of numerous transitions, use of procedure blanks and matrix spikes, and high purity of standards. The use of branched and linear PFOS standards should also be included in PFOS quantitative studies (instead of reporting total isomers only).

Greater emphasis should be put on the measurement of multiple ecological, biological, and physical variables in studies aiming at analyzing contaminants in species and more importantly when comparing data between studies. Researchers have only recently begun to orchestrate their sampling design in order to integrate a maximum number of parameters in their analyses but further expansion is possible. In addition to all these primary variables, the impacts of climate change will also have to be considered in analyses because changes in seasonal icing, temperature, or food webs can probably have great effects on the bioaccumulation and biomagnification of contaminants.

A complementary avenue of research to the determination of chemical concentrations in food webs is the toxic effect evaluation resulting from the biomagnification of PFC concentrations. Combining chemical assessment/monitoring with work on species/population biology, behavioral science, exposure biomarkers, or veterinary medicine would greatly contribute to scientific knowledge. The parallel work conducted between PFOS/PFOA assessment and the presence of pathology in Californian otters is a good example of a multidisciplinary approach. High concentrations of PFOA and PFOS in livers were found to be associated with infectious diseases detected in otters.[66]

Finally, a number of important points should be considered in studies in order to adequately assess the biomagnification and limit the variations within and between food web studies. First, samples should preferentially be collected during the same season of the same year and at the same location. The most species possible should be collected and stable isotope analyses should be analyzed to properly identify the trophic positions of species. Because of the fundamental differences in the bioaccumulation behavior of water- and air- breathing organisms, both groups should also be included in the analyses when possible (mammalian/birds and fish).[73] Additionally, chemical characteristics of compounds should be considered as different structural form including isomers that may have specific bioaccumulation potential. For example, PFOS has been strongly associated with serum protein (i.e., albumin)[101] indicating that the protein composition of analyzed tissue may affect the calculation of BMF and TMF. The expression of the data on a wet- or a specific protein-basis should therefore be adopted and standardized across the species studied. Standardizing data is a key element in comparison between studies. In some cases geometric means (based on log-transformed data) may be more representative of the environmental contamination than arithmetic means which is more affected by aberrant data. The report of range and median may offer solutions for the accurate comparison between contamination levels between tissue, species, and locations. Lastly, using PFC concentrations in a specific organ, instead of a whole burden estimate approach, may lead to overestimation of BMFs and TMFs.[1] Whole body residues in wildlife should be estimated (as done in harbor seal[14]) for more precise evaluation of biomagnification.

Ecotoxicological assessment of PFC exposure is a challenging task. Focusing on specific at-risk species and investigating both fresh and marine environments may be key elements to better understand the fate of PFCs. Investigating hotspots, such as developing nations, where the usage of these chemicals is increasing in an uncontrolled manner, is also very important.

■ ASSOCIATED CONTENT

Supporting Information. Latin names of species; mean or range of concentrations (ng/g ww) of some PFCs in aquatic invertebrates, fish, birds, reptiles, and marine mammals (2006−present); BMFs and TMFs in aquatic food webs (2006−present) by geographical locations; and additional references. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author
*E-mail: magali.houde@ec.gc.ca.

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