Quantifying Human Exposure to Chemical Pollutants from Domestic and Imported Food Consumption through Coupled Analysis and Modeling

by

Megha Bedi

BS in Biotechnology, Kurukshetra University, 2011

MS in Environmental Science and Technology, Thapar University, 2013

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This dissertation was presented

by

Megha Bedi

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and approved by

Dr. Carla Ng, PhD, Associate Professor, Department of Civil and Environmental Engineering, Department of Environmental and Occupational Health

Dr. Leanne Marie Gilbertson, PhD, Associate Professor, Department of Civil and Environmental Engineering, Department of Chemical and Petroleum Engineering

Dr. Vikas Khanna, PhD, Associate Professor, Department of Civil and Environmental Engineering, Department of Chemical and Petroleum Engineering

Dr. Peng Gao, PhD, Assistant Professor, Department of Environmental and Occupational Health, Department of Civil and Environmental Engineering

Dissertation Director: Dr. Carla Ng, PhD, Associate Professor, Department of Civil and Environmental Engineering, Department of Environmental and Occupational Health

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Megha Bedi, PhD

University of Pittsburgh, 2023

Chemicals are inevitably used in many industrial processes and consumer products and are critical to our daily activities. For instance, as flame retardants in fibers and molded plastics, stain resistant barriers in carpets and upholstery, grease and water-resistant coatings in cookware and food packaging, and pesticides to protect foodstuffs and crops. However, these chemicals and their byproducts are often released into the environment, during production, use, and disposal of products. In addition, the long-range atmospheric transport and movement of products across borders make them ubiquitous. They may be environmentally persistent and accumulate in organisms to exert toxic effects. Although many toxic chemicals have been regulated, they continue to be widely detected. In addition, many replacement chemicals, which were once believed to be safe, are now gaining attention due to concerns that they may be equally persistent and toxic.

Among the many potential intake routes, seafood consumption has been identified as a major non-occupational pathway for exposure to chemical contaminants. The objective of this work was to improve data on the occurrence of pollutants in seafood and quantify the risks involved with seafood consumption. This, coupled with data on bioaccumulation and toxicity of specific chemicals, substantially contributes to the overall body of knowledge on foodborne exposures, a growing public health concern.

In this work, 450+ legacy and emerging chemicals were analyzed, including pesticides, veterinary drugs, polybrominated diphenyl ethers (PBDEs), polycyclic aromatic hydrocarbons

(PAHs), polychlorinated biphenyls (PCBs), and per and polyfluoroalkyl substances (PFAS) in commercial seafood using liquid- and gas-chromatography coupled to mass spectrometry platforms. Our findings suggest that for individual compounds, the tested seafood was safe for human consumption. However, concerns over chronic exposure and uncertainties around mixture exposures persist.

Based on the measured concentrations, we developed exposure models and found that higher risks were associated with certain populations. Exposure modeling is therefore a powerful tool to identify which exposures may contribute most to body burdens and thus identify effective interventions to protect vulnerable populations. Overall, our findings warrant continued monitoring and identification of measures to reduce chemical amounts in seafood.

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Introduction

1.1 Motivation

1.1.1 Chemical Pollutants

Chemicals used in industrial applications and consumer products are critical to our daily activities for example as flame retardants in fibers and molded plastics,[1] fire suppressors in firefighting foams,[2] stain resistant barriers in carpets and upholstery,[3] and grease and water resistant coatings in cookware and food packaging.[3] However, the chemicals and byproducts associated with these innovations are often released into the ecosystem, during production, use, and disposal of products. In addition, atmospheric transport and movement of products across borders promotes long range transport of chemicals, making them ubiquitous. Many such chemicals are highly persistent and resistant to biodegradation, and may accumulate in environmental media or organisms where they exert toxic effects.[4] In humans, chemical pollutants have been linked with many adverse health effects on reproductive, neurological, endocrine, and immunological systems as well as developmental and behavioral impacts.[5,6] They may enter human bodies through various routes, among which food consumption has been identified as a major pathway.[1,7,8] Other less common exposure routes include dermal intake, dust ingestion, inhalation of contaminated air and drinking contaminated water.[7,9]

1.1.2 Seafood Consumption as an Exposure Route and Chemicals of Interest

Seafood, including fish and shellfish, is an integral part of a healthy diet, and a rich source of lean proteins, omega-3 fatty acids, vitamins, and minerals.[10,11] Consumption of seafood has been associated with reduced cardiac deaths and obesity, and improved infant health.[10–12] However, fish intake may pose adverse health effects due to the presence of hazardous chemical residues.[1,13–15] At the same time, seafood consumption has increased in the

US over recent decades, but from a seafood consumers' perspective, comprehensive data pertaining to which seafood to consume based on pollutant load and unsustainable practices, such as overfishing and habitat destruction, are lacking.

While chemicals such as antibiotics are intentionally applied to livestock, others are never added intentionally but enter ecosystems through environmental fate and transport, such as waste disposal from chemical industries. Antibiotics and other veterinary drugs help promote fish health and increase productivity. However, indiscriminate use of antibiotics has been associated with the development of antibiotic resistant bacteria.[16] Studies have also reported antibiotics above FDA-approved levels in farmed fish labeled as "antibiotic free".[17] Pesticides, on the other hand, may enter ecosystems indirectly through runoff from agricultural fields and bioaccumulate in aquatic food webs. Many banned organochlorine pesticides (OCPs) such as aldrin, chlordane, and the well-known dichloro-diphenyltrichloroethane (DDT) and its primary metabolite, dichloro-diphenyldichloroethane (DDE), have been found in edible fish and shellfish.[18–22]

In addition, many environmental contaminants used in industrial applications or generated during natural and anthropogenic activities have been widely detected in seafood.[1,14,23–29] For example, polybrominated diphenyl ethers (PBDEs) are extensively used as fire retardants in consumer products such as textiles and plastics.[30] Polychlorinated biphenyls (PCBs) were also widely used due to their fire resistant properties in applications such as electrical equipment and hydraulic systems and as additives in paints and plastics.[31] Per- and polyfluoroalkyl substances (PFAS) render oil and water resistant properties and are added to numerous consumer products such as grease-proof contact papers, cosmetics, coatings, paints, and firefighting foams.[3] On the other hand, polycyclic aromatic hydrocarbons (PAH) can be released from both natural and anthropogenic sources. They are released into the environment as a consequence of wildfires, but also through incomplete combustion within various industrial activities such as waste incineration, iron and steel production, cement manufacturing, and pesticide production.[32] Many of these chemicals have been banned and replaced by presumably safer alternatives. However, there are growing public health concerns over the safety of their replacements.

1.1.3 International Food Trade and Chemical Transfer

Practices like waste management (recycling, disposal or landfilling), emissions from construction materials, and food trade can effectively disseminate many environmental contaminants and may be responsible for their ubiquitous occurrence in the environment.[1] Chemicals contained in electronic waste have been identified as one of the most critical ongoing emissions pathways.[33] Many developed nations like the US and members of the EU export their e-wastes for processing and disposal to developing countries, including India and China.[34,35] Many e-waste dumping destinations are also major hubs for global aquaculture production, and actively export seafood to other parts of the world.[36] In 2016, Asia contributed 89% to global aquaculture production, China being the highest producer (61.5% of total aquaculture production), followed by India, Indonesia, and Vietnam.[36,37] Although the concept of e-waste dumping is not new, the impacts of contaminants being transferred across borders are still poorly quantified[38] and food as a means of transport has not been explored.[39]

1.2 Objectives

Human exposure to chemical residues in food and the associated health risks have been reported with little attention focused on the seafood industry. Previously, studies have determined levels of agricultural/aquacultural and industrial chemicals in commercial seafood. However, only a subset of these chemicals, particularly legacy chemicals, have been the focus. Little is known about the concentrations of chemicals still in active commerce, despite growing public health concerns over their safety.

Data on seafood consumption patterns, such as seafood-specific daily intakes for specific populations, are crucial for risk assessment, but such data are limited. Therefore, in an effort to help fill such gaps, we designed a mathematical model that uses international seafood trade data (instead of seafood consumption surveys) and published contaminant levels (PBDEs in this case) to quantify human exposure based. Furthermore, we screened commercial seafood for a wide suite of chemicals and used measured concentrations to build scenario-specific exposure estimates. We specifically focus on understanding exposures from a consumers' perspective and investigated if seafood origins, husbandry types (farmed and wild caught) and store preferences impact exposures, an aspect not yet been explored by others. To the best of our knowledge, we are the first US-based study to analyze 450+ compounds in seafood, providing a wider perspective than previously available on chemical residues in the US commercial seafood supply. Although, samples were collected from a single city, most of the stores surveyed belong to national chains with their associated supply chains, and therefore results are likely generalizable to the seafood-consuming US population.

The overall purpose of our study is to monitor the concentrations of chemical contaminants in edible fish and shellfish tissues to better understand dietary exposure to these hazardous compounds, which was achieved both by modeling (Objective 1) and analysis (Objectives 2 and 3).

The specific research objectives of this dissertation were as follows:

Objective 1**:** International food trade based mathematical model development to assess human exposure to PBDEs through seafood consumption

Objective 2: Documenting PFAS occurrence in seafood from a cross-section of retail stores in United States: Does consumer behavior impact exposure?

Objective 3: Levels of chemical residues including veterinary drugs, pesticides, and environmental contaminants in the commercial seafood supply in the United States.

1.3 Organization

The dissertation is structured as follows:

In Chapter 2.0, human exposure to PBDEs for the seafood-consuming adult Swiss population was estimated using two approaches. The first approach quantified exposures by estimating the composition of the Swiss seafood diet using international trade data from the UN Comtrade database and national statistics on total seafood consumption. The second approach was based on dietary survey data provided by the Swiss Federal Statistical Office as part of the menuCH study for exposure estimates. Literature was systematically reviewed to find PBDE levels in fish and other seafoods from food markets or freshwater resources from various countries. Meta-analyses of published PBDE concentrations was performed to estimate exposures based on a mathematical exposure model. Trade-data based exposures were compared with the survey-based exposures, to validate the efficacy of using widely available trade data in the absence of specific dietary surveys, which are rare.

In Chapter 3.0 we quantified the levels of PFAS in seafood from retail stores across the city of Pittsburgh to investigate whether customer choices impact exposures. Seafood samples were processed using QuEChERSER extraction and analyzed for 33 PFAS using ultra-high performance liquid chromatography coupled to tandem mass spectrometry (UHPLC-MS/MS) and to high resolution MS (HRMS). Scenario-specific (low and high exposure) risk assessment was performed based on tolerable weekly intakes (TWI) established by the European Food Safety Authority (EFSA).

Prior to sample collection, a thorough market survey was conducted to identify different seafood products including species, origins, and husbandry types (farmed or wild-caught) available in grocery stores in Pittsburgh. . We surveyed 11 stores including local retail stores, national grocery chains, dollar stores, major department stores, and international stores. A total of 46 samples representing variability across origins, prices, and husbandry types (farmed/wild-caught) were collected. Samples were packed and shipped to the United States Department of Agriculture- Agricultural Research Services (USDA-ARS), Wyndmoor, PA, where further analysis was performed. I trained on additional analysis methods at USDA-ARS under the supervision of Dr. Yelena Sapozhnikova who helped with the extractions, analysis, data collection, and reporting.

In Chapter 4.0 we measured levels of pesticides, veterinary drug residues and environmental chemicals (PCBs, PBDEs, PAHs) in the same sample set as discussed in Chapter 3.0 Samples were screened for 440+ legacy and emerging chemicals using low-pressure gas chromatography-tandem mass spectrometry (LPGC-MS/MS) and UHPLC-MS/MS. The risks associated with intake of target seafood were evaluated through maximum residue limits (MRLs), estimated daily intakes (EDI), and hazard quotients (HQ). We performed scenario-specific risk assessments considering low and high frequency seafood consumption. We specifically focused on vulnerable populations such as recreational anglers who eat comparatively more seafood than other consumers and may be at a greater risk of exposure.

Lastly, in Chapter 5.0, key findings of the dissertation are summarized, the significance of the work is highlighted and recommendations for future work are discussed.

2.0 Estimating Polybrominated Diphenyl Ether (PBDE) Exposure through Seafood Consumption Based on International Food Trade

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Seafood is a major source of human exposure to polybrominated diphenyl ethers (PBDEs). The intake of these globally distributed and bioaccumulative contaminants depends on both consumption patterns (which seafoods are consumed) and on their origins. Here, we investigate exposure to PBDEs through seafood consumption as a function of species, origins and consumption levels. We estimate the contribution of seafood consumption to PBDE exposures in the Swiss population using two approaches. The first approach estimates exposures by estimating the composition of the Swiss seafood diet using trade data and national statistics on total seafood consumption. This naïve approach could be used for any country for which no individually reported consumption data are available for a population. The second approach uses dietary survey data provided by the Swiss Federal Statistical Office as part of the menuCH study for exposure estimates. To support region- and species-specific estimates of exposures for both approaches, we built a database of PBDE concentrations in seafood by analysis of published PBDE levels in fish from food markets or freshwater resources from various countries. We find estimated PBDE exposures ranging from 0.15 to 0.65 ng/kg bw/day for the trade data-based diet. These were close to the median exposures of 0.68 ng/kg bw/day for the Swiss population based on the menuCH survey, indicating that the composition and consumption rate derived from trade data are appropriate for calculating exposures in the average adult population. However, it could not account for PBDE exposures of more vulnerable (high seafood consuming) populations captured only by the survey data. All estimates were lower than the PBDE Chronic Oral Reference Doses (RfD's) suggested by the EPA but could increase substantially to a value of 7 ng/kg bw/day if fish are sourced from the most contaminated origins, as in the case of Vietnamese shrimp/prawn, Norwegian salmon, and Swiss whitefish. Exposures as high as 8.50 ng/kg bw/day are estimated for the survey-based diet, which better captures the variability in consumption by individuals, including extreme high and low values. In general, the most frequently consumed species reported by Swiss consumers are consistent with those predicted using trade data.

2.1 Introduction

Polybrominated biphenyl ethers (PBDEs) are lipid-soluble[41] compounds used as flame retardants in synthetic fibers like rayon, nylon, polyester[42] and molded plastics.[43] There are 209 different PBDE congeners[44] based on the number (2–10) and configuration of bromines attached to diphenyl rings.[45] Three technical mixtures of PBDE homologues have been commercialized since the early 1970 s: (CDC, 2016) pentaBDE, octaBDE and decaBDE,[45] of which decaBDE is the most abundant in the environment.[46] PBDEs are released into the environment during manufacture, use and disposal of products, eventually making their way into ecosystems where they enter food chains, accumulating in fat-rich tissues. The commercial production of pentaBDE and octaBDE ceased in 2004 due to emerging recognition of their bioaccumulative, toxic and persistent nature,[47] and in 2008 deca-BDE was also banned by the European Court of Justice.[47,48] Despite the bans on PBDEs in the United States (U.S.) and European Union (E.U.)[45] and their inclusion under the Stockholm convention as Persistent Organic Pollutants (POPs) in 2009,[49] PBDEs continue to be a matter of concern to human health since they are persistent in the environment and are incorporated into materials that may still be in use or releasing PBDEs after disposal.[46,50,51] Animal studies have confirmed toxic effects including neurobehavioral changes (e.g. lower IQ), reproductive system damage, and thyroid and liver malfunctions due to PBDE exposure.[44,52,53]

PBDEs enter human bodies through dust ingestion and inhalation of contaminated air as well as food consumption,[54,55] with the latter being a major source of exposure.[56,57] Studies have confirmed that fish, meat and dairy products contribute significantly to daily PBDE intake.[58] For investigating fish intake as an exposure pathway, species-specific intake data are crucial. Some national agencies have been successful in conducting dietary surveys to furnish species-specific databases. For instance, the National Health and Nutrition Examination Survey (NHANES)[59] conducted by the Centers for Disease Control and Prevention (CDC) reported 24-h and 30-day species-specific fish consumption frequency for several regions in the United States. Similar surveys have also been conducted in many European countries. For instance the National Diet and Nutrition Survey (NDNS) in the UK[60] and the Belgium National Food Consumption Survey 2014–2015 in Belgium.[61] However, not all countries conduct these surveys, so alternate data sources are needed for generating seafood diets. Additionally, researchers have derived fish consumption patterns for Portugal and Greece among others countries, using information on trade data and fish landings.[62] However, in our understanding no study has attempted to validate trade-estimated seafood diets by comparing them with survey based dietary data. Here, we evaluate whether widely available trade data can generate reliable dietary estimates using pre-existing survey data for comparison.

Apart from being a tool for providing insight into typical diets for modern populations, international food trade data can also add an important dimension to the chemical exposure landscape: the transfer of contaminants across borders.[38,39] This is particularly appropriate for a globally distributed class of chemicals like PBDEs.[35] When in commerce, the majority of PBDEs were synthesized in the E.U., U.S., China, Israel and Japan.[52] However, practices like waste management (recycling, disposal or landfilling), emissions from construction materials, and food trade can effectively disseminate these contaminants and may be responsible for the ubiquitous occurrence of PBDEs in the environment.[54,63,64] PBDEs contained in electronic waste have been identified as one of the most critical ongoing emissions pathways.[33] Many developed nations like the U.S. and members of the E.U. export their e-wastes (containing PBDEs) for processing and disposal to developing countries, including India and China.[34,35] PBDEs emitted from e-waste make their way into the local environment and ultimately into the food chain.[65] Many e-waste dumping destinations are also major hubs for global aquaculture production, and actively export seafood to other parts of the world.[36] In 2016, Asia contributed 89% to global aquaculture production, China being the highest producer (61.5% of total aquaculture production), followed by India, Indonesia, and Vietnam.[36,37] Although the concept of e-waste dumping is not new, the im- pacts of contaminants being transferred across borders are still poorly quantified[38,63] and food as a means of transport has not been explored.[39] In this study, we estimate PBDE exposures via dietary intake of internationally traded seafood and compare methods to generate re- presentative diets, using both trade- based data and a pre-existing survey. We calculate PBDE exposures using both trade data from the UN Comtrade Database[66] and survey data from the menuCH National Nutrition Survey 2014/2015,[67] evaluating the influence of seafood origin on PBDE exposure.

2.2 Methods

2.2.1 Study Area

We selected Switzerland as our case study based on the role of food trade in its economy and the availability of dietary survey data. Fish consumption has increased substantially in Switzerland over the past decades: approximately 8.8 kg of fish were consumed annually per person in 2014, in comparison to only 6.4 kg in 1984.[68] Since fish bioaccumulate PBDEs from their surroundings,[69,70] this 37.5% increase in fish consumption could con- tribute to increased PBDE exposure. Moreover, Switzerland is among the countries with the highest share of foreign trade in gross domestic product (GDP),[71] implying that integration of seafood trade in our study would be relevant for this population.

Our study investigated PBDE intakes from seafood consumed by the Swiss population using two different approaches: trade data and survey data. Using trade data, we report here import volumes for individual seafood species (referred hereafter as "species-specific") and by the country of origin (referred hereafter as "origin-specific"). Using the survey data, we calculated daily seafood intakes for individual seafood species, but as origins of the seafood consumed are not reported by respondents in the menuCH survey, these are referred to hereafter as "species-specific but not origin-specific".

2.2.2 Construction of Seafood Consumption Characteristics

2.2.2.1 Swiss Diet Constructed from Trade Data and Domestic Catch

Seafood imports to Switzerland from the rest of the world, extracted from the UN Comtrade Database,[66] together with domestic fish catch, reported by the Swiss Federal Office of Fisheries Statistics,[68] were used to build a diet profile. All calculations are based on trade data from 2016. We assume the trade statistics to translate to consumption by adults, in order to compare with the menuCH survey of the adult Swiss population. However, national trade statistics account for the entire population; therefore, there is some uncertainty associated with assigning trade data to the diet of a particular population sector. Note that the term "seafood" is used here for all consumable aquatic species (marine or freshwater) in general.

Imports reported by Switzerland (mass imported; kg/year) were extracted for seafood including fish, mussels, and shrimp (these tend to dominate the Swiss diet) covering fresh, frozen, fresh fillet, and frozen fillet categories (Appendix A, Table1). Mass exported in kg/year for the same commodity codes as reported by Switzerland's trade partners was also obtained to assess discrepancies between partner-reported exports and Swiss-reported imports (Appendix A, Figure 1).[72]

From the list of total imported commodities, we report here the top 20 seafood types used for calculating "species-specific and origin-specific" PBDE exposures (Table 1; for a complete list of total seafood commodities imported see Appendix A, Table 2). We also included the complete list of imported species and not only the top 20 to calculate "species-specific but not origin-specific" PBDE exposures (see details in Section 2.5). Note that in Table 1 and Appendix A, Table 2 multiple entries may occur for related species, as reported in the UN Comtrade Database. For example, separate entries exist for Salmon, Trout and

Salmonidae, with the Salmonidae entry explicitly stating: "Salmonidae excluding 030211 and 030212", where 030211 and 030212 are entries for common species of Trout and Pacific/Atlantic/Danube Salmon, respectively. Since we have extracted all our trade data from Comtrade, we retained the same nomenclature.

Among the entire range of countries supplying seafood to Switzerland, we focused on the top three exporters for each seafood species/group. Together, these generally amounted to the highest trade quantity for a given seafood by a large margin; for instance, salmon imported from Norway, Denmark and the United Kingdom (UK) alone contributed 52% to the total Swiss imports of salmon from 31 nations. In the event of discrepancies between imported quantities reported by Switzerland and quantities reported by the partner nations as exported to Switzerland, imported quantities were used in diet generation and exposure calculations, since previous studies have found them to be more reliable.[72,73] Data on exports and re-exports of seafood from Switzerland were also extracted for comparison. However, these were found to be minimal in comparison to imports (Appendix A, Table 2) and therefore were excluded from all calculations.

Although perch fell below the top 20 seafood imports (traded quantity 14842 kg/year) it was added to the list of selected species, because it is both imported and locally caught,[68] a combination not found for any other selected fish. This allowed us to probe whether local or imported perch contributes more to PBDE exposure. Our analysis was therefore inclusive of 23 seafood species in total; 20 imported and 3 local, with both local and imported perch included.

Whitefish, roach and perch dominate the domestic Swiss fish catch,[68] and hence have been included in our analysis for the domestic component of exposure calculations. Data on catch quantity (kg/year) were extracted by the Swiss Federal Office of Fisheries Statistics.[68]

As reported, Switzerland caught 1,365,729 kg fish in 2016, contributing only approximately 2% of the country's fish intake. Whitefish (845,917 kg), perch (230,246 kg) and roach (119,176 kg) were the most widely caught fish species, contributing 62%, 17% and 9%, respectively, to the total domestic catch.

To translate the imported and local seafood proportions to amounts of each species consumed we used the average annual fish consumption reported by the Swiss Federal Statistical Bureau: Production and Consumption of fish.[68,74] This is equivalent to approximately 23 g/day, assuming that consumption is equally distributed over all days and over the entire Swiss population.

Table 1: Traded quantities of species selected for trade-data based diet generation

*Seafood species	Imports (kg/year)	Exports+ re-exports (kg/year)	Net quantity (kg/year)
Salmon	9519516	52577	9466939
Shrimp	4609169	29276	4579893
Catfish	2802212	4396	2797816
Flatfish	1595391	1200	1594191
Mussels	1443911	No Exports/Re-Exports	1443911
Gadiformes	1400404	No Exports/Re-Exports	1400404
Cod	1343495	2586	1340909
Seabream	1199876	160	1199716
Trout	1046693	282359	764334
Seabass	834985	No Exports/Re-Exports	834985
Tilapia	543341	3695	539646
Hake	387259	No Exports/Re-Exports	387259
Alaska Pollock	301844	1269	300575
Tuna	300673	4547	296126
Sardines	289433	5	289428
Sole	287062	No Exports/Re-Exports	287062
Mackerel	260307	1008	259299
Coalfish	247671	630	247041
Turbot	148239	No Exports/Re-Exports	148239
Swordfish	109512	No Exports/Re-Exports	109512

*top 20 in descending order of quantity traded

2.2.2.2 Swiss Dietary Survey (menuCH)

We received access to the detailed menuCH dietary survey data published by the Swiss Federal Food Safety and Veterinary Office.[67] These data represent a single day of consumption (24-hour dietary recall) by 2000 adult participants. On average this amounted to a total fish consumption of approximately 40 g/day for all surveyed participants (consumers and non-consumers) and included the following species: salmon, cod, tuna, shrimp, trout, perch, whitefish, sardines, seabream, pangasius, plaice, herring, flounder, hake, mackerel, sole, crab, mussels, anchovies, cuttlefish, squid, crayfish, oysters, Atlantic halibut, scallops, eel, clams, lobster and whiting. We did not include any processed fish in our calculations due to the unavailability of PBDE concentrations for them.

2.2.2.3 Additional Origin-Based Scenarios

As mentioned above, the transport of e-wastes for disposal and processing plays a key role in dispersing PBDEs into new environments.[33] At the same time, e-waste receiving nations like China, Vietnam, and Indonesia are also among the major exporters of seafood to Switzerland, based on UN Comtrade trade statistics. To inspect the different dimensions of the e-waste-food trade-PBDE exposure nexus we constructed 3 different extreme scenarios: (i) consumption only of seafood imported from Norway, a country with significant contribution to seafood exports to Switzerland that is also an e-waste source country, where PBDEs may be released during product use; (ii) consumption of only seafood imported from Vietnam, which has significant seafood exports to Switzerland and is an e-waste receiving country, where PBDEs may be released during e-waste disposal and processing[36,37] (iii) consumption of only locally produced fish from Switzerland, itself an e-waste source country. For these scenarios, 40 g of daily fish consumption by a Swiss adult weighing 72 kg was assumed, based on the average of the survey responses. PBDE concentrations in seafood from Norway did not include Norwegian whitefish since it is not imported at all, as informed by the UN Comtrade Database. For local exposures, we considered only whitefish since measured PBDE concentrations were available for Swiss whitefish, but not for perch or roach.

2.2.3 Global PBDE Levels in Seafood

We compiled global PBDE levels from the literature to translate consumption levels to exposures. PBDE concentrations in marine and freshwater species selected for exposure calculations in the current study were collected using two databases, Ei Compendex and Scopus, and two search engines, PubMed and Google Scholar. We used the search terms

“PBDE OR polybrominated diphenyl ether AND fish OR market basket study OR seafood intake” Publications from 2000 through 2018 were included. Among the screened papers, only sampling locations from Asia, Africa, North America, and Europe (specifically: Bangladesh, Belgium, Chile, China, Denmark, France, Germany, Greece, Iceland, Indonesia, Italy, Japan, Norway, Netherlands, Poland, Portugal, South Africa, Spain, Thailand, Turkey, UK, USA, and Vietnam) were included for further analysis, as these regions are among the dominant exporters of consumable aquatic species to Switzerland based on the UN Comtrade Database. We included only those studies where sampling was done from either food markets or fish farms. We excluded studies where sampling was done from known contaminated sites or potential point sources (e.g. rivers/lakes near industrial areas or municipal dump sites), because these could represent a biased sample. However, due to the unavailability of any market based study reporting PBDE concentrations in the fish locally caught in Switzerland (whitefish, roach and perch), we decided to include one study reporting PBDE concentrations in whitefish caught from Swiss lakes.[75] Refer to Appendix A Figure 2 for a Prisma-type flow diagram for this study.

Table 2 shows the origin-specific PBDE levels (pg/g wet weight) in seafood used in our analysis. Origin-based, species-specific exposure estimates were calculated using origin-specific PBDE concentrations (Table 2, column 4). In cases where a seafood species was associated with more than one concentration from the same origin (e.g. salmon from USA and Norway, shrimp from USA and China, catfish from USA and Vietnam, mussels from Spain, trout from USA, tilapia from USA and China, tuna from Japan, mackerel from Japan and carp from China), we used the geometric mean of PBDEs across a single origin in the final exposure calculations for that origin. For exposures where we did not consider origins, we used the geometric mean of PBDEs over all the available origins. For example, species average PBDE levels for salmon were calculated as the geometric mean of values reported in Norway, Belgium, USA, Japan, Spain and Chile (985 pg/g wet weight), which was then used for calculating PBDE exposures from salmon intake irrespective of origin (termed "species-specific but not origin-specific" exposure estimates).

The total PBDE concentrations for most studies (92%) were predominantly congeners 28, 47, 99, 100, 153, and 154. Since the congener profiles were in general similar across the selected studies, we used the sum of all PBDE congeners, referred to hereafter as total PBDEs. However, high BDE-209 concentrations were detected in a few studies.[41,76–78] This could potentially bias results for total PBDE exposure, since BDE-209 is considered less bioaccumulative and toxic than lower-brominated congeners. The only study for which this may be a concern is in Vietnamese shrimp, where BDE-209 was 46% of the total reported concentration,[77] and this was also a seafood-origin pair with one of the highest total PBDE concentrations. For the other studies in which BDE-209 was a dominant congener, catfish and tilapia from the USA and salmon from Spain, the total PBDE levels in these particular seafood-origin pairs were relatively low, as shown in Table 2. In all cases, for non-origin specific scenarios the use of geometric mean values to represent species averages minimized any undue influence from high BDE 209 contributions. For origin-specific calculations, the presence of high amounts of BDE 209 would only substantially affect exposures attributed to Vietnamese shrimp. Other congeners were frequently below the limit of detection.

The primary objective of the literature review was to find the PBDE levels measured in origins and species of interest. However, PBDE data were missing for some combinations of species and origins. In order to estimate PBDE concentrations for all fish and all origins considered in our analysis we made a number of assumptions. In the absence of data for a particular combination of origin country and seafood type we used either lipid-normalized

PBDE concentrations (ng/g wet weight/lipid percent) for the same fish but another region in close proximity[79,80] or PBDE values reported for the same origin country but for another fish having similar taxonomy to the fish of concern. Refer to Table 3 column 3 for the PBDE data substitutes (if used) within seafood species or origins and Table 3 column 4 for the lipid-normalized concentrations which were used for extrapolations across species. For exposure calculations we used wet weight concentrations (Table 3; column 5), since these are more representative of fish as consumed. Refer to Appendix A, Tables 3 and 4 for details on species and origin-specific assumptions and extrapolations.

Table 2: Global PBDE values in seafood.

Seafood species	Locations	PBDE congeners included in total[a]	Sampling year	∑PBDE[a] (pg/g wet weight)	Species average ∑PBDE[b] (pg/g wet weight)
Salmon	*Norway[81,82]	1, 2, 3, 7, 8, 10, 11, 12, 13, 15, 17, 25, 28, 30, 32, 33, 35, 37, 47, 49, 66, 71, 75, 77, 85, 99, 100, 105, 116, 119, 126, 138, 140, 153, 154, 155, 166, 181, 183, 190, 191, 196, 197, 206, 207, 208, 209	2002, 2007-2008	1783	985
	Belgium[83]	28, 47, 99, 100, 153, 154, 183, and 209	2005	1580	
	*USA[41,84,85]	17, 28, 47, 49, 66, 77, 85, 99, 100, 119, 138, 153, 154, 183, 196, 197, 206, 207, 209	2004, 2009, 2015-2016	1058	
	Japan[86]	28, 47, 99, 100, 153, 154	2002	835.75	
	Spain[78]	17, 28, 47, 66, 85, 99, 100, 153, 154, 183, 184, 191, 196, 197, 209	2003-2005	251	
	Chile[87]	1, 2, 3, 7,10, 13, 15, 17, 25, 28, 35, 47, 49, 66, 71, 75, 77, 85, 99, 100, 116, 119, 126, 138, 140, 153, 154, 155, 156), 81, 183, 197, 203, 207, 209	2006	1460	
Shrimp/ prawn	Vietnam[77]	47, 99, 100, 138, 153, 154, 156, 183, 206, 207, 209	2011	25100	310
	Belgium[83]	28, 47, 99, 100, 153, 154, 183, and 209	2005	61	
	*USA[84,85]	17, 28, 47, 66, 77, 85, 99, 100, 138, 153, 154, 183, 209	2004, 2015-2016	228	
	Japan[76]	17, 28, 47, 49, 66, 77, 99, 100, 119, 153, 154, 183, 184, 196, 197, 206, 207, 209	2004-2005	20	

	*China[14,88]	17, 28, 47, 66, 71, 85, 99, 100, 138, 153, 154, 183, 190, 209	2004-2005, 2006	111	
	Netherlands[89]	47, 99, 100, 153, 154	2003	1140	
Catfish	USA[41,85]	17, 28, 47, 66, 77, 85, 99, 100, 138, 153, 154, 183, 209	2004, 2009	779	364
	China[88]	17, 28, 47, 66, 71, 85, 99, 100, 138, 153, 154, 183, 190, 209	2006	270	
	*Vietnam[82,90]	28, 49, 71, 47, 66, 77, 100, 119, 99, 85, 126, 153, 138, 156, 184, 183, 191, 197, 196,208, 206, 209	2007-2008, 2008	229	
Mussels	Netherlands[89]	47, 99, 100, 153, 154	2003	1120	482
	USA[84]	17, 28, 47, 99, 100, 153, 154	2015-2016	398.1	
	Belgium[18]	28, 47, 49, 66, 85, 99, 100, 153, 154, 183	2002	690	
	*Spain[91,92]	47, 99, 100, 153, 154, 183	2000, 2006	175	
Cod	Belgium[83]	28, 47, 99, 100, 153, 154, 183, 209	2005	48	92
	Netherlands[89]	47, 99, 100, 153, 154	2003	410	
	USA[41]	17, 28, 47, 49, 66, 85, 99, 100, 119, 138, 153, 154, 183, 196, 197, 206, 207, 209	2008	31.8	
	European market[93]	47, 99	2014-2015	385.2	
	Norway[82]	28, 49, 71, 47, 66, 77, 100, 119, 99, 85, 126, 153, 138, 156, 184, 183, 191, 197, 196, 208, 206, 209	2007-2008	28	
Trout	Belgium[83]	28, 47, 99, 100, 153, 154, 183, 209	2005	270	976
	Switzerland[75]	28, 47, 99, 100, 153, 154, 183	2003	1300	
	*USA[84,85,94]	17, 28, 47, 66, 77, 85, 99, 100, 138, 153, 154, 183, 209	1996-1999, 2004, 2015-2016	4375	
	Italy[82]	28, 47, 49, 66, 71, 77, 85, 99, 100, 119, 126, 138, 153, 154, 156, 183, 191, 196, 197, 206,	2007-2008	413	

		208, 209			
	Denmark[82]	28, 47, 49, 66, 71, 77, 85, 99, 100, 119, 126, 138, 153, 154, 156, 183, 191, 196, 197, 206, 208, 209	2007-2008	355	
	Turkey[82]	28, 47, 49, 66, 71, 77, 85, 99, 100, 119, 126, 138, 153, 154, 156, 183, 191, 196, 197, 206, 208, 209	2007-2008	3831	
Tilapia	*USA[41,85]	17, 28, 47, 49, 66, 77, 85, 99, 100, 119, 138, 153, 154, 183, 196, 197, 206, 207, 209	2004, 2009	14	26
	*China[82,95]	28, 47, 49, 66, 71, 77, 85, 99, 100, 119, 126, 138, 153, 154, 156, 183, 191, 196, 197, 206, 208, 209	2004-2005, 2007-2008	51	
	Netherlands[82]	28, 47, 49, 66, 71, 77, 85, 99, 100, 119, 126, 138, 153, 154, 156, 183, 191, 196, 197, 206, 208, 209	2007-2008	27	
	Indonesia[82]	28, 47, 49, 66, 71, 77, 85, 99, 100, 119, 126, 138, 153, 154, 156, 183, 191, 196, 197, 206, 208, 209	2007-2008	22.75	
Hake	Spain[92]	47, 99, 100, 153, 154, 183	2006	221.1	221
Sardines	Spain[92]	47, 99, 100, 153, 154, 183	2006	710	169
	Japan[76]	17, 28, 47, 49, 66, 77, 99, 100, 119, 153, 154, 183, 184, 196, 197, 206, 207, 209	2004-2005	130	
	Belgium[83]	28, 47, 99, 100, 153, 154, 183, 209	2005	52	
Sole	Netherlands[89]	47, 99, 100, 153, 154	2003	440	731
	Spain[92]	47, 99, 100, 153, 154, 183	2006	241.5	
	USA[84]	17, 28, 47, 99, 100, 153, 154	2015-2016	3680	

Tuna	*Japan[76,86]	17, 28, 47, 49, 66, 77, 99, 100, 119, 153, 154, 183, 184, 196, 197, 206, 207, 209; 28, 47, 99, 100, 153, 154	2002, 2004-2005	29	55
	Spain[92]	47, 99, 100, 153, 154, 183	2006	558.3	
	Netherlands[89]	47, 99, 100, 153, 154	2003	10	
Mackerel	Belgium[83]	28, 47, 99, 100, 153, 154, 183, and 209	2005	200	876
	*Japan[76,86]	17, 28, 47, 49, 66, 77, 99, 100, 119, 153, 154, 183, 184, 196, 197, 206, 207, 209; 28, 47, 99, 100, 153, 154	2002, 2004-2005	950	
	Spain[92]	47, 99, 100, 153, 154, 183	2006	1123.7	
	Ireland[96]	28, 47, 49, 66, 71, 75, 77, 85, 99, 100, 119, 138, 154, 183, 190, 209	2003	2100	
	Netherlands[89]	47, 99, 100, 153, 154	2003	1150	
Swordfish	Spain[92]	47, 99, 100, 153, 154, 183	2006	977.7	978
Herring	Central North Sea[96]	28, 47, 49, 66, 71, 75, 77, 85, 99, 100, 119, 138, 154, 183, 190, 209	2003	7600	6046
	Netherlands[89]	47, 99, 100, 153, 154	2003	4810	
Whitefish	**Switzerland[75]	28, 47, 99, 100, 153, 154, 183	2003	4500	75000
	USA[97]	99, 100	1996-1999	1250000	
Alaska Pollock	PBDE DATA UNAVAILABLE WITHIN THE INCLUSIVE CRITERIA				
Seabream	Greece[93]	47, 99	2014-2015	4780	1157
	Japan[76]	17, 28, 47, 49, 66, 77, 99, 100, 119, 153, 154, 183, 184, 196, 197, 206, 207, 209	2004-2005	280	
Eel	Netherlands[89]	47, 99, 100, 153, 154	2003	4160	1767
	Belgium[18]	28, 47, 49, 66, 85, 99, 100, 153, 154, 183	2002	5525	
	Japan[76]	17, 28, 47, 49, 66, 77, 99, 100, 119, 153, 154, 183, 184, 196, 197, 206, 207, 209	2004-2005	240	
Perch	USA[23]	47, 99, 100, 153, 154	2000-2001	9301	9301
Plaice	North Sea[93]	47, 99	2014-2015	514.29	454
	Netherlands[89]	47, 99, 100, 153, 154	2003	400	

Halibut	PBDE DATA UNAVAILABLE WITHIN THE INCLUSIVE CRITERIA				
Crab	Thailand[77]	47, 99, 100, 138, 153, 154, 156, 183, 206, 207, 209	2011	3750	1285
	China[14]	28, 47, 66, 99, 100, 138, 153, 154, 183, 209	2004-2005	440	
Clams	Japan[86]	28, 47, 99, 100, 153, 154	2002	52.4	126
	USA[84]	17, 28, 47, 99, 100, 153, 154	2015-2016	303	
Scallop	Japan[77]	47, 99, 100, 138, 153, 154, 156, 183, 206, 207, 209	2011	5720	1057
	USA[84]	17, 28, 47, 99, 100, 153, 154	2015-2016	195.5	
Flounder	Netherlands[96]	28, 47, 49, 66, 71, 75, 77, 85, 99, 100, 119, 138, 154, 183, 190, 209	2003	15100	777
	Japan[76]	17, 28, 47, 49, 66, 77, 99, 100, 119, 153, 154, 183, 184, 196, 197, 206, 207, 209	2004-2005	40	
Coalfish	Netherlands[89]	47, 99, 100, 153, 154	2003	410	410
Squid	China[77]	47, 99, 100, 138, 153, 154, 156, 183, 206, 207, 209	2011	19420	19420
Carp	*China[88,95]	17, 28, 47, 66, 71, 85, 99, 100, 138, 153, 154, 183, 190, 209	2004-2005, 2006	87	575
	Belgium[18]	28, 47, 49, 66, 85, 99, 100, 153, 154, 183	2002	3800	
Seabass	Japan[76]	17, 28, 47, 49, 66, 77, 99, 100, 119, 153, 154, 183, 184, 196, 197, 206, 207, 209	2004-2005	330	330

[a] PBDE congeners measured by the study.
[b] Average total PBDEs reported (pg/g wet weight).
[c] PBDEs (pg/g wet weight) as geometric mean of values reported in column 4, rounded to the nearest whole number.
* Multiple studies reporting PBDE concentrations from the same origin, geometric mean concentration used.
** Swiss whitefish data from Swiss lakes, not market.

2.2.4 Exposure Calculations

PBDE exposures for the trade-data based approach were calculated using Equation 2.1 for both imported (20 species from top 3 exporters) and locally produced (3 species) seafood, as well as overall imported seafood (34 species; average PBDE concentrations over all origins). Total exposure (∑E), whatever the species or origin scenario, is reported in ng PBDEs/kg body weight (bw)/day. Calculations assumed an average Swiss adult weighs 72 kg (menuCH survey average weight of surveyed individuals). Because this is the trade-data based approach that could be used in the absence of specific reported consumption data (i.e. without a dietary survey available), we used the national-statistics based estimate of 23 g of fish consumed daily per person in Switzerland (*Cd*; *daily consumption*).[68,74]

$$\sum E = \sum_{i=1}^{n} \frac{(\frac{Q_i}{Q_t} * 100) * p * C_d * \sum PBDE}{BW} \quad (2.1)$$

Where, $\frac{Q_i}{Q_t} = proportion\ of\ total\ imports$ (%); $\left(\frac{Q_i}{Q_t} * 100\right) * p = proportion\ of\ diet$ (%) and $\left(\frac{Q_i}{Q_t} * 100\right) * p * C_d = daily\ seafood\ consumption\ (\frac{g}{day})$

Here, *PBDE* refers to the total (sum of individual PBDE congeners) average PBDE concentration in a particular seafood species. Although different PBDE congeners may be included in these sums, based on what was measured in specific studies cited in Table 2, we will refer hereafter only to total PBDEs. *Qi* is the quantity imported or locally produced (in units of kg/year) for a species *i* ranging from 1 to n, and the total quantity imported is *Qt* which is 47,969,288 kg for 2016. The quantity $\frac{Q_i}{Q_t}$ for a single seafood species represents it's percent proportion with respect to total imports. This, when multiplied by the parameter *p,* yields the proportion occupied by each seafood species with respect to total seafood consumption. Here, the parameter *p* takes the value of 0.98 or 0.02 to represent the percent of the Swiss seafood diet that is composed of imports or local products, respectively.

For the dietary survey-based approach, we calculated the PBDE exposure as the product of reported daily consumption by species and the average ∑PBDE concentration in that species (Table 2, column 5) calculated as the geometric mean of PBDE concentrations across all origins (because the survey did not include any information on seafood origin). Calculations were done using an average Swiss body weight of 72 kg as reported in menuCH. We also calculated PBDE exposures for each person (survey correspondent) for the fish species being consumed (here we used the individual body weights and amounts of seafood consumed), from which we constructed the distribution of PBDE exposures across individual fish consumers in Switzerland.

Note that all exposure estimates are for Swiss adults. The exposures were compared to available Chronic Oral Reference Doses (RfD) for PBDEs, representing the maximum acceptable oral dose in units of mg dose per kg body weight per day. We used a range of RfDs for PBDEs (100 ng/kg bw/day to 7000 ng/kg bw/day) representing the allowable doses for the most abundant PBDE congeners (penta, hexa, octa and deca-BDE) as suggested by the EPA.[45,51,98]

2.2.5 Uncertainty Assessment

Since our analysis is based on a number of assumptions, we considered the uncertainty that could be introduced by each component of our exposure estimation.

2.2.5.1 Diet Generation

The trade-estimated seafood diet we generated is simplified by including only the top 3 exporters (origins) for each species and only the top 20 seafood imports (species)**.** Using the sum of all imports and total fish import data, we account for fish species or quantities neglected by our analysis and investigate whether this introduces significant uncertainty to the outputs.

2.2.5.2 Daily Fish Intake

We assume the reported average daily consumption of 23 g of fish per person as a part in the Swiss diet all consists of fresh or frozen whole or fillet forms of imported and domestic fish. We further consider only the top 3 largest exporters of each seafood type to Switzerland and 23 types of seafood (local and imported) by weight. To assess if this point of uncertainty could be relevant, we calculated the daily consumption based only upon the quantity of imported and locally produced fish using the following equation 2.2.

$$C_d^* \frac{Q_{(Im+Lp)}}{P} \qquad (2.2)$$

The analysis based on fish consumption (C_d^*) was given by the ratio of the total fish quantity [imported (im) and locally caught (lp), $Q_{(Im+Lp)}; kg/year$] and the population of Switzerland in the same year ($P\ ; million\ people$). This was compared with the reported fish consumption (C_d) and any deviations were studied. Fish forms not included in our analysis (e.g., processed fish, fish products etc.) were considered responsible for any observed asymmetry in daily fish consumption.

2.2.5.3 PBDE Concentration in Fish

As mentioned earlier, we use assumptions to fill PBDE data gaps, which included estimating PBDE concentrations in target fish from data for other fish from similar origins. When comparing across species, we used lipid-normalized total PBDE concentrations (ng/g lipid weight), which we could convert back and forth from fresh weight for exposure calculations using Equation 2.3.

$$\sum PBDEs = \frac{\frac{ng\ PBDE}{g\ fish\ wet\ weight}}{\frac{g\ lipid}{g\ fish\ wet\ weight}} \qquad (2.3)$$

2.3 Results and Discussion

2.3.1 Trade-Based Seafood Diet

The Swiss seafood diet constructed using data from the UN Comtrade database and national statistics on domestic catch is shown in Figure 1. Combined with population-level consumption statistics this suggests that, on average, the Swiss population consumes around 10 g/day of salmon, shrimp, and cod alone, out of the total 23 g/day. Closer analysis of the top exporters to Switzerland indicates Vietnamese shrimp was the most consumed seafood type from a single exporting country, followed by Vietnamese catfish and Norwegian salmon. Native whitefish was also among the top 10 most consumed fish.

2.3.1.1 Sensitivity and Uncertainty Related to Diet Generation

Our trade-based analysis considers only the top 20 fish and their top 3 origins. These in total made up 20,919,367 kg in 2016, contributing 44% to the total imports. This implies that the remaining 56% of imports (species imported in smaller quantities and exporters beyond the top 3), collectively contribute a significant proportion to the Swiss seafood diet, adding uncertainty to our analysis. However, our approach could identify the most important traded commodities and, even for this restricted set, identification of species- and origin-appropriate PBDE data was a major challenge.

2.3.1.2 Sensitivity and Uncertainty Related to Daily Fish Intake

Based only on the total imports for selected fish commodities and locally caught fish, daily fish consumption calculated using Equation 2.2 amounted to 16.5 g per person daily. This is less than the value of 23 g (from total annual seafood consumption for the entire population) used as an input for the trade-based exposure calculations. The missing 7 g represents the species and/or origins not included in our analysis.

2.3.2 Seafood Diet Based on Direct Diet Survey

Most of the commonly consumed seafood species identified using the trade data were also found via the menuCH survey. Figure 2 shows proportions of seafood commodities most consumed in Switzerland according to the survey compared with those estimated using trade data. Refer to Appendix A, Table 5 for a complete list of seafood species with their daily consumption and proportion of diet for the survey-based diet and Appendix A, Table 6 for the trade-based diet.

Although the annual average statistics-based seafood consumption (23 g) and 24-h recall survey-based seafood consumption (40 g) differ in total amount, a comparison of the seafood diet structure shows strong similarities in the proportions occupied by various seafood species. As anticipated according to the trade-data-based diet, salmon was the most consumed fish in the country. Our results show that in the absence of available dietary data for a population, widely available food import data and national production statistics can serve as effective tools for constructing an estimated diet.

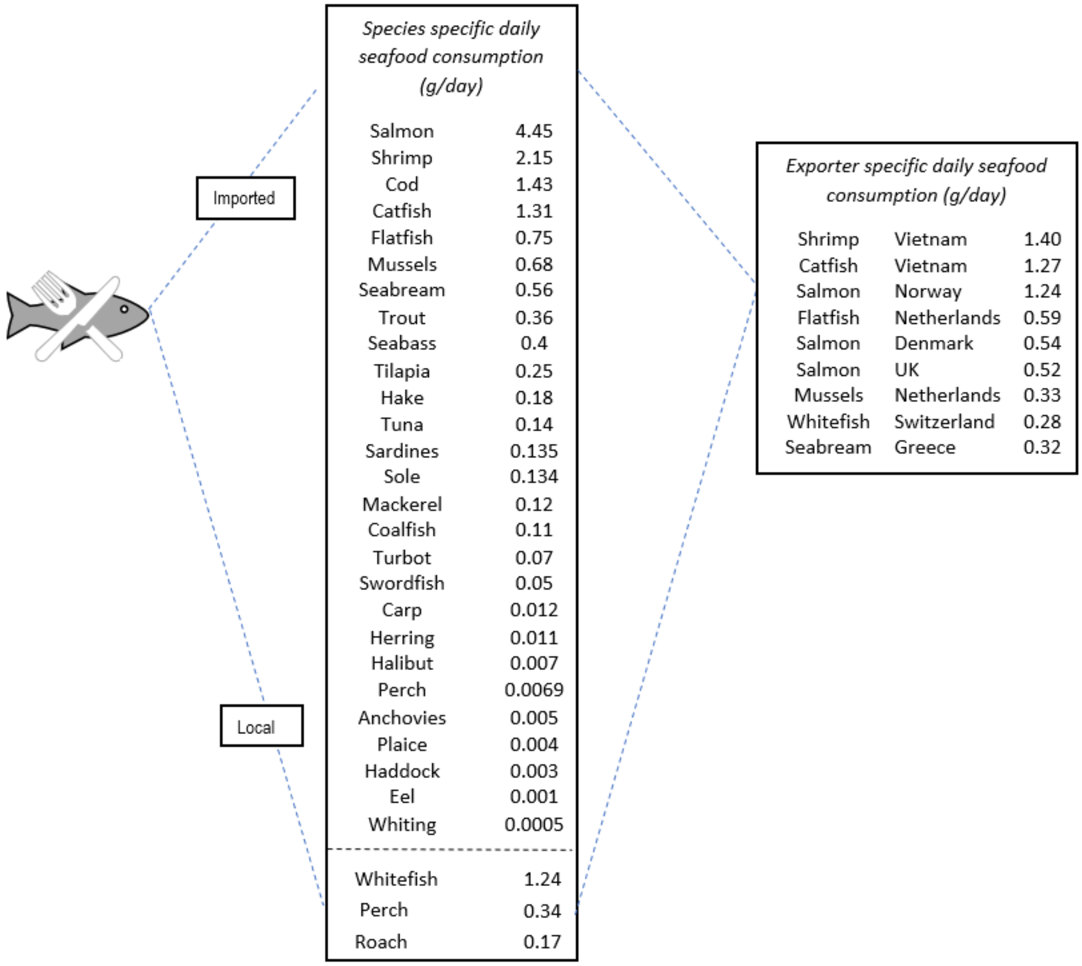


Figure 1: Species- and origin-specific seafood consumption in Switzerland based on international trade and domestic catch data.

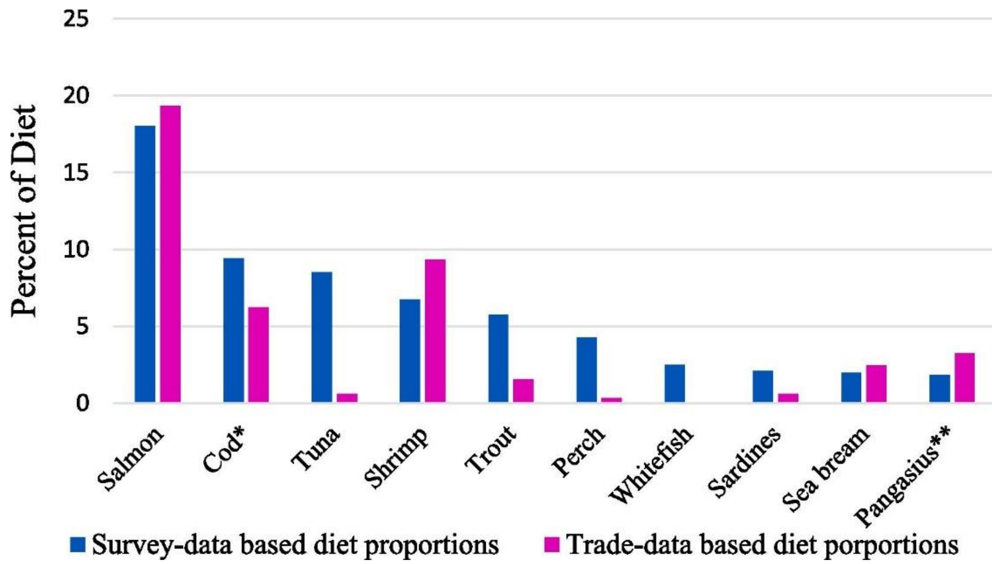


Figure 2: Proportion of most consumed seafood species based on the dietary survey (blue bars) compared to proportions based on trade data and local production (pink bars).

*Cod also includes Alaska pollock and Gadiformes. **UN Comtrade Database reports pangasius within the catfish category.

2.3.3 Input Data for Exposure Analysis

Table 3 shows the list of selected fish (imported and domestic) and the mean ΣPBDE (ng/g wet weight) reported in them by origin. Table 3 also provides the lipid-normalized ΣPBDE concentrations used for species substitutions. No species- and region-specific data were available for swordfish from Sri Lanka and perch from Vietnam, so they were not included in final exposure calculations.

Table 3: Species–origin combinations and ΣPBDE data used as input for analysis.

Seafood Species	Top exporters	Origin-species source for PBDE data used[a]	Lipid normalized ΣPBDE[b]	ΣPBDE[c]	Lipid % (reference)
Salmon	Norway	Norway- Salmon	7.44	2.50	33.6(81)
	Denmark	Belgium-Salmon	12.12	1.58	13(83)
	UK	Belgium-Salmon	12.12	1.58	13(83)
Shrimp/prawn	Vietnam	Vietnam-Shrimp	1930.77	25.10	1.3(83)
	Bangladesh	China-Shrimp*	8.51	0.11	1.3(88)
	Belgium	Belgium-Shrimp	4.69	0.06	1.3(83)
Catfish	Vietnam	Vietnam-Catfish	0.77	0.03	3.8(99)
	Netherlands	Netherlands-Herring	28.29	4.81	17(89)
	Italy	Spain- Sardines	10.00	0.71	7.1(83)
Flatfish	Netherlands	Netherland- Sole	44.00	0.44	1(89)
	Poland	Netherland- Sole	44.00	0.44	
	Germany	Netherland- Sole	44.00	0.44	
Mussels	Netherlands	Netherlands- Mussels	61.00	1.12	2(89)
	France	Spain-Mussels	12.49	0.35	2.8(91)
	Italy	Italy- Mussels	243.5	32.16	13.2 (100)
Gadiformes	Iceland	Norway- Salmon	7.44	2.50	33.6(81)
	France	Spain- Swordfish	13.81	0.98	7 (101)
	Denmark	Belgium- Salmon	12.12	1.58	13 (83)
Cod	China	China- Tilapia	0.40	0.03	7.3(102)
	Portugal	Spain- Swordfish	13.81	0.98	7 (101)
	Denmark	Central North Sea- Cod	107	0.385	0.36(93)
Seabream	Greece	Greece- Seabream	179.00	4.78	2.6(93)
	France	Greece- Seabream	179.00	4.78	
	Italy	Greece- Seabream	179.00	4.78	
Trout	Italy	Italy- Trout	13.32	0.41	3.1(83)
	France	Italy- Trout	13.32	0.41	
	Germany	Belgium- Trout	8.71	0.27	
Seabass	France	Mediterranean Sea- Seabass	28	1.70	6 (103)
	Italy	Mediterranean Sea- Seabass	28	1.70	
	Greece	Mediterranean Sea- Seabass	28	1.70	
Tilapia	Vietnam	Indonesia- Tilapia	0.31	0.02	7.3(102)
	China	China-Tilapia	0.018	0.03	7.3(102)
	Indonesia	Indonesia- Tilapia	0.31	0.02	7.3(102)
Hake	South Africa	Spain-Hake	31.59	0.22	0.7(104)
	Portugal	Spain- Hake	31.59	0.22	

	Germany	European market- Cod	107	0.385	0.36(93)
Alaska Pollock	China	China- Tilapia	0.27	0.02	7.3(102)
	Germany	European market- Cod	107	0.385	0.36(93)
	Denmark	European market- Cod	107	0.385	
Tuna	Vietnam	Japan- Tuna	1.89	0.02	1.1(86)
	Netherlands	Netherlands- Tuna	1.00	0.01	1(89)
	UK	Netherlands- Tuna	1.00	0.01	1(89)
Sardines	Portugal	Spain- Sardines	10.00	0.71	7.1(83)
	France	Spain- Sardines	10.00	0.71	
	Spain	Spain- Sardines	10.00	0.71	
Sole	Netherlands	Netherlands- Sole	44.00	0.44	1(89)
	France	Netherlands- Sole	44.00	0.44	
	UK	Netherlands- Sole	44.00	0.44	
Mackerel	Spain	Spain- Mackerel	7.49	1.12	15(96)
	Portugal	Spain- Mackerel	7.49	1.12	
	Netherlands	Netherlands- Mackerel	10.45	1.15	11(89)
Coalfish	Germany	Netherlands-Coalfish	41.00	0.41	1(89)
	China	China- Tilapia	0.40	0.03	7.3(102)
	Poland	Netherlands-Coalfish	41.00	0.41	1(89)
Turbots	Netherlands	Netherlands- Sole	44.00	0.44	1(89)
	Spain	Netherlands- Sole	44.00	0.44	
	France	Netherlands- Sole	44.00	0.44	
Swordfish	Sri Lanka	Data unavailable			
	Italy	Spain- Swordfish	13.81	0.98	7(101)
	France	Spain- Swordfish	13.81	0.98	
Perch	Netherlands	Netherlands- Herring	28.29	4.81	17(89)
	Germany	Netherlands- Herring	28.29	4.81	
	Indonesia	Vietnam- Perch	160.00	5.09	3.18(54)
	Domestic	Netherlands- Herring	26.72	4.81	17(89)
Whitefish	Domestic	Switzerland- Whitefish	103.45	4.50	4.3(75)
Roach	Domestic	Netherlands- Herring	28.29	4.81	17(89)

2.3.4 PBDE Exposure Calculations

2.3.4.1 Trade-Based Approach

Calculated PBDE exposures from the trade-based diet are shown in Table 4. The table shows the top 10 exposure values for imported or domestic fish and their origins (for a complete list see Appendix A, Table 8), indicating that shrimp imported from Vietnam contributes the most to PBDE exposure in the Swiss population (75% of the total exposures), congruent with the fact that it is exported in largest quantities. This is contrary to exposures as low as 0.004 ng/kg bw/day from Vietnamese catfish which, even after being the second-highest exported quantity, contributes less than many other seafood commodities (Appendix A, Table 9) due to low reported PBDE concentrations. European exporters were also found to have major contributions to PBDE exposures, as they are among the largest exporters of seafood to Switzerland. It is notable that domestic whitefish is also among the highest contributors to exposures contributing 3 percent to the total exposure estimates. Tilapia from Indonesia, sole from UK, and tuna from Vietnam and the UK were found to have the lowest species- and origin-specific PBDE contributions (Appendix A, Table 9).

Table 4: Origin – Specific PBDE Exposures based on Trade Data.

Fish Type	Top Exporters	Percent of Diet	PBDE Exposure (ng/kg bw/ day)
Shrimp/prawn	Vietnam	6.12	0.4914
Salmon	Norway	5.37	0.0306
Seabream	Greece	1.41	0.0216
Whitefish	Domestic	1.24	0.0178
Salmon	Denmark	2.35	0.0119
Salmon	UK	2.30	0.0116
Seabream	France	0.40	0.0063
Gadiformes	Iceland	1.09	0.0062
Seabream	Italy	0.35	0.0054
Mussels	Netherlands	1.45	0.0052

2.3.4.2 Survey-Based Approach

The PBDE exposures estimated across the surveyed fish consumers in Switzerland ranged between 0.011and 43.42 ng/kg bw/day (Figure 3). The median exposure (50th percentile) is 0.68 ng/kg bw/day. In

comparison, the calculated origin-specific trade-data based exposure is 0.65 ng/kg bw/day, surprisingly close to this value. This suggests the trade data are in fact a good proxy for the average exposure. We also find that the 95th percentile of the surveyed Swiss population is exposed to PBDE levels as high as 8.5 ng/kg bw/day. The analysis of survey data thus allows us to capture exposures of the more at-risk sectors of the population.

Species-specific but not origin-specific PBDE exposures were estimated to be 0.15 ng/kg bw/day using trade data. One reason for this low number is the fact that when we average PBDE concentrations across all origins, the overall PBDE concentration is reduced. To illustrate, Figure 4 shows the PBDE concentrations reported globally in salmon, shrimp and mussels, as well as their geometric means. Figure 4 also highlights the PBDEs that were used in our analysis. For instance, origin-based exposure estimates for salmon only account for Norway and Belgium, with individual values of 1783 pg/kg bw/day and 1580 ng/kg bw/day respectively. On the other hand, total trade-based estimates for salmon account for the average PBDE level of 985 ng/kg bw/day across Norway, Belgium, Chile, USA, Japan and Spain. We could therefore conclude that quantifying exposures according to origins gives us a more realistic understanding of a particular community's risk from PBDE exposure.

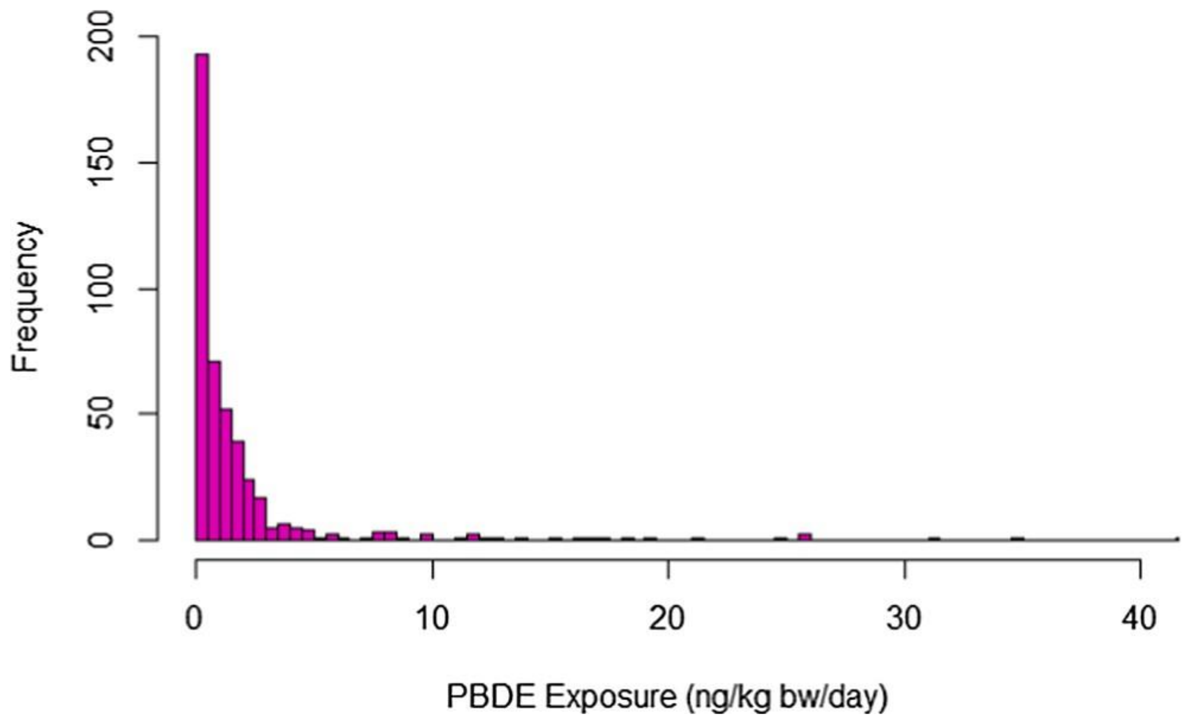


Figure 3: PBDE exposure range across fish consumers in Switzerland.

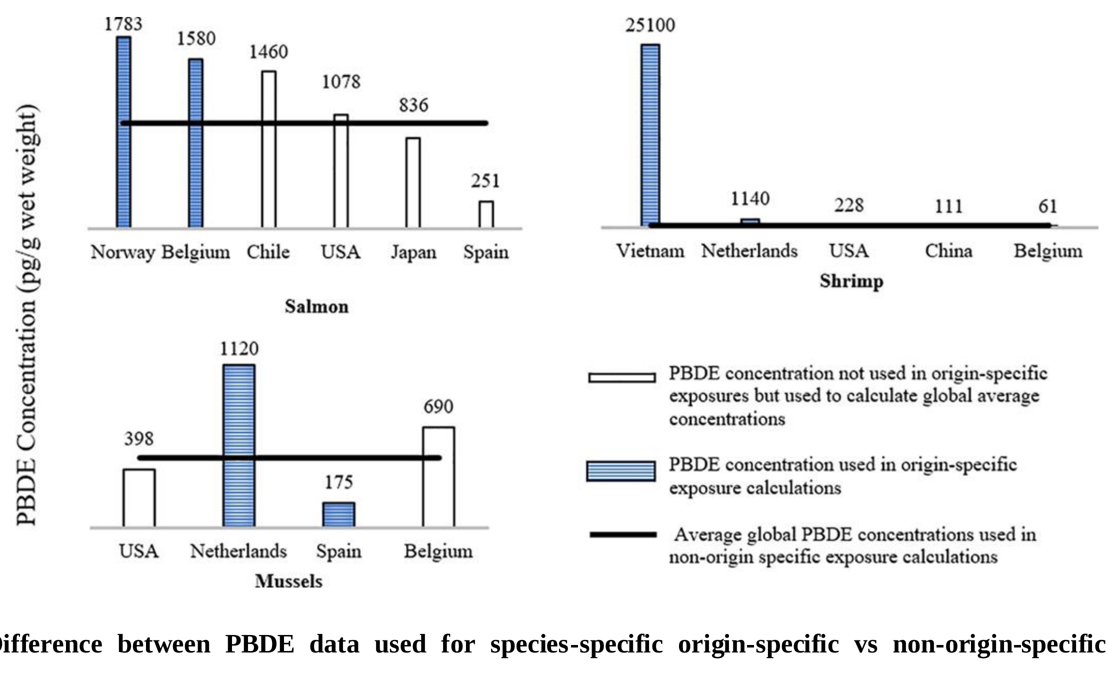


Figure 4: Difference between PBDE data used for species-specific origin-specific vs non-origin-specific exposures.

2.3.4.3 Comparison of Trade-Based and Survey-Based Approaches

Finally, we compare PBDE exposures by seafood species (irrespective of origin) based on geometric means of the global PBDE concentrations using both trade-based and survey-based diets. Table 5 shows the calculated PBDE intakes (top 10 exposures only based on trade-based diet and the corresponding exposures for the survey-based diet; refer to Appendix A, Tables 7 and 8 for a complete list). Salmon, perch, shrimp, trout and whitefish appear to be the most contaminated species for both the trade-based and survey-based diets.

The high exposure in the survey-based diet is driven by higher amounts of seafood eaten by some consumers that pushes up the average exposure from each species. This highlights a potential pitfall of using general annual statistics, since diets vary within populations and hence the risk of PBDE exposure may increase for groups that eat more trout, shrimp, perch or salmon (all having higher PBDE exposures) or have above average daily fish consumption. This was also illustrated by the distribution of PBDE exposures in survey respondents (Figure 4). However, all the exposures were found to be lower than the RfD range of 100 ng/kg bw/day to 7000 ng/kg bw/day.

Table 5: Species-specific trade-based diet versus survey-based diet PBDE exposures.

Seafood Species	Trade-based PBDE Exposure (ng/kg bw/day)	Survey-based PBDE Exposure (ng/kg bw/day)
Salmon	0.0612	0.0986
Whitefish	0.0181	0.0624
Perch	0.0109	0.221
Shrimp	0.0093	0.0116
Seabream	0.0089	0.0127
Flatfish	0.0076	0.0036
Trout	0.0067	0.0311
Catfish	0.0066	0.0036
Mussels	0.0045	0.0018
Roach	0.0033	Not reported as consumed

2.3.5 Origin Specific Scenarios

Table 6 shows PBDE exposures estimated for our three origin-specific scenarios. When considering the exporting e-waste source and sink countries selected for this analysis, seafood imports from Vietnam contribute most to PBDE exposure of the Swiss population. Although lower than the allowable reference dose range, these exposures surpass even the total PBDE exposure calculated using the top 3 exporters (0.65 ng/kg bw/day). The scenarios revealed that if Swiss adults consume only seafood imported from an e-waste sink country, as in the case of Vietnam, exposure can be as high as 7 ng/kg bw/day, which is very close to the PBDE exposure for high-risk consumers informed by the survey data (95th percentile, 8.5 ng/kg bw/day). Hence, origin- specific scenarios help provide us with a worst-case perspective on PBDE exposures.

The impact of Norwegian seafood alone was also found to be very close to the median PBDE exposures of 0.68 ng/kg bw/day as reported by the survey data. Norway recycles almost 80% of its e-waste in-state,[105] which reduces environmental impacts of e-waste exports, but also maintains the PBDEs in these products in circulation. Hence, the risk of exposures within Norway continues.

The consumption of only domestic whitefish (40 g per day) would lead to a lower PBDE exposure than consumption of seafood from Vietnam (20 g each of shrimp and catfish). This is consistent with the fact that Switzerland, like many other European nations, recycles only around 25% of its e-waste; the remainder is either untraced or sent out of state for disposal or processing.[105] Our analyses illustrate how choices around international seafood trade could result in increases or reductions in PBDE exposure, depending on the origins considered.

Table 6: Scenario-specific PBDE exposures for Swiss adults.

Parameters	Consumption of fish originating from e-waste source/ origin	Consumption of fish originating from e-waste dumping site/sink	Consumption of only local fish
Region	Norway	Vietnam	Switzerland
Species Included	Salmon and cod	Shrimp and catfish	Whitefish
∑PBDE concentration in selected seafood	Salmon (1.783); cod (0.028) ng/g wet weight	Shrimp (25.100); catfish (0.779) ng/g wet weight	4.50 ng/g wet weight
PBDE Exposure from consuming the scenario specific species	0.50 ng/kg bw/day	7.18 ng/kg bw/day	2.5 ng/kg bw/day

2.4 Conclusions

PBDE exposures as high as 8.5 ng/kg bw/day (for the 95th per- centile of the population) were found for the survey-based diet, where consumption amounts reflect more realistic averages for adult seafood consumers than the per capita consumption reported by national statistics. PBDE exposures from the trade-data based diet (origin-specific measures) were found to be very close to the median exposures of 0.68 ng/kg bw/day for the Swiss population, indicating that the per capita food balance derived from trade data is a good proxy for the average exposure, even though it could not account for the population variability captured by the survey data. However, in the absence of dietary survey data, the key species predicted using trade data were found to be consistent with those reported by Swiss consumers. Our analysis showed that tuna, sole and tilapia imported from the UK and Indonesia, were least contaminated with PBDEs. Vietnamese shrimp/prawn, Norwegian salmon and Swiss whitefish were found to be the most contaminated species–origin combinations. From the perspective of import-related exposures, our analysis identified Vietnam, Italy, Norway, and Greece as potential hot spots in the international seafood trade network, playing pivotal roles in bringing diet-borne PBDEs to Switzerland. Thus, if of sufficient quality, readily available trade data can provide important insights when specific data are lacking, and at the same time provides important information on the origin of foods.

3.0 Per- and Polyfluoroalkyl Substances (PFAS) Measured in Seafood from a Cross-Section of Retail Stores.

This chapter is reproduced in part from:

Bedi, M.; Sapozhnikova, Y.; Taylor R.; Ng, C. Per- and polyfluoroalkyl substances (PFAS) measured in seafood from a cross-section of retail stores: Does consumer behavior impact exposure? *Journal of Hazardous Materials (Under review)*

Seafood is a dominant source of human exposure to per- and polyfluoroalkyl substances (PFAS). Existing studies on foodborne PFAS exposure have focused on only a subset of these compounds and the impact of consumer choice (e.g., store, origin, husbandry) on exposure has not yet been explored. Here, we screen 33 legacy and emerging PFAS in 46 seafood samples from a cross-section of national and local stores. Low levels of 8 PFAS were measured in 74% of the samples, predominated by PFHxS (59%). Total PFAS ranged between 0.12 to 20 ng/g; highest levels measured in Estonia-sourced smelt. Highest median levels were of PFOA (0.84 ng/g) with elevated concentrations found in clams from China (2.4 ng/g). For an average consumption, exposures were below the tolerable weekly intakes (TWI) established by the European Food Safety Authority (EFSA). However, for more frequent consumption of flounder, catfish, and cod, exposures exceeded regulations which warrants the necessity of identifying vulnerable seafood-consuming populations. Consumer choices other than seafood species are less likely to impact exposures, highlighting the global nature of PFAS contamination. Because of the inclusion of

national grocery chains in our study, we expect the results be generalizable to the entire US population.

3.1 Introduction

Per- and polyfluorinated alkyl substances (PFAS) are synthetic compounds used for decades in consumer products and applications such as food packaging, non-stick cookware, firefighting foams, and stain and water repellent textiles.[2,3] The extremely strong perfluoroalkyl carbon moiety in their structure renders them resistant to environmental degradation, subsequently many PFAS are persistent.[28,106–108] Most PFAS are bioavailable and a number of them are known to bioaccumulate, and widespread in living organisms and the environment.[13,28,109,109–111]

Human exposure to PFAS is concerning because of known toxic health impacts such as immune suppression, thyroid disease, pregnancy-induced hypertension, and certain types of cancers.[28,112] Most of the adverse effects are associated with the long-chain perfluoroalkyl acids (PFAAs) containing 6 or more carbon atoms, including perfluorooctane sulfonic acid (PFOS) and perfluorooctanoic acid (PFOA), which were voluntarily withdrawn by industry under the USEPA Stewardship agreement.[113–115] Despite increasing global regulations on PFAS use, human biomonitoring studies have demonstrated widespread exposure to legacy PFAS.[112] Moreover, the introduction of replacement compounds such as short-chain PFAS is a common practice, and newer emerging PFAS are increasingly detected.[116,117]

Fish and other seafood are often reported as a dominant non-occupational source of human exposure to PFAS.[13,28,112,118,119] Concurrently, health benefits of seafood, including reduced risks of heart disease and obesity, have been widely acknowledged in the US and globally.[10,12]

Increasing consumption rates[120] have led to a subsequent proliferation of products on the market sourced from across the world. These products include both farm-raised and wild-caught seafood and, increasingly, can also include sustainability labelling, a designation that can be supported by various certification schemes (e.g. Marine Stewardship Council, MSC, Blue Ocean Institute, and Monterey Bay Aquarium Seafood Watch, among others). However, these labels can be problematic in not providing a holistic picture of fishery health and impact on ecosystems.[121] Moreover, a critical factor that remains largely unknown is whether different consumption patterns translate to differences in chemical exposures. Also, from a consumers' perspective, data pertaining to pollutant load based on seafood origins and supply chains are limited.

PFAS concentrations in edible seafood within the US seafood supply have been previously reported. In a recent study conducted in Washington, DC, 81 seafood samples from retail stores were analyzed for 20 PFAS. The highest concentration for the sum of PFAS (23 ng/g) was detected in canned clams from Asia, with PFOA dominating the PFAS profile.[122] Ruffle et al. analyzed 26 compounds in 70 seafood samples purchased from grocery stores.[29] In their study, total PFAS ranged between 0.50 to 22 ng/g with highest detection in walleye (*Sander vitreus*) from Lake Erie. Fair et al. determined levels of 11 PFAS in 39 edible fish from 3 river sites in South Carolina and found total PFAS ranging between 6.2 and 24 ng/g with highest levels in spot (*Leiostomus xanthurus*), a common choice among the Gullah-Geechee African American community and other fishers of the sampled region.[123] The overall trend observed in these studies reflects more frequent and higher detections of PFOS, PFOA, and PFUnDA with low or non-detectable levels of other PFAS in seafood. However, these datasets are limited to only a subset of PFAS particularly PFAAs and their precursors and few data exist for other compounds including emerging chemicals of concerns. Additionally, most studies focused on investigating PFAS occurrences in seafood without exploring the impact of seafood choices from a consumer' point of view.

The objectives of the present study were (1) to provide more data on the prevalence of PFAS in seafood to better understand the role of diet in PFAS exposure, (2) to use concentrations measured in samples to build scenario-based exposure estimates, and (3) to investigate if customer choices impact dietary exposures. PFAS levels in seafood are not regulated at the federal level in the US. We therefore referred to TWI of 4.4 ng/kg bw/week for Σ_4PFAS (PFOA, PFNA, PFHxS and PFOS) established by EFSA as the threshold value to assess potential risks associated with seafood consumption.[124]

3.2 Methods

3.2.1 Sample Preparation

A total of 46 samples consisting of 31 fish and 15 shellfish were purchased from grocery stores in Pittsburgh from January 2022 to April 2022: Salmon (Atlantic, Pacific, pink), cod (Alaskan, Pacific), tilapia, seabass, trout, yellowfin tuna, swai, smelt, flounder, perch, catfish, mahi-mahi, haddock, Alaska pollock, swordfish, mackerel, shrimp, crab, mussels, scallops, and clams (Appendix B, Table 10). These were the most commonly sold fish/shellfish found at local stores and were sourced from a variety of geographical origins. Fish fillet was primarily targeted so that the sample represented what people eat. Seafood samples were cleaned to remove any extraneous tissue such as skin, scales, fins, and tail and aliquots of ~25 g each were homogenized using a Robot Coupe RSI 2YI (Ridgeland, MS, USA) blender with dry ice and stored at -20˚C until analysis.

3.2.2 Materials

We monitored 33 PFAS including long and short-chain perfluoroalkane sulfonic acids (PFSAs) and perfluoroalkyl carboxylic acids (PFCAs), one perfluoroalkyl ether acid- HFPO-DA/GenX, three polyfluoroalkyl ether acids: ADONA, F53B major and minor, as well as several so-called precursor compounds (sulfonamides and fluorotelomers; see Table 7 for details). A 30-compound and a 4-compound mixture of PFAS standards from Wellington Laboratories (Guelph, Ontario, Canada) were combined to create a 500 ng/mL stock solution in methanol (MeOH) (Fisher Scientific, Pittsburgh, PA, USA). Twenty isotopically-labeled internal standards were also purchased from Wellington Laboratories and prepared as a 100 ng/mL stock solution in MeOH : d3NMeFOSAA, d5NEtFOSAA, M24:2FTS, M26:2FTS, M28:2FTS, M2PFDoA, M2PFTeA, M3HFPODA, M3PFBS, M3PFHxS, M4PFBA, M4PFHpA, M5PFHxA, M5PFPeA, M6PFDA, M7PFUdA, M8FOSA, M8PFOA, M8PFOS, M9PFNA. HPLC-grade water was purchased from Fisher Scientific while deionized water (18.2 MΩ-cm) was prepared in the lab using a Barnstead/Thermolyne (Dubuque, IA, USA) E-pure system.

Table 7: PFAS analyzed in seafood samples.

Compound	Acronym	# Carbon
Long-chain PFSAs		
Perfluorohexanesulfonic acid	PFHxS	6
Perfluoroheptanesulfonic acid	PFHpS	7
Perfluorooctanesulfonic acid	PFOS	8
Perfluorononane sulfonic acid	PFNS	9
Perfluorodecanesulfonic acid	PFDS	10
Short-chain PFSAs		
Perfluorobutanesulfonic acid	PFBS	4
Perfluoropentanesulfonic acid	PFPeS	5
Long-chain PFCAs		
Perfluorooctanoic acid	PFOA	8
Perfluorononanoic acid	PFNA	9
Perfluorodecanoic acid	PFDA	10
Perfluoroundecanoic acid	PFUnDA	11

Perfluorododecanoic acid	PFDoA	12
Perflurotridecanoic acid	PFTrDA	13
Perfluorotetradecanoic acid	PFTeA	14
Short-chain PFCAs		
Perfluoropentanoic acid	PFPeA	4
Perfluorohexanoic acid	PFHxA	5
Perfluoroheptanoic acid	PFHpA	6
Perfluoroalkyl ether carboxylic acid (PFECAs)		
Perfluoro-3-methoxypropanoic acid	PFMPA	4
Nonafluoro-3,6-dioxaheptanoic acid	NFDHA	5
Perfluoro (2-ethoxyethane) sulphonic acid	PFEESA	4
Perfluoro-4-methoxybutanoic acid	PFMBA	5
Hexafluoropropylene oxide dimer acid	HFPO-DA/Gen-X	6
Precursors		
4:2 fluorotelomer sulfonate	4:2 FTS	6
6:2 fluorotelomer sulfonate	6:2 FTS	8
8:2 fluorotelomer sulfonate	8:2 FTS	10
Perfluorobutyl sulfonamide	FBSA	4
Perfluorooctane sulfonamide	FOSA	8
Perfluorohexane sulfonamide	FHxSA	6
n-methyl perfluorooctane sulfonamidoacetic acid	NMeFOSAA	11
n-ethyl perfluorooctane sulfonamidoacetic acid	NEtFOSAA	12
Polyfluoroalkyl ether sulfonic acid (PFESAs)		
9-chlorohexadecafluoro-3-oxanone-1-sulfonic acid	9Cl-PF3ONS/ F 53B major/ 6:2 Cl-PFAES	8
11-chloroeicosafluoro-3-oxaundecane-1 sulfonic acid	11Cl-PF3OUS/ F 53B minor/ 8:2 Cl-PFAES	10
Polyfluoroalkyl ether carboxylic acid (PFECAs)		
h-perfluoro-3-[(3-methoxy-propoxy) propanoic acid	ADONA	7

3.2.3 PFAS Measurement

PFAS analysis was performed based on the quick, easy, cheap, effective, rugged, safe, efficient, and robust (QuEChERSER) extraction protocol previously reported.[125,126] This highly versatile protocol can be used to screen for a wide suite of chemicals with ultra-high performance liquid chromatography coupled to tandem mass spectrometry (UHPLC-MS/MS) and to high-resolution MS (HRMS), plus to low-pressure gas chromatography-tandem mass spectrometry (LPGC-MS/MS) for analysis of veterinary drugs, pesticides, PFAS and other environmental contaminants. In this work, which is a subset of a larger study, we only report the extraction protocol for PFAS,[127] in which 2.0 $\pm$ 0.1 g of sample was weighed into a 15 mL polypropylene tube and spiked with 40 µL of a 100 ng/mL internal standard mixture. Next, 10 mL acetonitrile/ water (4:1, v/v) was added to the tubes and shaken for 10 mins at 80% setting and maximum pulsation using a platform shaker (Glas-Col, Terre Haute, IN, USA), followed by centrifugation for 3 mins at 3711 relative centrifugal force (rcf) at room temperature. 1 mL of this extract was transferred to 2 mL polypropylene tubes and evaporated to ~0.2 mL under N_2 flow. The remaining extract was reconstituted to 0.4 mL using methanol. Following a brief vortex, tubes were ultracentrifuged for 5 mins at 12500 rcf at 4˚C and transferred into polypropylene autosampler vials for PFAS analysis.

PFAS analysis was performed using a previously reported method[127] using a Waters Acquity LC System coupled with a Q-Exactive Plus Hybrid Quadrupole-Orbitrap™ MS (Thermo Fisher Scientific, Bremen, Germany) and SCIEX 6500 QTRAP™ MS/MS system (Foster City, CA, USA). All solvent tubing on the LC was replaced with PEEK and a delay column was installed to separate remaining PFAS contamination in the system from the samples. Chromatographic separation was achieved over 15 min with 95:5 Water: MeOH (A) and MeOH (B) mobile phases containing 2 mM ammonium acetate. For HRMS, MS source settings were set to −2500 V spray voltage, 300 °C capillary temperature, 40 sheath gas, 10 auxiliary gas, 250 °C auxiliary gas temperature, and radio frequency of 50 for the S-lens RF. The mass spectrometer was operated in full-scan negative ionization mode (150−1000 *m/z*) at 70,000 resolution and automatic gain control at 3 x 10^6. For triple quadrupole MS/MS, a scheduled multiple reaction monitoring (MRM) method with a 30 s MRM window and target scan time 0.5 s was used. The source parameters were: curtain gas 40 au, ion spray voltage - 4500 V, source temperature 350˚C, ion source gas 1 and 2 at 50 au. The same LC system was used for both MS instruments connected through a contact closure.

For HRMS, data was first acquired in full scan (MS1) and processed with Trace Finder using retention time (t_R) and one precursor ion $[M-H]^-$ for identification and quantification of 33 PFAS. In total, 167 PFAS hits were recorded among 46 samples. Identification requirements for pesticides by HRMS in full scan requires a minimum of two ions with mass accuracy ≤ 5 ppm,[128] and a confirmation/fragment ion is (almost) always present and used to meet this criteria. However, PFAS compounds do not easily produce fragment ions in MS1, therefore, MS/MS (ddMS2) is used following MS1 analysis for their confirmation.[129] In our study we also used MS/MS triple quadrupole to confirm the identity and compare measured amounts of PFAS, where identification was based on t_R, two ion transitions and their ratios. Data produced by MS1 only *vs.* dd-MS2 and QQQ revealed 35% of detections were false positives when only using t_R and one precursor ion in full scan only mode. The measured amounts of confirmed PFAS by HRMS and QQQ were in excellent agreement.

3.2.4 Quality Assurance/Quality Control (QA/QC)

Reagent blank (1.6 mL water accounting for ~80% moisture content in fish), reagent spike (1.6 mL water + spike), two spike recovery fish samples, two duplicate extractions, and NIST

Standard Reference Materials (SRMs) 1947 and 1946 were used for QA/QC. Additionally, solvent blanks (methanol) were analyzed after every 10 injections, and after fortified samples to monitor for system contamination and/or carry over. A continuous calibration verification (CCV) standard of 1 ng/ml was injected at the start and end of the batch. Standards ranging from 0.05 ng/ml to 5 ng/ml (for 6:2 FTS, FBSA, FHxSA, FOSA, PFBS, PFDA, PFDS, PFHpA, PFHpS, PFHxA, PFHxS, PFMBA, PFMPA, PFNA, PFNS, PFOA, PFOS, PFPeA, PFPeS, and PFUdA), 0.1 ng/ml to 5 ng/ml (for PFDoA, PFTrDA, PFTeA, 8:2 FTS, and NFDHA) and 0.5 ng/ml to 5 ng/ml (for Gen-X, NMeFOSAA, and NEtFOSAA) were used to construct calibration curves with linear regression coefficients (r^2) > 0.98. The limit of quantification (lowest level of calibration in this case) was set between 0.1 and 1 ng/g (or ppb). No target analytes were detected above the LOQ in reagent blanks and solvent blanks. Experimental levels of PFOS in SRMs 1946 and 1947 were 1.5 ng/g and 5.9 ng/g wet weight, respectively, compared to the reference values of 2.2 ng/g and 5.9 ng/g wet weight.

3.2.5 Risk Assessment

We examined the risk of PFAS exposure based on per capita seafood consumption reported by Love et al. 2020, in which salmon, shrimp, tilapia, cod, catfish, crab, and flounder were identified as the top seafood species consumed in the United States.[130] Fish consumption (g/day) was translated into weekly PFAS exposures (ng/kg bw/week) for the sum of PFOA, PFOS, PFNA, and PFHxS using Equation 3.1:

$$\mathrm{EWI} = \left(\frac{\mathrm{Conc_{fish}} \times \mathrm{MS} \times \mathrm{MF}}{\mathrm{BW}}\right) \quad (3.1)$$

where, EWI is the estimated weekly intake in ng/kg bw/ week, $\mathrm{Conc_{fish}}$ is the total of PFOS, PFOA, PFHxS, and PFNA levels in seafood in ng/g, MS is the amount of seafood in the meal in g/meal, and MF is the meal frequency or number of meals per week. We calculate exposures for 1-3 seafood meals per week based on previously reported consumption frequencies.[123] Scenario-specific exposure estimates were calculated for (1) a low-exposure scenario representing an average seafood consumption of 18 g/day for both seafood consumers and non-consumers, and (2) a high-exposure scenario including only adult seafood consumers, defined as those reporting recent seafood consumption in a survey of U.S. consumers.[130] Estimated intake was compared with the TWI of 4.4 ng/ kg bw/week for the sum of PFOS, PFOA, PFHxS and PFNA established by EFSA.[124]

3.2.6 Statistical Analysis

Only the target compounds detected in at least one sample were included for further data analysis. Analyte concentrations that were below the quantification level were set at LOQ/2. Statistical analysis was performed using R.[131] To check if data conform to a normal distribution, a Shapiro-Wilk test was used, while Levene's test was used to check for homogeneity.[132] Non-parametric Mann- Whitney (Wilcoxon Rank Sum) tests were used to compare four groups of data: (1) fish vs shellfish, (2) farm raised vs wild caught, (3) comparison across stores (4) US vs internationally sourced. For comparisons, total PFAS concentrations (detects and non-detects) were used. All PFAS concentrations were log transformed to check for skewness.

3.3 Results

3.3.1 PFBS Found in Fish Reveals Contaminated Storage Bags

PFBS was the only compound detected in every seafood sample, with concentrations ranging from 0.3 to 342 ng/g. High PFBS concentrations were not expected in all samples since

PFBS is not bioaccumulative when compared with long-chain PFAS. The PFBS calibration curve was linear with $r^2 > 0.98$, calibration curve verifications were within 5% of the expected value, and spiked samples had near 100% recovery. We confirmed PFBS identity in fish samples with dd-MS2 by HRMS (Appendix B, Figure 3) and with 5 MRM transitions (299→80, 299→99, 299→119, 299→169, 299→219) and their ratios by MS/MS triple quadrupole. Since PFBS was not detected in the reagent blank, SRMs, or solvent blanks, we suspected samples may have been contaminated at some point between collection and extraction. Since all fish samples were stored in plastic food storage bags for ~ 3 months, we tested 3 plastic bags containing fish samples with lowest (0.3 ng/g), medium (44 ng/g) and highest (342 ng/g) PFBS levels measured in fish. Plastic bags were extracted using a recently developed protocol (Taylor, in preparation), with methanol using shaking and sonication. Reagent blanks and reagent spikes were included for quality control. PFBS was found in tested plastic storage bags, and just as in the case with fish samples, confirmed with dd-MS2 (Appendix B, Figure 4) and 5 MRM transitions and their ratios. Levels of PFBS found in the bags were similar, which may suggest that fish containing the highest levels of PFBS either had greater absorption from the bag or had a greater baseline level of PFBS present within the tissue.

We further tested two more samples of plastic storage bags: (1) this bag was used in the current study but not did not come in direct contact with seafood samples during any stage (designated as old), and (2) this plastic bag was not used in our study but is currently used in a PFAS dedicated lab (designated as new). We made sure that the piece of bag used for extraction was dye free and away from closure. We found average (n=3) PFBS concentration of 30.43 ng/g (SD=2.50 ng/g, RSD=8%) in the old bag. We also observed a significant difference in color of the extracts (Appendix B, Figure 5) and postulate the presence of PFBS in pigments used in the production of the older batch of bags or a potential cross-contamination during manufacturing. Although at lower concentration, PFBS was also detected in the newer batch of bags at average (n=3) concentration of 0.56 ng/g (SD=2.50 ng/g, RSD=29%). These findings prompted us to test other food storage bags (sandwich bags, zipper seal bags, freezer bags, snack bags) of different brands collected from local grocery stores and lab grade storage bags, and no PFBS was found in these bags. Overall, due to the external contamination from the bags, the starting level of PFBS in these samples cannot be confirmed. PFBS was therefore excluded from further comparison with other PFAS results.

3.3.2 PFAS Profile in Seafood

Of the 33 target analytes, 8 were detected above the detection limit in one or more samples, including 1 short-chain and 7 long-chain PFAAs (Appendix B, Table 11). ADONA, GenX, F 53B and PFAA precursors were not detected in any samples. As mentioned above, PFBS was found in plastic storage bags and hence was excluded from data analysis. PFHxS was most frequently detected in 59% of the seafood samples, followed by PFOA (13%), PFUnDA (11%), PFNA (11%), and PFOS (9%). With respect to detected levels, the PFAS profile was dominated by PFOA, with concentrations ranging between 0.12 and 2.40 ng/g (median concentration of 0.84 ng/g) (Figure 5). PFOS ranged between 0.20 and 0.80 ng/g (median concentration of 0.45 ng/g). Almost similar levels were observed for PFHxS and PFNA with median concentrations of 0.53 ng/g and 0.55 ng/g, respectively.

Of the 46 samples, 12 samples had no detectable levels of PFAS. Total detected PFAS ranged from 0.12 to 20 ng/g wet weight. The species-specific distribution shows that the highest PFAS levels were associated with bottom feeders (clams, crab, haddock, shrimp), followed by lean fish (flounder, catfish, cod) and then fatty fish (salmon, swordfish). Little or no PFAS were detected in some aquaculture species such as tilapia and trout (Figure 6). The origin-specific distribution revealed highest total PFAS levels detected in Estonia-sourced smelt (20 ng/g); PFNA dominated the PFAS profile at a concentration of 12 ng/g. Relatively high levels were also found in Canada-sourced clams (12 ng/g), and crab (3 ng/g) (Figures 7 and 8). In these samples, PFHxS (11 ng/g in clams and 3 ng/g in crab) dominated the PFAS profile. Highest levels of PFOA were found in China-sourced clams (~2 ng/g). We also studied the distribution of PFAS based on store categories (Figure 9).

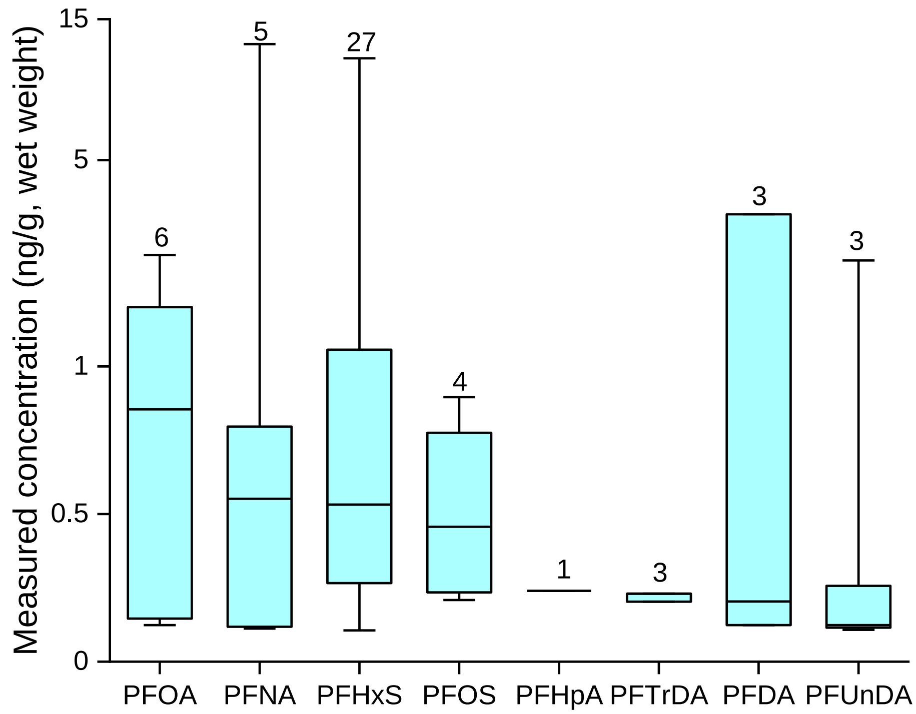


Figure 5: Measured PFAS concentrations (ng/g wet weight).

Only detected analytes are reported here. The box represents the 1st and 3rd quartile, solid line represents the median concentration, and the whiskers indicate minimum and maximum levels.

The number above each bar indicates the number of samples in which the specific analyte was detected, y-axis is log transformed.

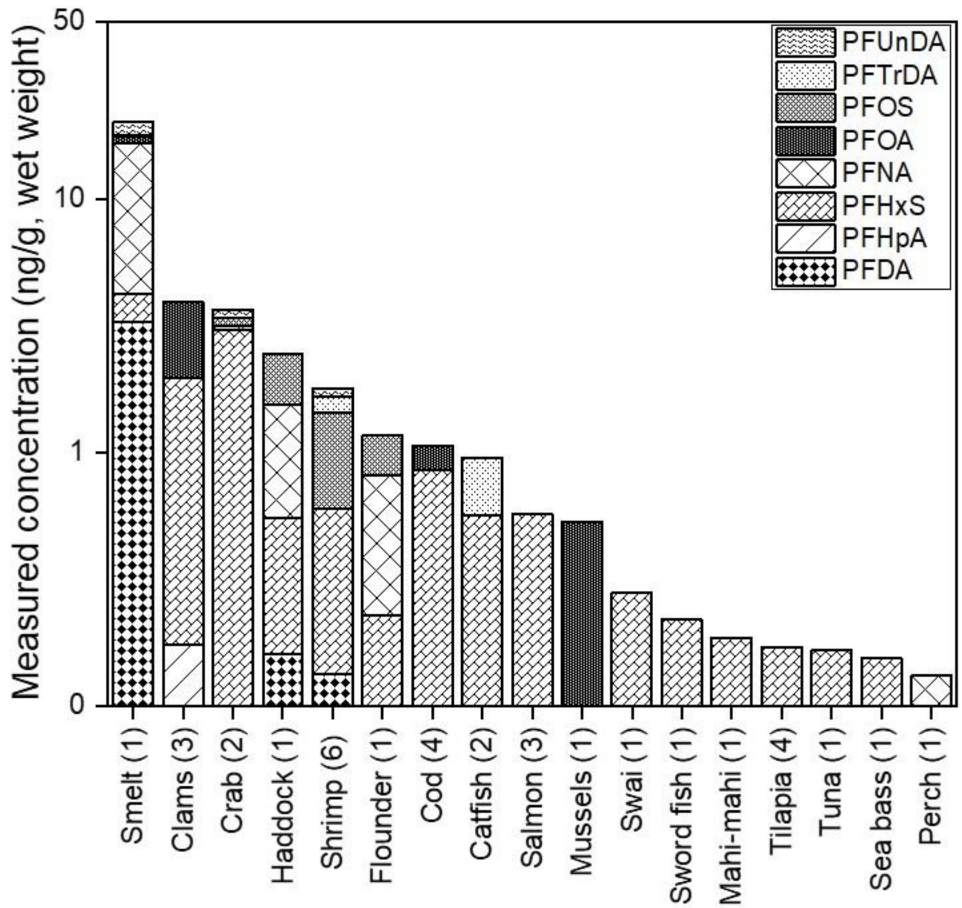


Figure 6: Distribution of PFAS in seafood.

The numbers in brackets next to seafood type on the x-axis labels represent the number of samples. In cases where more than one sample were analyzed for a seafood type, geometric mean concentrations were used for calculating seafood-specific distribution. Note the y axis is on a log scale.

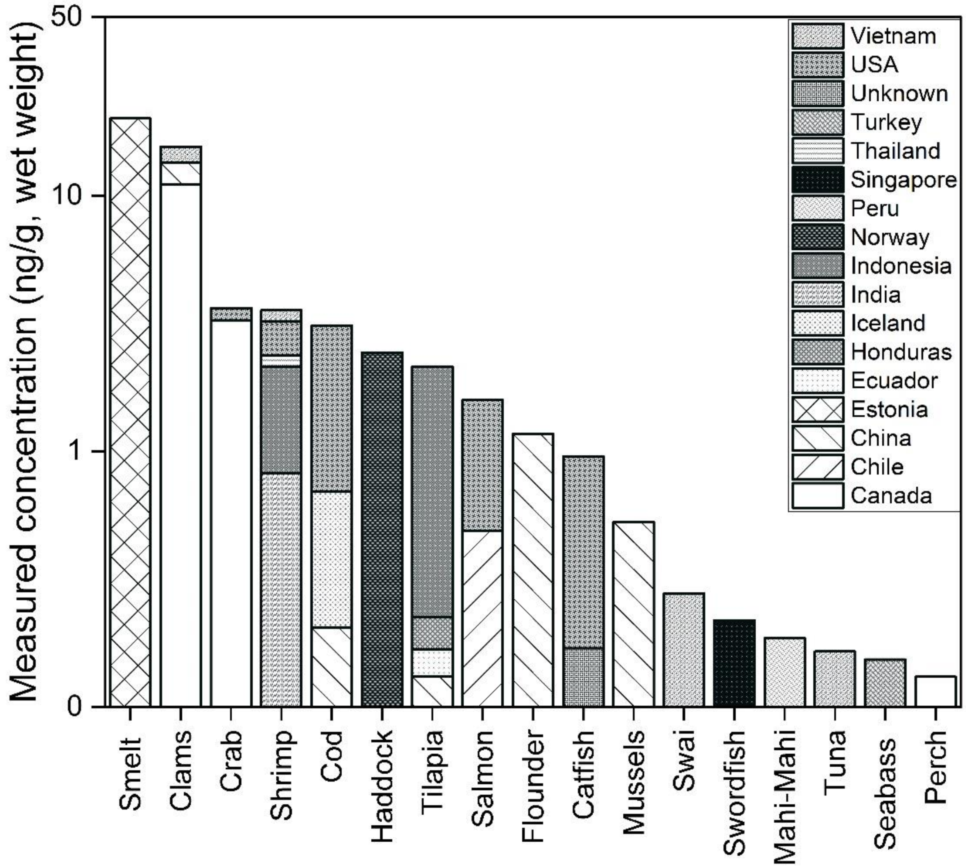


Figure 7: Seafood type-specific total PFAS concentration distributed by origin.

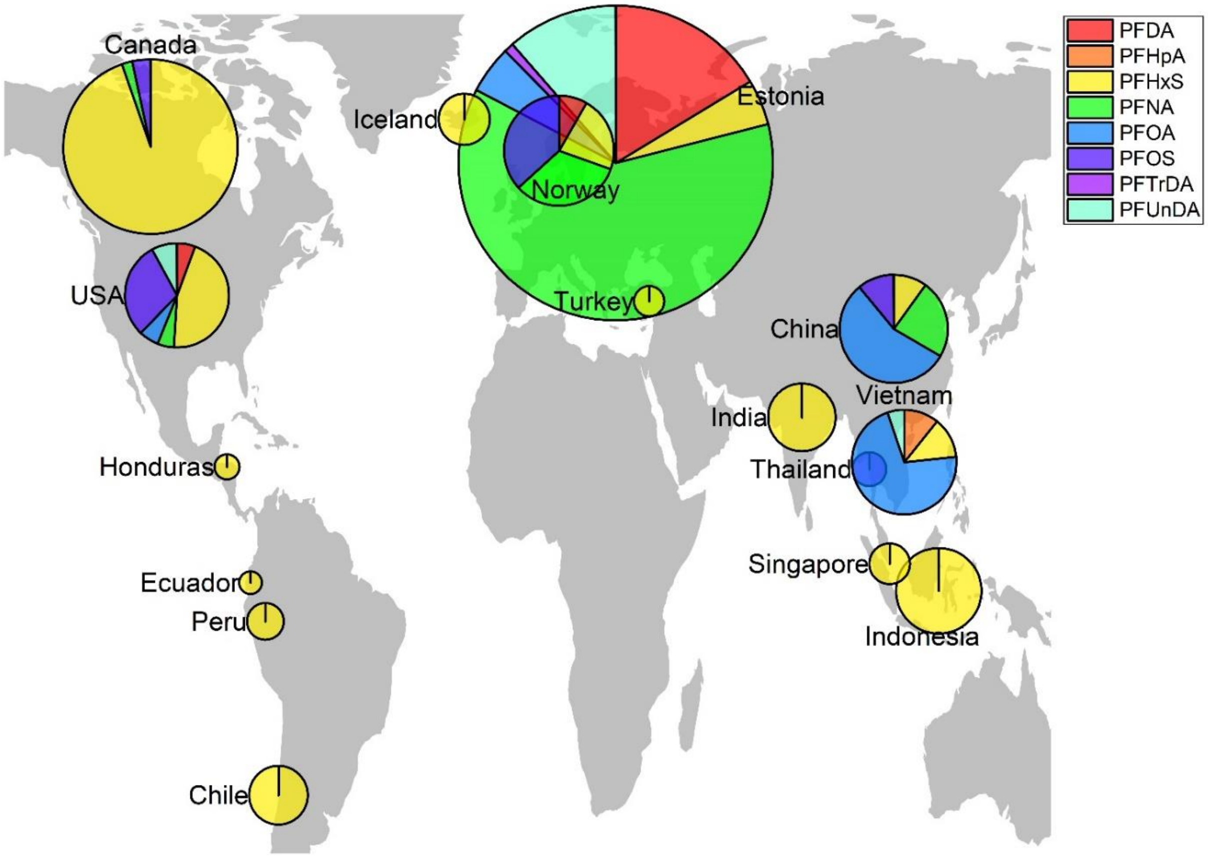


Figure 8: Origin-specific PFAS distribution.

The size of the pie is directly proportional to the total PFAS concentrations detected in seafood from the respective country. In case more than one sample had the same origin, geometric mean concentrations were used for calculating origin-specific distributions. Note the y-axis is log transformed.

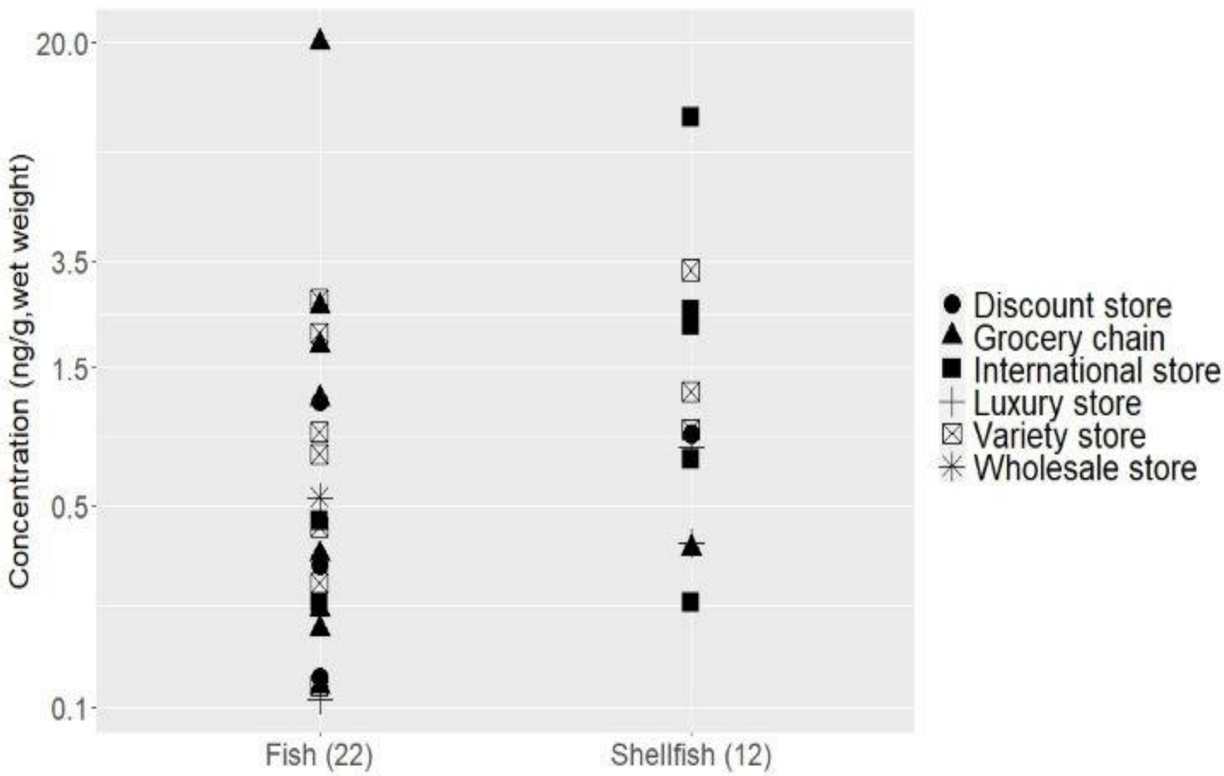


Figure 9: Store-specific PFAS distribution.

The number in the brackets on the x-axis show the number of samples in which PFAS were detected. Note that the y-axis is log transformed.

Seafood samples in which at least one PFAS was detected were divided into two groups: fish and shellfish. Median PFAS levels in shellfish (0.90 ng/g) were higher than in fish (0.44 ng/g). PFAS were detected at higher levels in fish purchased from national grocery chains and shellfish purchased from international stores. In the following sections, we discuss whether the observed variations across origins and stores are statistically significant.

3.3.3 Risk Assessment

We estimated weekly intake of Σ_4PFAS — PFOS, PFOA, PFHxS, and PFNA — for the top 7 consumed seafoods (tilapia, catfish, cod, flounder, salmon, crab, and shrimp) according to NHANES dietary surveys[130] (Figure 10, Appendix B, Tables 12 and 13). Estimated intakes for low and high exposure scenarios from a single meal/week ranged between 0.10 – 0.30 and 0.45 – 2.25 ng/kg bw/week, respectively.

For the low exposure scenario, considering an average seafood consumption of 18 g/meal, estimated PFAS intake was several times lower than the threshold established by EFSA. However, some seafood consumers may consume a relatively larger portion size than what an average adult consumes in the US when distributed across all meals. Considering this as the worst-case or high exposure scenario, one or more meals of flounder per week could lead to exposures above the threshold. Likewise, 3 or more meals/week each of catfish or cod will lead to exposures above the limit. For salmon, 4 or more meals/week would lead to PFAS exposure above the TWI. Shrimp was found to be the safest among all tested seafood types with a detectable PFAS concentration, needing at least 10 meals/week intake for exposures to reach the established limits. Note that the meals/week suggestions do not take into account any other contaminants that may be present. Geometric mean concentrations were used for number of samples > 1. Estimates are based on the sum of PFOA, PFNA, PFOS, and PFHxS. Non-detects were set at LOQ/2 (0.05 ng/g). The red dotted line is the TWI established by (4.4 ng/kg bw/week).

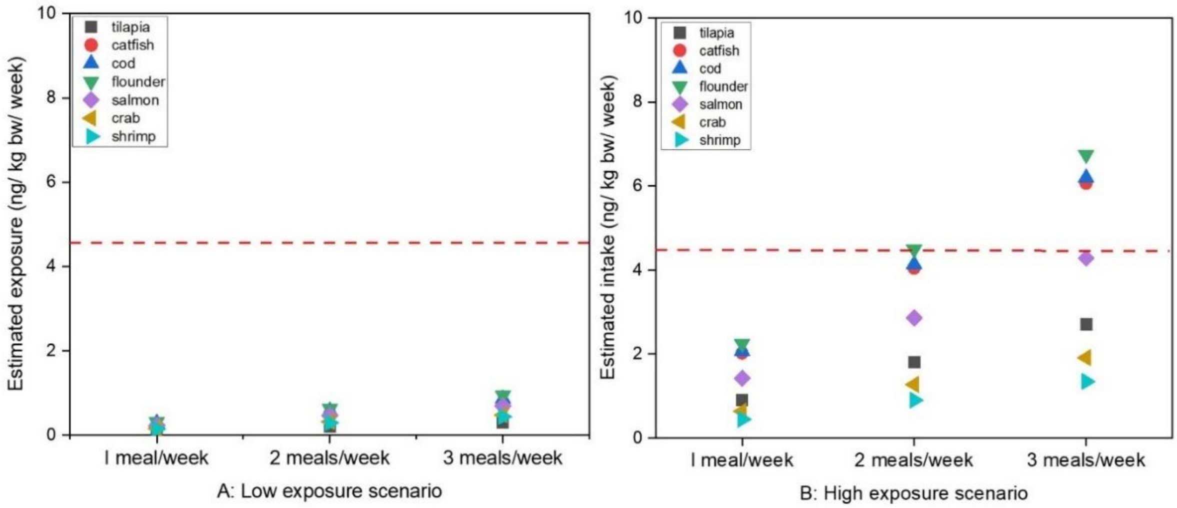


Figure 10:Estimated PFAS intake (ng/ kg bw/week) (A) low-exposure scenario and (B) high exposure scenario.

3.3.4 Impacts of Customer Choices

We compared total PFAS concentrations across four scenarios (1) fish and shellfish, (2) farm-raised and wild-caught, (3) among different stores, and (4) domestic and internationally-sourced, to investigate if customer preferences and seafood availability impact overall exposures. We first tested data to check if the assumptions of normal distribution and homogeneity of variance are met using Shapiro-Wilk and Levene's tests, respectively. The p-values for Shapiro-Wilk tests were frequently < 0.05, indicating that data were not normally distributed for most groups. All groups met the assumption of equal variance with p values >0.05. For group wise comparisons we used non-parametric Mann- Whitney (Wilcoxon Rank Sum) tests which does not require data to be normally distributed and dependent of each other.

We compared PFAS levels in seafood. The p-value for the Mann-Whitney test was > 0.05 (p-value= 0.12), indicating no statistical difference between the median PFAS concentrations in seafood. Further, the p-value for the Mann-Whitney test between farm-raised and wild-caught seafood was 0.11, indicating no statistical difference between median PFAS concentrations.

Mann-Whitney tests were also run to compare whether PFAS levels vary across stores to investigate if exposures might vary based on where one shops. We considered five store categories: (1) discount, (2) grocery, (3) variety, (4) international, and (5) luxury, and compared them pairwise. The p-values for all datasets were > 0.05, implying no statistical difference in median PFAS values across stores (Appendix B, Table 14). Finally, we investigated whether PFAS levels differ significantly between seafood sourced from the US and those with international origins. Here again, p-values for the Mann-Whitney test were > 0.05 (p-value= 0.35).

3.4 Discussion

We investigated PFAS levels in 46 seafood samples purchased from grocery stores in Pittsburgh, PA, USA. The sample set included farm-raised and wild-caught species originating from the US and internationally from 19 countries. A total of 33 PFAS including both legacy and emerging substances were analyzed, and measured concentrations were used to build exposure estimates for both low and high exposure scenarios. Furthermore, we investigate whether customer choices impact PFAS exposures.

Only 1 short chain and 7 long chain PFAAs were detected in these samples. PFBS was above detection limits in all samples, which was surprising and inconsistent with previous studies.[29,122,123,133–135] We confirmed the presence of PFBS using both HRMS and QQQ and found false-positive PFBS signal in seafood samples came from plastic food storage bags which were used to store samples. These findings prompted us to test other food storage bags of different brands collected from local grocery stores and lab grade storage bags, and no PFBS was found in these bags. Also, the extracts from these bags were clear confirming our hypothesis of possible PBFS contamination from pigments. PFBS is used in food contact materials and also as a replacement for PFOS substances.[136] A market survey from 2017 reported the increase of global manufacturing and consumption of PFBS from 2011 to 2015, mostly used as a surfactant.[137] PFBS is also a final degradation product of various PFBS-precursor compounds used in different applications.[138] Recently under EU REACH, PFBS along with Gen-X has been assigned the status of substance of very high concern.[139] We also found PFBS in other food packaging samples (Taylor, in preparation). It is generally thought that plastic food storage bags made of low-density polyethylene (LPDE) are not contaminated with PFAS. The recommendation resulting from our experiment is to avoid storing samples for PFAS analysis in plastic food storage bags, and to use polypropylene containers instead.

PFOS previously dominated detected PFAS in seafood.[29,123,133,140–144] However, inconsistent with these studies, PFHxS was the most highly detected PFAS in our samples; a comparatively lower detection was observed for PFOS. Following the phase-out of PFOS, shorter-chain alternatives including PFHxS have been used as replacements. This is also evident from the decreasing levels of PFOS in human serum, while no change and in some cases increasing levels have been reported for PFHxS.[145–149] The prevalence of PFHxS in human serum has also been previously reported to be associated with seafood consumption.[146,150,151] The higher detection of PFHxS in the current study is concerning since it has a long half-life in humans and can contribute significantly to overall body burdens of PFAS.[152]

For 12 of the 46 seafood samples, all 33 targeted PFAS were below the limit of detection, and overall, the majority of PFAS detections were at trace or low levels, which is consistent with the available US based studies.[29,122,123,134] PFOS and PFOA levels reported in our study are comparable to previous studies.[29,141,153] Particularly, elevated PFOA concentrations in wild Chinese clams was consistent with the latest studies.[122,154] The trend of comparatively higher levels of PFAS in bottom feeders, followed by lean fish and lowest levels in fatty fish and farmed seafood was also comparable with literature.[122] Higher levels in benthic organisms is most likely due to their ability to uptake PFAS from sediments.[155] Highest levels of PFAS were found in smelt sourced from Estonia, with a concentration of 20 ng/g. In agreement to our results, a study conducted in Finland reported the highest levels PFAS in smelt from the Baltic Sea when compared to other aquatic species.[142] In the Baltic study, median PFAS levels were 33 ng/g with highest contributions from PFOS (15 ng/g), PFNA (11 ng/g), and PFDA (3 ng/g). In our study, although PFOS was not detected in smelt, PFNA and PFDA had similar concentrations of 12 and 3 ng/g respectively.

For an average fish consumption of 18 g/meal, exposures were several orders of magnitude below the limits established by EFSA, suggesting selected seafood is unlikely to pose a risk to US consumers. However, this only holds true for the sum of specific PFAS established by EFSA; uncertainty remains about impacts associated with mixture exposures. Furthermore, the high-exposure scenario revealed that exposure may reach the TWI for certain populations. This highlights the need for understanding a community's dietary habits to identify vulnerable populations that are more likely to be exposed to higher levels of PFAS.

We did not find any evidence to support the hypothesis that shopping habits/choices impact exposures, which may alleviate concerns about disparities associated with location, accessibility, or affordability of certain seafoods. However, we do acknowledge that the large numbers of non-detects and smaller sample sizes within certain groups may have biased our hypothesis testing. Nonetheless, for certain seafood from specific origins such as Estonia-sourced smelt and China-sourced clams in which higher PFAS were detected in our study and previously reported as well, consumers may want to reduce their intake.

3.5 Conclusions

PFAS were measured in seafood samples purchased from a cross-section of grocery stores in Pittsburgh. Although the samples were collected in a single city, we included several national chains; as such, we expect these results can be to an extent generalized to the US population. Low levels of PFAS were detected in the majority of seafood samples. However, uncertainties persist around exposures from compound mixtures and chronic exposure. Therefore, continuous monitoring of seafood and complementary mixture toxicity studies would help improve the understanding of foodborne PFAS exposure, and the risks associated with it.

Exposure estimates based on average consumption rates and on a single meal/week were in compliance with the limits established by EFSA. However, risks associated with larger portions and more frequent consumption of seafood cannot be ruled out and warrant further research, specially to understand dietary habits of vulnerable populations (those who consume seafood more frequently than average consumers). From a seafood consumer's perspective, preference for a particular store, origin, or husbandry is unlikely to substantially impact exposures for these types of seafood. However, this also highlights that PFAS contamination is a global issue.

Chapter 4.0 Levels of Veterinary Drugs, Pesticides, and Environmental Pollutants in Seafood From Retail Stores in United States

This chapter is in preparation for submission to The Journal of Exposure Science and Environmental Epidemiology.

Bedi, M.; Sapozhnikova, Y.; Taylor R.; Ng, C. Levels of veterinary drugs, pesticides, and environmental pollutants in seafood from retail stores in United States *Journal of Exposure Science and* Environmental Epidemiology *(Under preparation).*

4.1 Introduction

Seafood, including fish and shellfish, is an integral part of a healthy diet, and a rich source of lean protein, omega-3 fatty acids, vitamins, and minerals.[10,11] Consumption of seafood has been associated with reduced cardiac deaths and obesity, and improved infant health. [10–12] However, fish intake may pose adverse health effects due to the presence of hazardous chemical residues. [1,13–15] While some chemicals such as veterinary drugs are intentionally introduced as medications to promote fish health,[156] others like pesticides and industrial chemicals enter aquatic ecosystems through environmental fate and transport, for example, waste disposal from chemical industries.[157] Human exposure to these chemicals has been linked to adverse effects on the reproductive, neurological, endocrine, developmental, and immunological systems,[5,16,156,158] and seafood specifically has been identified as a major exposure pathway for many of them. [159,160]

Fish can accumulate high levels of persistent organic pollutants (POPs), a class of ubiquitous toxic chemicals that are relatively resistant to environmental degradation.[143,159,161] In 1995, the Stockholm convention introduced a global ban on 12 POPs (popularly called the "dirty dozen") known for causing adverse impacts to human health and the environment.[162] Currently, the Stockholm Convention lists 30 POPs including pesticides, industrial chemicals, and their by-products.[163] Although chemicals on this list are eliminated or restricted for use in agriculture or industrial applications in most countries, a few continue to be used illegally, predominately in developing countries.[164] Many legacy organochlorine pesticides (OCPs) such as aldrin, chlordane, and the well-known dichlorodiphenyltrichloroethane (DDT) and its primary metabolite, dichlorodiphenyldichloroethane (DDE), have been found in edible fish and shellfish.[18–22] Legacy industrial chemicals which were once used in consumer products and applications such as polybrominated diphenyl ethers (PBDEs), polycyclic aromatic hydrocarbons (PAHs), and polychlorinated biphenyls (PCBs) have also been widely detected in seafood.[1,14,23–27]

Unlike pesticides and industrial chemicals, antibiotics are intentionally introduced into animal husbandry, including aquaculture, along with feed to reduce pathogens and promote growth. In the recent years, aquaculture has expanded rapidly to cater for increasing protein demand. In 2020, it accounted for 52% of the fish for human consumption, while China remained the major producer.[165] Intensification of agriculture can lead to infections and diseases, which are managed using veterinary drugs such as antibiotics.[166] However, indiscriminate use of antibiotics has been associated with the development of antibiotic resistance, a pressing public health problem according to the Centers for Disease Control and Prevention (CDC).[167] For this reason, many countries have restricted the use of certain antibiotics, and banned others for which no residues shall remain in animal tissues to ensure the consumers' safety. In the US, only the following antibiotics are approved for use in medicated feed: florfenicol, oxytetracycline dihydrate, sulfadimethoxine/ormetoprim, and sulfamerazine.[168] Even after imposing such regulations, many legacy veterinary drugs continue to be detected in seafood.[17,21,158,169,170]

Over the years, many legacy chemicals have been replaced by presumably safer alternatives. However, many of these replacement compounds are now regarded as chemicals of emerging concern, gaining attention due to findings that they may also be persistent and toxic. However, existing knowledge on levels of chemical residues in fish is focused primarily on legacy contaminants, and little is known about levels of emerging contaminants. The objective of the current study was to measure levels of both legacy and current use veterinary drugs, pesticides, and environmental contaminants (PBDEs, PAHs, and PCBs) in seafood to improve understanding of foodborne exposure to chemical contaminants. To complement this residue analysis, we performed scenario-specific risk assessments considering low- and high-frequency seafood consumption. We specifically focused on local populations such as recreational anglers who eat comparatively more seafood than other consumers and may be at a greater risk of exposure.[159]

4.2 Methods

4.2.1 Chemicals and Materials

Analytical standards for pesticides and veterinary drugs were received from the United States Environmental Protection Agency (U.S. EPA) National Pesticide Repository (Fort Meade, MD, USA.), Sigma-Aldrich (St. Louis, MO, USA.), Dr. Ehrenstorfer GmbH (Augsburg; Germany), ChemService (West Chester, PA, USA.), and LGC Standards (Manchester, NH, USA.). PCB congeners were obtained from AccuStandard (New Haven, CT, USA.). Standard solution mixtures were prepared at the following concentrations: pesticides at 13.3 µg/mL, except for stable organochlorine pesticides at 4.4 µg/mL; PAHs and PBDEs at 4.4 µg/mL; and PCBs at 1.3 µg/mL. For veterinary drugs, we performed an initial screening and identified 19 analytes in the samples based on 3 multiple reaction monitoring (MRM) transitions and retention time (t_R). The standard mixture of these analytes, at 4 µg/mL, was prepared and used for quantification. Isotopically labeled compounds used as internal and quality control (QC) standards were acquired from Cambridge Isotope Laboratories (Andover, MA, USA.), C/D/N Isotopes (Pointe-Claire, Quebec, Canada), AccuStandard, and Sigma-Aldrich and prepared as a 4 µg/mL stock solution for veterinary drug for analysis with LC and 4 µg/mL stock solution for pesticides and environmental contaminants for analysis with GC.

HPLC-grade organic solvents consisting of acetonitrile and methanol were purchased from Sigma-Aldrich and Fisher Scientific (Pittsburgh, PA, USA). HPLC-grade water was purchased from Fisher Scientific (Pittsburgh, PA, USA). Deionized water (18.2 MΩ cm) was prepared at the USDA laboratory using a Barnstead/Thermolyne (Dubuque, IA, USA) E-pure system. Salt-out partitioning was done using 15 mL polypropylene (PP) tubes containing 1.6 g of anhydrous $MgSO_4$ and 0.4 g NaCl from Agilent (Little Falls, DE, USA). Micro SPE cartridges containing 20 mg $MgSO_4$, 12 mg C18, 12 mg primary secondary amine (PSA), and 1 mg graphitized carbon black (GCB) were purchased from Archer Science (Lake Elmo, MN, USA).

4.2.2 Sample Collection

Overall, 46 seafood samples were collected from retail stores including national grocery chains in Pittsburgh, PA, USA from January 2022 through April 2022. The same set was also screened for PFAS, findings reported in *Bedi et al. 2023 (under review*) and included: catfish (n=2), clams (n=3), cod (n=4), crab (n=2), flounder (n=1), haddock (n=1), mackerel (n=2), mahi-mahi (n=1), mussels (n=2), perch (n=1), pollock (n=1), salmon (n=6), scallops (n=1), seabass (n=1), shrimp (n=7), smelt (n=1), swai (n=1), swordfish (n=1), tilapia (n=5), trout (n=1), and tuna (n=2). Sample selection was based on the availability at the time of survey and thus represents what consumers would typically buy. The samples originated from Canada, Chile, China, Estonia, Iceland, India, Indonesia, Norway, Peru, and 10 other regions worldwide. Appendix C, Table 15 provides further descriptions of the seafood products including point of origin, production method (farmed or wild-caught), and store type (discount, luxury, wholesale, variety, or grocery chain).

4.2.3 Sample Preparation

Samples were homogenized (~25 g aliquots) with dry ice using a Robot Coupe RSI 2YI blender (Ridgeland, MS, USA) and stored at -20˚C until analysis. Prior to homogenization, samples were cleaned to remove non-edible parts like skin, tail, shell, and bone. For sample extraction, we followed the quick, easy, cheap, effective, rugged, safe, efficient, and robust (QuEChERSER) protocol [125,126], in which 2.0 $\pm$ 0.1 g of sample was weighed into a 15 mL polypropylene tube and spiked with internal standard mixtures. : (To these tubes, 10 mL acetonitrile/ water (4:1, v/v) was added and the tubes were shaken for 10 min at 80% setting and maximum pulsation using a platform shaker (Glas-Col, Terre Haute, IN, USA), followed by centrifugation for 3 min at 3711 relative centrifugal force (rcf) at room temperature.

For UHPLC-MS/MS analysis, 0.2 mL of the extract (supernatant) was transferred to 2 mL polypropylene tubes and evaporated to just dryness under N_2 flow using a Rapid Vap Vertex N_2 evaporator by Labconco Corporation (Kansas, MO, USA) at 40°C. To this, 756 µL of aqueous mobile phase i.e., water (LC grade) and 20 µL of 200 ng/mL ^{13}C-phenacetin (QC standard) were added. The tubes were vortexed briefly and then ultracentrifuged for 5 min at 12500 rcf at 4°C. An aliquot of 0.6 mL of final extracts was transferred into polypropylene autosampler vials for analysis.

For LPGC-MS/MS, the remaining initial extract was decanted into 15 mL polypropylene tubes containing 2 g 4:1 (w/w) $MgSO_4$/NaCl, capped, shaken briefly by hand, and then on a platform shaker for 1 min at 80% setting and maximum pulsation. The tubes were then centrifuged for 3 mins at 3711 rcf at room temperature to separate the acetonitrile layer from water. Then, 1 ml of the acetonitrile upper layer was collected and 0.5 mL was passed through a micro-SPE cartridge containing 20 mg $MgSO_4$, 12 mg C18, 12 mg PSA, and 1 mg GCB at 5 µL/s using an automated Pal RTC system (Zwingen, Switzerland)

4.2.4 Instrumental Analysis

Low-pressure gas chromatography-tandem mass spectrometry (LPGC-MS/MS) was used to analyze pesticides and environmental contaminants and ultra-high performance liquid chromatography coupled to tandem mass spectrometry (UHPLC-MS/MS) was used for veterinary drugs. Additionally, some LC-amenable pesticides were analyzed by UHPLC-MS/MS. In total, we monitored 286 compounds using UHPLC-MS/MS and 252 compounds using LPGC-MS/MS, of which 93 analytes overlapped with UHPLC. Appendix C, Tables 16 and 17 provide list of all the target analytes, Appendix C, Table 18 shows the list of internal standards (IS) and quality control (QC) standards used.

UHPLC-MS/MS analysis was performed using a Shimadzu (Columbia, MA, USA) Nexera X2 UHPLC coupled with a Sciex (Framinhgham, MA, USA) QTRAP 6500 MS/MS. The analytical column was a Waters (Milford, MA, USA) Acquity BEH with 2.1 mm internal diameter, 100 mm length and 1.7 µm particle size fitted with a matching 5 mm VanGuard pre-column guard. The column temperature was 40°C and an injection volume of 10 µL was used. Mobile phase A and B were 100% water and 1:1 methanol/acetonitrile (v/v) respectively, both with 0.1% formic acid/10 mM ammonium formate. Flow was 0.45 mL/min using a gradient started at 5% B for 0.5 min, increased to 35% in one min, and to 100% after 8 min, which was held until 11 min. In the next 10 sec the solution went back to 5% B, which was held until 15 mins. During this time the column was allowed to re-equilibrate before the next injection. Curtain flow was 25 L/min, ion source gas 1 and 2 were at 60 L/min and 30 L/min, respectively, ion spray voltage was +5 kV, and the source temperature was 450°C. Three MRM transitions in positive electrospray ionization mode were monitored for each targeted analyte in scheduled MRM, with 45 s from the t_R with a target scan time of 0.25 s and dwell times automatically adjusted by the Sciex Analyst software.

LPGC-MS/MS analysis was performed based on a previously reported method using an Agilent 7890A/7010 GC–MS/MS instrument.[171] A 5 m, 0.18 mm i.d. uncoated pre-connected LPGC guard column (Restek, Bellefonte, PA, USA) was used at the inlet coupled to a 15 m, 0.53 mm i.d., 1 μm thickness film Rtx-5MS analytical column with an extra 1 m uncoated 0.53 mm i.d. integrated transfer line capillary. An injection volume of 3 μL final extract + 1 μL AP solution was used with a 1 μL air gap between them, a standard Agilent split/splitless inlet fitted with a Restek Topaz low-pressure drop splitless precision liner with glass wool was used for injection. Samples were injected at 280°C using a pressure pulse of 40 psi for 0.75 min, after which the split vent was initiated. The septum purge was closed for 3 min. Oven temperature started at 80°C for 1 min, which was ramped to 320°C at 45°C/min and held for 3.7 min to give a total run time of 10 min. The carrier gas was high purity helium starting at 2.25 mL/min for 3 min which was lowered to 1.5 mL/min until the end of the run. The transfer line was 280°C, the ion source was 320°C, and the quadrupoles were 150°C. Electron ionization (EI) was applied at 70 eV with 100 μA filament current. MassHunter software was used for instrument control and data processing.

To confirm if an analyte was present, we followed the identification requirements established by the European Union (EU).[128] An analyte was identified if: (1) retention time of an analyte (tR) was ≤ 0.1 min from the reference tR (2) a minimum of 2 fully overlapping precursor-product ion transitions were detected with S/N>3 and (3) ion ratios were within ±30% (relative) of average of calibration standards. We also used high resolution MS (Q-Orbitrap) to confirm the identity of compounds if required. Here, we looked for matching with analytical standards using NIST MS library ions (with mass accuracy ≤ 5 ppm) and S/N>3.

4.2.5 Quality Control

Reagent blank (1.6 mL water accounting for ~80% moisture content in fish), reagent spike (1.6 mL water + spike), spiked fish samples, and replicated samples were used for quality control. A continuous calibration verification (CCV) standard of 10 ng/mL was injected at the start and end of the batch. Solvent blanks were analyzed at the start, end, after every fortified sample, and after CCV to avoid carry over and monitor system contamination. The 19 compounds identified using UHPLC were used to prepare standard mixtures ranging between 1 ng/mL to 500 ng/mL and used to construct a 6-point calibration curve. The limit of quantification (lowest level of calibration in this case) was set at 1 ng/ml.

4.2.6 Risk Assessment

The risks associated with intake of analyzed seafood was evaluated through maximum residue limits (MRLs), estimated daily intakes (EDI), and hazard quotients (HQ) as described below.[172]

4.2.6.1 MRLs

To ensure a consumer's safety, maximum residue limits (MRL) may be established as the highest level of a chemical residue that is legally tolerated in or on food or feed.[173] In our study, we compared measured residual levels of pesticides and veterinary drugs in targeted seafood with MRLs established by the US, Canada, and the European Union (EU).[174] For PCBs, these limits are distinguished in some jurisdictions between non-dioxin like PCB congeners and the more toxic dioxin-like PCBs.[175] In this study, PCB concentrations for the sum of non-dioxin like PCB congeners (PCB 28, PCB 52, PCB 101, PCB 138, PCB 153, and PCB 180) were compared with the limit of 2000 ppb established by the U.S. Food and Drug Administration[176] and with the EU limit of 75 ppb (ng/g or µg/kg).[177] For dioxin-like PCBs (PCB 77, PCB 81, PCB 105, PCB 114, PCB 118, PCB 123, PCB 126, PCB 156, PCB 167, PCB 169, PCB 189), Toxic Equivalence (TEQ) values were calculated using Equation 4.1 and compared with the WHO-PCDD/F-PCB-TEQ (sum of the toxic equivalencies of the 17 most toxicologically significant dioxins and furans) level of 6.5 pg/g or 0.0065 ng/g.[177]

$$TEQ = \sum_{i=1}^{n} C_i \times TEF \qquad (4.1)$$

Here, C_i is the concentration of an individual PCB congener and TEF is the toxicity equivalence factor provided for this compound by the US EPA.[178]

For PAHs, we referred to maximum permitted levels of 30 ppb established by the EU for the sum of benzo(a)pyrene, benz(a)anthracene, benzo(b)fluoranthene, and chrysene in bivalve mollusks, and 12 ppb in smoked fish.[177] Although we only analyzed raw fish in our study, MRLs for smoked fish were used for comparison.

4.2.6.2 EDI and HQ

To assess potential health risks from the consumption of selected seafood, we next calculated EDIs using Equation 4.2.

$$\mathrm{EDI} = \left(\frac{\mathrm{C_{fish}} \times \mathrm{Cd}}{\mathrm{BW}}\right) \qquad (4.2)$$

where the EDI (ng/kg bw/day) is the estimated daily intake, C_{fish} (ng/g, ww) is the chemical concentration detected in seafood, and Cd (g/day) the amount of seafood consumed daily, for which the national average in the US is 18 g/day according to the National Health and Nutrition

Examination Survey (NHANES).[130] Since this value includes both consumers and non-consumers, resulting exposures are expected to be an under-estimation or represent a "low-exposure scenario".

We also determined exposure estimates for high-frequency seafood consumption using a deterministic or point-estimate approach, representing a worst-case or "high-exposure scenario".[179] Here the highest detected chemical concentrations and highest reported consumption rates were used for exposure estimation. High-frequency seafood consumption corresponds to > 3 meals/week and is reported at mean value of 108 g/day in the US. [180] Also, as reported previously, non-Hispanic Blacks consume some of the highest seafood among US populations, followed by Hispanics and non-Hispanic Whites.[180] We therefore include these populations in our high-exposure model to assess the associated risks. We also consider recreational anglers, who are reported to eat as much as 130 g/day of seafood. Although recreational anglers normally consume self-caught fish rather than store-bought, we include them in exposure modeling to assess the highest possible risks resulting from the highest measured concentrations. Consumers with similar seafood consumption patterns to recreational anglers will be at highest risk. Target populations for risk assessment (low- and high- exposure scenarios) are shown in Table 8. We further calculated the HQ as the ratio of the EDI to the oral reference dose (RfD_{oral}) (mg/kg/day), when such a value had been established by the US EPA.[181]

Table 8: Seafood consumption rates for US adult population.

Target population	Mean consumption (g/day)	References
US general population	18	Love et al., 2020a
High frequency seafood consumer	108	Love et al., 2020a, von Stackelberg et al., 2017
High frequency-Recreational anglers	130	von Stackelberg et al., 2017
High frequency-non-Hispanic White	107	von Stackelberg et al., 2017
High frequency-non-Hispanic Black	124	

High frequency- Hispanic	109	

4.3 Results

4.3.1 Chemical Residues in Seafood

Out of 445 analytes screened, 17 were detected at low frequencies. Overall, 16 species tested positive for at least one of the detected residues. Total concentrations of detected analytes ranged between non-detectable to 156 µg/kg. Species-specific highest residue levels were found in catfish (153 µg/kg), mackerel (36 µg/kg), mussels (34 µg/kg), salmon (24 µg/kg), and swordfish (14 µg/kg) (Figure 11). Higher levels were associated with then non-dioxin-like PCB 180, p,p'-DDE, and allethrin.

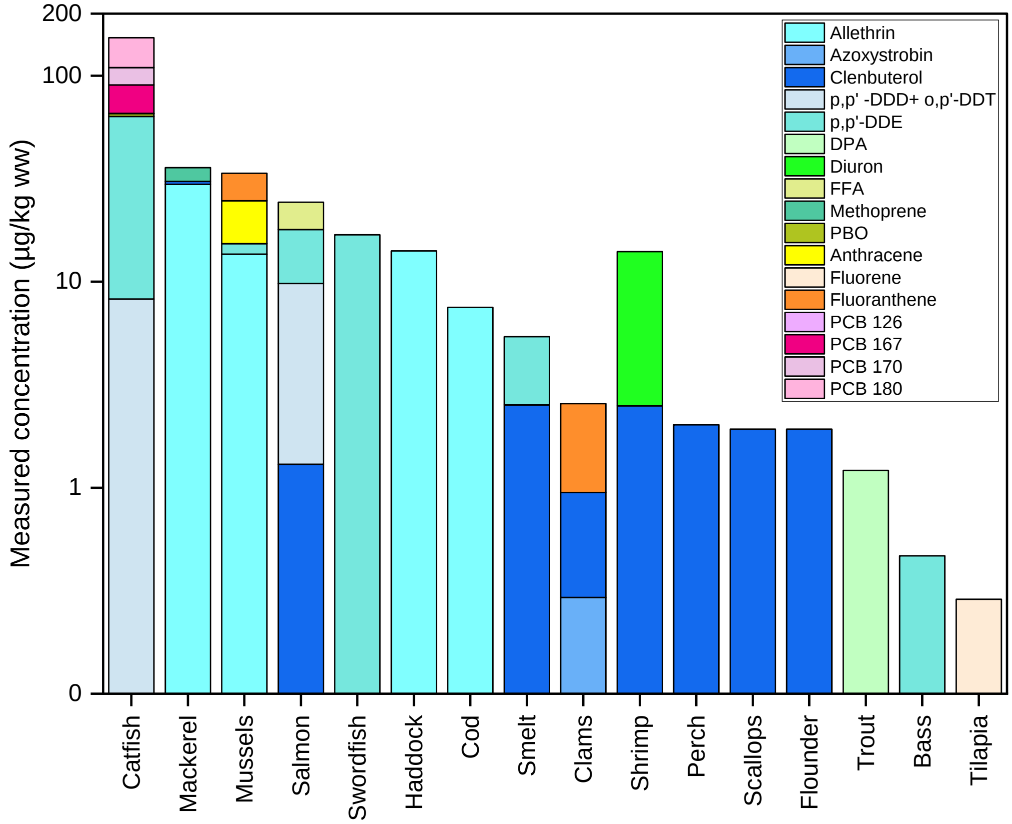


Figure 11: Total chemical profile in seafood.

Shades of blue/green represent pesticides and veterinary drugs, shades of orange/yellow represent PAHs, and shades of pink/purple represent PCBs.

4.3.2 Pesticides and Veterinary Drugs

Only 10 pesticides and veterinary drug residues, were detected at low occurrence frequencies, with concentrations ranging from 0.5 to 55 µg/kg ww (Table 9). The most frequently detected compounds were clenbuterol, p,p'-DDE and allethrin, with detection frequencies of 22%, 13%, and 11%, respectively. Azoxystrobin, diphenyl amine (DPA), diuron, methoprene, piperonyl butoxide (PBO) and florfenicol amine (FFA) were only detected in 2% of the samples. . Azinphos-methyl was detected in 100% samples using LCGC-MS/MS, which was not expected. To confirm its identity, high resolution MS with GC-Orbitrap MS was used to scan for 5 representative ions (*m/z* 81.06990, 91.05425, 107.08559, 132.04442, 160.05052) with a mass accuracy <5 ppm in a catfish sample. HRMS data showed that azinphos-methyl was not present in the selected sample and its detection by LPGC-MS/MS was a false-positive (Appendix C, Figure 6). We therefore removed azinphos-methyl from the list of detected analytes.

Out of the 46 seafood samples, 23 tested positive for at least one residue. Two residues were detected in one sample each of salmon (p,p' -DDD+ o,p'-DDT and p,p'-DDE), shrimp (clenbuterol and diuron), cod (allethrin, clenbuterol), smelt (p,p'-DDE and clenbuterol), catfish (p,p' -DDD+ o,p'-DDT and p,p'-DDE), and mackerel (allethrin and methoprene), while all other positive samples contained only one residue. Concentrations of all detected compounds were in compliance with MRLs established for the US. However, the average of ∑DDT (sum of p,p' -DDD, o,p'-DDT, and p,p'-DDE) (~22 µg/kg), allethrin (~16 µg/kg) and diuron (~12 µg/kg) levels exceeded EU guidelines. Specifically, DDT levels in Atlantic salmon, catfish, and swordfish, allethrin levels in haddock, mussel, and mackerel, and diuron levels in shrimp all violated EU MRLs.

Table 9: Veterinary drugs and pesticides concentrations and Maximum residue limits (MRLs).

Compound	Detection frequency (%)	Concentration (AVG ± STDEV), ppb (µg/kg) ww	Samples with detects	Concentration, ppb (µg/kg), ww	MRLs for US market, ppb (µg/kg)	MRLs for Canada and EU markets, ppb (µg/kg)
Clenbuterol	22	1.9 ± 0.8	Clams-Canada-wild	0.5	N/A	N/A
			Flounder-China-wild	1.9		
			Mackerel-Thailand-wild	1		
			Perch-Canada-wild	2		
			Atlantic salmon-Chile-farmed	1.3		
			Scallops-US-wild	1.9		
			Shrimp-US-wild	1.9		
			Shrimp-India-farmed	2.5		
			Shrimp-Vietnam-farmed	3.5		
			Smelt-Estonia-wild	2.5		
p,p'-DDE	13	14.1 ± 19.1	Atlantic salmon-Norway- farmed	8.1	5000[a]	5000 (Canada), 10 (EU)[c]
			Bass-Turkey-farmed	0.7		
			Smelt-Estonia-wild	2.9		
			Catfish-unknown	55.1		
			Swordfish-Singapore-wild	16.9		
			Clams-China-wild	1.6		
Allethrin	11	16.2 + 8.2	Cod-US-wild	7.5	N/A	100 (Canada)[c], 10 (EU)[c]
			Haddock-Norway-wild	14.1		
			Mussels-Chile-farmed	13.6		
			Mackerel-China-wild	29.7		
p,p' -DDD+ o,p'-DDT	4	8.3 + 0.15	Atlantic salmon-Norway- farmed	8.5	5000[a]	5000 (Canada), 10 (EU)[c]
			Catfish-unknown	8.2		
Azoxystrobin	2	0.5	Clams-China-wild	0.5	N/A	100 (Canada)[c], 10 (EU)[c]
DPA	2	1.2	Trout-Peru-farmed	1.2	N/A	100 (Canada)[c], 10 (EU)[c]
Diuron	2	11.5	Shrimp-US-wild	11.5	N/A	100 (Canada)[c], 10 (EU)[c]
FFA	2	6.4	Atlantic salmon-Chile-farmed	6.4	1000	800 (Canada), 1000 (EU)
Methoprene	2	5.1	Mackerel-China-wild	5.1	Exempt[b]	100 (Canada)[c], 10 (EU)[c]
PBO	2	2.1	Catfish-US-farmed	2.1	N/A	100 (Canada)[c], 10 (EU)[c]

N/A- MRL not established for the US, [a]MRL for DDT includes p,p' -DDD + o,p'-DDT+ p,p'-DDE, [b]exempt from the requirement of a tolerance in or on all food commodities when used to control insect larvae (MRL not required for use), [c]some markets defer to a default MRL value when a specific MRL has not been established for a commodity and active ingredient.

4.3.3 PCBs and PAHs

Among the monitored environmental contaminants, 4 PCB congeners and 3 PAHs were detected at low detection frequencies. Surprisingly, PBDEs were not found above the detection limits in any sample, perhaps showing the effectiveness of regulations in phasing out these substances. PCB congeners showed the following profile: PCB 180 (43.3 µg/kg) > PCB 167 (24.4 µg/kg ww) > PCB 170 (19.4 µg/kg ww) > PCB 126 (6.2 µg/kg ww). Levels of non-dioxin like PCBs (PCB 170 and PCB 180) were within the established tolerance limits. However, the TEQ for sum of detected dioxin-like PCBs (PCB126 and PCB 167) was above the WHO limits; the TEQ for PCB 126 + PCB 167 was 0.62 ng/g against the established maximum limits of 0.0065 ng/g (or 6.5 pg/g).

Fluorene, fluoranthene, and anthracene + phenanthrene (co-eluting together) were the only detected PAHs. Fluorene was found in farmed tilapia sourced from Honduras (0.5 µg/kg ww), anthracene + phenanthrene and fluoranthene in wild mussels from China (9.4 µg/kg and 8.9 µg/kg ww, respectively), and in wild Chinese clams (1.6 µg/kg ww). All PAH concentrations were within EU regulations for molluscs and smoked fish.

4.3.4 Risk Assessment

The EDIs of veterinary drugs and pesticides were calculated for all species in which EU MRLs were exceeded. All EDIs were well below oral RfDs.

Scenario-specific EDIs were calculated for compounds detected in seafood samples from grocery stores in Pittsburgh (Figure 12). The low-exposure scenario represented consumption rates for an average adult in the US, while the high-exposure scenario was based on conservative values and represented high frequency (HF) consumers such as recreational anglers. EDIs were also calculated for high frequency US consumers based on race (white, Black, and Hispanic).

For both low- and high-exposure scenarios, based on available RfDs, EDIs for DDT, diuron, DPA, anthracene (+phenanthrene), fluorene, and fluoranthene were within limits. However, EDIs for PCBs were above the established RfDs. In the case of the low-exposure scenario, the EDI was 2.4E-5 mg/kg/day or 24 ng/kg/day, which was ~20% higher than the RfDs (2E-5). For the high-exposure scenarios, EDIs for detected PCBs were more than 80% higher than the limits for all types of high-frequency consumer. The highest daily intakes were associated with recreational anglers and non-Hispanic Black consumers.

We also calculated HQs for the detected compounds when RfDs were available. In case of DDT, HQs were found in the range of 0.01-0.23 for high frequency consumer, highest for recreational anglers. For PCBs, HQs were >1 in case of both high and low exposure scenarios.

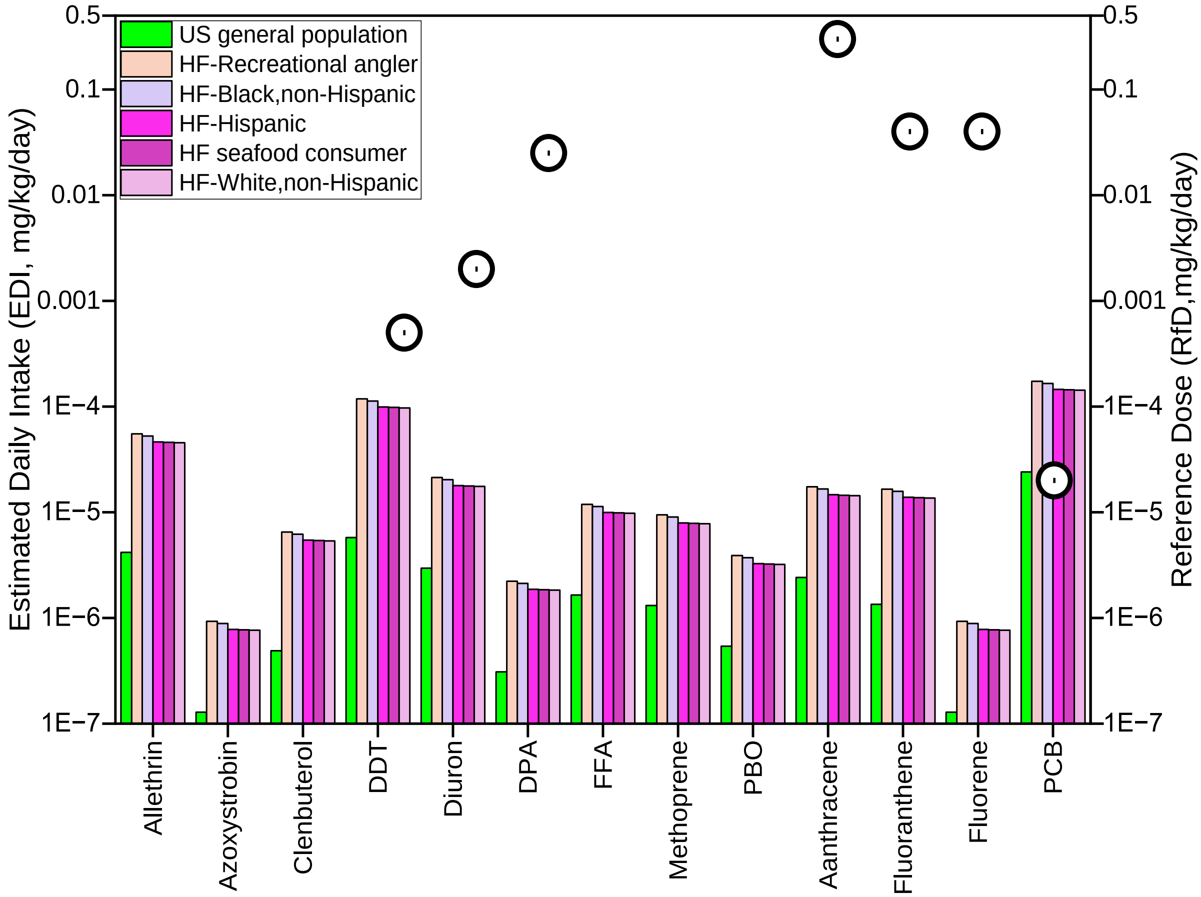


Figure 12: Exposure estimates (EDI, mg/kg/day) based on seafood consumption rates.

*DDT includes the sum of p,p' -DDD, o,p'-DDT, and p,p'-DDE; HF= high frequency; concentration of anthracene also includes phenanthrene.

4.4 Discussions

The presence of pollutant residues in food and the associated risks to human health have been reported, but relatively little attention has focused on commercially available seafood in the US. To the best of our knowledge, we are the first US based study to analyze 440+ compounds that provides a broad perspective on chemical residues in the commercial seafood supply. We screened 46 seafood samples purchased from retail stores across Pittsburgh, PA, USA. Although samples were collected from a single city, the stores surveyed are in many cases national chains, and therefore results can be expected to apply generally to the seafood consuming US population.

General trends in total concentrations indicate significantly higher levels of contaminants in bottom-feeders and benthic organisms such as catfish, mackerel, and mussels. These species are readily exposed to greater quantities of chemicals that accumulate in sediments. Detected compounds included allethrin, azoxystrobin, clenbuterol, DDT (p,p' -DDD, o,p'-DDT and p,p'-DDE), diuron, DPA, FFA, methoprene, PBO, anthracene, phenanthrene, fluorene, fluoranthene, and PCB congeners 126, 167, 170, and 180. Overall, 50% of the tested samples had detectable levels of at least one chemical. Clenbuterol was most frequently detected in 22% samples. Clenbuterol is a β-agonist used to improve feed efficiency and achieve higher muscle to fat ratio [182]. Although it is banned in many countries including the US, China and the EU, it has been widely detected in livestock.[183,184] However, clenbuterol has previously not been detected in seafood. Among the positive samples, 70% samples were wild caught from Canada, China, Thailand, Estonia, and the US pointing towards its widespread and non-judicious use and disposal. Thirteen percent of the samples tested positive for DDT metabolites and, consistent with previous studies, indicated that p,p'-DDE was the dominant component.[185–188] Interestingly, no PBDEs were detected in any samples, which is highly inconsistent with the most recent data,[188,189] and possibly reflects the effect of the PBDE ban. No prior knowledge exists on the occurrence of some of the residues detected in our study such as allethrin, azoxystrobin, DPA, diuron, and methoprene for US seafood. Some residues previously reported in commercial seafood such as oxytetracycline, erythromycin, sulfamethazine etc., were analyzed but not detectable in our samples.[17,169,190]

We observed that accumulation of certain chemical residues was highly species-specific. PCBs (126, 167, 170, and 180) were only detected in catfish. This sample also reported the highest ∑DDT levels (p,p' -DDD, o,p'-DDT and p,p'-DDE). This observation was also consistent with previous studies in which PCBs and DDT were predominately detected in catfish.[191,192] Catfish are bottom dwellers and accumulate chemicals from sediments. At the same time, catfish has relatively higher levels of lipids in its tissues and as a result lipid-soluble chemicals such PCBs and DDT have a greater tendency to accumulate in catfish than in other species. Similarly, we found detectable levels of FFA, a major metabolite of florfenicol, only in Atlantic salmon sourced from Chile. Florfenicol is a drug often used for disease control in Atlantic salmon aquaculture;[16,193] with 80% of its use in Chile.[194] In a previous study, FFA was detected in Atlantic salmon purchased in Canada.[190]

Measured levels of all the detected veterinary drugs and pesticide residues were in compliance with US and Canadian MRLs. However, levels of ∑DDT, allethrin, and diuron exceeded EU regulations. To investigate if the seafood with MRL exceedance is safe for consumption, we performed a risk assessment by calculating EDIs and HQs. Considering individual veterinary drug and pesticide residues, no risks were associated with species which exceeded MRLs, i.e., catfish, mussels, mackerel, and shrimp. Residual levels of PCBs detected in catfish were within US (2000 ppb) and EU (75 ppb for non-dioxin like PCBs) regulations. However, the TEQ for the sum of detected dioxin-like PCBs (PCB126 and PCB 167) was almost 100-fold higher than the WHO limits, suggesting that the analyzed catfish may not be safe for regular consumption.

Further, EDIs and HQs were also calculated for all the detected residues based on low and high exposure scenarios. For the low exposure scenario, EDIs ranged between 1.29E-7 and 2.4E-

5 mg/kg/day while for the high exposure scenario it ranged from 9.29E-7 to 0.00016 mg/kg/day. Generally higher EDIs were associated with recreational anglers and non-Hispanic Black populations who eat comparatively more seafood than others. EDIs for both scenarios were within the oral RfDs when available for all residues, except for PCBs. HQs for PCBs for both high and low exposure scenario were greater than 1. A HQ as high as 8 was observed for recreational anglers and non-Hispanic Black populations. Since catfish was the only species in which PCBs were detected, we conclude that catfish consumption is a major contributor of elevated risks associated with PCB exposure.

Our study shows that the US commercial seafood supply is contaminated by veterinary drugs and pesticides residues, although at low levels. Risk assessment confirmed that there were no safety concerns related with consumption of selected seafood. However, additional screening for environmental contaminants indicated risks of adverse effects from exposure to PCBs through catfish consumption. Catfish, which is a common sport fish, is also purchased for consumption from grocery stores, and can be found on fast food menus. It is a common choice, including for high-frequency consumers such as the non-Hispanic Black population. [195] Some consumers may also prefer to consume whole fish, which may have five- to ten- fold greater concentrations than fillets.[195] Thus, evaluating risks for high-frequency consumers may be critical in risk assessment for certain seafood and contaminant combinations. Nevertheless, these findings pertain to individual compounds only, and knowledge regarding mixture exposures remains a critical gap.

5.0 Summary and Future Work

5.1 Summary

Potential risks of foodborne exposure to toxic pollutants were investigated through coupled modeling and analysis in this dissertation. Our work focused on seafood as the intake route for human exposure to legacy chemicals as well as chemicals of emerging concern including veterinary drugs, pesticides, and environmental contaminants. We performed scenario-specific risk assessment considering seafood trade, geographic seafood origin, and frequency of seafood consumption within and among populations. We tested the hypothesis that shopping choices across stores, husbandry types (farmed and wild caught), and origins impact exposures.

A trade-data based mathematical model was successfully used to construct seafood-specific diets for the Swiss population and estimate tolerable daily intakes based on published PBDE levels in fish muscle tissue. Resulting exposures were found to be very close to the median exposures for the adult Swiss population (calculated using the menuCH dietary survey, a unique resource not typically available for national populations), indicating that the per capita food balance derived from trade data is a good proxy for average PBDE exposures. Our model could also be used to predict origin-specific exposures and identify potential hot spots in the international seafood trade network that play pivotal roles in bringing diet-borne contaminants to countries. Overall, with the help of this model, species- and origin-specific diets can be constructed for any country for which trade data are available, which when coupled with measured levels or published levels of contaminants can be used for risk assessment.

One key finding from this meta-analysis of global PBDE levels was that exposures vary based on seafood origins. To further improve the understanding on this aspect and to investigate if the observed differences are statistically significant, we designed our next goal. Here, instead of referring to published concentrations of pollutants, we measured the concentrations of a wide variety of potential seafood contaminants in commercially available seafood using advanced analytical chemistry techniques (high-resolution LC-MS and GC-MS platforms). We approached this by first examining the seafood market and the available products in the Pittsburgh region. Our approach for sample collection helped us capture a range of seafood consumers and evaluate whether shopper's choices matter to exposure.

We screened sampled seafood for 450+ pollutants including veterinary drugs, pesticides, and PFAS, PBDEs, PAHs, and PCBs. Our findings suggest that for individual compounds and low consumption (~18g/day), the analyzed seafood was safe for human consumption. Specific to PFAS, consumer habits are unlikely to substantially impact exposures, demonstrating the global distribution of these ubiquitous contaminants. However, this dissertation highlights that certain vulnerable populations who consume seafood more frequently than others may be at a higher risk of exposure to toxic chemicals. At the same, uncertainties around mixture exposure and chronic exposures exist and, therefore, continuous monitoring of seafood is needed to improve the overall understanding of foodborne chemical exposure, and the risks associated with it.

Thus, this dissertation contributes to efforts to improve data availability on the occurrence of both legacy and emerging pollutants in seafood. Such biomonitoring data are imperative for enforcing regulations on chemical use and establishing seafood consumption advisories to safeguard human health. Measured concentrations can also be used to feed into risk assessment models such as those designed to predict bioaccumulation and toxicity of chemical contaminants. In addition, we provide measurements of chemical levels in wild-caught fish which are indicators of ecological health. Thus, this dissertation also provides an insight into the health of aquatic environments, data crucial for conservation and management of water resources. This work is expected to improve risk assessment from both public health and ecological health perspectives.

5.2 Future Work

Most of the previous risk assessments have primarily taken average seafood intake rates into account, such that the estimated exposures represent both consumers and non-consumers. In contrast, in this dissertation, we also built exposure models representing different seafood consumers, especially those who comparatively eat more seafood than the average US population (termed “high-frequency” consumers). We selected race/ethnicity (Black/White and Hispanic/non-Hispanic) to represent high-frequency seafood consumers. Recreational anglers were also included to represent highest seafood intakes. Overall, we saw a significant difference in TWIs for these consumers (compared to the average US population). To fully identify vulnerable consumers and to increase the scope of risk assessments, future studies should consider other demographic groups such as age, gender education, and household income.

Of all the chemicals evaluated in this dissertation, PFAS were predominately detected in the targeted seafood samples. Previously, dietary exposure to PFAS has been indirectly linked to food packaging, and is thought to be the major contributor to overall PFAS exposure.[196] Foods are often packaged in materials to maintain their integrity, absorb moisture and/or grease, and increase shelf-life. However, synthetic agents which bring these properties to packaging often migrate into the food, thereby contributing to enhanced chemical exposures.[197] To date, studies have focused on correlations between consumption of packaged foods and human serum levels (only for a subset of chemicals like PFOS and PFOA),[196] or on identifying total fluorine in different packaged foods.[198] Limited public information is available on the specific PFAS structures used in packaging materials and their ability to migrate into food.

Therefore, we initiated a study to improve the understanding of PFAS occurrence in food packaging and their ability to migrate into food. This project is in collaboration with Dr. Yelena Sapozhnikova, USDA-ARS and Dr. Amina Salamova, Emory University, whereby we analyzed PFAS in globally sourced food packaging. Dr. Sapozhnikova led the non-target analysis to screen and identify all extractable fluorinated compounds in sampled materials using extraction and migration tests and instrumental analysis. Dr. Salamova led the targeted analysis to quantify concentrations of major PFAS identified based on non-target analysis.

Our initial contribution in this project was to conduct a food market survey and collect samples. Eighty-eight food samples were collected from 13 supermarkets in Pittsburgh, PA USA over 2 months in 2021. Samples were collected such that a variety of storage temperatures and food types *i.e*., dairy (18), bakery (19), meals (18), dry meats (5), produce (6), and others (22, which included mostly snacks such as chips, popcorn, and candy) would be captured. Different packaging types, including greaseproof papers, paperboard trays, wrappers, cardboard etc., were selected to represent food choices for different consumer groups (e.g. adults vs. children). Packaging was separated from the food, rinsed with water to remove particulates, and then stored in individual plastic storage bags.

The combined approach of targeted analysis (TA), total oxidizable precursor (TOP) assay and non-targeted analysis (NTA) was employed to identify and characterize PFAS chemicals that could be extracted from the food packaging. Overall, 66% of food packaging samples had detectable levels of at least one of the targeted 33 PFAS (Table 10 and Figure 13). More realistic migration tests were then conducted to study whether PFAS migrated into food simulants, and 4 migrated PFAS (PFHxS, PFHxA, PFHpA and 6:2 diPAP) were measured at ng/g levels with amounts increasing over the 10-day migration test (Table 11).

Table 10: Levels of detected PFAS in food packaging (ng/g) (unpublished data).

PFAS Analyte	# Detects	MIN	AVG	MAX
PFPeA	9	0.10	12.48	107.77
PFHxA	30	0.05	12.45	355.87
PFHpA	14	0.05	17.33	235.89
PFOA	31	0.06	0.25	0.99
PFNA	14	0.05	0.38	1.27
PFDA	12	0.05	0.48	1.80
PFUdA	12	0.07	0.57	2.88
PFDoA	10	0.06	0.87	4.47
PFTrDA	9	0.05	1.53	8.15
PFTeA	10	0.06	1.18	6.46
PFBS	2	0.22	2.48	4.74
PFPeS	1	0.26	0.26	0.26
PFHxS	28	0.05	3.95	90.74
PFOS	18	0.05	0.51	4.31
PFDS	1	0.07	0.07	0.07
HFPODA	4	0.10	0.14	0.24
6:2FTS	2	0.05	0.10	0.14
8:2FTS	4	0.08	0.24	0.61
NMeFOSAA	1	0.21	0.21	0.21
NEtFOSAA	7	0.10	0.20	0.37

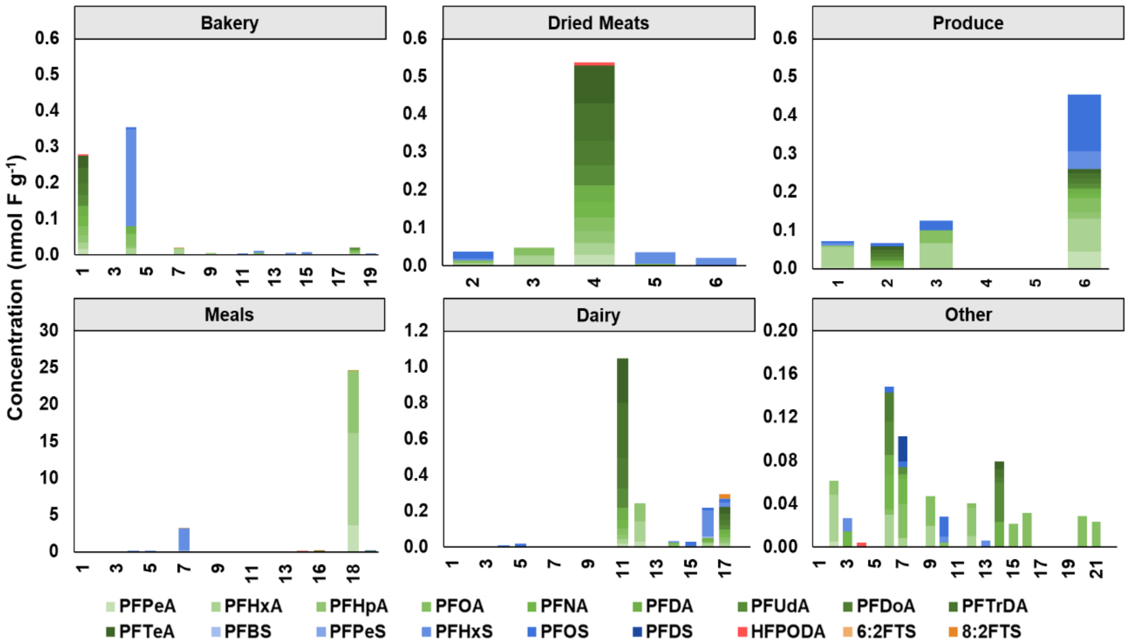


Figure 13.: Concentrations of PFAS (nmol of fluorine per gram of food packaging) detected via targeted analysis for each food category (unpublished data).

Table 11: Food packaging samples with PFAS detected during the migration study.

Food	Packaging material	PFAS	Concentration (µg/kg)			
			2 hr	24 hr	96 hr	240 hr
Cake	Paper	PFHxS	0.25	0.52	0.71	0.70
Salami	plastic and paper	PFHxA PFHpA	0.19 0.11	0.30 0.15	0.39 0.17	0.55 0.23
Tomato	foam and film	PFHxA	0.05	0.04	0.05	0.05
Cookie	Paper	6: 2 diPAP	0.2	0.5	0.7	0.7
Lamb kabab	Plastic	6: 2 diPAP	1.2	11.1	11.8	12.2

Following pollutant detections and exposure estimations, as next steps, the toxicity of the compounds detected in extraction and migration assays, and especially based on the mixture composition, should be assessed. Although biomonitoring data may provide an estimate of overall exposure to a substance, its presence in the body does not necessarily mean that it is causing harm. To quantify human health risks, we need to assess if the measured concentrations and resulting exposures are toxic. In future studies, the bioaccumulation potential and toxicity of PFAS at these relevant food-associated concentrations should be measured.

The zebrafish embryo developmental toxicity assay has been widely used for assessing PFAS toxicity and has shown to be a good proxy for toxic effects in mammalian species.[199,200] We conducted a pilot study in which fertilized zebrafish embryos were exposed to individual test PFAS (PFOA, K-PFBS, and PFHpA) for 5 days post-fertilization (120 hours) and the resulting impact on embryo survival and malformation endpoints were investigated. Some of the developmental malformations elicited due to exposures ranging from between 15-125 µM of test PFAS include failed swim bladder inflation, curved body axis, and yolk sac edema, observations that are consistent with previous studies.[200] At concentrations lower than 15 µM hardly any malformations were observed. However, these concentrations were much higher than what was detected in food packaging samples. Therefore, to assess PFAS toxicity at environmentally relevant concentrations, future studies need to focus on identifying possible molecular effects that could occur prior to the development of apparent malformations, for example through gene expression analysis.[201]

The food web is a complex system involving global chemical transport and subsequent human exposure.[39] Among the many risk assessment tools, exposure modeling is a powerful method to identify which chemical exposures may contribute most to body burdens. Although our projects offer insights into the utility of exposure modeling, for example by allowing us to identify vulnerable populations, more work needs to be done to fully realize its potential in risk assessment. From the quantification point of view, there are gaps in our knowledge with respect to levels of chemicals in food, which limits the establishment of interventions to protect human health. By analyzing a wider suite of chemicals, we have offered new insights into the occurrence of chemicals in food with a focus on commercial seafood. However, continued monitoring and identification of interventions is required to reduce chemical amounts not only in seafood, but other foodstuffs as well. In addition, although individual chemical concentrations may be low, simultaneous exposure to large numbers of chemicals may be a potential public health concern.[202] Therefore, future studies should also consider exposures to chemical mixtures for risk assessment. Overall, with enough data on occurrence of chemicals and advanced exposure models, risk assessment can improve. Moreover, the role of food-borne exposure on overall body burdens of chemicals can be better comprehended.

Appendix A Supporting Information for Chapter 2.0

Appendix A Table 1: Total imported commodities with Comtrade codes and import values (kg/year).

Code	Species and forms included	Net weight (kg/year)
030211	Fish; fresh or chilled, trout (Salmo trutta, Oncorhynchus mykiss, Oncorhynchus clarki, Oncorhynchus aguabonita, Oncorhynchus gilae, Oncorhynchus apache and Oncorhynchus chrysogaster), excluding fillets, livers, roes, and other fish meat of heading 0304	270817
030213	Fish; fresh or chilled, Pacific salmon (Oncorhynchus nerka, Oncorhynchus gorbuscha, Oncorhynchus keta, Oncorhynchus tschawytscha, Oncorhynchus kisutch, Oncorhynchus masou, Oncorhynchus rhodurus), not fillets, livers, roes, other fish meat of heading 0304	27379
030214	Fish; fresh or chilled, Atlantic salmon (Salmo salar) and Danube salmon (Hucho hucho), excluding fillets, livers, roes, and other fish meat of heading 0304	3166679
030219	Salmonidae (excl. of 0302.11 & 0302.12; excl. fillets/oth. fish meat of 03.04/livers & roes), fresh/chilled	58344
030221	Fish; fresh or chilled, halibut (Reinhardtius hippoglossoides, Hippoglossus hippoglossus, Hippoglossus stenolepis), excluding fillets, livers, roes, and other fish meat of heading 0304	14227
030222	Fish; fresh or chilled, plaice (Pleuronectes platessa), excluding fillets, livers, roes, and other fish meat of heading 0304	1218
030223	Fish; fresh or chilled, sole (Solea spp.), excluding fillets, livers, roes, and other fish meat of heading 0304	253295
030224	Fish; fresh or chilled, turbots (Psetta maxima, Scophthalmidae), excluding fillets, livers, roes, and other fish meat of heading 0304	145885
030229	Fish; fresh or chilled, flat fish, n.e.c. in item no. 0302.2, excluding fillets, livers, roes, and other fish meat of heading 0304	5833
030231	Fish; fresh or chilled, albacore or longfinned tunas (Thunnus alalunga), excluding fillets, livers, roes, and other fish meat of heading 0304	1990
030232	Fish; fresh or chilled, yellowfin tunas (Thunnus albacares), excluding fillets, livers, roes, and other fish meat of heading 0304	11549
030233	Fish; fresh or chilled, skipjack or stripe-bellied bonito, excluding fillets, livers, roes, and other fish meat of heading 0304	4197
030234	Fish; fresh or chilled, bigeye tunas (Thunnus obesus), excluding fillets, livers, roes, and other fish meat of heading 0304	3645
030235	Fish; fresh or chilled, Atlantic and Pacific bluefin tunas (Thunnus thynnus, Thunnus orientalis), excluding fillets, livers, roes, and other fish meat of heading 0304	8354
030236	Fish; fresh or chilled, southern bluefin tunas (Thunnus maccoyii), excluding fillets, livers, roes, and other fish meat of heading 0304	9
030239	Fish; fresh or chilled, tuna, n.e.c. in item no. 0302.3, excluding fillets, livers, roes, and other fish meat of heading 0304	1973
030241	Fish; fresh or chilled, herrings (Clupea harengus, Clupea pallasii), excluding fillets, livers, roes, and other fish meat of heading 0304	141
030242	Fish; fresh or chilled, anchovies (Engraulis spp.), excluding fillets, livers, roes, and other fish meat of heading 0304	9865

030243	Fish; fresh or chilled, sardines (Sardina pilchardus, Sardinops spp.), sardinella (Sardinella spp.), brisling or sprats (Sprattus sprattus), excluding fillets, livers, roes, and other fish meat of heading 0304	18612
030244	Fish; fresh or chilled, mackerel (Scomber scombrus, Scomber australasicus, Scomber japonicus), excluding fillets, livers, roes, and other fish meat of heading 0304	28287
030245	Fish; fresh or chilled, jack and horse mackerel (Trachurus spp.), excluding fillets, livers, roes, and other fish meat of heading 0304	1421
030246	Fish; fresh or chilled, cobia (Rachycentron canadum), excluding fillets, livers, roes, and other fish meat of heading 0304	149
030247	Fish; fresh or chilled, swordfish (Xiphias gladius), excluding fillets, livers, roes, and other fish meat of heading 0304	12890
030251	Fish; fresh or chilled, cod (Gadus morhua, Gadus ogac, Gadus macrocephalus), excluding fillets, livers, roes, and other fish meat of heading 0304	127395
030252	Fish; fresh or chilled, haddock (Melanogrammus aeglefinus), excluding fillets, livers, roes, and other fish meat of heading 0304	237
030253	Fish; fresh or chilled, coalfish (Pollachius virens), excluding fillets, livers, roes, and other fish meat of heading 0304	11458
030254	Fish; fresh or chilled, hake (Merluccius spp., Urophycis spp.), excluding fillets, livers, roes, and other fish meat of heading 0304	15560
030255	Fish; fresh or chilled, Alaska pollock (Theragra chalcogramma), excluding fillets, livers, roes, and other fish meat of heading 0304	374
030256	Fish; fresh or chilled, blue whitings (Micromesistius poutassou, Micromesistius australis), excluding fillets, livers, roes, and other fish meat of heading 0304	272
030259	Fish; fresh or chilled, n.e.c. in item no. 0302.5, excluding fillets, livers, roes, and other fish meat of heading 0304	13138
030271	Fish; fresh or chilled, tilapias (Oreochromis spp.), excluding fillets, livers, roes, and other fish meat of heading 0304	137
030272	Fish; fresh or chilled, catfish (Pangasius spp., Silurus spp., Clarias spp., Ictalurus spp.), excluding fillets, livers, roes, and other fish meat of heading 0304	986
030273	Fish; fresh or chilled, carp (Cyprinus carpio, Carassius carassius, Ctenopharyngodon idellus, Hypophthalmichthys spp., Cirrhinus spp., Mylopharyngodon piceus), excluding fillets, livers, roes, and other fish meat of heading 0304	15572
030274	Fish; fresh or chilled, eels (Anguilla spp.), excluding fillets, livers, roes, and other fish meat of heading 0304	40
030279	Fish; fresh or chilled, Nile perch (Lates niloticus) and snakeheads (Channa spp.), excluding fillets, livers, roes, and other fish meat of heading 0304	230
030281	Fish; fresh or chilled, dogfish and other sharks, excluding fillets, livers, roes, and other fish meat of heading 0304	59
030282	Fish; fresh or chilled, rays and skates (Rajidae), excluding fillets, livers, roes, and other fish meat of heading 0304	230
030283	Fish; fresh or chilled, toothfish (Dissostichus spp.), excluding fillets, livers, roes, and other fish meat of heading 0304	274
030284	Fish; fresh or chilled, seabass (Dicentrarchus spp.), excluding fillets, livers, roes, and other fish meat of heading 0304	803325

030285	Fish; fresh or chilled, seabream (Sparidae), excluding fillets, livers, roes, and other fish meat of heading 0304	1199876
030289	Fish; fresh or chilled, n.e.c. in heading 0302, excluding fillets, livers, roes, and other fish meat of heading 0304	2177446
030311	Fish; frozen, Sockeye salmon (red salmon) (Oncorhynchus nerka), excluding fillets/oth. Fish meat of 03.04/livers & roes	89152
030312	Fish; frozen, Pacific salmon (Oncorhynchus gorbuscha/keta/tschawytscha/ kisutch/masou/rhodurus) other than sockeye salmon (Oncorhynchus nerka), excluding fillets, livers, roes, and other fish meat of heading 0304	539031
030313	Fish; frozen, Atlantic salmon (Salmo salar) and Danube salmon (Hucho hucho), excluding fillets, livers, roes, and other fish meat of heading 0304	321516
030314	Fish; frozen, trout (Salmo trutta, Oncorhynchus mykiss, Oncorhynchus clarki, Oncorhynchus aguabonita, Oncorhynchus gilae, Oncorhynchus apache and Oncorhynchus chrysogaster), excluding fillets, livers, roes, and other fish meat of heading 0304	108988
030319	Fish; frozen, Pacific salmon (Oncorhynchus gorbuscha/keta/tschawytscha/kisutch/masou/rhodurus), excluding of 0303.11; excluding fillets/oth. Fish meat of 03.04/livers & roes	7465
030323	Fish; frozen, tilapias (Oreochromis spp.), excluding fillets, livers, roes, and other fish meat of heading 0304	269459
030324	Fish; frozen, catfish (Pangasius spp., Silurus spp., Clarias spp., Ictalurus spp.), excluding fillets, livers, roes, and other fish meat of heading 0304	37875
030325	Fish; frozen, carp (Cyprinus carpio, Carassius carassius, Ctenopharyngodon idellus, Hypophthalmichthys spp., Cirrhinus spp., Mylopharyngodon piceus), excluding fillets, livers, roes, and other fish meat of heading 0304	1400
030326	Fish; frozen, eels (Anguilla spp.), excluding fillets, livers, roes, and other fish meat of heading 0304	2941
030329	Fish; frozen, 98lalonga98e (excluding of 0303.21 & 0303.22), excluding fillets/oth. Fish meat of 03.04/livers & roes	16201
030331	Fish; frozen, halibut (Reinhardtius hippoglossoides, Hippoglossus hippoglossus/stenolepis), excluding fillets/oth. Fish meat of 03.04/livers & roes	1360
030332	Fish; frozen, plaice (Pleuronectes platessa), excluding fillets/oth. Fish meat of 03. 04/livers & roes	8257
030333	Fish; frozen, sole (Solea spp.), excluding fillets/oth. Fish meat of 03.04/livers & roes	33767
030334	Fish; frozen, turbots (Psetta maxima, Scophthalmidae), excluding fillets, livers, roes, and other fish meat of heading 0304	2354
030339	Fish; frozen, flat fish (excluding of 0303.31-0303.33), excluding fillets/oth. Fish meat of 03.04/livers & roes	2052
030341	Fish; frozen, albacore/longfinned tunas (Thunnus alalunga), excluding fillets/oth. Fish meat of 03.04/livers & roes	46
030342	Fish; frozen, yellowfin tunas (Thunnus albacares), excluding fillets/oth. Fish meat of 03.04/livers & roes	20139
030343	Fish; frozen, skipjack/stripe-bellied bonito (Euthynnus (Katsuwonus) pelamis), excluding fillets/oth. Fish meat of 03.04/livers & roes	564
030345	Fish; frozen, bluefin tunas (Thunnus thynnus), excluding fillets/oth. Fish meat of 03.04/livers & roes	119

030349	Fish; frozen, tunas (excluding of 0303.41-0303.46), excluding fillets/oth. Fish meat of 03.04/livers & roes	8932
030351	Fish; frozen, herrings (Clupea harengus, Clupea pallasii), excluding fillets, livers, roes, and other fish meat of heading 0304	23261
030353	Fish; frozen, sardines (Sardina pilchardus, Sardinops spp.), sardinella (Sardinella spp.), brisling or sprats (Sprattus sprattus), excluding fillets, livers, roes, and other fish meat of heading 0304	270821
030354	Fish; frozen, mackerel (Scomber scombrus, Scomber australasicus, Scomber japonicus), excluding fillets, livers, roes, and other fish meat of heading 0304	94884
030355	Fish; frozen, jack and horse mackerel (Trachurus spp.), excluding fillets, livers, roes, and other fish meat of heading 0304	135715
030357	Fish; frozen, swordfish (Xiphias gladius), excluding fillets, livers, roes, and other fish meat of heading 0304	10772
030363	Fish; frozen, cod (Gadus morhua, Gadus ogac, Gadus macrocephalus), excluding fillets, livers, roes, and other fish meat of heading 0304	298480
030365	Fish; frozen, coalfish (Pollachius virens), excluding fillets, livers, roes, and other fish meat of heading 0304	434
030366	Fish; frozen, hake (Merluccius spp., Urophycis spp.), excluding fillets, livers, roes, and other fish meat of heading 0304	141854
030367	Fish; frozen, Alaska pollock (Theraga chalcogramma), excluding fillets, livers, roes, and other fish meat of heading 0304	455
030368	Fish; frozen, blue whitings (Micromesistius poutassou, Micromesistius australis), excluding fillets, livers, roes, and other fish meat of heading 0304	732
030369	Fish; frozen, of Bregmacerotidae, Euclichthyidae, Gadidae, Macrouridae, Melanonidae, Merlucciidae, Moridae, Muraenolepididae, other than cod, haddock, coalfish, hake, Alaska pollock, blue whitings, excluding fillets, livers, roes, other fish meat of 0304	10211
030381	Fish; frozen, dogfish and other sharks, excluding fillets, livers, roes, and other fish meat of heading 0304	1941
030382	Fish; frozen, rays and skates (Rajidae), excluding fillets, livers, roes, and other fish meat of heading 0304 Species Included: -- Rays and skates (Rajidae)	4139
030383	Fish; frozen, toothfish (Dissostichus spp.), excluding fillets, livers, roes, and other fish meat of heading 0304	1839
030384	Fish; frozen, seabass (Dicentrarchus spp.), excluding fillets, livers, roes, and other fish meat of heading 0304	31660
030389	Fish; frozen, n.e.c. in heading 0303, excluding fillets, livers, roes, and other fish meat of heading 0304	459159
030431	Fish fillets; fresh or chilled, tilapias (Oreochromis spp.)	19266
030432	Fish fillets; fresh or chilled, catfish (Pangasius spp., Silurus spp., Clarias spp., Ictalurus spp.)	367782
030433	Fish fillets; fresh or chilled, Nile perch (Lates niloticus)	8233
030439	Fish fillets; fresh or chilled, carp (Cyprinus carpio, Carassius carassius, Ctenopharyngodon idellus, Hypophthalmichthys spp., Cirrhinus spp., Mylopharyngodon piceus), eels (Anguilla spp.), and snakeheads (Channa spp.)	11063
030441	Fish fillets; fresh or chilled, salmon, Pacific (Oncorhynchus nerka, Oncorhynchus gorbuscha, Oncorhynchus keta, Oncorhynchus	3634943

	tschawytscha, Oncorhynchus kisutch, Oncorhynchus masou and Oncorhynchus rhodurus), Atlantic (Salmo salar), Danube (Hucho hucho)	
030442	Fish fillets; fresh or chilled, trout (Salmo trutta, Oncorhynchus mykiss, Oncorhynchus clarki, Oncorhynchus aguabonita, Oncorhynchus gilae, Oncorhynchus apache and Oncorhynchus chrysogaster)	589304
030443	Fish fillets; fresh or chilled, flat fish (Pleuronectidae, Bothidae, Cynoglossidae, Soleidae, Scophthalmidae and Citharidae)	1081169
030444	Fish fillets; fresh or chilled, of the families Bregmacerotidae, Euclichthyidae, Gadidae, Macrouridae, Melanonidae, Merlucciidae, Moridae, and Muraenolepididae	1316376
030445	Fish fillets; fresh or chilled, swordfish (Xiphias gladius)	78045
030446	Fish fillets; fresh or chilled, toothfish (Dissostichus spp.)	8
030449	Fish fillets; fresh or chilled, other than fish of heading 0304.4	2569302
030451	Fish meat, excluding fillets, whether or not minced; fresh or chilled, tilapias (Oreochromis spp.), catfish (Pangasius spp., Silurus spp., Clarias spp., Ictalurus spp.), carp (Cyprinus carpio, Carassius carassius, Ctenopharyngodon idellus, Hypophthalmichthys spp., Cirrhinus spp., Mylopharyngodon piceus), eels (Anguilla spp.), Nile perch (Lates niloticus) and snakeheads (Channa spp.)	1803
030452	Fish meat, excluding fillets, whether or not minced; fresh or chilled, salmonidae	27684
030453	Fish meat, excluding fillets, whether or not minced; fresh or chilled, of the families Bregmacerotidae, Euclichthyidae, Gadidae, Macrouridae, Melanonidae, Merlucciidae, Moridae, and Muraenolepididae	15558
030454	Fish meat, excluding fillets, whether or not minced; fresh or chilled, swordfish (Xiphias gladius)	85
030461	Fish fillets; frozen, tilapias (Oreochromis spp.)	254479
030462	Fish fillets; frozen, catfish (Pangasius spp., Silurus spp., Clarias spp., Ictalurus spp.)	2395569
030463	Fish fillets; frozen, Nile Perch (Lates niloticus)	6379
030469	Fish fillets; frozen, carp (Cyprinus carpio, Carassius carassius, Ctenopharyngodon idellus, Hypophthalmichthys spp., Cirrhinus spp., Mylopharyngodon piceus), eels (Anguilla spp.), and snakeheads (Channa spp.)	3283
030471	Fish fillets; frozen, cod (Gadus morhua, Gadus ogac, Gadus macrocephalus)	917620
030472	Fish fillets; frozen, haddock (Melanogrammus aeglefinus)	5661
030473	Fish fillets; frozen, coalfish (Pollachius virens)	235779
030474	Fish fillets; frozen, hake (Merluccius spp., Urophycis spp.)	229845
030475	Fish fillets; frozen, Alaska pollock (Theraga chalcogramma)	282020
030479	Fish fillets; frozen, of the families Bregmacerotidae, Euclichthyidae, Gadidae, Macrouridae, Melanonidae, Merlucciidae, Moridae and Muraenolepididae other than cod, haddock, coalfish, hake, and Alaska pollock	43282
030481	Fish fillets; frozen, salmon, Pacific (Oncorhynchus nerka, Oncorhynchus gorbuscha, Oncorhynchus keta, Oncorhynchus tschawytscha, Oncorhynchus kisutch, Oncorhynchus masou, Oncorhynchus rhodurus), Atlantic (Salmo salar), and Danube (Hucho hucho)	1733351

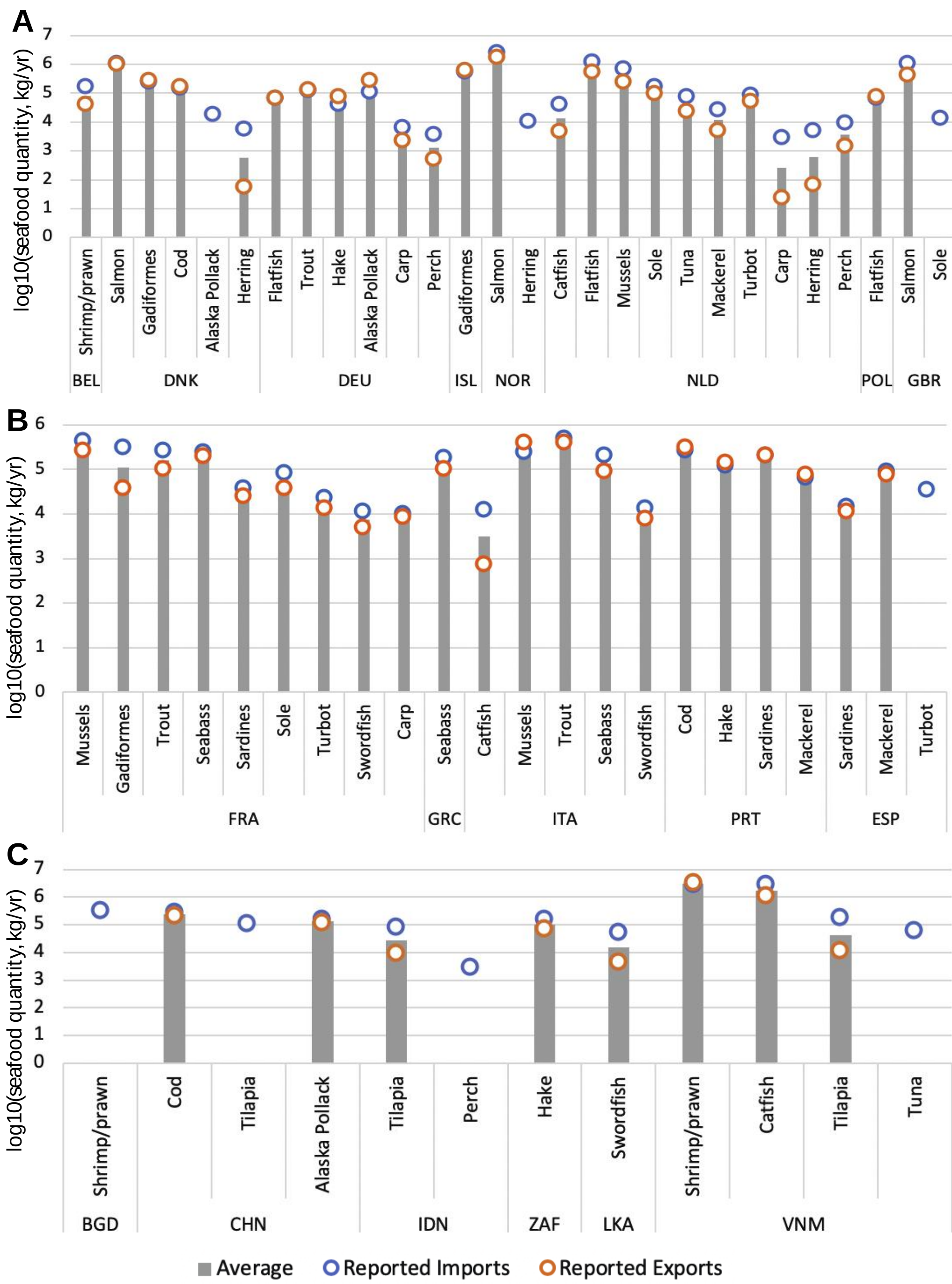
030482	Fish fillets; frozen, trout (Salmo trutta, Oncorhynchus mykiss, Oncorhynchus clarki, Oncorhynchus aguabonita, Oncorhynchus gilae, Oncorhynchus apache and Oncorhynchus chrysogaster)	77584
030483	Fish fillets; frozen, flat fish (Pleuronectidae, Bothidae, Cynoglossidae, Soleidae, Scophthalmidae and Citharidae)	506337
030484	Fish fillets; frozen, swordfish (Xiphias gladius)	7650
030485	Fish fillets; frozen, toothfish (Dissostichus spp.)	5977
030486	Fish fillets; frozen, herrings (Clupea harengus, Clupea pallasii)	1993
030487	Fish fillets; frozen, tunas (of the genus Thunnus), skipjack or stripe-bellied bonito (Euthynnus (Katsuwonus) pelamis)	239156
030489	Fish fillets; frozen, of fish n.e.c. in heading 0304.8	2352697
030491	Fish meat, excluding fillets, whether or not minced; frozen, swordfish (Xiphias gladius)	70
030493	Fish meat, excluding fillets, whether or not minced; frozen, tilapias (Oreochromis spp.), catfish (Pangasius spp., Silurus spp., Clarias spp., Ictalurus spp.), carp (Cyprinus carpio, Carassius carassius, Ctenopharyngodon idellus, Hypophthalmichthys spp., Cirrhinus spp., Mylopharyngodon piceus), eels (Anguilla spp.), Nile perch (Lates niloticus) and snakeheads (Channa spp.)	115169
030494	Fish meat, excluding fillets, whether or not minced; frozen, Alaska Pollock (Theraga chalcogramma)	18995
030495	Fish meat, excluding fillets, whether or not minced; frozen, of the families Bregmacerotidae, Euclichthyidae, Gadidae, Macrouridae, Melanonidae, Merlucciidae, Moridae and Muraenolepididae, other than Alaska Pollock (Theraga chalcogramma)	14977
030616	Crustaceans; frozen, cold-water shrimps and prawns (Pandalus spp., Crangon crangon), in shell or not, smoked, cooked or not before or during smoking; in shell, cooked by steaming or by boiling in water	144047
030617	Crustaceans; frozen, shrimps and prawns, excluding cold-water varieties, in shell or not, smoked, cooked or not before or during smoking; in shell, cooked by steaming or by boiling in water	4418151
030626	Crustaceans; not frozen, cold-water shrimps and prawns (Pandalus spp., Crangon crangon), in shell or not, smoked, cooked or not before or during smoking; in shell, cooked by steaming or by boiling in water; edible flour, meals, and pellets	23410
030627	Crustaceans; not frozen, shrimps and prawns excluding cold-water varieties, in shell or not, smoked, cooked or not before or during smoking; in shell, cooked by steaming or by boiling in water; edible flour, meals, and pellets	23561
030731	Mussels (Mytilus spp., Perna spp.), live, fresh or chilled	1443911
0302	Fish, fresh or chilled, excluding fish fillets and other fish meat of heading 03.04	8414138
0303	Fish, frozen, excluding fish fillets and other fish meat of heading 03.04	2960260
TOTAL IMPORTS		47969288

Appendix A Table 2: Total traded quantities for selected seafood commodities.

Seafood species	Imports (kg/year)	*Exports+ re-exports (kg/year)	Net quantity (kg/year)
Salmon	9,519,516	52,577	9,466,939
Shrimp	4,609,169	29,276	4,579,893
Catfish	2,802,212	4,396	2,797,816
Flatfish	1,595,391	1,200	1,594,191
Mussels	1,443,911	No exports or re-exports	1,443,911
Gadiformes*	1,400,404	No exports or re-exports	1,400,404
Cod	1,343,495	2,586	1,340,909
Seabream	1,199,876	160	1,199,716
Trout	1,046,693	282,359	764,334
Seabass	834,985	No exports or re-exports	834,985
Tilapia	543,341	3,695	539,646
Hake	387,259	No exports or re-exports	387,259
Alaska Pollock	301,844	1,269	300,575
Tuna	300,673	4,547	296,126
Sardines	289,433	5	289,428
Sole	287,062	No exports or re-exports	287,062
Mackerel	260,307	1,008	259,299
Coalfish	247,671	630	247,041
Turbot	148,239	No exports or re-exports	148,239
Swordfish	109,512	No exports or re-exports	109,427
Salmonidae**	102,229	1	102,228
Carp	31,318	4,885	26,433
Herring	25,395	1,126	24,269
Halibut	15,587	No exports or re-exports	15,587
Perch	14,842	No exports or re-exports	14,842
Anchovies	9,865	No exports or re-exports	9,865
Plaice	9,475	No exports or re-exports	9,475
Toothfish	8,098	No exports or re-exports	8,098
Haddock	5,898	No exports or re-exports	5,898
Rays and stakes	4,369	No exports or re-exports	4,369
Eel	2,981	No exports or re-exports	2,981
Dogfish	2,000	No exports or re-exports	2,000
Whiting	1,004	No exports or re-exports	1,004
Cobia	149	No exports or re-exports	149

* families Bregmacerotidae, Euclichthyidae, Gadidae, Macrouridae, Melanonidae, Merlucciidae, Moridae and Muraenolepididae other than cod, haddock, coalfish, hake, and Alaska pollock, **other than trout (Salmo trutta, Oncorhynchus mykiss, Oncorhynchus clarki, Oncorhynchus

aguabonita, Oncorhynchus gilae, Oncorhynchus apache and Oncorhynchus chrysogaster and Pacific salmon/Atlantic salmon/Danube salmon



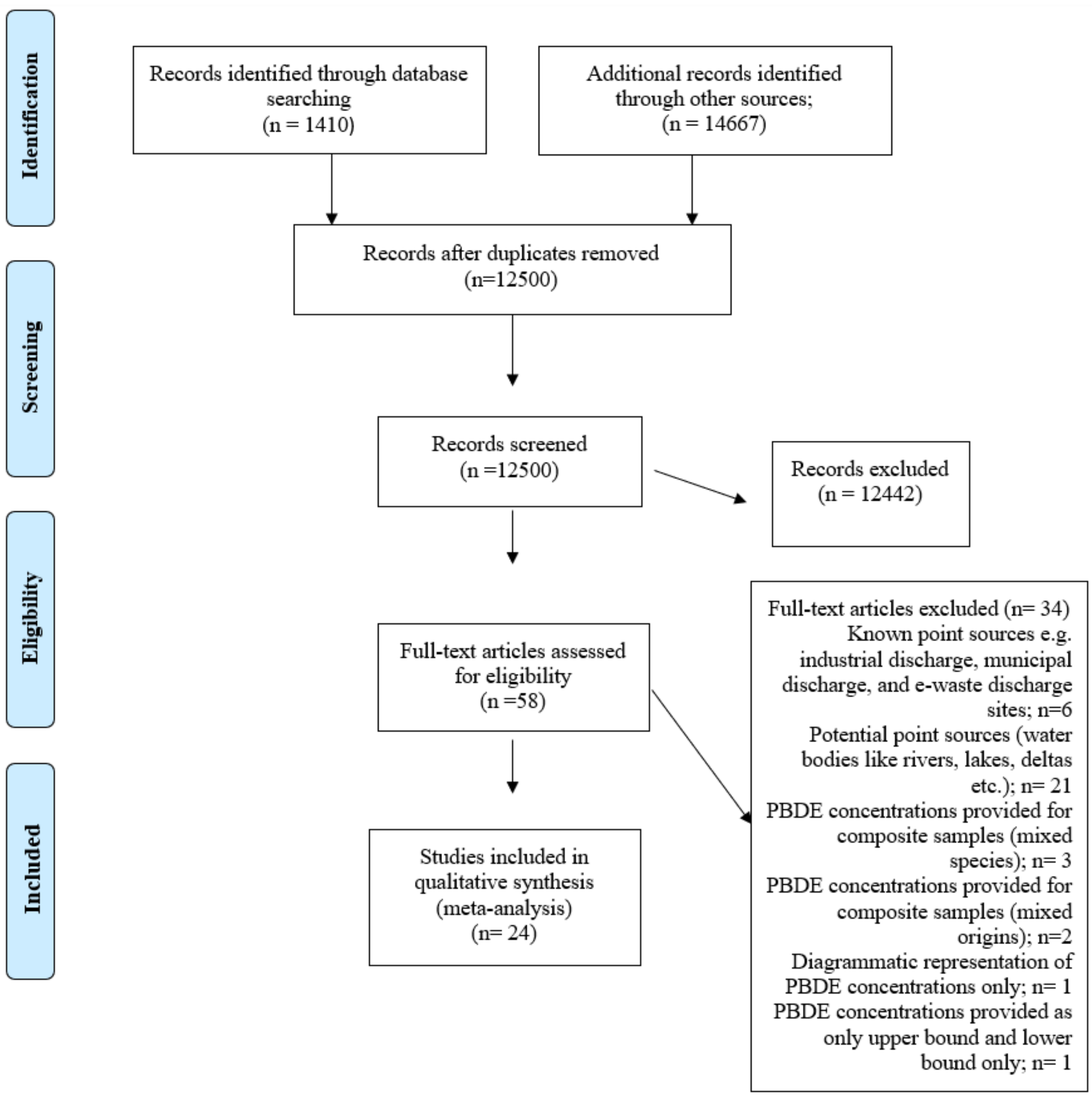
Appendix A Figure 1: Import/export trade data discrepancies for countries in (A) Northern Europe, (B) Southern Europe and (C) other parts of the world. Grey bars are means of imports and reported exports. Blue and orange circles are reported imports and reported exports.

Notes:

The disparities between imported quantities reported by Switzerland and exported quantities reported by its top trade partners were assessed (Appendix Figure A1). The mean fish quantities ($M_{fis\$}$) shown are an average of the imports reported (Im^S) by Switzerland (S) from partner country (P) and the exports reported (Ex^P) by the partner country to Switzerland (Equation A1).

$$\mathrm{M_{fish}} = \frac{\mathrm{Im_P^S + Ex_S^P}}{2} \qquad \text{(A1)}$$

All values were reported in log10kg/ year. Dominant regions (top 3) from where Switzerland imports its crucial fish (top 20 plus perch) were split across three regions; **Northern Europe** (Figure A1A: Belgium, Denmark, Germany, Iceland, Norway, Netherlands, Poland and United Kingdom); **Southern Europe** (Figure A1B: France, Greece, Italy, Portugal and Spain) and **Others** (Figure A1C: Bangladesh, China, Indonesia, South Africa, Sri Lanka and Vietnam). Counties are identified using standard alpha3 codes provided by the United Nation's Statistical Division have been used for countries.[203] For most of the fish types, there exists a difference between reported imports and exports, with reported import values being larger in mostcases. Since we use imports reported by Switzerland for the PBDE exposure calculations, this uncertainty does not impact our conservative (worst-case) estimates. Furthermore, we found that exports and re-exports reported (Table A2) were very small compared to the import quantities, andwithin the range of uncertainty for the imports themselves. These were therefore neglected in our exposure calculations.



Appendix A Figure 2: Systematic review flow diagram constructed using Prisma guidelines.

Appendix A Table 3: Fish characteristics used for species – origin substitutions.

Seafood species	Trophic level[204]	Habitat (adult fish)	Typical diet	Distinct feature/family
Catfish	Primary/ secondary	Freshwater	Aquatic flora; fauna found in lower trophic levels (insects, snails, small fish etc.)	Ray-finned fish
Herring	Primary	Saltwater	Filter feeder	Schooling fish, ray-finned, Family- Clupeidae
Sardines	Primary	Saltwater	Filter feeder	Schooling fish, ray-finned, Family- Clupeidae
Cod[205]	Tertiary	Saltwater	Pelagic fish like herring, silver hake, haddock, whiting, small mackerel etc.; small cod; carbs and other crustaceans	Family- Gadidae
Swordfish[206]	Tertiary	Saltwater	Cephalopods mainly squid and octopod, silver hake, mackerel, cods, bluefish are among the most consumed fish	Family- Xiphiidae
Seabass	Secondary	Saltwater	Small pelagic fish like sardine, mackerel, scads and anchovy; insects, frogs and small aquatic birds	Family-Lateolabracidae
Hake[205]	Secondary	Saltwater	Pelagic fish prey and invertebrates (mostly shrimp), larger sizes feed on congener, silver hake	Most abundant predator fish11, Family- Gadidae
Alaska Pollock	Secondary	Saltwater	Krill is the primary diet, also fishes and crustaceans	Schooling fish, National fish of Korea, Family- Gadidae
Turbot	Secondary	Saltwater	Bottom dwelling, near sand and gravel, crustaceans, small fish, worms and molluscs	Flatfish, Family- Scophthalmidae
Sole	Secondary	Saltwater	Bottom dwelling, near sand and gravel, crustaceans, small fish, worms and molluscs	Flatfish, Family- Soleidae

Carp	Primary/ secondary	Freshwater	Omnivorous, bottom dwelling, prefer insects, worms, crustaceans, crawfish, zooplanktons etc.	Schooling fish, ray finned, Family- Cyprinidae
Perch[207]	Secondary	Freshwater	Major preys include pelagic cyprinid, benthic shrimp and smaller nile perch, also consume minnows, roach, leeches and snails	Family-Percidae
Gadiformes	Secondary	Saltwater	Same as cod/pollock	Ray-finned, includes cod and its allies
Salmon	Tertiary	Saltwater	Opportunist feeders, shrimp is primary prey; pelagic fish like herring, mackerel, whiting; eels, squid etc.	Ray-finned, Family Salmonidae
Tilapia	Primary	Freshwater	Herbivore, algae or any aquatic plants	Family-Cichlidae
Coalfish[208]	Secondary	Saltwater	Crustaceans are most abundant; pelagic fish like herring, mackerel, sandeel, norway pout etc.	Family- Gadidae
Roach	Primary	Freshwater	Omnivorous; aquatic fauna, bottom dwelling invertebrates, worms etc.	Family-Cyprinidae
Haddock	Secondary	Saltwater	Bottom dweller; shrimps/ prawns, worms, molluscs etc.	Family- Gadidae
Whiting	Secondary	Saltwater	Bottom dweller; shrimps/ prawns, worms, molluscs etc.	Family- Gadidae
Anchovies	Primary	Saltwater	Filter feeder	Family- Engraulidae
Flounder	Secondary	Saltwater	Bottom dweller; shrimp/prawn, crustaceans etc.	Suborder-Pleuronectoidei (includes five families)
Crayfish	Primary/ secondary	Freshwater	Bottom dweller, omnivorous; vegetables, fish, insects etc.	Superfamily- Astacoidea and Parastacoidea

Lobster	Primary/ secondary	Freshwater/ saltwater	Bottom dweller, omnivorous; vegetables, fish, insects etc.	Family- Nephropidae

Notes:

PBDE data are key, as they drive our exposure estimates, yet data are not uniformly available forall species and origins. We therefore used various assumptions based on fish taxonomy and relatedPBDE concentrations to complete our dataset. First, we categorized the commercial seafood species in Switzerland according to their trophic level (primary consumers, secondary consumers, omnivores consuming both producers and consumers, and higher-trophic-level predators), habitat,or other distinct features.We assume that species with taxonomic similarities (e.g. similar trophic levels, belonging to samefamily or having similar features) will have similar PBDE levels, provided they are from similar geographic regions. Species having taxonomic similarities (shown in Table A4 as check marks) are assumed have similar PBDE concentrations if they are from the same environment, once differences in lipid content are accounted for by converting between lipid-normalized and wet- weight concentrations.

Appendix A Table 4: Seafood of interest and species with PBDE data available identified as having similar characteristics.

Seafood	Catfish	Herring	Cod	Sardines	Swordfish	Hake	Perch	Carp	Gadiformes	Seabass	Pollock	Turbot	Sole	Mussels	Shrimp	Squid
Catfish	√	√		√			√	√								
Gadiformes			√		√	√			√	√	√					
Cod			√		√	√			√	√	√					
Seabass			√			√			√	√	√					
Hake			√			√			√	√	√					
Alaska Pollock			√			√			√	√	√					
Turbot												√	√			
Swordfish			√		√				√							
Carp	√	√		√			√	√								
Perch	√	√		√			√	√								
Coalfish			√			√			√	√	√					
Roach	√	√		√			√	√								
Anchovies	√	√					√	√								
Lobsters															√	
Haddock			√		√	√			√	√						
Founder												√	√			
Crayfish															√	
Oysters														√		
Cuttlefish																√
Whiting			√		√	√					√					

Appendix Table 5: Seafood consumed according to menuCH survey responses.

Species or type	Total consumed byall respondents (g/day)	Average consumed per respondent (g/person/day)	Percentof diet
Salmon	14418.94	7.20	18.02
Cod, Atlantic	7528.65	3.764	9.41
Tuna	6818.75	3.40	8.52
Shrimp	5390.25	2.69	6.74
Trout	4591.76	2.29	5.74
Perch (+zander)	3422.28	1.71	4.28
Whitefish	1997	0.99	2.50
Sardines	1679.25	0.83	2.10
Sea bream	1589.75	0.79	1.99
Pangasius	1451.67	0.72	1.81
Plaice	1052.5	0.52	1.32
Herring	724	0.36	0.91
Flounder	673	0.33	0.84
Hake	617	0.30	0.77
Mackerel	614	0.307	0.77
Sole	605.5	0.302	0.76
Crab	576.179	0.28	0.72
Mussels	552.5	0.27	0.69
Anchovies	535.16	0.26	0.67
Cuttlefish	505.40	0.25	0.63
Squid	436	0.21	0.55
Crayfish	368.85	0.18	0.46
Oysters	354	0.17	0.44
Atlantic Halibut	248	0.12	0.31
Scallops	213.50	0.10	0.27
Swordfish	145.52	0.07	0.18
Eel	97	0.04	0.12
Clams	43.12	0.02	0.05
Lobster	32.34	0.01	0.04
Whiting	8	0.004	0.01

Notes: Each of the 2000 participants of the menuCH survey reported whether they consumed seafood during a 24-h recall period. Many individuals also reported using seafood as an ingredient while cooking an entrée, fish paste (fish not specified), fish sticks (fish not specified) or just fish (species not specified at all). All these data points were excluded from species-specific estimation. However, they were included in calculating the total average fish consumption of 40 g/day. Here we list the seafood species reported to be consumed along with the total quantity consumed, which was calculated as the sum of all individual responses during the survey period. Further, we calculate the average species-specific consumption per person for 2000 individuals. Finally, we report the proportion of the seafood diet occupied by each consumed species with respect to the 40 g daily consumption.

Appendix A Table 6: Seafood consumed according to trade data.

Species or type	Net quantity (kg/year)	Percent of total imports or local catch	Percent of diet	Daily consumption (g/day)
Salmon	9519516	19.84	19.44	4.47
Shrimp	4609169	9.60	9.41	2.16
Catfish	2802212	5.84	5.72	1.31
Flatfish	1595391	3.32	3.25	0.74
Mussels	1443911	3.01	2.94	0.67
Gadiformes	1400404	2.91	2.86	0.65
Cod	1343495	2.80	2.74	0.63
Seabream	1199876	2.50	2.45	0.56
Trout	1046693	2.18	2.13	0.49
Seabass	834985	1.74	1.70	0.39
Tilapia	543341	1.13	1.11	0.25
Hake	387259	0.80	0.79	0.18
Alaska Pollock	301844	0.629	0.616	0.1418
Tuna	300673	0.626	0.614	0.1413
Sardines	289433	0.60	0.59	0.136
Sole	287062	0.59	0.58	0.134
Mackerel	260307	0.54	0.53	0.122
Coalfish	247671	0.51	0.50	0.116
Turbot	148239	0.30	0.30	0.069
Swordfish	109512	0.22	0.22	0.051
Salmonidae	102229	0.21	0.20	0.048
Carp	31318	0.060	0.06	0.0147

Herring	25395	0.052	0.05	0.0119
Halibut	15587	0.032	0.031	0.0073
Perch	14842	0.030	0.0303	0.0070
Anchovies	9865	0.020	0.020	0.0046
Plaice	9475	0.019	0.019	0.0045
Toothfish	8098	0.016	0.016	0.0038
Haddock	5898	0.012	0.012	0.0028
Rays and stakes	4369	0.009	0.0089	0.0021
Eel	2981	0.006	0.0061	0.0014
Dogfish	2000	0.004	0.0041	0.0009
Whiting	1004	0.002	0.0021	0.0005
Cobia	149	0.0003	0.0003	0.0001
Whitefish	845917	61.94	1.23	0.28
Perch	230246	16.85	0.33	0.07
Roach	119176	8.72	0.174	0.04

Percent of total imports or local catch for each species was calculated for a total imported quantityof 47969288 kg or domestic catch quantity of 1365729 kg respectively.

Appendix A Table 7: Survey-based PBDE exposure estimates.

Seafood species	Consumption(g/day)	Average global PBDE concentration (ng/g wet weight)	PBDE level substitutes if used	PBDE exposure (ng/kg bw/day)
Salmon	7.2095	0.985	-	0.0986
Cod	3.7643	0.092	-	0.0048
Tuna	3.4094	0.055	-	0.0026
Shrimp	2.6951	0.310	-	0.0116
Trout	2.2959	0.976	-	0.0311
Perch	1.7111	9.301	-	0.2210
Whitefish*	0.9985	4.50	-	0.062406
Sardines	0.8396	0.169	-	0.0020
Sea bream	0.7949	1.157	-	0.0128
Pangasius	0.7258	0.364	Catfish	0.0037
Plaice	0.5263	0.454	-	0.0033
Herring	0.3620	6.046	-	0.0304
Flounder	0.3365	0.777	-	0.0036
Hake	0.3085	0.221	-	0.0009
Mackerel	0.3070	0.876	-	0.0037
Sole	0.3028	0.731	-	0.0031
Crab	0.2881	1.285	-	0.0051
Mussels	0.2763	0.482	-	0.0018
Anchovies	0.2676	6.046	Herring	0.0225
Cuttlefish	0.2527	19.420	Squid	0.0682
Squid	0.2180	19.420	-	0.0588
Crayfish	0.1844	0.310	Shrimp	0.0008
Oysters	0.1770	0.482	Mussels	0.0012
Halibut	0.1240	0.092	Cod	0.00015
Scallops	0.1068	1.057	-	0.0016
Swordfish	0.0728	0.978	-	0.0010
Eel	0.0485	1.767	-	0.0012
Clams	0.0216	0.126	-	0.000038
Lobster	0.0162	0.310	Shrimp	0.0001
Whiting	0.0040	0.092	Cod	0.000049
Total Exposure= 0.65 ng/kg bw/day				

*PBDE concentration here is for Switzerland since surveyed consumers noted that it was European whitefish.

Appendix A Table 8: Trade-based PBDE exposure estimates.

Seafood Species	Consumption (g/day)	Average global PBDE concentration (ng/g wet weight)	PBDE level substitutes if used	PBDE exposure (ng/kg bw/day)
Salmon	4.48	0.985	-	0.0613
Shrimp	2.16	0.31	-	0.0093
Cod	1.42	0.092	-	0.0018
Catfish	1.32	0.364	-	0.0067
Flatfish	0.75	0.731	Sole	0.0076
Mussels	0.68	0.482	-	0.0046
Seabream	0.56	1.157	-	0.0090
Trout	0.5	0.976	-	0.0068
Seabass	0.4	0.33	-	0.0018
Tilapia	0.25	0.026	-	0.0001
Hake	0.18	0.221	-	0.0006
Tuna	0.14	0.055	-	0.0001
Sardines	0.135	0.169	-	0.0003
Sole	0.134	0.731	-	0.0014
Mackerel	0.12	0.876	-	0.0015
Coalfish	0.11	0.41	-	0.0006
Perch	0.085	9.301		0.0110
Turbot	0.07	0.731	Sole	0.0007
Swordfish	0.05	0.978	-	0.0007
Carp	0.015	0.575	-	0.0001
Herring	0.012	6.046	-	0.0010
Halibut	0.007	0.092	Cod	0.000009
Anchovies	0.005	6.046	Herring	0.00042
Plaice	0.004	0.454	-	0.000025
Haddock	0.003	0.092	Cod	0.000004
Eel	0.001	1.767	-	0.000025
Whiting	0.0005	0.092	Cod	0.000001
Whitefish*	0.29	4.5	-	0.0181
Roach	0.04	6.046	Herring	0.0033
Total Exposure=0.15 ng/kg bw/day				

*PBDE concentration here is the specific concentration for the local/ Switzerland sourced whitefish since the trade data doesn't report any imports and it is only locally caught.

Appendix A Table 9: Trade-based origin-specific PBDE exposure estimates.

Seafood	Exporter	Imported quantity (kg/year)	Sum PBDEs (ng/g wet weight)	Percentof total imports	Percent proportionof diet	Fish consumption (g/day)	Total PBDE exposure (ng/day)	Total PBDE exposure (ng/kg bw/day)
Salmon	Norway	2630542	1.78	5.48	5.37	1.23605	2.20017	0.03056
	Denmark	1150148	1.58	2.40	2.35	0.54044	0.85389	0.01186
	UK	1122459	1.58	2.34	2.29	0.52743	0.83333	0.01157
Shrimp/prawn	Vietnam	2999681	25.1	6.25	6.13	1.40950	35.37850	0.49137
	Bangladesh	316610	0.11	0.66	0.65	0.14877	0.01636	0.00023
	Belgium	164000	0.06	0.34	0.34	0.07706	0.00462	0.00006
Catfish	Vietnam	2700230	0.22	5.63	5.52	1.26879	0.27913	0.00388
	Netherlands	43353	4.81	0.09	0.09	0.02037	0.09798	0.00136
	Italy	12546	0.71	0.03	0.03	0.00590	0.00419	0.00006
Flatfish	Netherlands	1244978	0.44	2.60	2.54	0.58500	0.25740	0.00357
	Poland	69228	0.44	0.14	0.14	0.03253	0.01431	0.00020
	Germany	67610	0.44	0.14	0.14	0.03177	0.01398	0.00019
Mussels	Netherlands	712557	1.12	1.49	1.46	0.33482	0.37500	0.00521
	France	440568	0.17	0.92	0.90	0.20702	0.03519	0.00049
	Italy	238499	0.17	0.50	0.49	0.11207	0.01905	0.00026
Gadiformes	Iceland	535083	1.78	1.12	1.09	0.25143	0.44754	0.00622
	France	306653	0.98	0.64	0.63	0.14409	0.14121	0.00196
	Denmark	253433	1.58	0.53	0.52	0.11908	0.18815	0.00261
Cod	China	280413	0.051	0.58	0.57	0.13176	0.00672	0.00009
	Portugal	272612	0.98	0.57	0.56	0.12810	0.12553	0.00174
	Denmark	158684	0.385	0.33	0.32	0.07456	0.02871	0.00040
Seabream	Greece	691010	4.78	1.44	1.41	0.32469	1.55204	0.02156
	France	200604	4.78	0.42	0.41	0.09426	0.45057	0.00626
	Italy	171736	4.78	0.36	0.35	0.08070	0.38573	0.00536
Trout	Italy	508818	0.41	1.06	1.04	0.23909	0.09803	0.00136
	France	257002	0.41	0.54	0.53	0.12076	0.04951	0.00069
	Germany	121569	0.27	0.25	0.25	0.05712	0.01542	0.00021

Seabass	France	246755	0.22	0.51	0.50	0.11595	0.02551	0.00035
	Italy	204907	0.22	0.43	0.42	0.09628	0.02118	0.00029
	Greece	172980	0.22	0.36	0.35	0.08128	0.01788	0.00025
Tilapia	Vietnam	177048	0.02	0.37	0.36	0.08319	0.00166	0.00002
	China	111225	0.051	0.23	0.23	0.05226	0.00267	0.00004
	Indonesia	82385	0.02	0.17	0.17	0.03871	0.00077	0.00001
Hake	South Africa	155846	0.22	0.32	0.32	0.07323	0.01611	0.00022
	Portugal	118892	0.22	0.25	0.24	0.05587	0.01229	0.00017
	Germany	40371	0.385	0.08	0.08	0.01897	0.00730	0.00010
Alaska Pollock	China	156928	0.051	0.33	0.32	0.07374	0.00376	0.00005
	Germany	100513	0.385	0.21	0.21	0.04723	0.01818	0.00025
	Denmark	17838	0.385	0.04	0.04	0.00838	0.00323	0.00004
Tuna	Netherlands	75955	0.02	0.16	0.16	0.03569	0.00071	0.00001
	Vietnam	57958	0.01	0.12	0.12	0.02723	0.00027	0.00000
	UK	40881	0.01	0.09	0.08	0.01921	0.00019	0.00000
Sardines	Portugal	212838	0.71	0.44	0.43	0.10001	0.07101	0.00099
	France	36613	0.71	0.08	0.07	0.01720	0.01221	0.00017
	Spain	14011	0.71	0.03	0.03	0.00658	0.00467	0.00006
Sole	Netherlands	173045	0.44	0.36	0.35	0.08131	0.03578	0.00050
	France	83037	0.24	0.17	0.17	0.03902	0.00936	0.00013
	UK	12901	0.44	0.03	0.03	0.00606	0.00267	0.00004
Mackerel	Spain	88292	1.12	0.18	0.18	0.04149	0.04647	0.00065
	Portugal	62504	1.12	0.13	0.13	0.02937	0.03289	0.00046
	Netherlands	25557	1.15	0.05	0.05	0.01201	0.01381	0.00019
Coalfish	Germany	123288	0.41	0.26	0.25	0.05793	0.02375	0.00033
	China	46349	0.51	0.10	0.09	0.02178	0.01111	0.00015
	Poland	38589	0.41	0.08	0.08	0.01813	0.00743	0.00010
Turbots	Netherlands	80357	0.44	0.17	0.16	0.03776	0.01661	0.00023
	Spain	33448	0.24	0.07	0.07	0.01572	0.00377	0.00005
	France	23534	0.24	0.05	0.05	0.01106	0.00265	0.00004
Swordfish	Sri Lanka	55007	PBDE DATA UNAVAILABLE					
	Italy	13319	0.98	0.98	0.03	0.03	0.00613	0.00009
	France	11949	0.98	0.98	0.02	0.02	0.00550	0.00008
	Netherlands	9588	4.81	4.81	0.02	0.02	0.02167	0.00030

	Germany	3475	4.81	4.81	0.01	0.01	0.00785	0.00011
	Indonesia	3085	PBDE DATA UNAVAILABLE					
	Domestic	230246	4.81	16.858	0.33	0.077	0.373019	0.00518
Whitefish	Domestic	845917	4.50	61.938	1.23	0.284	1.282134	0.01780
Perch	Domestic	119176	4.81	8.726	0.17	0.040	0.193076	0.00268

Appendix B Supporting information for Chapter 3.0

Appendix B Table 10: Details of seafood sample set.

Sample ID	Seafood	Point of origin	Production method	Storage condition	Store
01CAT-UNK-IS	Catfish	Unknown	Unknown	Fresh	International store
02-CAT-USA-VS	Catfish	USA	Farmed	Frozen	Variety store
03-CLA-CAN-IS	Clams	Canada	Wild	Frozen	International store
04-CLA-CHN-IS	Clams	China	Wild	Frozen	International store
05-CLA-VNM-IS	Clams	Vietnam	Farmed	Frozen	International store
06-COD-CHN-DS	Cod	China	Wild	Frozen	Discount store
07-COD-ISL-WC	Cod	Iceland	Wild	Frozen	Wholesale chain
08-COD-USA-VS	Cod	USA	Wild	Frozen	Variety store
09-COD-USA-VS	Cod	USA	Wild	Frozen	Variety store
10-CRA-CAN-VS	Crab	Canada	Wild	Fresh	Variety store
11-CRA-USA-LS	Crab	USA	Wild	Fresh	Luxury store
12-FLO-CHN-GC	Flounder	China	Wild	Frozen	Grocery chain
13-HAD-NOR-GC	Haddock	Norway	Wild	Frozen	Grocery chain
14-MAC-CHN	Mackerel	China	Wild	Frozen	International store
15-MAC-THA-IS	Mackerel	Thailand	Wild	Frozen	International store
16-MAH-PER-VS	Mahi-mahi	Peru	Wild	Frozen	Variety store
17-MUS-CHL-DS	Mussels	Chile	Farmed	Frozen	Discount store
18-MUS-CHN-IS	Mussels	China	Wild	Frozen	International store
19-PER-CAN-GC	Perch	Canada	Wild	Frozen	Grocery chain
20-POL-KOR-IS	Pollock	Korea	Wild	Frozen	International store
21-SAL-CHL-DS	Salmon	Chile	Farmed	Fresh	Discount store
22-SAL-CHL-VS	Salmon	Chile	Farmed	Frozen	Variety store
23-SAL-CHN-VS	Salmon	China	Wild	Frozen	Variety store
24-SAL-NOR-LS	Salmon	Norway	Farmed	Fresh	Luxury store
25-SAL-USA-VS	Salmon	USA	Wild	Frozen	Variety store
26-SAL-USA-GC	Salmon	USA	Wild	Frozen	Grocery chain
27-SCA-USA-DS	Scallops	USA	Wild	Frozen	Discount store
28-SEA-TUR-GC	Seabass	Turkey	Farmed	Frozen	Grocery chain
29-SHR-IND-VS	Shrimp	India	Farmed	Frozen	Variety store
30-SHR-IDN-VS	Shrimp	Indonesia	Farmed	Frozen	Variety store
31-SHR-THA-LS	Shrimp	Thailand	Farmed	Fresh	Luxury store
32-SHR-THA-IS	Shrimp	Thailand	Farmed	Frozen	International store

33-SHR-USA-DS	Shrimp	USA	Wild	Frozen	Discount store
34-SHR-USA-LS	Shrimp	USA	Wild	Frozen	Luxury store
35-SHR-VNM-GC	Shrimp	Vietnam	Farmed	Frozen	Grocery chain
36-SME-EST-GC	Smelt	Estonia	Wild	Frozen	Grocery chain
37-SWA-VNM-IS	Swai	Vietnam	Farmed	Frozen	International store
38-SWO-SGP-GC	Swordfish	Singapore	Wild	Frozen	Grocery chain
39-TIL-CHN-VS	Tilapia	China	Farmed	Fresh	Variety store
40-TIL-ECU-LS	Tilapia	Ecuador	Farmed	Fresh	Luxury store
41-TIL-HND-DS	Tilapia	Honduras	Farmed	Fresh	Discount store
42-TIL-IDN-GC	Tilapia	Indonesia	Farmed	Frozen	Grocery chain
43-TIL-TWN-IS	Tilapia	Taiwan	Farmed	Frozen	International store
44-TRO-PER-DS	Trout	Peru	Farmed	Fresh	Discount store
45-TUN-ESP-VS	Tuna	Spain	Wild	Frozen	Variety store
46-TUN-VNM-GC	Tuna	Vietnam	Wild	Frozen	Grocery chain

The sample set included 46 seafood consisting of 31 fish and 15 shellfish. Both farm raised and wild caught seafood were included,19 samples were farmed (~42%), 26 wild caught (~57%), and husbandry type for one sample was unknown. Seafood sourced from 19 origins were included: 26% from North America, 46% from Asia, 16% from South America, 10% from Europe, 2% from an unknown origin.

Stores were grouped to see if a customers' preference to shop at a specific store would impact PFAS exposure. We included 6 categories of stores based on accessibility and affordability. A store was categorized as a discount store (DS) if seafood prices were comparatively cheaper (Aldi and Dollar Tree); variety store (VS) if seafood prices were higher than the discount store but more range of products were sold, for example office supplies, home supplies, electronics, etc. (Walmart and Target); luxury store (LS) if seafood were expensive and products are mostly labeled and organic (Wholefoods); and grocery chain (GC) if prices maybe comparable with variety stores but mostly sell grocery items (Giant Eagle and Trader Joes). We also included 2 international stores (IS) (Lotus Food Co. and New Youngs Oriental Grocery) mainly representing South and

East Asian consumers and 1 wholesale chain (WC) (Costco), a very popular retailer among Americans. Variety and grocery chains included in our study have various stores across the city and are more accessible than others.

Appendix B Table 11: PFAS concentration (ng/g, wet weight) and descriptive statistics.

Sample ID	Seafood	Total PFAS (ng/g)	PFBS*	PFDA	PFHpA	PFHxS	PFNA	PFOA	PFOS	PFTrDA	PFUnDA
01CAT-UNK-IS	Catfish	0.23	0.34	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	0.23	<LOQ
02-CAT-USA-VS	Catfish	0.75	342.36	<LOQ	<LOQ	0.75	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
03-CLA-CAN-IS	Clams	11.06	0.78	<LOQ	<LOQ	11.06	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
04-CLA-CHN-IS	Clams	2.34	0.63	<LOQ	<LOQ	<LOQ	<LOQ	2.38	<LOQ	<LOQ	<LOQ
05-CLA-VNM-IS	Clams	2.09	3.15	<LOQ	0.24	0.27	<LOQ	1.58	<LOQ	<LOQ	<LOQ
06-COD-CHN-DS	Cod	0.31	1.96	<LOQ	<LOQ	0.31	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
07-COD-ISL-DS	Cod	0.53	1.74	<LOQ	<LOQ	0.53	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
08-COD-USA-VS	Cod	2.58	35.24	<LOQ	<LOQ	2.44	<LOQ	0.14	<LOQ	<LOQ	<LOQ
09-COD-USA-VS	Cod	1.97	13.54	<LOQ	<LOQ	1.85	<LOQ	0.124	<LOQ	<LOQ	<LOQ
10-CRA-CAN-VS	Crab	3.26	9.77	<LOQ	<LOQ	3.05	<LOQ	<LOQ	0.20	<LOQ	<LOQ
11-CRA-USA-LS	Crab	0.37	5.90	<LOQ	<LOQ	<LOQ	0.112	<LOQ	<LOQ	<LOQ	0.26
12-FLO-CHN-GC	Flounder	1.17	17.52	<LOQ	<LOQ	0.36	0.55	<LOQ	0.26	<LOQ	<LOQ
13-HAD-NOR-GC	Haddock	2.43	2.72	0.20	<LOQ	0.54	0.79	<LOQ	0.89	<LOQ	<LOQ
14-MAC-CHN	Mackerel	ND	1.10	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
15-MAC-THA-IS	Mackerel	ND	1.66	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
16-MAH-PER-VS	Mahi-mahi	0.27	1.84	<LOQ	<LOQ	0.27	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
17-MUS-CHL-DS	Mussels	ND	5.44	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
18-MUS-CHN-IS	Mussels	0.72	41.88	<LOQ	<LOQ	<LOQ	<LOQ	0.72	<LOQ	<LOQ	<LOQ
19-PER-CAN-GC	Perch	0.12	1.30	<LOQ	<LOQ	<LOQ	0.11	<LOQ	<LOQ	<LOQ	<LOQ
20-POL-KOR-IS	Pollock	ND	44.30	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
21-SAL-CHL-DS	Salmon	1.14	1.13	<LOQ	<LOQ	1.14	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
22-SAL-CHL-VS	Salmon	0.42	4.88	<LOQ	<LOQ	0.42	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
23-SAL-CHN-VS	Salmon	ND	0.40	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
24-SAL-NOR-LS	Salmon	ND	0.32	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
25-SAL-USA-VS	Salmon	0.90	4.57	<LOQ	<LOQ	0.89	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
26-SAL-USA-GC	Salmon	ND	0.54	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
27-SCA-USA-DS	Scallops	ND	0.15	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
28-SEA-TUR-GC	Seabass	0.19	0.89	<LOQ	<LOQ	0.18	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ

29-SHR-IND-VS	Shrimp	0.91	2.33	<LOQ	<LOQ	0.91	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
30-SHR-IDN-VS	Shrimp	1.23	5.10	<LOQ	<LOQ	1.23	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
31-SHR-THA-LS	Shrimp	ND	0.16	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
32-SHR-THA-IS	Shrimp	0.23	0.47	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	0.23	<LOQ
33-SHR-USA-DS	Shrimp	0.89	0.38	0.124	<LOQ	<LOQ	<LOQ	<LOQ	0.65	<LOQ	0.10
34-SHR-USA-LS	Shrimp	0.80	4.84	<LOQ	<LOQ	0.67	<LOQ	<LOQ	<LOQ	<LOQ	0.12
35-SHR-VNM-GC	Shrimp	0.35	1.02	<LOQ	<LOQ	0.24	<LOQ	<LOQ	<LOQ	<LOQ	0.11
36-SME-EST-GC	Smelt	20.04	20.98	3.27	<LOQ	0.94	12.35	0.98	<LOQ	0.20	2.28
37-SWA-VNM-IS	Swai	0.44	3.02	<LOQ	<LOQ	0.44	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
38-SWO-SGP-GC	Swordfish	0.34	1.70	<LOQ	<LOQ	0.34	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
39-TIL-CHN-VS	Tilapia	0.12	0.50	<LOQ	<LOQ	0.12	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
40-TIL-ECU-LS	Tilapia	0.10	0.58	<LOQ	<LOQ	0.10	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
41-TIL-HND-DS	Tilapia	0.13	0.88	<LOQ	<LOQ	0.12	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
42-TIL-IDN-GC	Tilapia	1.80	2.98	<LOQ	<LOQ	1.79	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
43-TIL-TWN-IS	Tilapia	ND	0.53	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
44-TRO-PER-DS	Trout	ND	0.63	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
45-TUN-ESP-VS	Tuna	ND	0.27	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
46-TUN-VNM-GC	Tuna	0.22	1.21	<LOQ	<LOQ	0.21	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
		SUM	593.70	3.60	0.24	31.20	13.93	5.95	2.02	0.66	2.89
		GM	2.03	0.44	0.24	0.58	0.59	0.60	0.42	0.22	0.25
		MEDIAN	1.68	0.20	0.24	0.53	0.55	0.85	0.46	0.23	0.12
		SD	50.16	1.47	0.00	2.07	4.79	0.80	0.28	0.01	0.86
		DF		7%	2%	59%	11%	13%	9%	7%	11%

*PFBS was found in plastic food storage bags used for samples storage and contaminated fish samples, these numbers do not represent PFBS in fish samples. All PFAS levels reported here were first found by HRMS, and then confirmed by QQQ. ND= not detected

Appendix B Table 12: Estimated PFAS exposure (ng/kg bw/week) for low exposure scenario.

	Sum PFOA+PFOS+PFNA +PFHxS (ng/g)	consumption (g/day)	Body weight (kg)	Exposure (ng/ kg bw/week)		
				1 meal/week	2 meals/week	3 meals/week
Tilapia	0.38	18	70	0.10	0.20	0.29
Catfish	0.90			0.23	0.46	0.69
Cod	1.12			0.29	0.58	0.86
Flounder	1.22			0.31	0.63	0.94
Salmon	0.90			0.23	0.46	0.69
Crab	0.62			0.16	0.32	0.48
Shrimp	0.57			0.15	0.29	0.44

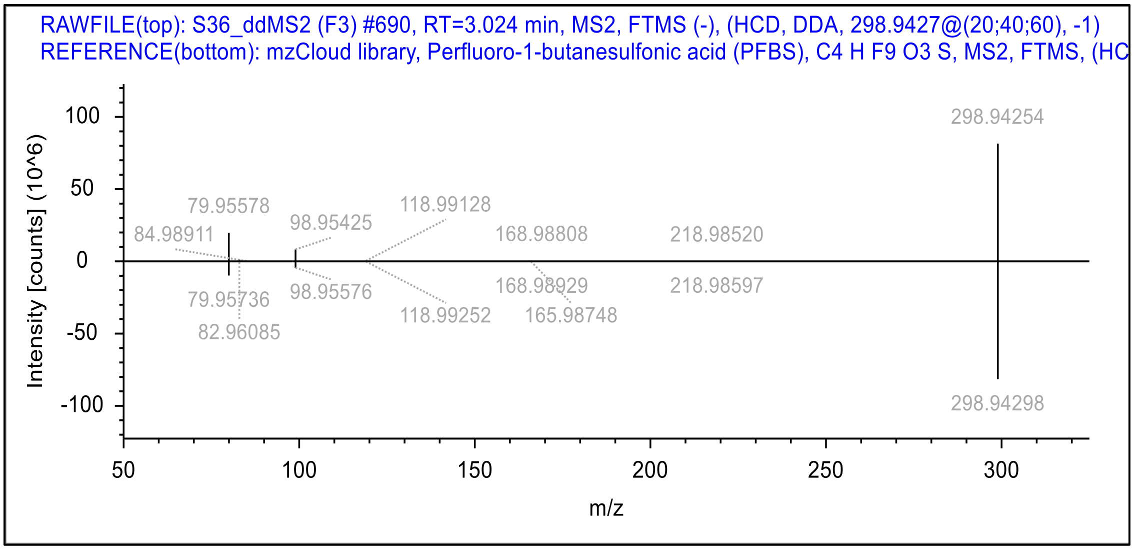
Appendix B Table 13: Estimated PFAS exposure (ng/kg bw/week) for high exposure scenario.

	Sum PFOA+PFOS+PFNA+PFHxS (ng/g)	consumption (g/day)	body weight (kg)	Exposure (ng/ kg bw/week)		
				1 meal/ week	2 meals/ week	3 meals/ week
Tilapia	0.38	166	70	0.90	1.80	2.70
Catfish	0.90	157	70	2.02	4.04	*6.06
Cod	1.12	129	70	2.06	4.13	*6.19
Flounder	1.22	129	70	2.25	*4.50	*6.74
Salmon	0.90	111	70	1.43	2.85	4.28
Crab	0.62	72	70	0.64	1.28	1.91
Shrimp	0.57	55	70	0.45	0.90	1.34

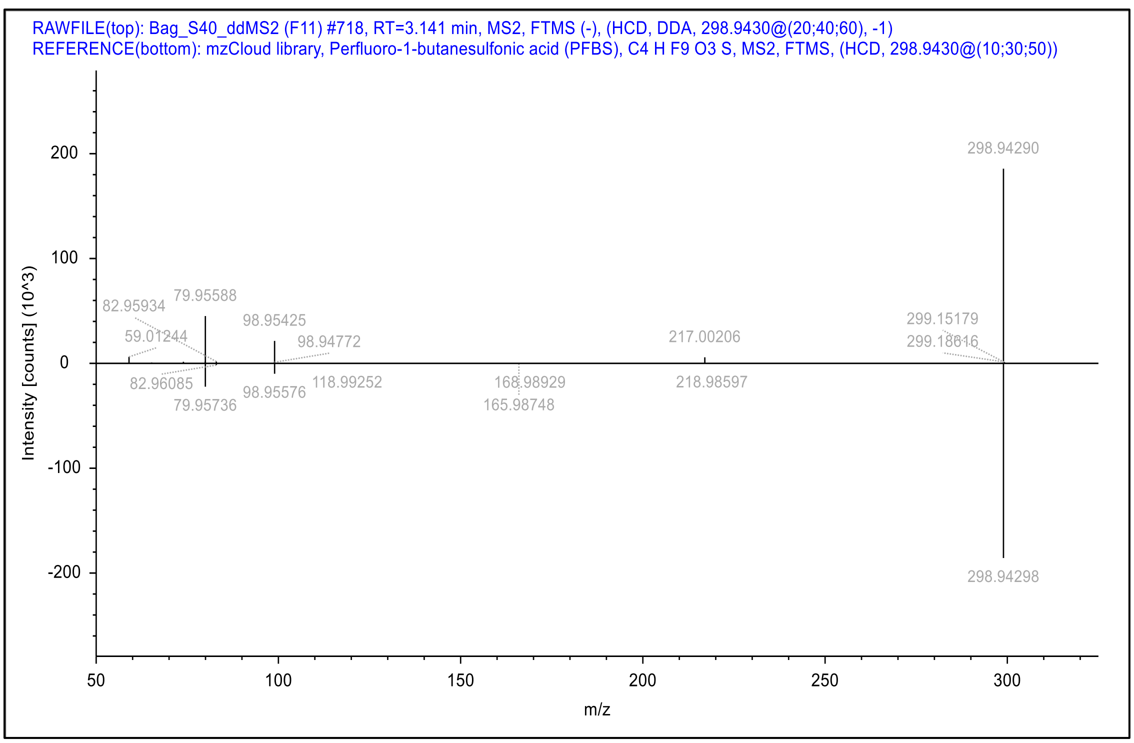
*exposures which are above the threshold recommended by EFSA (4.4 ng/kg bw/ week)

Appendix B Table 14: p-values for Mann-Whitney tests for store-specific data.

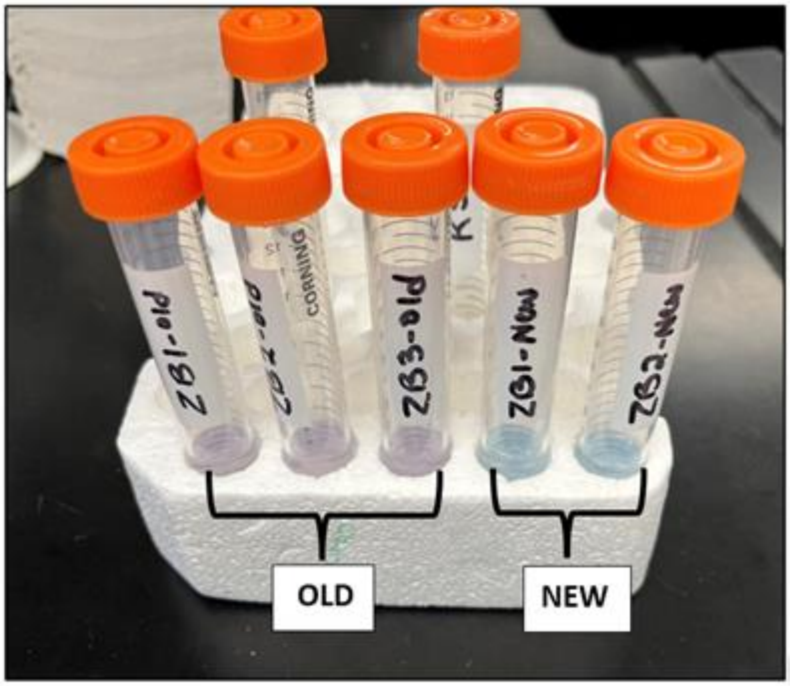
Store (number of samples, n)	International	Grocery	Discount	Variety	Luxury
International (n=7)	-	0.458	0.507	0.961	0.360
Grocery (n=9)	0.458	-	0.825	0.549	0.481
Discount (n=4)	0.507	0.825	-	0.373	0.628
Variety (n=10)	0.961	0.549	0.373	-	0.111
Luxury (n=3)	0.360	0.481	0.628	0.111	-



Appendix B Figure 3: Confirmation of PFBS identity in catfish sample. MzCloud MS2 identification: 97% match. Mass list MS1 identification: Sfit 84%, mzLogic score 95%.



Appendix B Figure 4: Confirmation of PFBS identity in ziplock bag sample. MzCloud MS2 identification: 87% match. Mass list MS1 identification: Sfit 76%, mzLogic score 84%.



Appendix B Figure 5: Food storage bag extracts.

Here, old signifies food storage bags used during various stages in our study but did not come in direct contact with fish samples and new signifies bags currently used in a PFAS dedicated lab and were not used in our study.

Appendix C Supporting information for Chapter 4.0

Appendix C Table 15: Details of seafood samples.

Sample ID	Seafood	Point of origin	Production method	Storage condition	Store
01CAT-UNK-IS	Catfish	Unknown	Unknown	Fresh	International store
02-CAT-USA-VS	Catfish	USA	Farmed	Frozen	Variety store
03-CLA-CAN-IS	Clams	Canada	Wild	Frozen	International store
04-CLA-CHN-IS	Clams	China	Wild	Frozen	International store
05-CLA-VNM-IS	Clams	Vietnam	Farmed	Frozen	International store
06-COD-CHN-DS	Cod	China	Wild	Frozen	Discount store
07-COD-ISL-WC	Cod	Iceland	Wild	Frozen	Wholesale chain
08-COD-USA-VS	Cod	USA	Wild	Frozen	Variety store
09-COD-USA-VS	Cod	USA	Wild	Frozen	Variety store
10-CRA-CAN-VS	Crab	Canada	Wild	Fresh	Variety store
11-CRA-USA-LS	Crab	USA	Wild	Fresh	Luxury store
12-FLO-CHN-GC	Flounder	China	Wild	Frozen	Grocery chain
13-HAD-NOR-GC	Haddock	Norway	Wild	Frozen	Grocery chain
14-MAC-CHN	Mackerel	China	Wild	Frozen	International store
15-MAC-THA-IS	Mackerel	Thailand	Wild	Frozen	International store
16-MAH-PER-VS	Mahi-mahi	Peru	Wild	Frozen	Variety store
17-MUS-CHL-DS	Mussels	Chile	Farmed	Frozen	Discount store
18-MUS-CHN-IS	Mussels	China	Wild	Frozen	International store
19-PER-CAN-GC	Perch	Canada	Wild	Frozen	Grocery chain
20-POL-KOR-IS	Pollock	Korea	Wild	Frozen	International store
21-SAL-CHL-DS	Salmon	Chile	Farmed	Fresh	Discount store
22-SAL-CHL-VS	Salmon	Chile	Farmed	Frozen	Variety store
23-SAL-CHN-VS	Salmon	China	Wild	Frozen	Variety store
24-SAL-NOR-LS	Salmon	Norway	Farmed	Fresh	Luxury store
25-SAL-USA-VS	Salmon	USA	Wild	Frozen	Variety store
26-SAL-USA-GC	Salmon	USA	Wild	Frozen	Grocery chain
27-SCA-USA-DS	Scallops	USA	Wild	Frozen	Discount store
28-SEA-TUR-GC	Seabass	Turkey	Farmed	Frozen	Grocery chain
29-SHR-IND-VS	Shrimp	India	Farmed	Frozen	Variety store
30-SHR-IDN-VS	Shrimp	Indonesia	Farmed	Frozen	Variety store
31-SHR-THA-LS	Shrimp	Thailand	Farmed	Fresh	Luxury store
32-SHR-THA-IS	Shrimp	Thailand	Farmed	Frozen	International store

33-SHR-USA-DS	Shrimp	USA	Wild	Frozen	Discount store
34-SHR-USA-LS	Shrimp	USA	Wild	Frozen	Luxury store
35-SHR-VNM-GC	Shrimp	Vietnam	Farmed	Frozen	Grocery chain
36-SME-EST-GC	Smelt	Estonia	Wild	Frozen	Grocery chain
37-SWA-VNM-IS	Swai	Vietnam	Farmed	Frozen	International store
38-SWO-SGP-GC	Swordfish	Singapore	Wild	Frozen	Grocery chain
39-TIL-CHN-VS	Tilapia	China	Farmed	Fresh	Variety store
40-TIL-ECU-LS	Tilapia	Ecuador	Farmed	Fresh	Luxury store
41-TIL-HND-DS	Tilapia	Honduras	Farmed	Fresh	Discount store
42-TIL-IDN-GC	Tilapia	Indonesia	Farmed	Frozen	Grocery chain
43-TIL-TWN-IS	Tilapia	Taiwan	Farmed	Frozen	International store
44-TRO-PER-DS	Trout	Peru	Farmed	Fresh	Discount store
45-TUN-ESP-VS	Tuna	Spain	Wild	Frozen	Variety store
46-TUN-VNM-GC	Tuna	Vietnam	Wild	Frozen	Grocery chain

Sample set reported in the current study are same as the one reported in Bedi et al. 2022 (under review) and consisted of 31 fish and 15 shellfish. Of the 46 samples, 42% were famed and 57% were wild caught, while for one sample data on husbandry type was unavailable. Seafood sourced from 19 origins were included: 26% from North America, 46% from Asia, 16% from South America, 10% from Europe, 2% from an unknown origin.

We surveyed the following types of grocery stores:

- Discount store: comparatively cheaper seafood
- Variety store: prices were higher than the discount store, but more range of products were sold, for example office supplies, home supplies, electronics, etc.
- Luxury store: seafood was expensive, and products were mostly labeled and organic
- Grocery chain: seafood prices maybe comparable with variety stores but mostly sell grocery items
- International stores: mainly representing South and East Asian consumers
- Wholesale chain: sold only wholesale items

Appendix C Table 16: List of target analytes by UHPLC-MS/MS (total 286).

Abamectin	Dimethomorph*	Mebendazole	Pyraclostrobin*
Acephate*	Dimetridazole hydroxy	Mebendazole-2-amino	Pyraflufen ethyl
Acequinocyl*	Dinotefuran	Melengesterol acetate	Pyrantel
Acetamiprid	Diuron	Meloxicam	Pyridaben*
Acetopromazine	Dodemorph*	Metalaxyl*	Pyrimethanil*
Albendazole	Doramectin	Methamidophos	Pyriproxyfen*
Albendazole sulfone	Doxycycline	Methamidophos*	Quinclorac
Albendazole-2-aminosulfone	Emamectin	Methidathion*	Quizalofop ethyl*
Albendozole sulfoxide	Enrofloxacin	Methiocarb*	Ractopamine
Aldicarb	Epoxiconazole	Methomyl	Robenidine
Aldicarb sulfone	Eprinomectin	Methoxyfenozide	Ronidazole
Aldicarb sulfoxide	Erythromycin A	Metoprolol	Roxithromycin
Amoxicillin	Ethiprole	Metronidazole	Saflufenacil
Ampicillin	Ethofumesate*	Metronidazole hydroxy	Salbutamol
Amprolium	Ethoprophos*	Minocycline	Salinomycin
Atrazine*	Etoxazole*	Monocrotophos*	Sarafloxacin
Azamethiphos	Fenamidone*	Morantel	Sethoxydim
Azaperol	Fenamiphos*	Nafcillin	Spinetoram
Azaperone	Fenarimol*	Nalidixic acid	Spiramycin
Azinphos ethyl*	Fenbuconazole	Naproxen	Spiromesifen*
Azinphos methyl*	Fenbuconazole*	Narasin	Spirotetramat
Azoxystrobin*	Fenbufen	Neospiramycin	Sulfachloropyridazine
Benzovindiflupyr	Fenhexamid*	Nitenpyran	Sulfaclozine
Bifenazate*	Fenobucarb*	Norfloxacin	Sulfadiazine
Bitertanol*	Fenoxaprop ethyl*	Norflurazon*	Sulfadimethoxine
Boscalid*	Fenoxycarb*	Novaluron	Sulfadoxine
Brilliant green	Fenpyroximate	Novobiocin	Sulfaethoxypyridazine
Brombuterol	Fenthion	Ofloxacin	Sulfamerazine
Buprofezin*	Fenthion sulfone*	Omethoate*	Sulfamethazine
Cambendazole	Fleroxacin	Orbifloxacin	Sulfamethizole
Carazolol	Flonicamid*	Ormetoprim	Sulfamethoxazole
Carbadox	Florfenicol	Oxacillin	Sulfamethoxypyridazine
Carbaryl*	Florfenicol amine	Oxadiazon*	Sulfamonomethoxine
Carbendazim	Flubendazole	Oxamyl	Sulfanilamide
Carbofuran*	Flubendazole-2-amino	Oxfendazole	Sulfapyridine
Chlorantraniliprole	Flufenacet*	Oxibendazole	Sulfaquinoxaline
Chlorfenvinphos*	Flumequin	Oxolinic acid	Sulfathiazole
Chlorimuron ethyl	Flumethasone	Oxydemeton methyl	Sulfisoxazole
Chlorpromazine	Flunixin	Oxyphenylbutazone	Tebuconazole*

Chlorsulfuron	Fluopyram*	Oxytetracycline	Tebufenozide
Cimaterol	Fluoxastrobin	Paclobutrazol*	Tebufenpyrad*
Ciprofloxacin	Flusilazole*	Penconazole*	Temephos
Clenbuterol	Flutolanil*	Penicillin G	Tetrachlorvinphos*
Clenbuterold	Flutriafol*	Penoxsulam	Tetraconazole*
Clethodim	Fluxapyroxad	Penthiopyrad*	Tetracycline
Clindamycin	Fosthiazate*	Phenothrin*	Thiabendazole
Clofentezine	Gamithromycin	Phenthoate*	Thiabendazole hydroxy
Clothianidin	Halofuginone	Phenyl butazone	Thiacloprid
Cortisone	Haloxon	Phenylthiouracil	Thiamethoxam*
Coumaphos	Hexaconazole*	Phosalone*	Thiobencarb*
Coumaphos*	Hexythiazox	Phosmet*	Thiodicarb
Crystal violet	Imazalil*	Picoxystrobin*	Thiophanate methyl
Crystal violet leuco	Imazethapyr	Piperonyl Butoxide*	Tiamulin
Cyantraniliprole	Imidacloprid	Pirimicarb*	Tildipirosin
Cyazofamid	Indoprofen	Pirimiphos methyl*	Tilmicosin
Cymoxanil	Indoxacarb*	Pirlimycin	Tolfenamic acid
Cyphenothrin	Iprodione*	Prednisolone	Topramezone
Cyphenothrin*	Ipronidazole	Prednisone	Triadimenol*
Cyprodinil*	Ipronidazole hydroxy	Prochloraz*	Triasulfuron
Danofloxacin	Iprovalicarb*	Profenofos*	Triazophos*
Dapsone	Isofenphos*	Promecarb*	Triclabendazole
Desethylene ciprofloxacin	Josamycin	Promethazine	Triclabendazole sulfoxide
Diazinon*	Ketoprofen	Propanil*	Trifloxystrobin*
Dichlormid*	Kitasamycin	Propargite*	Triflumizole*
Dichlorvos*	Kresoxim methyl*	Propiconazole*	Trimethoprim
Diclofenac	Levamisole	Propoxur*	Tulathromycin
Dicrotophos	Lincomycin	Propylthiouracil	Tylosin
Dicrotophos*	Linuron*	Propyphenazone	Virginiamycin
Difenoconazole*	Lufenuron	Propyzamide*	Xylazine
Difloxacin	Maduramicin	Prothioconazole	Zilpaterol
Diflubenzuron	Malachite green	Pymetrozine	
Diflufenzopyr	Malachite green leuco	Tebuthiuron*	
Dimethoate*	Marbofloxacin		

*analytes also analyzed by LPGC-MS/MS (93)

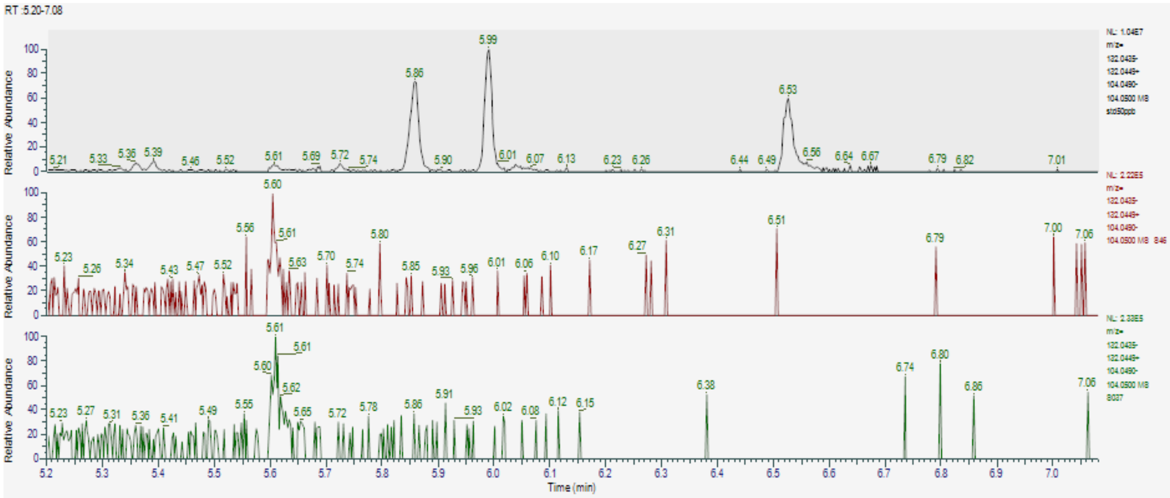
Appendix C Table 17: List of target analytes by LPGC-MS/MS (total 252).

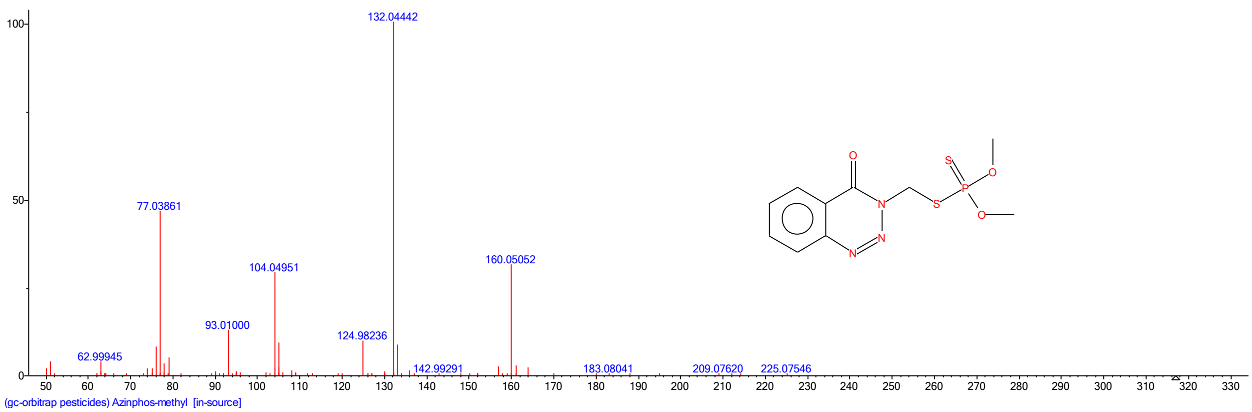
Acenaphthene	Dimethomorph*	Indeno(1,2,3-cd)pyrene	Penthiopyrad*
Acenaphthylene	Diphenylamine	Indoxacarb*	Permethrin, cis-
Acephate*	Disulfoton	Iprodione*	Permethrin, trans-
Aldrin	Dodemorph*	Iprovalicarb*	Phenanthrene
Allethrin	Endosulfan I	Isocarbofos	Phenothrin*
Anthracene	Endosulfan II	Isofenphos*	Phenthoate*
Atrazine*	Endosulfan sulfate	Isoproturon	Phorate
Azinphos ethyl*	Endrin	Kresoxim methyl*	Phosalone*
Azinphos methyl*	Endrin ketone	Lactofen	Phosmet*
Azoxystrobin*	Esfenvalerate	Linuron*	Phthalimide
Benfluralin	Ethalfluralin	Malathion	Picoxystrobin*
Benoxacor	Ethion	Metalaxyl*	Piperonyl Butoxide*
Benz(a)anthracene	Ethofumesate*	Methamidophos*	Pirimicarb*
Benzo(a)pyrene	Ethoprophos*	Methidathion*	Pirimiphos
Benzo(bjk)fluoranthene	Ethoxyquin	Methiocarb*	Pirimiphos methyl*
Benzo(c)fluorene	Etofenprox	Methoprene	Prochloraz*
Benzo(ghi)perylene	Etoxazole*	Methoxychlor	Procymidone
Bifenazate*	Etridiazole	Metribuzin	Profenofos*
Bifenthrin	Famoxadone	Mirex	Promecarb*
Bitertanol*	Fenamidone*	Monocrotophos*	Propanil*
Boscalid*	Fenamiphos*	Myclobutanil	Propargite*
Bromophos	Fenarimol*	Naphthalene	Propazine
Bromopropylate	Fenazaquin	Napropamide	Propetamphos
Bupirimate	Fenbuconazole*	Nitenpyram	Propham
Buprofezin*	Fenhexamid*	Norflurazon*	Propiconazole*
Cadusafos	Fenitrothion	o,p' -DDT	Propoxur*
Carbaryl*	Fenobucarb*	o,p'-DDD	Propyzamide*
Carbofuran*	Fenoxaprop ethyl*	o,p'-DDE	Pyraclostrobin*
Carbophenothion	Fenoxycarb*	Omethoate*	Pyrazophos
Carfentrazone	Fenpropathrin	o-Phenylphenol	Pyrene
Chinomethionate	Fensulfothion	Oxadiazon*	Pyridaben*
Chlordane, cis-	Fenthion	Oxadixyl	Pyrimethanil*
Chlordane, trans-	Fenthion sulfone*	Oxychlordane	Pyriproxyfen*
Chlordecone (Kepone)	Fenvalerate	Oxyfluorfen	Quintozene
Chlorfenapyr	Fipronil	p,p' -DDD	Quizalofop ethyl*
Chlorfenvinphos*	Fipronil sulfide	p,p'-DDE	Resmethrin
Chloroneb	Fipronyl desulfinyl	p,p'-DDT	Spirodiclofen
Chlorpropham	Flonicamid*	Paclobutrazol*	Spiromesifen*
Chlorpyrifos	Fludioxonil	Parathion	Sulprofos

Chlorpyrifos methyl	Flufenacet*	Parathion methyl	Tebuconazole*
Chrysene	Flufenoxuron	PBDE 100	Tebufenpyrad*
Clopyralid	Fluopyram*	PBDE 153	Tebuthiuron*
Coumaphos*	Fluoranthene	PBDE 154	Terbufos
Cyclopenta(cd)pyrene	Fluorene	PBDE 183	Terbuthylazine
Cyfluthrin	Fluridone	PBDE 28	Tetrachlorvinphos*
Cyhalothrin, lambda	Fluroxypyr-meptyl	PBDE 47	Tetraconazole*
Cypermethrin	Flusilazole*	PBDE 99	Tetradifon
Cyphenothrin*	Flutolanil*	PCB 105	Tetrahydrophthalimide
Cyproconazole	Flutriafol*	PCB 114	Tetramethrin
Cyprodinil*	Fluvalinate, tau	PCB 118	Thiamethoxam*
Deltamethrin	Folpet	PCB 123	Thiobencarb*
Diazinon*	Fonophos	PCB 126	Tolclofos methyl
Dibenz(ah)anthracene	HCH, alpha	PCB 156	Tralkoxydim
Dibenzo(a,e,h,l)pyrene	HCH, beta	PCB 157	Triadimenol*
Dichlormid*	HCH, delta	PCB 167	Triadimephon
Dichlorobenzophenone	HCH, gamma (Lindane)	PCB 169	Triallate
Dichlorvos*	Heptachlor	PCB 170	Triazophos*
Diclofop methyl	Heptachlor epoxide	PCB 180	Tribufos
Dicloran	Heptenophos	PCB 189	Tridiphane
Dicrotophos*	Hexachlorobenzene	PCB 77	Trifloxystrobin*
Dieldrin	Hexaconazole*	PCB 81	Triflumizole*
Difenoconazole*	Hexazinone	Penconazole*	Trifluralin
Dimethoate*	Imazalil*	Pendimethalin	Vinclozolin

Appendix C Table 18: List of standards.

13C12-DDE	LPGC-MS/MS (ISTD)
13C12-PCB 153	LPGC-MS/MS (ISTD)
Acenaphthylene-d8	LPGC-MS/MS (ISTD)
Benzo(a)pyrene-d12	LPGC-MS/MS (ISTD)
Benzo(g,h,i)perylene-d12	LPGC-MS/MS (ISTD)
FBDE 126	LPGC-MS/MS (ISTD)
Fluoranthene-d10	LPGC-MS/MS (ISTD)
Malathion-d10	LPGC-MS/MS (ISTD)
Naphthalene-d8	LPGC-MS/MS (ISTD)
Penicillin G- d7	LPGC-MS/MS (ISTD)
Phenanthrene-d10	LPGC-MS/MS (ISTD)
Pyrene-d10	LPGC-MS/MS (ISTD)
Azinphos methyl-d6	UHPLC-MS/MS (ISTD)
Clenbuterol-d9	UHPLC-MS/MS (ISTD)
Flunixin-d3	UHPLC-MS/MS (ISTD)
Malachite green leuco-d6	UHPLC-MS/MS (ISTD)
Malathion-d10	UHPLC-MS/MS (ISTD)
Phenylbutazone-d10	UHPLC-MS/MS (ISTD)
Ractopamine-d3	UHPLC-MS/MS (ISTD)
13C6-Sulfamethazine	UHPLC-MS/MS (ISTD)
Triphenyl phosphate-d_{15} (TPP-d_{15})	UHPLC-MS/MS (ISTD)
Atrazine-d_5	UHPLC+LPGC-MS/MS (ISTD)
Pyridaben-d_{13}	UHPLC+LPGC-MS/MS (ISTD)
^{13}C-phenacetin	QC standard





Appendix C Figure 6: Confirmation of Azinophos methyl absence in catfish samples.

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