FOOD RISK ASSESSMENT TO PERFLUOROALKYLS ACIDS IN THE FRENCH POPULATION

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Introduction

Perfluoroalkyl acids (PFAAs) are a large family of contaminants of anthropogenic origin that includes perfluorooctane sulfonate (PFOS) and perfluorooctanoic acid (PFOA). These substances are highly stable (having high thermal, chemical and biological resistance) and amphiphilic, giving them a surfactant property. Consequently, they are used in numerous industrial applications and common consumer products: stain- and water-resistant treatments (clothes, rugs, carpets, and furniture), non-stick coatings (kitchen utensils, paper including food packaging) and certain specialized applications (cosmetics, fire-fighting foam, plant protection products). Contrary to many persistent halogenated compounds (PCBs for instance), they do not accumulate in fatty tissues. Some PFAAs such as PFOS and PFOA persist in the environment and can accumulate in animals and humans (1).

Their apparent half-lives in humans are approximately 4 years (1). High concentrations are observed in liver, blood and kidneys. Toxicity studies have primarily examined PFOS and PFOA. The main toxic effects reported in animals have been observed in the liver, reproductive and developmental functions, the immune and hormonal systems and lipid metabolism. PFOS and PFOA are not genotoxic but have neoplastic-type effects. Recently, in a prospective study of a birth cohort from the National Hospital in the Faroe Islands, PFAAs were associated with a reduced humoral immune response to routine childhood immunizations in children (2). The tolerable daily intakes (TDI) generally accepted are for PFOS 150 ng/kg bw/day based on the effects on lipid and thyroid hormone levels observed in a 6-month toxicology study in monkey. For PFOA, the accepted TDI is 1.5 µg/kg bw/day based on a two-generation toxicology study showing some maternal hepatotoxicity (4).

PFAAs contaminate several compartments of the environment (water, soil, air) and accumulate in the food chain (3). Food, and particularly seafood products, is a significant source of exposure to PFAAs in humans (4).

To assess the risk led by food exposure to PFAAs, 16 of them were measured in the food samples collected for the second total diet study performed in France (5).

Materials and methods

Food sampling

Core foods were selected to be representative of the French population diet. The selection was based on the results of the second individual and national study on food consumption survey (6, 7).

The most consumed foods by adults and/or children were selected (consumer rate of at least 5%). In addition, the main known or assumed food contributors of the substances included in this study were also selected (if not already selected by the first criterion). The core foods (n=212) covered about 90% of the whole diet of adults and children, and were divided into 41 food groups.

The sampling was performed between June 2007 and January 2009 in eight great metropolitan regions (33 cities), and each food collected in a region was sampled during two different seasons, when possible.

To be as representative as possible of the French food consumption habits, each food sample was composed of up to 15 subsamples of equal weight of the same food, taking into account the market share, origin, species, processing and packaging, flavoring, etc to be representative of the French dietary habits. Altogether, around 20 000 products or subsamples were purchased, then prepared “as consumed” according to french cooking practices, e.g. vegetables and fruits were mainly washed and peeled, meat and seafood were cooked (braised, pan-fried, grilled, baked, deep-fried...). Finally, 15 subsamples were frozen and pooled by a single cryomilling

phase into 1 319 composite samples for analysis. More details about the methodology can be found in Sirot et al. (5). Concentrations of the 16 PFAAs were determined in 599 food samples.

Sample analysis

The analytical method included 16 PFAAs (5 perfluoroalkyl sulfonates including PFOS, and 11 perfluorocarboxylic acids including PFOA)(8). Solid food samples were lyophilized and extracted with methanol. After evaporation, food extracts are purified onto two consecutive SPE columns (copolymeric reversed phase and charcoal). Final purified extracts were analyzed by liquid chromatography coupled to tandem mass spectrometry (LC-MS/MS);electrospray ionization in the negative ion mode was preferred; two transitions at least were recorded per analyte. Water samples (100 mL), were directly deposited on a reversed-phase SPE column. For milk and dairy products, the samples were first extracted using acetone. For fish samples a dispersive SPE based on charcoal particles was used.

Quantification was performed according to the basic isotope dilution principles. Each sample was supplemented by two ^{13}C-labelled internal standards ($^{13}C_4$-PFOA and $^{13}C_4$-PFOS). An external standard (fluorometholone) was added at the end of the analytical process to determine extraction yields. Depending on the matrices, these yields ranged from 30 to 80%. Quality controls as well as analytical blank tests were performed for each series. The limits of detection and quantification, depending on the matrix and compound, ranged from 0.2 pg/g fresh weight (fw) to 3.73 ng/g fw.

Dietary exposure assessment

Values below the limits of detection or quantification are referred to as censored data. Censored data were processed according to the World Health Organization (WHO) recommendations (9). As the censoring rate was at least 60% for each PFAA: the lowerbound (LB) assumption, and the upperbound assumption (UB). The LB assumption corresponds to a scenario in which non-detected values are estimated to be 0 and the values detected, but not quantified, are estimated to be equal to the LOD. The UB assumption corresponds to a scenario in which non-detected values are estimated to be equal to the LOD and the values detected but not quantified are estimated to be equal to the LOQ. The LB scenario represents the minimum possible value, and the UB scenario represents the maximum possible value. To estimate population dietary exposure, the mean levels of the two seasons sampled were considered for each food.

Dietary exposure to each contaminant of interest in the population was calculated individually, for all INCA 2 study subjects (1918 adults aged 18 and over, and 1444 children aged 3 to 17), using the following formula:

$$E_{i,j} = \frac{\sum_{k=1}^{n} C_{i,k} \times L_{k,j}}{BW_i}$$

Where $E_{i,j}$ is dietary exposure to contaminant j of individual i, n is the number of foods in this diet, $C_{i,k}$ is the consumption of food k by individual i, $L_{k,j}$ is the level of contaminant j of food k, BW_i is the body weight of individual i.

For each subject, each food consumed was assigned the mean contamination level calculated for the two samples from each sampling wave from its region (in that event). In other cases (food not sampled in the region) it was assigned the average of the mean levels from the other regions.
Mean exposure as well as 95th percentile (P95) were calculated for adults and children. The percentages of consumers exceeding the TDIs for PFOS and PFOA were calculated with their confidence interval (CI_{95}).
For adults and children, the contribution of each food group to the exposure was calculated as the percentage of the exposure through the consumption of the food group in the total dietary exposure.

Interpretation of the data

The use of mean concentrations (in composite samples) in the calculations enables a realistic and appropriate estimate of dietary exposure over the long term to the extent that these estimates are compared to the health-based guidance values (tolerable daily intakes) for PFOS and PFOA, established by EFSA (4).

Results and discussion

Estimation of concentrations in foods

Out of 16 detected compounds, 14 were included in the analysis. Perfluorotridecanoic acid (PFTrDA) and perfluorotetradecanoic acid (PFTeDA) were not taken into account since only 40% and 32% respectively of the analyses could be interpreted for the analyzed matrices. The percentage of censored data (non-detected element) ranged from 91% (PFOS) to 100% (PFBA, PFDS, PFHpS and PFPA). Out of a total of 8,765 analyses, only 203 had a quantified result, and PFOS was the most frequently quantified compound (53 results, or 9% of the analyses). These observations were consistent with those published by the United Kingdom in 2009 (10).

As most of the compounds were not detected in the various matrices, considering the LB, almost all concentrations were equal to zero. More particularly, PFPA, PFHpS, PFDS and PFBA were not detected in any matrices. Water and seafood products were the foods for which the most substances were detected and quantified: six in water (PFBS, PFHpA, PFHxA, PFHxS, PFOA, PFOS) and molluscs and crustaceans (PFDA, PFDoA, PFNA, PFOA, PFOS, PFUnA), and five in fish (PFHpA, PFHxA, PFOA, PFOS, PFUnA).

PFOA was quantified in meats, poultry and game, delicatessen meats, seafood products, vegetables excluding potatoes, water and mixed dishes. The highest mean concentrations were found in mollusks and crustaceans: 0.007 µg/kg fw (LB) and 0.044 µg/kg fw (UB).

PFOS was quantified in meats, delicatessen meats, seafood products, vegetables excluding potatoes, water and mixed dishes. The highest mean concentrations were found in molluscs and crustaceans: 0.18 µg/kg fw (LB) and 0.19 µg/kg fw (UB). These concentrations were lower (up to a factor of 100) than those observed in Europe (4), and more specifically in the United Kingdom (10), but had the same order of magnitude as the levels observed in Asia and North America (4). However, the very low analytical limits of the methods used in the present study (by a factor of around 100) might explain the differences.

In water, the quantified results for PFOA and PFOS had the same order of magnitude as the concentrations used by EFSA in its report, which were respectively, 9 ng/L and 7 ng/L (4) and as the concentrations recently reported for treated water in France (11).

Table 1: Mean concentrations of PFOS and PFOA in different food groups

Food Group	Number of analyzed samples	PFOA		PFOS	
		LB	UB	LB	UB
Meat	64	0.001	0.056	0.003	0.048
Poultry and game	38	0.001	0.049	0	0.041
Delicatessen meats	79	0.001	0.064	0.004	0.060
Fish	46	0.001	0.023	0.089	0.099
Crustaceans & mollusks	37	0.007	0.044	0.180	0.189
Vegetables (excl. potatoes)	62	0.001	0.030	0	0.015
Water	6	0.001	0.016	0.001	0.002
Mixed dishes	19	0.001	0.035	0.001	0.041

Values expressed as ng/g fresh weight

In a few matrices, the concentration (LB) of some compounds (PFBA, PFUnA, etc.) was higher than that of PFOS and PFOA. For instance, mean PFBA concentration in chocolate was close to 1 ng/kg fw.

Estimation of the dietary exposure in the French population

In adults, mean exposure to PFOA for the UB was estimated at 0.74 ng/kg bw/day. Mean exposure to PFOS for the UB was estimated at 0.66 ng/kg bw/day. At the 95th percentile, UB exposure levels were estimated at 1.50 ng/kg bw/day for PFOA and 1.15 ng/kg bw/day for PFOS. Since there was a large amount of censored data, exposure concentrations greatly depended on the analytical limits. Given that these were very low, the estimated exposure were lower than those estimated in Germany and the United Kingdom, by a factor of approximately 2 to 100 (4).

In women of childbearing age, mean exposure to PFOS for the UB was estimated at 0.67 ng/kg bw/day. At the 95^{th} percentile, UB exposure concentrations were estimated at 1.62 ng/kg bw/day for PFOA and 1.17 ng/kg bw/day for PFOS.

In children, mean exposure to PFOS was estimated at 1.38 ng/kg bw/day. At the 95^{th} percentile, UB exposure concentrations were estimated at 3.24 ng/kg bw/day for PFOA and 2.88 ng/kg bw/day for PFOS.

Risk assessment

Considering the LB scenario, only the foods in which PFAAs were quantified appear as being contributors to exposure: these were primarily water (around 60% for PFOA) and seafood products (around 65% for PFOS). Even for the UB, EFSA's TDI values were not exceeded for PFOA or PFOS, in adults or in children. PFOA and PFOS therefore do not pose a health risk to the French population in the current state of knowledge. Nevertheless, some lack of data can be identified particularly with regard to their carcinogenic and endocrine disruptor potential.

Substance	TDI (4)		Adults			Children		
			Mean	95th percentile	%>TDI	Mean	95th percentile	%>TDI
PFOS	150 ng/kg bw/day	LB	0.04	0.13	0	0.05	0.19	0
		UB	0.66	1.15	0	1.38	2.88	0
PFOA	1 500 ng/kg bw/day	LB	0.01	0.03	0	0.01	0.04	0
		UB	0.74	1.50	0	1.55	3.24	0

Given the lack of data to establish health-based guidance values for PFAAs other than PFOA and PFOS, the risk assessment has not been performed. Oral long-term toxicological studies should therefore be initiated to determine health-based guidance values for these PFAAs.

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