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Dietary exposure to perfluoroalkyl acids, brominated flame retardants and health risk assessment in the French infant total diet study

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ABSTRACT

Perfluoroalkyl acids (PFAAs) and brominated flame retardants (BFRs) are widely used and present in human food. Due to the increased susceptibility to pollutants of the young children, we conducted a total diet study focusing on this population. Around 200 baby and common food composite samples, prepared "as consumed", have been analysed for PFAAS, hexabromocyclododecanes, polybrominated biphenyls, polybrominated diphenyl ethers and tetrabromobisphenol A. The dietary exposure of 705 children aged 1–36 months was assessed. PFAAS were detected only in one fish sample. Detection rates varied from 4 to 93% for BFRs, depending on the congeners. Regarding the provisional health-based guidance values set by EFSA in 2018 for PFOA and PFOS at 0.8 and 1.8 ng kg $bw^{-1}.d^{-1}$, respectively, 20–100% of children exceeded them, depending on the age. Efforts should be made to decrease the PFAAs contamination of common foods. This study also highlighted that for other PFAAs, toxicological studies are needed to set dietary health-based guidance values, to assess their related health risk. Conversely, dietary exposures to BRFs were much lower than the respective health based guidance values or margins of safety were high enough, and consequently not considered at-risk due to very low contamination of the infant specific foods.

1. Introduction

Early stages of life, i.e. the fetal and early postnatal periods, correspond to periods of increased susceptibility (Makri et al., 2004; Sly and Flack, 2008; Diamanti Kandarakis et al., 2009). Several pieces of evidence suggest that fetuses and infants may be more sensitive to pollutants (Landrigan et al., 2003). The French Agency for Food, Environmental and Occupational Health & Safety (ANSES) launched a specific TDS on infants to complete its overall chemical food safety program for the general population (Hulin et al., 2014). More than 500 chemical substances were analyzed in food products consumed by children under 3 years old, including persistent organic pollutants.

Perfluoroalkyl acids (PFAAs) are a large class of chemical contaminants of anthropogenic origin that includes perfluorooctane sulfonate (PFOS) and perfluorooctanoic acid (PFOA). These substances are highly stable, thermally, chemically and biologically, due to their strong carbon-fluoride bonds. They have surfactant properties and are used in numerous industrial applications and common consumer products: stain- and water-resistant treatments (clothes, rugs, carpets), non-stick coatings (kitchen utensils, paper including food contact materials) and certain specialized applications (fire-fighting foam). Due to their toxic properties, a group of renowned scientists published a statement, known as the "Madrid Statement", urging the international community to cooperate in limiting the production and use of PFAAs and in developing safer non fluorinated alternatives (scientists, governments, chemical and product manufacturers (Blum et al., 2015).

PFAAs contaminate several compartments of the environment (water, soil, air) and accumulate in the food chain (Kowalczyk et al., 2012). Food, particularly seafood products, is a significant source of exposure to PFAAs in humans (Cornelis et al., 2012; EFSA, 2008; Trudel et al., 2008; Rivière et al., 2014). PFOS and PFOA persist in the environment and can accumulate in animals and humans. High concentrations are generally observed in the liver, blood and kidneys. Toxicity studies on PFAAs generally only investigate PFOS and PFOA (Olsen et al., 2007). Their apparent elimination half-lives in humans are approximately 4–5 years (Olsen et al., 2007; Bartell et al., 2010). The main toxic effects reported in animals have been observed in the liver (Seacat et al., 2003), on reproductive and developmental functions and

The conclusions presented in the following article represent only the opinion of the authors.

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immune and hormonal systems (Seacat et al., 2002; Kang et al., 2016; Grandjean et al., 2012), neurobehavior (Johansson et al., 2008) as well as on lipid metabolism (EFSA, 2008). PFOS and PFOA have neoplastic effects but have not been shown to be genotoxic (EFSA, 2008).

Brominated flame retardants (BFRs) are mixtures of chemical substances produced and incorporated in many products due to their fire-retardant properties. They are incorporated in plastics, textiles as well as in electronic equipments. This class encompasses different compounds, including hexabromocyclododecanes (HBCDDs), polybrominated biphenyls (PBBs), polybrominated diphenyl ethers (PBDEs) and tetrabromobisphenol A (TBBPA). Food appears to be the main route of exposure for some BFRs such as PBDEs (Frederiksen et al., 2009; Domingo, 2012). The characterisation of chronic human toxicity of BFRs is difficult since they are often experimentally studied as mixtures. In experimental studies, these compounds have been shown to trigger neurodevelopmental effects (EFSA, 2011a).

For all these compounds, dietary intakes appear to be a major contributor to the overall exposure. On the other hand, some of these compounds trigger effects that can be of particular importance for the youngest population (behavioral, neurodevelopmental or endocrine disruptor effects). It is consequently deemed of importance to estimate the dietary intake of the youngest population to these compounds and to assess the risk related to these exposures. The objective of the present study is to assess the risk to children aged from 0 to 3 years of age related to the presence of PFAA and BFR compounds in food. Exposures were calculated using concentrations of 16 PFAAs, 8 PBDEs, 3 PBBs, 3 HBCDDs and TBBPA measured in food samples collected in the context of the infant total diet study (TDS) performed in France (Hulin et al., 2014).

2. Materials & method

2.1. Consumption data for children under 3

For children under 3 years of age, consumption data came from a national consumption survey conducted specifically on this population (Fantino and Gourmet, 2008). Briefly, this cross-sectional study was conducted from January to March 2005 by the Syndicat Français des Aliments de l'Enfance et de la Nutrition Clinique, © « Etude SOFRES 2005/Université de Bourgogne – Pr M. Fantino pour le Syndicat Français des Aliments de l'Enfance » (Fantino, 2005; Fantino and Gourmet, 2008). Individual, consecutive 3-day weight food records were collected from a sample of 705 children selected through proportionate quota sampling based on the living area, the age of the children, the occupation of the mother and the family socio-economic category. Totally or partially breastfed infants (during the survey period) were excluded from the study.

2.2. Food sampling

Food samples were collected as previously described (Hulin et al., 2014). To obtain a representative and general view of infant food consumption, food items were selected based on the results of the consumption survey (Fantino and Gourmet, 2008) based on two main criteria:

- The most consumed food in terms of quantity and/or percentage of consumers
- Food items that are known or supposed to be the main contributors to the exposure to one or more substances of interest

Food items were sampled in the same region and prepared as consumed by the same contractor (i.e. peeled, cooked, etc.) based on a result of a national study on parents' food preparation/cooking processes carried out by Anses (Hulin et al., 2014).

. The sampling plan included specific infant foods such as infant formulae or jarred baby foods that were updated before selection due to the changing market. Common foods (n = 95) such as vegetables, fruits or cakes, as they were not included in the previous French TDS. The sampling plan covered over 95% of the total diet of 0–3 years old children. To take into account seasonal variability, possible different flavours, and different ways of consuming or preparing foods, all the analysed samples, referred to as "composites" or "pools", were formed of 12 sub-samples of the same food and of equal weight. The products purchased were prepared in a way that reflected as closely as possible what is done in the home: preparation (removal of the non-edible part, washing of foods, etc.) and cooking (duration and power, addition or not of salt, fat, etc.). Specificities in infant food consumption and habits were considered. The infant formulas were diluted and heated most of the time, prepared baby dishes were reheated, vegetables (excluding raw vegetables), meat and fish were cooked according to the practices reported in the survey on practices (Hulin et al., 2014). The sampling phase took place between July 2011 and July 2012 in the center region of France.

2.3. Analytical procedure

2.3.1. Perfluoroalkyl acids

The analyses were performed in food items known or supposed to be contaminated by PFAAs (EFSA, 2012), corresponding to 198 samples out of 457, among which 22 common food samples and 176 infant food samples.

The analytical method was used to determine the concentration of 5 perfluoroalkyl sulfonates: PFOS, perfluorobutane sulfonate (PFBS), perfluorohexane sulfonate (PFHxS), perfluoroheptane sulfonate (PFHpS) and perfluoro[-1-]decanesulfonate (PFDS), 11 perfluorocarboxylic acids: PFOA, perfluorobutanoic acid (PFBA), perfluoropentanoic acid (PFPA) perfluorohexanoic acid (PFHxA), perfluoroheptanoic acid (PFHpA), perfluorononanoic acid (PFNA), perfluorodecanoic acid (PFDA), perfluoroundecanoic acid (PFUnA), perfluorododecanoic acid (PFDoA), perfluorotridecanoic acid (PFTrDA) and perfluorotetradecanoic acid (PFTeDA) and one perfluoroalkyl sulfonate (PFOSi) (Kadar et al., 2011). Solid food samples were freeze-dried and extracted with methanol. After evaporation, food extracts were purified onto two consecutive solid-phase extraction (SPE) columns (copolymeric reversed phase and charcoal). Final purified extracts were analysed by liquid chromatography tandem mass spectrometry (LC-MS/MS); electrospray ionisation in the negative ion mode was preferred and at least two transitions were monitored per analyte. Water samples (100 mL), were directly loaded on a reversed-phase SPE column. For milk and dairy products, samples were first extracted using acetone. For fish samples, a dispersive SPE based on charcoal particles was used.

Quantification was performed according to isotopic dilution principles. Each sample was spiked by two ^{13}C-labelled quantification standards ($^{13}C_4$-PFOA and $^{13}C_4$-PFOS) for quantification. A recovery standard (fluorometholone) was added at the end of the analytical process. Depending on the matrix, these recoveries ranged from 30 to 80%. Limits of detection (LOD) and quantification (LOQ), were determined based on the signal-to-noise ratio and depended on the matrix and analyte, overall, they ranged from 0.2 pg g^{-1} fresh weight (fw) to 3.7 ng g^{-1} fw. Repeatability of the signal was also dependent on the matrix, but was always better than 18.6% for all analytes.

2.3.2. Brominated flame retardants

The analyses were performed in food items known or supposed to be contaminated by BFRs (EFSA, 2010; EFSA, 2011a, b, c), corresponding to 205 samples out of 457, among which 36 common food samples and 169 infant food samples.

The extraction of fat was adapted to the physical characteristics of the samples (Cariou et al., 2006; Debrauwer et al., 2005). For all matrices, quantification standards were added before extraction (eight

$^{13}C_{12}$-labelled PBDE congeners, one $^{13}C_{12}$-labelled PBB congener and three $^{13}C_{12}$-labelled HBCD congeners). The solid samples were freeze-dried, ground, and extracted by Accelerated Solvent Extraction (ASE) using a Dionex™ ASE 300™. Pressure and temperature were set to 100 bars and 120 °C respectively. Liquid samples underwent protein precipitation through the addition of potassium oxalate. Two additional successive extractions using a solvent mixture of ethanol, ether and hexane were performed to extract the fat.

Purification involved three stages involving silica, Florisil® and charcoal-celite® columns. A recovery standard was added to each vial for each class of compounds ($^{13}C_{12}$-PBDE 138 for PBDEs and PBBs and fluorometholone for HBCDDs) just before injection.

Detection and identification of PBDEs and PBBs were carried out using a Hewlett–Packard 6890 gas chromatograph, equipped with a DB-5MS capillary column (30 m × 0.25 mm ID, 0.25 µm film thickness) coupled to a Jeol JMS-800D (Jeol, Tokyo, Japan), operating at a resolving power of 10 000 (10% valley). Concentrations of the following PBDE congeners were measured: BDE-28, -47, −99, −100, −153, −154, −183 and −209. Concentrations of PBB-52, PBB-101 and PBB-153 were also measured. For PBDEs, analytical limits in infant specific food items ranged from 0.01 to 1.4 pg g^{-1} fw and from 0.1 to 15 pg g^{-1} fw for common food items. For PBBs, analytical limits ranged from 0.007 to 5.4 pg g^{-1} fw depending on the matrix. Detection rates were 8, 4 and 12% for PBB-52, -101 and −153, respectively.

HBCDD were analysed by LC-MS/MS. HBCDD isomers were separated by reverse-phase chromatography using a Hypersil Gold column (100 mm × 2.1 mm; 1.9 µm, Thermo), with a mobile phase containing acetonitrile/methanol (1:1) (A) and 20 mM ammonium acetate (B). The detection and quantification MS instrument was a triple quadrupole 6410 (Agilent Technologies, Santa Clara, CA, USA), fitted with an electrospray ion source, operating in the negative ion mode. Analytical limits for infant specific food items ranged from 0.007 to 4 pg g^{-1} fw. For common food items, the median limit of detection ranged from 1.7 to 5 pg g^{-1} fw.

TBBPA was analyzed on a reversed-phase chromatography column (Gemini, 50 mm × 2 mm; 3 µm, Phenomenex) with a mobile phase containing acetonitrile + 0.1% acetic acid (A) and water + 0.1% acetic acid (B). The detection and quantification was achieved on an Orbitrap system (Exactive, Thermo) operating in the negative electrospray mode and full scan acquisition. Analytical limits were highly dependent on the matrix and ranged from 0.1 to 3 ng kg^{-1} fw.

2.3.3. Internal quality controls

LABERCA operates an ISO/IEC 17025:2005-certified Quality Assurance system requiring strict controls with regard to personnel, instrument conditions, and experimental situations.

Blank samples and quality control were analyzed and monitored in each series of ten to twenty samples: the signal of each compound in the blanks was checked to avoid contamination throughout the analytical procedure, and concentrations of analytes in quality control were monitored to ensure repeatability and followed in charts. In addition, every year the laboratory takes part in an interlaboratory comparison tests and achieves satisfactory results for both of these methods.

2.3.4. Exposure calculation

Censored data (results below the limits of detection (LOD) and quantification (LOQ)) were processed according to a substitution method that involved framing the actual level using the lowest (low assumption or lower-bound (LB)) and highest (high assumption or upper-bound (UB)) values possible. The low assumption was calculated by assuming that all values below the LOD were equal to zero and those between the LOD and the LOQ were equal to the LOD. The high assumption was calculated by assuming that all values below the LOD were equal to the LOD and those between the LOD and the LOQ were equal to the LOQ.

Using data on individual consumption and levels of PFAAs and BFRs measured in food, exposure was calculated with the following equation:

$$E_i = \sum_{k=1}^{n} \frac{C_{i,k} \times L_k}{BW_i}$$

where:

- E_i is the total daily exposure of an individual i (µg.kg body $weight^{-1}.day^{-1}$),
- $C_{i,k}$ is the daily consumption of the food k by an individual i ($g.day^{-1}$),
- L_k is the estimated level for the studied contaminant in the food k ($\mu g.g^{-1}$ fresh weight),
- BW_i is the body weight of the individual i (kg),
- n is the total number of foods consumed by the individual i.

For common food items, concentrations data were completed with data from the second French TDS focusing on the general population (Rivière et al., 2014).

According to WHO recommendations (GEMS/Food-EURO. 2013), exposure data were estimated according to both the upper bound hypothesis (LB and UB, respectively). In the present article health risk was assessed considering the worst case scenario, i.e., considering the UB hypothesis.

Mean and 90th percentile (P90) of exposure were calculated for the population divided into four age groups: 1–4 months, 5–6 months, 7–12 months and 13–36 months. The mean exposure of the 10% of the most exposed children (over the P90) was also calculated. The percentage (and corresponding confidence interval at 95%, CI95%) of children exceeding the respective health based guidance value was calculated for each age group. Margins of safety were calculated (when necessary) as the ratio between BMDLs and exposure (mean or P90). The ratio of the exposure through individual food items over the total exposure was calculated to determine the contribution (in %) of each food item to the total exposure. Food items contributing to more than 10% of the total exposure were identified as main contributors to the exposure.

2.4. Collective appraisal

The collective assessment of the risk linked to PFAA and BFR exposure has been conducted with the French Agency for Food, Environmental and Occupational Health & Safety (ANSES) Expert Committee on food contaminants.

3. Results and discussion

3.1. Contamination data

3.1.1. PFAAs

Analyses covered 96% of the diet theoretically contributing to the total exposure. PFAAs were not detected in any of the infant specific food items. For common foods, PFAAs were only detected in one fish sample (sole), PFOA concentration reached 30 ng kg^{-1} fw and PFOS concentration reached 277 ng kg^{-1} fw.

The foods presenting the highest concentrations of PFOA and PFOS in the child diet were crustaceans and mollusks that were previously analyzed, with respectively, 0.014 ng g^{-1} fw and 0.312 ng g^{-1} fw (Rivière et al., 2014).

In 2012, the European Food Safety Authority (EFSA) reported PFAAs concentration in fish ranging from 0.0064 to 18.2 ng g^{-1} fw for PFOA and from 0.04 to 211 ng g^{-1} fw for PFOS (EFSA, 2012). A Spanish study published in 2010 reported concentrations of PFOA and PFOS ranging from 0.17 to 0.72 ng g^{-1} fw and from 0.16 to 1.1 ng g^{-1} fw, respectively (Llorca et al., 2010). In both studies, detection rates were low (8% in the study reported by EFSA in 2012 for instance). The concentrations reported in our study are slightly lower than those previously reported.

Table 1
Mean concentrations (pg.g^{-1} fw) of BDE-209 and of the sum of the 7 PBDEs (BDE-28, BDE-47, BDE-99, BDE-100, BDE-153, BDE-14 and BDE-187) in food.

Food item	N	BDE-209					Sum 7 PBDEs			
		% detection	LB		UB		LB		UB	
			Mean ± SD	Min-max	Mean ± SD	Min-max	Mean ± SD	Min-max	Mean ± SD	Min-max
Infant specific foods										
Milk-based beverage	8	75	18.2 ± 11.8	0–31.2	21.8	13.0–31.2	0.95 ± 0.98	0–3.24	3.96 ± 1.06	1.73–5.02
Cereals	5	60	66.9 ± 95.6	0–211	90.4	3.95–211	3.67 ± 4.79	0.05–8.99	11.6 ± 3.42	7.32–15.3
Milk-based desserts	6	100	69.6 ± 62.5	17.1–180	69.6	17.2–180	3.22 ± 1.97	0.63–5.57	5.74 ± 1.56	4.22–8.61
Growing-up milk	9	44	5.64 ± 6.77	0–14.8	10.1	6.61–14.8	1.27 ± 1.22	0.43–4.28	2.49 ± 1.19	1.59–4.64
Soups and puree	11	73	16.6 ± 21.3	0–76.5	19.4	9.73–76.5	2.43 ± 2.25	0.32–7.88	4.43 ± 1.82	2.27–8.67
Fruit puree	4	75	32.9 ± 26.6	0–59.6	35.5	10.7–59.6	0.56 ± 0.67	0–1.35	4.81 ± 0.72	3.98–5.72
Vegetable-based ready-to-eat meal	20	60	17.6 ± 20.4	0–62.9	22.3	5.67–62.9	1.02 ± 1.06	0–4.24	3.61 ± 1.16	1.25–5.98
Meat/fish-based ready-to-eat meal	45	64	16.9 ± 21.9	0–125	20.8	8.56–125	4.35 ± 13.7	0.30–89.9	6.64 ± 13.2	2.33–90.3
Infant formula	28	61	11.4 ± 12.4	0–43.8	15.4	8.11–43.8	2.33 ± 2.64	0.34–8.43	4.38 ± 2.00	2.19–9.44
Follow-on formula	33	73	18.4 ± 21.0	0–104	21.8	10.8–104	2.19 ± 2.62	0.10–10.6	4.45 ± 2.12	1.69–11.4
Common foods										
Non-alcoholic beverages	1	100	9.68	9.68	9.68	9.68	0.83	0.83	1.34	1.34
Dairy-based desserts	1	100	73.7	73.7	73.7	73.7	4.62	4.62	8.01	8.01
Milk	1	0	0	0	8.93	8.93	0.66	0.65	2.49	2.49
Mixed dishes	1	0	0	0	37.7	37.7	6.58	6.58	14.0	14.0
Fish	1	0	0	0	20.4	20.4	31.2	31.2	31.8	31.8
Ultra-fresh dairy products	1	100	24.8	24.8	24.8	24.8	0	0	4.49	4.49
Meat	1	0	0	0	34.8	34.8	6.76	6.76	9.52	9.52
Poultry and game	1	100	28.4	28.4	28.4	28.4	1.01	1.01	5.96	5.96

N: number of composite samples analysed.
LB: Lower bound hypothesis; UB:Upper bound hypothesis.

3.1.2. BFRs

For PBDEs, overall analyses covered 96% of the contributing diet. Detection rates for the 7 PBDEs (BDE-28 + BDE-47 + BDE-99 + BDE-100 + BDE-153 + BDE-154 + BDE-183) ranged from 20% to 93% for BDE-183 and BDE-99, respectively. Highest mean concentrations were measured in dairy desserts and infant cereals for BDE-209 (respectively 69.57 and 66.94 pg g^{-1} fw considering the LB hypothesis) and in vegetables/meat or vegetable/fish ready to eat jars, infant cereals and dairy desserts for the sum of the 7 PBDEs (4.35 pg g^{-1} fw, 3.67 pg g^{-1} fw and 3.22 pg g^{-1} fw, respectively considering the LB hypothesis, Table 1). For common food items, highest BDE-209 mean concentrations were measured in a fish sample (31.2 pg g^{-1} fw), that was lower than the levels previously measured in common foods in the second French TDS (Rivière et al., 2014). In 2011, EFSA reported concentrations of PBDE in fish and seafood ten-fold higher than those reported in the present study (around 400 *versus* 40 pg g^{-1} fw; EFSA, 2011a). Similarly in infant food items, EFSA reported concentrations of BDE-209 of 130 pg g^{-1} fw *versus* 8–70 pg g^{-1} fw in the present study.

For HBCDDs, overall analyses covered 96% of the contributing diet. HBCDDs were detected in 82, 36 and 38% of the samples for isomers α, β and γ, respectively. Detection rates were very variable depending on the matrix analyzed (from 0 to 100%, in, respectively, cereals and dairy desserts and milk-based beverages). Measured concentrations in infant specific food items ranged from 2.46 to 42.85 pg g^{-1} fw (considering the sum of the three isomers and the UB hypothesis, Table 2). In one sample of infant formula, a concentration of 307 pg. g^{-1} fw was measured whereas all other infant formula samples had concentrations ranging from 0.22 to 8.15 pg. g^{-1} fw. A similar situation has been observed in the past where high concentrations of HBCDD were measured in different matrices (especially turkey and eggs, Anses, 2012). However, except an occasional contamination, no relevant hypothesis could be drawn to explain this observation. For common food items, highest mean concentrations were measured in fish (between 177 pg g^{-1} fw and 185 pg g^{-1} fw depending on the hypothesis) and in delicatessen meat (between 140 pg g^{-1} fw and 150 pg g^{-1} fw, depending on the hypothesis). EFSA, in 2011, reported concentrations of HBCDD in infant food in the same order of magnitude (between 10 and 30 pg. g^{-1} fw, EFSA, 2011c) than those reported in the present study.

For PBBs, overall, analyses covered 96% of the contributing diet. The three congeners analyzed were detected in 4–12% of samples tested. In infant specific food items, measured concentrations were close to the limits of detection, with values ranging from 0.26 to 4.88 pg g^{-1} (considering the UB hypothesis, Table 3) for the sum of the three congeners. Highest PBB-52 concentrations were measured in an infant specific dairy based dessert containing fruits (3.28 pg g^{-1} fw) and in a ready to eat jar containing salmon, rice and vegetables (1.23 pg g^{-1} fw). For common food items, only the BB-52 was detected in one fish sample and in one meat sample. These results are consistent with the poor use of these compounds in Europe since their ban in 2000 (EFSA, 2010). In 2010, EFSA reported concentrations of PBB in fish in the same order of magnitude than those reported here (between 1.86 and 18.9 ng kg^{-1} fw depending on the congener, EFSA, 2010).

Overall, analyses of TBBPA covered 94% of the contributing diet. TBBPA was detected in 30% of the samples. Highest mean concentrations were measured in croissant-like pastries (914 ng kg^{-1} fw, Table 4) and infant and follow-on formulae (between 45 and 60 ng kg^{-1} fw depending on the hypothesis), poultry (between 42 ng kg^{-1} fw and 54 ng kg^{-1} fw) and chocolate (between 32 and 62 ng kg^{-1} fw).

3.2. Exposure data

3.2.1. PFAAs

Considering the UB hypothesis with regards to censored data, mean daily exposures to PFOA ranged from 1.49 ng kg bw^{-1}.d^{-1} (90th percentile 1.77 ng kg bw^{-1}.d^{-1}) in the 1–4 months of age children to 2.95 ng kg bw^{-1}.d^{-1} (90th percentile 5.16 ng kg bw^{-1}.d^{-1}) in the 1 to 3-year old children (Table 5). For PFOS, the mean exposures ranged from 1.61 ng kg bw^{-1}.d^{-1} (90th percentile 3.56 ng kg bw^{-1}.d^{-1}) in the 5–6 months of age children to 2.66 ng kg bw^{-1}.d^{-1} (90th percentile 4.63 ng kg bw^{-1}.d^{-1}) in the 1–3 years of age children. The mean exposure of the most exposed children (whose exposure were higher than the 90th percentile), ranged from 6.25 to 7.45 ng kg bw^{-1}.d^{-1} for PFOA and from 5.54 to 6.37 for PFOS ng.kg bw^{-1}.d^{-1}. In 2012, EFSA reported exposures higher than those reported in the present study (EFSA, 2012). In newborns, reported exposures to PFOS and PFOA were 0.16 and 0.29 ng kg bw^{-1}.d^{-1}, respectively, whereas in young children

Table 2
Mean concentrations (pg.g^{-1} fw) of HBCDDs in food.

Food item	N	HBCDDα					HBCDDβ				
		%[a]	LB		UB		%	LB		UB	
Infant specific foods			Mean ± SD	Min-max	Mean ± SD	Min-max		Mean ± SD	Min-max	Mean ± SD	Min-max
Milk-based beverage	8	100	14.3 ± 9.87	1.69–27.2	14.3 ± 9.87	1.69–27.2	88	3.36 ± 2.49	2.49–6.57	3.39 ± 2.44	0.25–6.57
Cereals	5	40	11.0 ± 20.7	0–47.6	12.3 ± 19.9	1.19–47.6	0	0.00	0	0.44 ± 0.33	0.07–0.87
Milk-based desserts	6	100	26.8 ± 22.9	2.65–57.3	26.8 ± 22.9	2.65–57.3	83	6.94 ± 6.20	6.20–14.9	7.03 ± 6.09	0.52–14.9
Growing-up milk	9	89	3.56 ± 2.63	0–7.62	3.63 ± 2.53	0.67–7.62	67	0.80 ± 0.74	0.74–1.90	0.91 ± 0.63	0.11–1.90
Soups and puree	11	18	0.96 ± 2.72	0–9.06	1.48 ± 2.55	0.12–9.06	9	0.25 ± 0.83	0.83–2.77	0.38 ± 0.80	0.03–2.77
Fruit puree	4	75	4.28 ± 3.27	0–7.08	4.55 ± 2.81	1.08–7.08	25	0.48 ± 0.95	0.95–1.90	1.01 ± 0.72	0.17–1.90
Vegetable-based ready-to-eat meal	20	70	5.16 ± 6.05	0–22.6	5.67 ± 5.66	0.42–22.6	50	1.04 ± 1.39	1.39–4.83	1.27 ± 1.24	0.01–4.83
Meat/fish-based ready-to-eat meal	45	76	8.90 ± 12.1	0–51.7	9.16 ± 11.9	0.58–51.7	49	1.75 ± 3.20	3.20–14.1	1.87 ± 3.13	0.04–14.1
Infant formula	28	61	8.41 ± 36.7	0–196	8.74 ± 36.7	0.21–196	18	1.95 ± 9.54	9.54–50.6	2.20 ± 9.49	0.01–50.6
Follow-on formula	33	33	2.45 ± 6.26	0–33.2	3.13 ± 6.02	0.15–33.2	12	0.48 ± 1.76	1.76–9.46	0.72 ± 1.72	0.02–9.46
Common foods											
Non-alcoholic beverages	1	100	7.98	7.98	7.98	7.98	100	2.07	2.07	2.07	2.07
Dairy-based desserts	1	0	0	0	0.87	0.87	0	0	0	1.31	0.10
Milk	1	100	1.59	1.59	1.59	1.59	0	0	0	0.059	0.06
Mixed dishes	1	100	59.6	59.6	59.6	59.6	100	8.72	8.72	3.82	8.72
Fish	1	100	83.7	83.7	83.7	83.7	100	19.3	19.3	10.1	19.3
Ultra-fresh dairy products	1	0	0	0	1.96	1.96	0	0	0	2.07	0.29
Meat	1	0	0	0	3.99	3.99	0	0	0	1.72	0.11
Poultry and game	1	100	81.3	81.3	81.3	81.3	0	0	0	1.2	1.27

Food item	HBCDDγ					Sum of the HBCDDs			
	%	LB		UB		LB		UB	
Infant specific foods		Mean ± SD	Min-max	Mean ± SD	Min-max	Mean ± SD	Min-max	Mean ± SD	Min-max
Milk-based beverage	88	5.14 ± 3.70	0–11.2	5.31 ± 3.45	1.37–11.2	22.8 ± 15.9	2.19–44.4	23.0 ± 15.6	3.56–44.4
Cereals	0	0.00	0	1.85 ± 1.59	0.42–3.80	11.0 ± 20.7	0–47.6	14.6 ± 21.0	1.68–51.7
Milk-based desserts	83	8.87 ± 6.90	0–18.5	9.02 ± 6.68	0.89–18.5	42.6 ± 35.7	2.65–90.7	42.9 ± 35.4	4.06–90.7
Growing-up milk	67	0.96 ± 0.88	0–2.34	1.21 ± 0.62	0.45–2.34	5.32 ± 4.19	0–11.9	5.74 ± 3.74	1.47–11.9
Soups and puree	9	0.27 ± .91	0–3.01	0.61 ± 0.84	0.05–3.01	1.49 ± 4.45	0–14.8	2.46 ± 4.15	0.27–14.8
Fruit puree	50	1.24 ± 1.50	0–3.02	1.84 ± 0.86	1.12–3.02	5.99 ± 5.13	0–10.4	7.40 ± 4.18	2.37–11.2
Vegetable-based ready-to-eat meal	45	1.35 ± 1.83	0–6.23	1.71 ± 1.62	0.02–6.23	7.54 ± 9.09	0–33.7	8.65 ± 8.40	0.51–33.7
Meat/fish-based ready-to-eat meal	44	2.25 ± 3.92	0–16.4	2.54 ± 3.77	0.03–16.4	12.9 ± 19.0	0–82.3	13.6 ± 18.6	1.10–82.3
Infant formula	18	2.46 ± 11.5	0–60.8	2.89 ± 11.4	0.01–60.8	12.8 ± 57.7	0–307	13.8 ± 57.5	0.22–307
Follow-on formula	12	0.67 ± 2.51	0–13.8	1.03 ± 2.44	0.04–13.8	3.60 ± 10.5	0–56.4	4.88 ± 10.1	0.33–56.4
Common foods									
Non-alcoholic beverages	100	2.49	2.49	2.49	2.49	12.5	12.5	12.5	12.5
Dairy-based desserts	0	0	0	0.10	0.10	0	0	1.06	1.06
Milk	0	0	0	0.12	0.12	1.59	1.59	1.77	1.77
Mixed dishes	100	11.5	11.5	11.5	11.5	79.8	79.8	79.8	79.8
Fish	100	24.2	24.2	24.2	24.2	127	127	127	127
Ultra-fresh dairy products	0	0	0	0.67	0.67	0	0	2.92	2.92
Meat	0	0	0	1.22	1.22	0	0	5.32	5.32
Poultry and game	0	0	0	2.91	2.91	81.3	81.3	85.5	85.5

N: number of composite samples analysed.
LB: Lower bound hypothesis; UB: Upper bound hypothesis.
[a] Percentage of detection (%).

Table 3
Mean concentrations ($pg.g^{-1}$ fw) of PBBs in food.

	N	BB-52					BB-101				
		%[a]	LB		UB		%	LB		UB	
Infant specific foods			Mean ± SD	Min-max	Mean ± SD	Min-max		Mean ± SD	Min-max	Mean ± SD	Min-max
Milk-based beverage	8	0	0.00	0.00	0.13 ± 0.24	0.01–0.70	0	0.00	0	0.18 ± 0.24	0.01-µ0.75
Cereals	5	0	0.00	0.00	0.67 ± 0.31	0.34–0.98	0	0.00	0	0.78 ± 0.34	0.35–1.06
Milk-based desserts	6	17	0.08 ± 0.20	0–0.50	0.40 ± 0.21	0.11–0.67	0	0.00	0	0.38 ± 0.23	0.08–0.74
Growing-up milk	9	0	0.00	0.00	0.09 ± 0.07	0.01–0.24	0	0.00	0	0.14 ± 0.10	0.02–0.38
Soups and puree	11	0	0.00	0.00	0.06 ± 0.03	0.03–0.11	0	0.00	0	0.10 ± 0.03	0.06–0.15
Fruit puree	4	25	0.82 ± 1.64	0–3.28	2.06 ± 1.05	0.72–3.28	0	0.00	0	1.29 ± 0.58	0.70–1.95
Vegetable-based ready-to-eat meal	20	5	0.02 ± 0.08	0–0.34	0.37 ± 0.28	0.07–1.40	0	0.00	0	0.40 ± 0.26	0.10–1.06
Meat/fish-based ready-to-eat meal	45	4	0.03 ± 0.19	0–1.23	0.17 ± 0.20	0.03–1.23	2	0.01 ± 0.06	0–0.40	0.20 ± 0.12	0.05–0.68
Infant formula	28	14	0.07 ± 0.19	0–0.82	0.20 ± 0.18	0.06–0.82	0	0.00	0	0.24 ± 0.16	0.08–0.61
Follow-on formula	33	0	0.00	0.00	0.23 ± 0.18	0.04–0.86	0	0.00	0	0.24 ± 0.14	0.08–0.66
Common foods											
Non-alcoholic beverages	1	0	0	0	0.05	0.05	0	0	0	0.05	0.05
Dairy-based desserts	1	0	0	0	0.61	0.61	0	0	0	0.44	0.44
Milk	1	0	0		0.17	0.17	0	0	0	0.13	0.13
Mixed dishes	1	0	0	0	0.24	0.24	0	0	0	0.14	0.14
Fish	1	0	3.05	0	0.24	0.24	0	0	0	0.42	0.42
Ultra-fresh dairy products	1	0	0	0	0.37	0.37	0	0	0	0.36	0.36
Meat	1	0	0.001	0	1.43	1.43	0	0	0	1.34	1.34
Poultry and game	1	0	0	0	0.59	0.59	0	0	0	0.57	0.57

	BB-153					Sum of PBBs			
	%	LB		UB		LB		UB	
Infant specific foods		Mean ± SD	Min-max	Mean ± SD	Min-max	Mean ± SD	Min-max	Mean ± SD	Min-max
Milk-based beverage	0	0.00	0	0.15 ± 0.15	0.04–0.48	0.00	0.00	0.46 ± 0.63	0.07–1.93
Cereals	0	0.00	0	0.77 ± 0.37	0.31–1.27	0.00	0.00	2.22 ± 0.95	1.04–3.03
Milk-based desserts	0	0.00	0	0.31 ± 0.16	0.11–0.57	0.08 ± 0.20	0–0.50	1.09 ± 0.54	0.29–1.81
Growing-up milk	0	0.00	0	0.16 ± 0.16	0.02–0.54	0.00	0.00	0.39 ± 0.32	0.04–1.16
Soups and puree	0	0.00	0	0.10 ± 0.02	0.05–0.13	0.00	0.00	0.26 ± 0.07	0.17–0.37
Fruit puree	0	0.00	0	1.54 ± 1.04	0.43–2.79	0.82 ± 1.64	0–3.28	4.88 ± 2.49	207–7.65
Vegetable-based ready-to-eat meal	0	0.00	0	0.40 ± 0.33	0.10–1.56	0.02 ± 0.08	0–0.34	1.17 ± 0.82	0.27–4.02
Meat/fish-based ready-to-eat meal	0	0.00	0	0.16 ± 0.09	0.05–0.41	0.04 ± 0.24	0–1.62	0.53 ± 0.35	0.18–1.77
Infant formula	0	0.00	0	0.20 ± 0.13	0.07–0.55	0.07 ± 0.19	0–0.82	0.63 ± 0.43	0.23–1.85
Follow-on formula	0	0.00	0	0.20 ± 0.10	0.07–.43	0.00	0.00	0.68 ± 0.39	0.24–1.86
Common foods									
Non-alcoholic beverages	0	0	0	0.10	0.10	0	0	0.19	0.19
Dairy-based desserts	0	0	0	0.45	0.45	0	0	1.50	1.50
Milk	0	0	0	0.09	0.09	0	0	0.40	0.40
Mixed dishes	0	0	0	0.35	0.35	0	0	0.75	0.75
Fish	0	0	0	0.18	0.18	0	0	0.84	0.84
Ultra-fresh dairy products	0	0	0	0.25	0.25	0	0	0.98	0.98
Meat	0	0	0	1.20	1.20	0	0	3.98	3.98
Poultry and game	0	0	0	0.55	0.55	0	0	1.71	1.71

N: number of composite samples analysed.
LB: Lower bound hypothesis; UB: Upper bound hypothesis.
[a] Percentage of detection (%).

Table 4
Mean concentrations (ng.g^{-1} fw) of TBBPA in food.

Food item	N	% detection	LB		UB	
			Mean ± SD	Min-max	Mean ± SD	Min-max
Infant specific foods						
Milk-based beverage	8	0	0.00	0.00	10.4 ± 2.58	6.93–13.4
Cereals	5	0	0.00	0.00	34.8 ± 19.0	22.0–68.3
Milk-based desserts	6	0	0.00	0.00	11.6 ± 3.07	7.72–16.4
Growing-up milk	9	100	21.7 ± 21.2	6.79–75.0	21.7 ± 21.2	6.79–75.0
Soups and puree	11	0	0.00	0.00	8.37 ± 1.45	6.01–10 .8
Fruit puree	4	0	0.00	0.00	13.7 ± 3.17	8.97–15.6
Vegetable-based ready-to-eat meal	20	10	0.78 ± 2.4	0.00–9.13	10.4 ± 1.91	6.45–14.7
Meat/fish-based ready-to-eat meal	45	9	4.05 ± 21.2	0.00–141	12.7 ± 19.8	7.08–141
Infant formula	28	61	45.2 ± 57.2	0.00–321	48.6 ± 73.1	7.34–321
Follow-on formula	33	73	57.3 ± 115	0.00–581	60.1 ± 113.8	9.12–581
Common foods						
Butter	1	0	0.00	0.00	46.1	46.1
Non-alcoholic beverages	1	0	0.00	0.00	4.04	4.04
Delicatessen	3	0	0.00	0.00	20.5 ± 4.15	15.9–24.0
Chocolate	2	50	31.6 ± 44.7	0.00–63.2	61.9 ± 1.86	60.6–63.2
Dairy-based desserts	2	0	0.00	0.00	21.2 ± 0.98	20.521.9
Cheese	3	0	0.00	0.00	32.0 ± 5.97	25.3–36.9
Milk	4	0	0.00	0.00	10.8 ± 5.17	6.57–18.0
Eggs and derivatives	1	0	0.00	0.00	13.7	13.7
Mixed dishes	4	25	7.38 ± 14.8	0.00–29.5	26.9 ± 5.93	18.3–31.7
Fish	3	33.3	5.55 ± 9.6	0.00–16.6	18.4 ± 2.63	16.6–21.4
Potatoes and potato products	1	0	0.00	0.00	11.9	11.9
Pasta	1	0	0.00	0.00	20.8	20.8
Ultra-fresh dairy products	5	0	0.00	0.00	12.3 ± 3.78	7.80–16.9
Meat	2	50	10.7 ± 15.1	0.00–21.4	25.4 ± 5.60	21.4–29.3
Croissant-like pastries	1	100	914	913.64	914	914
Poultry and game	2	50	41.9 ± 59.3	0.00–83.8	53.6 ± 42.8	23.3–83.8

N: number of composite samples analysed.
LB: Lower bound hypothesis; UB: Upper bound hypothesis.
SD: standard deviation.

these exposures ranged from 0.20 to 17 ng kg bw^{-1}.d^{-1} for PFOA depending of the hypothesis with regards to censored data and from 0.58 to 14 ng kg bw^{-1}.d^{-1} for PFOS. In France, in the last total diet study, exposures to PFOA and PFOS of the 3–6 years of age children were estimated at 2.45 ng kg bw^{-1}.d^{-1} and 2.18 ng kg bw^{-1}.d^{-1}, respectively (Anses, 2011), which is the same range as for 1-3 years-old children of the present study.

Due to the very limited number of food where PFBS and PFHxA were detected, no conclusions can be drawn with regard to the exposures to these compounds.

Table 5
Dietary exposure to PFOA and PFOS and risk assessment (Upper bound hypothesis).

Substance	Age group	Reference dose (ng.kg bw^{-1}.d^{-1})	Mean (ng.kg bw^{-1}.d^{-1})	Standard deviation (ng.kg bw^{-1}.d^{-1})	90th percentile (ng.kg bw^{-1}.d^{-1})	Percentage of individuals exceeding the reference dose (IC 95%)
PFOA	1–4 mo	200	1.49	3,19	1.77	0
	5–6 mo		2.10	2,29	4.59	
	7–12 mo		2.42	1,84	4.71	
	13–36 mo		2.95	1,60	5.16	
PFOS	1–4 mo	80	1.83	2,66	2.04	0
	5–6 mo		1.61	1,99	3.56	
	7–12 mo		1.81	1,58	3.94	
	13–36 mo		2.66	1,43	4.63	
PFOA	1–4 mo	0.8	1.49	3,19	1.77	50.4 (39.4–61.5)
	5–6 mo		2.10	2,29	4.59	86.1 (75.4–96.9)
	7–12 mo		2.42	1,84	4.71	94.8 (90.8–98.8)
	13–36 mo		2.95	1,60	5.16	98.5 (97.3–99.6)
PFOS	1–4 mo	1.8	1.83	2,66	2.04	18.1 (9.6–26.7)
	5–6 mo		1.61	1,99	3.56	23.1 (10.0–36.2)
	7–12 mo		1.81	1,58	3.94	25.8 (17.8–33.7)
	13–36 mo		2.66	1,43	4.63	66.2 (62.0–70.5)
PFBS	1–4 mo	80 000	2.44	6.16	2.04	0
	5–6 mo		2.15	3.95	2.89	
	7–12 mo		2.36	2.57	5.13	
	13–36 mo		3.84	2.33	7.32	
PFHxA	1–4 mo	320 000	2.42	5.84	2.13	0
	5–6 mo		2.29	3.84	5.6	
	7–12 mo		2.7	3.24	6.69	
	13–36 mo		4.25	2.84	8	

Table 6
Dietary exposure to BDE-209, PBB and TBBPA, and risk assessment (Upper bound hypothesis).

Substance	Age group	Reference value (ng.kg $bw^{-1}.d^{-1}$)	Mean (ng.kg $bw^{-1}.d^{-1}$)	Standard Deviation (ng.kg $bw^{-1}.d^{-1}$)	90th percentile (ng.kg $bw^{-1}.d^{-1}$)	Margin of safety at the mean (ng.kg $bw^{-1}.d^{-1}$)	Margin of safety at the 90th percentile (ng.kg $bw^{-1}.d^{-1}$)
BDE 209	1–4 mo	$BMDL_{10}$ = 1 700 000	2.62	1,63	3.78	650 000	450 000
	5–6 mo		2.23	1,96	3.91	760 000	430 000
	7–12 mo		1.96	1,36	3.20	870 000	530 000
	13–36 mo		1.12	0,78	1.88	1 500 000	910 000
PBB	1–4 mo	NOAEL = 150 000	0.097	0,062	0.204	1 500 000	740 000
	5–6 mo		0.076	0,038	0.112	2 000 000	1300 000
	7–12 mo		0.063	0,028	0.098	2 400 000	1500 000
	13–36 mo		0.049	0,022	0.074	3 100 000	2000 000
TBBPA	1–4 mo	$BMDL_{10}$ = 16 000 000	9.94	12,72	31.3	1 610 000	511 000
	5–6 mo		5.60	9,37	16.3	2 857 000	982 000
	7–12 mo		3.28	5,02	8.39	4 878 000	1907 000
	13–36 mo		0.968	0,794	1.80	16 529 000	8 889 000

BMDL = Lower limit of the benchmark dose.

3.2.2. BFRs

Considering the UB hypothesis, mean daily exposure to BDE-209 ranged from 1.12 ng kg $bw^{-1}.d^{-1}$ to 2.62 ng kg $bw^{-1}.d^{-1}$, for the 1–3 years of age children and the 1–4 months of age children, respectively (Table 6). For the sum of the 7 PBDEs, mean exposures ranged from 0.448 to 0.926 ng kg $bw^{-1}.d^{-1}$ (Table 7). The 90th percentiles ranged from 1.88 to 3.91 ng kg $bw^{-1}.d^{-1}$ for BDE-209, whereas they ranged from 0.694 to 1.56 ng kg $bw^{-1}.d^{-1}$ for the sum of the 7 PBDEs depending on the age groups (4.30 ng kg $bw^{-1}.d^{-1}$). Two children had exposures of the 7 PBDEs much higher than the mean of their respective age groups. In both cases, these children consumed during the survey high quantities of salmon. Exposures of the 3–6 years of age children in France previously reported were in the same order of magnitude than those reported in the present study (ranging from 0.481 to 0.510 ng kg $bw^{-1}.d^{-1}$) whereas exposure to BDE-209 reported by EFSA were higher (ranging from 2.61 ng kg $bw^{-1}.d^{-1}$ to 6.02 ng kg $bw^{-1}.d^{-1}$ depending on the hypothesis for censored data, EFSA, 2011a). It is of interest to note that the ratio of exposures to BDE-209 to exposures to the sum of PBDEs is higher in the present study (around 3-fold) than in some previously reported studies (around 2-fold, Anses, 2011; EFSA, 2011a). This being possibly due to the increasing use of BDE-209 compared to that of the other congeners.

For the sum of HBCDDs and following the UB hypothesis, mean daily exposure ranged from 0.505 ng kg $bw^{-1}.d^{-1}$ for the 1–3 years of age children to 8.27 ng kg $bw^{-1}.d^{-1}$ for the 1–4 months of age children (Table 8). The 90th percentile ranged from 0.880 to 43.2 ng kg $bw^{-1}.d^{-1}$ for the same age groups, the last value being due to the atypical contamination value measured in one sample of infant formula. For this reason the median values have also been reported in Table 8.

. Mean exposures of the 3–6 years of age children previously reported in the previous total diet study ranged from 0.35 to 0.49 ng kg $bw^{-1}.d^{-1}$ (Anses, 2011). EFSA, in 2011, reported similar values (between 0.36 and 1.27 ng kg $bw^{-1}.d^{-1}$ for the sum of the three HBCDDs, EFSA, 2011c).

Mean exposure to the sum of the three PBBs ranged from 0.049 ng kg $bw^{-1}.d^{-1}$ in the 1–3 years of age children (90th percentile: 0.074 ng kg $bw^{-1}.d^{-1}$) to 0.097 ng kg $bw^{-1}.d^{-1}$ in the 1–4 months of age children (90th percentile: 0.204 ng kg $bw^{-1}.d^{-1}$, Table 7). These exposure values were in the same order of magnitude than those reported for the 3–6 years of age children in the previously conducted total diet study (Anses, 2011).

For TBBPA, mean daily exposures, following the UB hypothesis, ranged from 0.968 to 9.94 ng kg $bw^{-1}.d^{-1}$ for the 1–3 years of age group and the 1–4 months of age group, respectively (Table 7). One of the children from the 5–6 months of age group had exposure estimated at 77.1 ng kg $bw^{-1}.d^{-1}$, i.e. 14 times higher than the mean exposure of that group of age. The reason for this lying in the fact that this child consumed a follow-on formula highly contaminated compared to other formulae. In 2006, the United-Kingdom committee on toxicity of chemicals in food reported exposures similar to those reported in the present study in 1.5–4.5 years of age children (between 7.0 and 4.6 ng kg $bw^{-1}.d^{-1}$, COT, 2006).

3.3. Risk assessment

3.3.1. PFAAs

Both PFOA and PFOS bind to plasma protein and are non-genotoxic, therefore allowing the setting of a health based guidance value based on a threshold effect (US-EPA, 2009; EFSA 2018). US-EPA in 2009 set a Reference Dose (RfD) at 0.08 µg kg $bw^{-1}.d^{-1}$ for PFOS based on the effects observed on thyroid in a 182-day study in monkeys (Seacat et al., 2002). For PFOA, the American environmental protection agency (US-EPA) in 2009 also established a reference dose for PFOA set at 0.2 µg kg $bw^{-1}.d^{-1}$ based on a developmental study performed in mice (Lau et al., 2003). On the other hand, the EFSA set provisional tolerable daily intakes for PFOA and PFOS at, respectively, 0.8 and 1.8 ng kg $bw^{-1}.d^{-1}$ (EFSA, 2018). These health based guidance values were based on, the increase in serum total cholesterol in adults and a decrease in antibody response at vaccination in children for PFOS and on the increase in serum total cholesterol for PFOA.

Anses recently reported some health based guidance values for Perfluorobutanesulfonic acid (PFBS) and Perfluorohexanoic acid

Table 7
Dietary exposure to the sum of the 7 PBDEs (BDE28, BDE47, BDE99, BDE100, BDE153, BDE14 and BDE187) and risk assessment (Upper bound hypothesis).

Substance	Age group	Tolerable daily intake (ng.kg $bw^{-1}.d^{-1}$)	Mean (ng.kg $bw^{-1}.d^{-1}$)	Standard Deviation (ng.kg $bw^{-1}.d^{-1}$)	90th percentile (ng.kg $bw^{-1}.d^{-1}$)	Percentage of individuals exceeding the reference dose
Sum of the 7 PBDE	1–4 mo	10	0.926	0,455	1.56	0
	5–6 mo		0.553	0,330	1.01	
	7–12 mo		0.499	0,428	0.812	
	13–36 mo		0.448	0,477	0.694	

Table 8
Dietary exposure to HBCDDs and risk assessment (Upper bound hypothesis).

Age group	$BMDL_{10}$ (ng.kg $bw^{-1}.d^{-1}$)	Mean (ng.kg $bw^{-1}.d^{-1}$)	Standard Deviation (ng.kg $bw^{-1}.d^{-1}$)	Median (ng.kg $bw^{-1}.d^{-1}$)	90^{th} percentile (ng.kg $bw^{-1}.d^{-1}$)	Margin of safety at the mean (ng.kg $bw^{-1}.d^{-1}$)	Margin of safety at the median (ng.kg $bw^{-1}.d^{-1}$)	Margin of safety at the 90^{th} percentile (ng.kg $bw^{-1}.d^{-1}$)
1–4 mo	3000	8.27	18,27	0.662	43.2	363	4530	70
5–6 mo	3000	0.883	0,962	0.588	1.78	3400	5100	1690
7–12 mo	3000	0.827	0,696	0.574	1.79	3630	5230	1680
13–36 mo	3000	0.505	0,317	0.418	0.88	5940	7180	3410

(PFHxA) (0.08 and 0.32 mg kg $bw^{-1}.d^{-1}$, both based on renal toxicity; Anses, 2017a and 2017b).

With regard to PFOA and PFOS, based on the RfD set by the US EPA in 2009 for PFOA (0.2 µg kg $bw^{-1}.d^{-1}$) and PFOS (0.08 µg kg $bw^{-1}.d^{-1}$) the situation appears to not be of health concern (Table 5). However, in 2016, the US EPA reported lower RfD values, based on the result of pharmacokinetic modelling of serum values in animals in conjunction with the criteria of selected effects and their extrapolation to humans (respectively 20 and 30 µg kg $bw^{-1}.d^{-1}$ for PFOA and PFOS, respectively, US-EPA, 2016a and 2016b). We observed that for PFOS, no children included in the present study exceeded this RfD whereas for PFOA, only one child exceeded it. Considering the provisional health based guidance values set by EFSA in 2018 for PFOA and PFOS, high percentages of the 4 populations showed exceedances of the respective health based guidance values when considering the upper bound hypothesis (from 20% to almost 100% of the populations, Table 5).

For PFBS and PFHxA, mean and 90^{th} percentile exposures were much lower than the respective health based guidance values set by Anses (Anses, 2017a and 2017b). For the other PFAAs, given the absence of data that would enable a toxicological point of departure to be established, it was not possible to reach any conclusions as to the health risk associated with dietary exposure to these substances.

3.3.2. BFRs

None of the compounds analyzed in the present study are genotoxic, therefore allowing the setting of health based guidance values based on threshold effects (EFSA 2011a,b). These compounds are lipophilic and accumulate in the adipose tissues.

Regarding the 209 congeners of PBDEs, their chemical structure being similar to that of non-dioxin-like polychlorinated biphenyls (NDL-PCBs) and due to their common mechanism of action (Pellacani et al., 2012; Miller et al., 2012; Kodavanti et al., 2005) and pending the definition of a health-based guidance value for PBDEs, the French Agency for Food, Environmental and Occupational Health & Safety (ANSES) Expert Committee on food contaminants compared exposure to the following congeners: BDE-28,-47, −99, −100, −153, −154, −183 with the threshold of 10 ng/kg bw/day set for the six NDL-PCBs that are the most frequently found in food (AFSSA, 2007; Rivière et al., 2014). The European Food Safety Authority (EFSA) also set benchmark dose lower confidence limits (BMDLs) for a benchmark response of 10% ($BMDL_{10}$) for the four most "of concern" PBDEs based on their neurodevelopmental effects: 172 ng kg bw^{-1} for BDE-47, 4.2 ng kg bw^{-1} for BDE-99, 9.6 ng kg bw^{-1} for BDE-153 and 1700 µg kg bw^{-1} for BDE-209 (EFSA, 2011a). Regarding HBCDDs, EFSA identified neurodevelopmental effects on behavior as the critical endpoint, and derived a $BMDL_{10}$ of 0.79 mg kg bw^{-1}. Due to the limitations and uncertainties in current knowledge, EFSA concluded that it was inappropriate to use this BMDL to establish a health-based guidance value, and instead recommended using the margin of safety (MOS) approach for the risk characterisation of HBCDDs by comparing dietary intake with the estimated dietary human intake associated with the body burden at the $BMDL_{10}$, set at 0.003 ng kg $bw^{-1}.d^{-1}$. In its opinion on PBBs, EFSA could not define a health-based guidance value, but suggested comparing data on exposure to PBBs with a no observed adverse effect level (NOAEL) of 0.15 mg/kg bw/day based on the induction of hepatic carcinomas in rats (EFSA, 2010a). With regards to TBBPA, the toxicology point of departure ($BMDL_{10}$) was established in rat reprotoxicity study and based on the effects on the homeostasis of thyroid hormones (decrease of the circulating levels of hormone T4 in the first generation). It was set at 16 mg kg $bw^{-1}.d^{-1}$ (EFSA, 2011b). Due to its specific characteristics in terms of pharmacokinetics and toxicity, BDE-209 was considered separately from the other seven congeners, whose chemical structure and mechanism of action are similar to those of NDL-PCBs.

For the six NDL-PCBs the threshold value (10 ng/kg bw/day) was not observed to have been exceeded (Table 7). The margins of safety calculated for BDE-209 (with regard to the $BMDL_{10}$ of 1700 µg kg $bw^{-1}.d^{-1}$) ranging from 430 000 to 1,5 million, are much larger than the 2.5 margin deeming tolerable by EFSA (Table 6). For PBDEs, the situation is therefore deemed to be tolerable considering these health-based guidance values.

Regardless of the age group, the margins of safety calculated with regard to the $BMDL_{10}$ established by EFSA for the sum of the three HBCDDs (3000 ng kg $bw^{-1}.d^{-1}$) ranged 70 for the 1–4 months using the 90th percentile of exposure to 5940 using the median of exposure of the 13–36 months (Table 8). They were higher than the critical margin of safety value set at 25 to consider the exposure as being of no health concern.

The margins of safety calculated using the no adverse effect level observed by EFSA for the sum of the three PBBs (0.15 mg kg $bw^{-1}.d^{-1}$) ranged 740 000 to more the 3 000 000, depending on the age group and the exposure value (mean or P90) (Table 7). They are then considered as high enough to conclude that the situation is of no health concern.

For TBBPA, the margins of safety calculated using the $BMDL_{10}$ established by EFSA (16 mg kg $bw^{-1}.d^{-1}$), ranging 511 000 to more than 16 million (Table 7), are also large enough (higher than 1000 considered by EFSA as the critical margin of exposure) to conclude that the situation is of no health concern.

Overall, the risk related to the dietary exposures to these compounds appeared not to be of concern, for infants, similarly to the general population older than 3 years old (Rivière et al., 2014). However, it seems of importance to note that the present analysis focused on general infant population and then does not take into account some specific situations such as accidental contaminations. Moreover, the present study does not take into account breastfed infants where lipophilic compounds are known to accumulate (Colles et al., 2008).

3.4. Uncertainties

Some uncertainties are important to mention in parallel to the presented results. Indeed, risk analysis processes suppose some hypotheses that can lead to over or underestimation of the risk. The main identified uncertainties are the following. First, the selection of the samples that were analyzed. Indeed, we selected the food items known or supposed to be contaminated with the studied substances. Due to environmental persistence of some of these substances, food items that were not analyzed could be contaminated. This would lead to an underestimation of the overall exposure and consequently of the health

risk.

The available data to set health based guidance values are a source of uncertainty. For many perfluoroalkyl acids and brominated flame retardants, there is, as of today, not enough robust toxicological data to establish robust health based guidance values. Additionally, considering the population of interest of this study, one has to mention that some toxicological endpoints specific to this population could exist due to the development of the organisms. Efforts have been made to consider values that should be protective to the infant population, however, additional experimental data could lead to lower health based guidance values than the one considered in the present study, as it was the case for PFOS and PFOA with decreasing health-based guidance values with time. Moreover, synergistic or antagonistic effects could occur due to the exposure of substances from the same chemical family.

Some uncertainties are due to the consumption data used to perform exposure calculations. Since only main practices are considered in the present study, specific dietary habits that could lead to different exposure patterns are not observed.

Finally, analytical methodology could lead to uncertainties due to the precision of the method but also due to the limits of detection and quantification that can be achieved. This, indeed, has some impact on the exposure calculation as seen above for PFOS and PFOA. In the case of a limit of detection far above the concentrations measured in the food items, the upper bound hypothesis would lead to a significant overestimation of the exposure.

4. Conclusion

The results presented above allow to assess the risk related to the dietary exposure of some PFAAs and of some BFRs. For the compounds analyzed, dietary exposures appear to be of no health concern in the 0–3 years of age children with regard to the selected health based guidance values. However, considering the newly established RfD for PFOS and PFOA by US-EPA, for some children with specific diets the risk can not be excluded. This analysis also reveals that for some congeners (especially for some PFAAS), no health based guidance values are as of today available due to the paucity of robust toxicological data, preventing to perform a risk assessment. It is also of importance to consider that new toxicological data becoming available, health based guidance values could be lowered, especially for compounds for which some endocrine disruptor effects have been reported but no characterized enough as of today to set a health based guidance value.

Declaration of interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

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Appendix A. Supplementary data

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