Table 4. Median (range) of estimated adult daily dietary intakes in ng/kg b.w.

	PFOS	PFOA	Study location and year of sampling	Study information	Treatment of non-detects for intake estimation
FSA (2006)					
A	Lower bound: 10 Upper bound: 100	Lower bound: 1 Upper bound: 70	UK, 2004	Total diet study; yearly composite samples of 20 food groups that comprised an entire diet	Lower bound: <LOD = 0 Upper bound: <LOD = LOD
H	Lower bound: 30 Upper bound: 200	Lower bound: 3 Upper bound: 100			
Tittlemier et al. (2007)	1.8	1.1	Canada, 2004	Total diet study; 25 composite samples; only animal-derived food items and packaged food	<LOD = 0
Ericson et al. (2008)	Lower bound: 1.9/1.8[a] Upper bound: 2.4/2.3[a]	–	Spain, 2006	Total diet study; 36 composite samples; children 4–9 years	Lower bound: <LOD = 0 Upper bound: <LOD = LOD
Ericson et al. (2008)	Lower bound: 0.9 Upper bound: 1.1	–	Spain, 2006	Total diet study; 36 composite samples; adults	Lower bound: <LOD = 0 Upper bound: <LOD = LOD
Fromme et al. (2007c)	1.4 (0.6–4.4)	2.9 (1.1–11.6)	Germany, 2005	Duplicate diet study; 24 h food duplicates from 31 study subjects over 7 consecutive days	<LOD = 0.5 LOD

A: average food consumption.
H: high food consumption (97.5th percentile).
[a]Values for male and female.

were collected from four major retail food outlets and fast food restaurants, prepared as for consumption and combined to form composites. The composites did not represent the whole diet, but included foods with a high potential of contamination or foods with contact to food packaging. A concentration of zero was assigned if an analyte was not present at concentrations above the LOD. PFCs were detected in 9 of the analyzed composites. PFOS and PFOA were detected the most frequently, in 7 and 5 samples, respectively. The estimated daily intake of all analyzed substances for Canadians (>12 years old) was 250 ng/day. PFOS contributed 44% and PFOA 28% to the total amount of PFCs ingested. The authors calculated a daily dietary PFOS and PFOA intake of 1.8 $ng/kg_{body\ weight}$ and 1.1 $ng/kg_{body\ weight}$, respectively.

Ericson et al. (2008) measured different PFCs in 36 composite samples randomly purchased from Tarragona, Spain. They described similar results than the studies from Canada and Germany but higher intake levels for children compared to adult.

In a study conducted in Germany, PFCs were measured in 214 diet samples collected as food duplicates from 31 healthy subjects (15 female and 16 male) aged 16–45 years living in the southern parts of Germany (Fromme et al., 2007b, c). The participants collected daily duplicate diet samples over seven consecutive days in 2005. The median (90th percentile) daily intake of PFOS and PFOA was estimated as 1.4 $ng/kg_{body\ weight}$ (3.8 $ng/kg_{body\ weight}$) and 2.9 $ng/kg_{body\ weight}$ (8.4 $ng/kg_{body\ weight}$), respectively. PFHxS and PFHxA could be detected only in some samples above the limit of detection with median (maximum) daily intakes of 2.0 (4.0) $ng/kg_{body\ weight}$ and 4.3 (9.2) $ng/kg_{body\ weight}$, respectively. Because PFOSA could not be detected above the limit of detection of 0.2 ng/g this route of exposure seems to be of less significance under these study conditions for precursors of PFOS.

Migration from packaged foods and non-stick cookware

It is well known that perfluorinated substances like *N*-EtFOSA, *N*,*N*-Et_2FOSA, *N*-MeFOSA, and PFOSA were used in grease and water repellent coatings in food packing (Begley et al,. 2005; Tittlemier et al., 2006; Sinclair et al., 2007). As a consequence, food could become contaminated by this route and contribute to human body burdens of PFOS by degradation of the aforementioned precursors.

Individual perfluorooctane sulfonamides were detected at values from 0.014 ng/$g_{wet\ weight}$ (*N*-MeFOSA in Danish) to 22.6 ng/$g_{wet\ weight}$ (*N*-EtFOSA in pizza) in composite samples of all food groups collected from 1992 to 2004 Canadian TDS (Tittlemier et al., 2006). A median daily dietary intake of 73 ng per person for the sum of FOSAs was estimated. The authors concluded that the dietary exposure to perfluorooctane sulfonamides occurs predominantly via consumption of foods packaged in paper products that have likely been treated with perfluoroalkyl coatings (e.g. French fries, pizza, etc.). However, the concentration of FOSAs in certain foods has decreased in recent years likely due to the cease in production of perfluorooctylsulfonyl compounds, suggesting that dietary exposure has become less significant today.

Residual PFOA could be detected in PTFE cookware (4–75 ng/g), PTFE-coated dental floss, and in PTFE film (1800 ng/g) (Begley et al., 2005). The PFOA content of PTFE film used as sealant tape is specifically high because the film is produced at low temperatures, which reduces the likelihood of PFOA volatilization. Investigations on the migration into watery and fatty simulant foodstuff demonstrated only minor transfer of PFOA from PFTE-film and PFTE-coated cookware. This was also true for PFOA-containing microwave popcorn bags. A second group of researchers came to similar conclusions regarding PFTE-coated cookware (Powley et al., 2005). Sinclair et al. (2007) emphasized that the residual contents of PFOA and FTOH in brand new non-stick cookware was not completely removed during the fabrication process and was thus released into air, particularly during the first use of the items. However, after repeated use no FTOH was released into the gaseous phase while heating the pan. Results were not as clear regarding the release of PFOA. In some cases a distinct reduction of release was observed after the repeated use; in some cases no change was observed.

Overall, the results demonstrate that the general population is exposed to perfluorinated substances via food. In addition, localized higher dietary intakes are expected under some specific environmental conditions. For example, drinking water could be an important source of exposure in areas near environmental soil contamination or fluoropolymer or other fluorochemical production plants. At this point in time, it is unlikely that localized contamination of food or, e.g. contaminated pasture grass consumed by farm animals is also an important route for elevated PFC exposures in food-producing animals. Data on PFCs in cow's milk and feedstuff from the PFC-affected area of Sauerland, Germany do not indicate a significant contribution by this route (Wilhelm et al., 2008a). The levels of PFOS and PFOA in cow's milk ($n = 4$) were below 10 ng/l. PFOA, PFOS, and other PFC levels in corn ($n = 4$), pasture grass ($n = 4$), and maize ($n = 7$), which were grown on agriculture land with soil improver treatment were generally below 1 ng/g, only four samples had PFOA levels between 2 and 18 ng/g. However, consumption of fish and seafood could be another intake route of concern, especially for some regions (e.g. Baltic Sea or Lake Michigan) as indicated by reports of higher PFC concentrations in some samples obtained from these areas (Giesy and Kannan, 2001) and in residents that consumed locally obtained fish (Falandysz et al., 2006; Hölzer et al., 2008).

Human biomonitoring

Usually the internal exposure of PFCs is estimated based on concentrations in plasma, serum, or whole blood. Validation studies have shown that serum and plasma samples yield comparable results regarding PFOS, PFOA, and PFHxS concentrations (Ehresman et al., 2007). As yet, it was assumed that levels in whole blood are 50% below levels in serum or plasma, although the current results are not consistent. Samples with widely differing concentrations were analyzed by Ehresman et al. (2007) and a median plasma to whole blood ratio of 2.3 was observed for PFOS (ranges: 1.8–3.3 and 1.8–2.9 for whole blood collected in EDTA and heparin, respectively). For PFOA, the median ratio was 2.0; for PFHxS ratios were 2.4 or 2.1 depending on the anticoagulant used. A contrasting result was published by Kärrman et al. (2006a), who analyzed whole blood and plasma samples from 5 subjects. They found a plasma to whole blood ratio of 1.2 (PFHxS), 1.4 (PFOA), 1.2 (PFOS), 1.0 (PFNA) and 0.2 for PFOSA.

Biomonitoring of occupationally exposed populations

Results describing occupational exposure to PFCs are given in Table 5. Occupationally exposed workers have very high serum PFC concentrations as compared to non-occupationally exposed populations. Biomonitoring data regarding occupationally exposed populations are available from the two major producers, 3M and DuPont, only for the years 1995–2004. The workers included in the biomonitoring studies were involved in either the production of perfluorinated substances or in the incorporation of PFCs into their final products. The data suggest a reduction in PFC body burdens over time; however, more data are needed to allow a final conclusion about the temporal trend (US EPA, 2005). The main reasons for this observable trend are not apparent. They may include the phase out of POSF production by one producer, lower emissions from processes, better occupational safety, or a combination of the these factors.

Table 5. Perfluorinated substances in serum of occupationally exposed workers (data taken from Olsen et al., 2003a, c; US EPA, 2005; OECD, 2002; Olsen and Zobel, 2007)

Mean (range) in µg/l	Number of samples analyzed	Year	Location of production facility
PFOS			
2440 (250–12830)	90	1995	Decatur, AL, USA
1960 (100–9930)	84	1997	
1510 (90–10600)	126	1998	
1320 (60–10060)	263	2000	
1290 (60–4170)	188	2000–01	
1930 (100–9930)	93	1995	Antwerp, The Netherlands
1480 (100–4800)	65	1997	
800 (40–6240)	258	2000	
950 (40–6240)	196	2000–01	
860 (30–4790)	122	2000–01	Cottage Grove, MN, USA
PFOA			
1720	90 (M)	1995	Decatur, AL, USA
1400	84 (M)	1997	
1540 (20–6760)	126	1998	
1780 (40–12700)	263	2000	
1497 (25–4810)	54	2002	
1130 (<LOD–13200)	93	1995	Antwerp, The Netherlands
840 (10–7404)	258	2000	
2630 (920–5690)	30	2003	
5000 (<LOD–80000)	111	1993	Cottage Grove, MN USA
6800 (<LOD–114100)	80	1995	
6400 (100–81300)	74	1997	
850 (40–4730)	131(F)	2000	
4510 (7–92030)	17(M)	2000	
4300 (70–32600)	38	2002	
3210 (70–24000)	19	1984	Washington, WV, USA
2340 (60–18000)	22	1985	
1960 (60–11000)	22	1989–90	
1560 (120–4500)	80	1995	
1530 (20–9000)	72	2000	
494[a] (17–9550)	259	2004	

F: female; M: male; LOD: limit of detection.
[a]Median

Human biomonitoring of the general population

Comprehensive data on the internal exposure of the general population from different areas of the world are available and shown in Table 6.

In European studies, observed serum and plasma PFC concentrations range from 1 to 116 µg/l for PFOS and from 0.5 to 40 µg/l for PFOA, while in the US concentrations reach 656 µg/l (PFOS) and 88 µg/l (PFOA). Mean and median concentrations for some PFCs, such as PFOS, from North American populations appear to be slightly higher than European, Asian, and Australian populations studied. For example, in 40 pooled samples from Australia concentrations found were slightly higher than in Europe but lower than in the US (Kärrman et al., 2006b). According to an analysis of 473 samples from 9 countries, concentrations are highest in the US and Poland, medium in Belgium, Italy, Korea, Malaysia, Sri Lanka, and Brasil and lowest in India (Kannan et al., 2004). Large regional differences have also been observed in other investigations (Guruge et al., 2005; Harada et al., 2004; Olsen et al., 2003b). For example, in an US American study the median concentrations from 6 regions varied between 26.0 and 48.9 µg/l and the corresponding 90th percentiles between 48.7 and 105.3 µg/l (Olsen et al., 2003b).

Another commonly found substance that appeared to vary amongst populations was PFHxS. Concentrations reported were <0.4–40.0 µg/l for Europe, 0.1–20.9 µg/L for Asia and <0.4–712 µg/l for North America.

Table 6. Median (range) concentration of selected perfluorinated compounds in human plasma and serum of non-occupationally populations.

Concentration (μg/l)			n^a	Age (years)	Year	Country	Reference
PFOS	PFOA	PFHxS					
Europe							
34.2[d] (3.4–74)	5.0[d] (1.0–24.8)	3.0[d] (0.8–56.8)	66	19–75	1997–2000	Sweden	Kärrman et al. (2004) Kärrman et al. (2006a)
17.2 (4.5–27)	4.1 (1.1–12.8)	1.3 (1.1–1.4)	20	19–63	1998, 2000	Belgium	Kannan et al. (2004)
3.5 (2.5–8.0)	(<3)	1.3 (1.3–1.4)	8	20–59 F[b]	2001	Siena, Italy	Corsolini and Kannan (2004)
4.2 (1.0–10.3)	(<3)	1.7 (1.3–2.1)	42	20–59 M[c]	2001	Siena, Italy	
(16–116) [d]	(9.7–40) [d]	(<0.4–2.6) [d]	25	35–58	2003	Poland	Kannan et al. (2004)
15.2[d] (1.5–32.4)	3.4[d] (1.6–6.2)	5.8[d] (1.4–40.0)	48	20–60	2006	Tarragona, Spain	Ericson et al. (2007a)
22.3 (6.2–131)	6.8 (1.7–39.3)	–	105	5–84	2005	Northern Bavaria, Germany	Midasch et al. (2006)
13.7 (2.1–55.0)	5.7 (0.5–19.1)	–	356	14–67	2005	Southern Bavaria, Germany	Fromme et al. (2007a)
4.3 (1.6–26.2)	4.9 (2.0–11.5)	0.7 (<0.1–9.1)	80	5–6	2006	North Rhine-Westphalia,	Hölzer et al. (2008)
(1.0–92.5)	(0.7–15.3)	(<0.1–5.4)	256	18–69	2006	Germany	
Asia/Australia							
13.8[e,d] (4.0–40.4)	<6.7[d]	–	26	–	2002	Japan	Masunaga et al. (2002)
(<1–3.1)	(<3–3.5)	(<1.0–2.9)	45	17–48	1998, 2000	India	Kannan et al. (2004)
3.5–28.1[f]	2.5–12.4[f]	–	205	–	2003	Japan, various locations	Harada et al. (2004)
3.3 (0.4–18.2	4.0 (0.3–22.8)	0.4 (0.1–2.1)	38	24–61	2003	Sri Lanka	Guruge et al. (2005)
16.7[g] (10.4–31.9)	1.6[g] (<0.5–4.1)	–	21	21–56	2003	Japan	Inoue et al. (2004b)
(4.9–17.6)	(<0.5–2.3)	–	15	17–37 F	2003	Japan	Inoue et al. (2004a)
(3.0–92)[d]	(<15–256)[d]	(0.9–20.0)[d]	50	–	2003	Daegu, Korea	Yang et al. (2004)
27[g] (19–41)	–	(<2.7)	3	23–44	2002	Japan	Taniyasu et al. (2003)
22.4 (0.2–145)	4.3 (0.2–60)	–	119	29[h]	2002	China	Jin et al. (2007)
52.7[d]	1.59 [d]	1.88 [d]	85	7–66	2004	China	Yeung et al. (2006)
(3.4–92.2)	(0.4–25.5)	–	97	20–58	2003–2004	Japan, various locations	Harada et al. (2007a)
20.8 (12.7–29.5)	7.6 (5.0–9.9)	6.2 (2.7–19.0)	40[i]	–	2002–2003	Australia	Kärrman et al. (2006b)

North America							
28.4[g] (6.7–81.5)	6.4[g] (<5–35.2)	6.6[g] (<2.0–21.4)	65	–	–	USA, tissue banks	Hansen et al. (2001)
36.9[g] (2.8–57.9)	2.2[g] (0.5–5.5)	–	23[j]	–F	1994–2001	Northwest Territories, Canada	Tittlemier et al. (2004)
28.8[g] (3.7–65.1)	3.0[g] (<1.2–7.2)	–	56	<20	2002	Ottawa, Canada	Kubwabo et al. (2004)
35.8 (<4.3–1656)	4.7 (<1.9–52.3)	1.5 (<1.4–66.3)	645	20–69	2000–2001	USA, blood donors, 6 cities	Olsen et al. (2003b)
30.2 (<3.4–175)	4.2 (<1.4–16.7)	2.3 (<1.4–40.3)	238	65–96	2000	Seattle, USA	Olsen et al. (2004a)
(<1.3–164) [d]	(<3–88) [d]	(<0.4–32) [d]	175	17–72	2000–2002	4 cities in USA	Kannan et al. (2004)
36.7 (6.7–515)	5.1 (1.9–56.1)	3.8 (<1.4–712)	598	2–12	1994–1995	23 cities in USA	Olsen et al. (2004b)
29.5	2.3	1.6	178	30–60	1974	Maryland, USA	Olsen et al. (2005)
34.7	5.6	2.4	178	39–65	1989	Maryland, USA	Olsen et al. (2005)
55.8[g] (3.6–164)	4.9[g] (0.2–10.4)	3.9[g] (0.4–11.2)	20	23–67	2003	Atlanta, USA	Kuklenyik et al. (2004)
30.2	5.1	2.1	1562	12–>60	1999–2000	USA, NHANES study	Calafat et al. (2007)
31.1	11.6	2.0	23[j]	–	1990–2002	USA	Calafat et al. (2006a)
24.0[g]	4.0[g]	4.3[g]	54[j]	12–>60 F	2001–2002	USA, NHANES study	Calafat et al. (2006b)
40.2[g]	7.0[g]			12–>60 M			
15.8 (6.6–36.9)	2.4 (<1.0–4.7)	–	40	–	2005	St. Paul, USA	Olsen et al. (2007a)

[a]Number of samples analyzed.
[b]Female.
[c]Male.
[d]Computed from whole blood (i.e. multiplied whole blood concentration by a factor of 2).
[e]Geometric mean.
[f]Range of the geometric means of different regions.
[g]Arithmetic mean.
[h]Mean age.
[i]40 pooled samples made from 3802 individual samples.
[j]Pooled samples.

At present, there are no known explanations for the single exceptionally high concentrations observed.

In some recent studies, mean PFNA concentrations of 0.3–1.1 µg/l have been observed (Kärrman et al., 2006b; Calafat et al., 2006a; Ericson et al., 2007a). Calafat et al. (2007) found median PFNA concentrations (95th percentile) of 0.6 µg/l (1.7 µg/l) in 1562 serum samples collected from a representative US population 12 years of age and older in the 1999–2000 NHANES. Higher mean concentrations of 2.2 µg/l (males) and 2.9 µg/l (females) were found in a small study of 20 US citizens (Kuklenyik et al., 2004). Other PFCs, such as PFDeA or PFUA, were found at only very low concentrations, if at all.

Based on the three studies from Germany (Midasch et al., 2006; Fromme et al., 2007a; Hölzer et al., 2008), the following preliminary reference values of the general population (basis: 95th percentile values of the studies) for PFOA and PFOS in plasma of children and adults from Germany were recommended: PFOA – 10 µg/l for children, females, and males; PFOS – 10 µg/l for children, 20 µg/l for adult females, and 25 µg/l for adult males (Wilhelm et al., 2007). Reference values were normally established by the Biomonitoring Commission of the German Federal Environmental Agency (Ewers et al., 1999).

Sex-related differences in blood levels

In the majority of the studies, differences in blood levels of PFOS between sexes have been observed with higher levels in male donors (e.g. Corsolini and Kannan, 2004; Harada et al., 2004; Midasch et al., 2006; Kärrman et al., 2006b; Fromme et al., 2007a; Calafat et al., 2007; Hölzer et al., 2008). However, this observation could not be confirmed in other investigations (Olsen et al., 2003b, d, 2004a; Kannan et al., 2004; Kubwabo et al., 2004; Kärrman et al., 2004). Sex-related differences with respect to PFOA were reported in several investigations as well (Midasch et al., 2006; Kärrman et al., 2006b; Fromme et al., 2007a; Calafat et al., 2007; Hölzer et al., 2008). Similar differences have been reported in rats exposed to PFOA. Estimated half-lives were longer in males than females in a variety of rat strains (Kudo and Kawashima, 2003, and references therein). Renal clearance of PFOA is also higher in female mice. However, other studies suggest these sex-related differences are not consistent across other species, such as dogs, rabbits, and mice (Kudo and Kawashima, 2003).

Analysis of structural isomers in serum and plasma

Synthesis of PFCs mainly employs electrochemical fluorization (ECF) and fluorotelomerization. During ECF, the major technique of PFOS production, linear as well as branched isomers are generated, while during telomerization exclusively linear isomers are generated (Langlois and Oehme, 2006; Vyas et al., 2007).

The presence of PFOS and PFOA branched isomers was first noted in 2001 (Hansen et al., 2001). However, almost no data are available yet on the toxicokinetic behavior of the various isomers. In 70 serum and plasma samples collected in 1997–2003, the linear isomer of PFOS was found to be the most abundant. In Australian samples, the linear isomer comprised 58–70% of the total PFOS measured; it was 68% and 59% in samples collected in Sweden and Great Britain, respectively. These differences may be due to differences in isomer patterns in the source products from the various countries, or from differences in the major routes of human exposure amongst the countries (Kärrman et al., 2007b). Interestingly, the proportion of the linear isomer in a standard product after ECF (76–79%) is higher than its proportion in the blood of the general population. This could indicate differential uptake of the branched and linear PFOS isomers.

In another study the pattern of PFOA isomers in 16 pooled serum samples was investigated (De Silva and Mabury, 2006). Almost 98% of PFOA in serum presented itself in the linear form (L-PFOA) and only 2% as branched isomers. This was also true for PFNA and PFUnA. In contrast, a PFOA standard product synthesized by ECF contained only 80% as L-PFOA. The authors hypothesize that the high proportion of L-PFOA in serum is partly due to exposure to and metabolization of fluorotelomer alcohols and fluorotelomer olefins, two classes of PFCs synthesized by the telomerization process.

Exposure of the fetus

It is known from animal studies that PFCs are able to cross the placenta and enter the fetus. After providing ammonium perfluorooctanoate to pregnant rats, the PFOA concentration in fetal blood increased accordingly. The concentration in fetal blood reached about 42% of the mothers blood level (Hinderliter et al., 2005).

Results from studies that examined PFCs in maternal and cord blood are presented in Table 7. Concentrations of PFOS in maternal plasma from Inuit and Inuvialuit populations in the Arctic region of Canada were higher than those reported in study populations from Japan and Germany, but consistent with PFOS concentrations previously reported for North Americans (Tittlemier et al., 2004). In addition, PFOS in umbilical cord plasma was higher than the median PFOS concentration observed in cord serum from donors in Baltimore; however, individual concentrations in the American samples were as high as 35 µg/l (Apelberg et al., 2007).

Table 7. Median (range) concentration (μg/l) of perfluorinated substances in cord and maternal blood, serum, or plasma

PFOS		Mean ratio C/M	PFOA		Mean ratio C/M	Study population location	Number of samples analyzed	Age of donors (years)	Sampling years
Maternal	Cord		Maternal	Cord					
Tittlemier et al. (2004)									
36.9 [a]	16.7 [a]		2.2 [a]	3.4 [a]		Northwest Territories, Canada	10 maternal plasma; 13 cord plasma		1994–2001
Inoue et al. (2004a)									
8.1 (4.9–17.6)	2.5 (1.6–5.3)	0.3	– (<0.5–2.3)	– (<0.5)	–	Japan	15 blood	17–37	2003
Midasch et al. (2007)									
13.0 (7.8–16.4)	7.3 (3.3–9.5)	0.6	2.6 (1.5–4.0)	3.4 (1.5–4.6)	1.3	Bavaria, Germany	11 plasma	23–26	2003
Apelberg et al. (2007)									
	4.9 (<LOD–34.8)			1.6 (0.3–7.1)		USA	299 serum		2004–2005
Fei et al. (2007)									
35.3 [b] (6.4–107)	11.0 [b]	0.3	5.6 [b] (<1.0–41.5)	3.7 [b]	0.5	Denmark, first trimester	1399 plasma, 50 cord blood	30 (mean)	1996–2002
29.9 [b]		0.3	4.5 [b]		0.7	Second trimester	200 plasma		

[a]Mean of pooled samples; LOD: limit of detection.
[b]Mean values.

In the American study, no association between cord serum PFOA levels and the age or the education of the mother, or the sex of the child, could be identified.

In a Japanese study low concentrations of PFOS in cord blood and maternal blood were observed; the ratio between the two compartments was 0.3 (Inoue et al., 2004a). No association between the blood levels and body mass index, age, or sex of the child was found.

The analysis of cord plasma in a German population resulted in median concentrations of 13.0 μg/l for PFOS and 7.3 μg/l for PFOA (Midasch et al., 2007). The PFOS concentrations in cord plasma amounted on average to about 60% of the level in maternal plasma; however, PFOA concentrations were higher in cord than maternal plasma. This was also observed in the Canadian samples (Tittlemier et al., 2004). Midasch et al. (2007) discussed the higher cord plasma PFOA concentrations may be due to higher albumin content of cord than maternal blood, since PFOA has a high binding affinity to this protein (Han et al., 2003).

In a nationwide study, the Danish National Birth cohort, 1400 randomly selected women provided blood samples between gestational weeks 4 and 14 (Fei et al., 2007). From a subset of 200 of these mothers another sample was subsequently collected during the second trimester, as well as 50 cord blood samples. The PFOS and PFOA levels decreased with increasing parity and decreasing Body Mass Index. PFOA was highest in age group <25 years and lowest in age group ⩾35 years, but after adjustment for parity the differences were low. Concentrations in cord blood and mother's blood were highly correlated, with lower cord blood levels. Moreover, first and second maternal blood samples were correlated, with lower mean concentrations in the second sampling period.

Exposure of children

Only few scientific data on the internal exposure of children to PFC are available. In the context of an epidemiology study on infectious disease, serum samples of 598 children aged 2–12 years were collected in 1994 and 1995 in the USA (Olsen et al., 2004b). These samples were later analyzed for PFCs, and a median PFOS concentration of 36.7 μg/l (range: 6.7–515 μg/l) and a median PFOA concentration of 5.1 μg/l (range: <1.9–56.1 μg/l) were observed. For PFOA a decrease of the blood levels with age was found. The median as well as the 95% percentile were comparable to that of adults. Only the 95th percentile of PFHxS was higher in children (64 μg/l) in comparison to adults (8–9 μg/L).

For Europe, results are available only from one study of 80 children aged 5–6 years (Hölzer et al., 2008). In the control group of this study in which no known specific exposure occurred, PFOS concentrations of

1.6–26.2 μg/l (median: 4.3 μg/l) and PFOA concentrations of 2.0–11.5 μg/l (median: 4.9 μg/l) were observed. Again, in this study the internal exposure of the children were not increased in comparison to that of adults of the same region.

The first results on PFC levels in newborns were generated from the analysis of 61 blood samples of Hungarian newborns (Fromme et al., 2007d). The samples had been collected in 1996/97 during a nutrition study. The healthy newborns were 3–7 weeks old, weighed 1422–2339 g, and were exclusively breast-fed or bottle-fed when the blood was taken. Concentrations in newborns were 2.5–18.3 μg/l (median 7.3 μg/l) for PFOS and 0.8–16.9 μg/l (median: 3.6 μg/l) for PFOA. Breast-fed infants showed significantly higher PFOS, but not PFOA, concentrations in comparison to infants initially fed with formula.

Age-related exposure

Since PFCs such as PFOS and PFOA are very persistent contaminants that do not undergo metabolism, it might be expected that PFC body burdens would increase with age, as has been observed with other persistent organic compounds (Duarte-Davidson and Jones, 1994). However, most studies that have examined the association of age with PFC concentrations in blood (including plasma and serum) have not observed significant effects. Even in the large NHANES study, in which 54 pooled serum samples of the 2001/2002 survey and 1562 serum samples of the 1999–2000 survey were analyzed, there was no indication for an association of PFC concentrations with age (Calafat et al., 2006a; Calafat et al., 2007). In a small Spanish study, lower concentrations in subjects aged 55 years (±5 years) in comparison to those aged 25 years (±5 years) were found for only one of the PFC analytes monitored-PFHxS (Ericson et al., 2007a).

In contrast, the two studies from Germany did find an age-related increase in PFC (Fromme et al., 2007a; Hölzer et al., 2008). In the first investigation this association was found among women only (Fromme et al., 2007a). In the second study, the age of men was positively associated with the levels of PFOS, PFOA, and PFHxS in plasma, and the age of women with PFOA only (Hölzer et al., 2008). An age-related increase was identified in a large US American study with significant lower median PFOS and PFHxS concentrations in individuals younger than 40 years of age (Olsen et al., 2005). In Australia a significant increase of PFOS concentrations with age was found among female subjects (Kärrman et al., 2006b). In this investigation, concentrations of PFOA, PFHxS, and PFOSA were higher among adolescents (<16 years old) and among the elderly (>60 years old), while concentrations among subjects of medium age (16–60 years old) were lower.

Time trends of exposure

Currently, the time trend of the internal exposure in the general population has been investigated in some studies (Harada et al., 2004; Olsen et al., 2005, 2007a; Jin et al., 2007; Harada et al., 2007a; Wilhelm et al., 2008b).

The analysis of serum samples collected in Japan in 1983, 1987, 1991, 1995, and 1999 showed a significant increase in PFOA levels, while for PFOS no such increase could be observed (Harada et al., 2007a). In another Japanese study, serum samples collected in 1977, 1991, 1995, and 2003 from Akita and Miyagi regions were analyzed (Harada et al., 2004). In the samples from Miyagi, PFOS and PFOA concentrations increased 3- and 14-fold, respectively, from the years 1977 to 2003. In contrast, only a slight increase was observed for PFOA in samples from Akita for the time period 1991–2003.

Results of a Chinese study that analyzed serum samples from 1987, 1990, 1999, and 2002 also showed a considerable increase in PFOS and PFOA concentrations during this time period (Jin et al., 2007). While concentrations in the year 1987 hardly exceeded the limit of determination (0.01–0.03 μg/l), in 2002 they amounted to 22.4 μg/l (PFOS) and 4.9 μg/l (PFOA), respectively.

An increase in serum levels of PFOS and PFOA from 1974 and 1989 could be observed as well in two American studies (Olsen et al., 2003b; Olsen et al., 2005). As the authors emphasize, these results have to be interpreted with caution, since different analytical methods were employed and different matrices (serum collected in 1974 vs. plasma collected in 1989) were analyzed. Furthermore, preliminary results on 40 serum samples from 2005 and 100 serum samples from 2000 obtained from the same region indicated a reduction of PFOS and PFOA concentration by 40% to 50% (Olsen et al., 2007a).

From the PFC-affected area in the Sauerland, Germany 30 samples of young adults (20–31 years old) from the German Environmental Specimen Bank were analyzed for PFCs (Wilhelm et al., 2008b). The sampling time period covered 1977–2004. PFOA values ranged between 1.7 and 40.7 μg/l (median 6.1 μg/l), PFOS levels were 8.1–150.5 μg/l (median: 18.8 μg/l). Time trend analysis of PFOS and PFOA indicated a slight, but not significant, increase in concentrations from 1977 to about 1990, which was then followed by a decreasing tendency of the values. In contrast, there was a clear linear increase of PFHxS plasma concentrations (median, range: 1.7 μg/l, 0.49–4.6 μg/l) up to 2004.

Studies in other human tissues and body fluids

Human liver that was not suitable for transplantation and blood samples from 31 donors aged 5 to 74 years

were analyzed for various PFCs (Olsen et al., 2003d). PFOS concentrations in the liver ranged between <4.5 and 57 ng/g (mean: 18.8 ng/g) and in the serum between <6.1 and 58.3 μg/L (mean: 17.7 μg/l). If only values above the limit of determination were considered, the mean ratio of liver to blood concentration was 1.4. With respect to PFOA and PFHxS more than 90% of the samples did not contain residues above the limit of determination of the employed analytical method (17.9–35.9 ng/g and 3.4–18.5 ng/g, respectively).

Maestri et al. (2006) analyzed pooled tissue samples of seven deceased subjects aged 12–83 years at time of death. They employed an analytical method with a much higher sensitivity and observed PFOA concentrations of 3.1 ng/g in the liver and 3.0 ng/g in blood. The corresponding concentrations for PFOS were 13.6 ng/g (liver) and 5.1 ng/g (blood). The highest PFOA concentration was detected in lung tissue (3.8 ng/g), which also showed the second highest PFOS level (7.9 ng/g). The lowest concentrations were observed in nerve tissue (0.5 ng PFOA/g and 1.3 ng PFOS/g).

Within a pilot study in Germany, 10 liver samples of deceased subjects were analyzed and a mean PFOS concentration of 17.9 ng/g (range: 1.6–45.4 ng/g) and a mean PFOA concentration of 1.8 ng/g (range: 0.5–3.5 ng/g) were observed (Völkel et al., 2007). PFOS was detected in all samples above the limit of detection; whilst PFOA was detected in all but one sample. All the aforementioned studies obtained fairly similar concentrations of PFCs in liver. Concentrations of PFOA appear to be 10 times lower than concentrations of PFOS.

Very few data are currently available on the distribution of PFCs in other human tissues aside from liver and blood. PFCs were measured in bile and cerebrospinal fluid (CSF) (Harada et al., 2007b). The median concentration in bile was 27.9 μg PFOS/L and 1.0 μg PFOA/l with a serum to bile ratio of 0.60 (PFOS) and 0.21 (PFOA) ($n = 4$). In contrast, concentrations in a small number of CSF samples ($n = 7$) were very low, ranging from <0.04 to 0.07 μg PFOA/l and 0.07 to 0.20 μg PFOS/l. Concentrations in CSF reached on average only 1.8% (PFOA) and 0.9% (PFOS) of concentrations in serum. These data indicate only minor transfer of PFCs via the blood-brain-barrier, which is confirmed by the low concentrations in nerve tissue observed by Maestri et al. (2006).

Specific situations associated with increased exposure of the general population

In the scientific literature two incidents have been reported in which a contamination of drinking water with PFOA caused an increased internal exposure of the population; one occurring in the USA and the other in Germany (Emmett et al., 2006a, b; Hölzer et al., 2008; Wilhelm et al., 2008a). In the USA, a high contamination has been reported in the catchment area of a water supply in the vicinity of a fluoropolymer production facility in Ohio (Emmett et al., 2006a, b). The PFOA serum concentrations in the non-occupationally exposed general population in this area was high ($n = 371$, median = 354 μg/l), while the concentrations among subjects employed in the PFOA processing plant were higher ($n = 18$, median = 775 μg/l). The blood levels differed depending on the donors' use of water; the highest level was observed in subjects exclusively using water from the central water supply ($n = 291$, median = 374 μg/l). Slightly lower levels were reported for subjects who in addition used bottled water or spring water ($n = 26$, median = 320 μg/l), and levels were considerably lower if subjects used exclusively bottled water, cistern, or spring water ($n = 10$, median = 71 μg/l). No association of the blood PFOA concentrations with alcohol consumption, smoking, or consumption of meat or fish was found. However, an increasing number of meals prepared with locally grown vegetables or fruits was significantly associated with increasing blood PFOA concentrations. The authors conclude that drinking water is the major route of exposure for this population, while exposure through air can be neglected.

In Germany, in a region in North Rhine-Westphalia, PFC-contaminated inorganic and organic waste material was applied on a large agricultural area. Subsequently, increased PFOA concentrations were found in surface water as well as in drinking water (Wilhelm et al., 2008a). In a cross-sectional study, the internal exposure in 170 children and 521 adults living in the affected area and a control area was determined (Hölzer et al., 2008). The ratio of the geometric means of PFOA concentrations in the populations residing in the affected and control areas were 4.6 for children, 4.4 for male adults, and 8.3 for female adults. In addition, PFHxS concentrations in plasma (geometric means) were 53% (children), 14% (male adults), and 80% (female adults) higher in the affected region as compared to the control region. It was shown that the estimated consumption of drinking water was significantly associated with the plasma PFOA concentrations.

Breast milk

The mechanism by which perfluorinated substances are transferred from mother's blood to breast milk is not clear. But it is well known that PFCs are strongly bound to the protein fraction in blood (Han et al., 2003). The possibility of PFCs entering the milk and accumulating to levels observed in maternal plasma is therefore limited.

Up to now, PFOS and PFOA levels during lactation have been studied in two animal studies (Kuklenyik et al., 2004; Hinderliter et al., 2005). Testing an analytical method, Kuklenyik et al. (2004) measured PFCs in archived milk and serum samples of Sprague-Dawley rats collected at lactation day 14. In this experiment PFOS was administered by gavage (dose not available). In the two treated animals serum (and milk) concentrations were 196,000 μg/l (100,000 μg/l) and 116,000 μg/l (13,700 μg/l), respectively. PFOS was not detected (<0.5 μg/l) in any of the milk samples from the 8 control animals, whereas the mean concentration in the corresponding serum samples was 80 μg/l.

In another study, Hinderliter et al. (2005) dosed 20 time-mated rats by oral gavage once daily at concentrations of 3, 10, 30 mg ammonium PFOA salt/$kg_{body\ weight}$ starting on gestation day 4 until sacrifice. They found that the mean PFOA concentrations in milk were 1070, 2820, and 6160 μg/l at the three dose levels, respectively. The steady state concentrations in milk were approximately 10 times less than those in maternal plasma. Furthermore, the milk levels appeared to be generally comparable to the concentrations in pup plasma.

Concentrations of PFCs in human milk have been examined in a handful of studies, and the results are summarized in Table 8. In the first study, aimed to develop a reliable analytical method, two human milk samples were analyzed (Kuklenyik et al., 2004). PFOS and PFOA were not found (limit of detection: <0.30 and <0.2 μg/l). Only perfluoropentanoic acid (1.56 μg/l) in one of the samples and perfluorohexanoic acid (0.82 μg/l) in the second could be quantified.

Kärrman et al. (2007a) collected milk samples from 12 primiparous women during the third week after delivery in Sweden in 2004. While PFOS could be detected in all 12 milk samples with values ranging between 0.06 and 0.47 μg/l, PFOA could be quantified in one sample only, due to relatively high blank levels. PFHxS ranged from 0.03 to 0.17 μg/l and PFOSA was detected in 8 of 12 samples from LOD to 0.03 μg/l. PFNA was detected less frequently, in only 2 samples. PFUnDA was not detected at all. The PFOS milk level was on average 1% of the corresponding serum level, with a strong positive association between serum and milk levels (PFOS, $R^2 = 0.7$; PFHxS, $R^2 = 0.8$).

In another study, So et al. (2006) reported results of a Chinese study that included 19 primiparous volunteers recruited in 2004. The concentrations of PFOS and PFOA ranged from 0.05 to 0.36 μg/l and from 0.05 to 0.21 μg/l, respectively. The other PFCs were found in minor amounts only. For example, the maximum concentrations of longer chain PFCAs were all less than 0.1 ng/l – PFNA (0.06 μg/l), PFDA (0.02 μg/l), and PFUnDA (0.06 μg/l).

Nakata et al. (2007) analyzed the milk of 51 healthy Japanese mothers and observed PFOS and PFOA

Table 8. Median (range) concentration of perfluorinated substances in breast milk (values in squared brackets represents percentage of values >limit of detection)

PFOS (μg/l)	PFOA (μg/l)	PFHxS (μg/l)	Number of samples analyzed	Year of sampling	Donor location
So et al. (2006)					
0.10 (0.05–0.36) [100%]	0.11 (0.05–0.21) [100%]	0.01 (0.004–0.10) [100%]	19	2004	China
Kärrman et al. (2007a)					
0.17 (0.06–0.47) [100%]	[a]	0.07 (0.03–0.17) [100%]	12	2004	Sweden
Völkel et al. (2008)					
0.12 (0.03–0.31) [100%]	(<0.20–0.29) [11%]	–	57	2006	Bavaria, Germany
Bernsmann and Fürst (2008)					
0.08 (0.05–0.28) [66%]	0.14 (0.08–0.61) [54%]	[b]	183	2007	North Rhine-Westphalia, Germany
Nakata et al. (2007)					
0.01–0.40 [100%]	<LOD–0.34 [44%]	<LOD–0.03 [64%]	51		Japan

[a] Only one sample >0.01 (limit of detection), all other 11 samples with high background values.
[b] Only 2 positive samples (0.16 and 0.18 μg/l), all others <LOD.

concentrations of 0.01–0.40 μg/l and <LOD–0.34 μg/l, respectively. PFNA could be observed from <LOD to 0.15 μg/l and PFHxS from <LOD to 0.03 μg/l.

Völkel et al. (2008) reported results from breast milk samples collected in Germany (57 samples) and 13 archived samples from Hungary. The PFOS concentration in samples from Germany ranged from 0.03 μg/l to 0.31 μg/l, while the samples from Hungary showed significantly higher PFOS concentrations (median 0.33 μg/l, range 0.10–0.64 μg/l). In only 11 of 70 samples PFOA reached the limit of quantification of 0.2 μg/l; values ranged from 0.20 to 0.46 μg/l.

In a further investigation from Germany, Bernsmann and Fürst (2008) measured PFCs in 183 samples from North Rhine-Westphalia. The most frequently detected compounds were PFOS and PFOA, which could be detected in 99 and 120 samples, respectively. The concentrations of samples above limit of detection ranged from <0.01 to 0.28 μg/l (PFOS) and 0.03 to 0.39 μg/l (PFOA). PFHxS was detected only in 2 samples at concentrations of 0.16 and 0.18 μg/l.

Overall exposure assessment for adults

The widespread exposure of children and adults all over the world to PFCs suggests that the observed human body burdens are due to a ubiquitous source. With regard to the chemical and physical properties of PFCs, there are different possible routes for the assimilation of PFCs into the body. One set of routes is direct exposure to these substances via inhalation of air, ingestion of house dust, drinking water and food. With regard to the latter, we have to keep in mind that PFCs could be transferred to food during storage (from food packaging), preparation and bioaccumulation of PFCs via the food chain. Furthermore, a probable route of PFC exposure includes the intake of various precursors, which have been detected mainly in the gas phase of indoor and outdoor air and in some food products, potentially after migration from food packagaing. In addition, some precursors are metabolized in the body to their final persistent products, such as PFOS.

Exposure to PFOS and PFOA

Considering the potential routes of human exposure to PFOS and PFOA mentioned above, we estimated the overall mean and high daily intake for a non-occupationally exposed adult population (summarized in Table 9). Mean intake calculations were based on mean or median concentrations; high intake calculations were based on upper percentile or maximum concentrations. It was assumed that absorption from the gastrointestinal tract ands lungs was 100%.

Exposure via inhalation was estimated using the average of the mean daily inhalation values of females and males (13.3 m^3/day) (US EPA, 1997). For further calculation it was assumed that people generally spend 90% of the day in indoor environments. On this basis, outdoor exposure was estimated using median and maximum values from the winter and spring measurements of PFOS and PFOA in ambient air of 6 European measurement sites (Barber et al. 2007). Indoor air exposure was derived from Barber et al. (2007) using half of the limit of detection (PFOS) and mean value (PFOA) of 4 measurements carried out in Tromsø, Norway.

Exposure via non-dietary ingestion was estimated using median and maximum values measured in house dust of 67 Canadian homes (Kubwabo et al., 2005) combined with an average adult intake rate of 50 mg dust/day (US EPA, 1997), mean values and maximum values detected 2006 in drinking water samples from 14 German cities, Paris and Hampshire (UK) (Skutlarek et al., 2006) combined with adult median drinking water intake rate of 1.3 l/day (US EPA, 1997).

The dietary intake was estimated based on median and 95th percentile intake rates from a duplicate diet study in Germany (Fromme et al., 2007c), which is in accordance with data published previously from a total diet study in Canada (Tittlemier et al., 2007).

Based on these assumptions we can estimate a mean (and high) comprehensive daily intake of 1.6 $ng/kg_{body\ weight}$ (8.8 $ng/kg_{body\ weight}$) for PFOS and 2.9 $ng/kg_{body\ weight}$ (12.6 $ng/kg_{body\ weight}$) for PFOA, respectively.

As seen from Table 9 we can cautiously conclude that dietary exposure is the dominant intake pathway, responsible for 91% (PFOS) and 99% (PFOA) of the total intake of the general population using mean intake data. These results are in accordance with previously published findings. A simple one compartment toxicokinetic model showed that the dietary intake corresponds well with the plasma level of the same population (Fromme et al., 2007c).

Exposure to FOSE/FOSA and FTOH

Considering the potential routes of human exposure mentioned above, we estimated the overall mean and high daily intake for a non-occupationally exposed adult population (summarized in Table 10) to potential precursors of PFCAs and PFAS.

Outdoor exposure was estimated using median and maximum values of the sum of FTOHs and FOSAs/FOSEs analyzed from 7 air samples in Hamburg, Germany (Jahnke et al., 2007b). Indoor air exposure was derived from Barber et al. (2007) using median and maximum values of the sum of FTOHs from 4 indoor samples from Tromsø, Norway (Barber et al., 2007).

Table 9. Estimated adult daily intake of PFOS and PFOA for the general population. Mean intake based on mean or median concentrations; high intake based on upper percentile or maximum concentrations

	Concentration		Intake rate [a]	Intake (ng/day)		Daily intake pg/kg b.w. [b]	
	Mean	High		Mean	High	Mean	High
PFOA							
Indoor air	4.4 pg/m^3 [c]		12 m^3/day	0.053	0.053	0.9	0.9
Outdoor air	58.4 pg/m^3 [d]	552 pg/m^3 [d]	1.3 m^3/day	0.076	0.718	1.3	12.0
House dust	19.72 ng/g [e]	1234 ng/g [e]	50 mg/day	0.986	61.7	16.4	1028.3
Diet				169 [h]	689 [h]	2816.7	11483.3
Drinking water	1.0 ng/l [f]	4.0 ng/l [f]	1.3 l/day	1.3	5.2	21.7	86.7
Overall intake						2857.0	12611.2
PFOS							
Indoor air	23.7 pg/m^3 [g]		12 m^3/day	0.284	0.284	4.7	4.7
Outdoor air	4.5 pg/m^3 [d]	46 pg/m^3 [d]	1.3 m^3/day	0.006	0.060	0.1	1.0
House dust	37.8 ng/g [e]	5065 ng/g [e]	50 mg/day	1.9	253	31.7	4216.7
Diet				90 [h]	269 [h]	1500.0	4483.3
Drinking water	1.0 [f]	6.0 [f]	1.3 l/day	1.4	7.8	23.3	130.0
Overall intake						1559.8	8835.7

[a] US EPA (1997).
[b] Adult 60 kg.
[c] Mean of four indoor samples from one location (Barber et al., 2007).
[d] Median and maximum of means from 6 measurement sites (Barber et al., 2007).
[e] Median and maximum values (Kubwabo et al., 2005).
[f] Mean and maximum values (Skutlarek et al., 2006a).
[g] 0.5 of the detection limit (Barber et al., 2007).
[h] Median and 95th percentile (Fromme et al., 2007c).

Indoor air exposure to FOSAs/FOSEs was calculated using geometric mean concentration from 59 randomly selected homes of Ottawa, Canada (Shoeib et al., 2005a). For calculation of the high intake the 90th percentile of the estimated human exposure by inhalation was used from the same paper.

Mean exposure via non-dietary ingestion was estimated using geometric means of the sum of FTOHs and FOSAs/FOSEs measured in house dust of 66 Canadian homes (Shoeib et al., 2005a, b). The 95th percentile of dust exposure of adults was used to determine high intake levels (Shoeib et al., 2005b).

The dietary intake of FOSAs/FOSEs were calculated using median and 90th percentile intake rates for adults aged 40–64 years observed in a Canadian TDS (Tittlemier et al., 2006).

The overall mean (and high) daily intake level was of 0.14 ng/kg$_{\text{body weight}}$ (1.1 ng/kg$_{\text{body weight}}$) for FTOHs and 1.6 ng/kg$_{\text{body weight}}$ (11.0 ng/kg$_{\text{body weight}}$) for FOSAs/FOSEs, respectively.

Contribution of FTOHs and FOSAs/FOSEs to PFOA and PFOS exposure

There is growing evidence that numerous polyfluorinated substances undergo metabolic processes and can be converted in living organisms to PFOS and PFOA. As a result, their contribution to PFOS and PFOA exposure can be estimated by quantifying the amount of these precursor substances entering an organism. Nevertheless, we have to keep in mind that toxicokinetic data of these substances are limited and are missing for the inhalation pathway, which may be important for more volatile PFCs.

Dosing 8:2 FTOH by gavage to rats Fasano et al. (2006) estimated the total systemic absorption to be 49% and 57% at lower and 27% and 27% at higher doses for males and females, respectively. As seen before from the environmental degradation studies, the in vitro experiments with rat hepatocytes suggest that PFOA was not the main product of metabolism, since only 1.4% of 8:2 FTOH was converted to PFOA. Furthermore, Nabb et al. (2007) concluded that human hepatocytes produced 22-fold less PFOA compared to hepatocytes of mice and 9.5-fold less PFOA compared to hepatocytes of rats.

Early toxicological study demonstrated similar qualitative effects of *N*-EtFOSE and PFOS, leading to the hypothesis that the toxicity of the *N*-EtFOSE is primarily due to the conversion to its final metabolite PFOS (Butenhoff and Seacat, 2001). Manning et al. (1991) administered a single bolus of 50 mg radiolabeled *N*-EtFOSE to rats by gavage. The substance was slowly

Table 10. Estimated adult daily intake of FOSEs/FOSAs and FTOHs for the general population. Mean intake based on mean or median concentrations; high intake based on upper percentile or maximum concentrations

	Concentration		Intake rate [a]	Intake (ng/day)		Daily intake pg/kg b.w. [b]	
	Mean	High		Mean	High	Mean	High
$\sum FTOH$							
Indoor air	190 pg/m^3 [c]	527 pg/m^3 [c]	12 m^3/day	2.28	6.32	38.0	105.0
Outdoor air	139 pg/m^3 [d]	149 pg/m^3 [d]	1.3 m^3/day	0.18	0.19	3.0	3.2
House dust	123 ng/g [e]		50 mg/day	6.15	61 [h]	102.5	1016.7
Total intake						143.5	1124.9
$\sum FOSE/FOSA$							
Indoor air	2303 pg/m^3 [f]		12 m^3/day	27.6	123 [i]	460.0	2050.0
Outdoor air	49.6 pg/m^3 [g]	531 pg/m^3 [g]	1.3 m^3/day	0.064	0.69	1.1	11.5
House dust	259 ng/g [f]		50 mg/day	13.0	122 [h]	983.3	2033.3
Diet				59 [j]	280 [j]	216.7	6866.7
Total intake						1661.1	10961.7

[a] US EPA (1997).
[b] Adult 60 kg.
[c] Median and maximum of sum of 4:2FTOH, 6:2FTOH, 8:2FTOH, and 10:2FTOH (Barber et al., 2007).
[d] Median and maximum of sum of 4:2FTOH, 6:2FTOH, 8:2FTOH, and 10:2FTOH (Jahnke et al., 2007a).
[e] Geometric mean of sum of 6:2FTOH, 8:2FTOH, and 10:2FTOH (Shoeib et al., 2005b).
[f] Geometric mean of sum of *N*-EtFOSE, *N*-MeFOSE, *N*-EtFOSA, and *N*-MeFOSA (Shoeib et al., 2005a).
[g] Median and maximum of sum of *N*-EtFOSE, *N*-MeFOSE, *N*-EtFOSA, and *N*-MeFOSA (Jahnke et al., 2007a).
[h] Intake (95th percentile) derived from Shoeib et al. (2005b).
[i] Intake (90th percentile) derived from Shoeib et al. (2005a).
[j] Median and 90th percentile of sum of *N*-EtFOSA, *N*-MeFOSA, *N*,*N*-Et_2FOSA, *N*,*N*-Me_2FOSA, and PFOSA (Tittlemier et al., 2006).

absorbed from the gastro-intestinal tract and approximately 80% of the administered dose was recovered. The findings of the study indicate that *N*-EtFOSE is quickly and extensively metabolized to PFOSA with an elimination half-life of 16–20 h. In a second study Grossman et al. (1992) fed rats with a mean daily dose of 6.6 *N*-EtFOSA mg/kg$_{body\ weight}$ over a period of 56 days. They observed no detectable levels in blood samples, but its metabolite PFOSA, was present. The blood half-life of *N*-EtFOSA was expected to be 10.8 days with no tendency of the compounds to accumulate in adipose tissue.

In two studies Xu et al. (2004, 2006) elucidate the pathways for biotransformation of *N*-EtFOSE in vitro, and identify and characterize the enzymes catalyzing these processes. They observed that PFOSA is the major metabolite of *N*-alkylperfluorosulfonamides. As a major metabolic pathway PFOSA was subsequently transformed to PFOSA *N*-glucuronide, and to a lower extent, to the metabolically inert PFOS. The *N*-glucuronidation of PFOSA appears to be species dependent with higher *N*-glucuronosyltransferase activities in pooled liver microsomes from humans compared to other species studied. Overall, they concluded that PFOS is formed from PFOSA, but at a comparatively low rate.

Therefore, as a conservative estimate we assumed for further calculation that 5% of the FTOHs and 20% of the FOSAs/FOSEs were converted in the human body to PFOA and PFOS. It has to be noted that there are significant uncertainties using in vitro data or data observed from studies with rodents to predict rates of metabolism in humans. Using this somewhat rough approach and the intake data from Table 10 we can conclude that FTOHs have only a negligible contribution (<1%) on the total mean and high PFOA exposure of adults. Moreover, the contribution of the converted FOSAs/FOSEs to total PFOS exposure of the general population only reaches 10%.

Certainly, this somewhat preliminary estimation has various limitations. First of all, the database is very limited. Our knowledge of the occurrence and behavior of PFCs, especially in indoor air, ambient air and house dust needs to be expanded. Secondly, using the intake values from the UK TDS (FSA, 2006) the dietary intake was clearly higher than the estimates from the Canadian and German study (see Table 4). Furthermore, there are only limited data with regard to the dietary intake of other PFCs than PFOS and PFOA. Moreover, it should be noted that for some subsets of the population a higher exposure could be observed due to environmental contamination (Hölzer et al., 2008), or residence near a fluoropolymer production facility (Emmett et al., 2006a, b). Consumption of higher contaminated fish results under some circumstances and in some regions (e.g. Baltic Sea, Great Lakes) in higher intakes and body burdens of perfluorocarboxylates and sulfonates

(Falandysz et al., 2006). In addition, the significance of trace levels of PFCs in certain consumer articles is not clear yet, but it seems that the contribution to total exposure is quite low. For example Washburn et al. (2005) modeled the potential exposures during consumer use of articles containing PFOA. They estimated a hypothetical annual average intake as reasonable maximum aggregate exposure (RME) of an adult resident at approximately 2.2 ng PFOA/$kg_{body\ weight}$ from clothing and carpet. For the more typical exposure scenarios intake estimates were generally 1–2 orders of magnitude lower than the corresponding RME intakes.

Conclusion

For risk assessment purposes our exposure estimates could be compared to tolerable lifetime intake levels at which no appreciable health risks would be expected over a lifetime. Beyond this we compared our data to the tolerable daily intakes (TDI) recommended by scientific institutions.

A recent evaluation of PFOS was performed by the UK Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT, 2006a, b). For PFOS, the COT recommended a TDI of 300 ng/$kg_{body\ weight}$. For PFOA, a TDI of 3000 ng/$kg_{body\ weight}$ was established. Furthermore, the German Federal Institute for Risk Assessment (BfR, 2006) and the Drinking Water Commission of the German Ministry of Health (DWC, 2006) derived a provisional TDI of 100 ng/$kg_{body\ weight}$ for both PFOS and PFOA.

The total estimated average (and high) daily intakes of an adult population calculated above are in the low ng/$kg_{body\ weight}$ range; PFOS and PFOA estimated daily intakes are 1.6 ng/$kg_{body\ weight}$ (8.8 ng/$kg_{body\ weight}$) and 2.9 ng/$kg_{body\ weight}$ (12.6 ng/$kg_{body\ weight}$), respectively. The total estimated intake of PFOS and PFOA are well below the lowest recommended TDI values of 100 ng/$kg_{body\ weight}$.

In this paper we do not specifically estimate the exposure of children. It is obvious from biomonitoring data that the internal exposure of children is comparable to that of adults, but results are only based on a few studies (Olsen et al., 2004b; Hölzer et al., 2008; Fromme et al., 2007d). Overall, the exposure situation of children is not well understood, and therefore we cannot confidently make any statements on the risks of childrens' exposure to PFCs using the data currently available.

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References

Andersen, M.E., Butenhoff, J.L., Chang, S.C., Farrar, D.G., Kennedy, G.L., Lau, C., Olsen, G.W., Seed, J., Wallace, K.B., 2008. Perfluoroalkyl acids and related chemistries – toxicokinetics and modes of action. Toxicol. Sci. 102, 3–14.

Apelberg, B.J., Goldman, L.R., Calafat, A.M., Herbstman, J.B., Kuklenyik, Z., Heidler, J., Needham, L.L., Halden, R.U., Witter, F.R., 2007. Determinants of fetal exposure to polyfluoroalkyl compounds in Baltimore, Maryland. Environ. Sci. Technol. 41, 3891–3897.

Barber, J.L., Berger, U., Chaemfa, C., Huber, S., Jahnke, A., Temme, C., Jones, K., 2007. Analysis of per- and polyfluorinated alkyl substances in air samples from Northwest Europe. J. Environ. Monit. 9, 530–541.

Barton, C.A., Butler, L.E., Zarzecki, C.J., Flaherty, J., Kaiser, M., 2006. Characterizing perfluorooctanoate in ambient air near the fence line of a manufacturing facility: comparing modeled and monitored values. J. Air Waste Manag. Assoc. 56, 48–55.

Begley, T.H., White, K., Honigfort, P., Twaroski, M.L., Neches, R., Walker, R.A., 2005. Perfluorochemicals: potential sources of and migration from food packing. Food Add. Contam. 22, 1023–1031.

Bernsmann, T., Fürst, P., 2008. Determination of perfluorinated compounds in human milk. Prepared for DIOXIN 2008, Organohalogen Compounds 70, 718–721.

BfR (German Federal Institut for Risk Assessment), 2006. High levels of perfluorinated organic surfactants in fish are likely to be harmful to human health Statement No. 21/2006, 28 July 2006 〈http://www.bfr.bund./cd/8172〉 [accessed 4 January 2008].

Boulanger, B., Peck, A.M., Schnoor, J.L., Hornbuckle, K.C., 2005. Mass budget of perfluorooctane surfactants in Lake Ontario. Environ. Sci. Technol. 39, 74–79.

Butenhoff, J.L., Seacat, A.M., 2001. Comparative sub-chronic toxicity of perfluoroctane sulfonate (PFOS) and *N*-ethyl perfluorooctanesulfonamidoethanol (*N*-EtFOSE) in the rat. Toxicol. Sci. 60 (Suppl. 1), 348 (abstract 1655).

Calafat, A.M., Kuklenyik, Z., Caudill, S.P., Reidy, J.A., Needham, L.L., 2006a. Perfluorochemicals in pooled serum samples from the United States residents in 2001 and 2002. Environ. Sci. Technol. 40, 2128–2134.

Calafat, A.M., Needham, L.L., Kuklenyik, Z., Reidy, J.A., Tully, J.S., Aguilar-Villalobos, M., Naeher, L.P., 2006b. Perfluorinated chemicals in selected residents of the American continent. Chemosphere 63, 490–496.

Calafat, A.M., Kuklenyik, Z., Reidy, J.A., Caudill, S.P., Tully, J.S., Needham, L.L., 2007. Serum concentrations of 11 polyfluoroalkyl compounds in the US population: data from the National Health and Nutrition Examination Survey (NHANES) 1999–2000. Environ. Sci. Technol. 41, 2237–2242.

Corsolini, S., Kannan, K., 2004. Perfluorooctanesulfonate and related fluorochemicals in several organisms including humans from Italy. Organohalogen Compd. 66, 4079–4085.

COT (Committee on Toxicity of Chemicals in Food, Consumer Products and The Environment), 2006a. COT statement on the tolerable daily intake for perfluorooctanoic acid 〈http://www.food.gov.uk/multimedia/pdfs/cotstatementpfoa200610.pdf〉 [accessed 4 January 2008].

COT (Committee on Toxicity of Chemicals in Food, Consumer Products and The Environment), 2006b. COT statement on the tolerable daily intake for perfluorooctane sulfonate 〈http://www.food.gov.uk/multimedia/pdfs/cotstatementpfos200609.pdf〉 [accessed 4 January 2008].

D'eon, J.C., Mabury, S.A., 2007. Production of perfluorinated carboxylic acids (PFCAs) from the biotransformation of perfluoroalkyl phosphate surfactants (PAPS): exploring routes of human contamination. Environ. Sci. Technol. 41, 4799–4805.

De Silva, A.O., Mabury, S.A., 2006. Isomer distribution of perfluorocarboxylates in human blood: potential correlation to source. Environ. Sci. Technol. 40, 2903–2909.

Dinglasan, M.J., Yeh, Y., Edwards, E.A., Mabury, S.A., 2004. Fluorotelomer alcohol biodegradation yields poly- and perfluorinated acids. Environ. Sci. Technol. 38, 2857–2864.

Duarte-Davidson, R., Jones, K.C., 1994. Polychlorinated biphenyls (PCBs) in the UK population: estimated intake, exposure and body burden. Sci. Total Environ. 151, 131–152.

DWC (Drinking Water Commission), 2006. Provisional evaluation of PFT in drinking water with the guide substances perfluorooctanoic acid (PFOA) and perfluorooctane sulfonate (PFOS) as examples 〈http://www.umweltbundesamt.de/uba-info-presse-e/hintergrund/pft-in-drinking-water.pdf〉 [accessed 4 January 2008].

Ehresman, D.J., Froehlich, J.W., Olsen, G.W., Chang, S.-C., Butenhoff, J.L., 2007. Comparison of human whole blood, plasma, and serum matrices for the determination of perfluorooctanesulfonate (PFOA), and other fluorochemicals. Environ. Res. 103, 176–184.

Ellis, D.A., Martin, J.W., De Silva, A.O., Mabury, S.A., Hurley, M.D., Sulbaek Andersen, M.P., Wallington, T.J., 2004. Degradation of fluorotelomer alcohols: a likely atmospheric source of perfluorinated carboxylic acids. Environ. Sci. Technol. 15, 3316–3321.

Emmett, E.A., Shofer, F.S., Zhang, H., Freeman, D., Desai, C., Shaw, L.M., 2006a. Community exposure to perfluorooctanoate: relationships between serum concentrations and exposure sources. J. Occup. Environ. Med. 48, 759–770.

Emmett, E.A., Zhang, H., Shofer, F.S., Freeman, D., Rodway, N.V., Desai, C., Shaw, L.M., 2006b. Community exposure to perfluorooctanoate: relationships between serum levels and certain health parameters. J. Occup. Environ. Med. 48, 771–779.

Ericson, I., Gomez, M., Nadal, M., van Bavel, B., Lindstrom, G., Domingo, J.L., 2007. Perfluorinated chemicals in blood of residents in Catalonia (Spain) in relation to age and gender: a pilot study. Environ. Int. 33, 616–623.

Ericson, I., Marti-Cid, R., Nadal, M., van Bavel, B., Lindstrom, G., Domingo, J.L., 2008. Human exposure to perfluorinated chemicals through the diet: intake of perfluorinated compounds in foods from the Catalan (Spain) market. J. Agric. Food Chem. 56, 1787–1794.

EU (European Union), 2006. Directive 2006/122/ECOF of the European Parliament and of the Council of 12 December 2006. Official Journal of the European Union, L/372/32-34, 27.12.2006.

Ewers, U., Krause, C., Schulz, C., Wilhelm, M., 1999. Reference values and human biological monitoring values for environmental toxins. Int. Arch. Occup. Environ. Health 72, 255–260.

Falandysz, J., Taniyasu, S., Gulkowska, A., Yamashita, N., Schulte-Oehlmann, U., 2006. Is fish a major source of fluorinated surfactants and repellents in humans living on the Baltic coast. Environ. Sci. Technol. 40, 748–751.

Fasano, W.J., Carpenter, S.C., Gannon, S.A., Snow, T.A., Stadler, J.C., Kennedy, G.L., Buck, R.C., Korzeniowski, S.H., Hinderliter, P.M., Kemper, R.A., 2006. Absorption, distribution, metabolism, and elimination of 8-2 fluorotelomer alcohol in the rat. Toxicol. Sci. 91, 341–355.

Fei, C., McLaughlin, J.K., Tarone, R.E., Olsen, J., 2007. Perfluorinated chemicals and fetal growth: a study within the Danish National Birth Cohort. Environ. Health Perspect. 115, 1677–1682.

Fromme, H., Midasch, O., Twardella, D., Angerer, J., Boehmer, S., Liebl, B., 2007a. Occurrence of perfluorinated substances in an adult German population in southern Bavaria. Int. Arch. Occup. Environ. Health 80, 313–319.

Fromme, H., Albrecht, M., Angerer, J., Drexler, H., Gruber, L., Schlummer, M., Parlar, H., Körner, W., Wanner, A., Heitmann, D., Roscher, E., Bolte, G., 2007b. Integrated Exposure Assessment Survey (INES). Exposure to persistent and bioaccumulative chemicals in Bavaria, Germany. Int. J. Hyg. Environ. Health 210, 345–349.

Fromme, H., Schlummer, M., Möller, A., Gruber, L., Wolz, G., Ungewiß, J., Böhmer, S., Dekant, W., Mayer, R., Liebl, B., Twardella, D., 2007c. Exposure of an adult population to perfluorinated substances using duplicate diet portions and biomonitoring data. Environ. Sci. Technol. 41, 7928–7933.

Fromme, H., Völkel, W., Genzel-Boroviczény, O., Demmelmair, H., Gebauer, C., Koletzko, B., Raab, U., Twardella, D., 2007d. Internal exposure of newborns to perfluorinated substances and estimation of relevant intake pathways [in German, abstract]. Umwelt. Forsch. Prax. 12, 319.

Fromme, H., Nitschke, L., Kiranoglu, M., Albrecht, M., Völkel, W., 2008. Perfluorinated substances in house dust in Bavaria, Germany. Prepared for DIOXIN 2008, Organohalogen Compounds 70, 1048–1050.

FSA (Food Standards Agency), 2006. Fluorinated chemicals: UK dietary intakes. Food Survey Information Sheet 11/06, London, UK.

Giesy, J.P., Kannan, K., 2001. Global distribution of perfluorooctane sulfonate in wildlife. Environ. Sci. Technol. 35, 1339–1342.

Government of Canada, 2006. Perfluorooctane sulfonate and its salts and certain other compounds regulations. Can. Gazette Pt. 1 140 (50), 4265–4284.

Grossman, M.R., Mispagel, M.E., Bowen, J.M., 1992. Distribution and tissue eklimination in rats during and after prolonged dietary exposure to a highly fluorinated sulfonamide pesticide. J. Agric. Food Chem. 40, 2505–2509.

Gruber, L., Schlummer, M., Ungewiss, J., Wolz, G., Moeller, A., Weise, N., Sengl, M., Frey, S., Gerst, M., Schwaiger, J., 2007. Tissue distribution of perfluorooctansulfonate (PFOS) and perfluorooctanoic acid (PFOA) in fish. Organohalogen Compd. 69, 3.

Gulkowska, A., Jiang, Q., So, M.A., Taniyasu, S., Lam, P.K.S., Yamashita, N., 2006. Persistent perfluorinated acids in seafood collected from two cities of China. Environ. Sci. Technol. 40, 3736–3741.

Guruge, K., Taniyasu, S., Yamashita, N., Wijeratna, S., Mohotti, K.M., Seneviratne, H.R., Kannan, K., Yamanaka, N., Miyazaki, S., 2005. Perfluorinated organic compounds in human blood serum and seminal plasma: a study of urban and rural tea worker population in Sri Lanka. J. Environ. Monit. 7, 371–377.

Han, X., Snow, T.A., Kemper, R.A., Jepson, G.W., 2003. Binding of perfluorooctanoic acid to rat and human plasma proteins. Chem. Res. Toxicol. 16, 775–781.

Hansen, K.J., Clemen, L.A., Ellefson, M.E., Johnson, H.O., 2001. Compound-specific, quantitative characterization of organic fluorochemicals in biological matrices. Environ. Sci. Technol. 35, 766–770.

Harada, K., Saito, N., Sasaki, K., Inoue, K., Koizumi, A., 2003. Perfluorooctane sulfonate contamination of drinking water in the Tama River, Japan: estimated effects on resident serum levels. Bull. Environ. Contam. Toxicol. 71, 31–36.

Harada, K., Saito, N., Inoue, K., Yoshinaga, T., Watanabe, T., Sasaki, S., Kamiyama, S., Koizumi, A., 2004. The influence of time, sex and geographical factors on levels of perfluorooctane sulfonate in human serum over the last 25 years. J. Occup. Health 46, 141–147.

Harada, K., Nakanishi, S., Saito, N., Tsutsui, T., Koizumi, A., 2005a. Airborne perfluorooctanoate may be a substantial source contamination in Kyoto area, Japan. Bull. Environ. Contam. Toxicol. 74, 64–69.

Harada, K., Inoue, K., Morikawa, A., Yoshinaga, T., Saito, N., Koizumi, A., 2005b. Renal clearance of perfluorooctane sulfonate and perfluorooctanoate in humans and their species-specific excretion. Environ. Res. 99, 253–261.

Harada, K., Nakanishi, S., Sasaki, K., Furuyama, K., Nakayama, S., Saito, N., Yamakawa, K., Koizumi, A., 2006. Particle size distribution and respiratory deposition estimates of airborne perfluorooctanoate and perfluorooctanesulfonate in Kyoto area, Japan. Bull. Environ. Contam. Toxicol. 76, 306–310.

Harada, K., Koizumi, A., Saito, N., Inoue, K., Yoshinaga, T., Date, C., Fujii, S., Hachiya, N., Hirosawa, I., Koda, S., Kusaka, Y., Murata, K., Omae, K., Shimbo, S., Takenaka, K., Takeshita, T., Todoriki, H., Wada, Y., Watanabe, T., Ikeda, M., 2007a. Historical and geographical aspects of the increasing perfluorooctanoate and perfluorooctane sulfonate contamination in human serum in Japan. Chemosphere 66, 293–301.

Harada, K.H., Hashida, S., Kaneko, T., Takenaka, K., Minata, M., Inoue, K., Saito, N., Koizumi, A., 2007b. Biliary excretion and cerebrospinal fluid partition of perfluorooctanoate and perfluorooctane sulfunate in humans. Environ. Toxicol. Pharmacol. 24, 134–139.

Hekster, F.M., Laane, R.W., de Voogt, P., 2003. Environmental and toxicity effects of perfluoroalkylated substances. Rev. Environ. Contam. Toxicol. 179, 99–121.

Henderson, W.M., Smith, M.A., 2007. Perfluorooctanoic acid (PFOA) and perfluorononanoic acid (PFNA) in fetal and neonatal mice following in utero exposure to 8-2 fluorotelomer alcohol (FTOH). Toxicol. Sci. 95, 462–473.

Hinderliter, P.M., Mylchreest, E., Gannon, S.A., Butenhoff, J.L., Kennedy, G.L., 2005. Perfluorooctanoate: placental and lactational transport pharmacokinetics in rats. Toxicology 211, 139–148.

Hölzer, J., Midasch, O., Rauchfuss, K., Kraft, M., Reupert, R., Angerer, J., Kleeschulte, P., Marschall, N., Wilhelm, M., 2008. Biomonitoring of perfluorinated compounds in children and adults exposed to perfluorooctanoate (PFOA)-contaminated drinking water. Environ. Health Perspect. 116, 651–657.

Inoue, K., Okada, F., Ito, R., Kato, S., Sasaki, S., Nakajima, S., Uno, A., Saijo, Y., Sata, F., Yoshimura, Y., Kishi, R., Nakazawa, H., 2004a. Perfluorooctane sulfonate (PFOS) and related perfluorinated compounds in human maternal and cord blood samples: assessment of PFOS exposure in a susceptible population during pregnancy. Environ. Health Perspect. 112, 1204–1207.

Inoue, K., Okada, F., Ito, R., Kawaguchi, M., Okanouchi, N., Nakazawa, H., 2004b. Determination of perfluorooctane sulfonate, perfluorooctanoate and perfluorooctane sulfonylamide in human plasma by column-switching liquid chromatography–electrospray mass spectrometry coupled with solid-phase extraction. J. Chromatogr. B 810, 49–56.

Jahnke, A., Huber, S., Temme, C., Kylin, H., Berger, U., 2007a. Development and application of a simplified method for volatile polyfluorinated alkyl substances in indoor and environmental air. J. Chromatogr. A 1164, 1–9.

Jahnke, A., Ahrens, L., Ebinghaus, R., Temme, C., 2007b. Urban versus remote air concentrations of fluorotelomer alcohols and other perfluorinated alkyl substances in Germany. Environ. Sci. Technol. 41, 745–752.

Jahnke, A., Berger, U., Ebinghaus, R., Temme, C., 2007c. Latitudinal gradient of airborne polyfluorinated alkyl substances in the marine atmosphere between Germany and South Africa (53°N–33°S). Environ. Sci. Technol. 41, 3055–3061.

Jin, Y., Saito, N., Harada, K.H., Inoue, K., Koizumi, A., 2007. Historical trends in human serum levels of perfluorooctanoate and perfluorooctane sulphate in Shenyang, China. Tohoku J. Exp. Med. 212, 63–70.

Kärrman, A., van Bavel, B., Järnberg, U., Hardell, L., Lindström, G., 2004. Levels of perfluoroalkylated compounds in whole blood from Sweden. Organohalogen Compd. 66, 4058–4062.

Kärrman, A., van Bavel, B., Järnberg, U., Hardell, L., Lindström, G., 2006a. Perfluorinated chemicals in relation to other persistent organic pollutants in human blood. Chemosphere 64, 1582–1591.

Kärrman, A., Mueller, J.F., van Bavel, B., Harden, F., Toms, L.-M., Lindström, G., 2006b. Levels of 12 perfluorinated chemicals in pooled Australian serum, collected 2002–2003, in relation to age, gender, and region. Environ. Sci. Technol. 40, 3742–3748.