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REVIEW

Perfluorinated compounds – Exposure assessment for the general population in western countries

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Abstract

Perfluorinated compounds (PFCs) can currently be detected in many environmental media and biota, as well as in humans. Because of their persistence and their potential to accumulate they are of toxicological concern. The present review presents the current knowledge of PFC monitoring data in environmental media relevant for human exposure. In this context, PFC concentrations in indoor and ambient air, house dust, drinking water and food are outlined. Furthermore, we summarize human biomonitoring data of PFC levels in blood, breast milk, and human tissues. An estimate of the overall exposure of the general adult population is provided and compared with tolerable intake values.

Using a simplified model, the average (and upper) level of daily exposure including all potential routes amounts to 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 in adults in the general population. The majority of exposure can be attributed to the oral route, mainly to diet. Overall, the contribution of PFOS and PFOA precursors to total exposure seems to be limited.

Besides this background exposure of the general population, a specific additional exposure may occur which causes an increased PFC body burden. This has been observed in populations living near PFC production facilities or in areas with environmental contamination of PFCs. The consumption of highly contaminated fish products may also cause an increase in PFC body burdens.
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Keywords: PFOS; PFOA; PFC; Biomarkers; Human biomonitoring; Indoor air; House dust

Abbreviation: PFBS, perfluorobutane sulfonate; PFBA, perfluorobutanoate; PFC, perfluorinated chemical; PFDA, perfluorodecanoate; PFDoDA, perfluorododecanoate; PFDS, perfluorodecane sulfonate; PFDA, perfluorodecanoate; PFHpS, perfluoroheptane sulfonate; PFHpA, perfluoroheptanoate; PFHxA, perfluorohexanoate; PFHxS, perfluorohexane sulfonate; PFNA, perfluorononanoate; PFOA, perfluorooctanoate; PFOS, perfluorooctane sulfonate; PFOSA, perfluorooctane sulfonamide; PFOSF, perfluorooctanesulfonyl fluoride; PFUnDA, perfluoroundecanoate; *N*-EtFOSE, *N*-ethyl perfluorooctane sulfonamidoethanol; *N*-MeFOSE, *N*-methyl perfluorooctane sulfonamidoethanol; *N*-EtFOSA, *N*-ethyl perfluorooctane sulfonamide; *N*-MeFOSA, *N*-methyl perfluorooctane sulfonamide; *N*,*N*-Et_2FOSA, *N*,*N*-diethyl perfluorooctane sulfonamide; *N*,*N*-Me_2FOSA, *N*,*N*-dimethyl perfluorooctane sulfonamide; 4:2 FTOH, 1H,1H,2H,2H-perfluoro-1-hexanol; 6:2 FTOH, 1H,1H,2H,2H-perfluoro-1-octanol; 8:2 FTOH, 1H,1H,2H,2H-perfluoro-1-decanol; 10:2 FTOH, 1H,1H,2H,2H-perfluoro-1-dodecanol.

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Contents

Introduction

Perfluorinated compounds (PFCs) represent a large group of chemicals which are characterized by a fully fluorinated hydrophobic linear carbon chain attached to various hydrophilic heads. The chemical structures of some important PFCs are given in Fig. 1. PFCs have been produced since the 1950s and are widely used for many industrial purposes and consumer-related applications. This is due to their unique physico-chemical characteristics such as chemical and thermal stability, low surface free energy and surface active properties (Hekster et al., 2003; Lehmler, 2005). The C–F bond is particularly strong, and is resistant to various modes of degradation, including reaction with acids and bases, oxidation, and reduction (Kissa, 2001). This resistance contributes to the extraordinary stability of PFCs. While some PFCs undergo chemical transformations, these reactions occur mainly at the hydrophilic portions of the molecule, as opposed to the perfluorinated alkyl chains. The most commonly studied PFC substances are the perfluorinated sulfonates and the perfluorinated carboxylates. Among these, perfluorooctane sulfonate (PFOS) and perfluorooctanoate (PFOA) are of greatest concern. Both persist in humans and the environment.

PFOS, its precursors, and related compounds are used in many applications ranging from oil and water repellant coatings for carpets, textiles, leather, paper, cardboard, and food packing materials; electronic and photographic devices; and surfactants in diverse cleaning agents, cosmetics, and fire-fighting foams (OECD, 2002; Kissa 2001). PFOA, as its ammonium salt, is mainly used as an essential processing aid in the manufacture of certain fluoropolymers such as polytetrafluoroethylene (PTFE) and to a lesser extent in industrial applications as an antistatic additive and in the electronic industry (OECD, 2005).

There are two main processes used to commercially synthesize PFCs. PFOS, along with some other PFCs, are commercially synthesized by a process known as electrochemical fluorination (ECF), which uses an electric current to fully fluorinate organic feedstock dispersed in liquid hydrogen fluoride. During this non-selective process, the predominant perfluorinated alkyl chain

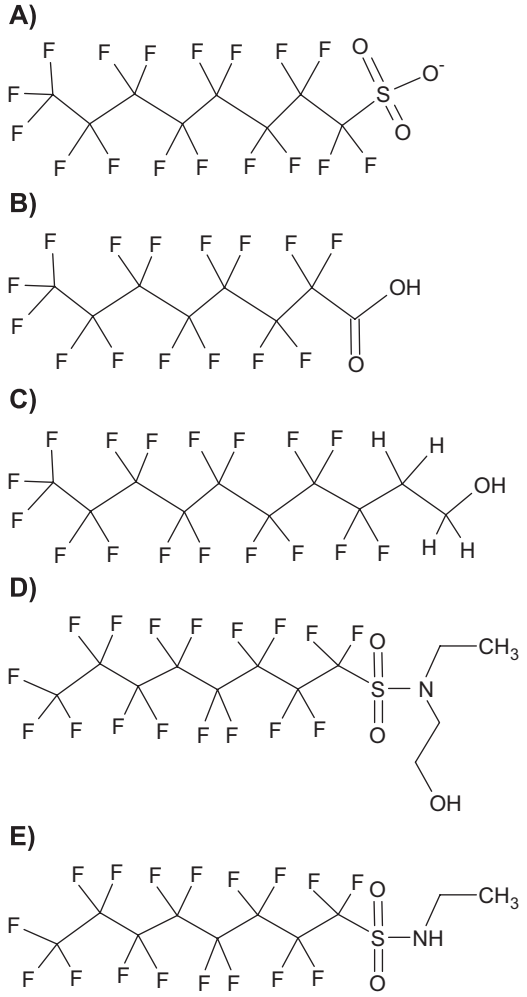

Fig. 1. Chemical structure of some typical perfluorinated substances. (A) Perfluorooctane sulfonate (PFOS), (B) perfluorooctanoate (PFOA), (C) 1-hydroxyethane-2-perfluorooctanol (8:2 FTOH), (D) *N*-ethyl perfluorooctane sulfonamidothanol (NEtFOSE), and (E) *N*-ethyl perfluorooctane sulfonamide (NEtFOSA).

length produced corresponds to the alkyl chain length of the organic feedstock used. However, other perfluoroalkyl homologues are also formed during ECF. For example, ECF of octanesulfonyl fluoride produces perfluorooctanesulfonyl fluoride (PFOSF) plus homologous sulfonyl fluorides and related fluorocarbons containing between 4 and 13 carbon atoms. Reaction by-products also include branched chain isomers. The resulting substances derived from various reactions with PFOSF, mainly perfluorooctane sulfonamides and perfluorooctane sulfonamide derivatives, are building blocks for different commercial perfluoroalkyl substances.

The other major commercially important process for PFC synthesis is telomerization. In this process, tetrafluoroethylene reacts with intermediate perfluoroalkyl iodides to form key compounds like fluoroalkyl silanes, carboxylates, acrylates and methacrylate polymers (Schultz et al., 2003). Branched chain isomers are not observed in the products formed by telomerization (Kissa, 2001).

The more persistent PFCs, such as PFOS and PFOA, can also be formed in the environment from abiotic and biotic transformation of commercially synthesized precursors. During ECF and subsequent commercial reactions, numerous substances such as perfluoroalkylsulfonamide alcohols were unintentionally produced, or remained as by-products in commercial products. Most of these substances can be converted in the ecosystem and in living organisms to persistent PFCs. For example, it has been demonstrated that perfluorooctane sulfonamides can be metabolized to PFOS (Xu et al., 2004; Tomy et al., 2004). It has to be noted that PFOS may therefore be the final degradation or metabolic product of many perfluorooctylsulfonyl substances (Hekster et al., 2003).

In addition, some precursors like fluorotelomer alcohols (FTOH) will be subsequently transformed into PFOA under environmental degradation processes (Ellis et al., 2004; Dinglasan et al., 2004; Wang et al., 2005). Furthermore, there is growing evidence from some studies that 8:2 FTOH is converted to PFOA after oral uptake in mice (Kudo et al., 2005; Henderson and Smith, 2007) and rats (Fasano et al., 2006; D'eon and Mabury, 2007). These findings were confirmed by in vitro studies using rat hepatocytes (Martin et al., 2005) and hepatocytes and microsomes from various species (Nabb et al., 2007) to study the metabolism of 8:2 FTOH.

From a regulatory point of view, PFOS is classified as very persistent, very bioaccumulative and toxic, thus fulfilling the criteria for being considered as a persistent organic pollutant under the Stockholm Convention (EU, 2006). In the European Union, the use of PFOS has been restricted and the PFOS Directive aims to end the use of all PFOS as soon as practical (EU, 2006). In particular, fire-fighting foams that have been placed on the market before 27 December 2006 can be used until 27 June 2011. Similar regulatory action has been taken in North America. In Canada, PFOS, its precursors, and salts are are being considered for addition to the list of Toxic Substances under the Canadian Environmental Protection Act 1999 (Government of Canada, 2006). This action would prohibit the manufacture, use, sale, offer for sale and import of PFOS, as well as manufactured items containing the perfluorooctylsulfonyl moiety. The United States Environmental Protection Agency (US EPA) has adopted federal Significant New Use Rules for PFOS and related substances for new manufacturers and new uses of these substances. These rules will allow the US EPA to evaluate any intended new uses, and subsequently restrict or prohibit these new uses.

In addition, one of the primary manufacturers of fluorinated chemicals in North America announced a

cease in production of perfluorooctanesulfonyl compounds in 2000. It was projected that from 2000 to 2002, the production of $C_8F_{17}SO_2$-containing compounds for US Food and Drug Administration-approved uses would decrease from 1,520,000 to 0 kg (US EPA 2002).

The toxicity of PFOS and PFOA has been studied extensively, mainly in rodents. Several reviews are available that discuss results from these studies (OECD, 2002; Kennedy et al., 2004; US EPA, 2005; Harada et al., 2005b; Andersen et al., 2008; Lau et al., 2007). Hepatotoxicity, developmental toxicity, immunotoxicity, hormonal effects and a carcinogenic potency are the effects of main concern. In contrast, epidemiologic data related to PFC exposure are limited. The data were collected mainly among PFC production plant workers and have not found consistent effects on morbidity and mortality in humans.

The persistence of PFCs in the environment, plus their potential to accumulate in organisms and to biomagnificate in the food chain is of particular toxicological concern. Several PFCs have been detected in nearly all environmental media and biota reflecting the widespread global pollution in all parts of the ecosystem (Giesy and Kannan, 2001). PFCs have also been detected in human blood and tissue samples from occupationally and non-occupationally exposed humans throughout the world. The persistence of certain PFCs may be a more relevant issue for humans versus other species. In contrast to investigations carried out in laboratory animals in which short half-lives of PFCs were observed, studies in retirees from PFC production facilities showed a mean elimination half-life of 3.8 years (PFOA) and 5.4 years (PFOS) (Olsen et al., 2007b). A widespread distribution of various PFCs and their corresponding degradation and metabolism products results in a very complex exposure situation. The contribution of single sources and pathways to the total exposure is currently not well defined.

The aim of this review was to compile in detail the current data available to define the environmental media responsible for human exposure to PFCs. For this purpose we used the results of different Medline inquiries to get an overwiew of the current scientific literature. We also included papers presented at conferences, reports from governmental, scientific and other institutions, and where possible, unpublished reports and other gray literature. In this context PFC concentrations in indoor and ambient air, house dust, drinking water, and food are outlined. Furthermore, we will summarize human biomonitoring data in blood, breast milk and human tissues. Current estimates of the overall exposure of the adult general population will also be addressed. All these data will be discussed in relation to present benchmark values used for risk assessment.

Environmental monitoring

For the assessment of human exposure to PFCs, different pathways have to be considered. Exposure via inhalation may result from outdoor air and indoor air PFC pollution, and from PFC in house dust. Oral exposure is mainly determined by contamination of food and drinking water. Ingestion of dust and soil due to hand-to-mouth activities may also contribute to the internal exposure for children. However, this paper will focus mainly on exposure pathways of adults. Data from PFC monitoring in environmental samples are discussed in the following sections.

Outdoor air

The neutral and more volatile PFCs [e.g. fluorotelomer alcohols (FTOHs), perfluorooctane sulfonamidoethanols (FOSEs), and perfluorooctane sulfonamides (FOSAs)] have been measured in outdoor air from various locations. Results from these analyses are given in Table 1.

In rural areas of Canada concentrations of 34 and 36 pg/m^3 (*N*-MeFOSE) and 68 and 85 pg/m^3 (*N*-EtFOSE) were found, respectively, while in urban sites concentrations were higher (101 pg *N*-MeFOSE/m^3 and 205 pg *N*-EtFOSE/m^3) (Martin et al., 2002). An urban–rural gradient was found in Germany too. Mean total concentrations of FOSEs/FOSAs (*N*-MeFOSE, *N*-EtFOSE, *N*-MeFOSA, and *N*-EtFOSA) of 50 pg/m^3 (9–142 pg/m^3) from an urban location (Hamburg) and 26 pg/m^3 (6–48 pg/m^3) from a rural site (Waldhof) were observed in 2005 (Jahnke et al., 2007b). Similar concentrations were found for FOSEs and FOSAs in northwestern Europe (Ireland, UK, Norway) (Barber et al., 2007). At 7 measuring sites in Ottawa concentrations of 76–99 pg *N*-MeFOSE/m^3 and 80–106 pg *N*-EtFOSE/m^3, were detected (Shoeib et al., 2005a). In the vicinity of a carpet processing factory in Griffin, GA, USA, total polyfluorinated sulfonamide (*N*-MeFOSE, *N*-EtFOSE, and *N*-EtFOSA) concentrations were found to be higher during one sampling event (1549 pg/m^3) probably due to specific meteorologic conditions and/or episodic point source release (Stock et al., 2004).

Measurements of single fluorotelomer alcohols in the North American troposphere ranged from 7 to 196 pg/m^3 (Martin et al., 2002), whilst mean total concentrations of FTOHs ranged from 11 to 165 pg/m^3 (Stock et al., 2004). In both studies higher concentrations were found in urban than rural settings. Similarly, in a German study, $\sum$FTOH concentrations in Hamburg were found to be 1.6 times higher compared to a rural area, reaching significance only for 4:2 FTOH and *N*-MeFOSE (Jahnke et al., 2007b). Furthermore, at four northwest European sampling sites comparable

Table 1. Concentration (range) of fluorinated organic compounds in gas and particulate phase of ambient air

Substance	Mean concentration (pg/m^3)	Sampling location	Sampling year	Number of samples (sampling sites)	Reference
N-MeFOSE	101 (86–123)	Canada, urban	2001	4	Martin et al. (2002)
	34, 36	Canada, rural		2	Martin et al. (2002)
	32, 16	Canada	2001–2003	2	Shoeib et al. (2004)
	83 (76–99)	Canada	2002–2003	7	Shoeib et al. (2005a)
	24–49[a]	UK, Norway, Ireland	2005–2006	(6)	Barber et al. (2007)
	41 (15–95)	Germany, Hamburg	2005	7	Jahnke et al. (2007a)
	8.6 (3.8–12)	Germany, Waldhof	2005	4	Jahnke et al. (2007a)
	(<1–11)	Oregon, USA, remote	2006	34	Piekarz et al. (2007)
N-EtFOSE	205 (51–393)	Canada, urban	2001	4	Martin et al. (2002)
	68, 85	Canada, rural		2	Martin et al. (2002)
	0.5 (0.3–1.0)	USA, Great Lakes	2003	8	Boulanger et al. (2005)
	9.8 and 8.5	Canada	2001–2003	2	Shoeib et al. (2004)
	88 (80–106)	Canada	2002–2003	7	Shoeib et al. (2005a)
	6.4–66[a]	UK, Norway, Ireland	2005–2006	(6)	Barber et al. (2007)
	13 (6.0–30)	Germany, Hamburg	2005	7	Jahnke et al. (2007a)
	16 (9.9–26)	Germany, Waldhof	2005	4	Jahnke et al. (2007a)
	(<1–3.7)	Oregon, USA, remote	2006	34	Piekarz et al. (2007)
N-MeFOSA	<5.3–6.1[a]	UK, Norway, Ireland	2005–2006	(6)	Barber et al. (2007)
	9.0 (3.4–20)	Germany, Hamburg	2005	7	Jahnke et al. (2007a)
	7.0 (3.8–11)	Germany, Waldhof	2005	4	Jahnke et al. (2007a)
N-EtFOSA	1.1 (0.4–2.2)	USA, Great Lakes	2003	8	Boulanger et al. (2005)
	<1.6–9.6	UK, Norway, Ireland	2005–2006	(6)	Barber et al. (2007)
	3.1 (1.3–5.9)	Germany, Hamburg	2005	7	Jahnke et al. (2007a)
	2.6 (1.5–3.4)	Germany, Waldhof	2005	4	Jahnke et al. (2007a)
	(<0.4–3.2)	Oregon, USA, remote	2006	34	Piekarz et al. (2007)
$\sum$FOSE/ FOSA	22–403 (<2–1549)[b]	Canada + USA	2001	26 (6)	Stock et al. (2004)
	39–89[b]	UK, Norway, Ireland	2005–2006	(6)	Barber et al. (2007)
	50 (9–142)[d]	Germany, Hamburg	2005	7	Jahnke et al. (2007a)
	26 (6–48)[d]	Germany, Waldhof	2005	4	Jahnke et al. (2007a)
4:2 FTOH	1.4–114	UK, Norway, Ireland	2005–2006	(6)	Barber et al. (2007)
	54 (22–117)	Germany, Hamburg	2005	7	Jahnke et al. (2007a)
	19 (3.3–45)	Germany, Waldhof	2005	4	Jahnke et al. (2007a)
6:2 FTOH	87 (30–196)	Canada, urban	2001	4	Martin et al. (2002)
	41, 16	Canada, rural		2	Martin et al. (2002)
	5–187[a]	UK, Norway, Ireland	2005–2006	(6)	Barber et al. (2007)
	66 (33–149)	Germany, Hamburg	2005	7	Jahnke et al. (2007a)
	64 (17–125)	Germany, Waldhof	2005	4	Jahnke et al. (2007a)
	4.6	Oregon, USA, remote	2006	34	Piekarz et al. (2007)
	14, 35, 55	Japan, three areas		24	Oono et al. (2008)
8:2 FTOH	55 (9–123)	Canada, urban	2001	4	Martin et al. (2002)
	40, 25	Canada, rural		2	Martin et al. (2002)
	(<LOD–20)	Canada, Arctic	2004	10	Stock et al. (2007)
	11.3–237 [a]	UK, Norway, Ireland	2005–2006	(6)	Barber et al. (2007)
	119 (62–275)	Germany, Hamburg	2005	7	Jahnke et al. (2007a)
	75 (33–112)	Germany, Waldhof	2005	4	Jahnke et al. (2007a)
	24	Oregon, USA, remote	2006	34	Piekarz et al. (2007)
	550, 698, 2031	Japan, three areas		24	Oono et al. (2008)

Table 1. (*continued*)

Substance	Mean concentration (pg/m^3)	Sampling location	Sampling year	Number of samples (sampling sites)	Reference
10:2 FTOH	29 (7–46)	Canada, urban	2001	4	Martin et al. (2002)
	20 and 15	Canada, rural		2	Martin et al. (2002)
	7.8–75[a]	UK, Norway, Ireland	2005–2006	(6)	Barber et al. (2007)
	35 (16–93)	Germany, Hamburg	2005	7	Jahnke et al. (2007a)
	23 (10–32)	Germany, Waldhof	2005	4	Jahnke et al. (2007a)
	15	Oregon, USA, remote	2006	34	Piekarz et al. (2007)
	64, 88, 229	Japan, three areas		24	Oono et al. (2008)
∑FTOH	11–165[c]	Canada + USA	2001	26 (6)	Stock et al. (2004)
	28[c]	Canada, Arctic	2004	10	Stock et al. (2007)
	19.3–527 [a,c]	UK, Norway, Ireland	2005–2006	(6)	Barber et al. (2007)
	288 (150–546)	Germany, Hamburg	2005	7	Jahnke et al. (2007a)
	181 (64–311)	Germany, Waldhof	2005	4	Jahnke et al. (2007a)
	41 (16.0–83)[c]	USA, urban	2006	8	Kim and Kannan (2007)

[a]Only gas phase analyzed.
[b]Sum of *N*-MeFOSE, *N*-EtFOSE, and *N*-EtFOSA.
[c]Sum of 6:2 FTOH, 8:2 FTOH, and 10:2 FTOH.
[d]Only gas phase.

concentrations from 19 to 527 pg/m^3 (∑FTOH) were observed (Barber et al., 2007).

As yet, only Jahnke et al. (2007b) analyzed for a correlation between the outdoor air temperature and the sum concentration of FOSEs/FOSAs and FTOHs observing a significant association ($r = 0.95$ and 0.97).

Air samples collected on board the German research vessel Polarstern during a cruise between Bremerhaven (Germany) and Capetown (Republic of South Africa) indicate a strong decreasing gradient from the European continent towards the southern hemisphere (Jahnke et al., 2007c). The study confirms that volatile PFCs are mainly restricted to the northern hemisphere, with maximum 8:2 FTOH concentrations of 190 pg/m^3 compared to 14 pg/m^3 (southern hemisphere). During a cruise crossing the North Atlantic and the Canadian Arctic Archipelago in July 2005 Shoeib et al. (2006) measured maximum concentrations of 22.7 pg/m^3 (8:2 FTOH) and 23.6 pg/m^3 (*N*-MeFOSE) in the gas and particulate phase. Air concentrations of these two PFCs were somewhat higher, but on the same order of magnitude as reported in urban regions like Toronto.

Results on outdoor air concentrations of the much less volatile PFOS, PFOA and similar compounds in the particulate phase are given in Table 2. In Japan, in an exposed urban setting (high traffic load) the mean PFOA concentration was 372 pg/m^3 and the mean PFOS concentration 5.6 pg/m^3, while in a rural area concentrations were 2.0 pg PFOA/m^3 and 0.6 pg PFOS/m^3 (Harada et al., 2005a). Other investigations in Japan confirmed the regional differences in PFOS concentrations between rural (0.6 pg/m^3) and urban (5.3 pg/m^3) settings (Sasaki et al., 2003).

Concentration differences were also noted in samples collected from urban and rural sites in Europe. Higher concentrations of PFOS and PFOA in the particulate phase from specific areas also indicate influence from fluoropolymer production facilities. While very low concentrations of PFOA were found in rural areas of Ireland and Norway, the PFOA concentration in Manchester (UK) was found to be 341 pg/m^3 in February/March and 16 pg/m^3 in November/December. It is probable that the very high concentrations of 552 and 101 pg/m^3 observed at the fourth site (Hazelrigg/UK), and potentially in Manchester could be explained by a nearby fluorpolymer production plant. In addition, considerably high concentrations were observed along the fence line of an industrial area in the USA where a fluoropolymer processing factory is situated. Depending on the wind direction, in a 10-week period PFOA concentrations ranged between 120,000 and 900,000 pg/m^3 (Barton et al., 2006).

Sugita et al. (2007) analyzed dust samples collected on quartz fiber filters using a sampler placed on the rooftop of a building located in Wako City, Japan, in 2006. The concentrations were lower in December compared to July and also on weekends compared to weekdays with means of 4.3 and 7.3 pg/m^3, respectively. According to the few data available, particulate phase concentrations in North America are similar for PFOS but lower for PFOA (Boulanger et al., 2005; Stock et al., 2007), than concentrations reported for Japan. However, this could be due to the preselection of low exposure areas

Table 2. Mean concentration (range) of PFOS and PFOA in particulate phase of ambient air

Mean concentration (pg/m^3)	Sampling location	Sampling year	Number of samples (sampling sites)	Reference
PFOS				
5.3 (2.3–22)	Urban, Japan	2001–2002	12	Sasaki et al. (2003)
0.6 (0.1–2.1)	Rural, Japan		12	
5.6 (2.5–9.8)	Urban, Japan	2001–2003	12	Harada et al. (2005a)
0.7 (0.5–1.2)	Rural, Japan		8	
2.9	Urban, Japan	2005	1	Harada et al. (2006)
2.2	Rural, Japan		1	
6.8	High traffic road, Japan		1	
5.9[a]	Canada, Arctic	2004	10	Stock et al. (2007)
6.4 (<LOD–8.0)	USA, Lakes Erie and Ontario	2003	8	Boulanger et al. (2005)
<45	Hazelrigg, UK	2005–2006	2 (spring)	Barber et al. (2007)
1.6			10 (winter)	
46	Manchester	2005–2006	2 (spring)	
7.1			1 (winter)	
1,0	Kjeller, Norway	2005	2	
<1.8	Mace Head, Ireland	2006	4	
7.3 (3.6–15.7)	Wako City, Japan	2006	26 (July)	Sugita et al. (2007)
4.3 (0.9–8.9)			27 (December)	
0.6 (0.4–1.2) [b]	Albany, New York, USA	2006	8 (summer)	Kim and Kannan (2007)
1.7 (0.9–3.0) [c]				
PFOA				
372 (72–919)	Urban, Japan	2001–2003	12	Harada et al. (2005a)
2.0 (1.6–2.6)	Rural, Japan		8	
15.2	Urban, Japan	2005	1	Harada et al. (2006)
205	Rural, Japan		1	
320	High traffic road, Japan		1	
1.4 [a]	Canada, Arctic	2004	10	Stock et al. (2007)
552	Hazelrigg, UK	2005–2006	2 (spring)	Barber et al. (2007)
101			10 (winter)	
341	Manchester, UK	2005–2006	2 (spring)	
16			1 (winter)	
1.5	Kjeller, Norway	2005	2	
8.9	Mace Head, Ireland	2006	4	
2.0 (0.8–4.2) [b]	Albany, New York, USA	2006	8 (summer)	Kim and Kannan (2007)
3.2 (1.9–6.5) [c]				

[a]Gas and particulate phase.
[b]Particulate phase.
[c]Gas phase.

for measurements in North America. Stock et al. (2007) described data from a remote Arctic site with mean concentrations of 5.9 pg/m^3 (PFOS), 0.2 pg/m^3 (PFHxS), 0.2 pg/m^3 (PFDS), 1.4 pg/m^3 (PFOA), 0.4 pg/m^3 (PFNA) and 0.4 pg/m^3 (PFDA), respectively.

Barber et al. (2007) found that PFOA was the prevailing analyte observed mainly in the particulate phase. Up to now, this point is not well understood. It can be hypothesized that source strength and different degradation processes on particulate matter were responsible for this observation.

Currently only very few studies on outdoor air PFC concentrations are available; these are mainly characterized by very small sample sizes or short sampling time periods. Overall, the studies indicate that a concentration gradient exist between urban, rural, and remote areas for FOSEs/FOSAs as well as for PFOS and PFOA. Substantially higher concentrations observed in specific locations also highlight the influence of possible point in addition to diffuse sources for these compounds. For some of the more volatile PFCs, a temperature dependency was found in one study; in a similar fashion, another study observed seasonal fluctuations of PFOS and PFOA concentrations. Beyond the effects of these seasonal and localized geographical factors no marked differences were found between PFC outdoor air concentrations from the western countries.

Indoor air

Findings on indoor air concentrations are given in Table 3. The most comprehensive data are available from Canada, where samples were taken from four private homes in the city of Ottawa between 2001 and 2003 (Shoeib et al., 2004) and an additional 59 randomly selected homes in 2002/2003 with a different sampling technique (Shoeib et al., 2005a). While in the first study analytes were actively sampled on polyurethane foam (PUF) and glass fiber filters, in the second investigation a passive sampling method using PUF-disks (21 days sampling time) was employed. Despite this methodological difference both studies found comparable concentrations with mean values of 1110 and 770 pg/m^3 (*N*-EtFOSE), 2590 and 1970 pg/m^3 (*N*-MeFOSE), as well as 73 and 35 pg/m^3 (*N*-MeFOSEA), for the two studies, respectively.

Considerably higher concentrations of 14,900 pg/m^3 FOSEs/FOSAs were observed in the gas phase of four indoor locations in Tromsø, Norway in 2005 (Barber et al., 2007). In this study fluorotelomer alcohols were determined in the gas phase for the first time at a geometric mean sum concentration of 11,075 pg/m^3. In the particulate phase only negligible amounts of the investigated PFCs could be found. The first measurements in a Norwegian office resulted in concentrations below those in private homes, probably due to the absence of typical sources such as carpets and upholstery for these compounds in offices (Jahnke et al., 2007a).

In Canada indoor to outdoor ratios reached 18 for *N*-MeFOSE and 8 for *N*-EtFOSE (Shoeib et al., 2005a), whilst in an earlier study indoor air levels exceeded outdoor air concentrations by about a factor of 100 (Shoeib et al., 2004). In the study of Barber et al. (2007) no outdoor concentrations from the vicinity of the measured indoor places are available. In comparison to other outdoor levels, however, an indoor to outdoor ratio of 30–570 ($\sum$FTOH) and 170–380 ($\sum$FOSAs/FOSEs), respectively, can be deduced.

In addition to neutral PFCs, Barber et al. (2007) analyzed various perflorocarboxylates (PFCAs) and perfluorosulfonates (PFAS) in the particulate phase of the four aforementioned sites in Tromsø. The highest concentrations were found for PFHxA and PFOA (17.1 and 4.4 pg/m^3, respectively), while among the sulfonates, only perfluorodecane sulfonate (2.6 pg/m^3) exceeded the limit of quantification.

Up to now, there are only very few data on indoor air concentrations of PFCs available. It can be concluded, that the indoor PFCA and PFAS levels were not significantly elevated above outdoor air, whilst concentrations of volatile polyfluorinated compounds appear to be considerably higher in indoor than in outdoor air. Because humans spend a lot of their time in indoor spaces much more data are needed to better characterize the exposure in the different indoor environments, such as residences and work places. Studies on seasonal variation and the influence of different furnishings will also provide important data to help examine exposure to PFCs.

Household dust

In the winter of 2002/2003, 66 randomly selected households in Ottawa, Canada were investigated (Shoeib et al., 2005a) for PFCs in dust. Dust samples were collected with a vacuum cleaner and 0.001–75.4 μg *N*-EtFOSE/g (geometric mean: 0.14 μg/g) and 0.003–8.8 μg *N*-MeFOSE/g (geometric mean: 0.11 μg/g) were found. The investigators observed a good correlation between the dust concentrations of FOSEs and the corresponding values in indoor air.

All other studies that have examined PFCs in dust have focused on the less volatile PFCAs and PFAS. In 16 Japanese houses concentrations between 0.011 and 2.5 μg PFOS/g dust (unsieved, only large particles removed) and between 0.070 and 3.7 μg PFOA/g dust were determined in dust collected from vacuum cleaner bags (Moriwaki et al., 2003). Median concentrations were 0.025 μg PFOS/g dust and 0.165 μg PFOA/g dust. A strong correlation was found between PFOS and PFOA ($r^2 = 0.99$), however the association dropped to $r^2 = 0.35$ when one outlier was removed. In another Japanese study, PFOS and PFOA were detected in all 7 collected dust samples (particle size of 75 μm to 1 mm) from 0.007 to 0.041 μg/g and 0.018 to 0.089 μg/g, respectively (Nakata et al., 2007).

In two North American studies, a wider variety of PFCAs and PFAS were studied. Dust from vacuum cleaner bags was collected in winter 2002/2003 from 67 Canadian homes and was sieved to a size of <150 μm (Kubwabo et al., 2005). The most frequently detected PFCs were PFOS at <0.002–5.065 μg/g (median: 0.038 μg/g; 33% of measurements below the limit of detection, 0.005 μg/g), PFOA at <0.002–1.231 μg/g (median: 0.020 μg/g; 37% <0.002 μg/g), and PFHxS at <0.002–4.305 μg/g (median: 0.023 μg/g; 15% $<$ 0.005 μg/g). PFC concentrations in the dust were statistically significantly correlated with the age of the houses and the floor covering. Older houses were characterized by lower concentrations of PFOS and PFOA, but not of PFHxS. All three compounds were positively correlated with each other and with the fraction of the floor covered with carpets.

Additionally, 112 dust samples were collected in 2000–2001 in Ohio and North Carolina and stored at room temperature in dark glass bottles (Strynar and Lindstrom, 2008). After sieving to <150 μm, samples were analyzed for a number of PFCAs and PFAS.

Table 3. Mean concentration (range) of volatile polyfluorinated compounds in indoor air

Substance	Concentration (pg/m^3)	Sampling location	Sampling year	Number of samples	Phase analyzed	Reference
N-MeFOSE	1970 (366–8190)	Canada	2002–2003	59[a]		Shoeib et al. (2005a)
	2590 (667–8315)	Canada	2001–2003	4	Particulate	Shoeib et al. (2004)
	6018	Norway	April–June 2005	4	Vapor	Barber et al. (2007)
	363	Norway	April–June 2005	4	Particulate	Barber et al. (2007)
	727, 798	Norway	2006	2 office	Vapor and particulate	Jahnke et al. (2007b)
N-EtFOSE	1100 (227–7740)	Canada	2002–2003	59[a]		Shoeib et al. (2005a)
	770 (364–1799)	Canada	2001–2003	4	Particulate	Shoeib et al. (2004)
	5755	Norway	April–June 2005	4	Vapor	Barber et al. (2007)
	76	Norway	April–June 2005	4	Particulate	Barber et al. (2007)
	305, 815	Norway	2006	2 office	Vapor and particulate	Jahnke et al. (2007b)
N-MeFOSEA	35 (12–109)	Canada	2002–2003	59[a]		Shoeib et al. (2005a)
	≈73 (LOD[b]–283)	Canada	2001–2003	4	Particulate	Shoeib et al. (2004)
N-MeFOSA	6608	Norway	April–June 2005	4	Vapor	Barber et al. (2007)
	6	Norway	April–June 2005	4	Particulate	Barber et al. (2007)
N-EtFOSA	59 (5.9–646)	Canada	2002–2003	59[a]		Shoeib et al. (2005a)
	6626	Norway	April–June 2005	4	Vapor	Barber et al. (2007)
	7	Norway	April–June 2005	4	Particulate	Barber et al. (2007)
	188, 158	Norway	2006	2 office	Vapor and particulate	Jahnke et al. (2007b)
4:2 FTOH	114	Norway	April–June 2005	4	Vapor	Barber et al. (2007)
	<20	Norway	April–June 2005	4	Particulate	Barber et al. (2007)
6:2 FTOH	2990	Norway	April–June 2005	4	Vapor	Barber et al. (2007)
	<40	Norway	April–June 2005	4	Particulate	Barber et al. (2007)
	177, 248	Norway	2006	2 office	Vapor and particulate	Jahnke et al. (2007b)
8:2 FTOH	2070 (261–28900)	Canada	2002–2003	52[a]		Shoeib et al. (2007)
	3424	Norway	April–June 2005	4	Vapor	Barber et al. (2007)
	<10	Norway	April–June 2005	4	Particulate	Barber et al. (2007)
	853, 421	Norway	2006	2 office	Vapor and particulate	Jahnke et al. (2007b)
10:2 FTOH	891 (104–9210)	Canada	2002–2003	52[a]		Shoeib et al. (2007)
	3559	Norway	April–June 2005	4	Vapor	Barber et al. (2007)
	13	Norway	April–June 2005	4	Particulate	Barber et al. (2007)
	898, 1.660	Norway	2006	2 office	Vapor and particulate	Jahnke et al. (2007b)

[a]Passive sampling over 21 days.
[b]LOD: limit of detection.

PFOS concentrations of <0.009–12.1 μg/g (mean: 0.76 μg/g; 5% < limit of quantification, 0.009 μg/g) and PFOA concentrations of 0.01–1.96 μg/g (mean: 0.29 μg/g; 4% < 0.01 μg/g) were found. For PFHxS the mean concentration was 0.87 μg/g, for PFHxA 0.12 μg/g and for PFHpA 0.11 μg/g. No differences were observed between the two sampling regions, but a significant correlation was found between PFOS and PFOA ($r = 0.87$).

In Germany, 12 dust samples were collected with a vacuum cleaner (Fromme et al., 2008) in a pilot study. Median (range) PFOS and PFOA concentrations in

the sieved fraction (<63 μm) were 0.016 μg/g (0.003–0.342 μg/g) and 0.011 μg/g (0.002–0.141 μg/g), respectively. Significantly lower median concentrations were observed in the unsieved samples (PFOS: 0.010 μg/g; PFOA: 0.007 μg/g) indicated that PFAS were mainly associated with smaller particles.

While only little information has been collected on the contamination of household dust at this point in time, the results indicate a large variability in the concentrations of the perfluorinated substances measured. Whilst the mean PFOS concentration in samples collected from Canadian and Japanese homes appear to be very similar, the mean PFOA concentration in Canada was 9 times lower than in Japan. On the other hand, very high concentrations were reported in the US study (Strynar and Lindstrom, 2008), where mean values exceed concentrations observed in the other countries by factors of 200 for PFOS and 150 for PFOA. The reasons for these differences, which may be partly due to methodological differences, are yet unknown.

Contamination of food and drinking water

Although dietary intake is assumed to be a major route of exposure for the general population, only few systematic data on PFC levels in foods are available. Often ecological or ecotoxicological questions are the focus of investigations on animals, so that information on the contamination of edible parts cannot be deduced. More detailed data are only available for PFC levels in fish, mainly in the context of surveys of fish caught in PFC-contaminated waters.

Commercially available food items

Only a limited number of studies have examined the presence of PFCs in commercially available food items. Details of these are provided in Table 4. These studies have analyzed only food items purchased from locations in North America and Western Europe; their main focus has been the analysis of PFCAs and PFAS.

Concentrations observed in all the studies conducted to date were in the sub- to low ng/g range. In 2000, the so-called "Multi-City-Study" conducted in 6 US cities observed PFOS was detected in 5 samples (milk and ground beef) and PFOA in 5 samples (green beans, apple, bread, and ground beef) at concentrations up to 0.85 $ng/g_{fresh\ weight}$ and 2.35 ng/g, respectively (US EPA, 2001). However, in only one of these instances (PFOS in ground beef) were the results from the duplicate consistent; for the remaining positive detections, PFCs were not detected in the duplicate analyzed. The UK Total Diet Study (TDS) found concentrations of PFOS, PFUA, PFDA, and PFTeDA up to 10 $ng/g_{fresh\ weight}$. These higher concentrations were all reported in the "potatoes" composite (which included potato chips, french fries, and other potato products) (FSA, 2006). The Canadian TDS observed concentrations up to 4.5 ng/g (PFNA in beef steak) (Tittlemier et al., 2007). The maximum concentration observed in a total of 36 composite samples purchased from local stores in Tarragona County, Spain was 0.84 $ng/g_{fresh\ weight}$ PFOS (Ericson et al., 2007b).

The German duplicate diet study was conducted in a slightly different fashion. As with the UK and Canadian TDSs, PFCs were analyzed in prepared and otherwise cooked food. However, the duplicate diet study did not analyze food items (or composites of similar food items) separately. Samples analyzed in this study were comprised of homogenized liquid or solid portions of whole meals. The maximum concentration observed in this study was 118 $ng/g_{fresh\ weight}$ PFOA; although most concentrations observed were less than 0.1 $ng/g_{fresh\ weight}$ (Fromme et al., 2007c).

Some of the studies have also analyzed for precursors to PFOS. These studies have mainly focused on PFOSA (US EPA, 2001; FSA, 2006; Fromme et al., 2007c); only the 2006 Canadian study has examined a wider range of perfluorooctanesulfonyl compounds (PFOSAs) in food items (Tittlemier et al., 2006).

The majority of food samples analyzed did not contain detectable PFCA or PFAS residues above the various limits of detection for the analytical methods employed. Generally, less than 50% of samples analyzed did not contain detectable levels of PFCAs or PFAS and in a study from Germany using 28 samples of packed and frozen French fries none reached the limit of detection of 1 ng/g for PFOS or PFOA (Stahl, 2007). A higher percentage of samples from the Canadian TDS contained PFOSAs (Tittlemier et al., 2006), even though PFOSA itself was not detected in samples from the other studies aside from one sample in the UK TDS (FSA, 2006). This may be due in part to the lower detection limit of the gas chromatographic–mass spectrometric method used in the Canadian study (Tittlemier et al., 2005).

Contamination of fish

PFOS and PFOA have been demonstrated to bioaccumulate in fish (Martin et al., 2003a, b; Gruber et al., 2007). Thus, fish is potentially an important dietary source of these PFCs for consumers. Freshwater and marine fish, and seafood, have been analyzed for PFCs in many studies.

Generally, PFOS has been found at higher levels in fish than PFOA. High PFOS concentrations of 59–297 $ng/g_{fresh\ weight}$ were found in muscle from fish caught in 1999 and 2000 in the American Great Lakes

(Giesy and Kannan, 2001, Kannan et al., 2005). By contrast, PFOA values did not reach the detection limit (LOD) of 36 ng/g (Kannan et al., 2005). Moreover, in China in 2004 freshly bought seafood (fish and shellfish edible portions) was analyzed for PFCs (Gulkowska et al., 2006). The PFOS concentrations ranged from 0.33 to 4.6 $ng/g_{wet\ weight}$; in one sample of shrimps a concentration of 13.9 ng/g was observed. In this study, the PFOA concentrations were between <0.25 and 1.7 ng/g and 45% of the samples contain levels below the LOD. In a Bavarian monitoring program that analyzed fish sampled from 15 bodies of water in 2005/2006, PFOS was found from 3.9 to 16.3 ng/g (19 eel samples), 7.1–14.7 ng/g (5 carp or perch), <1.0–1.3 ng/g (4 barbel), and 1.7–17.8 ng/g (5 pike) (LfU, 2007). In contrast, the PFOA concentrations in muscle of all measured fish ($n = 35$) ranged between <0.1 and 7.2 ng/g. In all 15 fish sampled in the Federal State of Hessen, Germany, PFOS and PFOA were below 1 ng/g; only in one carp a PFOS concentration of 1.8 ng/g was found (Stahl, 2007).

The difference between the observed PFOS and PFOA fish concentrations could suggest a lower potential of PFOA to bioaccumulate in fish than PFOS. Differences in bioconcentration and dietary accumulation of PFOS and PFOA have been demonstrated in laboratory experiments (Martin et al., 2003a, b; Gruber et al., 2007).

Fish sampled from areas that contain known point sources of PFCs, such as fluoropolymer or fluorochemical production plants, often contain higher PFC concentrations. For example, 3.0–52.5 ng/g PFOA were observed in fish (LfU, 2007) sampled from a waterbody with a known source of PFOA from a production plant in Bavaria. In addition, a survey on PFOS and PFOA levels in more than 200 fish was undertaken in the Federal State of North Rhine-Westphalia, Germany, in which a remarkable case of a contamination with PFCs became evident in 2006 (Wilhelm et al., 2008a). The highest level of PFOS (1100 $ng/g_{wet\ weight}$) was detected in a trout filet from a fish farm pond in the affected area. Fish (e.g. trout, chub, perch, zander) caught from contaminated rivers and lakes in 2006 and 2007 contained PFOS at levels between 6 and 425 $ng/g_{wet\ weight}$. PFOS in trout caught from non-contaminated creeks in North Rhine-Westphalia were <4 $ng/g_{wet\ weight}$. PFOA levels of fish were mostly below 2 $ng/g_{wet\ weight}$. The highest PFOA concentration (34 $ng/g_{wet\ weight}$) was measured in an eel sample. It should be noted that in the affected area only PFOA levels in surface waters were increased.

Similarly, elevated PFC concentrations were found in fish sampled from an area near a point source of PFCs. A second Bavarian Monitoring program analyzed 39 fish samples for PFOS and PFOA (LGL, 2007). The concentrations ranged from between LOQ (0.5 ng/g) and 80.3 ng/g for PFOS and between LOQ (1 ng/g) and 20.9 ng/g for PFOA. The highest concentrations of PFOA were found in eels and perches caught in rivers containing effluent from the point source. For both compounds, concentrations in fish living in fish ponds were lower compared to fish living in contaminated river water.

Some studies have found positive correlations between PFC body burdens and self-reported fish consumption. In Poland, blood samples from 45 donors living near the Baltic Sea were analyzed in 2004 (Falandysz et al., 2006). Subjects with a high consumption of regionally captured fish ($n = 15$) showed statistically higher PFC blood levels than the comparison groups. The authors concluded that the consumption of seafood was an important determinant for internal PFC exposure. The human biomonitoring study that examined residents in the affected North Rhine-Westphalia area also found a positive association between PFOS concentrations in plasma and consumption of locally caught fish, indicating that fish intake can be an important pathway for internal PFC exposure (Hölzer et al., 2008).

Contamination of drinking water

Current studies have shown that drinking water PFC concentrations are in the low ng/l range if there is no large point source of PFCs to the drinking water source. The analysis of potable water in Japan observed PFOS concentrations between 0.1 and 51 ng/l; the majority of results (8 of 9 waterworks) did not exceed 4 ng/l (Harada et al., 2003). Only in one waterworks concentrations of 43.7 and 51 ng/l were observed. The authors explain the high values by the fact that the waterworks draws water from the river Tama, which is contaminated upstream with PFOS by a wastewater treatment plant. In other investigations, the presence of potential sources of PFCs, such as an airport, has been observed to correlate with higher PFC surface water concentrations as well (Saito et al., 2004). In this study, concentrations of PFCs in drinking water from exposed areas ranged between 5.4 and 40.0 ng PFOS/l and 1.1 and 1.6 ng PFOA/l, while in areas with no known sources concentrations were only <0.1–0.2 ng PFOS/l and 0.1–0.7 ng PFOA/l.

Results from North America are generally similar. During the American "Multi-City-Study", PFOA was found at concentrations of 26 and 27 ng/l and PFOS at concentrations of 57 and 63 ng/l in tapwater from Columbus (US EPA, 2001). In the remaining 5 cities concentrations generally did not exceed the detection limit for PFOS (2.5 ng/l) and PFOA (7.5 ng/l). Only in one sample of potable water from Pensacola PFOS concentrations of 42 and 47 ng/l were found.

In Europe, Skutlarek et al. (2006) observed PFOA concentrations of <2–4 ng/l (13 of 16 were below the limit of detection) in 14 German, one French and one English drinking water samples. The PFOS and PFBS concentrations in these samples ranged between <2 and 6 ng/l (14 of 16 < LOD) and <2–20 ng/l (13 of 16 < LOD). In the vicinity of Lake Maggiore in Italy, concentrations of 8.1 ng/l (PFOS) and 2.4 ng/l (PFOA) were found in 6 samples of drinking water. These concentrations were very similar to the concentrations detected in the lake (Loos et al., 2007). The authors report that PFOS could not be detected in water samples from waterworks, which do not draw water from Lake Maggiore.

Contamination of drinking water by known sources

Worldwide two cases of PFOA contaminated drinking water have been studied in detail (Little Hocking, Ohio, USA and Sauerland, North Rhine-Westphalia, Germany).

Since 2004, drinking water wells in the Little Hocking Water Association, Ohio, a water catchment area in the vicinity of a localized PFOA source have been investigated. In this work, PFOA concentrations of 1900–10,100 ng/l (2004), 3900–18,600 ng/l (January 2005) and 1900–6600 ng/l (March 2005) were observed in four wells of the central water supply, as well as at the transit station to the distribution system 7200 ng/l (January 2005) (LHWA, 2005). A population-based study observed the highest PFOA concentrations in serum (median 374 ng/l) among those subjects which exclusively used water from the Little Hocking central drinking water supply (Emmett et al., 2006a). The private use of carbon water filters was associated with significant lower median blood levels, while subjects, who mostly drank water that originated from outside of the Little Hocking area, showed considerably lower serum PFOA concentrations.

The PFOA contamination in the Sauerland region was first discovered by Skutlarek et al. (2006). They reported levels of the sum of 7 PFCs in drinking water between 26 and 598 ng/l. The most abundant compound observed was PFOA; values in drinking water ranged from 22 to 519 ng/l. In 6 cities in this area concentrations above 100 ng/l were found. The proportion of PFOA in total PFCs detected was 50–80%. Industrial waste with high concentrations of PFCs was manufactured into soil improver by a recycling company and disseminated by framers on agricultural land in the rural area Sauerland. The use of the contaminated soil improver led to this substantial environmental pollution (details of this case are summarized in Wilhelm et al., 2008a). PFCs were washed from the highly contaminated area into small creeks and surface waters (Ruhr river, Möhne river, Möhne Lake) from which drinking water is drawn for several million residents of the Ruhr District. A survey performed between July 2006 and August 2007 showed that the sum of PFOS and PFOA levels in drinking water from the 17 waterworks along the Ruhr river were below 300 ng/l, mean levels were mostly between 50 and 100 ng/l (Wilhelm et al., 2008a). At the most affected waterworks of Möhnebogen, treatment with charcoal filtration effectively removed PFOA from drinking water. The initial PFOA concentrations of >500 ng/l observed in May 2006 rapidly declined to values mostly well below 100 ng/l after using charcoal filters. This concentration was set as a long-term minimum quality goal derived from a health-based precautionary value (DWC, 2006).

Dietary intake estimated from diet studies

At this point, only four studies which attempted to quantify the intake of PFCs via the diet have been published. Three of them used a market basket approach combining the measured concentrations in food composite samples with consumption patterns (FSA, 2006; Tittlemier et al., 2007; Ericson et al., 2008). The third study used a duplicate diet approach measuring PFC in duplicate portions of food prepared as for consumption (Fromme et al., 2007c). A summary of the results of these surveys is given in Table 4.

The first study analyzed PFCs in 20 composite food group samples from the 2004 UK TDS (FSA, 2006). The yearly composites were assembled by collecting retail food samples every fortnight from 24 locations in the UK and preparing as for consumption before compositing. PFOS was detected as the main analyte above LOD in potatoes (including chips, crisps, potato salad, hash browns, and croquettes), canned vegetables, eggs, and sugar and preserves. PFOA was detected only in the potato group. Based on the average and high (97.5th percentile) food consumption scenarios as derived from the nutritional surveys of British adults, the dietary intake of PFOS and PFOA was estimated. Concentrations below LOD were either substituted by the reporting limit (upper bound) or substituted with zero (lower bound). The estimated average daily intake was 100 ng/kg$_{body\ weight}$ (PFOS) and 70 ng/kg$_{body\ weight}$ (PFOA) (upper bound) or 10 ng/kg$_{body\ weight}$ (PFOS) and 1 ng/kg$_{body\ weight}$ (PFOA) (lower bound). The upper and lower bound intakes estimated using a high food consumption level were 200 ng/kg$_{body\ weigh}$ (PFOS) and 100 ng/kg$_{body\ weight}$ (PFOA) and 30 ng/kg$_{body\ weight}$ (PFOS) and 3 ng/kg$_{body\ weight}$ (PFOA), respectively.

Tittlemier et al. (2007) estimated the dietary exposure of Canadian teenagers and adults based on 25 composite samples collected in the 2004 TDS. Various food items

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 packaging. 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
∑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
∑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$_2$FOSA, *N*,*N*-Me$_2$FOSA, 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$_{\text{body weight}}$ 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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