Characterisation of human exposure pathways to perfluorinated compounds

- comparing exposure estimates with biomarkers of exposure

Line Småstuen Haug

Dissertation for the degree of Doctor Philosophiae (Dr. philos),
Faculty of Mathematics and Natural Sciences

UNIVERSITY OF OSLO

February 16th 2011

folkehelseinstituttet

ACKNOWLEDGEMENTS

Oslo, February 2011

Line Småstuen Haug

LIST OF PAPERS

Paper 1:   Haug LS, Thomsen C and Becher G. 2009. A sensitive method for determination of a broad range of perfluorinated compounds in serum suitable for large-scale human biomonitoring. *J. Chromatogr. A* 1216, 385-393.

Paper 2:   Haug LS, Thomsen C and Becher G. 2009. Time trends and the influence of age and gender on serum concentrations of perfluorinated compounds in archived human samples. *Environ. Sci. Technol.* 43, 2131-2136.

Paper 3:   Haug LS, Salihovic S, Jogsten IE, Thomsen C, van Bavel B, Lindström G and Becher G. 2010. Levels in food and beverages and daily intake of perfluorinated compounds in Norway. *Chemosphere* 80, 1137-1143.

Paper 4:   Haug LS, Thomsen C, Brantsæter AL, Kvalem HE, Haugen M, Becher G, Alexander J, Meltzer HM and Knutsen HK. 2010. Diet and particularly seafood are major sources of perfluorinated compounds in humans. *Environ. Int.* 36, 772-778.

Paper 5:   Thomsen C, Haug LS, Stigum H, Frøshaug M, Broadwell SL and Becher G. 2010. Changes in concentrations of perfluorinated compounds, polybrominated diphenyl ethers and polychlorinated biphenyls in Norwegian breast-milk during twelve months of lactation. *Environ. Sci. Technol.* 44, 9550-9556.

Paper 6:   Haug LS, Huber S, Schlabach M, Becher G and Thomsen C. 2011 Investigation on per- and polyfluorinated compounds in paired samples of house dust and indoor air from Norwegian homes *Environ. Sci. Technol.* doi: 10.1021/es103456h.

Paper 7:   Haug LS, Huber S, Becher G and Thomsen C. 2011. Characterisation of human exposure pathways to perfluorinated compounds - comparing exposure estimates with biomarkers of exposure. *Environ. Int.* 37, 687-693.

ABBREVIATIONS

ECF	electrochemical fluorination
ESI	electrospray ionisation mode
FFQ	food frequency questionnaire
GC	gas chromatography
ILC	interlaboratory comparison
LC	liquid chromatography
LC-MS/MS	liquid chromatography-triple quadrupole mass spectrometry
LOQ	limit of quantification
MLR	multiple linear regression
MRM	multiple reaction monitoring
MS	mass spectrometry
NFG study	Norwegian Fish and Game study
PBDE	polybrominated diphenylethers
PCB	polychlorinated biphenyls
PE	polyethylene
PK model	pharmacokinetic model
POP	persistent organic pollutant
PUF	polyurethane foam
SIM	selective ion monitoring
SPE	solid phase extraction
TDI	tolerable daily intake

For abbreviations of per- and polyfluorianted compounds and compound groups, see Table 1.

CONTENTS

1. INTRODUCTION

1.1 Background

A huge expansion within industry and technology has taken place in the 20th century, leading to development of numerous chemicals with properties favourable for specific purposes. Such chemicals are often present in consumer products we regularly come in contact with in everyday life. One large group of widely used chemicals is the per- and polyfluorinated compounds (PFCs). The PFCs consists of a carbon chain which is partly (poly) or fully (per) fluorinated and with different functional groups attached. The carbon chain can be either linear or branched. In Table 1 the PFCs studied in this thesis are listed together with the abbreviations.

Depending on the functional group, PFCs may be divided in two classes: ionic and neutral PFCs. Ionic PFCs such as perfluoroalkyl sulfonates (PFSAs) and perfluoroalkyl carboxylates (PFCAs) possesses an acidic group which is dissociated around neutral pH. PFCAs and PFSAs are highly resistant to physical, chemical and microbial degradation (Kissa 2001). Neutral PFCs such as perfluoroalkyl sulfonamides (FOSAs), perfluoroalkyl sulfonamidoethanols (FOSEs) and fluorotelomer alcohols (FTOHs) have a polar, non-ionic functional group. The chemical resistance, surface tension lowering properties and ability to create stable foams have made the PFCs extremely versatile, and they have been used in numerous consumer products and industrial processes such as in inks, varnishes, waxes, lubricants, hydraulic oils, fire fighting foams, food packaging, for metal plating and coating formulations, as water and oil repellents for leather, paper and textiles and as emulsifiers in fluoropolymer production (Kissa 2001;Prevedouros et al. 2006).

Table 1: List of PFCs studied in this thesis

	Compound	Abbreviation	Group abbreviation	
Perfluorinated compounds	Perfluorobutane sulfonate	PFBS	Perfluoroalkyl sulfonates (PFSAs)	Ionic PFCs
	Perfluoropentane sulfonate	PFPeS		
	Perfluorohexane sulfonate	PFHxS		
	Perfluoroheptane sulfonate	PFHpS		
	Perfluorooctane sulfonate	PFOS		
	Perfluorononane sulfonate	PFNS		
	Perfluorodecane sulfonate	PFDS		
	Perfluorobutanoate	PFBA	Perfluoroalkyl carboxylates (PFCAs)	
	Perfluoropentanoate	PFPeA		
	Perfluorohexanoate	PFHxA		
	Perfluoroheptanoate	PFHpA		
	Perfluorooctanoate	PFOA		
	Perfluorononanoate	PFNA		
	Perfluorodecanoate	PFDA		
	Perfluoroundecanoate	PFUnDA		
	Perfluorododecanoate	PFDoDA		
	Perfluorotridecanoate	PFTrDA		
	Perfluorotetradecanoate	PFTeDA		
	Perfluoropentadecanoate	PFPeDA		
	Perfluorohexadecanoate	PFHxDA		
	Perfluorooctadecanoate	PFODA		
	Perfluorooctane sulfonamide	PFOSA	Perfluoroalkyl sulfonamides (FOSAs)	Neutral PFCs
	N-Methylperfluorooctane sulfonamide	MeFOSA		
	N-Ethylperfluorooctane sulfonamide	EtFOSA		
	2-(N-Methylperfluoro-1-octanesulfonamido)- ethanol	MeFOSE	Perfluoroalkyl sulfonamidoethanols (FOSEs)	
	2-(N-Ethylperfluoro-1-octanesulfonamido)-ethanol	EtFOSE		
Polyfluorinated compounds	4:2 fluortelomer alcohol	4:2 FTOH	Fluorotelomer alcohols (FTOHs)	Ionic PFCs
	6:2 fluortelomer alcohol	6:2 FTOH		
	8:2 fluortelomer alcohol	8:2 FTOH		
	10:2 fluortelomer alcohol	10:2 FTOH		
	6:2 fluorotelomer unsaturated carboxylate	6:2 FTUCA	Fluortelomer unsaturated carboxylates (FTUCAs)	
	8:2 fluorotelomer unsaturated carboxylate	8:2 FTUCA		
	10:2 fluorotelomer unsaturated carboxylate	10:2 FTUCA		
	6:2 fluorotelomer sulfonate	6:2 FTS	Fluortelomer sulfonates (FTSs)	
	8:2 fluorotelomer sulfonate	8:2 FTS		

1.2 Production and use

PFCs have mainly been produced using two different processes, electrochemical fluorination (ECF) and telomerisation. In the ECF process an electric current is used to fully fluorinate the hydrocarbons dispersed in hydrogen fluoride. The predominant chain length corresponds to the alkyl chain length of the hydrocarbon. Because the process is neither effective nor selective, it yields numerous by-products including different chain length and branched isomers (Schultz et al. 2003). A lack of isomeric purity is a signature of this process. In the telomerisation process tetrafluoroethylene reacts with intermediate perfluoroalkyliodides. The fluoroalkyl chain generated during telomerisation processes are all linear and contain only even number of fluorinated carbons (Schultz et al. 2003).

The production of PFCs using the ECF process started around 1947, increased throughout the 1990s and maximum production was reached in 2000 (3M Company 2003;Kissa 2001). The ECF process was mainly used to produce PFOA and a line of perfluorooctane sulfonyl fluoride (PFOSF)-based products including PFOS. The global production of these products in 2000 was estimated to be around 3535 tonnes (Stock et al. 2010). In 2000, a phase-out of production of "perfluorooctanyl" compounds was announced by the main US manufacturer, 3M (3M Company 2000) after PFOS was found to be widespread in human populations and wildlife (Hansen et al. 2001;Kannan et al. 2001a;Kannan et al. 2001b). Subsequently, the US Environmental Protection Agency (US EPA) requested eight manufacturers to voluntarily eliminate their production and use of PFOA, its precursors and related chemicals (US EPA 2006a). For the period 1970 to 2002, Paul et al. (2008) estimated the total global production of PFOSF to be 96 000 tonnes. The FTOHs have been produced using the telomerisation process from the 1970s (Prevedouros et al. 2006). The annual production of FTOHs from 2000-2002 was estimated to be 5 000-6 500 tonnes, while a volume of around 12 000 tonnes in 2004 was estimated (Stock et al. 2010).

In 2004, the Climate and Pollution Agency (former Norwegian Pollution Control Authority) conducted a survey to explore uses of PFCs in Norway (Huse 2004). The largest quantities of PFCs were found to be used in fire extinguishers (15 tonnes/year) and textile protection (7-10 tonnes/year). The total annual amount of PFCs used was estimate to be in the range 23.2 to 26.2 tonnes (Huse 2004).

1.3 Physical-chemical properties and pharmacokinetics

Taves (1968) reported that human serum could contain organic fluorine. However it was not until 2001 when a sensitive and selective method for determination of PFCs had been developed, that the first study could confirm presence of PFCs in human serum (Hansen et al. 2001). Shortly after that, it was discovered that PFCs were ubiquitously distributed in wildlife (Kannan et al. 2001a;Kannan et al. 2001b). These early findings led to serious concerns about the persistence and bioaccumulative properties of PFCs.

Environmental losses of PFCAs and PFSAs through degradation are negligible due to the resistance to degradation (Kissa 2001). In contrast, neutral PFCs such as FOSAs, FOSEs and FTOHs, are usually not environmentally persistent, but may be transformed to persistent ionic PFCs in the environment (Ellis et al. 2004;Martin et al. 2006). It is not likely that FTOHs, FOSAs and FOSEs will undergo substantial bioaccumulation, as FTOHs and PFOSA have been demonstrated to be rapidly transformed and eliminated in fish (Brandsma et al. 2011). Among the ionic PFCs, PFSAs have been found to be more bioaccumulative than PFCAs of the same chain length. The bioaccumulation is directly related to the length of the carbon chain. PFCAs with seven fluorinated carbon or less and PFSAs with six fluorinated carbons or less, have not been found to be bioaccumulative (Conder et al. 2008).

Both neutral and ionic PFCs have been found to be widespread in the environment including the Arctic (Butt et al. 2010;Houde et al. 2006). In general, higher concentrations have been observed in samples collected close to urbanized/industrialized areas (Houde et al. 2006). As PFCs are neither produced nor used in the Arctic, their presence must be due to long-range transport. FOSA/FOSEs and FTOHs are found predominately in the air, while PFSAs, PFCAs and FTUCAs are mainly found in the aquatic phase (Stock et al. 2010).

Animal studies demonstrate that PFCs are well absorbed after oral administration (Hundley et al. 2006;Lau et al. 2007). It has been shown that FTOHs can be biotransformed to PFCAs (Nabb et al. 2007) and FOSA/FOSEs to PFSAs (Tomy et al. 2004). Ionic PFCs are distributed primarily in the extracellular space (Lau et al. 2007). Further they associate with proteins such as albumin and liver fatty acid-binding protein (Han et al. 2003), and undergo extensive uptake from enterohepatic circulation (Lau et al.

2007). The highest concentrations are found in blood, liver and kidney (Hundley et al. 2006;Johnson et al. 1979;Seacat et al. 2002;Seacat et al. 2003).

The ionic PFCs are primarily excreted through urine (Hundley et al. 2006). Rates of elimination differs considerably between species and sexes of a single species, and humans are thought to be very slow eliminators of PFCs compared to other species (Lau et al. 2007). This has been studied in retired fluorochemical production workers who had high initial serum concentrations (arithmetic mean = 799 ng/mL PFOS) (Olsen et al. 2007). Depuration followed a first-order kinetic, and geometric means of half-lives were 4.8 years for PFOS, 7.3 years for PFHxS, and 3.5 years for PFOA. The half-life range for PFOA was later confirmed in studies of general populations from Germany and the US exposed to PFOA through contaminated drinking water (Bartell et al. 2009;Hölzer et al. 2009; Seals et al. 2010). Two recent studies on exposures of professional ski waxing technicians indicated long elimination half-lives for PFNA, PFDA and PFUnDA as well (Freberg et al. 2010;Nilsson et al. 2010). In contrast the half-life of PFBS in six occupationally exposed workers was found to be around one month (Olsen et al. 2009a).

1.4 Toxicity and health effects

The toxicity of ionic PFCs, with special emphasize on PFOS and PFOA, have been reviewed by Lau et al. (2007) and Kennedy et al. (2004). Hepatotoxicity, developmental toxicity, immunotoxicity, neonatal mortality as well as hormonal effects have been demonstrated in animal studies. For instance, repeat-dose studies of PFOS in rodents and nonhuman primates indicated a potential to reduce body weight and body weight gain, increase liver weight, and reduce serum cholesterol. Similar effects have been seen for PFOA, except that no reduction in serum cholesterol was observed for nonhuman primates (Lau et al. 2007). A steep dose-response curve for mortality of PFOS was observed for sexual mature rats and primates (Lau et al. 2007). In a draft risk assessment, the US EPA concluded that "evidence was suggestive that PFOA is carcinogenic in humans" (US EPA 2005), and the majority of the EPA scientific advisory board members reviewing this draft concluded that PFOA was "likely to be carcinogenic in humans" (US EPA 2006b).

Several epidemiological studies have been conducted to investigate relationships between exposure to ionic PFCs, especially PFOS and PFOA, and possible health

outcomes. Among the outcomes studied are diabetes, cardiovascular diseases, cerebrovascular disease, elevation in uric acid, cholesterol level, thyroid function, immune function, liver and kidney function, sex hormones as well as reproductive and developmental outcomes as reviewed by Olsen et al. (2009b) and Steenland et al. (2010). The studies comprised wide ranges of exposures from highly exposed workers to background exposed populations. Occupational studies were often hampered by small sample sizes and the healthy worker effect. Several of the epidemiological studies were of the cross-sectional type, and it has been criticised that causal relationships between exposure and outcome could not be clearly established (Steenland et al. 2010).

1.5 Regulations

Based on the persistence, bioaccumulation potential, toxicity and the possibility of long range transport, PFOS, its salts as well as known precursors are regulated both nationally and internationally. In 2006, the European Union adopted Directive 2006/122/ECOF which restricts marketing and use of these chemicals (European Union 2006). PFOS and its salts were also found to fulfil the criteria of the Stockholm Convention on persistent organic pollutants (POPs), and were included in the list of restricted chemicals in 2009 (Annex B) (Stockholm convention on Persistent Organic Pollutants 2009). In Norway, it was forbidden from April 2007 to produce, import or sell impregnating agents and fire fighting foams containing 0.005 weight % or more of PFOS and related substances. Further, from July 2007 it was also forbidden to produce, import or sell textiles and other coated materials with concentrations of PFOS or related chemicals of 1 $\mu g/m^2$ or higher (Miljøverndepartementet 2007). The US EPA and eight major industrial companies launched the "2010/15 PFOA Stewardship Program" in 2006. In this program, the companies committed themselves to reduce global facility emissions and product content of PFOA and related chemicals by 95 percent by 2010, and to work toward eliminating emissions and product content by 2015 (US EPA 2006a).

1.6 Exposure assessment

The process of evaluating whether or not a population is exposed to a certain chemical to an extent that might cause adverse health effects, is called risk assessment. A

risk assessment can be divided in four steps, hazard identification, exposure assessment, effect assessment and risk characterisation (van Leeuwen and Vermeire 2007). This is illustrated schematically in Figure 1.
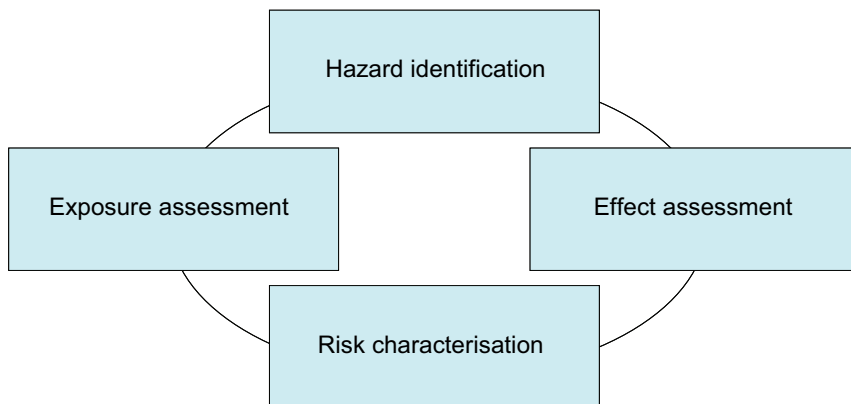
Figure 1. Schematic illustration of the four steps included in a risk assessment

The exposure assessment is important to gain insight in the concentrations/doses to which human populations are exposed to a certain chemical. There are two ways of performing an exposure assessment:

1. Measure concentrations of relevant chemicals in different exposure media (e.g. food, air and drinking water) and combine these concentrations with exposure factors (e.g. inhalation rate and volume/amount consumed). Such intake calculations give information on the **external doses** we are exposed to.

2. Measure concentrations of relevant chemicals in a suitable biological matrix (e.g. blood, breast milk and urine). This is called human biomonitoring. The measured concentrations are used to calculate the body burden (total amount in the body) of the chemicals based on knowledge on distribution of these chemicals in the human body. Such calculations give information on the **internal doses**.

For POPs, the internal dose reflects an integrated exposure over time comprising various sources and pathways. Biomonitoring data (e.g. blood concentrations) will also take individual differences into consideration (e.g. age and gender). In addition to giving

7

information on the internal dose of a chemical, biomonitoring is also applicable for identifying populations that might be at a higher risk, and for monitoring the efficacy of measures taken to reduce the environmental pollution. However, adequate collection of biological specimen can be resource-intensive. Further, biomonitoring does not give any information on the relative importance of different exposure pathways, which is of high importance when selecting appropriate actions to minimise exposure. Thus, the methods using internal and external doses are complementary.

1.7 Human biomonitoring (internal dose)

Following the first report of PFCs in human serum in 2001 (Hansen et al. 2001), a large number of studies have been conducted to explore ranges of PFCs in different populations. The pharmacokinetic data on PFCs suggest blood as a suitable sample matrix for monitoring the internal exposure of PFCs (Butenhoff et al. 2006). Both whole blood, plasma and serum have been used for biomonitoring. Whole blood has the advantage of representing the entire circulating fluid, but is impractical from an analytical point of view. A study by Ehresman et al. (2007) showed that whole blood concentrations can be converted to plasma or serum concentrations using a conversion factor of 2. In contrast Kärrman et al. (2006) found mean plasma to whole blood ratios of between 1.1 and 1.4 indicating partial distribution to cellular components. Further, the neutral PFOSA distributed preferentially to the cellular compartment with a plasma-to-whole blood ratio of 0.2.

Elevated serum concentrations have been seen in fluorochemical production workers, with mean concentrations of both PFOS and PFOA in the range of 500 to 7 000 ng/mL (Fromme et al. 2009). Increased PFOA concentrations have also been observed in a population living close to a manufacturing site (Emmett et al. 2006). Further, two Nordic studies have seen elevated concentrations of PFCAs in serum from professional skiwaxers (Freberg et al. 2010;Nilsson et al. 2010). No clear regional differences have been observed for general populations. However, there are indications of lower prevalence of PFCs in low income countries and slightly higher concentrations in North American populations than for European, Asian and Australian populations (Fromme et al. 2009;Kannan et al. 2004). Studies on general European populations report serum

PFOS concentrations in a range from 1 to 116 ng/mL and PFOA concentrations from 0.5 to 40 ng/mL around year 2000 (Fromme et al. 2009).

Several biological factors may influence the body burden of PFCs, including age, gender and ethnicity. An increase of contaminant levels in body fluids with age has been well documented for polychlorinated legacy POPs, such as polychlorinated biphenyls (PCBs) (Laden et al. 1999), however for PFCs, the age dependency seems to be more questionable (Fromme et al. 2009). Differences in blood concentrations of PFOS or PFOA between sexes have been observed in the majority of studies, but the findings are not entirely consistent (Fromme et al. 2009). A study from the US, indicated ethnic differences in PFC body burdens with mean serum concentrations of Mexican Americans lower than for non-hispanic whites (Calafat et al. 2007). Serum concentrations of PFCs are also influenced by other factors e.g. consumption of certain types of food. In a study from Poland, Falandysz et al. (2006) showed that individuals who reported a high intake of fish had higher concentrations of PFCs in their blood than those from who did not report high intake of fish. Results from Denmark showed positive associations between PFOS concentrations in serum and consumption of red meat, animal fat and snacks (Halldorsson et al. 2008).

Animal studies as well as human studies have demonstrated that PFCs can cross the placental barrier and thereby expose the foetus (Apelberg et al. 2007;Hinderliter et al. 2005;Inoue et al. 2004a;Monroy et al. 2008). PFCs have also been detected in breast milk, and in a limited study on 12 primiparous Swedish mothers, PFOS concentrations in breast milk of around 1% of those in serum were found (Kärrman et al. 2007). In a review by Fromme et al. (2009) ranges of PFC concentrations in breast milk from various studies are summarised. The reported concentrations of PFOS ranged from 0.01 to 0.47 ng/mL breast milk, while the concentrations of PFOA varied between 0.05 and 0.61 ng/mL.

1.8 Exposure pathways (external dose)

Humans can be exposed to PFCs via different pathways, as illustrated in Figure 2.
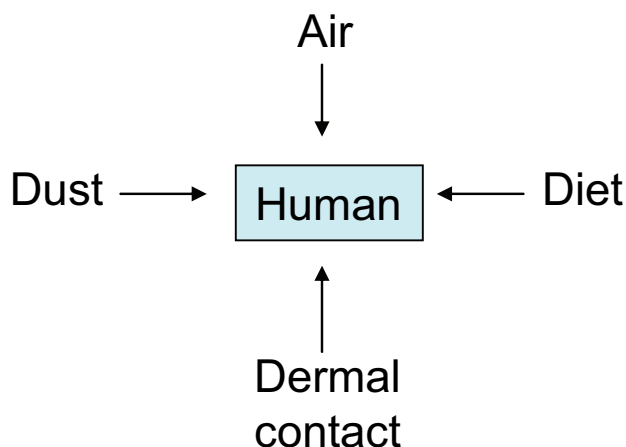
Figure 2. Sketch of possible exposure pathways to PFCs for humans

1.8.1 Exposure through diet

In general, food might be polluted with PFCs present in the environment. Meat etc. can also be contaminated through the domestic animals' feed. Further, it has been demonstrated that PFCs can migrate from food packaging and non-stick cookware which thus represents additional sources of exposure from food (Begley et al. 2005;Sinclair et al. 2007). Both ionic and neutral PFCs have been determined in samples of food as summarised by Egeghy and Lorber (2010), Fromme et al. (2009) and Vestergren and Cousins (2009). Ionic PFCs have in general been found in highest concentrations in samples of fish and shellfish (Ericson et al. 2008;Tittlemier et al. 2007), while the highest amounts of FOSAs have been observed in composite samples of fast food (Tittlemier et al. 2006).

Ionic PFCs have been determined in drinking water from several countries, and concentrations of PFOS and PFOA are usually in the low ng range (Mak et al. 2009). However, higher concentrations have been observed in areas with high industrial activity

10

(Ericson et al. 2009), near facilities manufacturing fluoropolymers (Emmett et al. 2006) and in an area where a contaminated soil conditioner had been applied on agricultural land (Hölzer et al. 2008).

1.8.2 Exposure through ingestion of house dust and inhalation of air

The large historical production volumes and widespread applications of PFCs in consumer products represent a potential for contamination of the indoor environment. Vapour pressures of PFCAs and PFSAs in dissociated forms are expected to be low, thus exposure from air primarily occurs through inhalation of neutral PFCs (Stock et al. 2010). Concentrations of PFCs in indoor air usually exceed the concentrations in outdoor air considerably, and thus indoor air is also suggested to be a source of PFCs in outdoor air (Harrad et al. 2010). Due to the low concentrations in outdoor air, exposure through inhalation of air is mainly through indoor air. Concentrations of PFCs in indoor air have been found to vary a lot between homes, e.g. in a study from Canada a range from 261 to 28 900 pg/m^3 was observed for 8:2 FTOH (Shoeib et al. 2008).

Ingestion of house dust is a potential exposure source for PFCs. In most studies on house dust ionic PFCs have been determined (Harrad et al. 2010), but neutral PFCs have been measured in certain cases as well (Shoeib et al. 2005). As for indoor air, the concentrations in house dust are quite variable. The distribution pattern is often following a lognormal distribution, with some samples having concentrations far exceeding the mean and median values of the dataset (Harrad et al. 2010). Kubwabo et al. (2005) reported concentrations of PFOS in the range 2.3 to 5 065 ng/g dust.

1.8.3 Dermal exposure

Dermal exposure to PFCs can occur through direct contact with consumer products. Three surveys have been conducted in Norway to explore ranges of PFCs in clothing (SFT 2006;Grønn hverdag 2010;Schulze and Norin 2006) and both ionic and neutral PFCs were detected. PFCs have also been found in carpets and textiles (Washburn et al. 2005), waxes and paints (Vejrup and Lindblom 2002;Washburn et al. 2005), food contact materials (Begley et al. 2005) and non-stick cookware (Sinclair et al. 2007). However, as the dermal absorption of ionic PFCs is thought to be low (e.g. the dermal absorption of ammonium perfluorooctanoate was only 0.048% (Fasano et al. 2005)), this pathway is thought to give only a minor contribution to the intake of PFCs.

1.8.4 Total exposure

For traditional POPs, such as dioxins and PCBs, the major exposure route for general populations is through the diet (Liem et al. 2000). However, as PFCs are used in consumer products indoors, the indoor environment could be a considerable source of PFCs in humans. Based on available exposure data from the literature, total intakes as well as relative proportions of the intakes for adults have been modelled for PFOS and PFOA (Egeghy and Lorber 2010;Fromme et al. 2009;Trudel et al. 2008;Vestergren and Cousins 2009). These studies indicate that consumption of food is generally the major source of exposure for background exposed adults. The contribution of precursor compounds (FTOHs, FOSAs and FOSEs) to the exposure of PFOS and PFOA have been evaluated by Vestergren et al. (2008), showing that in an intermediate exposure scenario 2-8% of the PFOS and PFOA exposure is from precursors, while in a high exposure scenario 28-80% of the exposure is from precursors. In these modelling studies, intakes have been calculated based on 2-3 scenarios by changing the concentrations in the exposure medias (e.g. high or low concentration in drinking water) and the exposure factors (e.g. high or low dust ingestion rate). So far, no studies have compared intakes from multiple exposure sources including dust, air and diet on an individual basis.

A breast-fed infant will be exposed to considerable amounts of PFCs during the breast-feeding period in the first months of life. Based on concentrations in Swedish breast milk samples, Kärrmann et al. (2007) estimated the daily intake of PFCs to be approximately 200 ng. However, infants may also ingest considerable amounts of dust by crawling on the floor and by putting toys and other objects in their mouth. In fact, the contribution from dust ingestion was estimated to be about the same as from food ingestion for 2 years old children in a study from the US (Egeghy and Lorber 2010). Thus, exploring multiple exposure pathways for infants is also important.

1.9 Comparison of external and internal doses (intakes vs blood concentrations)

As mentioned previously, exposure assessment using only internal or external doses have some limitations. However, these two methods give complementary information. The validity of the intake calculations can be examined in two ways; by exploring associations between calculated intakes and concentrations of PFCs in blood

using linear regression analyses, or by comparing calculated intakes with intakes back-calculated from serum concentrations using a pharmacokinetic (PK) model. In two studies where individual dietary intakes of PFCs were estimated and compared with corresponding serum concentrations, no significant relationship was found (Fromme et al. 2007;Kärrman et al. 2009). In the same studies, good agreements between intakes calculated using duplicate diet information and back-calculation from serum concentrations using a PK model were observed. In a modelling study by Vestergren and Cousins (2009) the total intake from multiple exposure pathways was compared to back-calculated intakes from serum concentrations. An agreement within a factor of 1.5-5.5 was observed. However, no studies have so far been able to compare biomonitoring data with total intakes from multiple exposure pathways for individuals.

2. AIM OF THE STUDY

The aim of this study was to characterise human exposure pathways of perfluorinated compounds by comparing estimates of exposure from food, drinking water, indoor air and house dust with biomarkers of exposure.

PFCs are present in many consumer products and are known to accumulate through the food chain. The fact that many Norwegians are high consumers of fish (EFSA 2004) and spend a lot of time indoors due to the climate, thus makes evaluation of these exposure pathways particularly important. Further, Norwegian mothers are among the most enthusiastic breast-feeders in the world, and more than 80% of all babies are breast-fed at the age of six months (Andreassen et al. 2001; Häggkvist et al. 2010). Thus, evaluation of the exposure of infants to PFCs through breast-feeding in relation to exposure from the indoor environment is also of particular interest in Norway.

To reach the overall aim, several sub goals were achived:

- High quality analytical methods to measure PFCs in human serum and breast milk were established (**Paper 1 and 5**)
- Temporal changes of PFC exposure in Norway were assessed by measuring PFC concentrations in pooled samples of serum collected over several decades (**Paper 2**)
- Changes in concentrations of PFCs in Norwegian breast milk during the course of lactation were studied (**Paper 5**)
- Concentrations of PFCs in samples of serum (**Paper 2, 4 and 7**) and breast milk (**Paper 5 and 7**) from selected Norwegian populations were determined
- Concentrations of PFCs in selected samples of Norwegian food and beverages were determined (**Paper 3**)
- Ranges of PFCs in paired samples of indoor air and house dust from a variety of Norwegian homes were explored (**Paper 6**)
- Predictors of serum PFC concentrations were identified (**Paper 2, 4, 5 and 7**)
- Dietary intakes of PFCs in selected Norwegian populations were estimated and food groups of main influence identified (**Paper 3, 4 and 7**)

- The PFC exposure through indoor environment, via inhalation of indoor air and dust ingestion, for a group of Norwegians was examined **(Paper 7)**
- Individual intakes of PFCs for selected groups of Norwegians were compared with concentrations of the corresponding PFCs determined in their serum **(Paper 4 and 7)**

3. SUBJECTS AND METHODS

This thesis is mainly based on analyses of samples collected in the BROFLEX study (described below). In addition, we had access to samples from other studies which gave us the opportunity to look further into some aspects related to exposure to PFCs.

3.1 The BROFLEX study

A study group of 41 volunteers from the Oslo area in Norway, hereafter called the 'BROFLEX study group', was established. As we also wanted to evaluate exposure of infants by analysing breast milk, only women were eligible for this study. The BROFLEX study group was restricted in size and geographic area for practical reasons. Colleagues from the Norwegian Institute of Public Health (NIPH) and women in the circle of acquaintances were invited to participate in the study. The study was approved by the Regional Committee for Medical Research Ethics (S-07110a, 2.2007.260). Written informed consent was obtained from all the women.

The following samples/information were collected from each woman/household:

- blood serum ($n = 41$)
- breast milk ($n = 19$)
- indoor air from the women's residence ($n = 41$)
- house dust from the women's residence ($n = 41$)
- a questionnaire ($n = 41$) covering demographic information, different life style factors as well as dietary habits (see Appendix 1, in Norwegian)

In addition, samples of selected food and beverages were collected (see below).
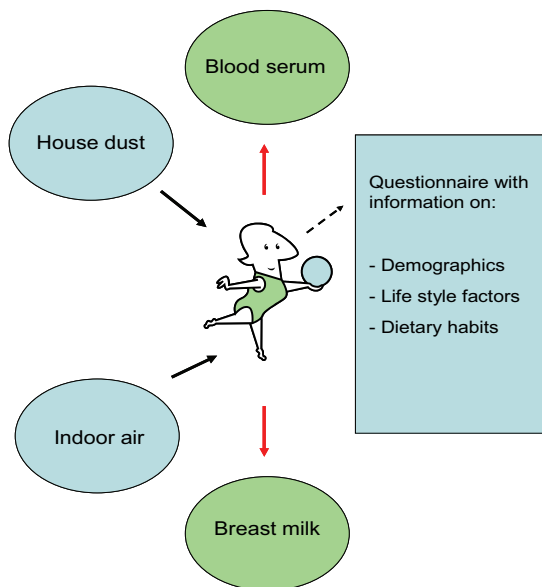
Figure 3. Overview of the individual samples and information collected in the BROFLEX study

3.1.1 Collection of blood serum

Blood was collected either by the womens' general practitioners or a medical laboratory technician at the NIPH. The sampling occurred between August 2007 and May 2008. Whole blood was collected in vacutainer tubes without anticoagulant, allowed to clot by placing in room temperature for 30-120 minutes, centrifuged (2500 rpm) until the serum was separated from the cells, and then the serum was transferred to a polyethylene (PE) container. If blood was drawn by a general practitioner, the serum was sent to NIPH by mail the same day. An amount of 3.5-13 mL of serum was obtained from each woman. The samples were stored below -18 °C until analyses.

3.1.2 Collection of breast milk

All breast-feeding women were encouraged to donate a sample of breast milk. Breast milk was collected by the women themselves. Breast milk was obtained by manual expression into a provided, pre-cleaned PE bottle. The mothers were free to collect the breast milk whenever they liked during the day, and sampling could occur on consecutive days as long as the breast milk was frozen between each sampling. Between 30 and 100

mL breast milk was obtained from the women. The samples were stored below -18 °C until analyses.

3.1.3 Sampling of indoor air and house dust

The vapour pressures of PFCAs and PFSAs in their dissociated form are expected to be very low (Stock et al. 2010), thus these PFCs are expected to be mainly bound to particles. Neutral PFCs have high vapour pressures and are found predominately in the gas phase (Stock et al. 2010). Therefore, only neutral PFCs were determined in the samples of indoor air, and the ionic PFCs in the samples of house dust. Concentrations of the neutral FOSAs/FOSEs were also determined in the samples of house dust, but were observed above the limit of quantification (LOQ) only in a few samples and in low concentrations, as expected.
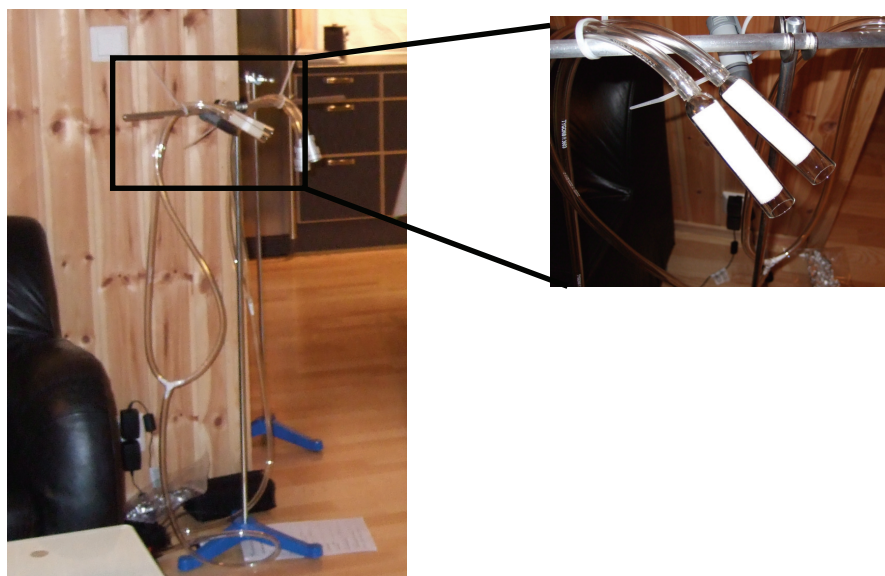
Figure 4. Illustration of sampling of indoor air

The samples of indoor air and house dust were collected between February and May 2008. Airborne PFCs in gaseous and particulate phase were trapped on tubes containing polyurethane foam (PUF)-XAD_2-PUF using low-volume air samplers, as shown in Figure 4. The pump speed was 4 L per minute per tube and the sampling lasted for 24 hours. Two parallel tubes were connected to the pump giving a total volume of 11.52 m^3 air sampled. The samples of air and dust were collected on two consecutive days in the living room, and house dust was collected by the research team at the end of the air sampling period. Deposited dust was sampled from elevated surfaces such as bookshelves and window sills. The samples were collected using a vacuum cleaner equipped with a special forensic nozzle with a one-way filter housing placed in front of the vacuum cleaner tube (see Figure 5).

Figure 5. Illustration of sampling of house dust

The air sampler tubes as well as the filter housing containing the house dust were wrapped in aluminium foil, each sample set packed in a PE bag and stored below -18 °C until analyses. Further information on collection of samples is given in **Paper 6** and Huber et al. (accepted for publication).

3.1.4 Sampling of food and beverages

At the beginning of the BROFLEX study in 2007, the knowledge on concentrations of PFCs in Norwegian food and beverages was very limited. Some data on fish and shellfish were available in reports from the Climate and Pollution Agency (former Norwegian Pollution Control Authority) and the Nordic Council of Ministers (Bakke et al. 2007;Bakke et al. 2008;Fjeld et al. 2005;Fjeld et al. 2009;Green et al. 2008;Kallenborn et al. 2004;Verreault et al. 2007). However, these samples had mainly been collected in costal near areas for environmental surveillance purposes. Thus, as a part of the BROFLEX study we collected samples of selected food and beverages to determine concentrations of PFCs (n=21). Except for drinking water, all samples were bought in grocery stores in the Oslo area. The samples comprised lettuce, carrot, potato, cheese, margarine, milk, bread, strawberry jam, pork meat, beef, chicken meat, egg, fish sticks, canned mackerel, farmed salmon, cod, cod liver, drinking water and tea. With the exception of cod, cod liver and drinking water, homogenates of three different brands or types were prepared. Samples of drinking water (n=3) were collected from the tap in households receiving water from different water works. All homogenates except cod liver, drinking water and tea were freeze dried prior to the analyses. Details on collection and analysis of these samples are given in **Paper 3**.

3.2 Time trend study

We had access to samples from a serum bio-bank established by the Division for Infectious Disease Control at the NIPH. The serum had been sampled from patients at different county hospitals, regardless of disease and the reason for hospitalisation, during the period 1976 to 2007 and stored below -18 °C. Serum from around 20 individuals were included in each pool (except 1997; n=14). The pools representing the years 1976 to 2002 had been prepared previously and used in a previous investigation (Thomsen et al. 2007), while the pools from 2003-2007 were prepared in 2008.

Two sample sets were established:

1. Pools of serum from men 40-50 years of age. One pool was prepared per year (1977, 1980, 1981, 1982, 1983, 1985, 1986, 1988, 1989, 1990, 1991, 1993, 1994, 1995, 1996, 1997, 1999, 2000, 2001, 2002, 2003, 2004, 2005, 2006)
2. Pools of serum from different age groups (e.g. 0-4, 5-14, 15-24 years) and genders collected in four different years (1976, 1987, 1998, 2007)

These samples gave us the possibility of exploring time trends as well as effect of age and gender on PFCs concentrations in Norwegian serum samples covering a period of almost 30 years. Further details on these samples are given in **Paper 2**.

3.3 Depuration rate study

In a study organised by the Department of Analytical Chemistry at the NIPH, nine Norwegian primiparous mothers and one mother breast-feeding her second child collected breast milk samples monthly from about two weeks after birth to up to twelve months (n=70). Each mother collected between 3 and 10 samples. Three mothers sampled breast milk in the period 2001-2003, while six sampled during 2005 and 2006, and one sampled in 2008-2009. Concentrations of PFCs were determined in the breast milk samples (n=68) to evaluate the changes in concentrations of PFCs during the lactation period. Further information on these samples is given in **Paper 5**.

3.4 Norwegian Fish and Game Study

NIPH has in collaboration with the Norwegian Food Safety Authority conducted a dietary survey in three parts, with special focus on consumption of fish and game, which are known to contain high levels of several environmental contaminants, and may thus be important with regard to dietary exposure of such compounds. Details on the Norwegian Fish and Game Study (NFG study) are given by Kvalem (2010). In the NFG study Part C, samples of serum were collected from a group of persons having a large variation in consumption of fish and shellfish. The participants also completed a 12-page food frequency questionnaire (FFQ) covering the consumption over the last 12 months for the

whole diet, in addition to a one-page query about demographic data. Thus, by determining PFCs in these serum samples, we could explore the influence of diet on PFC concentrations in serum in further detail. Results from this study are presented in **Paper 4**.

3.5 Analytical methods

3.5.1 Indoor air and house dust

Methods for sampling and determination of PFCs in indoor air and house dust were established and tested by the Norwegian Institute for Air Research (NILU). The collection of the BROFLEX samples was carried out by NIPH, while the PFC analyses were performed by NILU using liquid chromatography-time of flight-mass spectrometry (LC-TOF-MS) and gas chromatography-mass spectrometry (GC-MS). See **Paper 6** and Huber et al. (accepted for publication) for further information on determination of PFCs in indoor air and house dust.

3.5.2 Food and beverages

Samples of food and beverages were randomly purchased from grocery stores in Oslo by NIPH. All samples except cod liver, drinking water and tea were freeze-dried at NIPH, while MTM at Örebro University performed the PFC determinations according to their own procedures using liquid chromatography-triple quadrupole mass spectrometry (LC-MS/MS). For further details on determinations of PFCs in food and beverages see **Paper 3**.

3.5.3 Serum and breast milk

To accomplish this study, analytical methods for the determination of PFCs in human serum and breast milk had to be established at NIPH. A broad range of perfluorinated compounds likely to be present in human samples, were to be included in the methods. The established methods including results of the validation experiments are further discussed in paragraph 4.1 as well as in **Paper 1** (serum) and **Paper 5** (breast milk).

3.6 Quality control

To assure high quality of the determinations, all real samples (indoor air, house dust, food, drinking water, serum and breast milk) were analysed along with procedural and/or field blanks. No PFCs were observed above LOQ in any of the batches analysed for determinations of PFCs in serum or breast milk. For food and beverages the LOQs were calculated as three times the standard deviation of the method blanks, and none of the samples were thus corrected for PFCs in the blanks. A few PFCs were observed above the LOQs in the blanks analysed together with the samples of indoor air and house dust. Thus the concentrations of these PFCs were corrected by subtracting the mean blank concentrations.

In-house quality control samples were analysed together with the samples of food, serum and breast milk. In addition, the methods were also tested by participation in interlaboratory comparisons (ILC) or by analysing reference samples from previous ILCs. The results of these analyses were found satisfactory, and are presented along with the results in **Paper 1, 2, 3, 4, 5 and 7**. No in-house or external control samples were available for house dust or indoor air. However, the method for determination of PFCs in indoor air and house dust had previously been tested by spiking experiments and had been found adequate (Berger and Haukas 2005;Huber et al. accepted for publication).

3.7 Statistics

SPSS version 17.0 (SPSS Inc. Chicago, IL, USA) was used for the statistical analyses. A significance level of $p = 0.05$ was used. Bivariate correlations were explored using either Pearson Correlation or Spearman's Rank Correlation depending on the distribution of the data sets **(Paper 2, 4, 6 and 7)**. In the time trend study **(Paper 2)** the influence of sex on the concentrations of PFCs in serum was assessed using a paired sample t-test. Multiple linear regression (MLR) analyses were performed to identify predictors of PFCs in serum (**Paper 4 and 7**), indoor air or house dust **(Paper 6)**, as well as for assessing the relationship between estimated intakes and concentrations of PFCs in serum **(Paper 4 and 7)**. To estimate the slope of the concentrations over time in the study on depuration rates **(Paper 5)**, we used linear mixed effect models. Further details related to the statistical methods used are given in the papers **(Paper 2, 4, 5, 6 and 7)**.

3.8 Intake calculations

In this thesis, intakes have been estimated from consumption of food and drinking water, ingestion of dust and inhalation of indoor air. Dietary intakes have been estimated for up to ten PFCs, while intake calculations from ingestion of dust and inhalation of air have been performed only for PFOS and PFOA. For all intake estimates 100% absorption was assumed.

3.8.1 Dietary intakes

Dietary intakes have been estimated in three populations **(Paper 3, 4 and 7)** presented in this thesis. In Paper 3, only PFC concentrations measured in food and beverages collected in the BROFLEX study were used. These concentrations were combined with consumption data for the Norwegian general adult population from the NORKOST study (Johansson and Solvoll 1999). Dietary intakes for ten PFCs were estimated using consumption data for adults in general, and in addition intakes divided by sexes and three age groups (16-29, 30-59, 60-79 years) were also explored. For the NFG study, individual intakes of PFOS, PFOA and PFUnDA were estimated for all participants using information from the FFQ as well as all available information on PFC concentrations in Norwegian food and beverages (Bakke et al. 2007;Bakke et al. 2008;Fjeld et al. 2005;Fjeld et al. 2009;Green et al. 2008;Kallenborn et al. 2004;Verreault et al. 2007;**Paper 3**). Due to limited data on concentrations of the other PFCs in Norwegian food and beverages, calculations were limited to these three PFCs. Similar calculations were performed for PFOS and PFOA, for the women in the BROFLEX study group.

3.8.2 Intakes from ingestion of dust

Intakes of PFOS and PFOA through dust ingestion were calculated on an individual basis for the women in the BROFLEX study group using the concentrations of PFCs determined in their house dust and dust ingestion rates found in the literature. Harrad et al. (2010) have pinpointed the high uncertainty in dust ingestion rates published, as studies so far primarily have been designed for deriving soil ingestion rates (Stanek et al. 1997;Stanek and Calabrese 1995). Thus, we decided to use three different scenarios, assuming dust ingestion rates of either 50, 100 or 200 mg/day (US EPA 1997).

3.8.3 Intakes from inhalation of indoor air

For individual intakes of PFOS and PFOA from inhalation of indoor air, only biotransformations of FOSA/FOSEs to PFOS and FTOHs to PFOA have been considered. Similarly to ingestion of dust, we decided to establish intakes based on three scenarios using different biotransformation factors. The intakes were calculated by multiplying the sum FTOH or sum FOSA/FOSE concentrations with the respective biotransformation factor and inhalation rate. In accordance with Vestergren et al. (2008) factors of 0.01 (scenario 1), 0.2 (scenario 2) and 1 (scenario 3) were chosen for the biotransformation of FOSA/FOSEs to PFOS while 0.0002 (scenario 1), 0.005 (scenario 2) and 0.017 (scenario 3) were used for the biotransformation of FTOHs to PFOA. Similar to Egeghy and Lorber (2010), inhalation rates of 13.3 and 6.8 m^3 air per day were used for the women and infants, respectively.

3.8.4 Intakes through consumption of breast milk

Individual intakes through consumption of breast milk were calculated by multiplying the breast milk concentrations with a daily consumption of 700 mL breast milk.

3.8.5 Total intakes for the women

Three total intakes were calculated per individual, based on different scenarios. Due to high uncertainty regarding dust ingestion rates and biotransformation factors, three different exposure scenarios were established both for dust ingestion and inhalation of air. Intakes from food and drinking water were regarded as sufficiently certain, thus only one intake was calculated per individual for these exposure sources.

The three following total intakes were estimated:

- S1 (Total intake scenario 1): intake $_{food}$ + intake $_{drinking\ water}$ + intake $_{dust\ (scenario\ 1)}$ + intake $_{air\ (scenario\ 1)}$
- S2 (Total intake scenario 2): intake $_{food}$ + intake $_{drinking\ water}$ + intake $_{dust\ (scenario\ 2)}$ + intake $_{air\ (scenario\ 2)}$
- S3 (Total intake scenario 3): intake $_{food}$ + intake $_{drinking\ water}$ + intake $_{dust\ (scenario\ 3)}$ + intake $_{air\ (scenario\ 3)}$

3.8.6 Total intakes for the infants

Norwegian governmental authorities recommend exclusive breast-feeding the first half year (Norwegian Directorate of Health 2008), and more than 80% of all babies are

breast-fed at the age of six months (Andreassen et al. 2001;Häggkvist et al. 2010). Further, at this age infants may also ingest considerable amounts of dust by crawling on the floor and by putting toys and other objects in their mouth. Thus, for exposure of infants we chose to assess children six months of age, and included consumption of breast milk, ingestion of dust and inhalation of indoor air. Similarly to the total intakes for the women, three total intakes were calculated. The intake from breast milk consumption was identical for all three intakes. The same biotransformation factors and dust ingestion rates as for the women were used, while the inhalation rate was half of that for adults.

The three following total intakes were estimated:

- S1 (total intake scenario 1): intake $_{breast\ milk}$ + intake $_{dust\ (scenario\ 1)}$ + intake $_{air\ (scenario\ 1)}$
- S2 (total intake scenario 2): intake $_{breast\ milk}$ + intake $_{dust\ (scenario\ 2)}$ + intake $_{air\ (scenario\ 2)}$
- S3 (total intake scenario 3): intake $_{breast\ milk}$ + intake $_{dust\ (scenario\ 3)}$ + intake $_{air\ (scenario\ 3)}$

3.9 Comparisons between external and internal dose using PK modelling

The measured serum concentrations were compared with concentrations calculated from the total daily intakes using a first-order PK model as described by Egegy and Lorber (2010). In this model, the blood serum concentration is predicted as a function of dose, elimination rate and volume of distribution (i.e. the total amount of a PFC in the body divided by its concentration in the serum). This model is only applicable under steady state conditions, which was assumed. The dose was set to the total intakes of PFOS and PFOA (scenario 1, 2 and 3) in ng/kg bw/day. Elimination half-lives of 4.8 years (Olsen et al. 2007) and 2.3 years (Bartell et al. 2009) were applied for PFOS and PFOA, respectively, while the volumes of distribution were set to 220 mL/kg for PFOS and 140 mL/kg for PFOA, according to Andersen et al. (2006).

4. RESULTS AND DISCUSSIONS

4.1 Methods for determination of PFCs in serum and breast milk

In recent years several reviews have been published summarising methodologies for determination of PFCs (de Voogt and Saez 2006;Martin et al. 2004;van Leeuwen and de Boer 2007;Villagrasa et al. 2006). The first compound specific method for determination of PFCs in human serum was published by Hansen et al. (2001). This method included addition of an ion-paring agent to serum, extraction with methyl-tert-butylether, filtration and determination using liquid chromatography – tandem mass spectrometry in negative electrospray ionisation mode (ESI). This sample preparation method was time consuming, laborious and difficult to automate (van Leeuwen and de Boer 2007). Much effort has been used in the field, to develop more efficient methods which required less manual handling. This has resulted in development of methods using off-line solid phase extraction (SPE) (Kärrman et al. 2005;Kuklenyik et al. 2004), as well as methods using column switching LC-MS/MS (Holm et al. 2004;Inoue et al. 2004b;Kuklenyik et al. 2005). The methods using column switching LC-MS/MS are advantageous as they require a minimum of manual handling and are fast and were thus used as a starting point for developing a method for determination of PFCs in human serum. The method developed for serum was then modified to be applicable for breast milk. We were aiming at developing methods which were accurate, precise, fast and required small amounts of sample. These criteria were used as a basis for the method development process.

At our laboratory we had access to a standard column switching LC-MS/MS. Berger et al. (2004) compared three types of LC-MS instruments for analysis of PFCs, and concluded that LC-MS/MS instruments operated in negative ESI mode were suitable for determination of PFCs. One of the major advantages of that method is the opportunity to use MS/MS technology and multiple reaction monitoring (MRM) (Berger et al. 2004). Our aim was to establish a serum method comprising the following PFCs; PFBS, PFHxS, PFHpS, PFOS, PFDS, PFBA, PFPeA, PFHxA, PFHpA, PFOA, PFNA, PFDA, PFUnDA,

PFDoDA, PFTrDA, PFTeDA, PFOSA, MeFOSA, EtFOSA, MeFOSE and EtFOSE. The method for breast milk was limited to PFCs which had been found in considerable concentrations in human serum (i.e. PFOA, PFNA, PFDA, PFUnDA, PFHxS, PFHpS and PFOS).

The method development started with optimisation of MS parameters to achieve high sensitivity of all PFCs in both selective ion monitoring (SIM) mode and MRM mode. MeFOSE and EtFOSE had low sensitivity in both SIM and MRM mode and were thus left out of the method. Further, we discovered that the sensitivity of PFSAs and FOSAs were not sufficient in MRM mode. An approach called 'pseudo MRM' was then explored (Andreoli et al. 1999). With this 'pseudo MRM' technique, the parent ion is measured after application of a fragmentation voltage leading to fragmentation of interfering species but not the analyte. The experiments resulted in higher responses of both PFSAs and FOSAs, and thus, the 'pseudo MRM' approach was used for these compounds.

As an initial step in the pre-treatment of serum, proteins are usually removed by precipitation using organic solvents such as acetonitrile (Holm et al. 2004;Inoue et al. 2004b) or organic acids like formic acid (Kärrman et al. 2005). However, Kuklenyik et al. (2005) developed a method where no protein precipitation was required. The serum was just diluted with 0.1M formic acid. In our initial experiments with sample matrix, we tried this approach, but observed that the back-pressure on the SPE column increased between each injection and had to be replaced very frequently. This problem was solved by precipitation of the proteins using methanol prior to injection on the column-switching LC-MS/MS system. Also for precipitation of proteins in breast milk, organic solvents and organic acids have been used (Kärrman et al. 2007;Völkel et al. 2008), but enzymatic hydrolysis of proteins has also been applied (Mosch et al. 2010). We found that the proteins in breast milk were not completely precipitated using methanol, and thus a stronger precipitation agent, acetonitrile, was used. This was the major modification of our serum method to be applicable for analysing breast milk.

Background contamination of PFCs both from instruments and the laboratory in general was identified as one of the major problems related to determinations of PFCs at an early stage (Martin et al. 2004;Villagrasa et al. 2006). Such problems were avoided in our methods by minimising sample handling and by installing a Hypercarb guard column

between each of the LC pumps and the switching valves (Flaherty et al. 2005;Powely et al. 2005).

Thorough validations of the methods for determination of PFCs in both serum and breast milk were carried out. The methods were found to have comparable or higher sensitivity than what have been reported elsewhere (Hansen et al. 2001;Holm et al. 2004;Inoue et al. 2004b;Kärrman et al. 2005;Kärrman et al. 2010;Kuklenyik et al. 2005;So et al. 2006;Tao et al. 2008b;Völkel et al. 2008). The procedural blanks did not contain any of the PFCs above the LOQ. Further, the validation experiments proved the methods to have sufficient linearity, repeatability and accuracy. The methods have also been applied in several ILCs with satisfactory results (results are presented in **Paper 1, 2, 4, 5, and 7**)**.** The methods developed were thus found to be applicable for determination of a broad range of PFCs in serum and breast milk. Further, due to the limited manual handling the methods are appropriate for use in large-scale investigations comprising many samples.

4.2 Internal dose of PFCs

4.2.1 Concentrations in serum

Concentrations of PFC in serum have been explored in **Paper 2, 4 and 7.** In 2007 when the BROFLEX study began, no information on body burdens of PFCs in Norwegians was available, except for a limited study on twelve serum samples from women living in Northern Norway (Odland et al. 2005). During this project, concentrations of PFCs in serum from Norwegians have been measured in three study groups **(Paper 2, 4 and 7)**. First, we conducted a study to explore changes in serum concentrations over a time span of around 30 years **(Paper 2)**. In the NFG study group, we determined concentrations of PFCs in individual samples of serum from men and women between 18 and 79 years with a wide range of seafood consumption, sampled in 2003 **(Paper 4)**. The third study group comprised samples of serum from the 41 women in the BROFLEX study (age 25-46 years), collected between August 2007 and May 2008 **(Paper 7)**. In Figure 6, concentrations of the eight most prominent PFCs found in these samples are presented by year of sampling. For the time trend study, the pools of serum from women and men, 25 years of age and above, are shown in the Figure. Both for the

29

NFG samples (red squares) and the BROFLEX samples (green circles), the mean value of all samples is presented.

As can be seen in Figure 6, the PFC concentrations in serum increased from 1976 until the mid 1990s where they stabilized. For several PFCs decreasing concentrations were observed from around 2000. These trends are in accordance with the increasing production of PFCs until the phase-out of certain compounds starting in 2000 (Stock et al. 2010). No clear decline was observed for the long chain PFCAs (i.e. PFNA, PFDA, PFUnDA). This could be due to longer half-lives of these PFCs or differences in use. The concentrations of PFCs determined in the NFG study and the BROFLEX study fit well into the time trends (see Figure 6), and support the results obtained from the pooled samples in the time trend study. In a paper by Vestergren and Cousins (2009) our time trend data for PFOA, PFNA and PFOS are presented together with data from three US studies, showing similar trends. Also in a recent study on Swedish breast milk, similar temporal changes were observed for PFHxS, PFOS and PFOA (Sundström et al. 2011). In contrast, the PFC concentrations in Australian serum did not change considerably from 2002/2003 to 2006/2007 (Toms et al. 2009).

Six PFCs were found in all serum samples from both the NFG study and the BROFLEX study, i.e. PFOA, PFNA, PFDA, PFUnDA, PFHxS and PFOS. In these two studies and also in the time trend study the highest concentrations (in decreasing order) were observed for PFOS, PFOA, PFHxS and PFNA. The concentrations were in the range 1.8 - 133 ng/mL for PFOS, 0.28 – 22 ng/mL for PFOA, 0.053 - 14 ng/mL for PFHxS and < 0.050 - 4.3 ng/mL for PFNA. This is similar to what has been seen in other studies on general populations world-wide (Fromme et al. 2009;Houde et al. 2006;Lau et al. 2007;Vestergren and Cousins 2009) as well as in two other recent Norwegian studies (Rylander et al. 2009;Rylander et al. 2010).

The PFCs in serum from all three study groups included in this thesis were strongly intercorrelated. Correlations were observed within the PFCAs and the PFSAs, but also between those two groups of PFCs. Similar associations have also been seen in other studies world-wide (Kannan et al. 2004;Olsen et al. 2003). As stated by Olsen et al. (2003), PFCAs and PFSAs can not be converted directly into each other, thus correlations between these groups point to common sources of human exposure to these two PFC classes.
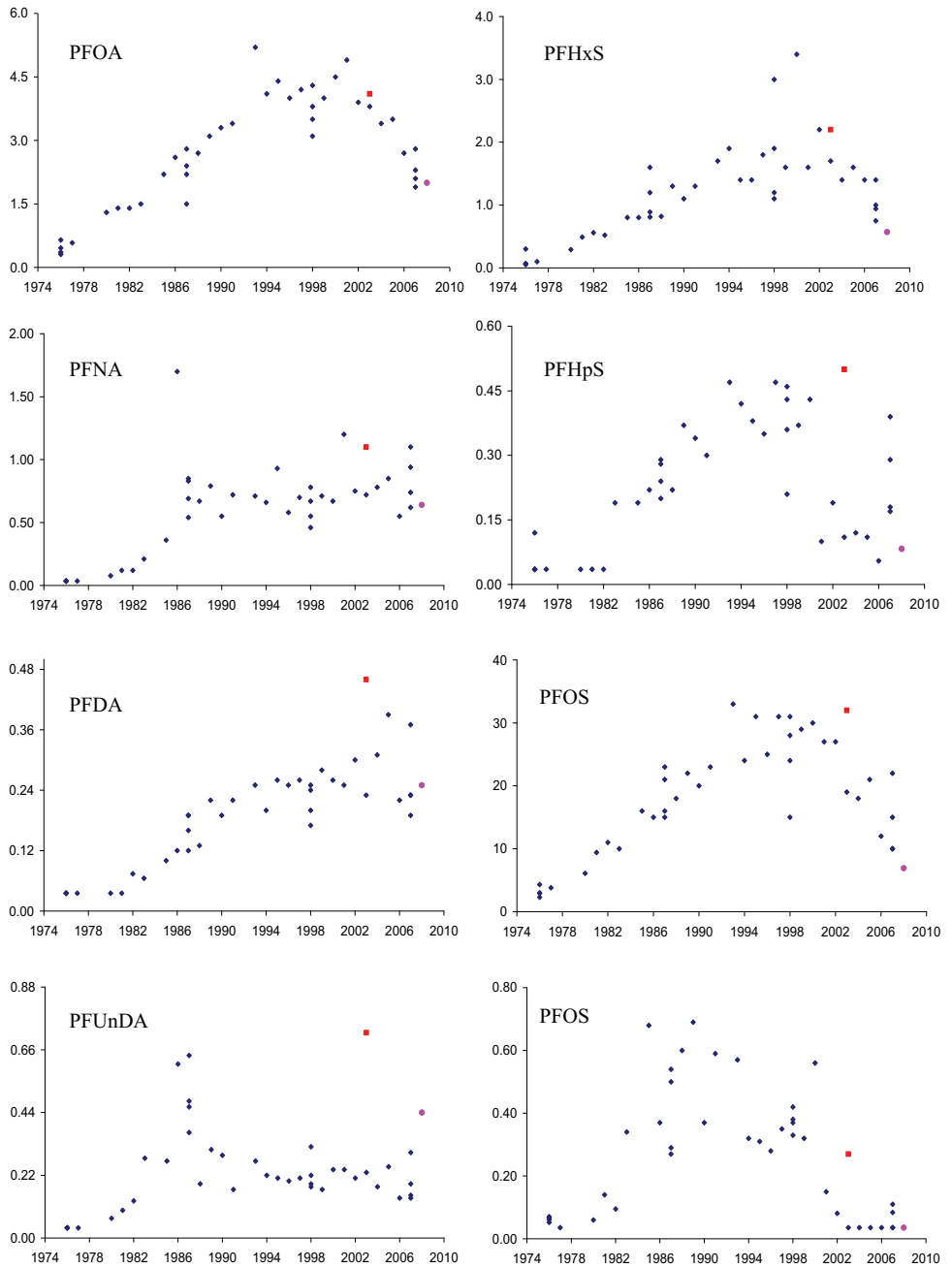
Figure 6: Concentrations of selected PFCAs and PFSAs in serum (y-axis; ng/mL) from the time trend study (pools of men and women ≥ 25 years of age), the NFG study (mean, red squares) and the BROFLEX study (mean, pink sircles) presented by year of sampling (x-axis; year)

The majority of the serum samples in the NFG study, had previously been analysed to determine PCBs and polybrominated diphenyl ethers (PBDEs). Strong relationships between concentrations of PFCs and PCBs were observed, while significant but weaker associations were seen between PFCs and PBDEs. This is in accordance with findings by Daillare et al. (2009). The strong associations between PFCs and PCBs were somewhat surprising, as in contrast to PCBs, PFCs do not accumulate in lipids and have thus been expected to behave differently. However, these findings indicate that the main exposure to PFCs occurs through the same pathways as for PCBs, while other sources may be important for the PBDEs.

4.2.2 Concentrations in breast milk

Concentrations of PFC in breast milk have been examined in **Paper 5** and **Paper 7.** Only PFOS and PFOA were found above LOQ in the samples. The PFOS concentrations were in the range 0.028 - 0.25 ng/mL breast milk, while the corresponding range for PFOA was <0.018 - 0.83 ng/mL breast milk. PFCs have not been previously determined in Norwegian breast milk samples, but the concentrations found are similar to what has been reported in other studies (Fromme et al. 2009;Fromme et al. 2010;Kärrman et al. 2010;Kim et al. 2011;Llorca et al. 2010;Roosens et al. 2010;So et al. 2006).

In paired samples of breast milk and serum from 19 women in the BROFLEX study, linear relationships with correlation coefficients (R^2) of 0.63 for PFOS and 0.99 for PFOA were observed. Further, the concentrations of PFOA and PFOS in breast milk were found to be 3.8 and 1.4% of the serum concentrations on volume basis, respectively. Also in two studies from Sweden (*n*=12) and Germany (*n*=44) positive correlations between concentrations of PFOS in serum and breast milk were observed, and around 1% the concentrations in serum were found in breast milk (Fromme et al. 2010;Kärrman et al. 2006). In a study from Korea (*n*=17), no significant relationships between concentrations of PFCs in breast milk and serum were observed (Kim et al. 2011). However the concentrations of PFOA and PFOS in breast milk were 3.4 and 0.5% of the serum concentrations, respectively. Despite the limited number of samples included in all these studies, the relative proportions of PFOS and PFOA in breast milk in relation to serum are similar.

Predominantly breast-fed infants consume a relatively high volume of breast milk daily. Thus, a considerable amount of the women's body burden of PFCs can be presumed to be eliminated during the course of lactation, even though the concentrations of PFCs in breast milk are low. Therefore the concentrations of PFCs in breast milk are expected to decrease during the lactation period. To verify this, concentrations of PFCs in samples from the depuration study were determined, and depuration rates calculated using linear mixed effect models. We found that the concentrations of PFOS and PFOA decreased significantly with around 3.8 and 7.8% per month of lactation. In a German study, breast milk was collected by mothers on a monthly basis in five months, but no significant downward trend was observed for PFOS in these samples (Fromme et al. 2010). The detection frequency of PFOA in that study was only 2%, thus no trends could be explored. The discrepancy between our study and the German study could be due to the low number of women included in both studies, as well as possible differences in breast-feeding frequency and sampling strategy. According to our models the reduction in PFOS concentration during five months would only be around 20%, thus the choice of statistical methods as well as the analytical precision may also influence the findings.

4.2.3 Isomers of PFOS

When using the ECF process for manufacturing, the PFC-products contain branched isomers (Kissa 2001). In this thesis, the relative contribution of branched PFOS isomers to the total amount of PFOS has been determined in serum samples from the time trend study **(Paper 2)** and the BROFLEX study **(Paper 7)**, as well as in breast milk from the depuration rate study **(Paper 5)** and the BROFLEX study **(Paper 7)**. In Table 2 is presented the mean and ranges of the relative proportion of branched PFOS isomers in the samples.

Table 2. Relative proportion of branched PFOS isomers (%) in samples of breast milk and serum (mean and ranges)

Study	Relative proportion of branched PFOS isomers, %		
	Min	Max	Mean
Serum, time trend study	22	47	32, 36, 40 and 43*
Serum, BROFLEX study	14	50	22
Breast milk, depuration rate study	6	36	18
Breast milk, BROFLEX study	9	29	17

* Mean of pools collected in 1976, 1987, 1998 and 2007

Overall, the relative proportions of branched PFOS isomers were in the range 6-50% of the total PFOS concentrations in the samples. In the time trend samples, the relative proportion of branched PFOS isomers increased from 1976 to 2007. The reason for this is not known, but in **Paper 2** we speculated if this could be due to changes in PFC usage during these years or differences in half-lives between linear and branched PFOS isomers. However, recent research has shown that branched PFOS isomers have shorter half-lives than linear PFOS (Benskin et al. 2009), thus increasing proportions of branched PFOS isomers during the period 1976 to 2007 could not be explained by differences in half-lives. Benskin et al. (2009) have postulated a hypothesis that isomer specific biotransformation rates of PFOS-precursors may explain the common observation of enrichment of the branched PFOS isomer profiles in humans. This remains to be confirmed.

The serum samples from the time trend study had a higher mean proportion of branched PFOS isomers than observed in the BROFLEX serum samples. However the min-max ranges were similar. The difference in mean values remains to be clarified. Similar ranges and mean values were found for the two sets of breast milk samples, and no statistical difference was seen between serum and breast milk samples in the BROFLEX study. The relative amounts of branched PFOS isomers in serum and breast milk were independent of the concentrations.

4.2.4 Predictors of serum concentrations

Predictors of serum PFC concentrations have been studied in **Paper 2, 4, 5 and 7.**

Age, gender and breast-feeding history

In the time trend study we examined the impact of age and gender on the concentrations of PFCs in four different years (1976, 1987, 1998 and 2007). No significant differences between genders were observed. Significant correlations between age and concentrations of most PFCs were seen in the samples from 2007, while the results for the other years were more variable. Strongest associations were observed for the PFCs with the longest carbon chains. In the time trend study, no additional information about the subjects, which may influence the serum concentrations, was available. In the NFG study and the BROFLEX study MLR analyses were performed to identify predictors of serum PFC concentrations. This statistical approach has the

advantage of being able to explore effects of several variables at the same time. In the NFG study both men and women were included, and the ages ranged from 18 – 79 years. Further, we had extensive information on the participants' dietary habits the last 12 months as well as demographic data. We found an effect of age on all PFCs, when adjusting for the other predictors of serum PFC concentrations. In contradiction, a significant association between PFC concentration and age was observed only for PFOA in the BROFLEX study. However, this might be due to the narrow age span for the women in this study group (25-46 years). The BROFLEX study group comprised only women, thus differences between genders could not be explored. Gender was included as a variable in the MLR models for the NFG study, but was not significant. This might be due to the associations to breast-feeding history which probably also explain the variation due to sex differences. Scientific papers on the effect of age and gender on concentrations of PFCs in serum are not consistent (Lau et al. 2007), and lack of appropriate information might be one reason for that.

Finding breast-feeding history as a significant predictor of PFC concentrations in the NFG study was somewhat surprising, as most of the women had not been breast-feeding for many years. This might indicate that the influence of breast-feeding on PFC concentrations in serum is high. This was confirmed in the BROFLEX study, where previous breast-feeding was a significant and strong predictor of all PFC concentrations in serum, except for PFUnDA. Time since previous breast-feeding gave the strongest effect, but duration of breast-feeding also influenced the PFC serum concentrations significantly. These findings are supported by the decreasing concentrations of PFCs in breast milk during the course of lactation, seen in the depuration rate study. In a study from the Danish national birth cohort, the duration of breast-feeding decreased with increasing concentrations of PFOS and PFOA in serum during pregnancy (Fei et al. 2010). Thus, the authors suggested that increased concentrations of PFOS and PFOA may reduce the ability to lactate. However, as these associations were not observed for primiparous women, they reported that a reverse causation might be possible, with lower PFC concentrations in the multiparous women who have breast-feed previous infants for a long period of time. Our findings of decreasing PFOS and PFOA concentrations in breast milk during the course of lactation, support the explanation of a reverse causation.

The NFG study was designed to evaluate the effect of diet, particularly fish and shell fish, on concentrations of environmental contaminants in serum. The serum concentrations of several PFCs were significantly associated with consumption of fish liver, lean fish and shrimps. The range between min and max consumption of various fish species was much smaller in the BROFLEX study e.g., NFG study; 0-8 g fish liver consumed per day while in the BROFLEX study 0-0.22 g fish liver was consumed per day. Nevertheless, associations between concentrations of some PFCs in serum and consumption of fish liver and shell fish were seen in the BROFLEX study as well. Seafood has also been identified as a predictor of serum PFC concentrations in other studies (Falandysz et al. 2006;Rylander et al. 2009;Rylander et al. 2010;Weihe et al. 2008). In the NFG study, also significant correlations between consumption of meat and concentrations of PFNA, PFDA, PFHpS and PFOS in serum were found. This is in agreement with results from the Danish national birth cohort, where red meat was identified as a determinant of PFOS and PFOA concentrations in plasma (Halldorsson et al. 2008). In another Danish study, frying as compared to cooking was identified as a predictor of PFOS and PFOA concentrations in plasma (Eriksen et al. 2010). We did not have access to information on processing methods for foods, and thus we were not able to examine this in our studies. Egg was also identified as a predictor of PFC concentrations in plasma in the Danish study (Eriksen et al. 2010), but this was neither seen in the NFG study nor the BROFLEX study. Seafood and meat are generally the food groups with highest concentrations of PFCs (Ericson et al. 2008;Tittlemier et al. 2007; **Paper 3**), thus our findings of these food groups being important predictors of serum PFC concentrations, are reasonable.

Area of residence

In the NFG study, the participants were recruited from both coastal and inland municipalities, and the serum PFC concentrations were found to be significantly higher in persons living in coastal municipalities as opposed to inland municipalities. Further investigation showed a higher frequency of eating self-caught fish in the coastal areas, and this coast-near fish is supposed to have higher concentrations of PFCs than fish caught in the open sea. Thus, the difference in serum PFC concentrations between costal

and inland counties might be due to different contamination levels of the seafood eaten, rather than the place of residence itself. In a recent Danish study, significant differences in PFOS and PFOA plasma concentrations between living in Copenhagen or living in Aarhus were seen (Eriksen et al. 2010). In this study differences in contamination of air and drinking water was suggested to be an explanation for the differences, in addition to possible variations in lifestyle.

Indoor environment

The BROFLEX study was designed to investigate relationships between concentrations of PFCs in serum and indoor air and house dust. Significant positive associations were seen for PFHxS and PFOA, and a similar tendency was also seen for PFOS, however statistically significance was not reached. This is the first study to explore relationships between concentrations of PFCs house dust and serum, thus no comparison with literature is possible. In the NFG study, where we modelled the influence of diet on PFC concentrations in serum, the lowest explained variances in the MLR models were obtained for PFOA and PFHxS. This might be due to house dust being a more important source of exposure for PFOA and PFHxS than for the other PFCs. This is in accordance with finding the strongest positive associations between serum and house dust concentrations for PFHxS and PFOA.

Concentrations of ionic PFCs in air are expected to be low (Egeghy and Lorber 2010), thus only neutral PFCs were determined in indoor air. As FOSA/FOSEs may be biotransformed to PFOS (Tomy et al. 2004), we explored the associations between FOSA/FOSEs in indoor air and PFOS in serum, but found no significant relationships. Correspondingly, biotransformation of FTOHs to PFOA can be expected (Nabb et al. 2007), but no relationships between FTOHs in indoor air and PFOA in serum were seen. This may indicate that ingestion of house dust affected the serum concentrations to a larger extent than inhalation of indoor air. However, the relationships between serum and indoor air involves biotransformation of 'precursors' in air to ionic PFCs in serum, and thus associations are more complex and maybe more difficult to observe.

4.3 External dose of PFCs

4.3.1 Exposure through diet

Exposure to PFCs through consumption of food and drinking water has been assessed in **Paper 3, 4 and 7**.

Concentrations in food and beverages

Concentrations of a wide range of PFCs were determined in 21 samples of Norwegian food and beverages. The concentrations of the ten most prominent PFCs are illustrated in Figure 7. Unlike other studies, a wide range of PFCs were detected in the samples, probably due to the high sensitivity obtained using the applied method. Both PFOS and PFOA were detected in almost all food samples, in the range 0.17 to 310 pg/g fresh weight. The concentrations of PFOS and PFOA varied between <0.030 to 9.5 ng/L for drinking water and tea. The highest PFC concentrations were found in the samples of fish, meat and egg, which are in accordance with findings in other studies (Ericson et al. 2008;Tittlemier et al. 2007).

The concentrations found are similar or lower than what has been reported in other studies (e.g. Bakke et al. 2007;Berger et al. 2009;Clarke et al. 2010;Del Gobbo et al. 2008; D'Hollander et al. 2010a; Ericson et al. 2008;Jogsten et al. 2009;Mak et al. 2009;Nania et al. 2009;Ostertag et al. 2009a;Tittlemier et al. 2007;van Leeuwen et al. 2009). Factors that could explain differences among studies could be geographical as well as temporal differences in use of PFC containing products, analytical methodology and sensitivity in the measurements of PFCs in food.
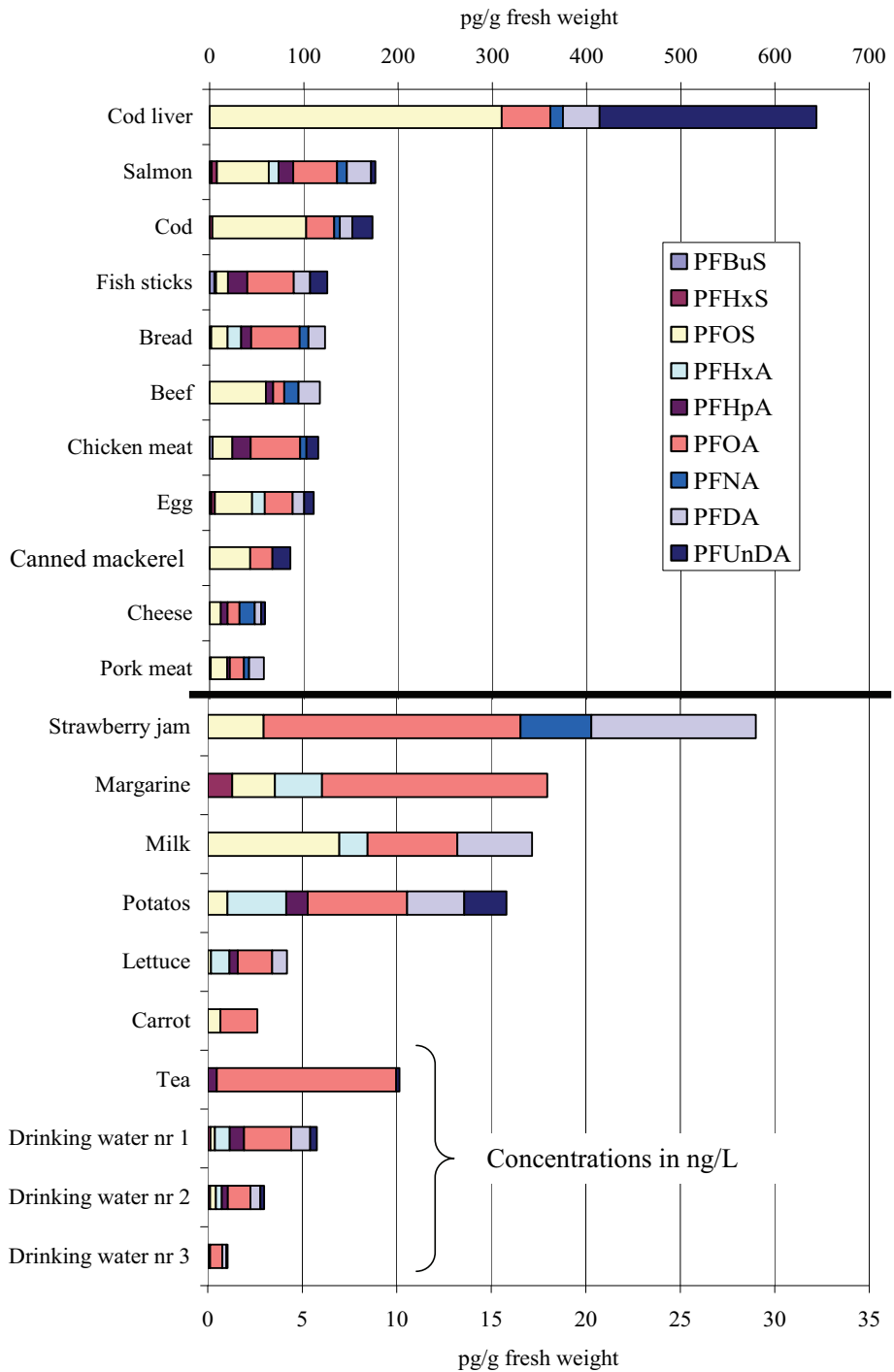
Figure 7. Concentrations of PFCs in samples of food and beverages presented in Paper 3

In Figure 8 dietary intakes of PFOS and PFOA estimated in **Paper 3, 4 and 7** are presented. The intakes in these three populations are not directly comparable as different FFQs have been used. In addition, only the PFC concentrations in food and beverages determined within this thesis have been used for the NORKOST intakes.
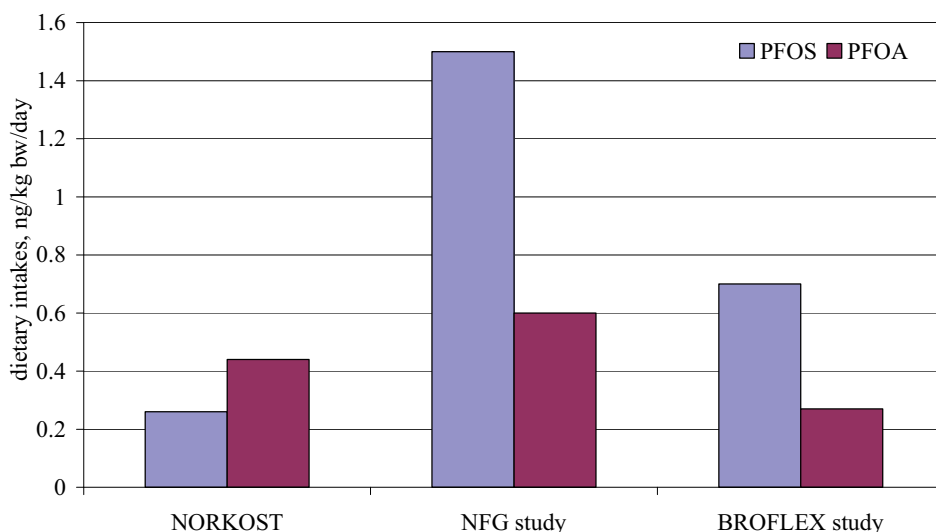
Figure 8. Dietary intake estimates for PFOS and PFOA from Paper 3, 4 and 7

The mean PFOS intakes varied between 0.26 and 1.5 ng/kg bw/day, while the mean PFOA intakes were in the range 0.24 - 0.60 ng/kg bw/day, when assuming a body weight of 70 kg (**Paper 3)**.

The dietary intakes estimated using NORKOST data were also divided by sex and age groups. Due to differences in amounts of various foods consumed, decreasing intakes were observed with increasing age, and higher intakes were estimated for males than for females. In contradiction to this, no age dependency was seen in a study by Ericsson et al. (2008). A significant difference in PFOS intakes between men and women was also observed in the NFG study, with mean intakes of 1.8 and 1.3 ng/kg bw/day, respectively. The PFOA and PFUnDA intakes were similar among men and women. The relative proportions of intakes from various food groups were assessed both in the NFG study and by using NORKOST data. In the NORKOST population fish and shellfish represented

40

only 8 and 19% of the total intakes of PFOA and PFOS, respectively. In the NFG study population fish and shellfish were the largest contributors to the PFOA and PFOS intakes, counting for 38 and 81% of the total intakes, respectively (see Figure 9). One plausible explanation for this difference is lower concentrations of PFCs in the samples of fish used in **Paper 3** than in **Paper 4** where additional samples were included in the estimations. Consumption of fish and shellfish were identified as significant predictors of serum PFC concentrations in both the NFG study and the BROFLEX study. Thus, a high relative contribution of fish and shellfish to the total PFC intakes as found in the NFG study is likely.
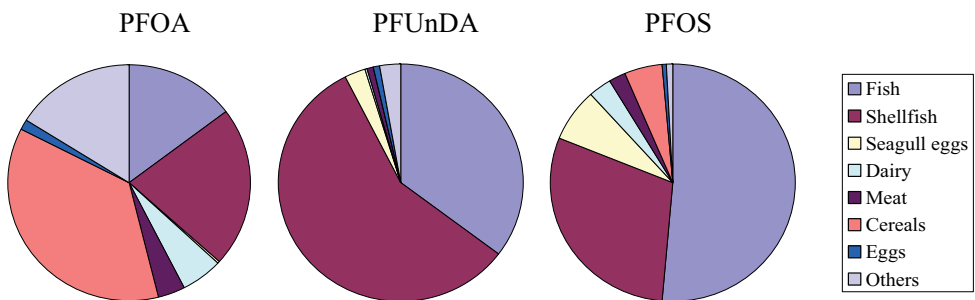
Figure 9. Relative contribution of different food groups to dietary intakes of selected PFCs for the participants in the NFG study

The intakes estimated in the three populations included in this thesis are similar or lower than what has been reported elsewhere (Clarke et al. 2010;Ericson et al. 2008;Fromme et al. 2007;Kärrman et al. 2009;Ostertag et al. 2009a;Ostertag et al. 2009b;Tittlemier et al. 2006;Tittlemier et al. 2007). Several factors may explain differences in estimated intakes; different contamination levels of PFCs in food and beverages, how the non-detects are treated in the data set, as well as different approaches used for intake calculations.

In our studies retrospective dietary assessments has been applied to estimate dietary intakes of PFCs. The intakes were estimated by combining information from FFQs with concentrations reported in food and beverages. Another method used for dietary intake calculation is the duplicate diet approach. In this approach the participants prepare and save identical portions of all consumed food and beverages consumed over a selected period of time. The duplicate diet approach have the advantages of obtaining accurate information on the quantity of food consumed, and the PFC concentrations are

determined in food which is identical to that consumed. However, this method imposes a large effort for the participants, and is very expensive. Thus, for duplicate diet studies collection of food is generally performed for a limited number of days (e.g. 7 days) and will only be representative for this period. Next, determination of PFCs in composite samples of different food types can be challenging due to the complexity of the matrix, and also because of 'dilution' of composites with food containing very low levels of PFCs (Tittlemier et al. 2007). Retrospective dietary assessment methods usually ask about food and beverages consumed in a larger time-span (e.g. 3-12 months back in time) and are advantageous with respect to obtaining information on foods and beverages which are not eaten very frequently. Further, this method gives information on the average dietary habits during an extended period of time, which is important for compounds with long half-lives.

4.3.2 Exposure through indoor environment

Exposure to PFCs through inhalation of indoor air and ingestion of house dust was explored in **Paper 6 and 7**.

Concentrations in indoor air and house dust

Concentrations of a broad range of PFCs were determined in paired samples of indoor air and house dust from the 41 households included in the BROFLEX study. The highest median concentrations of PFCAs in dust were found for PFHxA (28 ng/g), PFNA (23 ng/g), PFDoDA (19 ng/g) and PFOA (18 ng/g), while PFOS (3.1 ng/g), PFDS (1.1 ng/g) and PFHxS (0.60 ng/g) were the predominant PFSAs in dust. With the exception of PFPeA, the median concentrations of all PFCAs observed were higher than for the PFSAs. The concentrations of PFCAs in house dust were more evenly distributed than the PFSAs, where a few samples had considerably higher concentrations than the others (see Figure 1 in **Paper 6**). This was speculated to be due to a greater number of sources of PFCAs than PFSAs in indoor environments.

Compared to other studies, the PFC concentrations in the house dust samples are similar or lower than what has been found elsewhere (Björklund et al. 2009;D'Hollander et al. 2010b;Goosey and Harrad 2011;Huber et al. accepted for publication;Kato et al. 2009;Kubwabo et al. 2005;Moriwaki et al. 2003;Shoeib et al. 2005;Strynar and Lindstrom

2008;Zhang et al. 2010). Variation in PFC concentrations found among studies can be due to different use of products world wide, but as highlighted by Harrard et al. (2010), a variety of sampling strategies for house dust exists, which could influence the measured concentrations. In our study, the research team collected dust using a vacuum cleaner with a filter placed in the front of vacuum cleaner tube. Another commonly used approach is to analyse the content in a vacuum cleaner bag, which is either collected by the household residents or a research team. With respect to the sampling area, we collected dust from all elevated surfaces in the living room once. In some studies, when vacuum cleaner bags have been donated by the households, dust has been collected wherever the vacuum cleaner has been used during the period to fill this bag. The content in a vacuum cleaner bag which has been used for a period of time will give an integrated measure of the PFC concentrations. The approach with researcher collected dust will only reflect the concentrations in the dust collected at a specific point of time. A third approach commonly applied involves sampling of a standardised floor area. Harrard et al. (2010) pinpointed that in general, a systematic procedure for sampling performed by a research team is favourable, and that dust collected from elevated surfaces may reflect the exposure of adult better than dust collected from the floor.

The predominant PFCs in the indoor air were the FTOHs, with highest median concentrations of 8:2 FTOH (5173 pg/m^3), 10:2 FTOH (2822 pg/m^3) and 6:2 FTOH (933 pg/m^3). MeFOSE and EtFOSE were the dominating FOSA/FOSEs with median values of 265 and 78 pg/m^3. FTOHs are usually found in higher concentrations than FOSA/FOSEs in consumer products produced in recent years (Dorte Herzke, personal communication), thus our findings are reasonable. This is also supported by a recent study, where higher concentrations of FTOHs than FOSA/FOSEs were seen in most samples of indoor air collected in various shops selling products potentially containing PFCs (Langer et al. 2010). The concentrations of FTOHs observed in the BROFLEX study are similar to what has previously been found (Barber et al. 2007;Huber et al. accepted for publication;Shoeib et al. 2008), while the concentrations of FOSA/FOSEs generally were lower than reported elsewhere (Barber et al. 2007;Shoeib et al. 2004;Shoeib et al. 2005).

Associations within and between different groups of PFCs were studied in the samples of air and dust, and significant correlations were found within the group of PFSAs in dust as well as among FTOHs and FOSA/FOSEs in air. On the other hand, only

a few significant correlations were observed among the PFCAs. As summarised by D'Hollander et al. (2010a) significant relationships both among and between groups of PFCs have been observed in other studies which has been interpreted as an indicator for a common source. The reason for the lack of associations among most PFCAs in our study is not known.

FTOHs are likely to degrade to PFCAs in the atmosphere, thus being precursors of PFCAs (Ellis et al. 2004). Further, biotransformation of EtFOSA to PFOS has been reported (Tomy et al. 2004) and it has been anticipated that FOSA/FOSEs may also be transformed to PFSAs in the atmosphere. We found significant correlations between FOSA/FOSEs and PFSAs, while this was not seen for FTOHs and PFOA. This may indicate that, FOSA/FOSEs contribute to a larger extent to the indoor pollution with PFSAs than do FTOHs to PFOA pollution. A lack of correlation between FTOHs and PFOA does not mean that FTOHs are not degraded to PFOA, but other sources of PFOA are probably more pronounced. The distribution patterns of neutral PFCs in the indoor air samples were similar, in contrast to the large differences among samples of house dust. The reason for this remains to be clarified.

The PFC concentrations found in indoor air and house dust are likely influenced by several factors. In a study by Langer et al. (2010) on PFCs in indoor air from shops selling products potentially containing PFCs, large differences in distribution patterns were observed among the samples. These variations are probably due to differences in the content of PFCs in the products. To identify determinants of PFC concentrations in samples of indoor air and house dust in the BROFLEX study, the measured PFC concentrations were combined with information from the questionnaires using bivariate and multiple regression analyses. The age of the residence was found to significantly influence the concentrations of several PFCs in dust and air. Decreasing PFC concentrations were observed with increasing age of the residence. This might be related to differences in the construction of the buildings, the age and types of the building materials, but could also be related to differences in the residents' use of PFC-containing products. Also in a study from Canada, old houses had lower concentrations of PFHxS, PFOS and PFOA in house dust compared to new ones (Kubwabo et al. 2005). A suggested explanation for this was that old houses tended to have less carpeting than new ones. Carpets were also identified as a possible source of several PFCAs and PFSAs in a second study from Canada (Gewurtz et al. 2009). None of the houses in the BROFLEX

study had wall to wall carpets, however we explored possible associations between having a rug in the living room and the concentrations of PFCs in dust or air. With the exception of PFHxA, for which there was no association with the age of the residence, no significant associations were seen. Thus, the reason for lower concentrations of several PFCs observed in old houses compared to new ones in the BROFLEX study, remains to be clarified. In addition to the influence of the age of the residence on the PFC concentrations, significant relationships were observed for some other factors in the bivariate analyses, but only for one or two PFCs each. Due to the low number of samples analysed in this study, interpretations must be made with care. Associations seen only for a couple of PFCs can of course be due to different sources or specific physical-chemical properties for these compounds, but could also indicate that the relationships seen are accidental. Thus, no conclusions can be made based on those observations, and there is a need for further research to better understand the connection between use of various PFC containing products and concentrations in the indoor environment.

Intake estimates

Intakes of PFOS and PFOA from ingestion of house dust and inhalation of indoor air were estimated on an individual basis for the BROFLEX study group. Intakes were estimated according to three scenarios (see paragraph 3.8), due to high uncertainty in dust ingestion rates and biotransformation factors. The intakes for PFOS and PFOA from ingestion of house dust and inhalation of indoor air are illustrated in Figure 10 and 11, respectively and the median intakes were in the range 0.0004 to 0.077 ng/kg bw/day. For PFOS, intakes from dust were higher than for indoor air in scenario S1, while the opposite was seen for scenario S2 and S3 (Figure 10). For all three scenarios, higher proportions of the PFOA intakes from dust than indoor air were observed (Figure 11). In a recent study by Goosey and Harrad (2011), the median PFOS and PFOA intakes from dust ingestion (20 mg dust/day) were 0.05 and 0.06 ng/kg bw/day, respectively. This is higher than found for scenario S1 in our study, even though we assumed a higher dust ingestion rate (50 vs 20 mg/day).
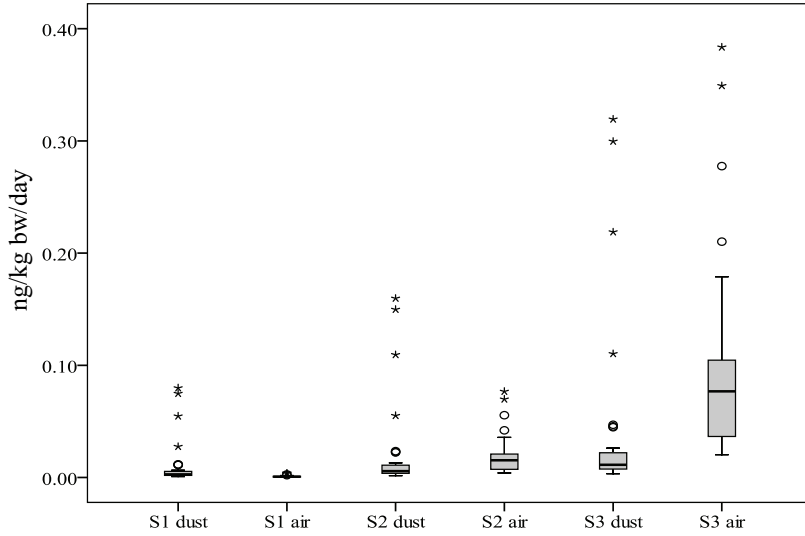
Figure 10. Boxplot of individual intakes for PFOS from ingestion of house dust and inhalation of indoor air according to three different scenarios (S1, S2 and S3)
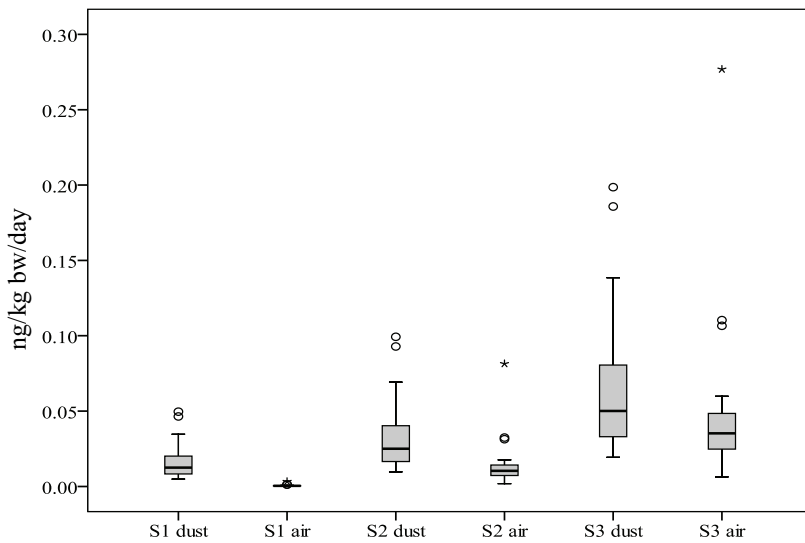
Figure 11. Boxplot of individual intakes for PFOA from ingestion of house dust and inhalation of indoor air according to three different scenarios (S1, S2 and S3)

A Swedish study reported median intakes of both PFOS and PFOA from dust ingestion to be 0.3 ng/day, which corresponds to 0.004 ng/kg bw/day when assuming a body weight of 70 kg (Björklund et al. 2009). This is in the same range as found for scenario S1 in our study, but the Swedish study was based on a dust ingestion rate of only 4.1 mg/day.

These results illustrate that there are not only variations in PFC concentrations observed among studies, but the results are also influenced by the dust ingestion rates and biotransformation factors applied. Hence there is a need for better characterisation of these factors, and preferably a harmonisation of use of those, to be able to draw firm conclusions regarding differences among studies.

4.3.3 Total exposure

Exposure to PFCs can occur through several pathways as illustrated in Figure 2. The total exposure to PFOS and PFOA for the BROFLEX study group was assessed by including consumption of food and drinking water, inhalation of PFC-precursors in indoor air and ingestion of house dust.

The median total intake of PFOS was estimated to be between 0.62 and 0.70 ng/kg bw/day depending on the dust ingestion rates and biotransformation factors applied (see Figure 12). Correspondingly, the median intakes of PFOA were in the range 0.26-0.33 ng/kg bw/day (see Figure 13). This is in the same range as has been modelled for PFOS and PFOA in studies on populations exposed to background contamination levels (Egeghy and Lorber 2010;Fromme et al. 2009;Vestergren and Cousins 2009).

Consumption of food was the dominating source of exposure for PFOS in all three scenarios (based on the median values), representing 88 to 99% of the total exposure for the individual women. Correspondingly, food consumption counted for 67 to 84% of the total PFOA exposure. Based on the assumptions in scenario S1, drinking water represented 0.68%, dust 0.41% and indoor air 0.10% of the median total intakes of PFOS. Drinking water represented 11%, dust 5.2% and indoor air 0.13% of the total intakes for PFOA in scenario S1.

Comparison with other studies is challenging as different sources of exposure have been assessed. Further, the exposure parameters used, such as dust ingestion rates, varies between studies. However, food has also been identified as the major exposure

source of PFOS and PFOA in other adult general populations (Egeghy and Lorber 2010;Fromme et al. 2009;Trudel et al. 2008;Vestergren and Cousins 2009).
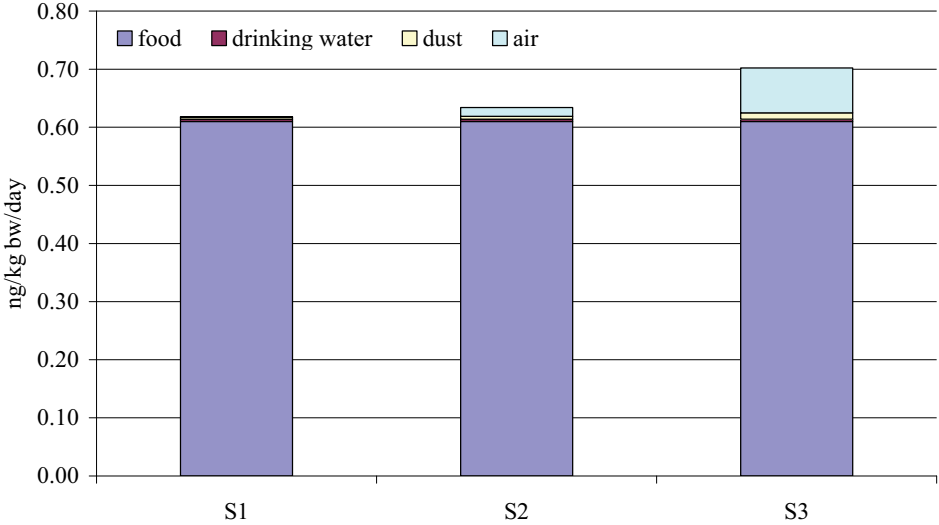
Figure 12. Total intakes of PFOS estimated for the BROFLEX study group

In a typical exposure scenario the median PFOS intakes from dust and drinking water represented only 6 and 22% of the total exposure for US adults, respectively (Egeghy and Lorber 2010). For PFOA, ingestion of dust and consumption of drinking water were also estimated to be minor exposure sources in background exposed populations reported by Vestergren and Cousins (2009).

Food is known to be the major source of exposure for POPs like dioxins and PCBs (Liem et al. 2000). The high positive correlations between PFCs and PCBs seen in serum from the NFG study, supports that food also is a major source of exposure for PFCs. However, when assessing the relative contribution of different exposure pathways on an individual basis, large variations were observed. This is illustrated in Figure 14 where the relative contribution of intakes from food, drinking water, house dust and indoor air (scenario 1) are shown for two women in the BROFLEX study group. The total intakes of PFOS were 0.27 and 0.30 ng/kg bw/day for Woman 1 and 2, respectively. The corresponding intakes of PFOA were 0.15 and 0.16 ng/kg bw/day, i.e. very similar.

48
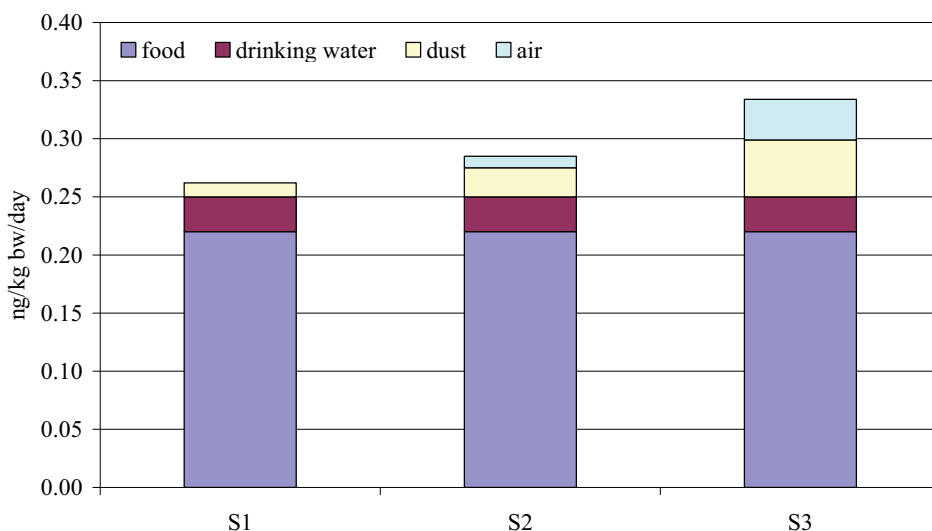
Figure 13. Total intakes of PFOA estimated for the BROFLEX study group

The relative importance of the PFOS exposure from dust and indoor air was quite high for some of the women (e.g. Woman 2), but for the majority of women more than 80% of the total exposure originated from food consumption (e.g. Woman 1). For PFOA the influence of the indoor exposure was in general higher than for PFOS. Dust and indoor air represented more than 40% of the PFOA exposure for one forth of the women in the scenario comprising high dust ingestion.

No other studies have so far assessed the PFC exposure from multiple sources on an individual basis. However the large variations observed among the individuals in this study (e.g. Woman 1 and 2 in Figure 14) underline the importance of performing such studies. Finding both PFC concentrations in dust and consumption of certain food types as predictors of serum PFC concentrations in the BROFLEX study group, also supports the large variations among individuals with respect to the relative contribution of different exposure pathways.

Benskin et al. (2009) hypothesized that isomer specific biotransformation rates of PFOS-precursors may explain the common observation of enrichment of the branched PFOS isomer profiles in humans. In the BROFLEX study group, we found significant associations between the proportion of branched PFOS isomers in serum and the relative contribution of the total PFOS intake from inhalation of precursors in indoor air (Scenario

1; R=0.33; *p*=0.038). Thus, one might speculate that the abundance of branched PFOS isomers in human serum is related to intake of PFOS precursors. This remains to be clarified.
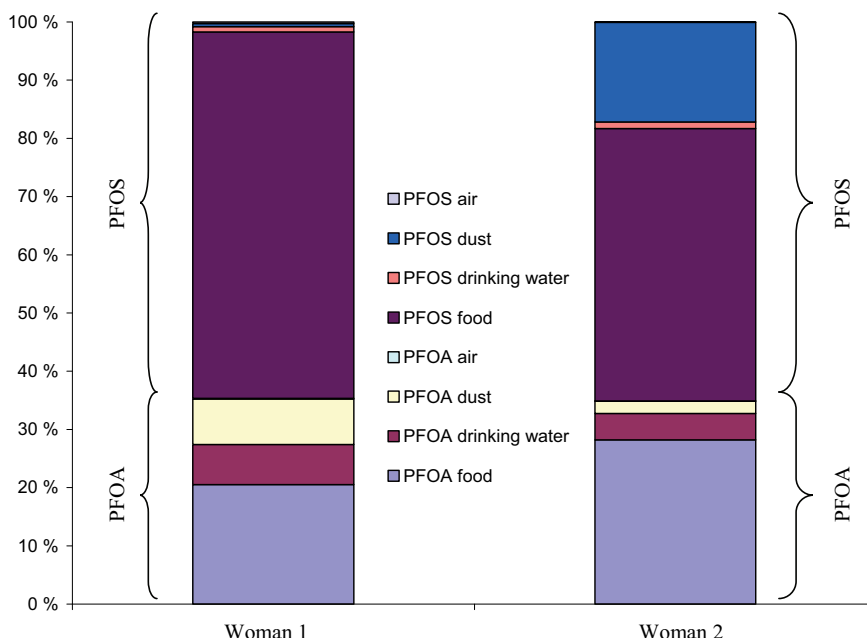
Figure 14. Relative contribution of intakes from food, drinking water, dust and indoor air for PFOS and PFOA for two of the women in the BROFLEX study group

4.3.4 Exposure of infants

The exposure of infants through breast-feeding was assessed in the depuration rate study and the BROFLEX study. Intakes of 61 ng/day for PFOA and 112 ng/day for PFOS were estimated in the depuration rate study using the median concentrations of the first sample donated by each mother. When assuming a body weight of 4 kg, this corresponds to 15 and 28 ng/kg bw/day. The median intakes estimated for infants in the BROFLEX study were 4.1 and 8.7 ng/kg bw/day for PFOA and PFOS, respectively. This is about a fourth to one third of the intakes found in the depuration rate study. Several of the mothers in the BROFLEX study collected breast milk after some months of breast-feeding. Thus, it is more appropriate to compare the BROFLEX intakes with intakes for

the depuration rate study based on the median values of all 70 samples collected during the lactation period. These intakes were similar.

Intakes of PFCs through breast-feeding have been calculated in several other studies. For PFOS, mean intakes in the range 5.7-28.7 ng/kg bw/day has been reported (Kim et al. 2011;Tao et al. 2008a;Tao et al. 2008b;Völkel et al. 2008) while for PFOA, estimated intakes of 4.7 ng/kg bw/day in a Korean study (Kim et al. 2011) and 9.6 ng/kg bw/day in a study including samples from Japan were reported (Tao et al. 2008a). Thus, the intakes of PFOS and PFOA through breast-feeding reported in this thesis are comparable to what has been reported elsewhere.

In the BROFLEX study, we assessed the exposure of PFOS and PFOA from multiple exposure pathways on an individual basis for infants at six months of age. We included intakes from consumption of breast milk, ingestion of dust and inhalation of indoor air. The median total intakes ranged from 8.7 to 9.1 ng/kg bw/day for PFOS and 4.3 to 4.9 ng/kg bw/day for PFOA, depending on the dust ingestion rates and biotransformation factors used. Based on the median values, breast milk represented more than 94 and 83% of the exposure to PFOS and PFOA, respectively. So far no other studies have compared exposure pathways for infants based on individual measurements of PFC concentrations in breast milk, house dust and indoor air. However, Fromme et al. (2010) found significant associations between concentrations of PFOS in breast milk and infants blood at the age of six months in a German study, indicating that breast milk is a major source of exposure for infants up to six months. Egeghy and Lorber (2010) estimated route specific PFOS intakes for 2-year old children, finding that food, ingestion of dust and drinking water represented 42, 36 and 20% of the total intake. Further, in a study by Trudel et al. (2008) more than half of the PFOS exposure for infants and toddlers in a high exposure scenario originated from contact with PFC containing consumer products. Thus, breast milk is the dominating source of PFCs exposure for exclusively or predominantly breast-fed infants, while the importance of the indoor environment increases after weaning.

4.4 Comparison of external and internal doses

Comparisons between external and internal doses of PFCs were performed in **Paper 4 and 7**.

4.4.1 Associations between estimated intakes and concentrations of PFCs in blood

For the NFG study significant associations between estimated total dietary intakes of PFOS, PFOA and PFUnDA, and measured serum concentrations of the corresponding compounds were found in both bivariate and MLR models. Bivariate associations for PFOS are illustrated in Figure 15.

In the BROFLEX study no significant associations were found between total intakes of PFOS and PFOA (scenario 1, 2 and 3) and the corresponding serum concentrations. However, when dividing the intakes by route of exposure a significant association between intakes from dust ingestion and the concentrations of PFOA measured in serum was seen.

Estimated daily intakes of PFOS ranging from 0.27-11 ng/kg bw, divided in quartiles
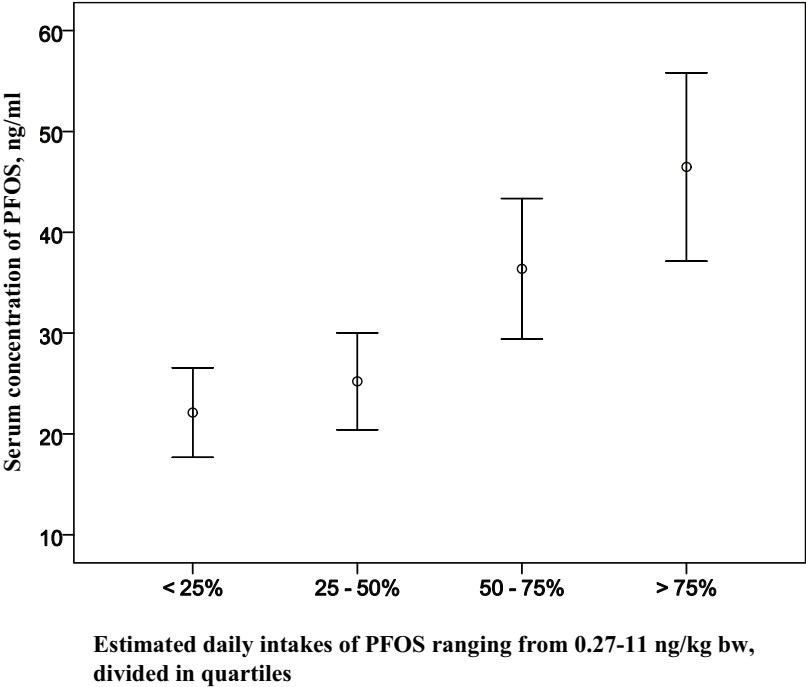
Figure 15. Relationship between estimated daily dietary intakes of PFOS divided in quartiles and the corresponding serum concentrations (mean and 95% CI), in the NFG-study

A similar tendency was found for PFOS, but the relationship was not statistically significant. No significant correlations to dietary intakes were observed. This could be due to the limited number of women included in the study, but could also be caused by

little variation in dietary habits, less detailed FFQs, as well as insufficient information on PFCs in food. Another plausible explanation could be that the predominance of PFC intakes through food results in a "baseline" serum concentration, while the concentration above this "baseline" might be driven by the wide variation in dust intakes. Hence an association with dust is more likely to be found than with food. Neither were there relationships between intake of PFOS and PFOA from precursors in air and serum concentrations. This might be due to an actual low relative contribution of precursors in indoor air to the total intakes, but could also be related to variations in biotransformations among individuals.

Fromme et al. (2007) examined relationships between concentrations of PFCs measured in serum and intakes calculated using duplicate diet samples collected over seven consecutive days. Kärrman et al. (2009) calculated intakes using concentrations determined in a one-day composite sample and compared with concentrations of PFOS and PFOA determined in serum. None of these studies found any significant relationships between dietary intakes and serum concentrations. However as pinpointed previously, for compounds with long half-lives such as most PFCs, the serum concentrations are accumulated from exposure during several years. Hence, the estimation of dietary intake using FFQs covering a longer time period, could have facilitated the finding of significant associations between diet and measured serum concentrations in the NFG study.

4.4.2 Comparing external and internal doses using PK modelling

In the BROFLEX study, the measured PFOS and PFOA concentrations in serum were compared with concentrations calculated from the total intakes using a PK model. The measured and calculated serum concentrations were found to be in the same range, indicating that the estimated intakes are reasonable. Similar results were seen in a German study, where a good agreement between intakes calculated using duplicate diet information and back-calculation from serum concentrations was observed (Fromme et al. 2007). PK modelling was also used to compare intakes modelled for the US population with intakes back-calculated from serum concentrations in the National Health and Nutrition Examination Survey (NHANES) 2003/2004 study, and similar central tendencies were observed (Egeghy and Lorber 2010). However, the intake data and the serum data in this study did not originate from the same individuals. Equivalent findings

were also reported from two other modelling studies (Trudel et al. 2008;Vestergren and Cousins 2009).

Despite the uncertainties associated with PK modelling, the results of our as well as other studies indicate that it can be a valuable tool in exposure assessment.

4.5 Tolerable daily intakes

The Scientific Panel on Contaminants in the Food Chain within the European Food Safety Authority (EFSA) has established tolerable daily intakes (TDI) for PFOS and PFOA of 150 ng/kg bw/day and 1500 ng/kg bw/day, respectively (EFSA 2008). In the NFG study, the maximum daily dietary intakes of PFOS and PFOA were 11 and 2.4 ng/kg bw/day, respectively. None of the women in the BROFLEX study had estimated total intakes above this. Thus, all adults included in this project had estimated intakes more than 14 (PFOS) and 625 (PFOA) times below the TDIs. One has to keep in mind that the intake calculations within this thesis were based on a limited number of samples, and thus do not necessarily reflect the whole range of intakes for the Norwegian population. For instance, it is expected that the actual intakes for high consumers of fish from coastal fishing grounds could be higher, and the margin to the TDIs would necessarily become lower.

The median total daily intakes of PFOS and PFOA per kg body weight for infants were 13-16 times higher than the corresponding estimates for adults. Thus, the maximum estimated intakes of PFOS and PFOA for infants 6 months of age (scenario 3) were only about 5 (PFOS) and 18 (PFOA) times below the TDIs. However, it has to be taken into account that TDIs are established for lifelong exposure and can not be applied to the relatively short period of breast-feeding.

4.6 Methodological strengths and limitations

The major strength of this work is the assessment of exposure to perfluorinated compounds from various angels. Due to practical reasons some of the studies were limited in size. However results from the different investigations all supported each other, increasing the strength of the individual studies. A wide range of PFCs was determined in the studies, being favourable because of the change in use of PFCs as a consequence of the phase-out and regulations of PFOS and PFOA. Below follows an overview of strenghts and limitations of the individual studies.

Table 3. Strengths (+) and limitations (-) in the studies included in this thesis

	Strengths/limitations	Consequences
	Time trend study	
+	Frequent sampling (almost every year) during 30 years	Advantageous for observing changes in concentrations over time
-	Only pooled samples were analysed	No information on variation between individuals could be obtained
-	This was a cross-sectional study	It was not possible to examine changes of PFC concentrations in pools of the same individuals at different points of time
-	For the serum pools from 1976, 1987 and 1998 information on each individual donor's age was not available	This complicates the assessment of the effect of age on PFC concentrations in serum
-	No information on diet etc. was available for the subjects	Could have an influence on the associations between age/gender and concentrations of PFCs in serum
	Concentrations in Norwegian food	
+	Low LOQs	We were able to detect low concentrations of several PFCs in the samples. This was advantageous to avoid overestimation of dietary intakes due to high LOQs
+	PFCs were determined in a broad range of food types	This is advantageous for calculating intakes
+	Consumption data from the NORKOST survey were used	The consumption data is representative for the Norwegian adult population
-	The NORKOST survey was carried out in 1997	The consumption patterns in Norway might have changed to some extent since then

	Strengths/limitations	Consequences
-	Only one sample of each kind was prepared and analysed (with the exception of drinking water)	No information on variation within a type of food or beverage could be obtained. This adds uncertainty to the intakes estimated
-	Only unprocessed food was analysed in this study	The measured concentrations do not necessary reflect the concentration in the food actually consumed

NFG study*

+	A comprehensive FFQ covering the consumption over the last 12 months for the whole diet was used	Favourable when assessing relationships between diet and measured serum concentrations for compounds with long half-lives such as PFCs
+	The FFQ has been validated and found satisfactory in a pregnancy sub-cohort	Limits the uncertainty in the consumption data
+	The study group comprised participants in a wide age-span, both men and women from both inland and costal municipalities throughout Norway which had a wide range of consumption, particularly of fish and shellfish	This is favourable when exploring relationships between diet and serum concentrations
+	The mean consume of fish and shellfish was comparable to the NORKOST survey which is representative to the general adult population	The results might be applicable to the general adult Norwegian population
-	The information on PFC concentrations in food from Norway is limited	This adds uncertainty to the estimated intakes

Depuration rate study

+	Frequent sampling and large number of breast milk samples obtained from each mother	This is favourable when exploring depuration rates
-	The number of mothers included was restricted	This has negative influence on the statistical power

BROFLEX study**

+	Unique design	Ability to assess multiple human exposure pathways of PFCs on an individual basis and compare with biomonitoring data
+	Comprehensive information was obtained from each individual	Allowed exploration of various factors in MLR analyses
-	The participants were not randomly selected	The samples are not necessarily representative for the Norwegian general population

	Strengths/limitations	Consequences
-	The number of investigated households was limited to 41 for practical reasons	This limits the statistical power
-	The FFQ was not as extensive as in the NFG study.	This could result in higher uncertainty in the calculations of dietary intakes. However, the intakes estimated were similar to what was observed in a study on pregnant women, where the FFQ used was equal to that in the NFG study (Anne Lise Brantsæter, personal communication)
-	The study includes sampling of indoor air and house dust only in the residence (not other microenvironments such as the work place) and only once	Variations in PFC concentrations over time and among microenvironments could not be considered
-	Due to the method used for collection of PFCs in air it was not possible to distinguish between PFC concentrations in gas and particulate phase.	The intakes of FOSA/FOSEs and FTOHs from air comprised the sum of the amount in gas phase and particulate phase. However, according to Barber et al. (2007) only a minor amount of neutral PFCs was found on particles in air in indoor environments
-	The exposure through inhalation of low contaminated outdoor air has been neglected	Could lead to a slight over-estimation of intake through inhalation
-	Exposure to PFCs through dermal absorption has not been included in this project.	This could result in an under-estimation of the total intakes. However, the dermal uptake is suggested to be low
-	Biotransformation of precursors have not been considered for exposure from food	This could result in an under-estimation of the total intakes.
-	Biotransformation of precursors have not been considered for exposure from dust	This could result in an under-estimation of the total intakes. However, neutral PFCs have high vapour pressures and are found predominately in the gas phase, and the concentrations of FOSAs, FOSEs and FTOHs in dust are thus thought to be low
-	Only indirect exposure through precursors was assessed for indoor air	This could result in an under-estimation of the total intakes. However, the vapour pressures of PFCAs and PFSAs in dissociated form are expected to be low, thus these PFCs are mainly bound to particles

* Strengths and limitations for the NFG study in general have also been thoroughly discussed by Kvalem (2010).
** Uncertainties associated with PK modelling has been thoroughly discussed elsewhere (Egeghy and Lorber 2010;Trudel et al. 2008;Vestergren and Cousins 2009)

5. CONCLUDING REMARKS AND FUTURE PERSPECTIVES

In serum samples from the Norwegian population collected almost annually between 1976 and 2007, we explored the changes in concentrations of a range of PFCs. The serum concentrations of most PFCs increased throughout the 1990s, which collate with increasing use of PFCs during this period. Declining concentrations of some PFCs (e.g. PFOS and PFOA) were seen from around year 2000 in line with the phase-out of these compounds. However, in the same period no reductions were observed for the longer chained PFCAs (i.e. PFNA, PFDA and PFUnDA). This could be due to longer half-lives or different use of these compounds. After the phase-out of PFOS and PFOA the production has shifted towards PFCs with shorter chain lengths. The phase-out out of high production volume chemicals may also lead to increased production of chemicals that might degrade to PFCAs and PFSAs. This underlines the importance of continuous human biomonitoring.

The levels of PFCs in Norwegian serum and breast milk studied in this thesis were compareable to those found in other studies from industrialised countries, indicating a similar degree of exposure. However, the concentrations in food, house dust and indoor air were generally lower. Comparison of studies on external exposure is challenging as different sampling strategies and analytical methods may have large impact on the results. To be able to reveal temporal and geographical variations, there is a need for harmonisation of sampling and analyses in the future.

When this project was started the knowledge on PFCs levels in breast milk and the impact of lactation on maternal body burdens was very limited. We found strong relationships between concentrations of PFOS in paired samples of serum and breast milk, and the same was seen for PFOA. Further, during the course of lactation declining concentrations of PFOS and PFOA were observed in breast milk, and previous breast-feeding was identified as an important factor for maternal serum PFC concentrations. These findings underline the necessity for obtaining information on breast-feeding in future studies on PFCs in women. Breast milk was found to be the major source of exposure to PFCs for exclusively or predominantly breast-fed infants, and the total daily intakes per kg body weight were 13-16 times higher than the corresponding intakes for

adults. The highest individual intakes were relatively close to the current TDIs for life long exposure.

Several factors influence the body burdens of PFCs, which reflects an integrated exposure over time comprising various sources. Major determinants of PFC concentrations in serum identified in this thesis were breast-feeding status, age, consumption of fish, shellfish and meat as well as concentrations of PFCs in house dust. Knowledge on and inclusion of such determinants are crucial when exploring associations between serum concentrations and e.g. health outcomes.

The knowledge on factors influencing the PFC levels in indoor environments is limited. An association between percentage of carpeting and concentrations of PFCs in the indoor environment has been reported, and in the BROFLEX study we found that older residences tend to have lower PFC levels in dust and air than new ones. The reasons for that remain to be clarified. More information on the variation of PFC concentrations within and between types of food and beverages is also required.

Total intakes through consumption of food and drinking water, ingestion of house dust and inhalation of indoor air were found to be comparable or lower than reported in other studies. This may partly be explained by the lower levels observed in our samples. However, there is a need for further knowledge on dust ingestion rates and biotransformation factors of precursor compounds. This has also been highlighted by Harrad et al (2010). Despite the underlying uncertainties, PK modelling indicated that the intakes estimated in the BROFLEX study are reasonable.

Food was generally the major source of exposure, especially fish and shellfish, and for the first time, strong relationships between measured concentrations of PFCs in serum and calculated dietary PFC intakes were reported. Nevertheless, in the BROFLEX study large individual variations were observed for the relative contributions of the various exposure pathways to the total intake of PFCs. This underlines the importance of performing studies considering multiple exposure sources on an individual basis. Further, the high influence of indoor exposure for several individuals as well as finding ingestion of house dust as a determinant of serum concentrations, highlights the importance of including indoor environment when characterising human exposure to PFCs. More efforts are needed to investigate other indoor environments, assess more homes and examine the variability within and between rooms. The contribution of various sources to PFC exposure might also differ between countries and regions.

Large variations between individuals were observed in the proportion of branched PFOS isomers in serum and breast milk. Higher proportions of branched isomers were observed for the women with the highest relative contribution to total PFOS intake from inhalation of precursors in indoor air. This agrees with the hypothesis that the abundance of branched PFOS isomers in human serum is related to the intake of PFOS precursors. Using the applied analytical method it was possible to distinguish between branched and linear PFOS, but with this method the individual branched isomers could not be quantified. Information on the relative contribution of the individual branched PFOS isomers in serum would be valuable to shed light on the impact of precursor compounds. More knowledge on biotransformation rates of precursors are also needed to understand their contribution to body burdens of ionic PFCs.

None of the participants in this study exceeded the TDIs established by The Scientific Panel on Contaminants in the Food Chain within EFSA. However in general, for instance for high consumers of fish from costal fishing grounds, the margins to the TDIs could be low. Further, for six months old infants, the maximum estimated intakes were relatively close to the current TDIs for lifelong exposure. Thus, given the high uncertainties both related to the TDIs and the intakes, all available strategies should be utilised to minimise human exposure to PFCs to limit the potential risk of adverse health effects.

6. REFERENCES

3M Company. 2000. Phase-out plan for PFOS-based products. U.S. Environmental Protection Agency Public Docket AR226-0588, US EPA, St.Paul, MN

3M Company. 2003. Environmental and health assessment of perfluorooctane sulfonic acid and its salts. Available: http://solutions.3m.com/wps/portal/3M/en_US/PFOS/PFOA/Information/Health-Environment/ [Accessed February 2011]

Andersen ME, Clewell III HJ, Tan YM, Butenhoff JL, Olsen GW. 2006. Pharmacokinetic modeling of saturable, renal resorption of perfluoroalkylacids in monkeys-Probing the determinants of long plasma half-lives. *Toxicology* 227, 156-164

Andreassen M, Bale M, Kaaresen PI, Dahl LB. 2001. Breastfeeding in Tromsø before and after 'the Baby-Friendly Hospital Initiative'. *Tidsskrift for den norske legeforening* 121, 3154-3158 [In Norwegian]

Andreoli R, Manini P, Bergamaschi E, Mutti A, Franchini I, Niessen WMA. 1999. Determination of naphthalene metabolites in human urine by liquid chromatography-mass spectrometry with electrospray ionization. *J. Chromatogr. A* 847, 9-17

Apelberg BJ, Goldman LR, Calafat AM, Herbstman JB, Kuklenyik Z, Heidler J, et al. 2007. Determinants of fetal exposure to polyfluoroalkyl compounds in Baltimore, Maryland. *Environ. Sci. Technol.* 41, 3891-3897

Bakke T, Boitsov S, Brevik EM, Gabrielsen GW, Green N, Helgason LB, et al. 2008. Mapping of selected organic contaminants in the Barents Sea 2007. Report number TA-2400/2008, Norwegian Pollution Control Authority, Oslo, Norway. Available: http://www.klif.no/publikasjoner/2400/ta2400.pdf [Accessed February 2011]

Bakke T, Fjeld E, Skaare BB, Berge JA, Green N, Ruus A, et al. 2007. Maping of metals and selected new organic contaminants 2006. Chromium, Arsenic, Perfluorated substances, Dichloroethane, Chlorianted benzenes, Pentachlorophenol, HCBD and DEHP. Report number TA-2284/2007, Norwegian Pollution Control Authority, Oslo, Norway. Available: http://www.klif.no/publikasjoner/2284/ta2284.pdf [In Norwegian, accessed February 2011]

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

Bartell SM, Calafat AM, Lyu C, Kato K, Ryan PB, Steenland K. 2009. Rate of decline in serum PFOA concentrations after granular activated carbon filtration at two public water systems in Ohio and West Virginia. *Environ. Health Perspect.* 118, 222-228

Begley TH, White K, Honigfort P, Twaroski ML, Neches R, Walker RA. 2005. Perfluorochemicals: Potential sources of and migration from food packaging. *Food Add. Contam.* 22, 1023-1031

Benskin JP, Holt A, Martin JW. 2009. Isomer-specific biotransformation rates of a perfluorooctane sulfonate (PFOS)-precursor by cytochrome P450 isozymes and human liver microsomes. *Environ. Sci. Technol.* 43, 8566-8572

Berger U, Glynn A, Holmstrom KE, Berglund M, Ankarberg EH, Tornkvist A. 2009. Fish consumption as a source of human exposure to perfluorinated alkyl substances in Sweden - Analysis of edible fish from Lake Vattern and the Baltic Sea. *Chemosphere* 76, 799-804

Berger U, Haukas M. 2005. Validation of a screening method based on liquid chromatography coupled to high-resolution mass spectrometry for analysis of perfluoroalkylated substances in biota. *J. Chromatogr. A* 1081, 210-217

Berger U, Langlois I, Oehme M, Kallenborn R. 2004. Comparison of three types of mass spectrometer for high-performance liquid chromatography/mass spectrometry analysis of perfluoroalkylated substances and fluorotelomer alcohols. *Eur. J. Mass Spectrom.* 10, 579-588

Björklund J, Thuresson K, de Wit CA. 2009. Perfluoroalkyl compounds (PFCs) in indoor dust: Concentrations, human exposure estimates, and sources. *Environ. Sci. Technol.* 43, 2276-2281

Brandsma SH, Smithwick M, Solomon K, Small J, de Boer J, Muir DCG. 2011. Dietary exposure of rainbow trout to 8:2 and 10:2 fluorotelomer alcohols and perfluorooctanesulfonamide: Uptake, transformation and elimination. *Chemosphere* 82, 253-258

Butenhoff JL, Olsen GW, Pfahles-Hutchens A. 2006. The applicability of biomonitoring data for perfluorooctanesulfonate to the environmental public health continuum. *Environ. Health Perspect.* 114, 1776-1782

Butt CM, Berger U, Bossi R, Tomy GT. 2010. Levels and trends of poly- and perfluorinated compounds in the arctic environment. *Sci. Total Environ.* 408, 2936-2965

Calafat AM, Wong L-Y, Kuklenyik Z, Reidy JA, Needham LL. 2007. Polyfluoroalkyl chemicals in the US population: Data from the National Health and Nutrition Examination Survey (NHANES) 2003-2004 and Comparisons to NHANES 1999-2000. *Environ. Health Perspect.* 115, 1596-1602

Clarke DB, Bailey VA, Routledge A, Lloyd AS, Hird S, Mortimer DN, et al. 2010. Dietary intake estimate for perfluorooctanesulphonic acid (PFOS) and other perfluorocompounds (PFCs) in UK retail foods following determination using standard addition LC-MS/MS. *Food Addit. Contam. Part A Chem. Anal. Control Expo. Risk Assess.* 27, 530-545

Conder JM, Hoke RA, de Wolf W, Russell MH, Buck RC. 2008. Are PFCAs bioaccumulative? A critical review and comparison with regulatory lipophilic compounds. *Environ. Sci. Technol.* 42, 995-1003

62

Dallaire R, Ayotte P, Pereg D, Dery S, Dumas P, Langlois E, et al. 2009. Determinants of plasma concentrations of perfluorooctanesulfonate and brominated organic compounds in Nunavik inuit adults (Canada). *Environ. Sci. Technol.* 43, 5130-5136

De Voogt P, Saez M. 2006. Analytical chemistry of perfluoroalkylated substances. *Trends Anal. Chem.* 25, 326-342

Del Gobbo L, Tittlemier S, Diamond M, Pepper K, Tague B, Yeudall F, et al. 2008. Cooking decreases observed perfluorinated compound concentrations in fish. *J. Agric. Food Chem.* 56, 7551-7559

D'Hollander W, de Voogt P, De Coen W, Bervoets L. 2010a. Perfluorianted substances in human food and other sources of human exposure. *Rev. Environ. Contam. Toxicol.* 179-215

D'Hollander W, Roosens L, Covaci A, Cornelis C, Reynders H, Campenhout KV, et al. 2010b. Brominated flame retardants and perfluorinated compounds in indoor dust from homes and offices in Flanders, Belgium. *Chemosphere* 81, 478-487

EFSA. 2004. Opinion of the Scientific Panel on Contaminants in the Food Chain on a request from the Commission to assess the health risks to consumers associated with exposure to organotins in foodstuffs. The EFSA Journal 102, 1-114

EFSA. 2008. Perfluorooctane sulfonate (PFOS), perfluorooctanoic acid (PFOA) and their salts. The EFSA Journal 653, 1-131

Egeghy PP, Lorber M. 2010. An assessment of the exposure of Americans to perfluorooctane sulfonate: A comparison of estimated intake with values inferred from NHANES data. *J. Expos. Sci. Environ. Epidemiol.* 1-19

Ehresman DJ, Froehlich JW, Olsen GW, Chang SC, Butenhoff JL. 2007. Comparison of human whole blood, plasma, and serum matrices for the determination of perfluorooctanesulfonate (PFOS), perfluorooctanoate (PFOA), and other fluorochemicals. *Environ. Res.* 103, 176-184

Ellis DA, Martin JW, De Silva AO, Mabury SA, Hurley MD, Andersen MPS, et al. 2004. Degradation of fluorotelomer alcohols: A likely atmospheric source of perfluorinated carboxylic acids. *Environ. Sci. Technol.* 38, 3316-3321

Emmett EA, Shofer FS, Zhang H, Freeman D, Desai C, Shaw LM. 2006. Community exposure to perfluorooctanoate: Relationships between serum concentrations and exposure sources. *J. Occup. Environ. Med.* 48, 759-770

Ericson I, Domingo JL, Nadal M, Bigas E, Llebaria X, van Bavel B, et al. 2009. Levels of Perfluorinated chemicals in municipal drinking water from Catalonia, Spain: Public health implications. *Arch. Environ. Contam. Toxicol.* 57, 631-638

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

Eriksen KT, Sørensen M, McLaughlin JK, Tjønneland A, Overvad K, Raaschou-Nielsen O. 2010. Determinants of plasma PFOA and PFOS levels among 652 Danish men. *Environ. Sci. Technol*. DOI: 10.1021/es100626h

European Union. 2006. Directive 2006/122/ECOF the European parliament and of the council of 12 December 2006 amending for the 30th time Council Directive 76/769/EEC on the approximation of the laws, regulations and administrative provisions of the Member States relating to restrictions on the marketing and use of certain dangerous substances and preparations (perfluorooctane sulfonates). Available:
http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2006:372:0032:0034:en:PDF
[Accessed February 2011]

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

Fasano WJ, Kennedy GL, Szostek B, Farrar DG, Ward RJ, Haroun L, et al. 2005. Penetration of ammonium perfluorooctanoate through rat and human skin in vitro. *Drug Chem. Toxicol.* 28, 79-90

Fei C, Mclaughlin JK, Lipworth L, Olsen J. 2010. Maternal concentrations of perfluorooctanesulfonate (PFOS) and perfluorooctanoate (PFOA) and duration of breastfeeding. *Scand. J. Work Environ. Health.* 36, 413-421

Fjeld E, Enge EK, Rognerud S, Rustadbakken A, Løvik JE. 2009. Environmental contaminants in fish and zooplankton from Lake Mjøsa-2008. Brominated flame retardants (PBDE, HBCDD), PCB, dioxin, chlorinated parafins, perfluorinated alkyl substances and mercury. Report number TA-2483/2009, Norwegian Pollution Control Authority, Oslo, Norway. Available: http://www.klif.no/publikasjoner/2483/ta2483.pdf [In Norwegian, accessed February 2011]

Fjeld E, Schlabach M, Berge JA, Green N, Eggen T, Snilsberg P, et al. 2005. Screening of selected new organic contaminants 2004.Brominated flame retardants, perfluorinated alkylated substances, irgarol, diuron, BHT og dicofol. Report number TA-2096/2005, Norwegian Pollution Control Authority, Oslo, Norway. Available: http://www.klif.no/publikasjoner/overvaking/2096/ta2096.pdf [In Norwegian, accessed February 2011]

Flaherty JM, Connolly PD, Decker ER, Kennedy SM, Ellefson ME, Reagen WK, et al. 2005. Quantitative determination of perfluorooctanoic acid in serum and plasma by liquid chromatography tandem mass spectrometry. *J. Chromatogr. B Analyt. Technol. Biomed. Life Sci.* 819, 329-338

Freberg BI, Haug LS, Olsen R, Daae HL, Hersson M, Thomsen C, et al. 2010. Occupational exposure to airborne perfluorinated compounds during professional ski waxing. *Environ. Sci. Technol.* 44, 7723-7728

Fromme H, Mosch C, Morovitz M, Alba-Alejandre I, Boehmer S, Kiranoglu M, et al. 2010. Pre- and postnatal exposure to perfluorinated compounds (PFCs). *Environ. Sci. Technol.* 44, 7123-7129

64

Fromme H, Schlummer M, Möller A, Gruber L, Wolz G, Ungewiss J, et al. 2007. Exposure of an adult population to perfluorinated substances using duplicate diet portions and biomonitoring data. *Environ. Sci. Technol.* 41, 7928-7933

Fromme H, Tittlemier SA, Völkel W, Wilhelm M, Twardella D. 2009. Perfluorinated compounds - Exposure assessment for the general population in western countries. *Int. J. Hyg. Environ. Health* 212, 239-270

Gewurtz SB, Bhavsar SP, Crozier PW, Diamond ML, Helm PA, Marvin CH, et al. 2009. Perfluoroalkyl contaminants in window film: Indoor/outdoor, urban/rural, and winter/summer contamination and assessment of carpet as a possible source. *Environ. Sci. Technol.* 43, 7317-7323

Goosey E, Harrad S. 2011. Perfluoroalkyl compounds in dust from Asian, Australian, European, and North American homes and UK cars, classrooms, and offices. *Environ. Int.* 37, 86-92

Green N, Schlabach M, Bakke T, Brevik EM, Dye C, Herzke D, et al. 2008. Screening of selceted metals and new organic contaminants 2007. Report number TA-2367/2008, Norwegian Pollution Control Authority, Oslo, Norway. Available: http://www.klif.no/publikasjoner/2367/ta2367.pdf [Accessed February 2011]

Grønn hverdag. 2010. Test av parkdresser 2010. Available: http://www.gronnhverdag.no/nor/Aktuelt/Parkdresser [In Norwegian, accessed February 2011]

Häggkvist A-P, Brantsæter AL, Grjibovski AM, Helsing E, Meltzer HM, Haugen M. 2010. Prevalence of breast-feeding in the Norwegian Mother and Child Cohort Study and health service-related correlates of cessation of full breast-feeding. *Public Health Nutr.* 13, 2076-2086

Halldorsson TI, Fei CY, Olsen J, Lipworth L, Mclaughlin JK, Olsen SF. 2008. Dietary predictors of perfluorinated chemicals: A study from the Danish National Birth Cohort. *Environ. Sci. Technol.* 42, 8971-8977

Han X, Snow TA, Kemper RA, Jepson GW. 2003. Binding of perfluorooctanoic acid to rat and human plasma proteins. *Chem. Res. Toxicol.* 16, 775-781

Hansen KJ, Clemen LA, Ellefson ME, Johnson HO. 2001. Compound-specific, quantitative characterization of organic: Fluorochemicals in biological matrices. *Environ. Sci. Technol.* 35, 766-770

Harrad S, de Wit CA, Abdallah MA-E, Bergh C, Björklund JA, Covaci A, et al. 2010. Indoor contamination with hexabromocyclododecanes, polybrominated diphenyl ethers, and perfluoroalkyl compounds: An important exposure pathway for people? *Environ. Sci. Technol.* 44, 3221-3231

Hinderliter PM, Mylchreest E, Gannon SA, Butenhoff JL, Kennedy J. 2005. Perfluorooctanoate: Placental and lactational transport pharmacokinetics in rats. *Toxicology* 211, 139-148

Holm A, Wilson SR, Molander P, Lundanes E, Greibrokk T. 2004. Determination of perfluorooctane sulfonate and perfluorooctanoic acid in human plasma by large volume injection capillary column switching liquid chromatography coupled to electrospray ionization mass spectrometry. *J. Sep.Sci.* 27, 1071-1079

Hölzer J, Goen T, Rauchfuss K, Kraft M, Angerer J, Kleeschulte P, et al. 2009. One-year follow-up of perfluorinated compounds in plasma of German residents from Arnsberg formerly exposed to PFOA-contaminated drinking water. *Int. J. Hyg. Environ. Health* 212, 499-504

Hölzer J, Midasch O, Rauchfuss K, Kraft M, Reupert R, Angerer J, et al. 2008. Biomonitoring of perfluorinated compounds in children and adults exposed to perfluorooctanate-contaminated drinking water. *Environ. Health Perspect.* 116, 651-657

Houde M, Martin JW, Letcher RJ, Solomon KR, Muir DCG. 2006. Biological monitoring of polyfluoroalkyl substances: A review. *Environ. Sci. Technol.* 40, 3463-3473

Huber S, Haug LS, Schlabach M. Per- and polyfluorinated compounds in house dust and indoor air from Northern Norway. Accepted for publication in Chemosphere.

Hundley SG, Sarrif AM, Kennedy GL. 2006. Absorption, distribution, and excretion of ammonium perfluorooctanoate (APFO) after oral administration to various species. *Drug Chem. Toxicol.* 29, 137-145

Huse A. 2004. Bruken av PerFluorAlkylStoffer (PFAS) i produkter i Norge. Materialstrømsanalyse. Report number TA-2031/2004, Norwegian Pollution Control Authority, Oslo, Norway. Available:
 http://www.klif.no/publikasjoner/kjemikalier/2031/ta2031.pdf [In Norwegian, accessed February 2011]

Inoue K, Okada F, Ito R, Kato S, Sasaki S, Nakajima S, et al. 2004a. Perfluorooctane sulfonate (PFOS) and related perfluorinated compounds in human maternal and cord blood samples: Assessment of PFOS exposure in a susceptible population during pregnancy. *Environ. Health Perspect.* 112, 1204-1207

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

Jogsten IE, Perello G, Llebaria X, Bigas E, Marti-Cid R, Kärrman A, et al. 2009. Exposure to perfluorinated compounds in Catalonia, Spain, through consumption of various raw and cooked foodstuffs, including packaged food. *Food Chem. Toxicol*. 47: 1577-1583

Johansson, L., Solvoll, K., 1999. Norkost 1997. Landsomfattende kostholdsundersøkelse blant menn og kvinner i alderen 16-79 år. Statens råd for ernæring og fysisk aktivitet, Oslo, Norway. Available: http://www.helsedirektoratet.no/vp/multimedia/archive/00003/IS-0168_3745a.pdf [In Norwegian, accessed February 2011]

Johnson DJ, Gibson SJ, Ober RE. 1979. Absorption of FC-95-14C in rats after a single oral dose. U. S. Environmental Protection Agency Public Docket AR226-0007, US EPA, St.Paul, MN

Kallenborn R, Berger U, Järnberg U. 2004. Perfluorinated alkylated substances (PFAS) in the Nordic environment. Report number TemaNord 2004:552. Nordic Counsil of Ministers,
Copenhagen, Denmark. Available: http://www.norden.org/da/publikationer/publikationer/2004-552/at_download/publicationfile [Accessed February 2011]

Kannan K, Corsolini S, Falandysz J, Fillmann G, Kumar KS, Loganathan BG, et al. 2004. Perfluorooctanesulfonate and related fluorochemicals in human blood from several countries. *Environ. Sci. Technol.* 38, 4489-4495

Kannan K, Franson JC, Bowerman WW, Hansen KJ, Jones JD, Giesy JP. 2001a. Perfluorooctane sulfonate in fish-eating water birds including bald eagles and albatrosses. *Environ. Sci. Technol.* 35, 3065-3070

Kannan K, Koistinen J, Beckmen K, Evans T, Gorzelany JF, Hansen KJ, et al. 2001b. Accumulation of perfluorooctane sulfonate in marine mammals. *Environ. Sci. Technol.* 35: 1593-1598

Kärrman A, Domingo JL, Llebaria X, Nadal M, Bigas E, van Bavel B, et al. 2010. Biomonitoring perfluorinated compounds in Catalonia, Spain: concentrations and trends in human liver and milk samples. *Environ. Sci. Pollut. Res.* 17, 750-758

Kärrman A, Ericson I, van Bavel B, Darnerud PO, Aune M, Glynn A, et al. 2007. Exposure of perfluorinated chemicals through lactation: Levels of matched human milk and serum and a temporal trend, 1996-2004, in Sweden. *Environ. Health Perspect.* 115, 226-230

Kärrman A, Harada KH, Inoue K, Takasuga T, Ohi E, Koizumi A. 2009. Relationship between dietary exposure and serum perfluorochemical (PFC) levels-A case study. *Environ. Int.* 35, 712-717

Kärrman A, van Bavel B, Järnberg U, Hardell L, Lindström G. 2005. Development of a solid-phase extraction-HPLC/single quadrupole MS method for quantification of perfluorochemicals in whole blood. *Anal. Chem.* 77, 864-870

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

Kato K, Calafat AM, Needham LL. 2009. Polyfluoroalkyl chemicals in house dust. *Environ. Res.* 109, 518-523

Kennedy G, Butenhoff J, Olsen G, O'connor J, Seacat AM, perkins R. 2004. The toxicology of perfluorooctanoate. *Crit. Rev. Toxicol.* 34, 351-384

Kim SK, Lee KT, Kang CS, Tao L, Kannan K, Kim KR, et al. 2011. Distribution of perfluorochemicals between sera and milk from the same mothers and implications for prenatal and postnatal exposures. *Environ. Pollut.* 159, 169-174

Kissa, E. 2001. Fluorinated surfactants and repellants. 2 ed., Marcel Dekker Inc. New York

Kubwabo C, Stewart B, Zhu JP, Marro L. 2005. Occurrence of perfluorosulfonates and other perfluorochemicals in dust from selected homes in the city of Ottawa, Canada. *J. Environ. Monitor.* 7, 1074-1078

Kuklenyik Z, Needham LL, Calafat AM. 2005. Measurement of 18 perfluorinated organic acids and amides in human serum using on-line solid-phase extraction. *Anal. Chem.* 77, 6085-6091

Kuklenyik Z, Reich JA, Tully JS, Needham LL, Calafat AM. 2004. Automated solid-phase extraction and measurement of perfluorinated organic acids and amides in human serum and milk. *Environ. Sci. Technol.* 38, 3698-3704

Kvalem HE. 2010. From food to blood - diet as a predictor of blood concentrations of dioxins and PCBs. PhD Thesis, Institute of Basic Medical Sciences, Faculty of Medicine, University of Oslo, Oslo, Norway

Laden F, Neas LM, Spiegelman D, Hankinson SE, Willett WC, Ireland K, et al. 1999. Predictors of plasma concentrations of DDE and PCBs in a group of U.S. women. *Environ. Health Perspect.* 107, 75-81

Langer V, Dreyer A, Ebinghaus R. 2010. Polyfluorinated compounds in residential and nonresidential indoor air. *Environ. Sci. Technol.* 44, 8075-8081

Lau C, Anitole K, Hodes C, Lai D, Pfahles-Hutchens A, Seed J. 2007. Perfluoroalkyl acids: A review of monitoring and toxicological findings. *Toxicol. Sci.* 99, 366-394

Liem AKD, Furst P, Rappe C. 2000. Exposure of populations to dioxins and related compounds. *Food Addit. Contam.* 17, 241-259

Llorca M, Farré M, Picó Y, Teijón ML, Álvarez JG, Barceló D. 2010. Infant exposure of perfluorinated compounds: Levels in breast milk and commercial baby food. *Environ. Int.* 36, 584-592

Mak YL, Taniyasu S, Yeung LWY, Lu GH, Jin L, Yang YL, et al. 2009. Perfluorinated compounds in tap water from China and several other countries. *Environ. Sci. Technol.* 43, 4824-4829

Martin JW, Ellis DA, Mabury SA, Hurley MD, Wallington TJ. 2006. Atmospheric chemistry of perfluoroalkanesulfonamides: Kinetic and product studies of the OH radical and Cl atom initiated oxidation of N-ethyl perfluorobutanesulfonamide. *Environ. Sci. Technol.* 40, 864-872

Martin JW, Kannan K, Berger U, de Voogt P, Field J, Franklin J, et al. 2004. Analytical challenges hamper perfluoroalkyl research. *Environ. Sci. Technol.* 38, 248A-255A

Miljøverndepartementet. 2007. Forbyr miljøgiften PFOS. Available: http://www.regjeringen.no/nb/dep/md/pressesenter/pressemeldinger/2007/forbyr-miljogiften-pfos.html?id=462603 [In Norwegian, accessed February 2011]

Monroy R, Morrison K, Teo K, Atkinson S, Kubwabo C, Stewart B, et al. 2008. Serum levels of perfluoroalkyl compounds in human maternal and umbilical cord blood samples. *Environ. Res.* 108, 56-62

Moriwaki H, Takata Y, Arakawa R. 2003. Concentrations of perfluorooctane sulfonate (PFOS) and perfluorooctanoic acid (PFOA) in vacuum cleaner dust collected in Japanese homes. *J. Environ. Monit.* 5, 753-757

Mosch C, Kiranoglu M, Fromme H, Völkel W. 2010. Simultaneous quantitation of perfluoroalkyl acids in human serum and breast milk using on-line sample preparation by HPLC column switching coupled to ESI-MS/MS. *J. Chromatogr. B* 878, 2652-2658

Nabb DL, Szostek B, Himmelstein MW, Mawn MP, Gargas ML, Sweeney LM, et al. 2007. In vitro metabolism of 8-2 fluorotelomer alcohol: Interspecies comparisons and metabolic pathway refinement. *Toxicol. Sci.* 100, 333-344

Nania V, Pellegrini GE, Fabrizi L, Sesta G, De Sanctis P, Lucchetti D, et al. 2009. Monitoring of perfluorinated compounds in edible fish from the Mediterranean Sea. *Food Chem.* 115, 951-957

Nilsson H, Kärrman A, Westberg H, Rotander A, van Bavel B, Lindström G. 2010. A Time Trend Study of Significantly Elevated Perfluorocarboxylate Levels in Humans after Using Fluorinated Ski Wax. *Environ. Sci. Technol.* 44, 2150-2155

Norwegian Directorate of Health. 2008. Norwegian Action Plan on Nutrition. Available: http://www.helsedirektoratet.no/vp/multimedia/archive/00026/IS-0238_26559a.pdf [Accessed February 2011]

Odland JØ, Heimstad E, Sandanger TM. 2005. Kartlegging av miljøgifter i humane blodprøver fra Taimyr, Russland og Bodø, Norge - en pilotstudie av "nye" miljøgifter. Report number TA 2103/2005, Norwegian Pollution Control Authority, Oslo, Norway. Available: http://www.klif.no/publikasjoner/overvaking/2103/2103.pdf [In Norwegian, accessed February 2011]

Olsen GW, Burris JM, Ehresman DJ, Froehlich JW, Seacat AM, Butenhoff JL, et al. 2007. Half-life of serum elimination of perfluorooctanesulfonate, perfluorohexanesulfonate, and perfluorooctanoate in retired fluorochemical production workers. *Environ. Health Perspect.* 115, 1298-1305

Olsen GW, Butenhoff JL, Zobel LR.2009b. Perfluoroalkyl chemicals and human fetal development: An epidemiologic review with clinical and toxicological perspectives, *Reprod. Toxicol*. 27, 212-230

Olsen GW, Chang SC, Noker PE, Gorman GS, Ehresman DJ, Lieder PH, et al. 2009a. A comparison of the pharmacokinetics of perfluorobutanesulfonate (PFBS) in rats, monkeys, and humans. *Toxicology* 256, 65-74

Olsen GW, Church TR, Miller JP, Burris JM, Hansen KJ, Lundberg JK, et al. 2003. Perfluorooctanesulfonate and other fluorochemicals in the serum of American Red Cross adult blood donors. *Environ. Health Perspect.* 111, 1892-1901

Ostertag SK, Chan HM, Moisey J, Dabeka R, Tittlemier SA. 2009b. Historic dietary exposure to perfluorooctane sulfonate, perfluorinated carboxylates, and fluorotelomer unsaturated carboxylates from the consumption of store-bought and restaurant foods for the Canadian population. *J. Agric. Food Chem.* 57, 8534-8544

Ostertag SK, Tague BA, Humphries MM, Tittlemier SA, Chan HM. 2009a. Estimated dietary exposure to fluorinated compounds from traditional foods among Inuit in Nunavut, Canada. *Chemosphere* 75, 1165-1172

Paul AG, Jones KC, Sweetman AJ. 2008. A first global production, emission, and environmental inventory for perfluorooctane sulfonate. *Environ. Sci. Technol.* 43, 386-392

Powely CR, George SW, Ryan TW, Buck RC. 2005. Matrix effect-free analytical methods for determination of perfluorinated carboxylic acids in environmental matrixes. *Anal. Chem.* 77, 6353-6358

Prevedouros K, Cousins IT, Buck RC, Korzeniowski SH. 2006. Sources, fate and transport of perfluorocarboxylates. *Environ. Sci. Technol.* 40, 32-44

Roosens L, D'Hollander W, Bervoets L, Reynders H, Van Campenhout K, Cornelis C, et al. 2010. Brominated flame retardants and perfluorinated chemicals, two groups of persistent contaminants in Belgian human blood and milk. *Environ. Pollut.* 158, 2546-2552

Rylander C, Brustad M, Falk H, Sandanger TM. 2009. Dietary predictors and plasma concentrations of perfluorinated compounds in a costal population from Northern Norway. *J. Environ. Public Health* doi:10.1155/2009/268219

Rylander C, Sandanger TM, Frøyland L, Lund E. 2010. Dietary patterns and plasma concentrations of perfluorinated compounds in 315 Norwegian women: The NOWAC postgenome study. *Environ. Sci. Technol.* 44, 5225-5232

Schultz MM, Barofsky DF, Field JA. 2003. Fluorinated alkyl surfactants, *Environ. Eng. Sci.* 20, 487-501

Schulze PE, Norin H. 2006. Fluormiljøgifter i allværsklær. Report 2/2006 from Norges Naturvernforbund. Available:
http://naturvernforbundet.no/getfile.php/Dokumenter/rapporter/2006%20og%202005/2_F luormiljogifter_i_allvaersklaer.pdf [In Norwegian, accessed February 2011]

Seacat AM, Thomford PJ, Hansen KJ, Clemen LA, Eldridge SR, Elcombe CR, et al. 2003. Sub-chronic dietary toxicity of potassium perfluorooctanesulfonate in rats. *Toxicology* 183, 117-131

Seacat AM, Thomford PJ, Hansen KJ, Olsen GW, Case MT, Butenhoff JL. 2002. Subchronic toxicity studies on perfluorooctanesulfonate potassium salt in cynomolgus monkeys. *Toxicol. Sci.* 68, 249-264

Seals R, Bartell SM, Steenland K. 2010. Accumulation and Clearance of PFOA in Current and Former Residents of an Exposed Community. *Environ. Health Perspect.* 119, 119-124

SFT 2006. Kartlegging av perfluoralkylstoffer (PFAS) i utvalgte tekstiler. Report number TA-2173/2006, Norwegian Pollution Control Authority, Oslo, Norway. Available: http://www.klif.no/publikasjoner/kjemikalier/2173/ta2173.pdf [In Norwegian, accessed February 2011]

Shoeib M, Harner T, Ikonomou M, Kannan K. 2004. Indoor and outdoor air concentrations and phase partitioning of perfluoroalkyl sulfonamides and polybrominated diphenyl ethers. *Environ. Sci. Technol.* 38, 1313-1320

Shoeib M, Harner T, Lee SC, Lane D, Zhu J. 2008. Sorbent-impregnated polyurethane foam disk for passive air sampling of volatile fluorinated chemicals. *Anal.Chem.* 80, 675-682

Shoeib M, Harner T, Wilford BH, Jones KC, Zhu JP. 2005. Perfluorinated sulfonamides in indoor and outdoor air and indoor dust: Occurrence, partitioning, and human exposure. *Environ. Sci. Technol.* 39, 6599-6606

Sinclair E, Kim SK, Akinleye HB, Kannan K. 2007. Quantitation of gas-phase perfluoroalkyl surfactants and fluorotelomer alcohols released from nonstick cookware and microwave popcorn bags. *Environ. Sci. Technol.* 41, 1180-1185

So MK, Yamashita N, Taniyasu S, Jiang QT, Giesy JP, Chen K, et al. 2006. Health risks in infants associated with exposure to perfluorinated compounds in human breast milk from Zhoushan, China. *Environ. Sci. Technol.* 40, 2924-2929

Stanek EJ, Calabrese EJ. 1995. Soil ingestion estimates for use in site evaluations based on the best tracer method. *Human Ecol. Risk Assess*. 1, 133-156

Stanek EJ, Calabrese EJ, Barnes R, Pekow P. 1997. Soil ingestion in adults-Results of a second pilot study. *Ecotoxicol. Environ. Saf.* 36, 249-257

Steenland K, Fletcher T, Savitz DA. 2010. Epidemiologic evidence on the health effects of perfluorooctanoic acid (PFOA). *Environ. Health Perspect.* 118, 1100-1108

Stock NL, Muir DCG, Mabury SA. 2010. Perfluoroalkyl compounds. In: Persistent organic pollutants, ed. Harrad S., Wiley, Chichester, UK, page 25-70

Stockholm Convention on Persistent Organic Pollutants (POPs). 2009. Available: http://chm.pops.int/ [Accessed February 2011]

Strynar MJ, Lindstrom AB. 2008. Perfluorinated compounds in house dust from Ohio and North Carolina, USA. *Environ. Sci. Technol.* 42, 3751-3756

Sundström M, Ehresman DJ, Bignert A, Butenhoff JL, Olsen GW, Chang SC, et al. 2011. A temporal trend study (1972-2008) of perfluorooctanesulfonate, perfluorohexanesulfonate, and perfluorooctanoate in pooled human milk samples from Stockholm, Sweden. *Environ. Int.* 37, 178-183

Tao L, Kannan K, Wong CM, Arcaro KF, Butenhoff JL. 2008b. Perfluorinated compounds in human milk from Massachusetts, U.S.A. *Environ. Sci. Technol.* 42, 3096-3101

Tao L, Ma J, Kunisue T, Libelo EL, Tanabe S, Kannan K. 2008a. Perfluorinated compounds in human breast milk from several Asian countries, and in infant formula and dairy milk from the United States. *Environ. Sci. Technol.* 42, 8597-8602

Taves DR. 1968. Evidence that there are two forms of fluoride in human serum. *Nature* 217, 1050-1051

Thomsen C, Liane VH, Becher G. 2007. Automated solid-phase extraction for the determination of polybrominated diphenyl ethers and polychlorinated biphenyls in serum-application on archived Norwegian samples from 1977 to 2003. *J. Chromatogr. B* 846, 252-263

Tittlemier SA, Pepper K, Edwards L. 2006. Concentrations of perfluorooctanesulfonamides in Canadian total diet study composite food samples collected between 1992 and 2004. *J. Agric. Food Chem.* 54, 8385-8389

Tittlemier SA, Pepper K, Seymour C, Moisey J, Bronson R, Cao XL, et al. 2007. Dietary exposure of Canadians to perfluorinated carboxylates and perfluorooctane sulfonate via consumption of meat, fish, fast foods, and food items prepared in their packaging. *J. Agric. Food Chem.* 55, 3203-3210

Toms LM, Calafat AM, Kato K, Thompson J, Harden F, Hobson P, et al. 2009. Polyfluoroalkyl chemicals in pooled blood serum from infants, children, and adults in Australia. *Environ. Sci. Technol.* 43, 4194-4199

Tomy GT, Tittlemier SA, Palace VP, Budakowski WR, Braekevelt E, Brinkworth L, et al. 2004. Biotransformation of N-ethyl perfluorooctanesulfonamide by rainbow trout (Onchorhynchus mykiss) liver microsomes. *Environ. Sci. Technol.* 38, 758-762

Trudel D, Horowitz L, Wormuth M, Scheringer M, Cousins IT, Hungerbuhler K. 2008. Estimating consumer exposure to PFOS and PFOA. Risk Analysis 28, 251-269

United States Environmental Protection Agency (US EPA). 1997. Exposure factors handbook. Available: http://www.epa.gov/ncea/pdfs/efh/efh-complete.pdf [Accessed February 2011]

United States Environmental Protection Agency (US EPA). 2005. Draft Risk Assessment of the Potential Human Health Effects Associated with Exposure to Perflouroctanoic Acids and Its Salts. Available: http://www.epa.gov/oppt/pfoa/pubs/pfoarisk.pdf [Accessed February 2011]

United States Environmental Protection Agency (US EPA). 2006a. U.S. EPA. 2010/2015 PFOA stewardship program. Available: http://www.epa.gov/oppt/pfoa/pubs/stewardship/ [Accessed February 2011]

United States Environmental Protection Agency (US EPA). 2006b. Scientific Advisory Board's Response to EPA's Draft Risk Assessment (letter). Available: http://www.epa.gov/sab/pdf/sab_06_006.pdf [Accessed February 2011]

Van Leeuwen CJ, Vermeire TG (eds). 2007. Risk assessment of chemicals. 2 ed., Springer, Dordrecht, The Netherlands

Van Leeuwen SPJ, de Boer J. 2007. Extraction and clean-up strategies for the analysis of poly- and perfluoroalkyl substances in environmental and human matrices. *J. Chromatogr. A* 1153, 172-185

Van Leeuwen SPJ, van Velzen MJM, Swart CP, van der Veen I, Traag WA, de Boer J. 2009. Halogenated Contaminants in Farmed Salmon, Trout, Tilapia, Pangasius, and Shrimp. *Environ. Sci. Technol.* 43, 4009-4015

Vejrup KV, Lindblom B. 2002. Analysis of perfluorooctanesulfonate compounds in impregnating agents, wax and floor polish products. Survey no. 17 from the Danish Environmental Protection Agency. Available: http://www.mst.dk/NR/rdonlyres/C2B54B41-7C66-4E2F-B2F9-A6ACAA69C37B/0/17.pdf [Accessed February 2011]

Verreault J, Berger U, Gabrielsen GW. 2007. Trends of perfluorinated alkyl substances in herring gull eggs from two coastal colonies in northern Norway: 1983-2003. *Environ. Sci. Technol.* 41, 6671-6677

Vestergren R, Cousins IT. 2009. Tracking the pathways of human exposure to perfluorocarboxylates. *Environ. Sci. Technol.* 43, 5565-5575

Vestergren R, Cousins IT, Trudel D, Wormuth M, Scheringer M. 2008. Estimating the contribution of precursor compounds in consumer exposure to PFOS and PFOA. *Chemosphere* 73, 1617-1624

Villagrasa M, de Alda ML, Barcelo D. 2006. Environmental analysis of fluorinated alkyl substances by liquid chromatography-(tandem) mass spectrometry: A review. *Anal. Bioanal. Chem.* 386, 953-972

Völkel W, Genzel-Boroviczeny O, Demmelmair H, Gebauer C, Koletzko B, Twardella D, et al. 2008. Perfluorooctane sulphonate (PFOS) and perfluorooctanoic acid (PFOA) in human breast milk: Results of a pilot study. *Int. J. Hyg. Environ. Health* 211, 440-446

Washburn ST, Bingman TS, Braithwaite SK, Buck RC, Buxton LW, Clewell HJ, et al. 2005. Exposure assessment and risk characterization for perfluorooctanoate in selected consumer articles. *Environ. Sci. Technol.* 39, 3904-3910

Weihe P, Kato K, Calafat AM, Nielsen F, Wanigatunga AA, Needham LL, et al. 2008. Serum concentrations of polyfluoroalkyl compounds in Faroese whale meat consumers. *Environ. Sci. Technol.* 42, 6291-6295

Zhang T, Sun HW, Wu Q, Zhang XZ, Yun SH, Kannan K. 2010. Perfluorochemicals in meat, eggs and indoor dust in China: Assessment of sources and pathways of human exposure to perfluorochemicals. *Environ. Sci. Technol.* 44, 3572-3579

2

3

4

5

Appendix

folkehelseinstituttet

Blir vi utsatt for miljøgifter fra innemiljøet?

Spørreskjema for deltakere *Konfidensielt*	
Navn	**Fødselsdato** (dd/mm/åååå)
Adresse	**Dato**
Hvor mange personer bor i boligen? Antall voksne…………………. Antall barn ………….. Barnas alder………………………	
Hvilken type bolig bor du i? (sett x ved det som passer) Enebolig/rekkehus ………….. Leilighet ……………… eventuelt etasje nr…………….	
Hvor lenge har du bodd i boligen? ………………….. år	
Når ble boligen bygget? ……………………..(ca årstall)	
Hvor stor er boligen? Totalt ………….kvm Stue……………kvm Ditt soverom…………..kvm	
Er det ventilasjonsanlegg i boligen? ☐ Ja ☐ Nei	
Hvordan varmes boligen opp? (sett x ved det som passer) Sentralfyr ☐ Elektrisk ☐ Vedfyring ☐ Olje/parafin ☐	

Finnes sterkt trafikkert(e) vei(er) mindre enn 500 m fra boligen?
(alltid minst en bil å se på veien hele dagen)

☐ Ja   ☐ Nei   Hvis ja, omtrent hvor langt unna er veien (i meter) …………………

Finnes industriområde(r) mindre enn 500 m fra boligen?

☐ Ja   ☐ Nei   Hvis ja, hvilken type industri?..

Luftes det daglig?

I stua: ☐ Ja   ☐ Nei   På soverommet: ☐ Ja   ☐ Nei

Røykes det i hjemmet?

☐ Ja   ☐ Nei

Hvis ja, i hvilke rom? (sett x ved det som passer)

Stue ☐   Kjøkken ☐   Soverom ☐   Bad ☐   Gang ☐   Arbeidsrom ☐

Hvis ja, hvor mange sigaretter røykes i hjemmet per dag? ……………..

Røyker du? (sigaretter, rullings)

Aldri røykt   Sluttet   Av og til   1-10 daglig   10-20 daglig   > 20

☐   ☐   ☐   ☐   ☐   ☐

Omtrent hvor mange timer per dag oppholder du deg i hvert av disse rommene?
(inkludert når du sover)

Stue ………   Kjøkken ………   Soverom………   Arbeidsrom ………

Har du/dere husdyr i leiligheten?

☐ Ja   ☐ Nei

Hvis ja, hvilke(t) husdyr? ……………………………………………………………………………

Har du følgende materialer i stuen? (spesifiser type materiale f.eks ull, syntetisk, bomull, vinyl og annet, og alder på materialene)

	Ja / Nei	Materiale	Alder (år)		
			Under 1 år	1-5 år	Mer enn 5 år
Vegg-til-vegg teppe	☐ Ja ☐ Nei				
Gulvteppe	☐ Ja ☐ Nei				
Gulvbelegg	☐ Ja ☐ Nei				
Polstret stol	☐ Ja ☐ Nei				
Polstret sofa	☐ Ja ☐ Nei				

Har du følgende materialer i ditt soverom? (spesifiser type materiale f.eks ull, syntetisk, bomull, vinyl og annet, og alder på materialene)

	Ja / Nei	Materiale	Alder (år)		
			Under 1 år	1-5 år	Mer enn 5 år
Vegg-til-vegg teppe	☐ Ja ☐ Nei				
Gulvteppe	☐ Ja ☐ Nei				
Gulvbelegg	☐ Ja ☐ Nei				
Madrass	☐ Ja ☐ Nei				
Overmadrass	☐ Ja ☐ Nei				
Teppe/dyne	☐ Ja ☐ Nei				
Pute	☐ Ja ☐ Nei				

Har du/dere en eller flere av følgende elektriske apparater:

	Ja	Nei	Antall i husholdningen	Alder på apparatet/apparatene		
				Under 1 år	1-5 år	Mer enn 5 år
TV						
TV med flatskjerm						
Video/DVD						
TVspillkonsoll						
CDspiller						
Stasjonær datamaskin						
Bærbar datamaskin						
Dataskjerm						
Flatskjerm til datamaskin						
Skriver/kopimaskin/telefax						
Radio/forsterker/høytalere						
Telefon og mobiltelefon						
Mikrobølgeovn						
Kaffetrakter						
Vannkoker						
Food processor/mikser						
Komfyr						
Kjøleskap						
Fryser						
Oppvaskmaskin						
Vaskemaskin						
Tørketrommel						
Gulvstøvsuger						
Sentralstøvsuger						
Annet:						

Hvor ofte og hvor lenge bruker du eller en av de andre i husholdningen følgende elektriske apparater: (hvis du har flere av en kategori summerer du bruken av disse, eks: hvis TV står på 5 dager i uka i 2 timer per dag, skriver du tallet 5 i kolonnen Ukentlig og 10 i kolonnen Timer i bruk)

	Daglig	Ukentlig	Månedlig	Timer i bruk
TV				
TV med flatskjerm				
Video/DVD				
CDspiller				
TVspillkonsoll				
Stasjonær datamaskin				
Bærbar datamaskin				
Dataskjerm				
Flatskjerm til datamaskin				
Skriver/kopimaskin/telefax				
Radio/Forsterker				
Telefon og mobiltelefon				
Mikrobølgeovn				
Kaffetrakter				
Vannkoker				
Food processor/Mikser				
Komfyr				
Oppvaskmaskin				
Vaskemaskin				
Tørketrommel				
Gulvstøvsuger				
Sentralstøvsuger				
Annet:				

Skaffer du/dere oftest nye eller brukte forbruksvarer? (sett kryss)

	Nesten alltid nytt	Oftest nytt	Oftest brukt	Alltid brukt
Bil				
Sofa/møbler				
Barneklær				
Egne klær				
TV/PC/stereoanlegg osv.				
Hvitevarer				

Hva slags type materiale er det på de klærne du bruker som er i direkte kontakt med huden? (sett x ved kategorien som passer best. 1 betyr at klærne kun er laget av naturlige materialer, 3 betyr at halvparten av innholdet er syntetisk og halvparten er naturlig, mens 5 betyr at klærne kun er laget av syntetiske materialer)

	1 = 100% naturlig materiale - - - - - - **5** = 100% syntetisk materiale				
	1	**2**	**3**	**4**	**5**
Undertøy					
Bukse/skjørt					
Bluse/kjole					
Sokker/strømper					

Hvor er TV'en(e) plassert? (du kan sette flere kryss)

Stue   Kjellerstue   Soverom   Gang   Annet sted

☐   ☐   ☐   ☐   ☐   .... (spesifiser)

Hvor er PC'en(e) plassert? (du kan sette flere kryss)

Stue   Hjemmekontor   Soverom   Gang   Annet sted

☐   ☐   ☐   ☐   ☐   .... (spesifiser)

Har dere klær av Gore-Tex® eller Gore-Tex® lignende materiale?

☐ Ja   ☐   Nei   hvis ja, antall:………

Har dere sko med Gore-Tex® eller Gore-Tex® lignende materiale?

☐ Ja ☐ Nei Hvis ja, antall par:………

Benytter du/dere kjeler eller stekepanner med Teflon® eller lignende belegg i matlaging?

☐ Ja ☐ Nei

Benytter du/dere kjøkkenredskaper med Teflon® eller lignende belegg i matlaging?

☐ Ja ☐ Nei

Har du vanligvis et arbeid du utfører andre steder enn hjemme? ☐ Ja ☐ Nei

Hvor mange timer jobber du da per dag? ……………………………….timer

Hvor mange dager i uka jobber du? ……………………………..dager

Hvilken andel av tiden jobber du med elektrisk utstyr (f.eks PC) ? ………prosent

Gi en kort beskrivelse av din jobb og materialer du jobber med:

……………………………………………………………………………………………………

 ……………………………………………………………………………………………………

Eier/benytter du en bil? ☐ Ja ☐ Nei
Hvis ja:
Hvilket merke har den? ………………………
Hvilken årsmodell er den? …………………..
I gjennomsnitt per dag, hvor mange timer tilbringer du i denne bilen? ……………timer

Bruker du noen andre biler i jobb eller privat? ☐ Ja ☐ Nei
Hvis ja:
Hvilket merke har den? ………………………
Hvilken årsmodell er den? …………………..
I gjennomsnitt per dag, hvor mange timer tilbringer du i denne bilen? ……………timer

Eier/benytter du en campingvogn? ☐ Ja ☐ Nei
Hvis ja:
Hvilken årsmodell er den? ………………….
I gjennomsnitt per år, hvor mange dager tilbringer du i denne campingvognen? ……………dager

Hvor ofte i gjennomsnitt blir ditt soverom og stuen støvsuget?

Stuegulv …………… (antall ganger) per ………........ *uke/måned* *(stryk det som ikke passer)*

Soveromsgulv …………… (antall ganger) per ………........ *uke/måned* *(stryk det som ikke passer)*

Når ble dette gjort forrige gang?........................

Hvor ofte i gjennomsnitt blir ditt soverom og stuen vasket?

Stuegulv …………… (antall ganger) per ………........ *uke/måned* *(stryk det som ikke passer)*

Soveromsgulv …………… (antall ganger) per ………........ *uke/måned* *(stryk det som ikke passer)*

Når ble dette gjort forrige gang?........................

Benytter du/dere poleringsmiddel for eksempel til polering av gulv, stuebord eller annet?

☐ Ja   ☐   Nei

Hvis ja, hva heter poleringsmiddelet? …………………………………………..

Har ett eller flere av følgende rom blitt renovert/pusset opp etter at blodprøven til prosjektet ble tatt?

	Ja	Nei	Hvis ja, hva har blitt gjort?
Stue			
Kjøkken			
Soverom			
Bad			
Gang			
Arbeidsrom			

Har du flyttet etter at blodprøven til prosjektet ble tatt?

☐ Ja   ☐   Nei

Har du/dere kjøpt noen nye møbler og/eller gulvtepper etter at blodprøven til prosjektet ble tatt?

☐ Ja   ☐   Nei

Hvis ja, spesifiser: ………………………………………………………………….

Har du/dere kjøpt noen nye elektriske artikler etter at blodprøven til prosjektet ble tatt?

☐Ja   ☐   Nei

Hvis ja, spesifiser: ……………………………………………………………………….

Hvilken utdannelse har du?

☐ 9 årig grunnskole

☐ 1-2 årig videregående

☐ 3 årig videregående

☐ Distrikthøyskole/universitet inntil 4 år

☐ Universitet/høyskole mer enn 4 år

Har du født barn?

☐ Ja   ☐   Nei

Hvis JA:

Ammet du?

1. barn født………………:	☐ Ja	☐ Nei	Eventuelt hvor lenge:
2. barn født………………:	☐ Ja	☐ Nei	Eventuelt hvor lenge:
3. barn født………………:	☐ Ja	☐ Nei	Eventuelt hvor lenge:

Hva veier du:

Hvor høy er du:

Er du født i Norge?   ☐ Ja   ☐   Nei

Er din mor født i Norge? ☐ Ja   ☐   Nei

Er din far født i Norge? ☐ Ja   ☐   Nei

Hvis NEI:

Hvilket land er du, din mor og far født i?

Du: …………………………………………

Mor: …………………………………………..

Far: …………………………………………...

Har du bodd i utlandet i mer enn 6 mnd?

☐ Ja   ☐ Nei

Hvis JA:

Hvor har du bodd lengst?

Norden	Europa	Afrika	Østen	Midtøsten	USA/Canada	Sør-Amerika	Oseania
☐	☐	☐	☐	☐	☐	☐	☐

KOSTHOLD

Hvor mange ganger <u>i livet</u> omtrent har du spist:

	Aldri	1-10	11-100	Mer enn 100
Gjedde				
Fiskemølje				
Måsegg				
Lever eller nyre fra vilt				
Krabber				

KOSTHOLDET DITT DET SISTE ÅRET

Viktig: *Velg å svare på antall ganger per **uke, måned, ELLER i året** for hver matsort ettersom hva som passer best!*

	Sett x	Sett antall i		
	Aldri	Uken	Måneden	Året
Pålegg og annet:				
Ost *(påleggsporsjoner)*				
Egg *(utenom middag)*				
Melk/yoghurt *(antall glass)*				

	Sett x	Sett antall i		
	Aldri	Uken	Måneden	Året
Peanøtter				
Tran				
Leverpostei				
Makrell/laks som pålegg				
Krabbepålegg				
Tunfisk i boks				
Svolværpostei (og andre fiskeleverposteier)				
Middagsporsjon:				
Hvitt kjøtt *(kylling, kalkun)*				
Svinekjøtt				
Oksekjøtt				
Sau/lammekjøtt				
Bearbeidet kjøtt *(deig, kaker, pølse)*				
Egg *(omelett, pannekaker m.m.)*				
Lever/nyre fra elg/vilt				
Lever/nyre fra okse, sau og gris				
Makrell, laks, ørret og sild				
Torsk, sei, flyndre				
Kolje/hyse				
Kveite/hellefisk				
Gjedde og abbor				
Bearbeidet fisk *(pinner/gratenger)*				

	Sett x	Sett antall i		
	Aldri	Uken	Måneden	Året
Lever fra torsk eller sei				
Skjell (Blåskjell/kamskjell)				
Reker				
Krabbe				
Middag uten kjøtt/fisk/egg *(grøt, vegetar)*				

FISK, KRABBE M.M.

Hvis du spiser selvfisket/selvfangede produkter som fisk, krabbe o.s.v. *(eller noen du kjenner fisker/fanger det for deg):*

Hva heter fjorden som sjømaten vanligvis kommer fra?

Oppgi fjordens navn:

Hva heter vannet som sjømaten vanligvis kommer fra?

Oppgi vannets navn:

Hvilken sjømat gjelder dette (krabbe, sei, ørret m.m.)?

Oppgi navn:

Takk for at du tok deg tid til å svare på spørreskjemaet!