Perfluorinated Chemicals: an emerging concern

Allsopp, M., Santillo, D., Walters, A. & Johnston, P.

Greenpeace Research Laboratories, Department of Biological Sciences, University of Exeter, Exeter EX4 4PS, UK

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Michelle Allsopp, David Santillo, Adam Walters and Paul Johnston

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CONTENTS

SUMMARY

Perfluorinated compounds (PFCs) are man-made chemicals. They never occur in nature. They are persistent in the environment, that is, they resist natural breakdown processes. This is due to the very strong carbon-fluorine bonds in the chain of the PFC molecule. Nevertheless, some PFCs can be transformed in the environment or in living organisms to form other, more stable PFCs. Research has revealed that some PFCs have the potential to bioaccumulate (build up) in the blood and liver of living organisms. Furthermore, studies on toxicity have shown that two PFCs, which are known contaminants of the global environment, namely perfluorooctane sulphonate (PFOS) and perfluorooctanoic acid (PFOA), exert many adverse effects on laboratory mammals and aquatic organisms. Some PFCs are thus persistent, bioaccumulative and toxic, three properties which mean they are particularly problematic in the environment and are of very high concern.

Perfluoroalkyl sulfonates, or PFOS-related chemicals, are PFCs that have been produced for over 50 years. They have properties of repelling both oil and water and, as a consequence, they have been used in producing protective coatings for carpet, leather, textiles and paper as well as being used as surfactants in a wide variety of applications. Other PFCs, perfluorinated carboxylates, which include PFOA and fluorotelomer alcohols, have also been produced for many years. They have similar uses to perfluoroalkyl sulfonates. One use of PFOA is for a process to produce non-stick coating on saucepans. The production of perfluoroalkyl sulfonates was stopped in the USA in 2003 because of concern that PFOS had been found as a widespread contaminate in wildlife and humans. Legislation is beginning to follow in other countries for PFOS-related chemicals. In the meantime, other PFCs are still being produced and used.

A global contamination problem.

PFCs are now ubiquitous global contaminants. These chemicals have been detected in indoor and outdoor air, in rivers, lakes and groundwater, in wastewater treatment effluent, in landfills and in the marine environment. PFCs have also been found in the body tissues of many different living organisms throughout the world including humans. During the past few years research has revealed that PFOS is the predominant PFC compound detectable in living organisms. Other PFCs, such as PFOA and long-chain perfluorocarboxylates, are also detectable but often at lower concentrations.

It has been observed that levels of PFCs in humans, wildlife and the environmental are generally higher near to urbanised or industrial areas compared with more rural or remote areas. The most likely explanation of this phenomenon is that urban and industrialised areas are in closer proximity to PFC sources. Nevertheless, PFCs have been found to contaminate even remote regions of the globe such as the Arctic. This has led to the belief that these chemicals undergo long-range transport on air currents to become widespread far from their sources. Some of the perfluorinated sulfonates are thought to undergo long-range transport from where they may also be transformed, either in the environment or in living organisms, to form PFOS. This is the reason why PFOS is so globally ubiquitous. Other fluorinated chemicals, the fluorotelomer alcohols, are volatile and are thought to be able to undergo long-range transport. These chemicals may break down in the environment or in living organisms to form more stable perfluorinated carboxylates. The presence of long-chain perfluorinated carboxylate chemicals in Arctic wildlife is likely to be due to the use of fluorotelomer alcohols.

Concentrations of PFCs in the Environment and in Living Organisms

Research on PFCs has mainly been conducted during the past few years. Many of the studies on concentrations of PFCs in the environment and in living organisms have focused on PFOS and sometimes also PFOA. Concentrations of other PFCs have been studied less frequently:

- In freshwater, studies found that concentrations of PFOS and PFOA generally fell in the range of <1-36 ng/l (ppt). Similar concentrations were found in coastal marine locations. In open ocean waters, levels are lower and are generally measured in pg/l (ppq) quantities. PFOS and PFOA were even detectable in the deep ocean at depths of >1000m. In coastal areas influenced by industrial inputs, and in an inland water body near to a fluorochemical manufacturing facility, concentrations of PFOS and PFOA were found to be an order of magnitude higher (>100 ng/l) than areas without direct industrial inputs. Studies in Japan reported PFOA contamination in drinking water in two areas, and in the USA, contamination of drinking water with PFOA occurred near to a manufacturing facility that used PFOA. Contaminated drinking water is a potential source of exposure to PFCs for humans.

- Concentrations of perfluoroalkyl sulfonamides in outdoor air have been reported up to 403 pg/m^3. Concentrations in indoor air were an order of magnitude higher and represent a potential exposure route in humans. PFOS and PFOA were also present in dust samples from homes that were tested in Japan. Inhalation of dust is a possible pathway of human exposure to these chemicals.

- Laboratory studies with fish have shown that perfluorinated sulfonates with a chain length of more than four, and perfluorinated carboxylates with a chain length of more than six, bioaccumulated in the blood and liver of fish as a result of exposure from contamination in the surrounding water and from contaminated food. In the environment, concentrations of PFOS reported in tissues of freshwater and marine fish ranged from <1 to 7900 ng/g wet weight (or ppb). Other perfluorinated sulfonates and carboxylates were also detected in fish.

- Studies in Japan, the USA and Italy have shown that liver samples from birds contain PFOS at concentrations of up to about 1780 ng/g wet weight. Levels in Arctic birds were lower, up to 26 ng/g wet weight. Comparatively high concentrations were also detected in eggs and in young chicks indicating that the developing young are exposed to PFOS.

- Marine mammals from a wide range of geographical locations have been shown to have concentrations of PFOS in liver tissue ranging up to about 1500 of ng/g wet weight. For polar bears in the Canadian Arctic, the concentrations in liver samples were even higher (1700 to >4000 ng/g). Such high levels reflect the top position of polar bears in the food chain. A number of perfluorinated carboxylates have also been detected in marine mammals including the polar bear.

- Comparatively high levels of PFOS have been found in mink (up to 5140 ng/g wet weight in liver) and otters (up to approximately 1000 ng/g) from the USA.

- In humans, concentrations of PFOS vary between countries but generally fall within the range of <1 to 200 ng/ml in blood serum, and more commonly in the range <1 to 30 ng/ml. Several perfluorinated carboxylates have also been detected in human blood.

PFOS and PFOA were found in samples of umbilical cord blood which indicates possible exposure to the foetus in the womb. In individuals who have been exposed to PFCs through their occupation, concentrations in blood are much higher than the general population (PFOS up to 12830 ng/ml, PFOA up to 81 300 ng/ml).

Toxic Effects

PFOS and PFOA were found to cause a wide range of toxic effects in exposed laboratory rats at doses higher than those currently found in wildlife. For instance PFOS and PFOA caused toxic effects on the liver, including reduced serum cholesterol levels and induction of enzymes associated with β-oxidation of fatty acids. PFOA caused adverse effects on the immune system and acted as a tumour promoter. PFOS caused adverse effects on development including death of rat pups. At levels lower than those present in wildlife, PFOS was found to act as an endocrine disruptor in rats, affecting the estrous cycle.

Some PFCs have been found to inhibit the communication system between cells in both mammalian cell lines *in vitro* and in rats. Disruption of this process results in abnormal cell growth and function and as such, the PFCs may pose a risk to the health of mammalian systems.

In humans exposed occupationally to PFCs there was an increase in deaths from certain cancers although the numbers of deaths in the studies were too small to make firm conclusions. One study found that exposure to PFOA was linked with changes in the levels of the hormones estradiol and testosterone, although another study found no effect on hormone levels. One study found an increase in cholesterol in workers exposed to PFOA whereas two others found no effect on this measure of liver toxicity.

PFOS and PFOA have been found to cause toxic effects on aquatic organisms at comparatively high concentrations. Adverse effects may occur on organisms at levels recorded in the environment following accidental spills of PFCs. Furthermore, one study indicated there was a small likelihood of causing adverse effects to freshwater plants and crustaceans at current environmental levels.

The Future

Although the production of PFOS-related compounds has ceased in the USA, the production has moved to perfluorobutyl sulphonate. This compound is persistent but not bioaccumulative. There little research on its toxicity but, unlike some other PFCs, it was not toxic to a communication system in mammalian cells. It is suspected that replacement of PFOS-related chemicals in the market are also being provided by fluorotelomer alcohols. These chemicals are believed to transform in living organisms to perfluorinated carboxylates which are persistent and bioaccumulative. There is little knowledge on the toxicity of perfluorinated carboxylates and they are already widespread environmental contaminants.

The US EPA has imposed a ban on the use of PFOS-related chemicals with the exception of a few essential uses. Similarly, the UK government have announced action to phase out PFOS-related chemicals and the European Commission is currently drafting proposals to restrict their marketing and use. However, with regard to other PFCs, such as PFOA, and the fluorinated telomers there is currently no legislation. This is of great concern considering that some these chemicals are persistent, bioaccumulative and possibly toxic. These chemicals are still being widely used despite their persistence and bioaccumulative properties while there is clearly a lack of knowledge on toxicity.

1. INTRODUCTION

Organofluorines are chemicals which contain both atoms of carbon and fluorine. There are about 30 natural organofluorine molecules (Hekster *et al.* 2003). These molecules contain only one fluorine atom per molecule. In contrast, man-made fluorinated organic compounds often contain many fluorine atoms, that is, they are polyfluorinated (Key *et al.* 1997). In fluorinated organic chemicals, a number of carbon-hydrogen bonds are replaced by carbon-fluorine bonds. In perfluorinated compounds (PFCs), all the carbon-hydrogen bonds are replaced with carbon-fluorine bonds (Renner 2001). PFCs are composed of a carbon-fluorine chain and generally have side moieties attached such as carboxylic acids or sulfonic acids. These compounds are respectively called perfluorinated carboxylates or perfluoroalkyl carboxylates (PFCA) and perfluorinated sulfonates or perfluoroalkyl sulfonates and they make up two major classes of PFCs (Giesy and Kannan 2002). The carbon-fluorine bond in PFCs is very strong and gives thermal and chemical stability to many PFCs (So *et al.* 2004). The stability that makes fluorinated compounds desirable for commercial use also makes them potentially significant environmental contaminants due to their resistance to natural breakdown processes, that is, their persistence (Key *et al.* 1997). Research over the past few years has shown that the PFC perfluorooctane sulfonate (PFOS) is now a widespread environmental contaminant and is found in living organisms globally.

1.1 Production and Uses

PFCs are manufactured because of their specific physical and chemical properties such as chemical and thermal inertness and special surface-active properties (Hekster *et al.* 2003). They repel both water and oil and act as surfactants, that is, they reduce surface tension and do so better than other surfactants (Renner 2001). These properties have led to the use of perfluorinated compounds in a wide variety of applications. For instance, their unique properties of repelling both water and oil has led to their use as coatings for carpet protection, textile protection, leather protection, and paper and board protection. They are also used in fire-fighting foams and as polymerisation aids. In addition they are used as speciality surfactants, for example, in cosmetics, electronics, etching, medical use and plastics (Hekster *et al.* 2003, So *et al.* 2004).

On the uses of PFCS, it has been reported that the use of the sulfonated fluorochemicals can be divided into 3 main categories, namely surface treatments, paper protectors and performance chemicals (Kannan *et al.* 2002b). Surface treatment applications are carried out to give resistance to soil, oil and water for carpet, fabric, upholstery and leather. The US EPA reported that 37% of the production of fluorinated surfactants is used for surface treatment applications (Kannan *et al.* 2002b). For paper protection, historically, sulfonated fluorochemicals were applied to paper products, such as plates, food containers and bags to provide grease, oil and water resistance. The US EPA reported that 42% of sulfonated fluorochemicals were used for coatings on paper products in 2000 (Kannan *et al.* 2002b). Performance chemicals are used for many different industrial, commercial and consumer applications including fire-fighting foams, mining and oil well surfactants, acid mist suppressants for metal plating and electronic etching baths, alkaline cleaners, floor polishes, photographic film, denture cleaners (Kannan *et al.* 2002b) and Sulfluramid, and insecticide used to control cockroaches, termites and ants (Kannan *et al.* 2004). The annual production of all PFOS-related chemicals in the USA was 3 thousand tonnes in 2000 (Stock *et al.* 2004). Table 1.1 gives estimates of the amounts of perfluoroalkylated substances used in various applications in the Netherlands and the UK.

Table 1.1 Estimated use and emissions of perfluoroalkylated substances in the Netherlands and the UK.

Type of Industry	Use in the Netherlands (tonnes/year)	Use in the UK (tonnes/year)	Emissions in the Netherlands (tonnes/year)[a]
Carpet	15	195[b]	10 (mostly wear)
Paper and Board	60-105 (not in NL)	60	23-41 (landfilled waste)
Textile	N.A.	-[b]	N.A. (100% mostly wear)
Leather	10-20	N.A	10-20 (mostly wear)
Fire-fighting foams	1-4	65	1-4 (use)
Speciality surfactants	N.A.	70	N.A
Polymerisation aid	>1	N.A.	>0.77

Source: Hekster *et al.* (2003)
N.A. not available
[a]These figures represent a worst case estimation
[b]Carpet and textiles together

PFCs have been produced by the 3M company since 1956. 3M have produced perfluoroalkylsulfonates by a process known as electrochemical fluorination. Perfluorooctane sulfonylfluoride (POSF) is the starting product for a range of different products (Hekster *et al.* 2003). POSF is chemically reacted to form PFOS and *N*-methyl and *N*-ethyl perfluorooctanesulfonamidoethanol (*N*-Me FOSE) and (*N*-EtFOSE) (Corsoloni and Kannan 2004, Hekster *et al.* 2003). These are the primary building block used in perfluorochemistry by the 3M company. The electrochemical fluorination process itself, besides making POSF, also generated other perfluorinated chemicals as by-products. (Hekster *et al.* 2003). POSF-based products may degrade or be metabolised to form PFOS, which is stable and chemically inert (Kannan *et al.* 2002a).

3M is the only major company known to use the electrochemical fluorination process (Renner 2001). Other companies use a different process for the production of PFCs namely the telomerization process. Perfluoroalkylethylates are produced (Hekster *et al.* 2003, Renner 2001). Telomerization has recently become more widely used in the production of many PFCs (So *et al.* 2004). Companies which use this process include AsahiGlass (Japan), AtoFina (France), Clariant (Germany), Daikin (Japan) and DuPont (United States) (Hekster *et al.* 2003, Renner 2001). DuPont make perfluorooctanoic acid (PFOA) from which Teflon is made, a non-stick coating used for saucepans (ENDS 2003). PFOA is used also used to make Goretex (Renner 2003). The telomerization process also results in the production of fluorotelomer alcohols (FTOHs), compounds consisting of a perfluorinated chain with two non-fluorinated carbons adjacent to a hydroxyl group attached to one end. FTOHs have recently been shown to break down in the environment to form perfluorinated carboxylates (see below). FTOHs are used as precursor molecules for the production of fluorinated polymers which, in turn, have similar uses to PFOS-based compounds such as in paper and carpet treatments (Dinglasan *et al.* 2004). They are also used in the manufacture of paints, adhesives, waxes, polishes, metals and electronics. The global production of FTOHs was estimated as 5 thousand tonnes during the years 2000-2002. 40% of the production occurred in North America (Dinglasan *et al.* 2004).

In May 2000, the 3M company announced that it would phase out the manufacture of materials based on perfluorooctanesulfonyl fluoride (POSF) by 2003 (Olsen *et al.* 2003, Stock *et al.* 2004). The decision was based on "[…] principles of responsible environmental management" (Hekster *et al.* 2003). It was due research showing that PFOS was widespread in human populations and wildlife (Olsen *et al.* 2003), and 3M were put under pressure from the United States Environmental Protection Agency to stop production (ENDS 2001, ENDS 2004a). For some applications, the production of perfluoroalkylated substances is being continued, but otherwise it is thought that 3M will replace the perfluorooctyl chemistry with the butyl equivalent (Hekster *et al.* 2003). It has been suggested that 3M's decision to move to perfluorobutane sulphonate (PFBS) is based entirely on the fact that it is less bioaccumulative than PFOS. There may not be a difference in the toxicity, but substances which do not bioaccumulate are less likely to reach toxic thresholds in the body (ENDS 2004a). In addition to PFBS other substitutes for PFOS – related chemicals are likely to be products made from perfluorinated telomers. Telomer manufacturers may take a large chunk of the market vacated by PFOS-based products (ENDS 2004a).

A recent report by the UK Environment Department (DEFRA) noted that uses of PFOS-related compounds in the UK had reduced markedly since 3M phased out production of these chemicals (see ENDS 2004c). It concluded that use had ceased for carpet, leather, paper and textile coatings, household cleaning products and pesticides. However, the Swedish Chemical Inspectorate, which has a register of product ingredients manufactured in or imported into Sweden, reported that PFOS-related substances were still present in some textile and leather protection products and household cleaners (ENDS 2004c).

1.2 Sources of PFCs and Environmental Fate

PFOS is widespread in the global environment and is present in the tissues of aquatic and terrestrial living organisms including humans. Other PFCs, including PFOA, perfluorooctanesulfonamide (PFOSA), perfluorohexanesulfonate (PFHS), PFBS and perfluorononanoic acid (PFNA) are also found in living organisms although often to a lesser extent than PFOS (So *et al.* 2004). The mechanisms and pathways leading to the presence of perfluorinated compounds in wildlife and humans are not well characterised, but it is likely there are multiple sources (Kannan *et al.* 2002a).

1.2.1 *Sources to the Environment Through Manufacture and Use*

The mechanisms by which volatile PFCs enter the environment may include release during manufacturing and application processes (Stock *et al.* 2004). For example, it has been demonstrated that the effluent from a fluorochemical manufacturing facility can be a source of perfluoroalkylated substances in the environment (Hekster *et al.* 2003). Emissions to the environment may also occur by leaching from consumer products and from waste products in landfills due to abiotic and/or biotic degradation processes (Stock *et al.* 2004). Specifically for fluorotelomers, it has been theorized that they can be released into the air during manufacture of surfactants or during application of stain protectors or can be released domestically. For example, there may be a residue left on treated materials that is not bound to the polymer and can therefore move into air. Also, these chemicals can be released through use or abrasion of a coated product because of the bond breaking between the surfactant and the polymer (Renner *et al.* 2003).

A study in the Netherlands estimated the emissions of perfluoroalkylated substances from various industrial applications (see table 1.1) (Hekster *et al.* 2003). It was noted that for treated

materials, it has been estimated that a very large amount of the applied PFCs will wear from the fibres and lead to emissions to the environment. For treated paper products, there are no studies but emissions may occur when the products are landfilled. Fire-fighting foams can result in direct releases to the environment (see also section 2.2). It has been estimated by the Association of Plastic Manufacturers Europe (APME) that when used as a polymerisation aid in global fluoropolymer production, 61% of the polymerisation aid is emitted to water, air or land and only 16% is present in the produced polymer (Hekster *et al.* 2003). When the results of the estimations for different uses of perfluoroalkylated substances were all considered, the study concluded that although the figures are estimations and some data are missing, several tonnes of perfluoroalkylated substances per year may be emitted to the Netherlands environment (Hekster *et al.* 2003).

1.2.2 *Sources of PFOS to the Environment*

POSF-based chemicals may degrade or be metabolised to PFOS, known as the final metabolite of POSF-based fluorochemicals. PFOS is stable, chemically inert and has the potential to bioaccumulate in living organisms (Corsolini and Kannan 2004). It has a high water solubility, which makes it less likely to partition to and be transported by air, (Giesy and Kannan 2002), and it is fairly involatile. These properties mean that it PFOS unlikely to enter the atmosphere directly and undergo long-range transport on air currents to remote regions (Shoeib *et al.* 2004, Stock *et al.* 2004). The same is also true for PFOA (Hekster *et al.* 2003). Although the environmental fate of PFOS is not completely understood, the accepted mechanism by which it occurs in remote areas is by other more volatile PFCs, such as perfluoroalkyl sulfonamides, acting as precursors which carry a PFOS moiety, being transported for long distances and then being degraded or metabolised to PFOS (Shoeib *et al.* 2004, So *et al.* 2004, Stock *et al.* 2004). There are data which show that PFCs produced by electrochemical fluorination can be broken down by microorganisms to PFOS and PFOA (Hekster *et al.* 2003). The 3M phase-out of perfluorooctyl chemistry will phase out the use of PFOS and those PFCs that break down to PFOS. If manufacturing is the main source of PFOS in the environment, then the phase-out should result in a substantial reduction of PFOS in the environment. However if PFOS is coming from existing products or from landfills there could still be significant environmental problem well in to the future (Renner 2001).

Tomy *et al.* (2004) carried out a study to investigate whether it was possible for fish to metabolise *N*-ethyl perfluorooctanesulfonamide (*N*-EtPFOSA) to PFOS and PFOA. *N*-EtPFOSA is commonly known as Sulfluramid and is used as an insecticide to control cockroaches, termites and ants. The study involved incubation of *N*-EtPFOSA with liver microsomes from rainbow trout *in vitro*. Results showed that PFOS increased with incubation time and, therefore, it was suggested that *N*-EtPFOSA could possibly undergo biotransformation in fish to PFOS. It was concluded that perfluorosulfonamides are precursors of PFOS in fish and that atmospheric *N*-EtPFOSA and PFOSA can be sources of environmental PFOS.

1.2.3 *Sources of Perfluoroalkyl Carboxylates (PFCAs) in the Environment*

PFOS and the longer chain PFCAs (>8 carbons) have been found in many living organisms but neither have generally been widely used directly in consumer or industrial materials. The only exceptions are their use in aqueous film-forming foams used for fire-fighting and for polymerisation aids in fluoropolymer manufacture. The widespread occurrence of PFOS and PFCAs in living organisms and in the environment therefore suggests these compounds are formed as degradation products of precursor chemicals (for PFOS see above) (Ellis *et al.* 2003). It has been hypothesised that this degradation could occur both in the environment and/or by

metabolism in living beings (Dinglasan *et al.* 2004). Plausible precursor molecules that could break down to yield PFCAs are fluorotelomer alcohols (FTOHs) (Ellis *et al.* 2004). Recent studies have shown that FTOHs can be broken down in the atmosphere to form PFCAs (Ellis *et al.* 2004) and by living organisms to yield PFCAs (Dinglasan *et al.* 2004). Studies also show that FTOHs are ubiquitous in the atmosphere of North America (Stock *et al.* 2004) and that they are capable of long-range transport in air (Ellis *et al.* 2003).

With regard to the breakdown of FTOHs in the atmosphere, these compounds were shown to degrade to PFCAs under laboratory conditions (Ellis *et al.* 2004). The study commented that atmospheric degradation of FTOHs is likely to contribute to the widespread dissemination of PFCAs in the environment. Furthermore, the pattern of the different PFCAs that were formed from the breakdown of FTOHs could account for the distinct contamination profile of PFCAs found in arctic animals once their individual bioaccumulation potentials were also considered. In addition, analysis of the PFCAs present in polar bear liver suggested that the sole input of one PFCA, namely perfluorononanoic acid (PFNA) was attributed to FTOHs as the source. Thus, long-range transport and degradation of FTOHs could explain the presence of long-chain PFCAs in arctic animals and may also explain the reported contamination profile. Calculations based on the experimental atmospheric breakdown of FTOHs indicated the delivery of approximately 0.1 – 10 tonnes/year to the Arctic, a figure which is comparable to the annual Arctic loading of persistent organochlorines such as hexachlorobenzene (1.8 tonnes/year).

A study on one FTOH compound ascertained that it could be broken down (biodegraded) by microorganisms from the environment to yield telomer acids and perfluorinated acids, specifically PFOA (Dinglasan *et al.* 2004). It was proposed that other FTOHs would similarly be biodegraded to yield other perfluorinated acids such as perfluorodecanoic acid and perfluorohexanoic acid. Thus the FTOHs represent potential environmental sources of perfluorinated acids via microbial biodegradation. It was suggested that this study has strong implications for other biological transformations that could take place in higher organisms since microorganisms can be seen as surrogates for metabolic reactions of higher organisms. One study has shown that an FTOH compound given to rats was metabolised to PFOA and another PFCA (see Dinglasan *et al.* 2004). Therefore, these metabolic reactions may serve as probable sources of PFOA and other carboxylic fluorinated acids that have been detected in wildlife.

1.2.4 *Sources of Perfluorinated Acids (PFAs) to the Environment*

A study on Teflon and other fluoropolymers was conducted to investigate whether chemicals were released from these products as a result of heating to high temperatures (Ellis *et al.* 2001). Teflonized engine additive Slick 50 and teflonized frying pans were heated to 500 ^{o}C and the emitted gases were collected and analysed. The gases produced on heating included trifluoroacetate (TFA) and other perhalogenated acids. TFA is expected to be long-lived in the environment. It was hypothesized that the thermal degradation of such polymers could lead to the formation of TFA. A study by a US non-governmental organisation, Environmental Working Group, also monitored gases that were released from Teflon-coated cookware heated to temperatures reached by conventional stoves (ENDS 2003). Fluoroacetic acids were among the chemicals released. The group linked the release of gases from the cookware with the deaths of pet birds which were reported to die after being exposed to fumes from heated non-stick pans.

2. LEVELS OF PFCs IN THE ENVIRONMENT

A number of PFCs have become widespread in the global environment and have been detected in air, freshwater and seawater (see section 2.1, 2.2, 2.3). The sorption of PFOS to sediment and sludge has been shown to be strong (Hekster *et al.* 2003). PFCs in the environment are generally a concern because there is no known route of degradation either in the environment or by living organisms. Furthermore some are bioacculmulative (Martin *et al.* 2004b). PFCs do not accumulate in fatty substances but in the blood and liver of living organisms (Hekster *et al.* 2003, Renner 2001). PFCs have been detected in both aquatic and terrestrial wildlife and in humans from all over the world (see section 3). They are potentially harmful (Giesy and Kannan 2002) and have elicited various toxic effects in laboratory animals (see section 4)

2.1 The Atmosphere

PFOS is fairly involatile and it has been hypothesised that the presence of PFOS in remote regions is not due to its transport on air currents but to the atmospheric transport of more volatile precursor compounds such as perfluoroalkyl sulfonamides (PFASs) (Shoeib *et al.* 2004). Such chemicals have been detected in both indoor and outdoor air samples as discussed below.

PFASs were detected in the atmosphere at all six locations that were tested in North America (Stock *et al.* 2004). The chemicals that were found included *N*-ethyl perfluorooctane sulfonamide (*N*-EtPFOSA), *N*-methyl perfluorooctane sulfonamidoethanol (*N*-MeFOSE) and *N*-ethyl perfluorooctane sulfonamidoethanol (*N*-EtFOSE). Mean concentrations of total PFASs ranged from 22 to 403 pg/m^3. Concentrations were higher in samples from urbanised areas compared to rural areas. In particular, high concentrations of *N*-MeFOSE were present in one area where carpet manufacturing and treatment processes occurred. It is possible that these high concentrations were due to this point source although further studies are being conducted to confirm this.

A study was conducted to investigate the level of PFASs in indoor and outdoor air in Ottawa, Canada (Shoeib *et al.* 2004). Results showed that the mean level of *N*-MeFOSE in indoor air was 1968 pg/m^3. This was considered to be very high. Outdoor air contained concentrations were 25-fold lower. Similarly, high indoor air concentrations were found for *N*-EtFOSE (mean 1033 pg/m^3) and outdoor air concentrations were 13 times lower. *N*-ethyl perfluorooctane sulphonamide (*N*-EtPFOSA) and *N*-methyl perfluorooctane sulfonanidethylacrylate (*N*-Me FOSEA) were detected at levels one order of magnitude lower in indoor air than *N*-MeFOSE and *N*-EtFOSE. The study noted that high indoor concentrations are significant since people generally spend a large proportion of time indoors and exposure via inhalation should be considered in human exposure assessments. The study also concluded that indoor air may be a key source of these chemicals to the outdoor environment.

A study on Lake Ontario detected *N*-EtFOSE and *N*-EtFOSA in air samples from over the lake (Boulanger *et al.* 2005). Mean concentrations were 0.5 and 1.1 pg/m^3 respectively, far lower than in other studies (see above). The study noted that the concentrations sampled above the water were most likely lower because other studies had sampled above land closer to urban areas. The study also detected PFOS in the particulate phase, but not in the gaseous phase of air samples, in 4 out of eight samples at a mean concentration of 6.4 pg/m^3. This is the first time that PFOS has been detected in samples of air.

A study in Japan investigated the concentrations of PFOA and PFOS in dust samples taken from vacuum cleaner dust in Japanese homes (Moriwaki *et al.* 2003). These chemicals were present in all samples taken from 16 Japanese homes. PFOS was detected at concentrations ranging from 11-2500 ng/g and PFOA, 69-3700 ng/g. The results suggested that the sources of PFOS and PFOA in the dust samples were similar, or that the compounds coexisted in the sources. The study concluded the absorption of dust in the home is possibly one of the pathways of human exposure to PFOS and PFOA, and that humans may suffer from chronic exposure to these chemicals from absorption of house dust.

A similar study (Costner *et al* 2005) conducted in the United States also found both PFOA and PFOS in all dust samples analysed (seven pooled samples from different states). Reported levels of PFOS were in a similar range to the Japanese study (76-1174 ng/g) though PFOA was detected at lower levels (18-205 ng/g).

2.2 Freshwater and Sediments

Sinclair *et al.* (2004) measured PFOS and PFOA in water samples collected from Michigan waters of the Great Lakes. Concentrations up to 29 ng/l were found for PFOS and background concentrations were in the range of 2 to 5 ng/l. For PFOA, the maximum concentration was 36 ng/l and background concentrations were in the range of <8 to 16 ng/l. The concentrations of PFCs in freshwater samples from the USA in this study are similar to those found from freshwater samples from Lake Biwa in Japan which ranged from <4 to 7.4 ng/l for PFOS (Taniyasu *et al.* 2003). Another study in Japan found a wider range of contamination levels for PFOS (0.24 – 37.32 ng/l) and PFOA (0.1 – 456.41 ng/l) in rivers (Saito *et al.* 2004). In a study conducted on water samples from Nordic countries, PFOA concentrations were again slightly higher than PFOS concentrations (Berger *et al.* 2004). Median concentrations in lake water were 7.8 ng/l for PFOA and <1ng/ml for PFOS. PFOA was also detected in rainwater at a median concentration of 13.1 ng/l.

A study of sediments from Nordic countries found differences between the countries. Samples from Sweden, Iceland and Faeroe Islands hardly contained any detectable PFCs whereas those from Norway were dominated by PFOS and PFOA and those from Finland were dominated by PFOS (Berger *et al.* 2004). In sewage sludge samples, PFOS and PFOA were the dominating PFCs. Total PFCs ranged from 150 pg/g wet weight to 3800 pg/g wet weight. For sewage effluent samples, the median concentration of PFOA was 20.5 ng/l and for PFOS was 12.7 ng/l (Berger *et al.* 2004).

A study was conducted for Lake Ontario to determine the major sources of perfluorooctane surfactants to the Lake (Boulanger *et al.* 2005). The greatest source came from inflow from lake Erie. The second major source was from wastewater discharge to the lake. The study noted that previous research had identified the presence of PFOS and PFOA in samples from wastewater treatment plants. It is believed that the cleaning and care of surface-treated products, such as carpets and clothing by consumers, and use in industrial processes causes the release of PFCs to municipal wastewater treatment systems (Boulanger *et al.* 2005).

It was reported that levels of PFOS in the middle stream of the Tama River in Japan were exceptionally high (up to 157 ng/l) (see Harada *et al.* 2003, see Taniyasu *et al.* 2003). A further study on waters from the middle stream of the Tama River was undertaken to confirm the findings (Harada *et al.* 2003). The study found that the source of the high PFOS contamination was a sewage treatment works that discharged into the river. Concentrations in the discharge water were 303-440 ng/l. The study also analysed PFOS in drinking water from different

waterworks in Japan. In most drinking water, PFOS levels were less than 4 ng/l. However, in drinking water sourced from the middle stream of the Tama River there was heavy contamination (measurements of 43.7 and 50.9 ng/l). In another study on Japanese surface waters, comparatively high levels of PFOA (40 ng/l) were also found in drinking water in the Osaka area (Saito *et al.* 2004). Drinking water represents a possible source of human exposure to PFCs in these areas.

A study on levels of PFOS and PFOA along the Tennessee River USA indicated that effluent from a fluorochemical manufacturing facility was one likely source of these chemicals to the river water (Hansen *et al.* 2002). The study showed that levels of PFOS increased downstream of the facility from an average of 32 ± 11 ng/l before the facility to 114 ± 19 ng/l after the facility. PFOA was not detectable before the plant but was detectable downstream of the plant at an average concentration of 394 ± 128 ng/l.

The company DuPont manufactures Teflon at a plant on the Ohio River West Virginia, USA. At the site, local groundwater and the river were found to be contaminated with PFOA (see ENDS 2004a). Drinking water supplies to around 12 000 people were contaminated with up to 10 ppb (ug/l) of PFOA. Local residents filed a legal action against the company alleging that it had knowingly contaminated water near the site. DuPont have since reached a financial settlement with local residents and agreed to provide six communities with water treatment facilities designed to achieve the lowest practicable levels of PFOA (ENDS 2004e).

Perfluorinated surfactants are used in aqueous film forming foam (AFFF) formulations. These formulations are used in fire-fighting to extinguish hydrocarbon-fuel fires that occur at fire-training sites as well as in emergency situations. A study at two military bases in the USA where fire-training had taken place 7 to 10 years previously, detected perfluorinated carboxylates (including PFOA) in groundwater samples from the site (Moody and Field 1999). The maximum concentration of PFOA found was 6570 µg/l (i.e. 6 570 000 ng/l). Further research showed that perfluoroalkyl sulfonates were present in ground water at one site (see Schultz *et al.* 2004). Fluorotelomer sulfonates were also detected in groundwater at one of the military sites where these chemicals had been present in the AFFF formulations (Schultz *et al.* 2004).

2.3 Seawater

A study on concentrations of PFCs in the North Sea reported concentrations of PFOA of around 500 pg/l in the open sea whereas PFOS was below the limit of detection (Caliebe *et al.* 2004). However, a study of PFCs in open ocean waters of the Pacific and Atlantic Oceans detected both PFOA and PFOS in pg/l concentrations, although PFOA was the more dominant chemical (Taniyasu *et al.* 2004). For example, the concentrations in the central to eastern Pacific waters were 15-62 pg/l for PFOA and 1.1 to 20 pg/l for PFOS. The study noted that these values appeared to be background values for remote marine waters far from local sources. The study also reported that PFOS and PFOA were detectable in trace quantities in samples collected from the open ocean at depths of >1000 m. A study of seawater from Nordic countries similarly found PFOA (median 5.2 ng/l) to be present in higher concentrations than PFOS (median <1ng/l) (Berger *et al.* 2004).

Coastal (offshore) waters had concentrations of PFOS and PFOA an order of magnitude higher than the open ocean waters of the Pacific and Atlantic (Taniyasu *et al.* 2004). For instance, in waters of Tokyo Bay PFOA ranged from 1.8 – 192 ng/l (1 800-192 000 pg/l) and PFOS ranged from 0.338 – 57.7 ng/l (338 – 57 7000 pg/l). Therefore levels of PFOA were again somewhat

higher than PFOS. High concentrations of PFOA and PFOS in Tokyo Bay compared with open ocean waters suggest sources associated with urban and industrial areas in Tokyo. A study on PFCs in coastal waters of Hong Kong and South China reported that PFOS and PFOA were detectable in all samples that were analysed (So *et al.* 2004) Concentrations ranged from 0.02 to 12 ng/l (i.e. 20 - 12 000 pg/l) for PFOS and 0.24 to 16 ng/l (249 - 16 000 pg/l) for PFOA. Other PFCs were also detectable in about 90% of the samples at concentrations less than those for PFOS and PFOA. These included perfluorooctanesulfonamide (PFOSA) perfluorohexanesulfonate (PFHS), perfluorobutanesulfonate (PFBS) and perfluorononanoic acid (PFNA).

Notably high concentrations of PFCs were detected in waters from one area on the west coast of Korea (So *et al.* 2004). For instance, concentrations of PFOS were 730 ng/l (730 000 pg/l) and of PFOA were 320 ng/l (320 000 pg/l). The study noted that the area where the sample was taken was heavily influenced by the effluents from a number of local industries. Apart from this "hotspot" area, levels of PFCs from Korean waters were comparable to those of Hong Kong and China.

Taniyasu *et al.* (2004) made the observation that PFOA pollution is more ubiquitous than PFOS in oceanic waters. Conversely, PFOS appears to be the predominant compound in wildlife samples collected from several areas. It was noted that this discrepancy suggests that the bioaccumulation potential of PFOA is comparatively lower than PFOS.

2.4 Landfill

In a study in Nordic countries, high levels were detected in landfill effluent (Berger *et al.* 2004). The median concentrations for PFOA and PFOS were 297 ng/l and 65.8 ng/l respectively.

3. LEVELS OF PFCs IN LIVING ORGANISMS

3.1 Bioaccumulation

Bioaccumulative substances are of great concern because of their potential to attain toxicologically significant tissue and organ residue concentrations in higher-trophic-level species such as predatory fish, birds mammals and humans (Kelly *et al.* 2004). Unlike many persistent and bioaccumulative environmental pollutants, PFOS and other PFCS do not accumulate in lipids of the body. Instead, these chemicals accumulate in the blood and in the liver and gallbladder (Renner 2001, Martin *et al.* 2003a). Wildlife studies show that organisms that consume fish, such as predatory birds and mink, contain greater concentrations of PFOS than their food sources. Such higher concentrations in higher trophic level organisms indicates that PFCs may have significant bioaccumulation potential (Martin *et al*. 2003).

In one study on bioaccumulation of PFCs in fish, rainbow trout were exposed to perfluorinated sulfonates and carboxylates in the surrounding water (Martin *et al.* 2003a). Following exposure, PFC concentrations were found to be greatest in the blood of the fish followed by the kidney then the liver, then gallbladder, then adipose tissue and finally muscle tissue. This is different to many other persistent organic pollutants (POPs) such as the organochlorines, which accumulate preferentially in the adipose (fat) tissue. Perfluorinated carboxylates with a carbon-fluorine chain of more than six and perfluorinated sulfonates with a chain length of more than four were found to accumulate in the blood and liver of the rainbow trout. Bioconcentration factors ranged from 4.0 to 23 000 and generally increased with increasing chain length. The bioconcentration factor is the concentration in fish compared to the concentration in water. Bioconcentration factors were greatest in blood for the perfluorinated carboxylates and in the liver for

perfluorinated sulfonates. It is thought that PFCs enter into enterohepatic circulation in fish, which means they are continuously circulated between the blood, liver, gallbladder and intestines. In another study on fish, the common shiner, the bioaccumulation factor for PFOS was reported to vary between 6 300 and 125 000 (see Hekster *et al.* 2003).

A study on wild fish from different coastal regions of Japan detected PFOS in all tissue samples of the fish (Taniyasu *et al.* 2003). Bioconcentration factors for PFOS in livers of fish were estimated from the results for two species of marine fish and one freshwater species. Bioconcentration factors for PFOS ranged from 274 to 41 600.

A study was carried out to investigate dietary accumulation of PFCs in fish (Martin *et al.* 2003b). Juvenile rainbow trout were fed for 34 days on food spiked with various perfluorosulfonates and perfluorocarboxylates. The fish were sacrificed at varying time intervals during and after the feeding study and the PFCs in their tissues were analysed. The results showed that PFCs had accumulated in the tissues of the fish and bioaccumulation factors ranged from 0.038 to 1.0. The bioaccumulation factors of less than 1 indicated that PFCs will not biomagnify in juvenile rainbow trout, but from this it cannot be assumed that this will be the case in mature rainbow trout or other fish. The bioaccumulation factors increased with increasing length of the perfluorinated chain, as was also the case in the water exposure study discussed above (Martin *et al.* 2003a). Perfluorinated sulfonates bioaccumulated to a greater extent than perfluorinated carboxylates. For example, the bioaccumulation for the perfluorinated sulphonate PFOS, which has a perfluorinated chain length of eight, was similar to perfluoroundecanoic acid (PFUnA), a perfluorinated carboxylate with a chain length of ten. The study also showed that the half-life of PFOS in the fish was 13 days. Half-lives estimated for mammals are greater. For instance, in male rats the half-life was 89 days, in monkeys it was 180 days and in humans it was 1 428 days. The reason for the much lower half-life in fish was suggested as being due to a more rapid elimination from gills to water than from lungs to air, and possibly because animals with a larger body size have a slower elimination rate than those with smaller bodies.

An experimental study on captive mink found that the more PFOS in the diet of the mink, the higher the concentration of PFOS that was found in the liver (Kannan *et al.* 2002d). Biomagnification factors were calculated for the mink livers and were estimated to range from 11 to 23 with a mean value of 18. This value is similar to or greater than the biomagnification factors reported for PCBs or PCDD/Fs in mink livers.

The ability of a chemical to bioaccumulate in aquatic organisms has been assessed by using its partition coefficient, $K_{ow.}$ This has been adopted in some policies to assess the bioaccumulation potential of chemicals. However, its use is limited because it does not take into account other air-breathing organisms and therefore may be inaccurate. Presently, there is evidence that the K_{ow} classification of chemicals is not an adequate model to identify substances with a bioaccumulative potential in food webs that include mammals, birds and humans (Kelly *et al.* 2004). For instance, PFOS does not meet the current K_{ow} criterion for bioaccumulative substances and does not biomagnify in fish. However, studies show that PFOS is efficiently absorbed via dietary exposures, biomagnifies and persists in the liver and blood of air-breathing animals and is inherently toxic (Kelly *et al.* 2004).

3.2 Freshwater Invertebrates and Fishes

PFCs have been found in freshwater fish from the Great Lakes, Japan and the Canadian Arctic (respectively Taniyasu *et al.* 2003, Martin *et al.* 2004a, Martin *et al.* 2004b). A study of PFCs in a food web in Lake Ontario showed that some PFCs, including PFOS and PFOA, bioaccumulated in fish (Martin *et al.* 2004a). It also suggested that biomagnification, that is, a progressive increase in levels of PFCs in the bodies of organisms going up through the food chain, may be occurring at the top of the food web for PFOS, perfluorodecanoic acid (PFDA) perfluoroundecanoate (PFUnA) and perfluorotridecanoate (PFTrA).

The study on the Lake Ontario food web analysed various PFCs in 3 species of fish. The mean PFOS concentrations in whole body homogenates of the fish were 450 ng/g wet weight for sculpin, 110 ng/g wet weight for smelt and 46 ng/g wet weight for alewife. Other PFCs that were detected in the fish included the homologous series of perfluoroalkyl carboxylates (PFCAs) – perfluorooctanoate (PFOA), perfluorononanoic acid (PFNA), perfluordecanoate (PFDA), perfluoroundecanoate (PFUnA), perfluorododecanoate (PFDoA), PFTrA, perfluorotetradecanoate (PFTA) and perfluoropentadecanoate (PFPA). PFCs were also detected in 2 aquatic invertebrates, *Mysis* and *Diporeia*, which were studied. *Mysis* had a PFOS concentration of 13 ng/g wet weight and *Diporeia*, 280 ng/g wet weight respectively. The high concentrations in *Diporeia* were unusual because, of the species analysed, it occupied the lowest trophic level in the food web. It was hypothesised that the sediments of the lake were a major source of PFCs to the food web rather than the water and that the chemicals are consequently taken up by *Diporeia* which is a benthic organism.

A study of fish from Michigan waters of the Great Lakes and inland water bodies of New York detected PFOS in the livers of a number of species that were tested (Sinclair *et al.* 2004). Concentrations ranged from <7 to 381 ng/g wet weight, which, it was noted were similar to concentrations found in fish liver from Tokyo Bay in another study. PFOS was also detected in fish eggs at concentrations approximately twice those as in the livers from the same species of fish. The authors stated that this suggests that PFOS is actively transferred from adult female fish to their eggs. Furthermore, occurrence of PFOS in eggs has implications for early life stage effects. Other PFCs, namely PFOA, FOSA and PFHS were not detectable in fish livers or fish muscle in this study. This result is different to the study of fish from Lake Ontario where PFOA was detected in whole body homogenates of fish tissue.

A study of fish in Nordic countries found that PFOS was the predominant PFC (Berger *et al.* 2004). The highest concentration of PFCs detected was for Finnish pike, a top predator (PFOS 551 ng/g wet weight, PFOSA 141 ng/g wet weight). A study in Japan analysed concentrations of PFOS in 3 species of fish from Lake Biwa (Taniyasu *et al.* 2003). Concentrations in blood ranged from 33 to 834 ng/ml and in livers from 3 to 310 ng/g wet weight.

A study on organisms from the Canadian Arctic collected fish from the mouth of the Great Whale River at Kuujuarapik and from Lake Minto, Quebec (Martin *et al.* 2004b). PFOS was found in all samples of fish liver at concentrations ranging from 5.7 to 50 ng/g. FOSA was detected in fish liver at similar concentrations to PFOS (2.0 to 18 ng/g). The study noted that this differs from birds and mammals in which levels of FOSA are usually lower than PFOS. PFOA was below the limit of detection in the fish. However, other PFCs, some from a homologous series of PFCAs, were detectable. Those compounds which were found in fish liver included PFNA, PFDA, PFUnA, PFDoA, PFTrA and PFTA. PFPA was not detectable.

3.3 Marine Fish

A study on fish from different coastal regions of Japan investigated concentrations of PFCs in samples of blood and liver (Taniyasu *et al.* 2003) PFOS was detected in all samples and the concentrations in blood ranged from 1 to 834 ng/ml and in liver from 3 to 7900 ng/g wet weight. The concentrations in fish varied depending on species and location. Perfluorohexane sulphonate (PFHS) was also detected in about one third of the samples tested, at maximum concentrations of 121 ng/ml in blood and 19 ng/g wet weight in liver. No perfluorobutane sulphonate (PFBS) was found in any of the fish.

A study on marine fish from Nordic countries found a high variability in PFC levels reflecting differences in trophic levels, feeding habits and location (Berger *et al.* 2004). PFOS was the predominant compound in most fish samples. The least contaminated fish originated from the Faeroe Islands. Around Iceland, fish contained unusually high levels of perfluorodecane sulphonate (PFDcS) (median 10 ng/g wet weight) and perfluorohexanoic acid (PFHxA) was present at concentrations of >1ng/g wet weight. It was suggested that the different patterns of contamination indicated country specific contamination with PFCs. Overall, the marine fish that were analysed from Nordic countries in this study were approximately ten times less contaminated compared to freshwater species from Nordic countries.

A study on fish collected from the Mediterranean, specifically the Italian coast, investigated bluefin tuna (*Thunnus thynnus*) and swordfish (*Xiphias gladius*) (Kannan *et al.* 2002a). Concentrations of PFOS in blood ranged from 4 to 52 ng/ml and in liver ranged from <1 to 87 ng/g wet weight. Perfluorooctanesulfonamide (FOSA) was detected in all blood samples of fish that were analysed at concentrations of 1.1 to 28 ng/ml. FOSA was also found in freshwater fish from the Canadian Arctic (Martin *et al.* 2004b) but not fish from Lake Ontario (Martin *et al.* 2004a). PFHxS was detected in one of the five livers of swordfish that were analysed at a concentration of 10 ng/g wet weight. PFOA was not found in any of the fish samples above the limit of detection. The study also analysed livers from Atlantic salmon from the northern Baltic Sea. None of the 22 samples contained PFOS. It was suggested that the lack of PFCs in these fish could be due to their long fasting periods.

A study in the USA analysed PFOS in oysters from 77 different sites in the Gulf of Mexico and from Chesapeake Bay in the USA (Kannan *et al.* 2002b). PFOS was detected in 64% of the oyster samples. It was only detected in one sample from Chesapeake Bay. The concentrations of PFOS in the oysters ranged from <42 to 1 225 ng/g in a dry weight basis.

3.4 Birds

PFOS has been found in birds from across the United States, from the Canadian Arctic, from Italy and from Japan (respectively Kannan *et al.* 2001a, Martin *et al.* 2004b, Kannan *et al.* 2002a and Taniyasu *et al.* 2003). In a study of the Canadian Arctic, PFOS was detected in liver samples from the common loon (mean 20 ng/g, range 11-26 ng/g) and northern fulmar (mean 1.3 ng/g, range 1.0-1.5 ng/g), but not the black guillemot (Martin *et al.* 2004b). These levels were at the lower end of the range compared to fish-eating birds from the USA (Kannan *et al.* 2001a), as discussed below. FOSA was detected in the common loon (mean 5.9 ng/g, range 2.0-13 ng/g) but not in the other two species. Samples were analysed for the homologous series of PFCAs, but most were either not detectable or present at only trace levels except for PFUnA (mean 1.3 ng/g) and PFTrA (mean 0.88 ng/g) in the common loon.

A study on the presence of PFOS in fish-eating water birds from across the USA was conducted (Kannan *et al.* 2001a). PFOS was found in most samples of blood and liver tissue from the birds

that were analysed. Concentrations in blood plasma for birds from the Great Lakes region ranged from <1 to 2030 ng/ml, and concentrations in liver tissue for birds from various locations ranged from <12 to 1780 ng/g wet weight. PFOS was also detected in yolk from bird eggs. For example, egg yolks of double-crested cormorants and ring-billed gulls contained PFOS at concentrations ranging from 21 to 220 ng/g wet weight and 30 to 126 ng/g respectively. PFOS was found in most of the blood samples that were taken from nestling bald eagles. Blood plasma from nestling eagles in midwestern United States contained PFOS at a mean level of 330 ng/ml and range 1-2220 ng/ml. The presence of PFOS in nestling eagles may indicate exposure from egg proteins and through diet. The study detected PFOS (3.0 – 34 ng/ml) in blood serum of albatrosses from Midway Atoll, North Pacific Ocean and commented that this suggests the widespread distribution of sulfonated PFCs in remote marine locations. In addition, the study noted that results showed that birds from more urbanized areas had higher levels of PFOS than those from more remote areas which suggested greater exposure to PFOS for birds in more urbanized areas.

A study of cormorants from the coast of Sardinia, Italy, found PFOS in liver tissue at concentrations ranging from 32 to 150 ng/g wet weight (Kannan *et al.* 2002a). The authors commented that these concentrations were similar to, or lower than those found for fish-eating birds of the Great Lakes in the USA (see above, Kannan *et al.* 2001a). PFOA was also detected in the liver from the cormorants at concentrations of 29 to 450 ng/g wet weight. These were, on average, 1.7-fold greater than PFOS concentrations. The results suggested that sources of PFOS and PFOA may be similar for these birds. FOSA was detected in one out of twelve cormorant livers at a concentration of 89 ng/g wet weight.

A study in Japan and Korea determined PFOS and other PFCs in several species of birds from different locations (Kannan *et al.* 2002c). Like the above studies discussed here, PFOS was found in nearly all the samples of bird livers that were analysed, which suggests the widespread occurrence of this chemical. The concentrations of PFOS detected in bird livers fell within the range of those from birds collected across the USA (see above, Kannan *et al.* 2001a). The greatest concentration of PFOS was 650 ng/g wet weight. Results suggested that urbanized and industrialized areas are major sources of exposure to PFOS whilst remote areas are less so. The study noted that mean concentrations of PFOS in livers or cormorants from Japan were 6-fold greater than those found in livers of cormorants from Sardinia (see above, Kannan *et al.* 2002a) and 5-10 fold greater than those found in white-tailed sea eagles from eastern Germany. The study detected perfluorooctanesulfonamide (FOSA) and perfluorohexanesulfonate (PFHS) in 5-10 % of the bird livers that were analysed and also PFOA. While PFHS and PFOA were found to occur sporadically in samples, FOSA was limited to a certain region suggesting localised sources.

A study was conducted in the Baltic to investigate the trends of PFOS levels with time using guillemot eggs (Holmström *et al*. 2005). An archive of frozen eggs was available for the study. PFOS was measured in eggs dating from 1968 to 2003. Results showed that there was an almost 30-fold increase in PFOS concentrations during this time period. For instance, in 1968 the concentration from pooled eggs was 25 ng/g wet weight and by 2003 the concentration was 614 ng/g. The study noted that the presence of currently high concentrations of PFOS in the guillemot eggs suggests a possible risk of reproductive interference. However, toxicity studies on one species of bird, the northern bobwhite, reported that developmental effects on chicks only occurred at concentrations that were a factor of 50 higher than in the guillemot eggs (Giesy and Jones 2004).

3.5 Amphibians

One study in the literature contained information on PFOS in amphibians in the US (Giesy and Kannan 2001). PFOS was detected in liver of the yellow-blotched map turtle from Mississippi (39-700 ng/g wet weight) and green frogs from Southwest Michigan (<35-290 ng/g). It was also detected in blood plasma of snapping turtles from Michigan (1-170 ng/ml).

3.6 Marine Mammals

PFOS has been found in marine mammals from a wide range of geographical regions (Kannan *et al.* 2001b). One study detected PFOS in tissues from marine mammals from the east and west coast of the US, Alaskan coastal waters, the northern Baltic Sea, the Arctic (Spitsbergen) and Sable Island in Canada (Kannan *et al.* 2001b). In this study, 247 tissue samples from 15 species of marine mammals were analysed for PFOS. Table 3.1 shows the mean concentrations of PFOS found in liver samples of the marine mammals in the USA. Mean levels of PFOS in dolphins from the east coast USA were generally higher than seals and sea lions (pinnipeds) from the west coast USA. The study commented that the lower concentrations in pinnipeds may suggest less exposure to PFOS and/or a greater ability to metabolise and excrete fluorinated organic chemicals possibly through annual moulting.

In Alaskan waters, PFOS was detected in the livers of 5 of 13 northern fur seals and all 17 samples of polar bear liver. The presence of PFOS in these animals suggests the transport and distribution of PFOS to remote marine locations. PFOS was not detectable in blood of Stellar sea lions collected from the south east coast of Alaska.

Table 3.1 Mean Concentrations of PFOS in Livers from Marine Mammals in the USA

Location	**Species**	**Mean and (range) PFOS concentrations in Liver (ng/g, wet weight)**
East Coast USA (Florida)	pygmy sperm whale (n= 2)	**14.8** (6.6-23.0)
	short-snouted spinner dolphin (n = 3)	**123** (78.7-168)
	striped dolphin (n = 2)	**212** (36.6-388)
	rough-toothed dolphin (n = 2)	**54.2** (42.8-65.6)
	bottlenose dolphin (n = 20)	**489** (48.2-1520)
West Coast USA	California sea lion (n = 6)	**26.6** (4.6-49.4)
	elephant seal (n = 5)	**9.3** (<5-9.8)
	harbour seal (n = 3)	**27.1** (10.3-57.1)
Alaska	northern fur seal (n = 13)	(<10-122)
	polar bear (n = 17)	**350** (175-678)

Source: Kannan *et al.* (2001b)

Blood samples of ringed seals from Spitzbergen in the Arctic contained PFOS at concentrations in the lower end of the range of those detected in the study (means of 8.1 ng/ml in 1996 and 10.1 ng/ml in 1998). Similarly, in another study blood plasma from ringed seals in the Canadian Arctic and Norwegian Arctic contained PFOS concentrations within the same range (respectively <3-12 and 5-14 ng/ml) (Giesy and Kannan 2001). In a further study, livers from

ringed seals in the Canadian Arctic had PFOS at concentrations of 10 to 37 ng/g (Martin *et al.* 2004b).

A study of Arctic animals measured PFOS in the livers of seven polar bears from the Canadian Arctic (Martin *et al.* 2004b). Concentrations of PFOS ranged from 1700 to >4000 ng/g, mean 3100 ng/g. This is 10-fold higher than polar bears from Alaska (mean 350 ng/g, see above). The study noted that the bears from the Canadian Arctic were at a considerably lower latitude than those from Alaska and so were perhaps closer to regional sources of PFOS. It also commented that it can be generalised from the data that were collected, that mammals feeding at higher trophic levels have higher concentrations of PFOS than mammals feeding at lower trophic levels. On this basis, a polar bear is at the top of a food chain and would therefore be expected to contain comparatively high levels of PFOS. The study also investigated the levels of other PFCs. PFOA was detectable in polar bear livers at concentrations ranging from 2.9 to 13 ng/g. A number of perfluoroalkyl carboxylates (PFCAs) were also detected in polar bear liver. The PFCAs were a homologous series ranging in length from 9-15 carbons and included perfluorononanoate (PFNA) (mean 180 ng/g), perfluorodecanoate (PFDA) (mean 56 ng/g), perfluoroundecanoate (pFUnA) (mean 63 ng/g), perfluorododecanoate (PFDoA) (mean 6.2 ng/g), perfluorotrideconoate (PFTrA) (mean 11 ng/g), perfluorotetradecanoate (PFTA) (mean 0.51 ng/g) and perfluoropentadecanoate (PEPA) (mean <0.5 ng/g). There is little information on these chemicals in wildlife and this was the first report of their presence in marine mammals. Some of the compounds were also detectable in ringed seals from the Canadian Arctic.

Samples of blood from ringed seals in the northern Baltic Sea contained PFOS at levels that were 15-fold greater than those from Spitzbergen in the Arctic (means 133 ng/ml in 1996, 242 ng/ml in 1998) (Kannan *et al.* 2001b). These results can be explained by the fact that the Baltic has industrialised regions and is therefore closer to sources of PFCs than the Arctic. Grey seals from the northern Baltic had blood concentrations of PFOS (mean 25.5 ng/ml in 1998) that were similar to grey seals from Sable Island in Canada (mean 27.7 ng/ml in 1998). As a general observation, the study noted that PFOS did not appear to increase with age of marine mammals, unlike certain other persistent pollutants such as PCBs.

A study of PFCs in liver tissue from harbour porpoises in Northern Europe found PFOS to be the predominant compound (Van de Vijver *et al.* 2004). The study investigated harbour porpoises from the coastal waters around Iceland, Norway and Denmark and from the German Baltic Sea. Contamination with PFOS was considered to be heavy in the animals. Concentrations in liver tissue of the 41 animals that were tested ranged from 26 to 1149 ng/g wet weight. PFNA (<14 to 47 ng/g wet weight), PFDA, PFUnA and PFDoA were also detected in liver tissue from some of the harbour porpoises and PFOA was only detected in one animal. Concentrations of all PFC compounds, discounting PFOA, were found to be higher in porpoises from the Baltic Sea compared to Iceland and Norway. For example, concentrations of PFOS in the German Baltic were (mean values) 534±357 ng/g, in Iceland were 38±14 ng/g and in Norway were 213±195 ng/g. It was suggested that this is because the Baltic Sea region is relatively highly industrialised compared to Iceland and Norway and is known to have higher levels of other pollutants. In addition, there is no known production of PFCs in Iceland and Norway. Even though levels of PFCs were lower in harbour porpoises from Iceland and Norway, the presence of these chemicals in the animals further confirms their contamination of more remote marine environments. In another study, concentrations of PFOS in ringed seals and grey seals from the Baltic Sea were measured (Kannan *et al.* 2002a). Concentrations in liver tissue (130 to 1100 ng/g wet weight) were in the same range as those of harbour porpoises from

the region (26 to 1149 ng/g, see above). As in harbour porpoises, PFOA was rarely detected in seals (2 of the 52 animals) from the Baltic.

A study of marine mammals from the southern North Sea indicated that their tissues contained PFOS (Van de Vijver *et al.* 2003). The animals had been stranded along the Belgian, Dutch, and French North Sea coast. PFOS was detected in the livers of harbour porpoises (12-395 ng/g wet weight), harbour seals (<10-532 ng/g), grey seals (11-233 ng/g), sperm whales (19-52 ng/g) white beaked dolphins (14-443 ng/g), white-sided dolphins (<10-26 ng/g) and a striped dolphin (11 ng/g). PFOS was below the limit of detection in hooded seal and fin whale. The study noted that the concentrations of PFOS that were observed in white-beaked dolphins from the North Sea were in the same range than those of striped dolphins and bottlenose dolphins from the coastal waters of Florida in the study by Kannan *et al.* (2001b). The study also suggested that the feeding ecology of the marine mammals, either in inshore or in offshore waters, was likely to affect the level of PFOS contamination in the animals. For instance, those feeding in inshore coastal waters may be more highly contaminated due to feeding nearer to PFC sources than offshore feeders. In the study, results showed that the offshore feeders, namely, the sperm whale, fin whale and white-sided dolphin, had comparatively lower tissue concentrations of PFOS than coastal species such as grey and harbour seal, harbour porpoise and white-beaked dolphin. The study noted that PFOS concentrations up to 50 ng/g wet weight in sperm whales, which feed on abyssal cephalopods and bottom-dwelling species, suggest that PFCs have reached deeper water layers. Results from this study also indicated that PFOS may have the potential for biomagnification.

Other PFCs were detected in livers of three of the nine species of marine mammals that were tested from the North Sea (Van de Vijver *et al.* 2003). Perfluorononanoic acid (PFNA) was detected in a sperm whale (240 ng/g wet weight) and a white-beaked dolphin (480 ng/g wet weight). Perfluorodecanoic acid (PFDA) was detected in 3 white-beaked dolphins (90 to 120 ng/g wet weight), and perfluoroundecanoic acid (PFUA) was detected in a harbour porpoise (110 ng/g wet weight), in a sperm whale (50 ng/g wet weight), in a white-sided dolphin (60 ng/g wet weight) and in 3 white-beaked dolphins (50 to 150 ng/g wet weight). PFOA and perfluorododecanoic acid (PFDoA) were not found in any species. As in other studies on PFCs in marine mammals, in this study PFOS was the predominant compound of all the PFCs that were investigated.

In a study of marine mammals from the Italian coast of the Mediterranean Sea, PFOS was found in the liver of striped dolphins (16.3 to 40 ng/g wet weight), a common dolphin (940 ng/g), bottlenose dolphins (<1.4 to 110 ng/g) and a long-finned pilot whale (270 ng/g) (Kannan *et al.* 2002a). FOSA was also detected in livers of bottlenose dolphins (30-139 ng/g) and a long-finned pilot whale (50 ng/g), but not in striped dolphins. The study remarked that occurrence of FOSA in marine mammals from the Mediterranean is indicative of the presence of specific sources.

3.7 Terrestrial and Aquatic Mammals

A study on animals from the Canadian Arctic found PFOS in samples of liver from arctic foxes (mean 250 ng/g, range 6.1-1400 ng/g) and in mink (mean 8.7 ng/g, range 1.3 to 20 ng/g) (Martin *et al.* 2004b). Samples were analysed for a homologous series of perfluoroalkyl carboxylates (PFCAs). Arctic fox liver contained mean concentrations of perfluorononanoate (PFNA) at 22 ng/g, perfluorodecanoate (PFDA), 14 ng/g, perfluoroundecanoate (PFUnA), 13 ng/g, perfluorododecanoate (PFDoA), 1.5 ng/g, and perfluorotrideconoate (PFTrA), 2.2 ng/g.

Mink liver contained mean concentrations of PFNA at 16 ng/g, PFDA at 3.7ng/g and PFUnA at 4.3ng/g.

A study of mink from various locations across the USA found comparatively high concentrations of PFOS in these animals (Kannan *et al*. 2002d). Mink are top carnivores in aquatic ecosystems. PFOS was found in all of the 112 mink livers that were analysed at concentrations ranging from 20 to 5140 ng/g wet weight. These concentrations were far higher than those found for mink in the arctic (see above, Martin *et al.* 2004b). The greatest concentrations of PFOS in mink from the USA were apparent in those that were collected near to urbanised or industrial locations. Perfluorooctanesulfonamide (PFOSA), perfluorohexanesulfonate (PFHxS) and PFOA were detected in some of the animals, though generally at lower concentrations than PFOS. Maximum concentrations for FOSA were 590 ng/g, for PFHxS, 85 ng/g, and for PFOA, 27 ng/g.

Kannan *et al.* (2002d) also assessed concentrations of PFCs in otters from the USA. Otters are top predators of riverine food chains. PFOS was detected in all 20 otter livers that were found which, like the results for mink, confirmed that PFOS is a widespread contaminant of these animals. Concentrations of PFOS ranged from 25 to 994 ng/g wet weight, mean 303 ng/g. Concentrations of PFOS were again greatest in animals that were collected from more urbanised areas suggesting that urbanised areas are the primary sources of fluorochemicals to the environment. FOSA, PFHxS and PFOA were detected in the livers of some of the otters at generally lower concentrations than PFOS.

A study on 3 beef cattle from Japan detected PFOS in blood samples (mean 530 pg/ml or 0.53 ng/ml) (Guruge *et al.* 2004a). The study noted that the concentrations were at least one order of magnitude lower than fish from Japan. Other PFCs, namely perfluorohexanoic acid (PFHxA), perfluordecanoic acid (PFDA), perfluorononanoic acid (PFNA), PFOA and perfluoropentanoic acid (PFPeA) were also detected in the cattle, generally at lower levels than PFOS.

3.8 Humans

3.8.1 *PFCs in Blood*

A study by Kannan *et al.* (2004) assessed the level of various PFCs in human blood serum from a number of countries. The samples were collected in city locations and from a diverse age range of individuals. As such, it was suggested that the samples provided a reasonable representation of the populations in question. PFOS was the most predominant compound and was detectable in most samples. Table 3.2 shows the mean level of PFOS in human serum for all the countries that were included in the study. The greatest mean concentrations (> 30 ng/ml) were found in the USA and Poland. The mean concentrations of PFOS for Japan, Korea, Malaysia, Belgium and Brazil were between 10 and 25 ng/ml, and the means from Italy and Colombia were between 4 and 10 ng/ml. The lowest levels were present in India (< 3 ng/ml). Only 51% of the serum samples from India contained PFOS at concentrations greater than 1ng/ml. Overall, the results suggested that the amount of exposure to PFOS both within and between the different countries is quite variable.

Table 3.2 Concentrations of PFOS in human serum from different countries

Country	Mean and (Range) PFOS in Sera (ng/ml)
USA (Michigan, Kentucky and New York) (n=175)	49.5 (<1.3 - 164)
Colombia (n=56)	8.2 (4.6 - 14)
Brazil (n=27)	12.1 (4.3 - 35)
Italy (n=50)	4.3 (<1 - 10.3)
Poland (n=25)	44.3 (16 - 116)
Belgium (n=20)	13.9 (4.5 - 27) (values are for blood plasma)
India (n=45)	2.0 (<1 - 3.1)
Malaysia (n=23)	12.4 (6.2 - 18.8)
Korea (n=50)	21.1 (3.0 - 92)
Japan (n=38)	17.1 (4.1 - 40.3)

Source: Table adapted from Kannan *et al.* (2004).

A number of other studies have also investigated the level of PFOS in human blood. Studies were conducted in USA (Olsen *et al.* 2003, Kuklenyik *et al.* 2004), northern Canada (Tittlemier *et al.* 2004), Japan (Masunaga *et al.* 2002, Taniyasu *et al.* 2003) and Sweden (Kärrman *et al.* 2004). Table 3.3 shows the mean and the range of PFOS concentrations reported in these studies. It is possible to convert the values for whole blood to the approximate equivalent of serum or plasma by dividing by 2. The mean concentration of PFOS in serum for the USA (34.9 ppb) is again in the category of >30 ng/ml (Olsen *et al.* 2003). The study commented that there was one very high value (1656 ng/ml) which is similar to concentrations found for persons with occupational exposure to PFCs. The next highest value to this was much lower at 329 ng/ml. The mean concentration of PFOS in blood plasma from individuals in northern Canada (36.9 ng/ml) is similar to other mean values for the USA (Tittlemier *et al.* 2004). This study noted that the results confirm that populations residing in the Northwest and Nunavut Territories in northern Canada are exposed to fluorinated organic chemicals.

Results from a study in Sweden showed a mean equivalent concentration of PFOS in serum of 9.1 ng/ml (Kärrman *et al.* 2004). Levels were within the same range as those found for Belgium (e.g. mean 13.9 ng/ml) in the study by Kannan *et al.* (2004). For Japan, two studies showed somewhat lower ranges and mean concentrations (e.g. equivalent mean sera concentrations 4 and 4.5 ng/ml) (Masunaga *et al.* 2002, Taniyasu *et al.* 2003) as opposed to 17.1 ng/ml reported in the study by Kannan *et al.* (2004). In one of the studies on Japan, (Masunaga *et al.* 2002), it was noted that levels of PFOS in human blood from Japan were lower than levels found in the USA and that this shows that the Japanese are less exposed to PFOS. A possible reason for the difference is the fact that major Japanese producers of perfluorinated surfactants reportedly do not use PFOS derivative as intermediates. However, the study commented that Japanese people may still be exposed to PFOS through imported products and/or global scale environmental transport.

Table 3.3 Concentration of PFOS and PFOSA in human blood from different countries

Country	Number of samples	PFOS (ng/ml)	PFOSA (ng/ml)	Reference
USA, Atlanta	20	serum 3.6 - 164	< limit of detection to 0.9	Kuklenyik *et al.* 2004
USA	645	serum <4.3 - 1656 mean 34.9	<1.6 - 60.1 mean 2.0	Olsen *et al.* 2003
Northern Canada	NA	plasma 2.8 - 57.9 mean 36.9	NA	Tittlemier *et al.* 2004
Japan	26	whole blood 2.0 - 20.2 mean 8.1	<1.3 - 4.8 mean 1.7	Masunaga *et al.* 2002
Japan	10	whole blood 2.4 - 14 mean 9	NA	Taniyasu *et al.* 2003
Sweden	66	whole blood 1.7 - 37 mean 18.2	0.4 - 22.9 mean 4.1	Kärrman *et al.* 2004

NA not available

In the study by Kannan *et al.* (2004), both the concentration and frequency of occurrence of other PFCs in serum samples, namely PFOA, perfluorohexanesulfonate (PFHxS) and perfluorooctanesulfonamide (PFOSA) were relatively lower than for PFOS. However in a study on USA residents, Kuklenyik *et al.* (2004) detected PFOA and PFHxS in all samples, though again at lower concentrations than PFOS. In the study by Kannan *et al.* (2004), concentrations of PFOA in serum were generally 2 to 7-fold lower than PFOS concentrations. An exception was Korea where samples contained higher concentrations of PFOA than PFOS. This suggested the presence of specific sources of exposure in Korea. A study in Sri Lanka also reported that levels of PFOA in human serum (0.24 ng/ml) were higher than levels of PFOS (0.13 ng/ml) (Guruge *et al.* 2004b). The study by Kannan *et al.* (2004) investigated the relationships between PFOS and PFOA, PFHxS and PFOSA to establish whether there were any links between sources of exposure. In some cases relationships were present and in others not. These results indicated that there were varying exposure patterns for these chemicals in different countries, an issue which clearly warrants further investigation.

In other studies on PFCs in human blood, it is also apparent that concentrations of other PFCs are generally lower than concentrations of PFOS. For instance, table 3.3 shows that the range and mean concentrations of PFOSA are lower than for PFOS in the USA, Japan and Sweden.

The study by Kannan *et al.* (2004) also tested human serum for several other PFCs besides PFOA, PFHxS and PFOSA. Perfluorodecanesulfonate (PFDS) was present in some samples. PFDS is an impurity in POSF-based products. Perfluoroheptanoic acid (PFHpA), perfluorononanoic acid (PFNA) and perfluorodecanoic acid (PFDA) were also detectable in serum. Some of these long-chain perfluorocarboxylates have also been reported to be present in samples from wildlife (see section 3.6). Kannan *et al.* (2004) remarked that the results indicated that several PFCs coexisted in human blood and that hazard assessment for PFCs in humans should take into consideration the occurrence of all these chemicals. In a study on blood

samples from Atlanta in the USA, a number of long-chain perfluorocarboxylates including PFNA were detected in human blood and from the results it was suggested that exposure to these chemicals may be widespread (Kuklenyik *et al.* 2004).

In a study of PFCs in human blood in Sweden, several PFCs were also detected (Kärrman *et al.* 2004). For example, perfluorononanoic acid (PFNA) was found in most samples. Perfluorodecane acid (PFDA) and perfluoroundecanoic acid (PFUnDA) were found in about 65% of samples at concentrations of 0.1-0.7 ng/ml. Perfluorodecane sulphonate (PFDS), perfluorohexanoic acid (PFHxA), perfluorododecanoic acid (PFDoDA) and perfluorotetradecanoic acid (PFTDA) were present in 3-8% of the samples at concentrations of 0.3-5 ng/ml. The only compound which was not detectable in the samples was perfluorobutane sulphonate (PFBuS).

A study on levels of PFCs in human blood in Sri Lanka investigated the difference between samples taken from residents of an urban area compared to a rural population (Guruge *et al.* 2004b). The results showed that for all the PFCs monitored, the concentrations were significantly higher in samples of serum from the urban location compared to the rural location. For example, levels of PFOS were approximately 10-fold higher in the urban area. The other chemicals that were investigated included perfluorohexanesulfonate (PFHS), perfluorododecanoic acid (PFDoA), perfluoroundecanoic acid (PFUnA), perfluorodecanoic acid (PFDA), perfluorononanoic acid (PFNA), PFOA and perfluoroheptanoic acid (PFHpA). The results suggested that exposure to PFCs is higher in urban locations, as may be expected, because of proximity to sources of the chemicals.

The age of animals and humans may affect the level of some persistent, bioaccumulative chemicals in body tissues because, as more of these chemicals are taken in over time, they can build up to higher levels in the body. For PFCs, Kannan *et al.* (2004) reported that age did not appear to affect the concentration of PFOS or PFOA in humans. Olsen *et al.* (2003) also found no effect of age on concentrations of PFCs in human blood from the USA.

The levels of some persistent organic chemicals in mammals and humans are affected by gender. This occurs because females pass on some of the chemicals stored in their bodies to their young during development in the womb and via milk during breast feeding. This lowers the body burden of such chemicals in females. This phenomenon is known to occur for environmental pollutants such as PCBs and dioxins. For PFCs, a study of concentrations of PFOS and PFOA in human blood from a number of countries found there was no difference between levels in males and females (Kannan *et al.* 2004). However, a study of PFCs in human blood samples from the USA, Oslen *et al.* (2003) reported that males had significantly higher levels of PFOS, PFOA and PFHS in serum than females. A study in Korea also found significantly higher levels of PFOS in males than females but not PFOA, PFOSA or PFHxS (Yang *et al.* 2004). Finally, a study in Japan reported that males had significantly higher blood concentrations of PFOS than females (Harada *et al.* 2004). It also found significantly higher concentrations of PFOA in blood for males in 2 out of 3 locations that were studied. Taken together, results for effects of gender on levels of PFCs are mixed and not conclusive.

3.8.2 *PFCs in Umbilical Cord Blood and Human Milk*

In a study of PFCs in human blood samples from northern Canadian populations, Tittlemier *et al.* (2004) detected PFOS (mean concentration 16.7ng/ml) and PFOA (mean concentration 3.4 ng/ml) in samples of umbilical cord blood plasma. The study reported that the presence of fluorinated organic chemicals in cord blood plasma indicates that exposure occurs *in utero* (i.e.

to the developing infant in the womb). Another study in Japan reported the presence of PFOS in cord blood serum at concentrations of 1.6 to 5.3 ng/ml (Inoue *et al.* 2004). The study detected PFOA in a small number of serum samples from the mothers but not in cord blood serum. The study concluded that foetuses in Japan may be exposed to relatively high levels of PFOS.

Two human milk samples were analysed for a number of different PFCs including PFOS, PFOA and PFOSA (Kuklenyik *et al.* 2004). In one sample only perfluoropentanoic acid (PFPeA), at 1.56 ng/ml, was found and in the other sample only perfluorohexanesulphonate (PFHxA), at 0.82 ng/ml. The study suggested that PFCs may, therefore, be not as prevalent in human milk as in blood, but studies with a much larger sample size are needed to confirm this because the sample size was so limited.

3.8.3 *PFCs in Occupationally Exposed Individuals*

A study was conducted to analyse PFOS in blood samples from individuals who worked in fluorochemical production in Decatur, Alabama, and in Antwerp, Belgium (Olsen *et al.* 1999). In 1995, the mean serum level for 178 employees was 2.19 parts per million (ppm) and the range was 0 to 12.83 ppm. For comparison with the above data on levels in the general population, the values would be mean 2190 ng/ml and range 0 to 12830 ng/ml. In 1997, PFOS was monitored again in 149 employees and the mean was 1.75 ppm (or 1750 ng/ml), range 0.1 to 9.93 ppm (or 100-9930 ng/ml). Considering the mean levels of PFOS in serum from the workers, these values are two orders of magnitude greater than mean values for the general population.

A further study was carried out on workers involved in the production of ammonium perfluorooctanoate (Olsen *et al.* 2000). The study analysed blood samples from the workers for PFOA. In 1997, the mean PFOA concentration in the serum of 74 workers was 6.4 ppm (or 6400 ng/ml), and the range was 0.1 to 81.3 ppm (or 100 – 81300 ng/ml). The mean value is three orders of magnitude greater than levels found in the general population.

4. TOXICITY

4.1 Binding to Blood Proteins

PFOS is known to accumulate in the liver and blood of exposed animals. It has been proposed that interaction of man-made chemicals with certain proteins in blood serum (serum proteins) might disturb the normal functioning of the endocrine (hormonal) system. A study was conducted to investigate the binding of PFOS with serum proteins to assess whether PFOS was likely to cause endocrine disruption by this mechanism (Jones *et al.* 2003). The study found that at very high concentrations, PFOS bound weakly to fish blood serum proteins and caused the displacement the hormones estradiol and testosterone. It also bound to bird blood serum proteins and displaced cortisone. Although PFOS interfered with the binding of hormones to serum proteins, it only did so at extremely high concentrations. At the concentrations which are found in wildlife this effect did not occur. The study concluded that based on current environmental concentrations of PFOS in fish and birds, no effects on hormone binding to serum proteins would be expected.

4.2 Cellular Effects

At a cellular level, it is known that cells have channels which run through the cell membrane to connect them with neighbouring cells. Signalling molecules pass through these channels to synchronise tissue function, a process called gap junctional intercellular communication. This process is necessary for normal cell growth and functioning. Disruption of the process results in

abnormal cell growth and function. It has been hypothesised that the inhibition of gap junctional intercellular communication is associated with tumour promotion. In addition, chronic (long-lasting) disruption of gap juctional intercellular communication could lead to neurological, cardiovascular, reproductive, and endocrinological dysfunction. Experiments have shown that certain PFCs inhibit gap junction intercellular communication (Hu *et al.* 2002). Two cell lines, rat liver cells and dolphin kidney epithelial cells, were exposed to PFOS, perfluorooctane sulfonamide (PFOSA) and perfluorohexane sulfonic acid (PFHA) *in vitro*. Results showed that these compounds inhibited gap junctional intercellular communication in a dose-dependent manner. The study commented that previous work also showed that PFOA and perfluorodecanoic acid (PFDA) inhibited this process. It was found that the inhibition by PFCs depended on the number of carbons in the chain length of the molecule, such that perfluorinated sulfonic acid compounds with less than 5 carbons or more than 16 did not inhibit gap junctional intercellular communication. Hu *et al.* (2002) also studied the effect of PFOS on gap juctional intercellular communication in the liver of rats. After 3 days of exposure, gap junctional intercellular communication was significantly reduced in the liver. Results for the cell lines and on the rats were reported to be comparable, and this suggested that the inhibitory effects of PFOS on gap junctional intercellular communication were not species specific nor tissue specific and can occur both *in vitro* and *in vivo*. It was concluded that PFOS poses a risk to the health of mammalian systems by interrupting gap junctional cellular communication. It was noted that it would not be possible to determine whether PFOS would pose a risk to human health due to its effects on this process.

Some of the effects on gap junction intercellular communication are thought likely to be due to alterations in membrane fluidity (Hu *et al.* 2003). A study on the effects of PFOS on cell membranes confirmed that this compound significantly increased membrane fluidity in fish leukocytes (white blood cells) *in vitro* (Hu *et al.* 2003). Perfluorohexane sulfonic acid (PFHS) and perfluorobutane sulfonic acid (PFBS) had no effect on membrane fluidity. In the same study, PFOS, but not PFHS or PFBS, was also found to affect cell membrane permeability. PFOS had the effect of increasing cell permeability to two other compounds that were tested, one of these being dioxin (2,3,7,8-TCDD). The increased permeability meant that there was increased uptake of this compound across the cell membrane and into the cell. The study noted that both the effects on cell permeability and on membrane fluidity occurred *in vitro* and that additional studies are needed to confirm whether these effects occur *in vivo*. Nevertheless, the authors commented that given that the tissue concentrations measured in some organisms can reach 1-10 mg/kg, it would be expected that these effects may occur *in vivo* at these concentrations. If the effects on membrane fluidity occurred, it is not known whether adverse effects to the whole organism are likely. All that is known from previous studies is that alterations in membrane fluidity are a consequence of diseased or abnormal conditions.

4.3 Toxicity to Nematode Worms

A study was conducted on the toxicity of PFOS, PFOA and perfluorononanoic acid (PFNA) on the nematode worm *Caenorhabditis elegans* (Tominaga *et al.* 2004). At concentrations of 10 pM (5.38 ng/L)PFOS and 1 nM PFNA the number of eggs and worms in the fourth generation of worms decreased significantly. The study concluded that low doses of PFOS and PFNA can strongly disrupt fecundity in *C.elegans*. It was noted that nematodes play essential roles in food chains and the results of the study may be ecologically relevant for the protection of ecosystems.

4.4 Toxicity to Birds

The reproductive toxicity of PFOS to birds has been investigated in two species, namely the Northern bobwhite quail (*Colinus virghinianus*) and the mallard (*Anas platyrhynchos*) (Giesy and Jones 2004). The birds were given doses of 10, 50 or 150 mg PFOS/kg in the diet. In the mallard, doses of 50 and 150 mg/kg PFOS were overtly toxic and the study at these doses was stopped. At 10 mg/kg PFOS there was no effect on body weight or food consumption in the birds. However, in both species, a dose of 10 mg/kg PFOS resulted in an increased incidence of small testes in adult males. Post-reproductive regression of the testes is a normal physiological process, but the treatment with PFOS appeared to accelerate this process. The toxicological and potential ecological significance of this effect is unknown. In both species, PFOS was measurable in the yolk of eggs that were laid by exposed females. The health of the chicks was investigated. In bobtail quail chicks up to 14 days old, but not in mallard chicks, the results indicated there was an overall effect on chick health that was described as 'failure to thrive'. Based on the results of this reproductive toxicological study, and based on levels of PFOS in wild birds that were measured before the year 2000, the study performed a hazard assessment which suggested that in most circumstances, the concentrations found in bird tissues do not seem to pose a significant threat to the health of wild birds. Nevertheless, it was also noted that further studies would be prudent based on the results, and that the levels measured in birds in the environment were mainly recorded before 2000 and may not accurately represent current levels because of the recent cessation of PFOS production in the US.

A report by the US non-governmental organisation Environmental Working Group noted the mysterious deaths of pet birds that were exposed to fumes from heated Teflon coated pans. A study by the organisation showed that a cocktail of hazardous chemicals were released to the air from Teflon coated pans heated for 2-5 minutes on a conventional stove. The report linked the deaths of the birds with the releases of the chemicals (ENDS 2003). Another study showed that heating of Teflon to 500 ^{0}C resulted in the release of trifluoroacetic acid, a persistent chemical (Ellis *et al.* 2001).

4.5 Toxicity to Rodents

PFCs have been found to cause a variety of toxicological effects in rodents. These effects include hepatomegaly (liver enlargement), proliferation of peroxisomes and endoplasmic reticulum and, induction of cytochrome P450 enzymes in the liver (Adinehzadeh *et al.*1999). PFOA has been shown to be a strong tumour promoter, showing a 56% tumour incidence in 12 months of dietary exposure at 0.02% (w/w). However the structurally similar perfluorodecanoic acid (PFDA) was not a tumour promoter (see Adinehzadeh *et al.*1999). Another long term feeding study showed that PFOA exposure at 300 ppm in the diet over 2 years increased cancers of the liver (liver adenomas) and pancreas (pancreatic acinar cell adenoma) (see Olsen *et al.* 1998).

According to Renner (2001), a study on rats showed that the lowest dose at which weight loss occurred in the animals after giving PFOS was 0.4 mg/kg/day (the lowest observed adverse effect level or LOAEL). This corresponded to a liver concentration of 58 ppm. In wild mink, the greatest concentration that was found in livers was 6 ppm. Mink could be more or less sensitive to PFOS than rats, so it is possible that current environmental levels of PFOS may already be causing adverse effects in such wildlife species (Renner 2001).

4.5.1 *Effects on the Liver*

PFOS and PFOA have been found to cause hepatic (liver) peroxisome proliferation in rats that were given a single injection (100 mg/kg) of these chemicals (Berthiaume and Wallace (2002).

Peroxisomes are organelles that are present in the cells of animals and are involved in β-oxidation of fatty acids (i.e. their metabolism), synthesis of bile acids and cholesterol and, metabolism of amino acids and purines (Giesy and Kannan 2002). Effects resulting from peroxisome proliferation include increase in liver weight, induction of enzymes associated with β-oxidation of fatty acids and lowering of serum cholesterol. In a study on PFOA and PFOS (Berthiaume and Wallace 2002), these chemicals resulted in induction of enzymes associated with β-oxidation of fatty acids and lowering of serum cholesterol (Berthiaume and Wallace (2002). PFOA but not PFOS also caused an increase in liver weight and both chemicals caused a decrease in body weight. The study concluded that acute administration of PFOS and PFOA in rats causes hepatic peroxisome proliferation. PFOA, but not PFOS, was also found to affect the functioning of mitochondria in the liver.

Kawashima *et al.* (1995) investigated peroxisome proliferation and liver toxicity in response to administering repeated low doses of PFOA and perfluorodecanoic acid (PFDA) to rats. Both chemicals caused peroxisome proliferation in the liver and an increase in liver cell size. They also caused effects in parameters that are responses of peroxisome proliferation including induction of several enzymes and proteins. For example, they induced peroxisomal β-oxidation, microsomal l-acylglycerophosphocholine acyltransferase and cytosolic long-chain acyl-CoA hydrolase. PFDA caused increases in lipid droplets in hepatocytes (liver cells), an effect typical of acute metabolic disorders and considered to be an indication of toxicity to hepatocytes. The study concluded that both PFOA and PFDA are peroxisome proliferators in rats at low doses and that PFDA is more toxic to hepatocytes than PFOA. In another study, PFDA was shown to cause increases in liver phosphocholine and other effects related to phospholipid metabolism in rats (Adinehzadeh *et al.*1999).

4.5.2 ***Effects on the Immune System***

The thymus and spleen are organs which both play central roles in the immunological defences of higher animals. These organs can be highly sensitive to damage by toxic chemicals and are, therefore, often investigated for immunotoxicological effects. A study on chemicals which cause peroxisome proliferation, including PFOA, also reported loss of weight of the thymus and spleen (thymic and splenic atrophy) in exposed mice (see Yang *et al.* 2001). Further investigation of PFOA in this regard confirmed the findings and also found that the weights of the organs recovered after cessation of treatment with PFOA (Yang *et al.* 2001). It was hypothesised that these effects on the immune system resulted from altered fatty acid transport and/or metabolism. In a laboratory setting, atrophy of the thymus and spleen is sometimes associated with disturbances in the normal cellular structure of the organ, as well as various functional alterations of immune response, leading to impaired resistance to experimental infections and tumour growth (Yang *et al.* 2002).

This latter study also reported that PFOA is potently immunosuppressive in mice (Yang *et al.* 2002). Immunosuppression can lead to increased incidence and severity of infection and tumour frequency. The study exposed mice to PFOA and tested the immune response to the introduction of horse red blood cells. The number of splenocytes (cells of the immune system) that produced antibodies to the horse red blood cells was dramatically decreased in PFOA treated mice. The study concluded that PFOA causes a pronounced suppression of adaptive immunity in mice. In considering humans who have been occupationally exposed to PFCs, the study noted that the doses of PFOA that caused immunosuppression in mice were considerably higher than levels in such exposed humans.

4.5.3 *Effects on Development*

A review of developmental effects caused by PFOS lists a number of adverse effects of this chemical after comparatively high dose administration to rats (Lau *et al.* 2004). The developmental effects include reduction of fetal weight, cleft palate, anasarca (edema), delayed ossification of the bones, cardiac abnormalities and death in newborns. A study on developmental effects in rats also reported significant increases in liver weight in newborns exposed to PFOS *in utero* (Lau *et al.* 2003). It was suggested that the developing liver is a potential target for PFOS action. In addition, pups that survived beyond the first few days had growth retardation (a reduction in body weight gain) and had reduced serum levels of thyroxine, a thyroid hormone. The results on growth retardation suggested that PFOS may interfere with cellular or functional maturation of target organs possibly via alteration of thyroid hormones.

Administration of high doses of PFOS to rats and mice during pregnancy causes death of the pups to occur soon after birth (Lau *et al.* 2004). In rats, that were given at dose of 10 mg/kg throughout pregnancy all the pups died, and at a dose of 3 mg/kg 50% survived. In mice, most pups died after the mothers were given a dose of 15 or 20 mg/kg during pregnancy and 50% survived at a dose of 10 mg/kg. Death of rat pups occurred after dosing during different periods of the pregnancy but mortality was greatest when exposure to PFOS was given late in gestation. The results of these studies suggested that death in newborns is most likely caused by adverse impacts on maturation of the lungs and pulmonary function.

N-ethyl-*N*-(2-hydroxyethyl)-perfluorooctanesulfonamide (*N*-EtFOSE) is a building block for perfluorooctane sulfonyl fluoride (POSF)–related products for commercial applications and can be degraded metabolically and in the environment to PFOS. Research on the impacts of *N*-EtFOSE showed that when administered to pregnant rats, like PFOS, it caused mortality of the pups (Lau *et al.* 2004). Two other PFCs, potassium PFBS and potassium PFHS, were not found to produce any adverse effects on development in rats (Lau *et al.* 2004).

4.5.4 *Effects on the Neuroendocrine System*

Austin *et al.* (2003) reported that many of the toxicological effects observed in animals after exposure to PFOS suggested the involvement of the central nervous system, specifically the neuroendocrine system. A study was conducted to investigate the effects of PFOS on the neuroendocrine system in rats (Austine *et al.* 2003). Adult female rats were injected with PFOS at a dose of 1 or 10 mg/kg body weight for 2 weeks. Analysis of rat tissues at the end of the treatment period revealed that PFOS was found in all tissues, including the brain, which suggested it had crossed the blood-brain barrier. PFOS was shown to disrupt the regularity of the estrous cycle and this indicated that PFOS can function as an endocrine disruptor. At the higher dose, PFOS caused a reduction in body weight and significantly increased serum corticosterone levels. Overall, the results indicated that PFOS had marked effects on the neuroendocrine system. Importantly, it was noted that the low dose of PFOS that was given which effected the estrous cycle was lower than levels present in wildlife. Levels in the serum of the treated rats were similar to levels in humans who had been occupationally exposed to PFOS. Therefore, changes in the neuroendocrine functions found in the study may have implications for individuals occupationally exposed to PFOS. In addition, human blood contains several perfluorinated compounds, such as PFOA, which are thought to have similar effects to PFOS.

4.6 Toxicity to Monkeys

According to Renner (2001), the US Environmental Protection Agency conducted a study on rhesus monkeys which showed that no monkeys survived beyond 3 weeks into treatment with

PFOS at a dose of 10 mg/kg/day. At a dose of 4.5 mg/kg/day, no monkeys survived beyond 7 weeks into treatment. A study on cynomolgus monkeys showed they died at doses as low as 0.75 mg/kg/day. There were also changes in the livers of the monkeys and significant reductions in blood cholesterol.

4.7 Toxicity to Humans

Both PFOS and PFOA have long half-lives in the human body (8.67 years and 1 - 3.5 years respectively) (Hekster *et al.* 2003). The excretion from the body is slow and occurs via the urine and faeces. PFOS and PFOA are both widely distributed in the body, especially in blood plasma, liver and kidney (Hekster *et al.* 2003).

A study was undertaken which evaluated the mortality of male and female workers who had been employed for at least one year at a facility that produced perfluorooctanesulphonyl fluoride (POSF)-based fluorochemicals (Alexander *et al.* 2003). A total of 2083 workers were identified who were eligible to be included in the study and among these there were 145 deaths. The workers were categorised into those with high exposure to PFOS, those with low exposure and those with no exposure. Results showed that the overall mortality rates were below those expected for most causes of death. There were two exceptions, namely a higher than expected number of deaths from liver cancer and bladder cancer. For liver cancer, there were 2 deaths which was approximately 3 times greater that expected. These results were of interest because studies on laboratory rodents show that the liver is the primary target organ for PFOS. One of the workers who died had been in highly exposed work for 14 months and the other was in the low exposure group for 11 years. The study commented that these results are difficult to interpret because they are based on only two cases and it is possible that the finding is due to chance. For bladder cancer, 3 workers died from this disease and all were in the high exposure group for more than 5 years. The study commented that the fact that all 3 cases worked for a long duration in high exposure jobs warrants further evaluation. Bladder cancer is not a known effect of PFOS exposure in animal studies. The study concluded that there was excess occurrence of death from bladder cancer, but it is not clear whether this can be attributed to exposure to fluorochemicals alone, and/or to an unknown bladder carcinogen encountered in the workplace and/or to non-occupational exposures such as smoking. Also the possibility of chance could not be ruled out with only 3 observed cases.

Another study on mortality was conducted on individuals who were occupationally exposed to PFOA (Gilliland and Mandel 1993). The incidence of mortality from cardiovascular and gastrointestinal diseases and all cancers combined was not increased. However, the risk of mortality from prostate cancer was increased with increasing duration of work for those in jobs exposed to PFOA. For instance, ten years of employment in exposed jobs was associated with a 3.3-fold increase in prostate cancer mortality. These results were, however, based on only 4 deaths among exposed workers. The study suggested that because there were only a small number of cases, the results should be interpreted cautiously since the increase in prostate cancer deaths could be due to chance or unrecognised confounding from exposure to other factors. Further research on prostate cancer risk from PFOA exposure was suggested.

A study was conducted on the health of 115 male individuals who were occupationally exposed to PFOA (Gilliland and Mandel 1996). This chemical is known to cause effects on the liver in rats including changes in cholesterol, lipoproteins and hepatic enzymes. The study on the exposed workers was carried out to assess whether such changes also occurred in humans exposed to PFOA. Exposure in the workers was determined by measuring total serum fluorine.

Results of the study showed that exposure to PFOA was not associated with causing significant clinical hepatic (liver) toxicity. For instance, total serum fluorine was not associated with cholesterol or lipoproteins. For enzymes indicative of liver injury, there was some evidence of an exposure-related increase in a small subset of obese workers. It was noted that, in this regard, PFOA may modulate hepatic responses to obesity and to alcohol. Another study on male individuals who were occupationally exposed to PFOA also reported there was no significant effect on hepatic enzymes, cholesterol or lipoproteins in relation to serum levels of PFOA (Olsen *et al.* 2000). Unlike the previous study, this study found no evidence that PFOA may modulate hepatic responses to obesity and alcohol.

A study on male individuals who worked in fluorochemical production also investigated hepatic effects due to exposure (Olsen *et al.* 1999). Associations between serum concentrations of PFOS with levels of cholesterol, lipoproteins and hepatic enzymes were assessed. PFOS was measured because the fluorochemicals to which the workers were exposed may be expected to transform metabolically to PFOS. Like PFOA, PFOS has also been found to accumulate in the liver and cause lowering of serum cholesterol in laboratory rodents. This effect has also been found in rhesus monkeys. The study results indicated that there was no association between serum levels of PFOS (at levels less than 6 ppm) and serum levels of cholesterol, lipoproteins or hepatic enzymes. Indeed there were no substantial changes in any of these markers of toxicity.

PFOA has been shown to increase levels of the hormone estradiol in rats fed 100 ppm for up to 13 weeks but there was no effect on testosterone levels. According to Olsen *et al.* (1998) , an earlier study of effects on reproductive hormones in workers exposed to PFOA indicated a positive association between total serum fluorine and estradiol and a negative association with testosterone. Thus estradiol levels apparently increased with increasing exposure to PFOA, as in the study with rats, and testosterone decreased. In order to confirm this, Olsen *et al.* (1998) conducted a further study on male individuals who were exposed to PFOA in the workplace. In contrast, this latter study found that there were no significant changes in estradiol, testosterone or other reproductive hormones with serum levels of PFOA. The authors concluded that the results provided reasonable assurance that significant hormonal changes among the male employees was not apparent in relation to their measured serum PFOA levels.

DuPont manufactures telomers. Its has a Teflon manufacturing facility on the Ohio river in West Virginia, USA. The river, groundwater, the local drinking water supply and local landfills were found to be contaminated with PFOA. Local residents commissioned an epidemiology study. It reported there was a statistically significant excess of prostate cancer and female reproductive cancers in local residents compared with the US average. Examination of health certificates of 5000 of the DuPont employees showed an excess of other cancers such as non-Hodgkins lymphoma, leukaemia and multiple myeloma (ENDS 2004a). Another study was commissioned by DuPont to investigate health of its employees at the plant (see ENDS 2004a). No excess risk of cancer was found but there was a slight (about 10%) increase in serum cholesterol and also a rise in serum triglycerides among some individuals who had serum PFOA levels of greater than 1000 ppb (DuPont 2005).

4.8 Toxicity to Aquatic Organisms

A review of aquatic toxicity studies, mainly published by industry, reported that PFOS is moderately acutely toxic and slightly chronically toxic to aquatic organisms (Hekster *et al.* 2003). Further studies on aquatic toxicity of PFOS and other PFCs are discussed below.

A study was carried out to test the toxicity of PFOS in various small freshwater organisms including the green algae *Selenastrum capricornutum* and *Chlorella vulgaris*, the floating macrophyte *Lemna gibba* and the invertebrates *Daphnia magna* and *Daphnia pulicaria* (Boudreau *et al.* 2003). These organisms represent lower trophic levels in aquatic ecosystems that play important functions in freshwater communities, such as nutrient cycling and energy transfer up the foodchain. All the organisms were adversely affected by acute exposure to PFOS concentrations between 31.1 and 169 mg/l in the surrounding water. For example, *L. gibba* underwent growth inhibition whilst *D. magna* and *D. pulicaria* experienced immobility and a reduction in mean number of young in each brood. While adverse effects occurred at around at mg/l concentrations, environmental concentrations of PFOS are typically in the low ng/l to low μg/l range. The study commented that in this regard, the results indicated a small likelihood of causing adverse effects to freshwater plants and crustaceans. In addition, PFOS may accumulate to adverse effect levels in locations such as vernal pools subject to high evaporation and no outflow or spill events may result in short-term high concentrations. The authors suggested further studies on long-term effects in aquatic species should be conducted.

A study was conducted on the toxicity of PFOA on zooplankton communities set up in the laboratory (Sanderson *et al.* 2003). The introduction of PFOA at concentrations of 10 and 70 mg/l caused the structure of the ecosystem to change. The overall species richness was significantly reduced such that the ecosystem went from a more diverse community dominated by larger species, towards a less diverse community dominated by smaller species. These smaller species that increased in number were less sensitive to adverse effects of PFOA. The study suggested that further investigations needed to be carried out to test environmentally relevant concentrations of PFOA on freshwater ecosystems.

A study on the aquatic midge *Chironomus tentans* found that it was not sensitive to exposure to PFOA but was highly sensitive to PFOS (MacDonald *et al.* 2004). Midge larvae did not survive exposure to 100 μg/l in the water. At doses of 50 μg/l or greater, there was a significant reduction in midge survival, a significant decline in growth and adverse impacts on emergence of adult midges from larvae. This concentration is much lower than adverse impacts recorded on other aquatic organisms in other studies (e.g. see above) in which effects occurred in the mg/l range. Aquatic midges represent an important food source for aquatic organisms such as fish and ducks. Although the adverse effects on midges in this study occurred at concentrations that normally exceed environmental concentrations (e.g. 25-144 ng/l), higher concentrations of PFOS have been reported in the environment following accidental spills of PFOS, and this brings into concern possible adverse impacts on aquatic midges.

Oakes *et al.* (2004) investigated reproductive impairment and biochemical changes in fish (the fathead minnow, *Pimephales promelas*) following exposure to PFOA. Exposure to water concentrations of 0.3 to 100 mg/l did not cause an increase in mortality of the fish. However PFOA did significantly alter the levels of circulating steroid hormones in the fish and, as also seen in rats, it increased peroxisome-associated enzyme activity. With regard to steroid hormones, levels of testosterone were significantly reduced in male and female fish at PFOA water concentrations of greater than 1.0 mg/l. 17β-estradiol levels were also altered in female fish at concentrations of PFOA above 30 mg/l. Such reductions in steroid hormones, however, only appeared to have a modest effect on reproduction in the fish. For instance, there was a trend towards reduced egg production and oviposition (egg laying) with increasing concentrations of PFOA. It was suggested that further studies needed to be carried out on reproduction effects to investigate effects in subsequent generations of fish after exposure of the parents. The study concluded that while PFOA appeared to be relatively non-toxic at

environmentally relevant concentrations, exposure to higher levels found in environmental spills may impact in reproduction. For example, total perfluorinated solvents downstream of spills have been found to range up to 17 mg/l (Oakes *et al.* 2004).

In summary, a diversity of adverse effects have been reported in organisms exposed to various PFCs. Although these effects often occur only at levels higher than those expected to be encountered in the environment at present, this is not always the case. Some species appear to be markedly more sensitive than others. Precise details of the mechanisms and potency of toxic effects are still relatively poorly understood for this group, for which the scale and extent of environmental contamination has only recently emerged. Moreover, what limited information does exist focuses primarily on PFOS, PFOA and a small number of other PFCs. A common characteristic of much of the research published to date is a call for further research to elucidate fate and effects of this chemical group.

5. CURRENT POLICY ON PFCs

5.1 United States Environmental Protection Agency

In 2000, the 3M company made a decision to cease the manufacture of PFOS related chemicals by 2003 (see section 1.1). It later transpired that the decision to phase out "perfluorooctanyl chemistry" by 3M was prompted by pressure from the US Environmental Protection Agency (EPA). Research was accumulating on the presence of PFCs in human blood from around the world and on adverse effects in laboratory animals, and the EPA threatened 3M with regulatory action if it did not stop the perfluorooctanyl chemistry voluntarily (ENDS 2001, ENDS 2004a).

The US EPA has since imposed a ban on the use of PFOS with only a few essential uses in aviation, photographic and microelectronics industries being exempted (ENDS 2004a). The "significant new use" rule that was proposed in October 2000 for 75 perfluorinated sulfonates requires firms intending to manufacture or import the chemicals to notify the EPA which could then impose restrictions. This effectively prohibits their manufacture or import into the US apart from the exceptions listed (ENDS 2002a).

The US EPA have also turned attention to the perfluorinated carboxylate breakdown product and manufacturing aid PFOA (Renner 2004). It produced a draft risk assessment of PFOA in April 2003 (ENDS 2004a) in which it identified "potential human health concerns" (ENDS 2003). It planned a public meeting to negotiate an "enforceable consent agreement" with manufacturers to submit information to a specified schedule. The completed draft risk assessment on PFOA is due to be published by US EPA in early 2005 (http://www.epa.gov). DuPont is the principle manufacturer of PFOA since 3M stopped their production of PFOS related chemicals. The US EPA have recently filed a claim against DuPont seeking penalties for withholding the results of human blood sampling information that documents levels of PFOA in individuals near a DuPont facility in West Virginia (http://www.epa.gov).

5.2 OECD

A risk assessment was conducted by the OECD on PFOS (ENDS 2002b). It concluded that PFOS is persistent, bioaccumulative and toxic to mammals. The US EPA have a request for international measures to be taken on PFOS but OECD did not recommend action for a ban. It did recommend that governments contact PFOS manufacturers in their countries (Italy, Japan, Switzerland and the UK) to determine whether the companies have plans to phase out PFOS production.

5.3 Europe

The European Commission is currently drafting proposals to restrict the marketing and use of PFOS (ENDS 2004a).

The UN Economic Commission for Europe's 1979 Convention on long-range transboundary air pollution has 8 protocols. One of the protocols, which was adopted in 1998, was for regulation of persistent organic pollutants (POPs). At a recent meeting of the executive committee, Sweden proposed that PFOS should be included on the POPs list (ENDS 2004b).

5.4 UK

In June 2004, the UK government announced unilateral action to phase out PFOS and related compounds (ENDS 2004a). The Department of Environment, Food and Rural Affairs (DEFRA) published a risk reduction strategy for PFOS and related compounds which recommended a ban on these substances. It noted that a few industries would be temporarily exempt, but this would be conditional on the development of alternatives and the disposal of all PFOS-bearing wastes by high temperature incineration (ENDS 2004c). For instance, it recommended setting a phase-out timetable for photographic, photolithographic and fire fighting applications, and an immediate phase out for chromium plating since alternative technologies already exist in this sector. For aviation fluids, an unlimited derogation was given subject to compliance with guidance and best practice, including disposal of PFOS wastes by high temperature incineration. DEFRA warned all users that it will be highly likely that EU legislation will be following behind the UK proposals (ENDS 2004d). Although the 3M company have withdrawn its PFOS related chemicals in the US, DEFRA believes there are at least two other producers, one in Germany and the other in Italy (ENDS 2004a).

To summarise, in addition to voluntary action taken by manufacturers, some legislative measures are now being developed in Europe, notably in the UK. There is also the possibility that some PFCs, particularly PFOS, may qualify as persistent organic pollutants (POPs) under relevant international law.

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