ENVIRONMENTAL WORKING GROUP

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December 6, 2002

Ms. Dorothy Sussman
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Dear Ms. Sussman:

We are writing to nominate the category of perfluorinated chemicals for inclusion in future releases of the Centers for Disease Control and Prevention's (CDC's) National Report on Human Exposure to Environmental Chemicals (the "Report").

Justification for this nomination is drawn from our review of the US Environmental Protection Agency's public Administrative Record on perfluorinated chemicals (AR-226), a collection of over 1130 documents, including PFC studies conducted over the past 30 years and accumulated by the Agency primarily over the past two years. These studies document the widespread use of PFCs in consumer products, their toxicity, and the universal occurrence of these chemicals in the general population, at concentrations that exceed standard safety margins for public health protection.

At your request we can provide copies of any of the scientific materials referenced in our written justification for our nomination, which is attached to this letter.

Thank you for your consideration.

Sincerely,

Kristina Thayer, Ph.D.
Senior Scientist

Jane Houlihan
Vice President for Research

Perfluorinated chemicals: Justification for Inclusion of this Chemical Class in the National Report on Human Exposure to Environmental Chemicals

Environmental Working Group
Washington, D.C.
December 6, 2002

Kristina Thayer, Ph.D.
Jane Houlihan

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Chapter 1: Overview

The Environmental Working Group nominates the category of perfluorinated chemicals (PFCs) for inclusion in future releases of the Centers for Disease Control and Prevention's (CDC's) National Report on Human Exposure to Environmental Chemicals (the "Report").

Justification for this nomination is drawn from our review of the US Environmental Protection Agency's public Administrative Record on perfluorinated chemicals (AR226), a collection of over 1130 documents, many of which describe studies of PFCs conducted over the past 30 years. The Agency compiled this record primarily over the past two years, coinciding with 3M's phaseout period of one branch of PFCs - a phaseout triggered by company tests from the late 1990s that showed the widespread presence of a pertinent biomarker in human serum (PFOS, or perfluorooctane sulfonate), near global environmental contamination of wildlife by PFOS, and low-dose mortality of adult monkeys dosed with PFOS and neonate rats exposed to PFOS *in utero*.

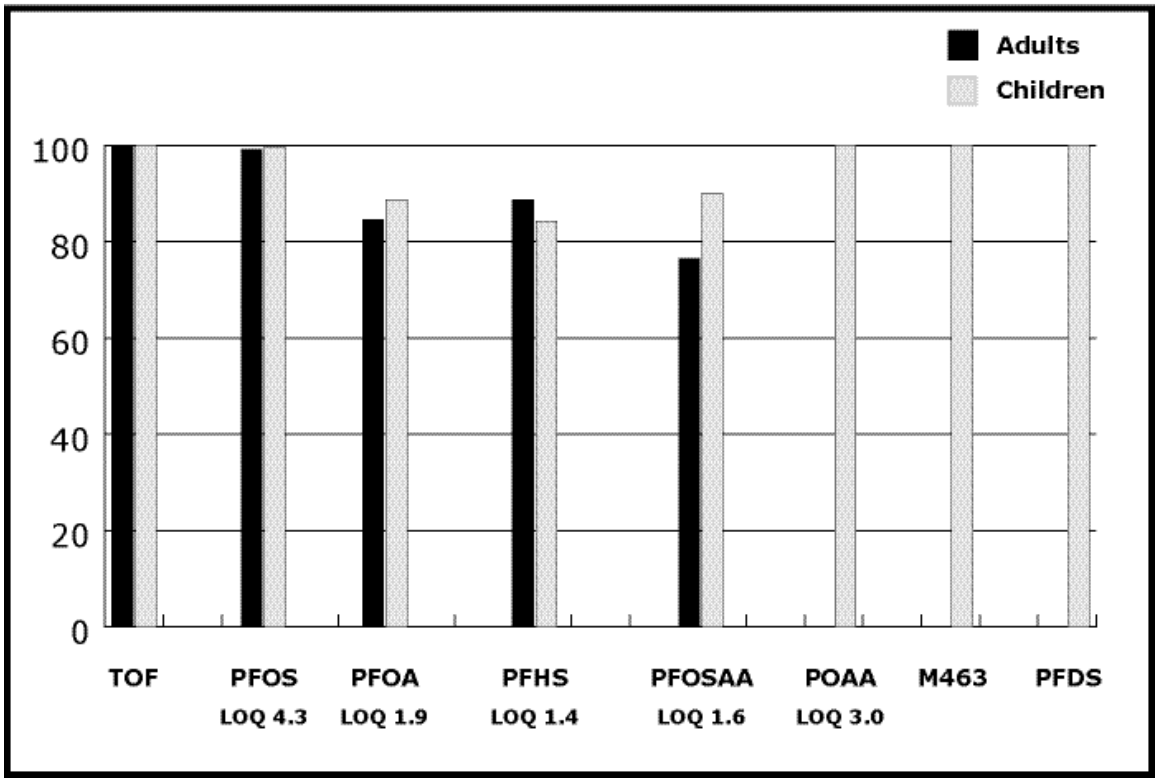
Collectively, the studies in the public record document:

- The continued widespread use of PFCs in consumer products;
- The theoretically infinite persistence of ultimate PFC breakdown products in the environment;
- The toxicity of PFCs spanning multiple mammalian systems and modes of action; and
- The universal occurrence of perfluorinated chemicals in the general population, at concentrations that exceed standard safety margins for public health protection.

Industries worldwide incorporate millions of pounds of PFCs each year into consumer products. These range from food wraps and packaging to spray-on treatments for carpet, upholstery, clothing and leather; and from non-stick cooking pans to cosmetics, hair care formulas, and floor care products. Scotchgard™, Teflon®, Stainmaster® and Zonyl® are just four examples of consumer product lines that contain these chemicals.

Industry scientists have detected PFCs in archived human blood samples dating back to 1957 (Tables 1-4). Scientists found PFCs in every recent sample tested from nearly 3000 people in the US, including blood samples from 599 children, 238 elderly Washington residents, and approximately 2000 blood bank donors (Figure 1).

Figure 1. Percent of individuals with serum levels above the limit of quantitation (LOQ)



For TOF, PFOS, PFOA, PFHS, PFOSAA see Tables 5 and 6 for details. Percent detection data for POAA, M463, PFDS are presented in a 3M pilot study (3M 1999d). Adult data for POAA, M463, and PFDS are not presented in the public record.

Studies show that the ultimate perfluorinated breakdown products of PFCs do not hydrolyze, photolyze, or biodegrade under environmental conditions, and cannot be metabolized in biota. These products include PFOS and the Teflon® manufacturing aid PFOA, or perfluorooctanoic acid.

Unlike other persistent organic pollutants, all of which have some capacity to degrade in the environment, PFCs will persist indefinitely even if banned, and will continually redistribute throughout the environment, the food chain, and the human population. PCBs and DDT have declined in total global mass in the decades following their respective bans in many countries, but the same will not be true for PFOS. The persistence of PFCs heightens the importance of tracking human exposures through tools like biomonitoring.

PFCs are linked to a broad range of adverse health effects. In lab animals these effects include liver toxicity, tumors of multiple organs, death by wasting at relatively low doses, and increased toxicity to

developmentally exposed rats (OECD 2002, US EPA 2002). Studies of exposed workers have found that PFCs are associated with increased levels of cholesterol and triglyceride, as well as elevated rates of cerebral vascular disease, bladder cancer and tumors of the male reproductive tract (OECD 2002, US EPA 2002a, US EPA 2002b). The PFCs that have been studied thus far cause similar types of toxicity, indicating that the effects of individual PFCs may be cumulative, and that many PFCs could be considered to fall within a common toxicity chemical class, much like dioxin-like PCBs.

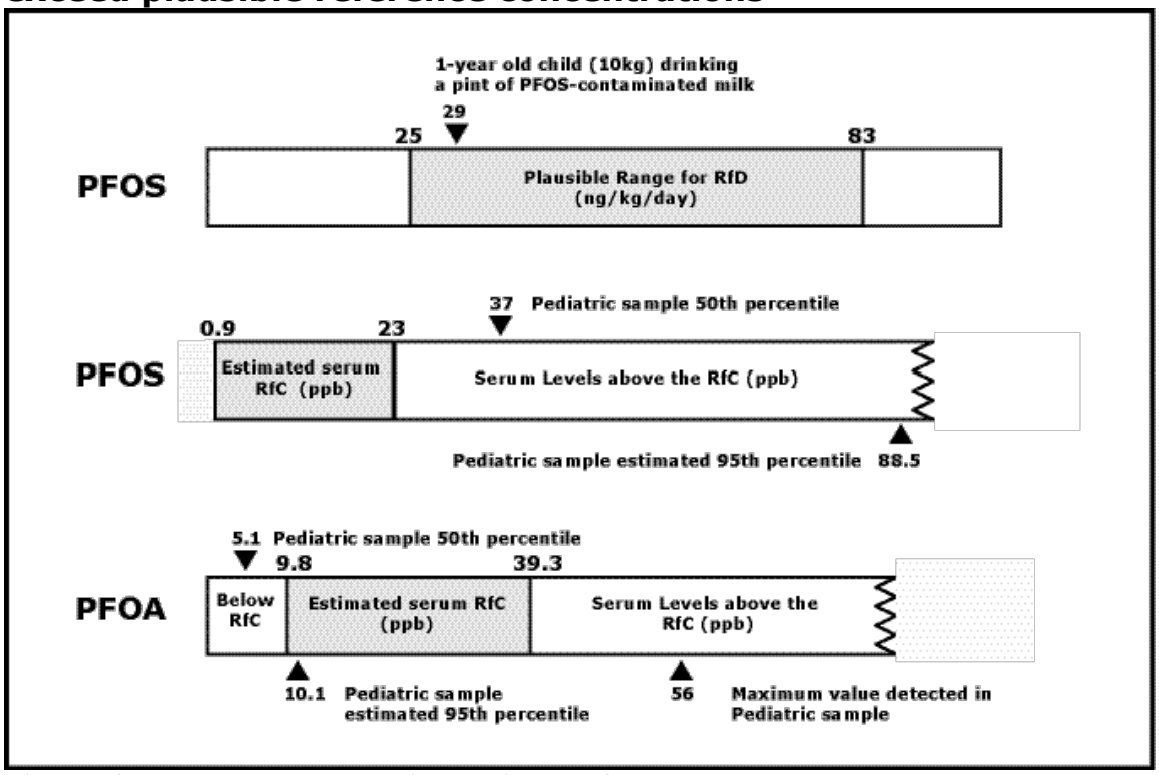
The occurrence of both PFOS and PFOA in human serum exceeds plausible reference concentration ranges derived from animal studies (Figure 2). More than half of the children and adults tested during the past decade showed PFOS serum levels higher than an upperbound reference concentration (derived by applying a composite uncertainty factor of 300 to a rat serum level at the No Observed Adverse Effect Level (NOAEL) based on liver toxicity). The estimated 95th percentile exposure for children is nearly four times the upperbound reference concentration.

As shown in Figure 2, a one-year-old child weighing 10 kilograms could exceed a reasonable reference dose for PFOS through a single exposure route, a pint of milk, consumed each day.

PFOA levels in the blood of more than five percent of children and adults tested fall in the range of a plausible reference concentration. The maximum level detected among samples from 599 children was 1.5 times an upperbound reference concentration (derived by applying a composite uncertainty factor of 3000 to a rat serum level at the Lowest Observed Adverse Effect Level (LOAEL) associated with altered liver, kidney, spleen and seminal vesicle weight).

Both PFOS and PFOA persist in the human body for long periods of time. Through ongoing monitoring of a handful of occupationally exposed retired workers, 3M has most recently estimated a human half-life of 8.7 years for PFOS, and 4.4 years for PFOA (Burris, et al. 2002). The estimated human half-lives for both these compounds have increased as 3M has tracked workers more thoroughly (Burris, et al. 2000, Olsen, et al. 1999).

Figure 2. In more than half of all children tested, PFC levels exceed plausible reference concentrations



RfC = Reference concentration; RfD = Reference dose
See Tables 5, 6 and 9 for serum concentrations and RfD/RfC details.

In recent studies, scientists have detected PFCs in tap water and food. In June 2001, 3M reported finding PFCs in public drinking water sampled from the tap in two of six cities (3M 2001c), indicating the possibility of widespread contamination of drinking water supplies in areas not associated with PFC manufacturing. PFOA has been detected in tap water from multiple towns on the Ohio River near a DuPont PFC plant (West Virginia Department of Environmental Protection 2002).

Both market basket studies and studies of wildlife around the world indicate that the food chain may be broadly contaminated with PFCs. In food purchased from supermarkets in six cities, laboratory analyses detected PFCs in six of 11 food types tested. Analyses showed PFOS in 22% (4/18) of milk samples and PFOS or PFOA in 17% (3/18) of ground beef samples. PFOA was also found in green beans, apples, and bread (3M 2001d).

In a series of studies conducted primarily over the past five years, scientists have detected PFCs in at least 55 species of vertebrates in 13 countries and three continents, including species in remote areas – albatross in Midway Atoll, Alaskan polar bears, and seals in Arctic

areas of Norway and Canada (Giesy and Kannan 2001a, Kannan, et al. 2001c). The widespread distribution of PFCs in wildlife suggests that the food chain has been contaminated through diffuse, broad transport of PFCs on a near global scale.

Under the terms of a phaseout agreement submitted to EPA, 3M discontinued the manufacture of 13 key PFOS-related chemicals by December 31, 2000 (US EPA 2002d), but human exposures to the chemicals will persist. Other countries, including Japan and Italy, have PFOS-related chemical production capabilities. It was not definitively stated in a recent review published by the Organization for Economic Cooperation and Development (OECD), whether production in these countries has stopped (OECD 2002).

PFOS will persist in the environment indefinitely, irrespective of current production volumes, and will continue to redistribute globally through transport in the atmosphere, water, and sediment. Even following a complete, worldwide cessation of the manufacture of PFOS-related chemicals, the total mass of PFOS in the environment will continue to increase through time as precursor chemicals are degraded or metabolized to PFOS. It is not known if exposures in the general population will decline substantially, or at all, over the next generation.

Evidence in the public record shows that product lines previously dominated by PFOS chemicals are likely being replaced with alternate perfluorinated chemicals, including PFOA (US EPA 2002b); chemicals that break down to the four-carbon chain equivalent of PFOS (perfluorobutane sulfonate, or PFBS) (3M 2002b); and telomer alcohols, some of which break down to PFOA and PFOA homologues (DuPont 2002a, DuPont 2002c, Purdy 2002).

No studies appear in the record estimating relative contributions of ambient air, drinking water, food, and consumer product exposures to body burdens of PFCs in the general population. Without these estimates and underlying models, biomonitoring will be the only available tool to assess changes in exposure during the current fluxes in PFC use, in the wake of 3M's PFOS phaseout.

The number of perfluorinated chemicals used in industrial applications and consumer products is large. To prioritize these chemicals, we have categorized PFCs identified by various agencies (primarily the US EPA and FDA) into 10 groups based on patterns of human exposure, toxicity, biopersistence and availability of analytical method. The 10 groups of PFCs we have identified are:

Group 1: Two perfluorinated chemicals for which current body burdens of the general population and expected future use and exposure patterns raise human health concerns (PFOS and PFOA).

Group 2: (single chemical) A four-carbon homologue to PFOS that represents a PFOS replacement in 3M's new Scotchgard formulations, perfluorobutane sulfonate (PFBS). 3M is also planning on using potassium perfluorobutane sulfonate (KBPS) in a new flame retardant to replace the brominated flame retardants used in clear polycarbonate plastic (Mullen 2001).

Group 3: Nine perfluorinated chemicals that have been detected in the general population or wildlife, including four metabolic precursors of PFOS, two homologues of PFOS (six-carbon and ten-carbon chains), and three metabolites of fluorinated telomer alcohols and/or telomer acrylates that are used in product lines that directly compete with the 3M product lines based on PFOS-related chemistry (3M 1999a, DuPont 2002a, DuPont 2002b, DuPont 2002c).

Group 4: Seven telomer alcohol or telomer acrylate metabolites for which methods have been developed for animal tissue. The majority, if not all, of these compounds are homologues of the eight-carbon PFOA (carbon chain lengths of 7, 10, 11, 12, and 14).

Group 5: Three perfluorinated homologues of PFOS and PFOA (the seven- and nine-carbon homologues of PFOS and the nine-carbon homologue of PFOA) which lack analytical data for biota in the public record, but which are used in PFC products or production processes, and for which analytical methods would be analogous to existing methods.

Group 6: Thirteen PFOS-related compounds or mixtures that collectively (10) or individually (3) were produced in quantities over a million pounds per year and never tested in the general population.

Group 7: Seventeen perfluorinated compounds identified by the TSCA Interagency Testing Committee (ITC) in their 49th report to the EPA Administrator as possible PFOS replacements (US EPA 2002e). In 1998, these PFCs had production volumes greater than 10,000 pounds, but less than 1 million pounds.

Group 8: Sixteen perfluorinated compounds that the FDA has approved as indirect food additives.

Group 9: Fifty perfluorinated compounds identified by the TSCA Interagency Testing Committee in their 46th report to the EPA Administrator (US EPA 2000b) as potentially persistent and bioaccumulative.

Group 10: Approximately 90 compounds related to PFOS chemistries, phased out of production by 3M, and subject to Significant New Use Rule by EPA.

Chapter 2: Justification for inclusion of PFOS and PFOA in CDC biomonitoring program

Sections below present the justification for including PFCs in CDC's biomonitoring program, framed around the selection criteria presented in CDC's Federal Register Notice of October 7, 2002 (Center for Disease Control 2002). These justifications focus primarily on PFOS and PFOA (Group 1 in the chemical groupings we constructed to aid CDC in prioritizing PFC testing). Information relevant to CDC's selection criteria for all 10 groups of PFCs is summarized in Chapter 3 of this document.

(1) Independent scientific data which suggest that the potential for exposure of the US population to a particular chemical is changing (i.e., increasing or decreasing) or persisting.

The potential for exposure to particular PFCs is changing
Studies in the public record show that people are exposed to PFCs through consumer products containing the chemicals, and through drinking water and food contaminated with PFCs from the environment. The contribution of each of these exposure routes to body burdens of PFCs in the general population has not been defined.

Patterns of PFC use in consumer products are changing as a result of 3M's phaseout of PFOS-related chemicals. Information in the public record suggests that replacement chemicals could include PFOA (US EPA 2002b); chemicals that break down to the four-carbon chain equivalent of PFOS (perfluorobutane sulfonate, or PFBS) (3M 2002b); and telomer alcohols, some of which break down to PFOA and PFOA homologues (DuPont 2002a, DuPont 2002c, Purdy 2002).

As PFOS-related chemicals are phased out of use, those that are metabolic and degradation precursors of PFOS in the environment should decline in overall mass through time, concomitant with an overall increase of PFOS mass in the environment. The rate at which this transformation will occur is undefined. The possibility continues for sustained widespread exposures to PFOS precursors. And as precursors are transformed to PFOS through time, the possibility exists for ever-increasing exposures to PFOS through exposure routes driven by environmental contamination (tap water and food, for example), even as exposures to PFOS from consumer products decline.

PFOS has been found in milk and ground beef (3M 2001d) and drinking water in certain US cities (3M 2001c). The extent of PFOS contamination is so thorough that control animals used in toxicology studies have background levels of PFOS on par with the non-worker human population in the US (OECD 2002), and is likely to increase with time. PFOS is the ultimate breakdown product for all PFOS precursors, as it is not known to hydrolyze, photolyze, or biodegrade under environmental conditions, and cannot be metabolized in biota.

As formulations in commercial products shift, exposures to chemicals chosen as PFOS alternates will increase. If PFOA and its precursors are widely selected as PFOS alternatives, PFOA exposures, already exceeding standard safety margins in the general population (Figure 2), could increase.

Currently, neither EPA nor the manufacturer is able to define the source of widespread occurrence of PFOA in the general population, since the chemical is not intended to appear in finished commercial products. One possible source is PFOA produced through the oxidation or metabolism of telomer-based fluorochemicals that DuPont uses in their Zonyl® product line (DuPont 2002a, DuPont 2002c). The Zonyl® product line is used in various consumer products including carpet and upholstery protection, glass or other hard surface cleaners, floor polishes (DuPont 2001). Recently, the FDA approved the use of Zonyl® products for use on paper and paperboard for food contact, including uses such as food wraps, pizza boxes and butter boxes (DuPont 2002b). Along with DuPont, several other companies (Asahi Glass, Atofina, Clariant, Daikin) are member companies of the Telomer Research Program (TRP) (Telomer Research Program 2000), and presumably produce or use telomer fluorochemicals.

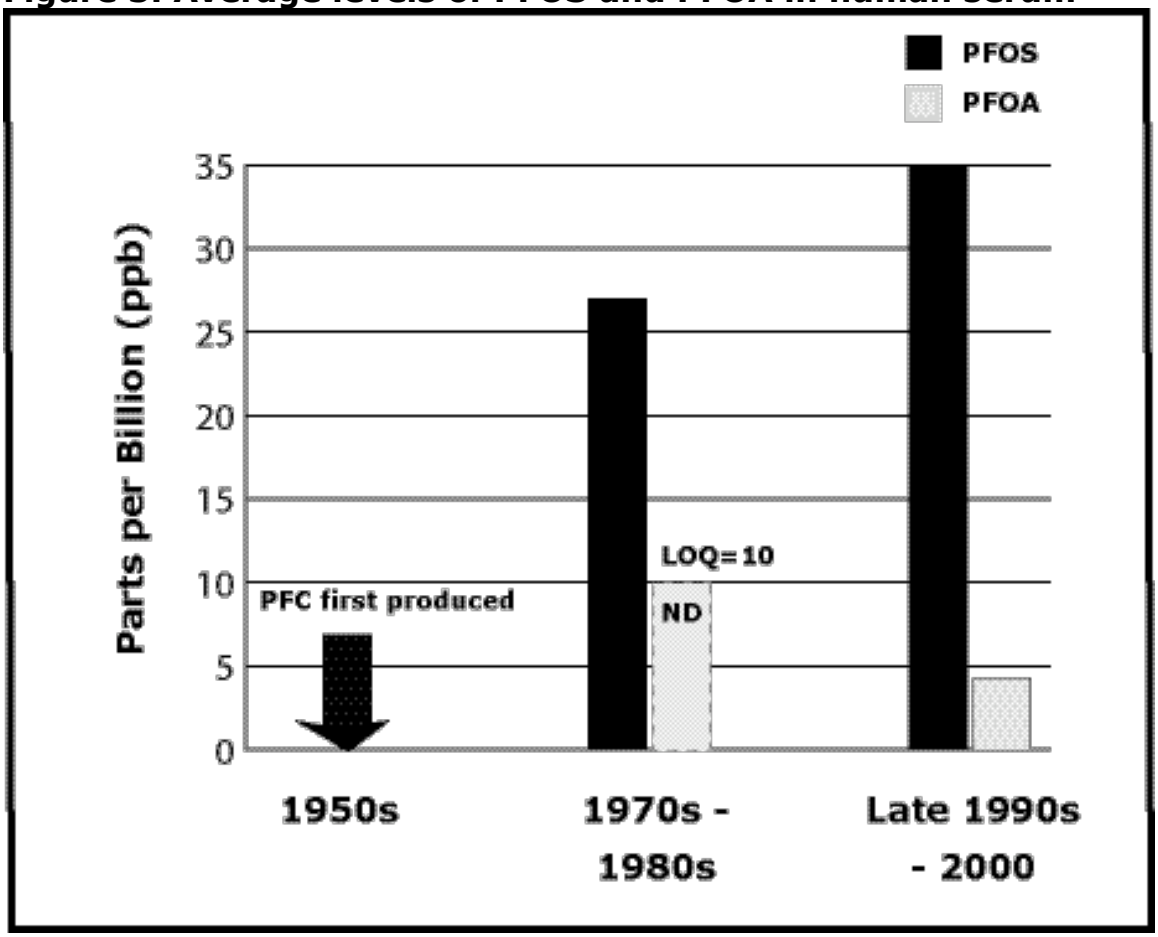
Regardless of the extent to which telomers contribute to current PFOA exposures, the selection of relevant telomers as substitutes for PFOS will result in increasing PFOA exposures for the general population.

Current PFOA body burdens could also stem from water, food, or air contaminated with PFOA. PFOA has been detected in public water supplies (3M 2001c), and in various foods in a market basket survey, including ground beef, green beans, apples, and bread (3M 2001d). The selection of PFOA and its telomer precursors as PFOS substitutes will likely increase the levels and extent of PFOA contamination in public drinking water supplies, food, and air as greater amounts of PFOA and its precursors are emitted to the environment from manufacturing facilities and consumer products.

The potential for exposure to PFCs is persisting

PFCs have been detected in human blood samples dating back to 1957, and in every recent sample tested from nearly 3000 people in the US, including blood samples from 599 children, 238 elderly Washington residents, and approximately 2000 blood bank donors. Human body burdens of PFOS have increased over the past 50 years (Figure 3) and are now readily detected in all segments of the US population. Certain PFCs are detected in higher levels in children than in adults.

Figure 3. Average levels of PFOS and PFOA in human serum



* Levels shown represent the average of the arithmetic mean serum levels derived in the following studies: PFOS = 1970s to 1980s (MRFIT data 1976, 1980), 1990s-2000 (Intergen, Sigma, US blood banks 1998 and US Commercial sources 1999); PFOA = 1990s-2000 (US Commercial sources 1999, US American Red Cross 2000). See Table 2 for details.

Human exposures to PFCs through consumer products are expected to persist and increase. Use of PFCs and other organic fluorinated compounds have increased during the past decade. The public record

contains no evidence that the trend of increasing PFC use would be expected to change.

Human exposures through routes dominated by environmental contamination will persist indefinitely - the ultimate degradates and metabolites of PFCs are not known to further degrade or metabolize, and are characterized by theoretically infinite environmental persistence.

Levels of PFCs in non-worker populations. Organic fluorinated compounds have been detected in the general population for at least the past 45 years (3M 1999b) (Table 2 and 4). A 1998 analysis of historical blood samples conducted by 3M indicates that PFOS was not detected in samples collected from 1948 to 1951, but was found in samples stored since 1957 (Table 2). PFOS was first produced in the early 1950s. Studies of PFOS in blood samples collected during the 1990s show that average levels range from 33 to 52.3 ppb, although concentrations as high as 1656 ppb have been detected most recently (Table 2).

The first report of PFOA in the general population was in 1976 (Guy, et al. 1976), a finding that prompted 3M and DuPont to begin conducting worker biomonitoring studies. 3M did not detect PFOA in a 1998 analysis of archived blood samples collected between1948 and 1951 (PFOA was first produced in the early 1950s), although the detection limit was higher than even current levels of serum PFOA (Figure 3). Analysis of non-worker samples collected during the 1990s using a more sensitive analytical technique found that the median PFOA concentrations ranged from 4.2 to 5.6 ppb (Tables 3) (3M 1999b, US EPA 2002b). The highest non-worker concentrations of PFOA detected thus far occur in children (Table 4).

Body burdens of other PFOS-related compounds (PFHS, M570 and M566) are highest in children (Tables 5-7). 3M attributes these findings to different exposure scenarios rather than metabolic differences between children and adults (Olsen, et al. 2002). PFHS (like PFOA) is not a precursor, metabolite or residual of PFOS; it is a used in fire fighting foams and post-market carpet treatment applications. M570 is a PFOS-precursor chemical and a metabolite of compounds used in Scotchgard products designed for carpet and textile surface treatments. Children may have higher body burdens of these PFHS and M570 because they have more contact with the carpet compared to adults (Olsen, et al. 2002). M566 is not associated with any one type of consumer product (Olsen, et al. 2002).

PFCs are persistent in the human body

Human half-lives have been estimated for PFOS, PFOA, and PFHS. All three chemicals have half-lives measured in years. Through ongoing monitoring of a handful of occupationally exposed retired workers, 3M has most recently estimated a human half-life of 8.7 years for PFOS, and 4.4 years for PFOA (Burris, et al. 2002). The estimated human half-lives for both these compounds have increased as 3M has tracked workers more thoroughly (Burris, et al. 2000, Olsen, et al. 1999). 3M has been unable to estimate a study-wide half-life for perflurohexane sulfonate (PFHS) because levels of PFHS have increased in three of nine participating retired workers. Exclusion of these 3 subjects resulted in an estimated half-life range of 2.9 – 30.1 years (Burris, et al. 2002).

Rat studies underestimate the elimination of PFOS, PFOA, and PFHS (OECD 2002, US EPA 2002b). For example, virtually all PFHS in the liver of treated rats was eliminated during a 28-day recovery period (3M 1999a); current human half-life estimates range up to 30.1 years. The half-life of PFOS is estimated as greater than 89 days in rats, 220 days in monkeys, and 8.7 years in humans. The half-life of PFOA in male rats (who eliminate PFOA slower than female rats) is 5 to 7 days (US EPA 2002b), and in humans is 4.4 years.

Recently, 3M conducted a 28-day oral toxicity study in rats followed by a 28-day recover period for a fluorinated telomer alcohol and acrylate. 3M found that certain perfluorinated metabolites of these compounds (referred to as M513 and M613) did not decrease in rat liver during the recovery time, suggesting that these chemicals may also persist in humans for long-periods of time (3M 1999a).

PFCs in the food chain indicate long-term exposure potential

Both market basket studies and studies of wildlife around the world indicate that the food chain may be broadly contaminated with PFCs. In food purchased from supermarkets in six cities, laboratory analyses detected PFCs in six of 11 food types tested. Analyses showed PFOS in 22% (4/18) of milk samples and PFOS or PFOA in 17% (3/18) of ground beef samples. PFOA was also found in green beans, apples, and bread (3M 2001d).

In a series of studies conducted primarily over the past five years, scientists have detected PFCs in at least 55 species of vertebrates in 13 countries and three continents. These species include mammals such as whales and polar bears; reptiles such as turtles; fish, including

brown trout, Chinook salmon, bluefin tuna and swordfish; and various fish-eating water birds from the bald eagle to the common loon (Giesy and Kannan 2002a, Kannan, et al. 2002d).

PFOS has been detected in wildlife at concentrations above average levels detected in occupationally exposed plant workers. For example, four Caspian tern eggs in Michigan were observed to have an average whole egg concentration of 2605 ng/g (Giesy and Kannan 2001a), and nine minks in South Carolina were observed to have an average liver concentration of 2085 ng/g (Giesy and Kannan 2001b), while blood concentrations of five cell operators in a fluorochemical manufacturing 3M plant in Decatur, Alabama averaged 1320 ng/mL in 2000.

PFOS has been detected in remote areas far from manufacturing facilities and consumer applications. It has been detected in Alaskan polar bears (detected in 17 of 17 tested polar bears, average liver concentration = 350 ng/g) (Giesy and Kannan 2001c), midwestern bald eagle nestlings (in 33 nestlings all under 70 days old the average blood plasma concentration was 330 ng/mL) (Giesy and Kannan 2001a), a great egret from Swan Lake National Wildlife Refuge in Sumner, Missouri (liver concentration = 171 ng/g) (Giesy and Kannan 2001c), bottlenose dolphins from the Adriatic Sea off the coast of Riccione, Italy (detected in 3 of 3 bottlenose dolphins, average blood concentration = 143 ng/mL) (Giesy and Kannan 2001c) and Laysan albatrosses from Sand Island, a wildlife refuge in Midway Atoll (detected in 6 of 6 albatrosses, average blood concentration = 16 ng/mL) (Giesy and Kannan 2001a).

PFOA and perfluoroctanesulfonamide (FOSA) have also been detected in species across the globe. PFOA has been detected in double crested cormorant eggs from Lake Winnipeg in Manitoba Canada (average yolk concentrations of 3 eggs = 162 ng/g) (Giesy and Kannan 2001a), and in cormorants in Japan (detected in 12 of 12 cormorants, average liver concentration = 153 ng/g) (Giesy and Kannan 2001a). Off of the Italian coast, FOSA has been detected in a Delphinus whale (liver concentration = 878 ng/g) (Giesy and Kannan 2001c), and in swordfish (detected in 7 of 7 swordfish, average blood concentration = 7 ng/mL) (Giesy and Kannan 2001d).

The widespread distribution of PFCs in wildlife suggests that the food chain has been contaminated through diffuse, broad transport of PFCs on a near global scale and provides more evidence that human exposures are expected to persist regardless of current production volumes.

(2) Seriousness of health effects known or suspected to result from exposure to the chemical (for example, cancer, birth defects, or other serious health effects).

In laboratory animals, the PFCs cause low dose mortality and significant toxicity to many organ systems and metabolic pathways. For example, both PFOS and PFOA cause liver, mammary gland and pancreatic tumors. PFOS also causes thyroid tumors while PFOA causes testicular tumors. Non-tumor effects are seen in many other tissues. In addition, available data suggests young animals are more sensitive to PFCs than adults. Not only do PFOS and PFOA cause death in offspring at doses that don't affect parental mortality, but the PFOS has been found to cause hypothyroidism in young rats – at the lowest dose tested. Congenital hypothyroidism is a significant risk factor for impaired brain development.

Laboratory animal findings

Mortality. PFCs can cause mortality in laboratory animals at much lower doses than most other industrial chemicals. For example, PFOS causes significant mortality in adult monkeys exposed to 0.75 mg/kg/d for up to 26 weeks (OECD 2002). A 4.5 mg/kg/d dose of PFOS results in 100% mortality in monkeys within 7 weeks (OECD 2002). Exposure to a 3 mg/kg/d dose of PFOA for up to 26 weeks may also cause mortality in monkeys (US EPA 2002b). By way of comparison, monkey can survive exposure to 20 mg/kg/d of DDT for 130 months (Takayama, et al. 1999).

PFOS and PFOA are more toxic to animals exposed *in utero* than to adult animals because they cause death in developmentally exposed animals at doses that do not cause parental mortality (OECD 2002, US EPA 2002b).

Tumors. Both PFOS and PFOA have been shown to cause tumors of the liver, mammary gland and pancreas in rats (3M 2000a, OECD 2002, US EPA 2002a). The pancreatic tumors caused by PFOS were islet cell carcinomas (3M 2000a), while PFOA causes pancreatic acinar cell adenomas (US EPA 2002a). In addition, PFOS also causes thyroid follicular cell adenomas (3M 2000a, OECD 2002) and PFOA causes testicular (Leydig cell) tumors (US EPA 2002a).

Target organs. The highest concentrations of PFCs are found in blood and liver tissue. Thus, it is not surprising that PFCs cause significant

liver toxicity (Butenhoff, et al. 2002, OECD 2002, Pastoor, et al. 1987, US EPA 2002b). PFOS and PFOA also cause altered organ weight and/or histopathology in many non-liver tissues, including the brain, thyroid, adrenal, kidney, spleen, heart, pituitary, salivary gland, ovary, testes, prostate, pancreas, stomach, thymus, bone marrow, lymph nodes and bile duct (OECD 2002, US EPA 2002a)(Table 8).

Laboratory animal studies that show that the liver, thyroid, kidney, and immune system are common targets of many heavily fluorinated compounds (3M 1999a, DuPont 2002a, Gutshall, et al. 1989, Langley and Pilcher 1985, Van Rafelghem, et al. 1987, Van Rafelghem, et al. 1987). Studies have shown each of these organs and systems to be targets of multiple PFCs:

- Liver - PFOS, PFOA, PHDA, PFHS, telomer BA, telomer ethoxylate, telomer urethane polymer
- Thyroid - PFOS, PFOA, PFDA, telomer BA, telomer ethoxylate, telomer urethane polymer
- Kidney - PFOS, PFOA, telomer BA, telomer ethoxylate
- Immune System - PFOS, PFOA, telomer ethoxylate

Although the liver is considered a primary target organ for PFOS and PFOA, several studies have detected lower dose effects in other tissues. For example, ovarian tubular hyperplasia occurred at a dose of PFOA (1.6 mg/kg/d; the lowest dose tested) that did not cause liver toxicity (US EPA 2002a). Similarly, PFOS caused mammary gland tumors at 0.5 ppm (also the lowest concentration tested), a dose that did not cause liver toxicity to female rats (OECD 2002).

Endocrine and lipid metabolic toxicity. PFOA, PFOS and the fluorinated telomer alcohols impact various endocrine systems and lipid metabolism.

Thyroid toxicity. The PFCs that have been tested most thoroughly for thyroid hormone effects, PFOS and PFDA, have been found to cause hypothyroidism (3M 2001b, Gutshall, et al. 1989, Harris, et al. 1989, Langley and Pilcher 1985, US EPA 2002a, Van Rafelghem, et al. 1987). PFOS caused hypothyroidism in neonatal rats at the lowest maternal dose tested (3M 2001b). To date, this finding of hypothyroidism in young rats is the one of the lowest dose effects of PFOS known. Developmental hypothyroidism is a well-characterized risk factor for abnormal neural development and mental retardation. Failure of the fetus to produce sufficient thyroid hormone (congenital hypothyroidism) results in cretinism – a condition characterized by

permanent physical and intellectual impairment. Effects include failure to grow, delayed skeletal development, slow metabolism, decreased psychomotor function, lethargy, severe mental retardation, and hearing loss.

Although children treated for congenital hypothyroidism (via administration of thyroid hormone) fare better than untreated children, treated children still appear to have intellectual and motor impairment (reading comprehension and arithmetic skills, balance, extremity coordination, fine motor skills, quality of movement and head movement are all impaired) compared to euthyroid (normal) children (Bargagna, et al. 1997, Bargagna, et al. 1999, Bargagna, et al. 2000, Rovet and Ehrlich 2000). These effects are not surprising given the critical role thyroid hormones have on late stage brain differentiation, including effects on synaptogenesis, axogenesis, dendritic arborization, myelination, and neuronal migration.

As discussed above, PFOS causes thyroid follicular cell adenomas. Many chemicals that cause hypothyroidism have been shown to cause histopathological effects in follicular cells. The state of hypothyroidism leads to a similar trajectory of thyroid pathology that includes follicular cell hyperplasia, hypertrophy, adenoma, and carcinoma. Decreased levels of thyroid hormones, thyroxin (T4) and triiodothyronine (T3) cause increased production of thyroid stimulating hormone (TSH). In turn, increased TSH signals the thyroid gland to produce more T4 and T3, causing thyroid follicular cells to increase in both size (hypertrophy) and number (hyperplasia) (Hill, et al. 1998, Hurley 1998).

Studies with sufficient statistical power to detect changes in thyroid hormone levels have not been conducted for PFOA. However, a small sample size monkey study (4-6 males per sex) did find a trend towards decreased triiodothyronine (T3) and thyroxin (T4) (US EPA 2002a, Environ 2002). In rat studies, non-statistically significant increases in thyroid C-cell hyperplasia and adenomas have been observed (US EPA 2002a). The thyroid C-cells, which do not participate in iodine metabolism, produce calcitonin. The thyroid gland does not appear to have been studied in a recently conducted multi-generation study for PFOA (York 2002).

The fluorinated telomer alcohols also affect the thyroid gland. Although detailed study information is claimed as CBI (Confidential Business Information) and redacted from the public record, presentations made by the Telomer Research Group to the US EPA indicate that the thyroid

was a target for all of the fluorinated telomers tested (telomer BA, telomer ethoxylate, telomer urethane polymer) (DuPont 2002a). In addition, PFOA is a metabolic product of telomer 8:2, which is a mixture of telomers (DuPont 2002c).

Concentrations of certain telomer alcohol and acrylate metabolites have been shown to remain at relatively constant levels in individual rat livers during a 28-day recovery period following 28-days of oral exposure (3M 1999a). Other metabolites of the fluorinated telomers have not been fully identified (3M 1999a).

Reproductive hormone levels. PFOS and PFOA have been linked with altered estradiol levels, although the direction of effect differs. In general, PFOS is associated with decreased estradiol in monkeys (OECD 2002) and PFOA causes increased estradiol levels in rats (Biegel, et al. 1995, Biegel, et al. 2001, Cook, et al. 1992, Liu, et al. 1996) (US EPA 2002a). The increased estradiol caused by PFOA may be due to increased liver activity of aromatase, an enzyme that converts testosterone to estradiol (Liu, et al. 1996). Long-term exposure to PFOA also causes decreased serum and testicular testosterone levels (Biegel, et al. 1995, Cook, et al. 1992).

Pancreatic toxicity. Both PFOS and PFOA cause pancreatic toxicity. PFOS causes pancreatic islet cell carcinomas (3M 2000a), while PFOA causes pancreatic acinar cell adenomas (US EPA 2002a). Alterations in pancreatic function can affect insulin and glucose regulation. Although diagnostic tests of glucose regulation (i.e. glucose or insulin tolerance test) have not been conducted, PFOA and PFOS have both been associated with increased glucose levels in monkey and/or rat studies (3M 2001b, OECD 2002, US EPA 2002a). Increased glucose levels have also been found in fetal rats exposed to PFOS *in utero* (3M 2001b).

Lipid metabolism. In adult monkeys and rats, PFOS causes decreased levels of cholesterol (3M 2001b, OECD 2002) and high-density lipoprotein (HDL) or "good" cholesterol (OECD 2002), and increases levels of low-density lipoprotein (LDL) or "bad" cholesterol (3M 2001b). PFOA may be associated with increased cholesterol levels, although this finding was based on a measure from one surviving monkey in a high dose group that caused mortality (US EPA 2002a, US EPA 2002b). PFOA has also been associated with decreased triglyceride levels in monkeys (US EPA 2002a).

Although PFOS causes decreased cholesterol in adult animals, it has the opposite effect on fetus and neonates. In fetal or neonatal rats exposed *in utero*, PFOS causes increased cholesterol, HDL and LDL and decreased triglycerides (3M 2001bb). Maternal cholesterol depletion does not appear to be the cause of the neonatal mortality found at low dose exposures to PFOS (3M 2001b, OECD 2002).

Immunotoxicity. Both PFOS and PFOA cause toxicity to tissues involved in regulating immune response. For PFOS, these effects include depletion of in the number and size of lymphoid follicles in the thymus, bone marrow, spleen, and lymph node. PFOA causes histological effects in the thymus, lymph node, and bone marrow and decreased thymus weight (Yang, et al. 2000, Yang, et al. 2002).

Mode of action. The toxic mechanism of action for PFOS and PFOA are not fully understood. PFOS and PFOA are both uncouplers of oxidative phosphorylation (Keller, et al. 1992, Keller, et al. 1992) and peroxisome proliferators (Berthiaume and Wallace 2002), but it is not known if these modes of action account for all effects caused by these compounds. For example, while peroxisome proliferation is linked to liver and Leydig cell tumors, it has not been clearly linked to mammary gland fibroadenomas and pancreatic tumors. Moreover, several studies for PFOS and PFOA have found liver or Leydig cell toxicity without evidence of peroxisome proliferation. For example, the most recent hazard assessment for PFOS concluded that "there was no evidence of peroxisome proliferation in the livers of treated animals" and thus, the rat "hepatocellular adenomas do not appear to be related to peroxisome proliferation" (OECD 2002). Two recent studies have found that PFOS and PFOA also inhibit gap junctional intercellular communication (GJIC) and cause peroxisome proliferation (Hu, et al. 2002, Upham, et al. 1998).

Increased developmental susceptibility. Rats exposed *in utero* are especially susceptible to effects from PFOS and PFOA exposure. Both compounds cause mortality in young rats at doses that do not cause parental mortality (OECD 2002, US EPA 2002b). PFOS also causes delayed ossification (bone formation), cryptorchidism (undescended testicles), cleft palate, delayed reflex and physical development (pinna unfolding and eye opening) and possible alterations in sex ratio (increased percent male fetuses) (OECD 2002). In addition, PFOS caused congenital hypothyroidism, which would be expected to cause delays of physical growth and impaired brain development (3M 2001b). PFOA causes decreased body weights and delayed sexual

development in both male and female (delayed preputial separation and vaginal opening) rats exposed *in utero* (US EPA 2002b).

In addition to the mortality findings described above, there are other indications that PFOS and PFOA are more toxic to developmentally exposed animals. For example, a NOAEL of 0.1 mg/kg/d was established for F0 generation male rats, but a NOAEL could not be established for adult F1 generation male rats (OECD 2002). PFOA-induced immunotoxicity may also be enhanced when exposure occurs during development. For example, PFOA caused decreased spleen weight in F1 generation male rats at the lowest dose tested (1 mg/kg/d), 30 times lower than the dose of PFOA that caused decreased spleen weight in parental animals (30 mg/kg/d) (York, 2002). Body weight, seminal vesicle weight, thymus weight, and testicular weight were also significantly affected by PFOA at lower doses in adult F1 males compared to F0 males.

Human findings

Several occupational studies have been conducted in 3M plant workers in Decatur, AL; Cottage Grove, MN; and Antwerp, Belgium. Cottage Grove is the primary site of PFOA production in the US, while PFOS has been produced primarily in Decatur and Antwerp. However, most, but not all, 3M perfluorinated production workers have higher serum levels of PFOS and PFOA than the general population (Table 1 and 3). These studies all have significant limitations (such as estimated PFC exposure, small sample size, young cohort age, multiple chemical exposure or differences in study populations) which make drawing conclusions difficult. Nevertheless, exposure to PFOS and/or PFOA has been associated with adverse health findings in 3M workers. Levels of PFOS in some workers, which are as high as 12 ppm, are within the range of PFOS detected in rat serum (4.3 to 7.6 ppm) at the 2-year chronic toxicity/carcinogenicity study Lowest Observed Adverse Effect Levels (LOAEL), which is based on liver toxicity

Mortality/Cancer. Retrospective cohort mortality studies have been conducted at 3M plants in Decatur, AL and Cottage Grove, MN. In these studies, serum levels of fluorochemicals were not measured. Instead, exposure was estimated based on job function. Cause of death was determined via death certificates. Workers in high PFOS exposure occupations at 3M's Decatur, AL plant were found to be more likely to die from bladder cancer when compared to the general population of Alabama (standardized mortality ratios or SMR = 12.77, 95% CI = 2.63 – 37.35). Other cancers that had SMRs greater than 1,

although not statistically significant, were cancer of the esophagus, liver, breast, urinary organs and skin.

Several SMRs above 1 were found in Cottage Grove workers (based on Minnesota mortality rates) in definite and probably PFOA exposure categories. Elevated SMRs include cerebrovascular disease, cancers of the large intestine, pancreas, prostate, skin, testis and other male genital organs. In addition, 3M workers at the Cottage Grove, MN plant were more likely to die from bladder cancer, regardless of job function, than the general population (Alexander 2001b, Alexander 2001c).

Episodes of care. An "episode of care" study was conducted at the Decatur, AL plant to assess the relationship between high fluorochemical exposure and health care service sought from the onset of a health condition until resolution or solution of the condition. In workers with the highest and longest exposure to fluorochemicals, increased relative risk ratio for each episode of care (RREpC) was observed for male reproductive tract cancers, gastrointestinal tract neoplasms (especially benign colonic polyps), disorders of the biliary tract and pancreas, cystitis and lower urinary tract infections. Additionally, Decatur workers, regardless of exposure category, had an elevated RREpC for all cancers, and this risk ratio was greatest for workers with the highest and longest exposure to fluorochemicals.

Clinical chemistry/ hormone/hematology findings. A cross-sectional study of 3M workers at the Decatur, AL and Antwerp, Belgium plants was conducted in 2000 to determine whether PFOS or PFOA were associated with hematology, clinical chemistries or hormone measurements in a group of volunteer employees. The data were analyzed by multivariable regression analysis, which included: production job (yes or no), plant, age, body mass index (BMI), cigarettes per day, drinks per day and years worked at the plant. In addition, for PFOS, employees were divided into quartiles based on serum PFOS levels. These data were also analyzed as part of a longitudinal study that included medical surveillance data from 1994/95, 1997 and 2000. Only 41 workers participated in all 3 surveillance periods.

In the cross-sectional study, higher serum PFOA and PFOS levels were significantly associated with increased cholesterol and triglycerides (US EPA 2002a). The positive association with PFOA and triglycerides remained even after both serum PFOA and PFOS levels were included in the analysis. Likewise, PFOA was negatively associated with high density lipoprotein (HDL) or "good" cholesterol even when PFOS levels

were accounted for. In the longitudinal study, PFOA was positively associated with serum cholesterol and triglycerides in the Antwerp employees. These associations were strongest in the 21 Antwerp employees who participated in all 3 study periods. PFOS and PFOA were also both positively associated with triiodothyronine (T3); and male employees in the highest PFOS exposure group had significantly decreased thyroid hormone binding ratio, which is a measure of T3 uptake, than those in the lowest PFOS quartile. Employees in the highest serum PFOS quartile also had significantly higher triglyceride, bilirubin, alkaline phosphatase, and alanine aminotransferase (ALT) values. In addition, a greater percentage of male workers in the Decatur plant in the highest PFOS quartile had liver enzyme levels above the reference range.

Analysis of cross-sectional data from Cottage Grove workers collected in 1993 and 1995 found that workers in the highest exposure PFOA category (> 30 ppm) had 10% higher estradiol levels than other PFOA employee groups. This effect was not statistically significant, which could be due to the small sample size in the high exposure group (only 4 in 1993 and 5 in 1995) (Olsen, et al. 1998). PFOA has been shown to increase estradiol in animal studies (Biegel, et al. 1995).

Elevated values of liver enzymes in DuPont workers exposed to PFOA have also been described in DuPont internal correspondence made public via legal discovery. DuPont began assessing potential worker effect in the 1970's after 3M discovered PFOA in the blood of their workers. DuPont found that "minor elevations of many blood tests did occur in larger-than-anticipated numbers ……one of the liver function tests (SGOT) is most frequently elevated in the operator [PFOA exposed] group" (internal DuPont correspondence from W.A. Bower) (Bilott 1978).

(3) Proportion of the US population likely to be exposed to levels of chemicals of known or potential health significance.

The calculations presented in this section show that the occurrence of both PFOS and PFOA in human serum exceeds plausible reference concentrations ranges derived from animal studies (Figure 2). A comparison of PFOS and PFOA levels in the general population, relative to reference concentrations derived from rat serum and dosing levels at the most sensitive endpoints, shows the following:

- More than half of the children and adults tested during the past decade showed PFOS serum levels higher than an upperbound

reference concentration (derived by applying a composite uncertainty factor of 300 to a rat serum level at the No Observed Adverse Effect Level (NOAEL) based on liver toxicity). The estimated 95th percentile exposure for children is nearly four times the upperbound reference concentration.

- A one-year-old child weighing 10 kilograms could exceed a reasonable reference dose for PFOS through a single exposure route – a pint of milk, consumed each day (Figure 2).

- PFOA levels in the blood of more than five percent of children and adults tested fall in the range of a plausible reference concentration. The maximum level detected among samples from 599 children was 1.5 times an upperbound reference concentration (derived by applying a composite uncertainty factor of 3000 to a rat serum level at the Lowest Observed Adverse Effect Level (LOAEL) associated with altered liver, kidney, spleen and seminal vesicle weight).

<u>Comparison of human and rat serum levels of PFOS and PFOA</u>

The US EPA has not has yet established a reference dose (RfD) or reference concentration (RfC) for PFOS or PFOA, but a sufficient number of studies are available from which to estimate a potential RfD. The analysis that we outline below is not meant to portray a definitive risk assessment for PFOS or PFOA, but is meant to put current exposure levels in context with a plausible range for a reference dose or concentration.

Both of these chemicals are animal carcinogens and also causes non-cancer effects, and it is unclear which type of effect (cancer or non-cancer) will ultimately drive risk assessment. For our analysis, we use the NOAEL approach and selection of uncertainty factors that we believe is not likely to underestimate the RfD that is ultimately calculated for PFOS and PFOA (Table 9).

The study we use to derive a RfD for PFOS is a rat chronic toxicity/carcinogenicity study, the study which tested the lowest doses of PFOS compared to all other available studies. The lowest dietary concentration of PFOS tested in this study was 0.5 ppm, or approximately 0.025 mg/kg/d assuming that a rat ingests 5% of its body weight per day. At this dose, a statistically significant increase in mammary fibroadenomas was observed. In addition, statistically

significant increases in cystic hepatocellular degeneration were observed in males at all doses.

With respect to non-tumor effects, it is unclear whether this dose is considered to be a LOAEL (Lowest Observed Adverse Effect Level) or a NOAEL (No Observed Adverse Effect Level); it is referred to as both in the most recent OECD hazard assessment for PFOS. The summary and conclusion section of the assessment states that "In males, the LOAEL was 0.5 ppm, and a NOAEL was not established" (p. 7). Later in the draft, the liver lesions were attributed to "old age of the animals and is not considered to be treatment-related" (p. 335). However, we note that the lesions were significantly increased compared to control animals. Moreover, the control levels had background serum levels of PFOS that ranged from 24.9 to 2670 ppb, depending on week of assessment and sex. In fact, high levels of PFOS were detected in control animals in all the studies that measured serum and liver levels of PFOS.

We present a range for a plausible RfD based on the 0.5 ppm concentration, considered first as a LOAEL and then as a NOAEL. Details of specific uncertainty factors assumed and assumptions made are presented in Table 9. Comparison of estimated rat serum levels at the RfD and human serum levels shows that the majority of people in the US do not have an adequate margin of exposure for PFOS. Serum levels in workers overlap with rat serum levels at an unambiguous LOAEL (2 ppm).

The study we use to derive a RfD for PFOA is a rat multigenerational study. The lowest dose tested in this study, 1 mg/kg/d, has unambiguously been interpreted as a LOAEL. Significant changes in liver, kidney, spleen, and seminal vesicle weight were observed in adult F1 generation male rats. Again, we note that control animals in this study – as in other studies – have significant background levels of PFOA. We estimated a RfD of 0.333 µg/kg/mg for PFOA by dividing 1 mg/kg/d LOAEL by 3000. This incorporates a 10X factor to account for a lack of a NOAEL for both the reproduction and chronic toxicity/carcinogenicity studies. Details of specific uncertainty factors assumed and assumptions made are presented in Table 9.

To estimate animal serum data at the PFOA RfD, serum levels from a 26-week monkey study were used because these data were not presented for the rat multigenerational study. The monkey serum data were then divided 3000 to estimated serum levels at the RfD of 0.333 µg/kg/mg (Table 9). Monkey serum levels may be higher than rat

serum levels for a given dosing level, since PFC clearance times in monkeys appear to be higher than in rats. In this respect, our derived reference concentrations may be unconservative.

PFOS and PFOA in the diet

3M recently sponsored a study that measured levels of PFOS and PFOA found in various food products. In food purchased from supermarkets in six cities, laboratory analyses detected PFCs in six of 11 food types tested. Analyses showed PFOS in 22% (4/18) of milk samples and PFOS or PFOA in 17% (3/18) of ground beef samples. PFOA was also found in green beans, apples, and bread (3M 2001d). PFOS and PFOA were not detected above the limit of quantification in pork, chicken, eggs, hot dogs, or catfish.

PFOS. Based on a RfD for PFOS of 0.025 μg/kg/d (Table 9), a small child could exceed the "safe" daily dose of PFOS by simply ingesting one pint of milk containing PFOS at the average level found in four contaminated samples tested.

$$424 \text{ g of milk} \times \frac{0.681 \text{ g of PFOS}}{1 \times 10^{9} \text{ g milk}} = 2.89 \times 10^{-7} \text{ g } (0.289 \text{ μg}) \text{ PFOS per pint of milk}$$

$$\frac{0.289 \text{ μg PFOS}}{10 \text{ kg child}} = 0.029 \text{ μg/kg}$$

- 1 pint of milk = 424 grams milk
- 0.681 ppb = the average amount of PFOS found in contaminated milk (0.573, 0.605, 0.693, 0.852)

Thus, one pint of contaminated milk could have 0.289 μg of PFOS. If a 10 kg child were to ingest this pint of milk, the dose of PFOS to that child would be 0.029 μg/kg, exceeding a RfD of 0.025 μg/kg/d. This analysis does not account for other exposure to PFOS that are likely to occur due to the persistence of this compound and from continued exposure to consumer products still in existence that were treated with the old 3M formulations of PFOS-related compounds (such as carpet and upholstery).

PFOA. For PFOA, ingestion any one food item would not be sufficient to exceed our estimated RfD, but PFOA exposure from a 100g apple could account for about 5 percent of a daily dose equivalent to the reference dose:

$$100 \text{ g apple} \times \frac{1.74 \text{ g of PFOA}}{1 \times 10^{9} \text{ g apple}} = 1.74 \times 10^{-7} \text{ g } (0.174 \text{ μg}) \text{ PFOA per apple}$$

$\frac{0.174\ \mu g\ PFOS}{15\ kg\ child} = 0.012\ \mu g/kg$

- 1.74 ppb = the average amount of PFOA found in apples (2.35, 1.13 ppb; a value of 14.7 ppb was not included because it was considered by 3M's contract lab to be suspect)

PFOA is also found in drinking water in certain cities, and is a breakdown product of certain telomer alcohols used in consumer products. PFOA exposure routes are not currently well understood - the EPA recently stated that "blood sample analysis data indicate low level exposures to the general population that are unexplained at this time" (US EPA 2002f).

(4) Need to assess the efficacy of public health actions to reduce exposure to a chemical in the US population or a large component of the US population (for example, among children, women of childbearing age, the elderly).

A public health action was initiated two years ago to reduce exposures to PFOS in the US population. Under the terms of a phaseout agreement submitted to EPA, 3M discontinued the manufacture of 13 key PFOS-related chemicals by December 31, 2000 (US EPA 2002d).

The phaseout was triggered by company tests from the late 1990s that showed the widespread presence of a pertinent biomarker in human serum (PFOS, or perfluorooctane sulfonate), near global environmental contamination of wildlife by PFOS, and low-dose mortality of adult monkeys dosed with PFOS and neonate rats exposed to PFOS *in utero*. Current levels of PFOS in blood exceed acceptable margins of exposure for the majority of the population tested.

Biomonitoring will be a critical tool to assessing the efficacy of 3M's PFOS phaseout in reducing exposures in the general population. Many factors, described below, contribute to uncertainty in the magnitude of exposure reductions that can be achieved by the phaseout.

New sources of PFOS in consumer products may continue to appear on the market. Both Japan and Italy retain the capacity to produce PFOS-related chemicals, although it is unclear if production is occurring (OECD 2002). PFOS products already in home or store shelves will continue to be used for a number of years. Some products containing perfluorinated chemicals are characterized by indefinite shelf-lives.

These factors could delay population-wide reductions in exposures to PFOS from consumer products.

PFOS exposures from environmental contamination could increase in spite of the phaseout. As PFOS-related chemicals are phased out of use, those that are metabolic and degradation precursors of PFOS in the environment should decline in overall mass through time, concomitant with an overall increase of PFOS mass in the environment. The rate at which this transformation will occur is undefined. As precursors are transformed to PFOS through time, the possibility exists for ever-increasing exposures to PFOS through exposure routes driven by environmental contamination (tap water and food, for example), even as exposures to PFOS from consumer products decline.

PFOS has been found in milk, ground beef, and drinking water (3M 2001d, 3M 2001c). The extent of PFOS contamination is so thorough that control animals used in toxicology studies have background levels of PFOS on par with the non-worker human population in the US (OECD 2002), and is only likely to increase with time. For all PFOS-related chemicals in the environment, PFOS will be the ultimate breakdown product, as it is not known to hydrolyze, photolyze, or biodegrade under environmental conditions, and cannot be metabolized in biota.

In addition to assessing changes in PFOS levels among the general population, biomonitoring should also be used to assess the magnitude of increases in exposure to chemicals chosen to replace PFOS in relevant consumer products. Potential replacements include PFOA and telomer alcohols that may break down to PFOA, and PFBS (perfluorobutane sulfonate). Studies available in the public record show that many perfluorinated chemicals have patterns of toxicity similar to those of PFOS. Monitoring PFOS substitutes in the general population will be an important component of showing the efficacy of PFOS phaseout actions in protecting public health.

(5) Existence of an analytical method that can measure the chemical or its metabolite in blood or urine with adequate accuracy, precision, sensitivity, specificity, and speed.

Several peer-reviewed papers or entries into EPA's administrative record AR226 describe analytical techniques for PFCs. The PDF versions of these references are included with submission of these comments.

(6) Incremental analytical cost (in dollars and personnel) to perform the analyses (preference is given to chemicals that can be added readily to existing analytical methods).

We did not attempt to estimate incremental analytical cost for measuring the PFCs and fluorinated telomer alcohols.

Chapter 3: Recommendations for Chemical Groups as Framework for Testing Prioritization, and Justification for Inclusion of Each Group in CDC Biomonitoring Program

We are nominating the chemical class of PFCs as a whole for inclusion in future releases of the Report, but we would also suggest the groupings of ~180 individual PFCs shown in Table 10 as a framework for prioritization. These groups, described below, are based on our present understanding of current margins of exposure where data are available; expected chemical use and exposure patterns; and availability of an analytical method, as evidenced by either the presence of relevant analytical results in the public record, or published methodologies.

In this chapter we summarize the justification for nomination of each grouping of PFCs to the Report, framed around the selection criteria presented in CDC's Federal Register notice of October 7, 2002 (Center for Disease Control 2002). We did not attempt to estimate incremental analytical costs for each group; so that selection criteria is not discussed here.

Group 1: Two perfluorinated chemicals for which current body burdens of the general population and expected future use and exposure patterns raise human health concerns (PFOS and PFOA).

Uses – PFOS is a breakdown product of certain perfluorinated chemicals used for fifty years, through 2001, in paper, food wraps, carpet, clothing, and furniture surface treatments as part of the 3M company's Scotchgard™ and Scotchban™ product lines. PFOS-related compounds also have performance chemical uses in industry (3M 1999c). PFOS itself was used as an ingredient in aqueous fire-fighting foams (AFFF) (OECD 2002).

PFOA is used in the manufacture of Teflon® and is a breakdown product of certain fluorinated telomer alcohols (DuPont, 2002c), which are used in carpet and upholstery protection, glass or other hard surface cleaners, floor polishes, and packaging for greasy foods. Asahi Glass, Atofina, Clariant, Daikin and DuPont are member companies of the Telomer Research Program (TRP) (Telomer Research Program 2000).

Potential for human exposures to change or persist – PFOS and PFOA have no known environmental or metabolic breakdown mechanism under environmental conditions.

PFOS was detected in every recent blood sample tested, from more than 3000 people (3M 1999b, Olsen, et al. 2002, Olsen, et al. 2002, Olsen, et al. 2002). PFOS has been phased out of production in the U.S., but its possible continuing manufacture in other countries (such as Japan or Italy) (OECD 2002), extreme environmental persistence, and continuing long-range transport raises questions on the magnitude of exposure reductions by 3M's recent phaseout.

PFOA was detected recently in greater than 99 percent of adult and pediatric blood samples (Olsen, et al. 2002, Olsen, et al. 2002, Olsen, et al. 2002). PFOA exposures are expected to rise as PFOA-related chemicals replace PFOS chemicals in consumer products (US EPA 2002b)(p. 11-12).

Known or suspected health effects – In laboratory animals, PFOS and PFOA cause liver, mammary gland and pancreatic tumors. PFOS also causes thyroid tumors, and PFOA causes testicular tumors. PFOS and PFOA also cause low dose mortality, immune system toxicity and altered lipid metabolism. Many of the lowest dose effects are non-cancer effects of the immune and endocrine systems. In addition, available data suggests young animals are more sensitive to PFCs than adults. The most described mode of actions for PFOS and PFOA are uncoupling of oxidative phosphorylation, inhibition of gap junctional intercellular communication (GJIC) and peroxisome proliferation (Hu, et al. 2002, OECD 2002, Starkov and Wallace 2002, Upham, et al. 1998, US EPA 2002b).

Proportion of the population likely to be exposed to levels of chemicals of known or potential health significance – PFOS serum levels in more than half of the 599 children (Olsen, et al. 2002) and 883 adults (Olsen, et al. 2002, Olsen, et al. 2002) tested exceed a reasonable upperbound estimate for reference concentration (Figure 2). PFOA serum levels in more than five percent of 599 children (Olsen, et al. 2002) and 645 adults (Olsen, et al. 2002) tested exceed estimated reference concentration. Maximum detected levels exceed a reasonable upperbound estimate for reference concentration (Figure 2).

Need to assess the efficacy of public health actions to reduce exposure to a chemical in the U.S. population - This factor is discussed on pages 25 to 26.

Analytical method available? Published methodology is available for both chemicals [Hansen 2001; Attachment A].

Group 2 (single chemical): A four-carbon homologue to PFOS that represents a PFOS replacement in 3M's new Scotchgard formulations, perfluorobutane sulfonate (PFBS).

Uses – New replacement for PFOS chemistries in Scotchgard products.

Potential for human exposures to change or persist – The public record indicates that PFBS-related chemistries will now replace PFOS chemistries in 3M's Scotchgard formulations, indicating the potential for significant new PFBS exposures (3M 2002b). 3M is also planning to use potassium perfluorobutane sulfonate (KBPS) in a new flame retardant to replace the brominated flame retardants used in clear polycarbonate plastic (Mullen 2001). The clearance time for PFBS from the rat liver following 28-days of exposure is 14 days, but rats have been shown to be poor indicators of persistence in humans – the six-carbon PFOS homologue known as perfluorohexane sulfonate (PFHS) was also almost entirely eliminated from the rat liver in this same study (3M 1999a), but has recently been estimated to have a half-life on the order of years in humans (3M 2002a).

Known or suspected health effects - Limited Confidential Business Information (CBI) regarding PFBS toxicity (28-day toxicity) and liver elimination was inadvertently made public in an AR226 entry (3M 1999a, 3M 2000b).

This study shows that PFBS, like PFOS, caused decreased total protein, globulin, aspartate aminotransferase activity (in males) and prothrombin time (in females). The effect on prothrombin was still present 2 weeks after the end of dosing. Only one dose was tested, so a NOAEL was not determined (3M 1999a). This same 28-day study was not adequate to describe PFOS toxicity, which was used as a positive control. In this study, PFOS only caused decreased total cholesterol, alterations in hematology measures (like those described for PFBS) and liver toxicity. Effects on other known target tissues of PFOS were not observed. Clearly, a 28-day toxicity study is not adequate to fully characterize PFC toxicity (3M 1999a).

Although the majority of PHBS in the liver at the end of the dose period was eliminated within 28 days in the recovery group, rats have been shown to be poor indicators of persistence in humans. Rat elimination data points to potential for long human half-life in that the

pattern of PFBS elimination from rat liver resembles that for PFHS, a chemical which has a half-life on the order of years in humans (3M 1999a, 3M 2000b, 3M 2002a)

Proportion of the population likely to be exposed to levels of chemicals of known or potential health significance - Using PFOS as an indicator, broad exposure to PFBS is expected as it replaces the PFOS-based Scotchgard market. The extent to which these exposures will be mitigated or amplified by differing environmental and metabolic characteristics is unknown.

Analytical method available: Analytical data has been published for rat liver concentration [3M 1999a; Attachment C].

Group 3: Nine perfluorinated chemicals that have been detected in the general population or wildlife, including four that are metabolic precursors of PFOS, two that are homologues of PFOS (six-carbon and ten-carbon chains), and three that are metabolites of fluorinated telomer alcohols and/or telomer acrylates.

Uses – These chemicals are metabolic PFOS-precursors (PFOSAA, M570, M556, PFOSA), PFOS homologues (PFHS, PFDS) or metabolites of telomer alcohols and acrylates (POAA, M463, M513). All of these chemicals are associated with the same surface treatment and paper protection applications described for PFOS and PFOA. Telomer alcohols and acrylates are used product lines that directly compete with the 3M product lines based on PFOS-related chemistry (Scotchgard™, Scotchban™, and Fluorad™) (3M 1999c). Asahi Glass, Atofina, Clariant, Daikin and DuPont are member companies of the Telomer Research Program (TRP) (Telomer Research Program 2000). More information for each compound is presented in Table 10. So far, through our scrutiny of the public record, we are unable to establish the chemical identity of M463. Hopefully, DuPont or 3M will share that information with CDC.

Potential for human exposures to change or persist – As PFOS is phased out of use, its metabolic precursors in the environment should, theoretically, decline, and the concentrations of PFOS should build up in the environment. The rate at which this transformation will occur is completely undefined. The possibility continues for sustained widespread exposures to PFOS precursors.

Broad exposure to breakdown products of telomer alcohols and acrylates is expected, and may increase depending on the extent to

which it replaces the PFOS-based Scotchgard market. Continued exposure to higher carbon chain PFOS homologues (> 10) may occur, as these chemicals are not covered under 3M's phaseout plan (US EPA 2002c, US EPA 2002d).

Known or suspected health effects – These PFCs have not been as well studied as PFOS or PFOA, but existing data suggests they are likely to cause similar toxicity. For example, PFOS, PFOA, PFOSA, PFOSAA and some of their precursors (N-EtFOSA, N-EtFOSE, and N-EtFOSAA) all inhibit mitochondrial respiration (Starkov and Wallace 2002). In fact, PFOSA is five times more potent than 2,4-dinitrophenol in uncoupling of oxidative phosphorylation; 2,4-DNP is a positive control for uncoupling of oxidative phosphorylation (3M 1998, Starkov and Wallace 2002). PFOSA and PFHA, like PFOS and PFOA, inhibit gap junctional intercellular communication (Hu, et al. 2002, Upham, et al. 1998). Thus, not only is the final breakdown product of these chemicals toxic, but metabolic precursors of PFOS are also toxic.

Structure activity studies suggest that the length of the fluorinated tail and the functional group are important determinants of toxicity. For GJIC, carbon lengths of 7 to 10 were most effective and was not the nature of the functional group (Hu, et al. 2002, Upham, et al. 1998). However, for peroxisome proliferation, the presence of a carboxylic acid moiety does seem to be important (DePierre 2002)) (Ikeda, et al. 1985).

These *in vitro* findings are supported by laboratory animal studies that show that the liver (PFOS, PFOA, PHDA, telomer BA, telomer ethoxylate, telomer urethane polymer), thyroid (PFOS, PFOA, PFDA, telomer BA, telomer ethoxylate, telomer urethane polymer), kidney (PFOS, PFOA, telomer BA, telomer ethoxylate), and immune system (PFOS, PFOA, telomer ethoxylate) are common targets of many heavily fluorinated compounds (DuPont 2002a, Gutshall, et al. 1989, Langley and Pilcher 1985, Van Rafelghem, et al. 1987, Van Rafelghem, et al. 1987). The thyroid effects include hypothyroidism for PFOS and PFDA.

Proportion of the population likely to be exposed to levels of chemicals of known or potential health significance - Data to allow estimation of a reference dose for chemicals in this group is generally not as robust as data for PFOS and PFOA. Critical studies such as the chronic toxicity/carcinogenicity and multigenerational study are not available for the vast majority of these compounds. However, *in vitro* studies show that these compounds have intrinsic toxicity, so it is not the case

that *in vivo* toxicity is necessarily the result of toxic metabolites such as PFOS or PFOA (Starkov and Wallace 2002, Upham, et al. 1998).

Analytical method available? Published methodology is available for all chemicals [Hansen 2002, Olsen 2002a, 3M 1999a, 3M date not specified; Attachments A, B, C, D].

Group 4: Seven telomer alcohol metabolites for which methods have been developed for animal tissue. The majority, if not all of these compounds are homologues of PFOA (referred to by carbon chain lengths as C7, C10, C11, C12, and C14). The names of some of these compounds may be redundant. For example, M563 may represent C11, because the majority of C11 mass is comprised of M563.

Uses – These chemicals are metabolites of telomer alcohols and acrylates, which are used for the same surface treatments and paper protection applications as PFOS-related compounds.

Potential for human exposures to change or persist – Exposures are expected to persist and are likely to increase as industry moves away from PFOS-related chemicals to telomer based mixtures. Many of these chemicals can be detected in fish liver samples (C7, C10, C11, C14) (Mabury 2002, Muir, et al. 2002). In fact, C7 was detected in fish liver at approximately the same concentration as C8 (PFOA) (Muir, et al. 2002). These compounds may also be metabolically inert. For example, C12 concentrations in rat liver did not decrease to any significant extent in a 28-day recovery group (3M 1999a). Even PFOS concentrations decreased to a greater extent in this study. Several telomer alcohols have been detected in the air in Ontario (Martin in press).

Known or suspected health effects – Overall, studies of these chemicals are not available in the public record, but their toxicity is likely to be similar to other PFCs (see health effect discussion for Group 1 and 3). However, PFDA has been studied in some detail and is well-known to cause liver toxicity, altered lipid metabolism and hypothyroidism (Gutshall, et al. 1989, Langley and Pilcher 1985, Van Rafelghem, et al. 1987, Van Rafelghem, et al. 1987, Van Rafelghem, et al. 1988).

Proportion of the population likely to be exposed to levels of chemicals of known or potential health significance – The data required to make this determination are unavailable. Depending on the extent to which these chemicals share target organs and modes of action with PFOS

and PFOA, they will amplify exposure levels in the general population that exceed standard safety margins considering PFOS and PFOA alone. However, there is ample cause for concern given the presence of PFOA homologues detected in wildlife and the similarity of toxic effects associated with PFDA to those of PFOA and PFOS.

Analytical method available? Published methodology is available for all chemicals [3M 1999a, 3M 1999d; Attachments C, E].

Group 5: Three perfluorinated homologues of PFOS and PFOA (the seven- and nine-carbon homologues of PFOS and the nine-carbon homologue of PFOA) which lack analytical data for biota in the public record, but which are used in PFC products or production processes, and for which analytical methods would be analogous to existing methods

Uses – Used in PFC products or production processes (Purdy 2002).

Potential for human exposures to change or persist – No information available in the public record.

Known or suspected health effects – Overall, studies of these chemicals are not available in the public record, but their toxicity is likely to be similar to other PFCs (see health effect discussion for Groups 1 and 3).

Proportion of the population likely to be exposed to levels of chemicals of known or potential health significance – The data required to make this determination are unavailable. Depending on the extent to which these chemicals share target organs and modes of action with PFOS and PFOA, they will amplify exposure levels in the general population that exceed standard safety margins considering PFOS and PFOA alone.

Analytical method available? Analytical methods would be analogous to existing methods (Purdy 2002).

Group 6: Thirteen PFOS-related compounds or mixture that collectively (10) or individually (3) were produced in quantities over a million pounds per year and never tested in the general population. Of these chemicals, information is available in the public record for two – NEtFOSE and MEtFOSE, which are the focus of the discussions below.

Uses – N-EtFOSE-related chemicals were used for paper and packaging protection applications (Scotchban™). Specific uses included food contact applications (plates, food containers, bags, and wraps), as well as non-food contact applications (folding cartons, containers, carbonless forms, and masking papers) (3M 1999c). MeFOSE-related chemicals were used in surface treatment applications such as carpet, apparel, upholstery, leather protection (Scotchgard™) (3M 1999c). Information on uses for the other 11 chemicals is generally unavailable in the public record.

Potential for human exposures to change or persist – Exposures are expected to eventually decline since these chemicals have been phased out of production. However, many consumers are likely still exposed to these chemicals via products purchased before the Scotchgard™ and Scotchban™ lines were reformulated. Other countries retain the capacity to produce these chemicals (such as Italy and Japan) (OECD 2002).

Known or suspected health effects – A recent TSCA 8(e) submission indicates that N-EtFOSE caused a significant trend towards increased incidence of thyroid follicular cell adenoma in a cancer bioassay (3M 2001a).

Proportion of the population likely to be exposed to levels of chemicals of known or potential health significance – There is not enough information available to assess this directly because these chemicals have not been measured in the general population. However, several metabolites of N-EtFOSE (PFOSAA), and MeFOSE (M570) have been found in non-worker populations (Figure 1).

Analytical method available? No information available in the public record.

Group 7: Seventeen perfluorinated compounds identified by the TSCA Interagency Testing Committee (ITC) in their 49th report to the EPA Administrator as possible PFOS replacements. In 1998, these PFCs had production volumes greater than 10,000 pounds, but less than 1 million pounds.

Uses – PFOS was used in surface treatment, paper and package protection and as an industrial performance chemical. Replacements for PFOS would be expected to have these same uses.

Potential for human exposures to change or persist - Prior to 3M's PFOS phaseout, industry produced each of these chemicals in quantities between 10,000 and 1,000,000 pounds per year, indicating a potential for substantial human exposure that may increase for any of these chemicals selected as PFOS replacements.

Known or suspected health effects - No information available in the public record.

Proportion of the population likely to be exposed to levels of chemicals of known or potential health significance - Levels of these chemicals in the general population are unavailable in the public record. Toxicological significance of potential exposures is undefined. Depending on the extent to which these chemicals share target organs and modes of action with PFOS and PFOA, they will amplify exposure levels in the general population that exceed standard safety margins considering PFOS and PFOA alone.

Analytical method available? No information available in the public record.

Group 8: Sixteen perfluorinated compounds that the FDA has approved as indirect food additives.

Uses – Full range of uses is not defined, but PFCs are used as food package coatings for grease repellency (e.g., pizza boxes, butter boxes, microwave popcorn bags, fast food french fry boxes).

Potential for human exposures to change or persist – Estimates of human exposures to all PFC indirect food additives are available from FDA. The popularity of food items associated with food contact uses of PFCs indicates the likelihood of substantial, persistent exposures.

Known or suspected health effects - No information available in the public record.

Proportion of the population likely to be exposed to levels of chemicals of known or potential health significance - Levels of these chemicals in the general population are unavailable in the public record. Toxicological significance of potential exposures is undefined. Depending on the extent to which these chemicals share target organs and modes of action with PFOS and PFOA, they will amplify exposure levels in the general population that exceed standard safety margins considering PFOS and PFOA alone.

Analytical method available? No information available in the public record.

Group 9: Fifty perfluorinated compounds identified by the TSCA Interagency Testing Committee (ITC) in their 46th report to the EPA Administrator. Thirty-eight of the 50 PFCs listed in the ITC report were identified because they satisfied criteria for persistence (ultimate degradation > 2-3 months) and bioconcentration potential (log octanol-water partition coefficient 3-6) and production/importation criteria described by the ITC in its 45th Report (US EPA 2000b). Twelve other PFCs were added from studies submitted to EPA under TSCA's Section 8(e) requirements (notices of substantial risk), because these chemicals are structurally similar the original 38.

Uses – Individual chemical uses are not easily obtained.

Potential for human exposures to change or persist - These chemicals are believed to be persistent and bioaccumulative, indicating the potential for substantial and sustained human exposure, depending on chemical production quantities, uses, disposal practices, and environmental transport properties.

Known or suspected health effects – For several of these chemicals (noted in Table 10) manufacturers have notified the EPA of scientific findings that indicate the potential for substantial risk via a TSCA 8(e) submission.

Proportion of the population likely to be exposed to levels of chemicals of known or potential health significance - Levels of these chemicals in the general population are unavailable in the public record. Toxicological significance of potential exposures is ill-defined. Depending on the extent to which these chemicals share target organs and modes of action with PFOS and PFOA, they will amplify exposure levels in the general population that exceed standard safety margins considering PFOS and PFOA alone.

Analytical method available? No information available in the public record.

Group 10: Approximately 90 compounds related to PFOS chemistries, phased out of production by 3M, and subject to Significant New Use Reporting by EPA.

Uses – Individual chemical uses are not easily obtained.

Potential for human exposures to change or persist - PFOS was detected in every recent blood sample tested, from more than 3000 people. PFOS-related chemicals have been phased out of production in the U.S., but their continued manufacture in other countries, extreme environmental persistence, and apparent capacity for long-range transport raises questions on possibility of exposure reductions.

Known or suspected health effects – The toxicity of some of these chemicals has been discussed previously in this document. However, the majority have not been tested in any detail.

Proportion of the population likely to be exposed to levels of chemicals of known or potential health significance – PFOS serum levels in more than half of 599 children tested exceed a reasonable upperbound estimate for reference concentration (Figure 2). Data to allow estimation of a reference dose for other chemicals in this class is generally not as robust, or not available.

Analytical method available? No information available in the public record for chemicals not already presented in other groups.

Table 1. Occupational PFOS serum levels (OECD 2002)

Occupational exposures		
Plant Location	**Mean (ppm)**	**Range (ppm)**
Cottage Grove Plant, Minnesota 1997 (n = 74) *not the primary location of US PFOS production (AR226-0548; p. 14_)	0.82	0.05 – 6.25
Decatur, Alabama 1995 (n = 90) 1997 (n = 84) 1998 (n = 126) 2000 (n = 263)	 2.44 1.96 1.51 1.32	 0.25 – 12.83 0.10 – 9.93 0.09 – 10.6 0.06 – 10.06
Antwerp, Belgium 1995 (n = 93) 1997 (n = 65) 2000 (n = 258)	 1.93 1.48 0.80 GM = 0.44*	 0.10 – 9.93 0.1 – 4.8 0.04 – 6.24 (0.38 – 0.51)**
Building 236 2000 (n = 45)	 0.182	 <0.037 – 1.036
Sagamihara, Japan (1999) (processing PFOS) n = 32	0.135	0.0475 – 0.628

* GM is geometric mean; ** 95% CI of the geometric mean

Table 2. PFOS serum levels in non-worker populations (OECD 2002, 3M 1999b)

General population exposures		
Source	**Mean (ppb)**	**Range (ppb)**
Korean Was era U.S. military recruits (1948 to 1951) 10 samples with 10 donors per sample [Analyzed in 1998 (3M 1999b)]	Not detected	Not detected
Swedish samples (1957)(n = 10)	2	Not detected - 2
Michigan Breast Cancer Study (1969-71) (n = 5)	33	Not detected - 59
Swedish samples (1971)(n = 10)	1	Not detected - 1
Multiple Risk Factor Intervention Trial (MRFIT) (1976) (6 pooled samples with unknown number of donors per sample)	31	14 - 56
MRFIT samples (1980) (3 pooled samples with unknown number of donors per sample)	23	14 - 41
China samples (Linxian, rural province) (1994) (n = 6)	Not detected	Not detected
MRFIT samples (1985) (n =3)	31	Not detected – 44
China samples (Shandong, rural province) (1984) (n = 6)	Not detected	Not detected
Non-occupational (n = 31) (corporate staff or managers) St. Paul, Minnesota (1998)	47	28 - 96
Non-occupational (1999) (plant management) Sagamihara, Japan (n = 32) Tokyo, Japan (n = 30)	40.3 52.3	31.9 – 56.6 33 – 96.7
Commercial Sources, U.S. (1998) Intergen (n = ~500 donors) Sigma (n = ~200 donors)	44 33	43-44 26 - 45
U.S. Blood Banks (1998) (n = ~340 – 680 donors)	29.7	9 - 56
Other Commercial Sources, U.S. (1999) (n = 35 lots)	35	5 - 85
European Blood Banks (1999) Belgium (6 pooled samples) Netherlands (5 pooled samples) Germany (6 pooled samples)	17 53 37	4.9 – 22.2 39 – 61 32 – 45.6
U.S. Blood Banks (2000) American Red Cross ages 20 – 69 (n = 645)	34.9*	4.3 - 1656
Samples in U.S. children (1995) Pediatric Study ages 2 – 12 from 23 states (n – 599)	37.5*	6.7 - 515
Samples in elderly in Seattle, WA (1999) Cognition Study ages 65 – 96 (n = 238)	31.0*	3.4 - 175

* Geometric Mean

Table 3. Occupational PFOA serum levels (US EPA 2002)

Occupational exposures			
Plant Location	**Mean (ppm)**	**Range (ppm)**	**95% CI**
Cottage Grove Plant, Minnesota 1993 (n = 111) 1995 (n = 80) 1997 (n = 74) *primary US site for PFOA production (AR226-0548; p. 14)	 6.4 6.8 5.0	 0.1 – 81.3 0.0 – 114.1 0.0 – 80.0	Not presented
Decatur, Alabama 1995 (n = 90) 1997 (n = 84) 1998 (n = 126) 2000 (n = 263)	 1.46 1.57 1.54 (GM = 0.90*) 1.78 (GM = 1.13*)	 Not reported Not reported 0.02 – 6.76 0.04 – 12.70	 Not presented Not presented 0.72 – 1.12 0.99 – 1.30
Antwerp, Belgium 1995 (n = 93) 2000 (n = 258)	 1.13 0.84 (GM = 0.33*)	 0.0 – 13.2 0.01 – 7.04	 Not presented 0.27 – 0.40
Building 236 2000 (n = 45)	 0.106 (GM = 0.053*)	 0.008 – 0.668	 0.037 – 0.076

* GM = Geometric Mean

Table 4. PFOA serum levels in non-worker populations (US EPA 2002)

General population exposures			
Source	**Mean (ppb)**	**Range (ppb)**	**95% CI**
Korean Was era U.S. military recruits (1948 to 1951) 10 samples with 10 donors per sample (Analyzed in 1998 (US EPA 1999))	ND (LOD = 10 ppb)	ND (LOD = 10 ppb)	
Swedish samples (1957)(n = 10)	ND (LOD = 10 ppb)	ND (LOD = 10 ppb)	
Michigan Breast Cancer Study (1969-71) (n = 5)	ND (LOD = 10 ppb)	ND (LOD = 10 ppb)	
Swedish samples (1971)(n = 10)	ND (LOD = 10 ppb)	ND (LOD = 10 ppb)	
Blood bank samples from 5 US cities (Guy, et al. 1976) (n = 106 but samples pooled for FOC identification)	Identified; not quantified	Identified; not quantified	
Multiple Risk Factor Intervention Trial (MRFIT) (1976) (6 pooled samples with unknown number of donors per sample)	ND (LOD = 10 ppb)	ND (LOD = 10 ppb)	
MRFIT samples (1980) (3 pooled samples with unknown number of donors per sample)	ND (LOD = 10 ppb)	ND (LOD = 10 ppb)	
China samples (Linxian, rural province) (1994) (n = 6)	ND (LOD = 10 ppb)	ND (LOD = 10 ppb)	
MRFIT samples (1985) (n =3)	ND (LOD = 10 ppb)	ND (LOD = 10 ppb)	
China samples (Shandong, rural province) (1984) (n = 6)	ND (LOD = 10 ppb)	ND (LOD = 10 ppb)	
Non-occupational (n = 31) (corporate staff or managers) St. Paul, Minnesota (1998) **only 4 employees were above the detection limit of 10 ppb)	12.5	Not reported	Not presented
U.S. Blood Banks (1998) (n = ~340 – 680 donors) *** detected in 1/3 of pooled samples, but quantifiable in only 2	17	12 - 22	Not presented
Commercial Sources, U.S. (1999) (n = 35 lots)	3	1 - 13	Not presented
U.S. Blood Banks (2000) American Red Cross ages 20 – 69 (n = 645)	5.6 (GM = 4.6*)	1.9 – 52.3	4.3 – 4.8
Samples in U.S. children (1995) Pediatric Study ages 2 – 12 from 23 states (n – 598)	5.6 (GM = 4.9*)	1.9 – 56.1	4.7 – 5.1
Samples in elderly in Seattle, WA (1999) Cognition Study ages 65 – 96 (n = 238)	GM = 4.2*	1.4 – 16.7	3.9 – 4.5

* GM is geometric mean

Table 5. PFC serum levels in children (samples drawn in 1994-1995, ages 2-12, n = 599) (Olsen 2002a)

Compound	Geometric mean	Average	Median	95th percentile	Range/ < LLOQ(N)**
PFOS ($C_8F_{17}SO_3$-)	37.5 ppb* (95%CI: 36.0 - 39.1) M: 40.1 F: 35.2	43.5 ppb	36.7 ppb	90.2 ppb	6.7 - 515 ppb <4.3 (0)
PFOA ($C_7F_{15}CO_2$-)	4.9 ppb* (95%CI 4.7 – 5.1) M: 5.2 F: 4.7	5.6 ppb	5.1 ppb	10.2 ppb	<LLOQ (1.9) -56.1 ppb <1.9 (5)
PFHS ($C_6F_{13}SO_3$-)	4.5 ppb* (95%CI: 4.1 - 5.1) M: 5.3 F: 3.9	15.0 ppb	3.8 ppb	71.3 ppb	<LLOQ (1.4) - 711.7 ppb <1.4 (92)
PFOSAA [$C_8F_{17}SO_2N(C_2H_5)$-CH_2CO_2-]	3.3 ppb (95%CI 3.1 – 3.6) M: 3.3 F: 3.4	4.4 ppb	3.7 ppb	10.4 ppb	<LLOQ (1.6) - 23.8 ppb <1.6 (67)
M570 [$C_8F_{17}SO_2N(CH_3)$-CH_2CO_2-]	1.9 ppb (95%CI 1.7 – 2.1) M: 2.0 F: 1.8	3.4 ppb	1.8 ppb	12.5 ppb	<LLOQ (1.0) - 48 ppb <1.0 (140)
M556 [$C_8F_{17}SO_2NH$-CH_2CO_2-]	2.4 ppb (95%CI 2.2 – 2.5)	***	***	***	<LLOQ (2.5)-9.9 ppb <2.5 (457)
PFOSA ($C_8F_{17}SO_2NH_2$)	***	***	***	***	*** <1.0 (457)
TOF	38.9 ppb* (95%CI 37.2 – 40.7) M: 41.6 F: 36.4	not presented	not presented	not presented	9.6 – 803.7

* Significant sex difference ; ** LLOQ = lower limit of quantitation; *** Not presented because too few samples exceeded the LLOQ
TOF = total organic fluorine = the percent of each of the seven fluorochemicals' molecular weight that was attributed to organic fluorine [PFOS (64.7%); PFHS (61.9%); PFOA (69%); PFOSAA (55.3%); PFOSA (64.7%); M570 (56.6%); and M556 (58.1%)] multiplied by the concentration measured for each fluorochemical and then summed across all seven fluorochemicals

Table 6. PFC serum levels in adults (samples drawn in 2000, focusing on ages 20-69, n = 645) (Olsen 2002b)

Compound	Geometric mean	Average	Median	95th percentile	Range/ < LLOQ(N)**
PFOS ($C_8F_{17}SO_3$-)	34.9 ppb* (95%CI 33.3 – 36.5) M: 37.8 F: 32.1	43.7 ppb	35.8 ppb	90.5 ppb	<LLOQ (4.3) - 1656 ppb <4.3 (1)
PFOA ($C_7F_{15}CO_2$-)	4.6 ppb* (95%CI 4.3 – 4.8) M: 4.9 F: 4.2	5.6 ppb	4.7 ppb	12.9 ppb	<LLOQ (1.9) - 52.3 ppb <1.9 (2)
PFHS ($C_6F_{13}SO_3$-)	1.9 ppb* (95%CI 1.8 – 2.0) M: 2.2 F: 1.6	2.9 ppb	1.6 ppb	9.6 ppb	<LLOQ (1.4) - 66.3 ppb <1.4 (72)
PFOSAA [$C_8F_{17}SO_2N(C_2H_5)$-CH_2CO_2-]	2.0 ppb (95%CI 1.9 – 2.1) M: 1.9 F: 2.1	3.0 ppb	1.4 ppb	7.6 ppb	<LLOQ (1.6) - 60.1 ppb <1.6 (101)
M570 [$C_8F_{17}SO_2N(CH_3)$-CH_2CO_2-]	1.3 ppb (95%CI 1.3 – 1.4) M: 1.3 F: 1.3	1.8 ppb	0.9 ppb	5.3 ppb	<LLOQ (1.0) - 19.0 ppb <1.0 (63)
M556 [$C_8F_{17}SO_2NH$-CH_2CO_2-]	***	***	***	***	<LLOQ-12.9 ppb <2.5 (145)
PFOSA ($C_8F_{17}SO_2NH_2$)	***	***	***	***	*** <1.0 (196)
TOF	31.7 ppb (95%CI 30.4 - 33) M: 41.6 F: 36.4	Not presented	Not presented	Not presented	5.7 – 1083.2

* Significant sex difference
** LLOQ = lower limit of quantitation
*** Not presented because too few samples exceeded the LLOQ
TOF = total organic fluorine = the percent of each of the seven fluorochemicals' molecular weight that was attributed to organic fluorine [PFOS (64.7%); PFHS (61.9%); PFOA (69%); PFOSAA (55.3%); PFOSA (64.7%); M570 (56.6%); and M556 (58.1%)] multiplied by the concentration measured for each fluorochemical and then summed across all seven fluorochemicals

Table 7. PFC serum levels in elderly adults (focusing on ages 65-96, n = 238) [Olsen 2002c)

Compound	Geometric mean	Median	Cumulative 90%	Range/ < LLOQ(N)**
PFOS ($C_8F_{17}SO_3$-)	31.0 ppb (95%CI 28.8 – 33.4) M: 30.2 F: 31.9	30.2 ppb	61.3 ppb	<LLOQ (3.4) – 175.0 ppb <3.4 (1)
PFOA ($C_7F_{15}CO_2$-)	4.2 ppb (95%CI 3.9 – 4.5) M: 4.0 F: 4.4	4.2 ppb	7.8 ppb	<LLOQ (1.4) – 16.7 ppb <1.4 (5)
PFHS ($C_6F_{13}SO_3$-)	2.2 ppb (95%CI 2.0 – 2.4) M: 2.3 F: 2.1	2.3 ppb	6.4 ppb	<LLOQ (1.4) – 40.3 ppb <1.4 (58)
PFOSAA [$C_8F_{17}SO_2N(C_2H_5)$-CH_2CO_2-]	1.5 ppb (95%CI 1.4 – 1.7) M: 1.4 F: 1.6	1.6 ppb	5.3 ppb	<LLOQ (1.6) – 21.1 ppb <1.6 (115)
M570 [$C_8F_{17}SO_2N(CH_3)$-CH_2CO_2-]	1.2 ppb (95%CI 1.1 – 1.3) M: 1.3 F: 1.1	1.3 ppb	3.0 ppb	<LLOQ (1.0) – 6.6 ppb <1.0 (83)
M556 [$C_8F_{17}SO_2NH$-CH_2CO_2-]	***	***	***	<LLOQ (1.0) – 4.8 <1.0 (230)
PFOSA ($C_8F_{17}SO_2NH_2$)	***	***	***	Not presented (too few exceeded LLOQ) <1.0 (238)
TOF	28.2 ppb (95%CI 26.4 – 30.1)	Not presented	Not presented	3.7 – 133.1

** LLOQ = lower limit of quantitation
*** Not presented because too few samples exceeded the LLOQ
TOF = total organic fluorine = the percent of each of the seven fluorochemicals' molecular weight that was attributed to organic fluorine [PFOS (64.7%); PFHS (61.9%); PFOA (69%); PFOSAA (55.3%); PFOSA (64.7%); M570 (56.6%); and M556 (58.1%)] multiplied by the concentration measured for each fluorochemical and then summed across all seven fluorochemicals

Table 8. Comparative toxicity of PFOS and PFOA

Tissue	PFOS	PFOA
Adrenal	Monkey adrenal cortex congestion, hemorrhage, lipid depletion (OECD 2002) Rat ↑ absolute and relative adrenal weight (M) (OECD 2002)	Monkey Adrenal lipid depletion (US EPA 2002) Rat Non-significant increase in pheochromocytomas (M) (US EPA 2002); non-significant increase in adrenal nodular hyperplasia (M) (US EPA 2002); ↑ relative weight of adrenal (US EPA 2002); ↑ absolute adrenal weight (US EPA 2002); ↑ thickness and vacuolation of adrenal cortex zona glomerulosa (US EPA 2002)
Brain	Monkey Rat delays in reflex (surface righting, acoustic startle) ; delayed physical development (pinna unfolding, eye opening) (OECD 2002)	Monkey ↓ activity; ataxia (US EPA 2002); ↓ absolute brain weight (F) (US EPA 2002) Rat ataxia (US EPA 2002)
Cardiovascular Effects & Lipid Metabolism	Monkey ↓ cholesterol (OECD 2002); ↓ HDL (OECD 2002) Rat inhibition of cholesterol synthesis; ↓ HMG-CoA (rate limiting enzyme in cholesterol synthesis); ↓ cholesterol esterification enzyme (ACAT); ↓ serum cholesterol; ↑ free cholesterol; ↓ serum triglyceride (3M 2001b)	Monkey ↑ cholesterol (based on 1 surviving male); ↓ absolute and relative heart weight (F) (US EPA 2002) Rat inhibition of cholesterol synthesis; ↓ HMG-CoA (rate limiting enzyme in cholesterol synthesis); ↓ cholesterol esterification enzyme (ACAT); ↓ serum cholesterol; ↑ free cholesterol; ↓ serum triglyceride (Haughom and Spydevold 1992)
Clinical Chemistry & Liver Enzyme	Monkey ↓ serum potassium (F) (OECD 2002); ↓ inorganic phosphate (F) (OECD 2002)(p. 296); ↑ bilirubin (M) (OECD 2002) Rat ↓ hematocrit (M), ↓ erythrocyte, ↓ hemoglobin, ↓ leukocytes, ↓ reticulocyte counts (F); ↑ glucose (M); ↑ blood urea nitrogen; ↑ creatinine phosphokinase (F); ↑ alkaline phosphatase; ↑ plasma glutamic oxalacetic activity (F); ↑ pyruvic transaminase activity (F) (rat) (OECD 2002)	Monkey ↓ erythrocytes (based on 1 surviving male); ↓ protein and albumin (based on 1 surviving male); ↓ hemoglobin (based on 1 surviving male); ↓ hematocrit (based on 1 surviving male); ↑ platelets (based on 1 surviving male); ↑ prothrombin and activated prothrombin time (based on 1 surviving male); ↓ alkaline phosphatase; trend toward increase glucose during first month; ↑ SGOT; ↑ SGPT (US EPA 2002a) Rat ↓ erythrocytes (M) (US EPA 2002a); ↓ leukocyte (M); ↓ hemoglobin (M); ↑ glucose (M); ↑ BUN (M); ↑ alkaline phosphatase (M); ↑ urinary albumin (US EPA 2002a)

M = male; F = female

Tissue	PFOS	PFOA
Developmental Toxicity	Rabbit ↓ fetal body weight; delayed ossification (OECD 2002) Rat ↓ fetus and neonatal body weight; ↑ number of male fetuses; skeletal variations (incomplete skull closure; delayed ossification of the pectoral girdle, rib cage, vertebral column, pelvic girdle, limbs); rib and sternebrae skeletal variations; cryptorchidism, cleft palate, subcutaneous edema; delays in reflex (surface righting, acoustic startle) and physical development (pinna unfolding, eye opening); decreased implantation site; live litter size; eye lens abnormalities – this effect later attributed to sectioning errors, although lens defects were not seen in controls (OECD 2002)	Rabbit Skeletal variation (extra rib) (US EPA 2002a)(p. 225) Rat ↓ fetal and pup weight (US EPA 2002); delayed preputial separation; annular constriction of tail (M); delayed vaginal opening (US EPA 2002); eye lens abnormalities – this effect later attributed to sectioning errors) (US EPA 2002a)
Endocrine	Monkey ↓ estradiol, estrone, TSH, T4, T3 (small n) (OECD 2002) Rat Hypothyroidism (3M 2001b)	Rat ↑ serum estradiol and ↓ testosterone (M) (US EPA 2002a)
Gastrointestinal	Monkey anorexia, emesis, black stool, dehydration, diarrhea; increased bile acid concentration (M) (OECD 2002) Rat lesions of the stomach, intestine; discoloration of glandular mucosa of stomach; mucosal hyperkeratosis and/or acanthosis in forestomach; mucosal hemorrhage in glandular stomach (OECD 2002)	Monkey anorexia, black stool, diarrhea, frothy emesis; dehydration (US EPA 2002a) Rat salivary gland sialadenitis (M) (US EPA 2002a) Mouse bile duct proliferation (US EPA 2002a)
Immune System	Rat lesions of the thymus, bone marrow, spleen, lymph node (depletion of in number and size of lymphoid follicles)(OECD 2002)	Monkey Bone marrow hypocellularity; atrophy of spleen and lymph node lymphoid follicle (US EPA 2002a) Rat ↓ absolute spleen weight (M); ↓ absolute thymus weight (M) (US EPA 2002a, Yang, et al. 2002); ↓ leukocyte (M) (US EPA 2002a); ↓ total number of thymocytes and splenocytes ; ↓ number of thymocytes and splenocytes expressing CD4 helper T-cell and/or CD8 cytotoxic T-cell; ↓ number of T and B cells in splenocytes; ↓ thymocyte proliferation (Yang, et al. 2000)

M = male; F = female

Tissue	PFOS	PFOA
Kidney	Rat ↑ relative kidney weight (OECD 2002)	Rat ↑ kidney weight (US EPA 2002a); biphasic kidney weight response – □ at high dose; slight dilation of kidney pelvis (M) (US EPA 2002b)
Liver	Monkey yellowish-brown or other discoloration ; □ alkaline phosphatase; ↑ absolute and relative liver weight ; centrilobular or diffuse hepatocellular vacuolation/hypertrophy (OECD 2002) Rat ↑ relative and absolute liver weight; hepatocyte necrosis; hepatocyte cytoplasmic hypertrophy; discoloration and/or enlargement; liver adenoma, centrilobular or diffuse hepatocellular vacuolation/hypertrophy; centrilobular eosinophilic hepatocytic granules; centrilobular hepatocytic pigment; lymphohistiocytic infiltrate (OECD 2002)	Rat liver adenoma (M); ↑ hepatic palmityl CoA oxidase activity (indication of peroxisome proliferation); multifocal cytoplasmic hypertrophy in hepatocytes; ↑ absolute and relative liver weight; liver discoloration: cystoid degeneration, megalocytosis; portal mononuclear cell infiltration (M) (US EPA 2002a) Mouse Hepatocellular hypertrophy; hepatocellular degeneration and/or necrosis; cytoplasmic vacuoles; liver discoloration; ↑ absolute and relative liver weight (US EPA 2002a)
Lungs	Monkey moderate diffuse atrophy of serous alveolar cells characterized by decreased cell size and loss of cytoplasmic granules (OECD 2002)	Rat alveolar macrophages (M); lung hemorrhage (M); vascular mineralization (F) (US EPA 2002a) Mouse cyanosis (US EPA 2002a)
Muscular	Rat muscle atrophy (OECD 2002)	
Pancreas	Monkey moderate diffuse atrophy of pancreatic acinar cells with decreased cell size and loss of zymogen granules (OECD 2002) Rat pancreatic islet cell carcinoma (3M 2000a)	Rat pancreatic acinar cell proliferation/adenoma (M) (US EPA 2002a)
Pituitary	Rat □ absolute pituitary weight (M) (OECD 2002)	Monkey ↑ relative pituitary weight (M) (US EPA 2002a)
Reproductive Organs - Female	Rat mammary fibroadenoma; □ uterine weight (dams); □ gestation length (OECD 2002)	Rat mammary fibroadenoma; ovarian tubular hyperplasia (US EPA 2002); delayed vaginal opening (US EPA 2002b)

M = male; F = female

Tissue	PFOS	PFOA
Reproductive Organs - Male	Rat □ absolute weight of seminal vesicle; □ absolute weight of prostate (OECD 2002)	Rat Leydig cell adenoma; Leydig cell hyperplasia; testis/epidiymis vascular mineralization; ↑ testis weight (US EPA 2002a); ↑ relative organ weight of epididymides, testes, seminal vesicles; □ absolute prostate weight; delayed preputial separation (US EPA 2002b)
Thyroid	Monkey □ thyroid hormone (OECD 2002) Rat follicular cell adenoma (OECD 2002); hypothyroidism (3M 2001b); □ absolute thyroid/parathyroid weight (M) (OECD 2002)	Monkey "Apparent downward trends in thyroid hormone levels returned to pre-study levels after cessation of exposure" (small n) (Environ International Corporation (Environ) 2002) Rat possible thyroid C-cell adenoma (M-low dose); possible thyroid C-cell hyperplasia (F) (US EPA 2002a)
Skin	Rat Epidermal hyperkeratosis and/or acanthosis (OECD 2002)(p. 300);	

M = male; F = female

Table 9. PFOS and PFOA reference dose (RfD) and comparison of rat and human serum levels.

PFOS RfD										
Critical Study	**Critical Effect**	**Critical Effect Level**	**UF_A**	**UF_H**	**UF_L**	**UF_S**	**UF_D**	**MF**	**Composite UF**	**RfD (μg/kg/d)**
2-year dietary study	cystic hepatocellular degeneration; mammary gland fibroadenomas	0.5 ppm (~ 0.025 mg/kg/d)	10	10	1	1	1	3[a]	300	0.083
2-year dietary study	cystic hepatocellular degeneration; mammary gland fibroadenomas	0.5 ppm (~ 0.025 mg/kg/d)	10	10	3[b]	1	1	3[a]	900 (~1000)	0.025

PFOS estimated rat serum RfC and human serum [c]		
Rat serum levels at critical effect (ppb)	**Composite UF**	**Hypothetical Rat serum levels at RfD (ppb); also referred to as RfC**
907 (min) to 6960 (max)	300	3 (min) to 23 (max)
907 (min) to 6960 (max)	1000	0.9 (min) to 6.96 (max)
Child median serum concentration (range)		**36.7 (6.7 – 515)**

PFOA RfD										
Critical Study	**Critical Effect**	**Critical Effect Level**	**UF_A**	**UF_H**	**UF_L**	**UF_S**	**UF_D**	**MF**	**Composite UF**	**RfD (μg/kg/d)**
2-generation study	changes in spleen, kidney, liver, seminal vesicle weight	1 mg/kg/d (LOAEL)	10	10	10	1	1	3[a]	3000	0.333

PFOA estimated monkey serum RfC and human serum [c]		
Male monkey serum levels at 3 mg/kg/d (ppb)	**Composite UF**	**Hypothetical Monkey serum levels at RfD (ppb); also referred to as RfC**
29,400 (min) to 118,000 (max)	3000	9.8 (min) to 39.3 (max)
Children median serum concentration (range)		**4.9 [<LOQ(1.9) – 56.1]**

[a] Modifying factor of 3 to account for the extreme biopersistence and long human half-life
[b] A 3 fold-factor to account for significant effects on mammary glands and liver observed at the lowest dose tested (0.5 ppm)
[c] Assuming a linear relationship between ingested dose and serum levels in the low dose range

Table 10. Perfluorinated or perfluorinated-related compounds

Chemical	CAS number/ PMN	Use
Group 1: Two perfluorinated chemicals for which current body burdens of the general population and expected future use and exposure patterns raise human health concerns		
Perfluorooctane sulfonate (PFOS)	2795-39-3	Breakdown product of certain perfluorinated chemicals used for fifty years, through 2001, in paper, food wraps, carpet, clothing, and furniture surface treatments. Also used in fire-fighting foams
Perfluorooctanoic acid (PFOA)	3825-26-1	Used in the manufacture of Teflon, breakdown product of certain fluorinated telomer alcohols, which are used in carpet and upholstery protection, glass or other hard surface cleaners, floor polishes, and packaging for greasy foods.
Total Organic Fluorine (TOF)		
Group 2 (single chemical): A four-carbon homologue to PFOS that represents a PFOS replacement in 3M's new Scotchgard formulations, perfluorobutane sulfonate (PFBS)		
Perfluorobutane sulfonate (PFBS)		PFBS based chemistry to replace perfluorooctane sulfonate (PFOS)-based surfactants; rat liver concentrations decrease in 28 day recovery group, but so did PFHS which has been estimated to have a human half-life on the order of years. In addition, the highest non-worker concentrations of PFHS are found in children (Olsen, et al. 2002); no toxicity information publicly available
Group 3: Nine perfluorinated chemicals that have been detected in the general population or wildlife, including four that are metabolic precursors of PFOS, two that are homologues of PFOS (six-carbon and ten-carbon chains), and three that are metabolites of telomer alcohols and acrylate that could replace PFOS chemistries in consumer products		

Perfluorinated sulfonates		
Perfluorohexane sulfonate (PFHS)	NA	Not a precursor, metabolite or residual of PFOS (Olsen, et al. 2002); used in fire-fighting foams and certain post-market carpet treatment applications (Olsen, et al. 2002); highest non-worker concentrations found in children (Tables 5-7); detected in bird liver extract (3M date not specified)
N-ethyl perfluorooctanesulfonamidoacetate or Perfluorooctane sulfonylamido(ethyl)acetate (PFOSAA)	2991-51-7	Biomarker for consumer exposure to perfluorinated chemicals found in paper and packaging; PFOSAA is a residual of N-EtFOSE-related chemistry; can metabolize to PFOSA and M556, which in turn can metabolize to PFOS (Olsen, et al. 2002); widely detected in humans (Tables 5-7)
N-methyl perfluorooctanesulfonamidoacetate (M570)	NA	Biomarker for consumer exposure to perfluorinated chemicals used in surface treatment (such as carpet, apparel, upholstery, leather); M570 is a residual of MeFOSE-related chemistry; can metabolize to PFOSA and M556, which in turn can metabolize to PFOS (Olsen, et al. 2002); highest non-worker concentrations found in children (Tables 5-7)
Perfluorooctanesulfonamidoacetate (M556)	NA	PFOS precursor compound; metabolite of M570 and PFOSAA; (Olsen, et al. 2002); highest non-worker concentrations found in children (Tables 5-7)
Perfluorooctanesulonylamide (PFOSA)	754-91-6	PFOS-precursor compound; metabolite of M570 and PFOSAA; not readily found in humans above the limit of quantitation (Tables 5-7);

		detected in bird liver extract (3M date not specified)
Perfluorodecanesulfonate (PFDS) Ammonium salt	67906-42-7	Detected (but not quantified – no standard, but response factor could be extrapolated from homologs) in children's blood (all individuals) and bird liver extract samples (3M date not specified, 3M 1999d);detected at high concentrations by Danish EPA in impregnating agents (used for tents, sleeping bags, etc) (Danish EPA 2002)
Perfluorinated carboxylic acid metabolites of telomer alcohol and/or telomer acrylate		
Perfluorooctanoate (POAA)		Metabolite of unspecified telomer alcohol and/or telomer acrylate (3M 1999a); found in male rat following a 28-day recovery period (AR226-0951); name found in (3M date not specified); detected (but not quantified) in pilot children's blood study (all individuals); estimated detection limit is 3 ppb (3M 1999d)
M463		Metabolite of unspecified telomer alcohol and/or telomer acrylate; no standard available for confirmation (3M 1999a); detected (but not quantified) in pilot children's blood study (all individuals); estimated detection limit is 3 ppb (3M 1999d)
Perfluorodecanoate (M513)		Metabolite of unspecified telomer alcohol and/or telomer acrylate; liver concentrations did not diminish in 28-day recovery group – even PFOS concentrations decreased to a greater extent (3M 1999a); name found in (3M date not specified); not detected in pilot children's blood study, but estimated detection limit is 12 ppb (3M 1999d)

Group 4: Seven telomer alcohol/acrylate metabolites for which methods have been developed for animal tissue		
Perfluorinated carboxylic acid metabolites of telomer alcohol and/or telomer acrylate		
M563 * M563 is the mass of perfluoroundecanoic acid (C11)		Metabolite of unspecified telomer alcohol and/or telomer acrylate; no standard available for confirmation (3M 1999a)
M363		Metabolite of unspecified telomer alcohol and/or telomer acrylate; no standard available for confirmation (3M 1999a)
Perfluoroheptanoic acid (a C7 carboxylic acid)	375-85-9	Perfluorinated telomer breakdown product, Not quantitated in humans, C7 found at about the same levels at PFOA in fish livers (Muir, et al. 2002)
Perfluorodecanoic acid (PFDA) (a C10 carboxylic acid)	335-76-2	Perfluorinated telomer breakdown product, Not quantitated in humans, but has been detected in fish liver (Mabury 2002); causes hypothyroidism (Van Rafelghem, et al. 1987)
Perfluoroundecanoic acid (a C11 carboxylic acid)		Perfluorinated telomer breakdown product, Not quantitated in humans, found in fish livers (Mabury 2002)
Perfluorododecanoic acid or Perfluorododecanoate (a C12 carboxylic acid); M613 is the Mass of perfluorododecanoic acid (C12)	307-55-1	Metabolite of unspecified telomer alcohol and/or telomer acrylate; liver concentrations did not diminish in 28-day recovery group – even PFOS concentrations decreased to a greater extent (3M 1999a); name found in (3M date not specified); found in fish liver (Mabury 2002)
Perfluorotetradecanoic acid (a C14 carboxylic acid)	376-06-7	Perfluorinated telomer breakdown product, Not quantitated in humans; found in fish (Mabury 2002)
Group 5: Three perfluorinated homologues of PFOS and PFOA (the seven- and nine-carbon homologues of PFOS and the nine-carbon homologue of PFOA) which lack analytical data for biota in the public record		

PFOS homologues for compounds in which analytical techniques could easily be developed		
Perfluoroheptane sulfonate (ammonium salt)	68259-07-4	By product of PFOS and PFOS-precursor synthesis and would be expected to be found in tissues because longer and shorter chain homologs are; analytical technique identical to PFOS (personal communication with Rich Purdy)
Perfluorononane sulfonate (ammonium salt)	17202-41-4	By product of PFOS and PFOS-precursor synthesis and would be expected to be found in tissues because longer and shorter chain homologs are; analytical technique identical to PFOS (personal communication with Rich Purdy)
PFOA homologues for compounds in which analytical techniques could easily be developed		
Perfluorononanoic acid (C9)	375-95-1	Perfluorinated telomer breakdown product, Not quantitated in humans; not because it has been used as internal standard – thus, method is available (personal communication with Rich Purdy)
Group 6: Twelve PFOS-related compounds previously produced in quantities over a million pounds per year and never tested in the general population		
1-octanesulfonamide, 1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8,8- heptadecafluoro-N-(2-hydroxyethyl)-N-ethyl- (N-EtFOSE alcohol)	1691-99-2	Also on the EPA SNUR and TSCA ITC 46th report list. N-EtFOSE-related chemicals are used for paper and packaging protection applications (Scotchban™). Specific uses include food contact applications (plates, food containers, bags, and wraps), as well as non-food contact applications (folding cartons, containers, carbonless forms, and masking papers) (3M 1999c); Significant trend towards increased incidence of thyroid follicular cell adenoma noted in cancer bioassay (3M 2001a)

1-octanesulfonamide, 1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8,8-heptadecafluoro-N-(2-hydroxyethyl)-N-methyl- (N-MeFOSE alcohol)	24448-09-7	Also on the EPA SNUR and TSCA ITC 46th report list. MeFOSE-related chemicals are used in surface treatment applications such as carpet, apparel, upholstery, leather protection (Scotchgard™)
Perfluoropentane (C5)	678-26-2	Also appears in 46th ITC Report
Perfluoro-N-methylmorphine	382-28-5	
Perfluorohaxane (C6)	355-42-0	Also appears on list of 17 possible PFOS replacements
Perfluorheptane (C7)	335-57-9	
Perfluorooctane	307-34-6	
Perfluoro-2-butyltetrahydrofuran (cyclic perfluoroether)	335-36-4	
Perfluorotripropylamine	338-83-0	
Perfluorotributylamine	311-89-7	
Perfluorotriamylamine	338-84-1	
Perfluoro-N,N,N',N'-tetrapropyl hexanediamine	143356-32-5	
Group 7: Seventeen perfluorinated compounds identified by the TSCA Interagency Testing Committee (ITC) in their 49th report to the EPA Administrator as possible PFOS replacements (US EPA 2002e). In 1998, these PFCs had production volumes greater than 10,000 pounds, but less than 1 million pounds.		
Perfluoroalkyl Alcohols		
1-Dodecanol, 3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,1 1,11,12,12,12-heneicosafluoro-	865-86-1	
1-Tetradecanol, 3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,1 1,11,12,12,13,13,14,14,14-pentacosafluoro-	39239-77-5	
1-Hexadecanol, 3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10, 11,11,12,12,13,13,14,14,15,15,16,16, 16-nonacosafluoro-	60699-51-6	
1-Octadecanol, 3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10, 11,11,12,12,13,13,14,14,15,15,16,16, 17,17,18,18,18-tritriacontafluoro-	65104-67-8	

Perfluoroalkyl Esters		
2-Propenoic acid, 3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,1 1,11,12,12,12-heneicosafluorododecyl ester	17741-60-5	
2-Propenoic acid, 3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecyl ester	27905-45-9	
2-Propenoic acid, 3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,1 1,11,12,12,13,13,14,14,15,15,16,16, 16-nonacosafluorohexadecyl ester	34362-49-7	
2-Propenoic acid, 3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,1 1,11,12,12,13,13,14,14,14-pentacosafluorotetradecyl ester	34395-24-9	
2-Propenoic acid, 3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10, 11,11,12,12,13,13,14,14,15,15,16,16, 17,17,18,18,18-tritriacontafluorooctadecyl ester	65150-93-8	
Perfluoroalkyl Iodides		
Dodecane, 1,1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10-heneicosafluoro-12-iodo-	2043-54 -1	
Octane, 1,1,1,2,2,3,3,4,4,5,5,6,6-tridecafluoro-8-iodo-	2043 -57 -4	
Tetradecane, 1,1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8,9 ,9,10,10,11,11,12,12-pentacosafluoro-14-iodo-	30046 -31 -2	
Eicosane, 1,1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8,9, 9,10,10,11,11,12,12,13,13,14,14,15,15,16,16,17, 17,18,18-heptatriacontafluoro-20-iodo-	65104 -63 -4	
Octadecane, 1,1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11, 12,12,13,13,14,14,15,15,16,16-tritriacontafluoro-18- iodo-	65150 -94 -9	
Hexadecane,	65510 -55 -6	

1,1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10, 1,11,12,12,13,13,14,14-nonacosafluoro-16-iodo-		
Perfluoroalkyl Acids and Salts		
Octanoic acid, pentadecafluoro	335-67-1	
Butanedioic acid, sulfo-, 1,4-bis(3,3,4,4,5,5,6,6,7,7,8,8,8,-tridecafluorooctyl)ester, sodium salt	54950-05-9	
Group 8. Sixteen perfluorinated compounds which the FDA has approved as indirect food additives		
Ammonium bis(2,2-bis((perfluoroalkyl(C2-18)ethyl)thio methyl)-3 hydroxypropyl) phosphate	977169-39-3	
Ammonium bis(2-(N-ethyl(perfluorooctane)sulfonamido) ethyl)phosphate	030381-98-7	also on the EPA SNUR
Ammonium 5,5-bis((perfluoroalkyl(C2-18)ethyl)thiomethyl)-2-hydroxy-2-oxo-1,3,2-dioxaphoshorinane	977169-38-2	
Ammonium mono(N-ethyl-2-perfluoroackylsulfonamidoethyl) phosphate	977094-94-2	
Diammonium 2,2-bis((perfluoroalkyl(C2-18)ethyl)thiomethyl)-3-hydroxypropyl phosphate	977169-40-6	
Diethanolamine mono- and bis(1H,1H,2H,2H-perfluoroalkyl) phosphate	977042-24-2	
Pentanoic acid, 4,4-bis ((gamma-omega-perfluoro-C8-20-alkyl)thio) derivatives, compounds with diethanolamine	071608-61-2	
Perfluorocarbon resin	031692-93-0	
Perfluorohexane	000355-42-0	
Perfluoromethyl vinyl ether	001187-93-5	
Perfluoro-2-phenoxypropyl vinyl ether	024520-19-2	
Perfluoropropyl vinyl ether	001623-05-8	Also found on the TSCA ITC 46th report
Perfluoro(propylvinyl ether)-tetrafluoroethylene copolymer	026655-00-5	
Poly(choline chloride methacrylate-CO-2-ethoxyethylacrylate-CO-glycidylmethacrylate-CO-N-methylperfluorooctanesulfonamidoethyl acrylate	092265-81-1	

Tetraammonium 2,2-bis(perfluoroalkyl(C2-18)ethyl)thiomethyl-1,3-bis (dihydrogenphosphate)propane	977169-41-7	
Tetrafluoroethylene-perfluoromethyl vinyl ether-perfluoro-2-phenoxypropylvinyl ether terpolymer	026658-70-8	
Group 9. Fifty perfluorinated compounds identified by the TSCA Interagency Testing Committee in their 46th report to the EPA Administrator (US EPA 2000b). Thirty-eight of the 50 PFCs listed in the ITC report were identified because they satisfied the DEBITS criteria of persistence (ultimate degradation > 2-3 months) and bioconcentration potential (log octanol-water partition coefficient 3-6) and production/importation criteria described by the ITC in its 45th report. Twelve other PFCs were added from TSCA 8(e) submissions because they are structurally similar the original 38. An asterisk identifies the TSCA 8(e) compounds		
Perfluoroalkyl Acids and Salts (n=7)		
1-Decanesulfonic acid, 1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8,9, 9,10,10,10-heneicosafluoro-	000335-77-3	
1-Octanesulfonic acid, 1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8,8-heptadecafluoro-*	001763-23-1	also on the EPA SNUR list
1-Octanesulfonic acid, 1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8,8-heptadecafluoro-, potassium salt*	002795-39-3	PFOS
Ammonium perfluorooctanoate* (PFOA)	003825-26-1	PFOA
1-Hexanesulfonic acid, 1,1,2,2,3,3,4,4,5,5,6,6,6-tridecafluoro-, potassium salt*	003871-99-6	
Hexanoic acid, undecafluoro-, ammonium salt*	021615-47-4	
1-Octanesulfonic acid 1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8,8-heptadecafluoro-, lithium salt	029457-72-5	also on SNUR; pesticide
Perfluoroalkyl Sulfonamides (n=13)		
1-Octanesulfonamide, 1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8,8-heptadecafluoro- (PFOSA)	000754-91-6	also on the SNUR (PFOSA)
1-Octanesulfonamide,	001691-99-2	also on the EPA SNUR list and HPV list

1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8,8-heptadecafluoro-N-(2-hydroxyethyl)- N-ethyl- (N-EtFOSE alcohol)		(N-EtFOSE alcohol)
1-Octanesulfonamide, ethyl-1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8,8-heptadecafluoro-* (EtFOSA)	004151-50-2	also on the EPA SNUR; pesticide (EtFOSA)
1-Octanesulfonamide, 1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8,8-heptadecafluoro-N-(2-hydroxyethyl)- N-methyl-* (N-MeFOSE alcohol)	024448-09-7	also on the EPA SNUR list and HPV list (N-MeFOSE alcohol)
1-Butanesulfanamide, ethyl-1,1,2,2,3,3,4,4,4-nonafluoro-N-(2-hydroxyethyl)-	034449-89-3	
1-Butanesulfonamide 1,1,2,2,3,3,4,4,4-nonafluoro-N-(2-hydroxyethyl)-N-methyl-	034454-97-2	
1-Hexanesulfonamide, ethyl-1,1,2,2,3,3,4,4,5,5,6,6,6-tridecafluoro-N-(2-hydroxyethyl)-	034455-03-3	
2-Propanoic acid, 2-[methyl[(nonalfuorobutyl)sulfonyl] amino]ethyl ester	067584-55-8	
2-Propenoic acid, 2-methyl (undecafluoropentyl)sulfonyl amino ethyl ester	067584-56-9	
1-Pentanesulfonamide, ethyl-1,1,2,2,3,3,4,4,5,5,5-undecafluoro-N-(2-hydroxyethyl)-	068555-72-6	
1,1,2,2,3,3,4,4,5,5,5-Undecafluoro- N-(2-hydroxyethyl)-N-methylpentane-1-sulphonamide	068555-74-8	
1-Hexanesulfonamide, 1,1,2,2,3,3,4,4,5,5,6,6,6-tridecafluoro-N-(2-hydroxyethyl)-N-methyl-	068555-75-9	
1-Butanesulfonamide, 3- (dimethylamino)propyl-1,1,2,2,3,3,4,4,4-nonafluoro-	068555-77-1	
Perfluorinated Quaternary Ammonium Chemicals (n=2)		
1-Propanaminium,3 (((heptadecafluorooctyl)sulfonyl) amino)-N,N,N-trimethyl-, iodide	001652-63-7	Also on the EPA SNUR list
1-Propanaminium,3	038006-74-5	Also on the EPA SNUR list

[[(heptadecafluorooctyl)sulfonyl] amino]-N,N,N-trimethyl-, chloride		
Perfluoroalkanes (n=3)		
Octafluoropropane	000076-19-7	
Dodecafluoropentane	000678-26-2	
Hexafluoro-1,2- bis(trifluoromethyl)cyclobutane	002994-71-0	
Fluoroalkyl Ethers (n=6)		
2,2,3,3-Tetrafluoro-3-methoxy- propionic acid methyl ester*	000755-73-7	
Propane, 1,1,1,2,2,3,3-heptafluoro- 3-[(trifluoroethyenyl)oxy]-	001623-05-8	Also on the FDA list of indirect food additives
Propane, 1-(1-(difluoro(1,2,2,2-tetrafluoroethoxy)methyl)-1,2,2,2-tetrafluoroethoxy)-1,1,2,2,3,3,3-heptafluoro-	003330-14-1	
Heptafluoropropyl 1,2,2,2- tetrafluoroethyl ether	003330-15-2	
Propanoic acid, 3-1-difluoro(trifluoroethenyl)oxymethyl-1,2,2,2-tetrafluoroethoxy-2,2,3,3-tetrafluoro-, methyl ester	063863-43-4	
3,5-Dichloro-4-(1,1,2,2-tetrafluoroethoxy)aniline	104147-32-2	
Fluoroalkyl Iodides (n=3)		
1-Iodoperfluorobutane	000423-39-2	
1,1,1,2,2,3,3,4,4-Nonafluoro-6-iodohexane	002043-55-2	
Perfluoroalkyl(C2-C18)ethyl iodide	068188-12-5	
Gamma, Omega-Perfluoroalkyl Alcohols (n=3)		
3,3,4,4,5,5,6,6,7,7,8,8,8- Tridecafluoro-1-octanol	000647-42-7	
3,3,4,4,5,5,6,6,6-Nonafluoro1-hexanol	002043-47-2	
2-Perfluoroalkyl (C6-C12) ethanol	068391-08-2	
Perfluoroalkyl Sulfonyl Fluorides (n=4)		
Nonafluorobutanesulfonyl fluoride	000375-72-4	
Methyl fluorosulfonate*	000421-20-5	
Cyclohexanesulfonyl fluoride, decafluoro(pentafluoroethyl)-	068156-06-9	
Cyclohexanesulfonyl fluoride, decafluoro(trifluoromethyl)-	068318-34-3	
Perfluoroglycol Acid Fluorides (n=5)		
Propanoyl fluoride, 2,3,3,3-tetrafluoro-2-(1,1,2,3,3,3-hexafluoro-2-(1,1,2,2-tetrafluoro-2-	004089-58-1	

(fluorosulfonyl)ethoxy) propoxy)-		
3-Pentanone, 1,1,2,2,4,4,5,5- octafluoro-1,5-dimethoxy-*	001422-71-5	
Methyl 2,2-difluromalonyl fluoride*	069116-71-8	
Propanoic acid, 2,2,3,3-tetrafluoro-3-1,2,2,2-tetrafluoro-1- (fluorocarbonyl)ethoxy-, methyl ester*	069116-72-9	
Propanoic acid, 3-(2-(1,2-difluoro- 2-oxo-1-(trifluoromethyl)ethoxy)- 1,2,2-trifluoro-1-(trifluoromethyl) ethoxy)-2,2,3,3-tetrafluoro-, methyl ester	069116-73-0	
Perfluoroalkyl Carboxylic Acid Fluorides (n=2)		
Pentadecylfluorooctanoyl fluoride	000335-66-0	
Tridecafluoroheptanoyl fluoride	000375-84-8	
Perfluorinated Chemicals Not Assigned to a Structural Class (n=2)		
1-Hexene, 3,3,4,4,5,5,6,6,6-nonafluoro-	019430-93-4	
Perfluoroalkyl (C4-C10) ethyl mercaptan	068140-20-5	
Group 10: Approximately 90 compounds related to PFOS chemistries, phased out of production by 3M, and subject to Significant New Use Reporting by EPA.		
Final rule. March 11, 2002 (FR Vol 67, Number 47, pages 11007-11013). No comments were received on these chemicals and 3M discontinued their manufacture before December 31, 2000 (n=13)		
1-Octanesulfonamide, N,N',N''-[phosphinylidynetris(oxy-2,1-ethanediyl)] tris[N-ethyl-1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8,8-heptadecafluoro-	2250-98-8	
1-Octanesulfonamide, N,N'- [phosphinicobis(oxy-2,1- ethanediyl)]bis[N-ethyl-1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8,8heptadecafluoro-,,ammonium salt	30381-98-7	also on EPA indirect food additive list
Benzoic acid, 2,3,4,5-tetrachloro-6-[[[3-[[(heptadecafluorooctyl)sulfonyl]ox y]phenyl]amino]carbonyl]-, monopotassium salt	57589-85-2	
1-Octanesulfonamide, N-ethyl-1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8,8-heptadecafluoro-N-[3-(trimethoxysilyl)propyl]-	61660-12-6	

1-Octanesulfonamide, N-ethyl-,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8,8-heptadecafluoro-N-[2-(phosphonooxy)ethyl]-,diammonium salt	67969-69-1	
Sulfonamides, C4-8-alkane-perfluoro, N-ethyl-N-(hydroxyethyl), reaction products with 1,1'-methylenebis[4-isocyanatobenzene]	68608-14-0	
2-Propenoic acid, 2-methyl-,octadecyl ester, polymer with 1,1- dichloroethene, 2-[[(heptadecafluorooctyl)sulfonyl]methylamino]ethyl 2-propenoate, N-(hydroxymethyl)-2-propenamide, 2-[methyl[(nonafluorobutyl)sulfonyl] amino]ethyl 2-propenoate, 2-[methyl[(pentadecafluoroheptyl)sulfonyl]amino]ethyl 2-propenoate, 2-[methyl[(tridecafluorohexyl)sulfonyl]amino]ethyl 2-propenoate and 2-[methyl[(undecafluoropentyl)sulfonyl]amino]ethyl 2-propenoate	70776-36-2	
2-Propenoic acid, 2-methyl-, polymers with Bu methacrylate, lauryl methacrylate and 2-[methyl[(perfluoro-C4-8-alkyl)sulfonyl]amino]ethylmethacrylate	127133-66-8	
Fatty acids, C18-unsatd., trimers, 2-[[(heptadecafluorooctyl)sulfonyl]methylamino]ethyl esters	148240-78-2	
Sulfonamides, C4-8-alkane, perfluoro, N-(hydroxyethyl)-N-methyl, reaction products with 1,6-diisocyanatohexane homopolymer and ethylene glycol	148684-79-1	
Sulfonamides, C4-8-alkane, perfluoro, N-ethyl-N-(hydroxyethyl)-, polymers with 1,1'-methylenebis[4-isocyanatobenzene] and polymethylenepolyphenylene isocyanate, 2-ethylhexyl esters, MeEt ketone oxime-blocked	178535-22-3	
Polymethylenepolyphenylene isocyanate and	P-94-2205	

bis(4-NCO-phenyl)methane reaction products with 2-ethyl-1-hexanol, 2-butanone, oxime, N-ethyl-N-(2- hydroxyethyl)- 1-C4-C8 perfluoroalkanesulfonamide		
Fatty acids, C18-unsatd., dimers, 2-[methyl[(perfluoro-C4-8-alkyl)sulfonyl]amino]ethyl esters	P-96-1645 306974-63-0	
Perfluoroalkyl sulfonates: EPA Proposed Significant New Use Rule – Supplemental proposed rule. March 11, 2002 (FR Vol 67, Number 47, pages 11014-11030); 3M was not the only manufactorer of these compounds (n=75)		
1-Octanesulfonyl fluoride, 1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8,8-heptadecafluoro-	307-35-7	
1-Decanesulfonyl fluoride, 1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heneicosafluoro-	307-51-7	
2-Propenoic acid, 2-methyl-, 2-[ethyl[(heptadecafluorooctyl)sulfon]amino]ethyl ester	376-14-7	
2-Propenoic acid, 2- [butyl[(heptadecafluorooctyl) sulfonyl]amino]ethyl ester	383-07-3	
1-Hexanesulfonyl fluoride, ,1,2,2,3,3,4,4,5,5,6,6,6-tridecafluoro-	423-50-7	
2-Propenoic acid, 2- [ethyl[(heptadecafluorooctyl) sulfonyl]amino]ethyl ester	423-82-5	
1-Octanesulfonamide, 1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8,8-heptadecafluoro- (PFOSA)	754-91-6	also on the TSCA ITC 46th report (PFOSA)
1-Propanaminium, 3-[[(heptadecafluorooctyl)sulfonyl] amino]-N,N,N-trimethyl-,iodide	1652-63-7	also on the TSCA ITC 46th report
1-Octanesulfonamide, N-ethyl-,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8,8-heptadecafluoro-N-(2-hydroxyethyl)- (N-EtFOSE alcohol)	1691-99-2	also on the HPV list and TSCA ITC 46th report
1-Octanesulfonic acid, 1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8,8-	1763-23-1	also on the TSCA ITC 46th report

heptadecafluoro-		
1-Octanesulfonic acid, 1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8,8-heptadecafluoro-, potassium salt	2795-39-3	PFOS
Glycine, N-ethyl-N-[(heptadecafluorooctyl)sulfonyl]-, potassium salt	2991-51-7	
1-Octanesulfonamide, N-ethyl-1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8,8-heptadecafluoro- (EtFOSA)	4151-50-2	also on the TSCA ITC 46th report; pesticide (EtFOSA)
2-Propenoic acid, 2-methyl-, 2-[[(heptadecafluorooctyl)sulfonyl]methylamino]ethylester	14650-24-9	
1-Nonanesulfonic acid, 1,2,2,3,3,4,4,5,5,6,6,7,7,8,8,9,99-nonadecafluoro-, ammonium salt	17202-41-4	
1-Octanesulfonamide, 1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8,8-heptadecafluoro-N-(2-hydroxyethyl)- N-methyl- (N-MeFOSE alcohol)	24448-09-7	also on the HPV list and TSCA ITC 46th report
2-Propenoic acid, 2-[[(heptadecafluorooctyl)sulfonyl] methylamino]ethyl ester	25268-77-3	
1-Octanesulfonic acid, 1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8,8-heptadecafluoro-, ammonium salt	29081-56-9	
Poly(oxy-1,2-ethanediyl), .alpha.-[2-[ethyl[(heptadecafluorooctyl) sulfonyl]amino]ethyl]-.omega.-hydroxy-	29117-08-6	
1-Octanesulfonic acid, ,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8,8-heptadecafluoro-, lithium salt	29457-72-5	pesticide-use
1-Octanesulfonamide, 1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8,8-heptadecafluoro-N-methyl-	31506-32-8	
1-Propanaminium, 3-[[(heptadecafluorooctyl)sulfonyl]	38006-74-5	also on the TSCA ITC 46th report

amino]-N,N,N-trimethyl-, chloride		
1-Propanaminium, N-(2-hydroxyethyl)-N,N-dimethyl-3-[(3-sulfopropyl)[(tridecafluorohexyl)su]amino]-,inner salt	38850-58-7	
1-Hexanesulfonic acid, 1,1,2,2,3,3,4,4,5,5,6,6,6-	55120-77-9	
Cyclohexanesulfonic acid, decafluoro(pentafluoroethyl)-, potassium salt	67584-42-3	
1-Decanesulfonic acid, ,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8,9,910,10,10-heneicosafluoro-,ammonium salt	67906-42-7	
Cyclohexanesulfonic acid, nonafluorobis(trifluoromethyl)-, potassium salt	68156-01-4	
2-Propenoic acid, 2- [butyl[(heptadecafluorooctyl) sulfonyl]amino]ethyl ester, telomer with 2-[butyl[(pentadecafluoroheptyl)sulfo]amino]ethyl 2-propenoate, methyloxirane polymer with oxirane di-2-propenoate, methyloxirane polymer with oxirane mono-2-propenoate and 1-octanethiol	68298-62-4	
2-Propenoic acid, eicosyl ester, polymer with 2-[[(heptadecafluorooctyl)sulfonyl]methylamino]ethyl 2-propenoate, hexadecyl 2-propenoate, 2-[methyl[(nonafluorobutyl)sulfonyl]amino]ethyl 2-propenoate, 2- [methyl[(pentadecafluoroheptyl) sulfonyl]amino]ethyl 2-propenoate, 2-[methyl[(tridecafluorohexyl) sulfonyl]amino]ethyl 2-propenoate, 2- [methyl[(undecafluoropentyl) sulfonyl]amino]ethyl 2-propenoate and octadecyl 2-propenoate	68329-56-6	
2-Propenoic acid, polymer with 2-[ethyl[(heptadecafluorooctyl) sulfonyl]amino]ethyl 2-methyl-2-propenoate and octadecyl 2-propenoate	68541-80-0	
2-Propenoic acid, butyl ester, polymer with 2-[[(heptadecafluorooctyl)sulfonyl]me]ethyl 2-propenoate, 2- [methyl[(nonafluorobutyl) sulfonyl]a]ethyl 2-propenoate, 2-	68555-90-8	

[methyl[(pentadecafluoroheptyl)sulfonyl]amino]ethyl 2-propenoate, 2- [methyl[(tridecafluorohexyl) sulfonyl]amino]ethyl 2-propenoate and 2-[methyl[(undecafluoropentyl)sulfonyl]amino]ethyl 2-propenoate		
2-Propenoic acid, 2-methyl-, 2-[ethyl[(heptadecafluorooctyl)sulfon]amino]ethyl ester, polymer with2- [ethyl[(nonafluorobutyl) sulfonyl]am]ethyl 2-methyl-2-propenoate, 2-[ethyl[(pentadecafluoroheptyl)sulfonyl]amino]ethyl 2-methyl-2-propenoate, 2-[ethyl[(tridecafluorohexyl)sulfonyl]amino]ethyl 2-methyl-2-propenoate, 2-[ethyl[(undecafluoropentyl)sulfonyl] amino]ethyl 2-methyl-2-propenoate	68555-91-9	
2-Propenoic acid, 2-methyl-, 2-heptadecafluorooctyl) sulfonyl]methylamino]ethyl ester, polymer with 2-methyl[(nonafluorobutyl)sulfonyl]amino]ethyl 2-methyl-2-propenoate, 2-[methyl[(pentadecafluoroheptyl) sulfonyl]amino]ethyl 2-methyl-2-propenoate, 2-[methyl[(tridecafluorohexyl)sulfonyl]amino]ethyl 2-methyl-2-propenoate, 2-[methyl[(undecafluoropentyl) sulfonyl]amino]ethyl 2-methyl-2-propenoate	68555-92-0	
2-Propenoic acid, 2-[[(heptadecafluorooctyl)sulfonyl] methylamino]ethyl ester, telomer with 2-[methyl[(nonafluorobutyl)sulfonyl]amino]ethyl 2-propenoate, .alpha.-(2-methyl-1-oxo-2-propenyl)-.omega.- hydroxypoly(oxy-1,2-ethanediyl), alpha.-(2-methyl-1-oxo-2-propenyl)-omega.-[(2-methyl-1-oxo-2-propenyl)oxy]poly(oxy-1,2-ethanediyl), 2-[methyl[(pentadecafluoroheptyl) sulfonyl]amino]ethyl 2-propenoate, 2- [methyl[(tridecafluorohexyl)sulfonyl]amino] ethyl 2-propenoate, 2-	68586-14-1	

[methyl[(undecafluoropentyl)sulfonyl] amino]ethyl 2-propenoate and 1-octanethiol		
1-Octanesulfonamide, N-ethyl-1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8,8-heptadecafluoro-N-(2-hydroxyethyl)- reaction products with N-ethyl-1,1,2,2,3,3,4,4,4-nonafluoro-N-(2-hydroxyethyl)-1-butanesulfonamide, N-ethyl-1,1,2,2,3,3,4,4,5,5,6,6,7,7,7-pentadecafluoro-N-(2-hydroxyethyl)- 1-heptanesulfonamide, N-ethyl-1,1,2,2,3,3,4,4,5,5,6,6,6-tridecafluoro-N-(2-hydroxyethyl)-1-hexanesulfonamide, N-ethyl-1,1,2,2,3,3,4,4,5,5,5-undecafluoro-N-(2-hydroxyethyl)-1-pentanesulfonamide, polymethylenepolyphenylene isocyanate and stearyl alc.	68649-26-3	
Chromium, diaquatetrachloro[.mu.-[N-ethyl-N-[(heptadecafluorooctyl)sulfonyl]glycinato-.kappa.O:.kappa.O']]-.mu.-hydroxybis(2-methyl-1-propanol)di-	68891-96-3	
2-Propenoic acid, 2-[[(heptadecafluorooctyl)sulfonyl]methylamino]ethyl ester, polymer with 2- [methyl[(nonafluorobutyl)sulfonyl]amino]ethyl 2-propenoate, 2-[methyl[(pentadecafluoroheptyl)sulf]amino]ethyl 2-propenoate, 2-[methyl[(tridecafluorohexyl) sulfonyl]amino]ethyl 2-propenoate, 2-[methyl[(undecafluoropentyl)sulfonyl]amino]ethyl 2-propenoate andalpha.-(1-oxo-2-propenyl)-.omega.-methoxypoly (oxy-1,2-ethanediyl)	68867-60-7	
2-Propenoic acid, 2-methyl-, 2-[ethyl[(heptadecafluorooctyl)sulfonyl]amino]ethyl ester, telomer with 2-[ethyl[(nonafluorobutyl)sulfonyl] amino]ethyl 2-methyl-2-propenoate, 2-[ethyl[(pentadecafluoroheptyl)sulfonyl]amino]ethyl 2-methyl-2-propenoate, 2-	68867-62-9	

ethyl[(tridecafluorohexyl)sulfonyl]amino]ethyl 2-methyl-2-propenoate, 2-[ethyl[(undecafluoropentyl)sulfonyl]amino]ethyl 2-methyl-2-propenoate, 1-octanethiol and .alpha.-(1-oxo-2-propenyl)-.omega.-methoxypoly(oxy-1,2-ethanediyl)		
2-Propenoic acid, eicosyl ester, polymers with branched octylacrylate, 2-[[(heptadecafluorooctyl)sulfonyl]me thylamino]ethyl acrylate, 2-[methyl [(nonafluorobutyl)sulfonyl]amino]ethyl acrylate, 2- [methyl[(pentadecafluoroheptyl)sulfonyl]amino]et hyl acrylate, 2-[methyl[(tridecafluorohexyl)sulfony l]amino]ethyl acrylate, 2-[methyl[(undecafluoropentyl)sulfony l]amino]ethyl acrylate, polyethylene glycol acrylate Me ether and stearyl acrylate	68909-15-9	
Poly(oxy-1,2-ethanediyl), .alpha.-[2-[ethyl[(heptadecafluorooctyl)sulfonyl]amino]ethyl]-.omega.-methoxy-	68958-61-2	
1-Octanesulfonic acid, 1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8,8-heptadecafluoro-, compd. with 2,2'-iminobis[ethanol]	70225-14-8	
2-Propenoic acid, 2-methyl-, methyl ester, polymer with ethenylbenzene, 2-[[(heptadecafluorooctyl) sulfonyl]methylamino]ethyl 2-propenoate, 2-[methyl[(nonafluorobutyl)sulfonyl]amino]ethyl 2-propenoate, 2- [methyl[(pentadecafluoroheptyl) sulfonyl]amino]ethyl 2-propenoate, 2-[methyl[(tridecafluorohexyl)sulfonyl]amino]ethyl 2-propenoate, 2- [methyl[(undecafluoropentyl) sulfonyl]amino]ethyl 2-propenoate and 2-propenoic acid	71487-20-2	

1-Propanesulfonic acid, 3-[[3-(dimethylamino)propyl][(tridecafluorohexyl)sulfonyl]amino]-2-hydroxy-,monosodium salt	73772-32-4	
1-Propanaminium, N-(2-hydroxyethyl)- 3-[(2-hydroxy-3-sulfopropyl)[(tridecafluorohexyl)sulfonyl]amino]-N,N-dimethyl-,hydroxide, monosodium salt	81190-38-7	
Sulfonamides, C4-8-alkane, perfluoro, N-(hydroxyethyl)-N-methyl, reaction products with epichlorohydrin, adipates (esters)	91081-99-1	
1-Propanesulfonic acid, 3-[[3-(dimethylamino)propyl][(heptadecafluorooctyl)sulfonyl]amino]-2-hydroxy-, monosodium salt	94133-90-1	
Sulfonamides, C7-8-alkane, perfluoro, N-methyl-N-[2-[(1-oxo-2-propenyl)oxy]ethyl], polymers with2-ethoxyethyl acrylate, glycidyl methacrylate and N,N,N-trimethyl-2- [(2-methyl-1-oxo-2-propenyl)oxy]ethanaminium chloride	98999-57-6	
1-Heptanesulfonic acid, 1,1,2,2,3,3,4,4,5,5,6,6,7,7,7-pentadecafluoro-, lithium salt	117806-54-9	
Sulfonamides, C4-8-alkane, perfluoro, N-methyl-N- (oxiranylmethyl)	129813-71-4	
Fatty acids, C18-unsatd., trimers, 2-[methyl[(tridecafluorohexyl)sulfonyl]amino]ethyl esters	148240-80-6	
Fatty acids, C18-unsatd., trimers, 2- [methyl [(pentadecafluoroheptyl)sulfonyl]amino]ethyl esters	148240-82-8	
1-Octanesulfonamide, 1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8,8- -N-methyl-, reaction products with benzene-chlorine-sulfur chloride (S2Cl2) reaction products chlorides	182700-90-9	
2-Propenoic acid, 2-methyl-, butyl ester, polymer with 2-	L-92-0151	

[ethyl[(heptadecafluorooctyl)sulfonyl]amino]ethyl 2-methyl-2-propenoate, 2-[ethyl[(nonafluorobutyl) sulfonyl]amino]ethyl 2-methyl-2-propenoate, 2-[ethyl[(pentadecafluoroheptyl)sulfonyl]amino]ethyl 2-methyl-2-propenoate, 2-ethyl[(tridecafluorohexyl)sulfonyl] amino]ethyl 2-methyl-2-propenoate and 2-propenoic acid		
Sulfonamides, C4-8-alkane, perfluoro, N-[3-(dimethylamino)propyl], reactionproducts with acrylic acid	P-80-0183 192662-29-6	
Fatty acids, linseed-oil, dimers, 2-[[(heptadecafluorooctyl) sulfonyl]methylamino]ethyl esters	P-83-1102 306973-46-6	
Propanoic acid, 3-hydroxy-2- (hydroxymethyl)-2-methyl-, polymer with 2-ethyl-2-(hydroxymethyl)-1,3-and N,N',2-tris(6-isocyanatohexyl)imidodicarbonic, reaction products with N-ethyl-1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8,8-heptadecafluoro-N-(2-hydroxyethyl)- 1-octanesulfonamide and N-ethyl-1,1,2,2,3,3,4,4,5,5,6,6,7,7,7-pentadecafluoro -N-(2-hydroxyethyl)- 1 heptanesulfonamide, compds. With triethylamine	P-84-1163 306975-56-4	
Propanoic acid, 3-hydroxy-2- (hydroxymethyl)-2-methyl-, polymerwith 1,1'-methylenebis[4-isocyanatobenzene] and 1,2,3-propanetriol, reaction products with N-ethyl-1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8,8-heptadecafluoro-N-(2-hydroxyethyl)- 1-octanesulfonamide and N-ethyl-1,1,2,2,3,3,4,4,5,5,6,6,7,7,7-pentadecafluoro-N-(2-hydroxyethyl)- 1-heptanesulfonamide,compds. With morpholine	P-84-1171 306975-57-5	
Sulfonamides, C4-8-alkane, , N-(hydroxyethyl)-	P-86-0301	

N-methyl, reaction products with 12-hydroxystearic acid and 2,4-TDI, ammonium salts	306973-47-7	
2-Propenoic acid, 2-methyl-, dodecyl ester, polymers with 2- [methyl[(perfluoro-C4-8-alkyl)sulfonyl]amino]ethyl acrylate and vinylidene chloride	P-86-0958 306975-62-2	
Sulfonamides, C4-8-alkane, perfluoro, N-ethyl-N- (hydroxyethyl), reaction products with 2-ethyl-1-hexanol andpolymethylenepolyphenylene isocyanate	P-89-0799 160901-25-7	
Sulfonamides, C4-8-alkane, perfluoro, N-methyl-N-[(3-octadecyl-2-oxo-5-oxazolidinyl)methyl]	P-90-0111 306974-19-6	
Poly(oxy-1,2-ethanediyl), .alpha.- hydro-.omega.-hydroxy-, polymer with 1,6-diisocyanatohexane, N-(2-hydroxyethyl)-N-methyl perfluoro C4- 8-alkane sulfonamides-blocked	P-91-1419 306975-84-8	
2-Propenoic acid, 2-methyl-, dodecyl, polymers with N-(hydroxymethyl)-2-propenamide, 2-[methyl[(perfluoro-C4-8-alkyl)sulfonyl]amino]ethyl methacrylate, stearyl methacrylate and vinylidene chloride	P-93-1444 306975-85-9	
1-Hexadecanaminium, N,N-dimethyl-N-[2-[(2-methyl-1-oxo-2-propenyl)oxy]ethyl]-, bromide, polymers with Bu acrylate, Bu and 2-[methyl[(perfluoro-C4-8-alkyl)sulfonyl]amino]ethyl acrylate	306976-25-0	
2-Propenoic acid, 2-methyl-, 2-methylpropyl ester, polymer with 2,4-diisocyanato-1-methylbenzene, 2-ethyl-2-(hydroxymethyl)-1,3-propanediol and 2-propenoic acid, N-ethyl-N-(hydroxyethyl)perfluoro-C4-8-alkanesulfonamides-blocked	P-94-0927 306976-55-6	

Siloxanes and Silicones, di-Me, mono[3-[(2-methyl-1-oxo-2-propenyl)oxy]propylgroup]-terminated, polymers with 2- [methyl[(perfluoro-C4-8-alkyl)sulfonyl]amino]ethyl acrylate and stearyl methacrylate	P-94-2206 306974-28-7	
Sulfonamides, C4-8-alkane, perfluoro,N,N'-[1,6-hexanediylbis[(2-oxo-3,5-oxazolidinediyl)methylene]]bis[N- methyl-	P-95-0120 06980-27-8	
Sulfonic acids, C6-8-alkane, perfluoro, compds. with polyethylene-polypropylene glycol bis(2-aminopropyl) ether	P-96-1262 306974-45-8	
2-Propenoic acid, 2-methyl-, 2-(dimethylamino)ethyl ester, telomer with 2-[ethyl[(perfluoro-C4-8-alkyl)sulfonyl]amino] ethyl methacrylate and 1-octanethiol, N-oxides	P-96-1424 306977-10-6	
Sulfonamides, C4-8-alkane, perfluoro, N-[3-(dimethyloxidoamino)propyl], potassium salts	P-96-1433 179005-06-2	
1-Decanaminium, N-decyl-N,N-dimethyl-, salt with 1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8,8-heptadecafluoro-1-octanesulfonic acid (1:1)	P-97-0790 251099-16-8	
2-Propenoic acid, butyl ester, polymers with acrylamide, 2- [methyl[(perfluoro-C4-8-alkyl)sulfonyl]amino]ethyl acrylate and vinylidene chloride	P-98-0251 306978-04-1	
2-Propenoic acid, 2-methyl-, 3-(trimethoxysilyl)propyl ester, polymers with acrylic acid, 2- [methyl[(perfluoro-C4-8-alkyl)sulfonyl]amino]ethyl acrylate and propylene glycol monoacrylate, hydrolyzed, compds. with 2,2'- (methylimino)bis[ethanol]	P-98-1272 306977-58-2	
Hexane, 1,6-diisocyanato-,homopolymer, N-(hydroxyethyl)-N-methyl perfluoro-C4-8-alkane sulfonamides- and stearyl alc.-blocked	P-99-0188 306978-65-4	
Poly(oxy-1,2-ethanediyl), .alpha.-[2-(methylamino)ethyl]-.omega.- [(1,1,3,3-tetramethylbutyl)phenoxy]-, N-[(perfluoro-C4-8-alkyl)sulfonyl]derivs.	P-99-0319 306979-40-8	

Polymethylenepolyphenylene isocyanate and bis(4-NCO-phenyl)methane reaction products with 2-ethyl-1-hexanol, 2-butanone, oxime, N-ethyl-N-(2-hydroxyethyl)- 1-C4-C8 perfluoroalkanesulfonamide	CAS# P-94-2205	

References:

1. 3M. (date not specifed) Laboratory report of fluorochemicals in wild bird livers U.S. EPA Administrative Record AR226-0079: Report prepared for 3M, St. Paul, MN by 3M Environmental Laboratory Fluorine Analytical Chemistry Team (FACT). Study No. FACT-TOX-010.

2. 3M. (1998) Summary of the effects of PFC's on mitochondrial bioenergetics in vitro. U.S. EPA Administrative Record AR226-0169.

3. 3M. (1999a) Report of data for exploratory 28-day oral toxicity study in rats: telomer alcohol, telomer acrylate, [(CBI)], PFHS, PFOS. NOTOX project number 242933. Report prepared for 3M, St. Paul, MN by 3M Environmental Laboratory Fluorine Analytical Chemistry Team (FACT). Study No. FACT-TOX-120.3; NOTOX#24933 U.S. EPA Administrative Records AR226-0951 (metabolites) and AR226-1030a (full report).

4. 3M. (1999b) Perfluorooctane Sulfonate: current summary of human sera, health and toxicological data. U.S. EPA Administrative Record AR226-0548. Laboratory Fluorine Analytical Chemistry Team (FACT). Study No. FACT-GEN-011

5. 3M. (1999c) Fluorochemical use, distribution and release overview. U.S. EPA Administrative Record AR226-0550.

6. 3M. (1999d) Laboratory report: Analysis of FCs in samples of children's sera. U.S. EPA Administrative Record AR226-0961. Report prepared for 3M, St. Paul, MN by 3M Environmental

7. 3M. (2000a) TSCA 8(e) substantial risk notice: potassium perfluorooctanesulfonate (CASRN 2795-39-3) U.S. EPA Administrative Record AR226-1022.

8. 3M. (2000b) Attachment to Letter to C. Auer dated May 4, 2000 regarding the exploratory 28-day oral toxicity study with telomer alcohol, telomer acrylate, PFBS, PFHS, PFOS (positive control) by daily gavage in the rat followed by a 14/28 day recover period. NOTOX project 24933. U.S. EPA Administrative Record AR226-0153.

9. 3M. (2001a) TSCA 8(e) supplemental notice (Docket 8EHQ-1288-0373): N-ethyl perfluorooctanesulfonamid oethanol (N-EtFOSE) (CASRN 1691-99-2). U.S. EPA Administrative Record AR226-1021.

10. 3M. (2001b) TSCA 8(e) supplemental submission Docket No. 8EHQ-998-374 Perfluorooctane Sulfonate (PFOS): CAS# 2795-39-3 U.S. EPA Administrative Record AR226-1030a - sub Docket #42534, 2001.

11. 3M. (2001c) Executive Summary: Environmental monitoring - multi-city study water, sludge, sediment, POTW effluent and landfill leachate samples U.S. EPA Administrative Record AR226-1030a111.

12. 3M. (2001d) Analysis of PFOS, FOSA, and PFOA from various food matrices using HPLC electospray/mass spectrometry. In: Report prepared for 3M, St. Paul, MN by Centre Analytical Laboratories, Inc.. (State College, PA). Study No. 023-057:US EPA AR226-1030a.

13. 3M. (2002a) Interim Report #2: Determination of serum half-lives os several fluorochemicals U.S. EPA Administrative Record AR226-1086: Conducted by Occupational Medicine, Medical Department, 3M Company, St. Paul, MN, 2002.

14. 3M. (2002b) PFBS is a sustainable replacements for perfluorooctane sulfonate (PFOS)-based surfactants. http://cms.3m.com/cms/US/en/2-68/iilziFT/view.jhtml

15. Alexander B. (2001b) Mortality study of workers employed at the 3M Decatur facility. Final Report. Division of Environmental and Occupational Health, School of Public Health, University of Minnesota, April 26, 2001: Reviewed in "Letter from Mr. Charles Auer and Draft Hazard Assessment of PFOA and its Salts with Page 8 was corrected on 4/15/02" U.S. EPA Administrative Record AR226-1093, 2001b.

16. Alexander B. (2001c) Mortality study of workers employed at the 3M Decatur facility. Final Report. Division of Environmental and Occupational Health, School of Public Health, University of Minnesota, April 26, 2001: Reviewed in: Draft Assessment of perfluorooctane sulfonate and its salts, 2001c.

17. Bargagna S, Chiovato L, Dinetti D, Montanelli L, Giachetti C, Romolini E, Marcheschi M, Pinchera A. (1997) Neuropsychological development in a child with early-treated congenital hypothyroidism as compared with her unaffected identical twin. Eur J Endocrinol 136:100-4.

18. Bargagna S, Dinetti D, Pinchera A, Marcheschi M, Montanelli L, Presciuttini S, Chiovato L. (1999) School attainments in children with congenital hypothyroidism detected by neonatal screening and treated early in life. Eur J Endocrinol 140:407-13.

19. Bargagna S, Canepa G, Costagli C, Dinetti D, Marcheschi M, Millepiedi S, Montanelli L, Pinchera A, Chiovato L. (2000) Neuropsychological follow-up in early-treated congenital hypothyroidism: a problem-oriented approach. Thyroid 10:243-9.

20. Berthiaume J, Wallace KB. (2002) Perfluorooctanoate, perflourooctanesulfonate, and N-ethyl perfluorooctanesulfonamido ethanol; peroxisome proliferation and mitochondrial biogenesis. Toxicol Lett 129:23-32.

21. Biegel LB, Liu RC, Hurtt ME, Cook JC. (1995) Effects of ammonium perfluorooctanoate on Leydig cell function: in vitro, in vivo, and ex vivo studies. Toxicol Appl Pharmacol 134:18-25.

22. Biegel LB, Hurtt ME, Frame SR, O'Connor JC, Cook JC. (2001) Mechanisms of extrahepatic tumor induction by peroxisome proliferators in male CD rats. Toxicol Sci 60:44-55.

23. Bilott R. (1978) Lab test summaries for Dupont PFOA workers. Legal discover document. AJP001419; EID080234.

24. Burris JM, Olsen G, Simpson C, Mandel J. (2000) Determination of serum half-lives of several fluorochemicals: Interim Report #1. In: Study Sponsor: 3M Company, Corporate Occupational Medicine Department. US EPA AR226-0611.

25. Burris JM, Lundberg JK, Olsen G, Simpson C, Mandel J. (2002) Determination of serum half-lives of several fluorochemicals: Interim Report #2. In: Study Sponsor: 3M Company, Corporate Occupational Medicine Department. US EPA AR226-1086.

26. Butenhoff J, Costa G, Elcombe C, Farrar D, Hansen K, Iwai H, Jung R, Kennedy G, Jr., Lieder P, Olsen G, Thomford P. (2002) Toxicity of Ammonium Perfluorooctanoate in Male Cynomolgus Monkeys after Oral Dosing for 6 Months. Toxicol Sci 69:244-257.

27. Center for Disease Control. (2002) Final selection criteria and selection of nominations for chemicals or categories of environmental chemicals for analytical development and inclusion in future releases of the National Report on Human Exposure to Environmental Chemicals. Federal Register October 2, 2002, Volume 67, Number 194:62477-62478.

28. Cook JC, Murray SM, Frame SR, Hurtt ME. (1992) Induction of Leydig cell adenomas by ammonium perfluorooctanoate: a possible endocrine-related mechanism. Toxicol Appl Pharmacol 113:209-17.

29. Danish EPA. (2002) Analysis of PFOS-compounds in consumer products by means of chemicals analysis and according to product register information. OECD electronic PFOS forum.

30. DePierre JW. Effects on rodents of perfluorofatty acids. In: The Handbook of Environmental Compounds: Volume 3 Anthropogenic Compounds - Organofluorines (Neilson AH, ed), 2002;203 - 248.

31. DuPont. (2001) DuPont Zonyl Flurosurfactants for household and I&I applications. In: Reorder No.: H-91366.

32. OECD. (2002a) The updated copy of DuPont Product Stewardship on December 17, 2001. U.S. EPA Administrative Record AR226-1069.

33. DuPont. (2002b) FDA approves Zonyl for paper protection. http://www.dupont.com/corp/news/product/2002/pn07_22_02a_pf.html

34. DuPont. (2002c) The updated copy of the Telomer Research Program Presentation January 31, 2002. U.S. EPA Administrative Record AR226-1066.

35. Environ International Corporation (Environ). (2002) A Hazard Narrative for Perfluorooctanoate (PFOA).

36. Giesy JP, Kannan K. (2001) Global distribution of perfluorooctane sulfonate in wildlife. Environ Sci Technol 35:1339-42.

37. Giesy JP, Kannan K. (2001a) Perfluorooctanesulfonate and related fluorochemicals in fish-eating water birds. Prepared for 3M, St. Paul, MN June 20, 2001 US EPA Administrative Record 226-1030a.

38. Giesy JP, Kannan K. (2001b) Perfluorooctanesulfonate and related fluorochemicals in mink and river otters. Prepared for 3M, St. Paul, MN June 20, 2001 US EPA Administrative Record 226-1030a.

39. Giesy JP, Kannan K. (2001c) Perfluorooctanesulfonate and related fluorochemicals in marine mammals. Prepared for 3M, St. Paul, MN June 20, 2001 US EPA Administrative Record 226-1030a.

40. Giesy JP, Kannan K. (2001d) Perfluorooctanesulfonate and related fluorochemicals in fish tissues. Prepared for 3M, St. Paul, MN June 20, 2001 US EPA Administrative Record 226-1030a.

41. Giesy JP, Kannan K. (2002) Perfluorochemical surfactants in the environment. Environ Sci Technol 36:146A-152A.

42. Gutshall DM, Pilcher GD, Langley AE. (1989) Mechanism of the serum thyroid hormone lowering effect of perfluoro-n- decanoic acid (PFDA) in rats. J Toxicol Environ Health 28:53-65.

43. Guy WS, Taves DR, Brey WS. (1975) Organic fluorocompounds in human plasma: prevalance and characterization. In: Biochemistry involving carbon-fluorine bonds. A symposium sponsored by the Division of Fluorine and Biological Chemistry at the 170th meeting of the American Chemical Society. Chicago, IL. August 26, 1975. Washington DC:American Chemical Society, 1976;117 - 134.

44. Hansen KJ, Johnson HO, Eldridge JS, Butenhoff JL, Dick LA. (2002) Quantitative characterization of trace levels of PFOS and PFOA in the Tennessee River. Environ Sci Technol 36: 1681-5.

45. Harris MW, Uraih LC, Birnbaum LS. (1989) Acute toxicity of perfluorodecanoic acid in C57BL/6 mice differs from 2,3,7,8-tetrachlorodibenzo-p-dioxin. Fundam Appl Toxicol 13:723-36.

46. Haughom B, Spydevold O. (1992) The mechanism underlying the hypolipemic effect of perfluorooctanoic acid (PFOA), perfluorooctane sulphonic acid (PFOSA) and clofibric acid. Biochim Biophys Acta 1128:65-72.

47. Hill RN, Crisp TM, Hurley PM, Rosenthal SL, Singh DV. (1998) Risk assessment of thyroid follicular cell tumors. Environ Health Perspect 106:447-57.

48. Hu W, Jones PD, Upham BL, Trosko JE, Lau C, Giesy JP. (2002) Inhibition of gap junctional intercellular communication by perfluorinated compounds in rat liver and dolphin kidney epithelial cell lines in vitro and Sprague-Dawley rats in vivo. Toxicol Sci 68:429-36.

49. Hurley PM. (1998) Mode of carcinogenic action of pesticides inducing thyroid follicular cell tumors in rodents. Environ Health Perspect 106:437-45.

50. Ikeda T, Aiba K, Fukuda K, Tanaka M. (1985) The induction of peroxisome proliferation in rat liver by perfluorinated fatty acids, metabolically inert derivatives of fatty acids. J Biochem (Tokyo) 98:475-82.

51. Kannan K, Franson JC, Bowerman WW, Hansen KJ, Jones PD, Giesy JP. (2001) Perfluorooctane sulfonate in fish-eating water birds including bald eagles and albatrosses. Environ Sci Technol 35:3065-70.

52. Kannan K, Choi JW, Iseki N, Senthilkumar K, Kim DH, Giesy JP. (2002) Concentrations of perfluorinated acids in livers of birds from Japan and Korea. Chemosphere 49:225-31.

53. Keller BJ, Marsman DS, Popp JA, Thurman RG. (1992) Several nongenotoxic carcinogens uncouple mitochondrial oxidative phosphorylation. Biochim Biophys Acta 1102:237-44.

54. Keller BJ, Yamanaka H, Thurman RG. (1992) Inhibition of mitochondrial respiration and oxygen-dependent hepatotoxicity by six structurally dissimilar peroxisomal proliferating agents. Toxicology 71:49-61.

55. Langley AE, Pilcher GD. (1985) Thyroid, bradycardic and hypothermic effects of perfluoro-n-decanoic acid in rats. J Toxicol Environ Health 15:485-91.

56. Liu RC, Hurtt ME, Cook JC, Biegel LB. (1996) Effect of the peroxisome proliferator, ammonium perfluorooctanoate (C8), on hepatic aromatase activity in adult male Crl:CD BR (CD) rats. Fundam Appl Toxicol 30:220-8.

57. Mabury SA. (Year) Fascinating fluorofacts of perfluorinated alkylcarboxylates and sulfonates. In: Society of Environmental Toxicology and Chemistry (SETAC). November 16-20, Salt Lake City, Utah, USA., 2002.

58. Martin JW, Muir, D.C.G., Moody, C.A., Ellis, D.A., Kwan, W.C. Solomon, K.R. and Mabury, S.A. (in press) Collection of airborne fluorinated organics and analysis by gas chromatography/chemical ionization mass spectrometry. Analytical Chemistry.

59. Muir DCG, Scott B, Spencer C, Teixeira C, Alaee M, Cannon C, Wang X, Yang F, Mabury SA, Martin J. (Year) Latitudinal trends of perfluorinated acids and brominated diphenyl ethers in eastern North America inferred from lake water and dated sediment cores. In: Society of Environmental Toxicology and Chemistry (SETAC). November 16-20, Salt Lake City, Utah, USA., 2002.

60. Mullen R. (2001) 3M develops flame retardants. Chemical Week February 7, 2001.

61. OECD. (2002) Draft Assessment of perfluorooctane sulfonate (PFOS) and its salts: Complete assessment. September 16, 2002 ENV/JM/RD(2002)17.

62. Olsen GW, Gilliland FD, Burlew MM, Burris JM, Mandel JS, Mandel JH. (1998) An epidemiologic investigation of reproductive hormones in men with occupational exposure to perfluorooctanoic acid (Reviewed in "Letter from Mr. Charles Auer and Draft Hazard Assessment of PFOA and its Salts with Page 8 was corrected on 4/15/02" U.S. EPA Administrative Record AR226-1093). J Occup Environ Med 40:614-22.

63. Olsen GW, Burris JM, Mandel JH, Zobel LR. (1999) Serum perfluorooctane sulfonate and hepatic and lipid clinical chemistry tests in fluorochemical production employees. J Occup Environ Med 41:799-806.

64. Olsen GW, Burris JM, Lundberg JK, Hansen KJ, Mandel JH, Zobel LR. (2002a) Final Report: Identification of fluorochemicals in human sera. III. Pediatric participants in a group A streptococci clinical trial investigation U.S. EPA Administrative Record AR226-1085: Study conducted by Corporate Occupational Medicine, Medical Department, 3M Company, 220-3W-05, St. Paul, MN, 2002.

65. Olsen GW, Burris JM, Lundberg JK, Hansen KJ, Mandel JH, Zobel LR. (2002b) Final Report: Identification of fluorochemicals in human sera. I. American Red Cross Adult Blood Donors U.S. EPA Administrative Record AR226-1083: Study conducted by Corporate Occupational Medicine, Medical Department, 3M Company, 220-3W-05, St. Paul, MN, 2002.

66. Olsen GW, Burris JM, Lundberg JK, Hansen KJ, Mandel JH, Zobel LR. (2002c) Final Report: Identification of fluorochemicals in human sera. II. Elderly participants of the adult changes in thought study, Seattle, Washington U.S. EPA Administrative Record AR226-1083: Study conducted by Corporate Occupational Medicine, Medical Department, 3M Company, 220-3W-05, St. Paul, MN, 2002.

67. Pastoor TP, Lee KP, Perri MA, Gillies PJ. (1987) Biochemical and morphological studies of ammonium perfluorooctanoate-induced hepatomegaly and peroxisome proliferation. Exp Mol Pathol 47:98-109.

68. Purdy, R. (2002) Former 3M Senior Ecotoxicologist, personal communication.

69. Rovet JF, Ehrlich R. (2000) Psychoeducational outcome in children with early-treated congenital hypothyroidism. Pediatrics 105:515-22.

70. Starkov AA, Wallace KB. (2002) Structural determinants of fluorochemical-induced mitochondrial dysfunction. Toxicol Sci 66:244-52.

71. Takayama S, Sieber SM, Dalgard DW, Thorgeirsson UP, Adamson RH. (1999) Effects of long-term oral administration of DDT on nonhuman primates. J Cancer Res Clin Oncol 125:219-25.

72. Telomer Research Program. (2000) Telomer Research Program update and status Report, presented to U.S EPA, OPPT 23 October, 2000 and Draft Protocols. Reviewed in US EPA AR226-0947.

73. Upham BL, Deocampo ND, Wurl B, Trosko JE. (1998) Inhibition of gap junctional intercellular communication by perfluorinated fatty acids is dependent on the chain length of the fluorinated tail. Int J Cancer 78:491-5.

74. US EPA. (1999) 3M submission: Perfluorooctane sulfonate: Current summary of human sera, health and toxcicology data U.S. EPA Administrative Record AR226-0548.

75. US EPA. (2000a) Forty-fifth report of the TSCA Interagency Testing Committee to the Administrator, Receipt of report and request for comments; Notice. Federal Register December 1, 2000, Volume 65, Number 232: 75543-75550

76. US EPA. (2000b) Forty-sixth report of the TSCA Interagency Testing Committee to the Administrator of the Environmental Protection Agency; Receipt of report and request for comments. Federal Register December 1, 2000, Volume 65, Number 232:75551-75561

77. US EPA. (2001) Analysis of PFOS, FOSA, and PFOA from various food matrices using HPLC electrospray/mass spectrometry U.S. EPA Administrative Record AR226-1030a154: 3M study conducted by Centre Analytical Laboratories, Inc.,

78. US EPA. (2002a) Draft hazard assessment of PFOA and its salts February 20, 2002 U.S. EPA Administrative Record AR226-1079.

79. US EPA. (2002b) Revised draft hazard assessment of PFOA and its salts November 4, 2002 U.S. EPA Administrative Record AR226-in progress addition.

80. US EPA. (2002c) Perfluoroalkyl Sulfonates; Proposed Significant New Use Rule. Action: Supplemental proposed rule. Federal Register March 11, 2002, Volume 67, Number 47:11014-11030.

81. US EPA. (2002d) Perfluoroalkyl Sulfonates; Proposed Significant New Use Rule. Action: Final Rule. Federal Register March 11, 2002, Volume 67, Number 47:11007-11013

82. US EPA. (2002e) Forty-ninth report of the TSCA Interagency Testing Committee to the Admintrator of the Environmental Protection Agency; Receipt of report and request for comments. Federal Register March 6, 2002, Volume 67, Number 44:10297-10307.

83. US EPA (2002f). Memorandum, dated September 27, 2002, from Charles M. Auer to Oscar Hernandez, Mary Ellen Weber, and Ward Penberthy re Revision of PFOA hazard assessment and next steps. US EPA Administrative Record Number AR226-1127.