Chapter 4
PFAS Biomonitoring in Higher Exposed Populations

Geary W. Olsen

Abstract Perfluoroalkyl and polyfluoroalkyl substances (PFAS) have a wide range of applications as a result of their chemical and thermal stability of the C-F bond and their hydrophobic and lipophobic characteristics. Because of these unique physical and chemical properties there have been numerous industrial and consumer applications. These characteristics have also resulted in the widespread presence and persistence of PFAS in the environment and detection in biological tissue in humans.

In general, biomonitoring trend studies of the PFAS, in particular PFOS and PFOA, within the general population have shown marked declines in PFOS since a May 2000 phase-out announcement by a major manufacturer. The trends, however, for PFOA are more inconclusive as multiple manufacturers of PFOA and its various precursors (e.g., fluorotelomer alcohols) remain.

Higher exposed populations can be defined by identifiable exposures (e.g., environmental, occupational) that have resulted in serum, plasma, or whole blood concentrations of PFASs that are substantively larger than those reported in the general population. Although some investigators refer to these populations as 'highly exposed', this description does not sufficiently describe the magnitude of exposure that occurs within these populations and/or individuals. Thus, the term 'higher' is preferred.

For the purpose of this chapter, higher exposed populations and their serum concentrations are described into three categories: (1) PFAS manufacturing and 'downstream' production workers; (2) communities affected by specific identifiable sources of PFAS exposure (above background levels) through municipal and/or private water sources; and (3) medical, occupational, and consumer PFAS-related exposures that were targeted to a well-defined group of individuals. Each of these three higher exposure populations are reviewed separately for their biomonitoring data and then compared jointly.

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PFAS manufacturing workers had serum concentrations 2–3 orders of magnitude higher than those reported in the general population. Depending upon the communities whose drinking water sources were affected with PFAS, these populations tended to have average serum concentrations ranging between 2× and <1 order of magnitude higher than the general population. Individuals, however, within these communities may have had comparable concentrations to those at the higher levels within the manufacturing sector. Likewise, depending on the specific medical, occupational, and/or consumer exposures, there may have been substantively higher exposures to PFOS and PFOA than reported in the general population.

Keywords Perfluorochemicals • Perfluoroalkyl and polyfluoroalkyl substances • PFAS • Perfluorooctanesulfonate • PFOS • Perfluorooctanoate • PFOA • Biomonitoring

4.1 Introduction

4.1.1 Brief Review of General Population Trends

As discussed in Chap. 1 (Lau 2014), perfluoroalkyl and polyfluoroalkyl substances (PFAS) have a wide range of applications as a result of their chemical and thermal stability of the C-F bond and their hydrophobic and lipophobic characteristics. Because of these unique physical and chemical properties there are numerous industrial and consumer applications. These include surfactant (e.g., use in fluoropolymer synthesis, coatings, and aqueous film-forming-foams (AFFF)) and polymer applications (e.g., use in textiles as stain and soil repellents (e.g., carpet, clothes) and grease-proof, food contact paper) (Buck et al. 2011).

Because of their widespread presence and persistence in the environment and detection in biological tissue in humans, there has been an effort to understand PFAS exposure sources and pathways as well as potential associations with human health. In particular, this exposure research has focused on 'long chain' PFASs defined as perfluoroalkyl sulfonic acids with six or more perfluorinated carbons and perfluoroalkyl carboxylic acids with six or more perfluorinated carbons, respectively (Buck et al. 2011).

Multiple sources of potential exposure to PFAS in the environment have been identified in the general (nonoccupational) human population. These sources include food intake and packaging, drinking water (municipal and private wells), indoor (house and office) and outdoor air, and dust (Fromme et al. 2009; Domingo 2012). Dietary intake has been considered an important source of human exposure by some investigators (Fromme et al. 2009; Domingo 2012) but others have questioned this assumption noting the declining PFOS concentrations in the general

population without comparable declines of PFOS in the diet suggesting indirect sources of exposure through transformation of precursors (D'Eon and Mabury 2011; Buck et al. 2011). Although precursors of perfluorooctanesulfonate (PFOS) and perfluorooctanoate (PFOA) have not been considered a major source of exposure, subgroups of the population may be at higher risk. In general, PFAS in municipal water supplies are measured in the very low ng/L levels unless the community has been affected by specific industrial and/or environmental exposures (Fromme et al. 2009).

As detailed in the previous chapter, PFAS biomonitoring trend studies of general populations have been conducted in the United States (Kato et al. 2011; Olsen et al. 2012a), Australia (Toms et al. 2014), Germany (Yeung et al. 2013a, b), Norway (Nøst et al. 2014), and Sweden (Glynn et al. 2012; Sundström et al. 2011). Few trend studies have involved repeated measurements from the same, albeit small number, of individuals (Olsen et al. 2012a; Nøst et al. 2014). The other biomonitoring trend studies were periodic cross-sectional analyses of a general population. Collectively, these studies have analyzed and reported on 23 PFASs although only two, PFOS and PFOA, were routinely reported in these and many other studies. In general, these biomonitoring trend studies have shown declines in PFOS in the general population since the May 2000 announcement of the phase-out of perfluorooctanyl related materials by the 3M Company (3M). Results, however, for PFOA were more inconclusive as other manufacturers of PFOA remained after this phase-out including production of potential PFOA precursors (e.g., 8:2 fluorotelomer alcohol) (Buck et al. 2011; Fasono et al. 2006).

The 23 PFASs included a series of perfluoroalkyl sulfonic acids [perfluorobutanesulfonate (PFBS), perfluorohexanesulfonate (PFHxS), several precursors of PFOS, the homologue series of perfluoroalkyl carboxylic acids (C4 through C12), and their various precursors. The precursors of PFOS included N-ethyl perfluorooctanesulfonamidoacetate (EtFOSAA), an oxidation product of N-ethyl perfluorooctanesulfonamidoethanol (EtFOSE) which was primarily used in the building block of the phosphate ester in paper and packaging protectant applications, and N-methyl perfluorooctanesulfonamidoacetate (MeFOSAA), an oxidation product of N-methyl perfluorooctanesulfonamidoethanol (MeFOSE) that was primarily incorporated into polymer surface treatments for carpet and textile applications (Buck et al. 2011; Yeung et al. 2013b). Both compounds likely metabolize to perfluorooctanesulfonamidoacetate (FOSAA) and then to perfluorooctanesulfonamide (FOSA) (Xu et al. 2004, 2006). FOSA metabolizes to PFOS. FOSA can also be a metabolite of EtFOSE-based polyfluoroalkyl phosphate ester (di-SAmPAP) used in food contact paper. Precursors of perfluoroalkyl carboxylic acids include several polyfluoroalkyl phosphate esters which are a class of fluorotelomer-based commercial products of various fluorinated chain lengths with phosphate mono-, di-, or triesters (Yeung et al. 2013b) and the 8:2 fluorotelomer alcohol (Fasono et al. 2006, 2009).

4.1.2 Higher Exposed Populations

For the purpose of this chapter, "higher exposed" populations were defined by identifiable exposures (e.g., environmental, occupational) that resulted in larger serum, plasma, or whole blood concentrations of PFASs than those reported in the general population. Although some investigators refer to these populations as 'highly exposed', this description does not sufficiently describe the magnitude of exposure that occurs in these populations. A community may be referred to as "highly exposed" to PFASs but could be orders of magnitude lower than an occupationally exposed population, or, as will be discussed later, comprise individuals that may have exposures higher than individuals who are occupationally exposed through manufacturing. Unlike the general population, biomonitoring of higher exposed human populations have, in general, reported fewer PFAS compounds. This may be due to the specificity of exposure and therefore more targeted measurements. Nevertheless, PFOS and PFOA remain the most frequently measured compounds regardless of the type of population studied.

For the purpose of this chapter, higher exposed populations are categorized as follows: (1) PFAS manufacturing and 'downstream' production workers; (2) communities affected by specific identifiable sources of PFAS exposure (above background levels) through municipal and/or private water sources; and (3) medical, occupational, and consumer PFAS-related exposures that were targeted to a well-defined group of individuals. Each of these three categories will be reviewed separately for the biomonitoring (serum, plasma, whole blood) data reported, and then compared jointly in the chapter summary.

Provided in this chapter are summaries of PFAS concentrations measured in these higher exposed populations. The primary PFASs reviewed are PFOS and PFOA due to the frequency of measurement and reports. Not discussed in this chapter are the analytical methods and quality control procedures that were employed by the study investigators. An overview of the analytical laboratory methods that have evolved over time to measure PFASs can be found in Chap. 2. The original papers cited in this chapter should be examined by the reader to assess the precision and reliability of the analytical capabilities that were employed by the study investigators at the time of their analyses.

4.2 PFAS Manufacturing and 'Downstream' Production

Prior to its phase-out of perfluorooctanyl chemistry, the 3M Company was considered the primary manufacturer of perfluorooctanesulfonyl fluoride (POSF)-related materials but only one of several manufacturers/users of PFOA. Furthermore, there were other fluorochemical manufacturers whose product line (e.g., fluorotelomer alcohols) may degrade, to a limited degree, to PFOA. At 3M, POSF and PFOA were manufactured through electrochemical fluorination (ECF) that yielded

characteristic linear to branch isomer ratios (Buck et al. 2011). PFOA can also be manufactured by telomerization that results in a linear isomer. Because of its widespread environmental presence and persistence, in 2006 the US EPA invited eight fluoropolymer and telomer manufacturers to participate in a global stewardship program focused on the goal of working towards the elimination of PFOA and precursor chemicals as well as higher homologues by 2015 (US EPA 2006). These companies were Arkema, Asahi, BASF (successor to Ciba), Clariant, Daikin, 3M/Dyneon, DuPont, and Solvay Solexis.

Similar agreements have been obtained in other nations including perfluorocarboxylic acids in Canada (Environment Canada 2010) and PFOS in European Union countries (European Parliament 2006). PFOS was listed as an Annex B (restricted in its use) substance in the Stockholm Convention on Persistent Organic Pollutants (UN Environmental Programme 2009). Upon 3M's phase-out of PFOS production, the production of POSF–related materials in some countries, particularly China, increased (Zhang et al. 2012; Xie et al. 2013).

Among the fluorochemical, fluoropolymer and fluorotelomer manufacturers, 3M and DuPont have frequently published their biomonitoring data and therefore this information was available in peer-reviewed scientific literature and publicly accessible repositories of information (e.g., AR-226 docket of the US EPA). One other company, Miteni, had published company-specific biomonitoring (PFOA) data in the published scientific literature (Costa et al. 2009), prior to this company's phase-out of PFOA. It is possible that other PFAS biomonitoring analyses of fluorochemical and fluoropolymer manufacturing workers may have been analyzed but such information was not available in the published scientific literature.

4.2.1 3M Company

There have been four 3M Company manufacturing plants involved with the manufacture of PFAS-related materials located in the United States (Cottage Grove, Minnesota; Decatur, Alabama; Cordova, Illinois) and Belgium (Antwerp).

4.2.1.1 Cottage Grove (Minnesota)

The Cottage Grove plant manufactured the ammonium salt of perfluorooctanoic acid (APFO). APFO rapidly dissociates in the blood to PFOA (the anion) where it is bound to proteins. APFO production began at the Cottage Grove plant in 1947 and was phased-out after the May 2000 announcement by the company. Primary users included external customers (major customer was DuPont) and internal applications within the 3M/Dyneon operations. The production of APFO was a multistep process that included the following steps (Olsen et al. 2000, 2003a): electrochemical fluorination, stabilization, fractionation, distillation, purification, the addition of ammonium, drying of the salt, and packaging. The production of the

APFO could result in potential for inhalation exposure of the vapor or particulate from regular production tasks and equipment cleaning responsibilities (Raleigh et al. 2014). Exposure may also have occurred from incidental spills and background air concentration levels. Dermal and ingestion were other potential exposure pathways although deemed less likely than inhalation.

Salts of perfluorooctanesulfonate (PFOS) were manufactured at Cottage Grove but since the 1970s perfluorooctanesulfonyl fluoride (POSF), the starting material for related materials, was manufactured, through the ECF process, elsewhere (Decatur and Antwerp). Salts of shorter chain PFASs have also been manufactured at Cottage Grove (Olsen et al. 2003a, 2009).

Serum total organic fluorine (TOF) was used to estimate Cottage Grove workers' serum PFOA concentrations in the 1980s until 1993 when PFOA was then speciated by high performance liquid chromatography mass spectrometry (Gilliland and Mandel 1996; Olsen et al. 1998, 2000). TOF was considered not sufficiently specific for PFOA due to the potential for other perfluoroalkyl exposures to contribute. This includes the longer chain PFOS and more recently short-chain perfluoroalkyls at this facility (e.g., lithium bis(trifluoromethane-sulfonyl)imide, potassium salt of perfluorobutanesulfonate). Historic TOF measurements at Cottage Grove also used a higher limit of quantitation (LOQ) < 1.0 ppm (Gilliland and Mandel 1996). As a consequence, many jobs with PFOA exposures could not be quantified. For example, of the 115 Cottage Grove workers who volunteered for the 1990 fluorochemical medical surveillance program, 23 (20 %) had TOF values reported <1.0 ppm (Gilliland and Mandel 1996).

Beginning in 1993, measurement of serum concentration of PFOA was included in the periodic voluntary medical surveillance programs in the chemical division. The median PFOA concentrations reported in 1993 (n = 111), 1995 (n = 80), 1997 (n = 74), and 2000 (n = 148) were 1,100 ng/mL, 1,200 ng/mL, 1,300 ng/mL, and 810 ng/mL, respectively, with mean concentrations approximately five times higher as a consequence of the log normal distribution (Olsen et al. 2000, 2003a; Olsen and Zobel 2007). The great majority of participants were male workers. The highest PFOA concentration measured was 114,100 ng/mL in 1997 (Olsen et al. 2000). PFOA and PFOS concentrations were production process-related as seen in Fig. 4.1 for the 117 male employees who participated in 2000. These data indicate TOF would be a biased estimate for either PFOA or PFOS at the Cottage Grove facility.

Because of these limitations using TOF to estimate PFOA at the Cottage Grove site, Raleigh et al. (2014) incorporated PFOA air sampling data, both personal and environmental, in their task-based job/department exposure matrix for their Cottage Grove cohort mortality and cancer incidence study. Industrial hygiene data characterizing APFO exposure in the air within the chemical division (205 personal samples and 659 area samples) were collected between 1977 and 2000. These samples represented all processes and tasks related to APFO production. Production processes prior to 1977 involved the same procedures and tasks but exposure was less due to lower production volume. An air (mg/m^3) time-weighted average (TWA) was calculated for APFO exposure for specific department, job, work area, equipment, tasks, and year groupings to create an exposure data matrix that contained 23

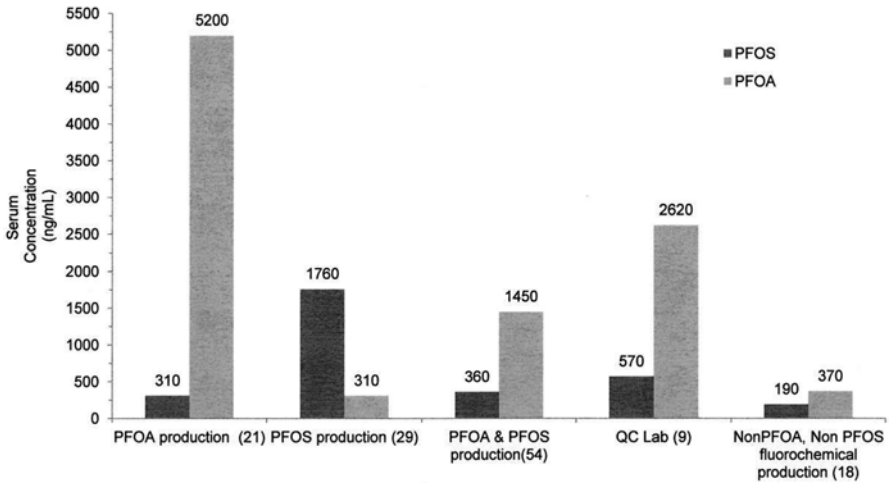

Fig. 4.1 Cottage Grove Manufacturing site, geometric mean serum PFOS and PFOA concentrations, medical surveillance program by major job classifications, (N = 117) male employees, 2000

departments and 45 job titles within the chemical division for all production years (1947–2002). This task-based exposure model incorporated the amount of time spent during an 8 h shift in up to three predefined work task areas: (1) exposure-associated tasks in the production area, (2) nonexposure associated tasks in the production area, and (3) tasks outside the production area. TWAs for jobs in APFO production ranged from 1×10^{-4} mg/m^3 to 4.0×10^{-1} mg/m^3. TWAs estimated for non-APFO production areas within the chemical division were estimated to range between 1×10^{-8} mg/m^3 and 3×10^{-5} mg/m^3. Exposures within the non-chemical division were considered to be between 1×10^{-8} mg/m^3 and 1×10^{-6} mg/m^3.

As a measure of external validity, Raleigh et al. (2014) reported PFOA concentrations for the year 2000 fluorochemical medical surveillance program's 50 participants who worked only in the APFO-related manufacturing area had a geometric mean serum PFOA concentration of 2,538 ng/mL (95 % CI 1,626–3,961 ng/mL). Those who partially worked in the APFO production area had a geometric mean PFOA of 979 ng/mL (95 % CI 565 ng/mL–1,695 ng/L). Those who never worked in the PFOA manufacturing area but still within the chemical division had a geometric mean PFOA of 282 ng/mL (95 % CI 194–410 ng/mL).

Materials derived from perfluorobutanesulfonyl fluoride (PBSF) have been introduced by 3M as replacement chemistry for some PFOS-related materials. The N-alkyl derivatives of perfluorobutanesulfonamides are used in various applications including fabric, carpet, and upholstery protectants as well as surfactant applications. Atmospheric degradation of N-methyl perfluorobutanesulfonamidoethanol has been shown to produce among other degradation products, PFBS (D'eon et al. 2006). Six Cottage Grove employees who had finished a semi-annual batch production of the potassium salt of PFBS participated in a 6-month follow-up pharmacokinetic-related study (Olsen et al. 2009). At study onset, shortly after

production was completed, the employees' mean serum PFBS concentration was 397 ng/mL (range 92–921 ng/mL). At study completion the geometric mean serum elimination half-life was calculated at 25.8 days (95 % CI 16.6–40.2) as compared to 4.8 years (95 % CI 4.0–5.8) for PFOS in a study of 26 retired fluorochemical production workers (Olsen et al. 2007). Urine was a major route of PFBS elimination as concentrations early in the study ranged from 5 to 173 ng/mL and declined during the study such that all measurements by end-of-study were less than the LOQ (5 ng/mL). ECF production of PBSF occurs at the 3M Antwerp and Cordova plants. Production of PFBS-related materials has occurred at all four 3M plants (Cottage Grove, Decatur, Cordova, Antwerp).

4.2.1.2 Decatur (Alabama)

The 3M Decatur manufacturing site consists of two plants: Specialty Film (film plant) and Specialty Materials (chemical plant) (Olsen et al. 1999b, 2003b). PFASs were not significantly used in the film plant except for one product line. On the other hand, hundreds of different manufacturing processes were run in the chemical plant with the majority batch operations that occurred in several buildings. The three major product groups were: protective chemicals, performance chemicals, and fluoroelastomers. Raw materials and intermediates for each product group went through several different production buildings before packaging and shipment. Perfluorooctanesulfonyl fluoride (POSF) was the base chemical until its phase-out announced in 2000. Essentially, octyl mercaptan reacted with chlorine and ammonium to produce octanesulfonyl fluoride (OSF). OSF became the cell feed for ECF to produce POSF, the precursor to the production of a variety of perfluorinated amides, alcohols, acrylates, and other fluorochemical polymer materials manufactured as protective and performance chemicals. PFOA was also manufactured by ECF for limited time periods at Decatur. This production occurred in the majority of months in 1969, 1977, 1978, 1999, and 2000 and a few months in 1967, 1970, and 1972–1974 (personal communication, David Courington). PFOA was also produced as a by-product (residual) of POSF ECF. Also manufactured were intermediate products and surface active chemicals (e.g., AFFFs). PFHxS was produced via the ECF process for use primarily in performance chemicals such as fire suppression liquids. Fluoroelastomers were manufactured from combinations of tetrafluoroethylene, chlorotrifluoroethylene, hexafluoropropylene and vinylidene fluoride. Upon the phase-out of PFOS, the shorter chain PBSF replaced POSF as the basic building block for protective and performance chemicals. ECF production of PBSF occurs at the Cordova, Illinois and Antwerp, Belgium manufacturing plants. The ECF operations at Cottage Grove and Decatur were demolished after the company's phase-out of perfluorooctanyl products (Olsen et al. 2012 b).

Prior to 1995, serum TOF was measured in the Decatur voluntary medical surveillance examinations. Beginning in 1995, PFOS was specifically measured by liquid chromatography-tandem mass spectrometry (LC-MS/MS) during these examinations (Olsen et al. 1999a), as well as PFOA. In 1998 a random sample of the

chemical and film plant employee population was examined for several PFASs with statistical analyses stratified by the workers' major job categories (Olsen et al. 1999b, 2003b). A total of 126 chemical plant employees participated in the random sample (80 % of targeted sample). Presented in Table 4.1 are measures of central tendency from this study. The geometric mean serum concentrations for PFOS and PFOA were 941 ng/mL and 899 ng/mL, respectively. The highest PFOS and PFOA concentrations were 10,600 ng/mL and 6,760 ng/mL, respectively. [Note: The highest PFOS concentration ever reported at Decatur was 12,830 ng/mL in an employee in the 1995 voluntary medical surveillance examinations (Olsen et al. 1999a).] Presented in Fig. 4.2 are the geometric mean (GM) concentrations reported for five PFASs stratified by seven major job categories from this Decatur random sample of employees. Findings from this study showed that combined serum concentrations of PFOS and PFOA accounted for 86 % of the serum TOF that was measured. This suggested historical TOF measurements could not be considered specific to any one PFAS.

In 2000, at the onset of the company's announced phase-out, a total of 263 Decatur employees voluntarily participated in the medical surveillance program (Olsen et al. 2001a, 2003a; Olsen and Zobel 2007). Except for PFOA, the serum concentrations were comparable to those measured in the 1998 random sample (Table 4.1). The geometric mean serum PFOA concentration had increased due to the start-up of ECF production of PFOA in 1999.

A total of 24 of the 26 retirees that were followed for 5 years to estimate their serum elimination half-life were from the Decatur plant (Olsen et al. 2007). The other two retirees were from the Cottage Grove plant. This study calculated geometric mean half-lives of PFOS and PFOA of 4.8 years (95 % CI 4.0–5.7) and 3.5 years (95 % CI 3.0–4.1). Russell et al. (2014) estimated the half-life for PFOA among those retirees (n = 7) whose initial concentrations were >500 ng/mL was 3.0 years (95 % CI 2.4–3.8). This would result in minimal bias (1 %) in the calculation of an intrinsic half-life for PFOA due to the highly elevated initial concentrations and long sampling duration of almost two half-lives. Analysis of the apparent half-lives of retirees whose initial concentrations were less than 500 ng/mL had biased upward estimates up to 13 % with the lowest initial concentrations (~70 ng/mL) (Russell et al. 2014).

4.2.1.3 Cordova (Illinois)

3M Cordova manufactures specialty chemicals, adhesives, and fluorinated chemicals for the company's internal and external customers. As part of this product-mix, the plant manufactures PBSF, C3/C4 acid fluorides, and hydrofluoroethers. Unlike Cottage Grove or Decatur, the Cordova plant was not a primary manufacturer of APFO or PFOS-related materials, One production that did occur was that of a post-market carpet protectant. Voluntary biomonitoring of Cordova employees was conducted in 1997 (n = 66). Median concentrations of PFOS and PFOA were 151 ng/mL and 100 ng/mL, respectively.

Table 4.1 PFAS measures of central tendency, Decatur biomonitoring random sample (1998) and medical surveillance results, Decatur and Antwerp, 2000

	Decatur 1998 random sample				Decatur 2000 medical surveillance				Antwerp 2000 medical surveillance			
	(N = 126 employees)				(N = 263 chemical employees)				(N = 258 employees)			
	AM	Range	GM	95 % CI	AM	Range	GM	95 % CI	AM	Range	GM	95 % CI
PFOS	1,505	91–10,600	941	790–1,130	1,320	60–10,060	910	820–1,020	800	40–6,240	440	380–510
PFOA	1,536	21–6,760	899	720–1,120	1,780	40–12,700	1,130	990–1,300	840	10–7,040	330	270–400
PFHxS	345	5–1,880	180	150–220	300	7–1,670	180	160–210	170	1–1,430	70	60–80
N-Me-FOSE-AcOH	150	8–992	81	70–100	250	8–992	110	100–130	150	3–1,060	60	50–70
N-Et-FOSE-AcOH	23	1–269	8	6–10	60	3–440	40	10–40	20	3–140	9	8–10

AM = Arithmetic Mean
GM = Geometric Mean

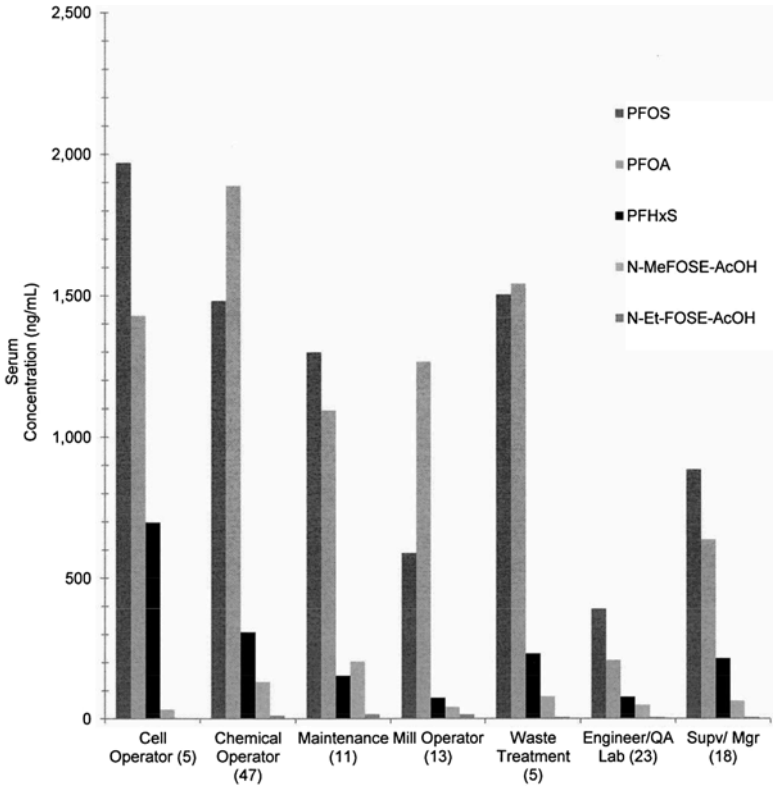

Fig. 4.2 Decatur manufacturing site, geometric mean serum PFOS and PFOA serum concentrations (ng/mL) by major job classifications, random sample (N = 128), 1998

4.2.1.4 Antwerp (Belgium)

Beginning in the mid-1970s and similar to Decatur production processes, POSF was the base material produced by ECF at the Antwerp plant that was the precursor to the production of PFOS-based protective and performance materials (Olsen et al. 2001b). Also manufactured were intermediate products, end-products (PFOA), inerts, and surface active chemicals (fire fighting foams). Synthetic fluoroelastomers were manufactured from hexafluoropropylene and vinylidene fluoride. Nonfluorochemical production involved phenolic resins, acrylate polymers and adhesives, polyurethane polymers, and acrylates.

Beginning in 1995, voluntary participation by employees in medical surveillance activities involved LC-MS/MS measurement of PFOS and PFOA (Olsen et al. 1999a, 2001b, 2003c; Olsen and Zobel 2007). These analyses showed serum PFOS,

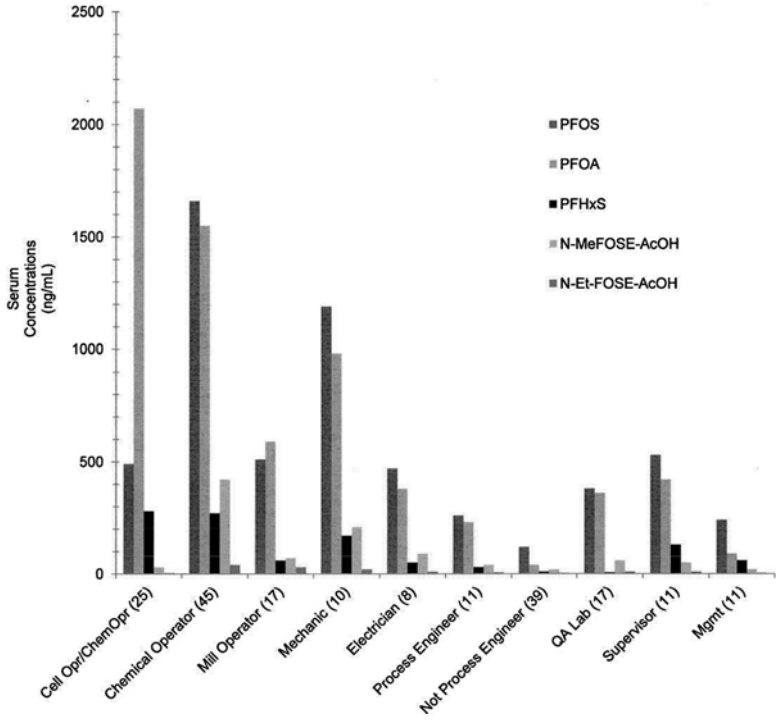

Fig. 4.3 Antwerp manufacturing site, geometric mean serum PFOS and PFOA concentrations (ng/mL), by major job classifications, medical surveillance program (N = 258), 2000

PFOA, and other PFAS-related serum levels were generally lower than those observed among Decatur employees. For example, in 1995 and 1997 the mean PFOS concentrations in Antwerp workers were 1,930 ng/mL and 1,480 ng/mL compared to the Decatur workforce at 2,440 ng/mL and 1,960 ng/mL, respectively (Olsen et al. 1999a, b).

In the 2000 voluntary medical surveillance examinations, the Antwerp mean serum PFOS and PFOA concentrations were 800 ng/mL and 840 ng/mL, respectively. The distributions were log normal as the geometric means were 440 ng/mL and 330 ng/mL, respectively (Table 4.1). Highest PFOS and PFOA concentrations measured in 2000 at Antwerp were 6,240 ng/mL and 7,040 ng/mL, respectively. Figure 4.3 shows the geometric mean concentrations for five PFASs stratified by seven major job categories from the 2000 Antwerp medical surveillance data.

4.2.1.5 Decommission, Demolition and Disposal Activities (3M Cottage Grove and Decatur)

PFAS biomonitoring was conducted among workers who decommissioned, demolished and disposed of former PFAS manufacturing facilities (Olsen et al. 2012b). These facilities included the APFO manufacturing buildings at Cottage Grove and

the ECF cell building operations at Decatur. Decommission work involved pipe and equipment removal and disposal. Because of the uniqueness of this work, the extent of potential exposures was unknown. Therefore, as part of the decommissioning work, an exclusion work zone was established that required anyone entering the area to have appropriate training, personal protective equipment, and participate in a medical monitoring program. The latter included baseline and end-of-project blood collections for the determination of PFOA and PFOS serum concentrations. A total of 204 individuals (primarily contract workers) completed the baseline and end-of-project assessments. Of these individuals, 120 (59 %) had PFOA and PFOS baseline concentrations comparable to that measured in the general population (Kato et al. 2011; Olsen et al. 2012a). Among these 120 individuals their matched pair median change and interquartile range for PFOA was 5.3 ng/mL (0.5–32.6) and 0.7 ng/mL ((−1.0)–4.7), respectively. Their mean matched-pair changes were PFOA 44.2 ng/mL ($p<0.0001$) and PFOS 4.2 ng/mL ($p<0.0001$). These biomonitoring results suggested an increase in serum PFOA concentrations, and lesser so for PFOS, among workers who were engaged in this decommissioning, demolition, and disposal work.

4.2.2 DuPont Washington Works (Parkersburg, WV)

Fluoropolymer production began at the DuPont Washington Works plant in 1951 (Woskie et al. 2012). APFO was used as a surfactant in the emulsion polymerization of tetrafluoroethylene (TFE) to make polytetrafluoroethylene (PTFE) whose variety of products, included use in non-stick pans and water repellent clothing. Brand names were sold under the labels Teflon® and Gore-tex®. PFOA was not considered incorporated into the final product of these fluoropolymers (Kreckmann et al. 2009). Other production applications included wire and cable, inert tubing, and semiconductors. APFO was also used in co-polymer production of fluorinated ethylene propylene (FEP) and perfluoroalkoxy (PFA) polymer. Depending on time periods, PFOA was used as either a powder or premixed liquid form for these polymer and co-polymer production processes.

TOF was measured as a surrogate for PFOA in the blood prior to laboratory capabilities to speciate for PFOA. Between 1972 and 1981 whole blood analysis for TOF used the Wickbold torch method followed by a spectrophometric method of detection (Woskie et al. 2012). Beginning in 1981, the whole blood analyses were converted to a gas chromatography with electron capture detector method (GC-ECD) that specifically quantified PFOA. Beginning in 2003, PFOA measurements were subsequently analyzed using high pressure LC/MS-MS methods using a serum matrix. Based on an analysis of 114 samples by both the Wickbold and GC-ECD methods, a correction factor was applied to the TOF data to convert to GC-ECD PFOA analysis equivalents and then these whole blood PFOA measurements were subsequently adjusted to serum PFOA equivalents.

Kreckman et al. (2009) used actual serum PFOA measurements from 1,025 Washington Works workers that were obtained in a cross-sectional health study in 2004. They combined these data with current job titles to derive three relative APFO similar exposure categories. The mean of the serum PFOA measurements for each job exposure category served as an intensity factor. The job exposure categories were applied to historical job titles and validated with PFOA measurements collected among voluntary participants between 1979 and 2002. A cumulative exposure matrix was derived.

Woskie et al. (2012) expanded on this methodology to predict serum PFOA levels over time at this DuPont Washington Works site for the following eight plant workplace categories:

1. Fine powder/granular polytetrafluoroethylene (PTFE) job categories (direct exposure to PFOA).
2. Fluorinated ethylene propylene (FEP) and perfluoroalkoxy fluoropolymer (PFA) job categories (direct exposure to PFOA).
3. Non-PFOA use in Teflon polymer and co-polymer production job category (intermittent direct or plant background PFOA exposure). Included two subcategories:
   (3a) Teflon polymer co-polymer production department category (intermittent direct PFOA exposure). This included ethylene-tetrafluoroethylene fluoropolymer and fluorotelomer co-polymer operations.
   (3b) Tetrafluoroethylene (TFE) monomer operation category (plant background PFOA exposure).
4. Maintenance job category (intermittent direct or plant background PFOA exposures). Included two subcategories:
   (4a) Assigned to Teflon/co-polymer maintenance job category (intermittent direct PFOA exposure).
   (4b) Not assigned to Teflon/co-polymer maintenance job category (plant background PFOA exposure).
5. Non-Teflon/co-polymer production division with no PFOA-use job category (plant background PFOA exposure). Included two subcategories:
   (5a) Jobs considered potentially exposed to PFOA in either (1), (2), (3), or (4) above (intermittent direct PFOA exposure).
   (5b) Jobs not exposed to PFOA (plant background PFOA exposure).

Linear mixed models were developed to predict serum PFOA concentrations for each DuPont plant employee and year of their work history for the above eight job category/job group combinations. These retrospective models took into account individual and repeated measures from a collective sample of 2,125 serum measurements from 1,308 workers collected between 1979 and 2004. Of the 2,125 samples, the median and mean serum PFOA concentrations were 580 ng/mL and 2,050 ng/mL, respectively. The highest PFOA measurement was 59,400 ng/mL that was measured in a worker involved with PTFE production. Figure 4.4 shows the median

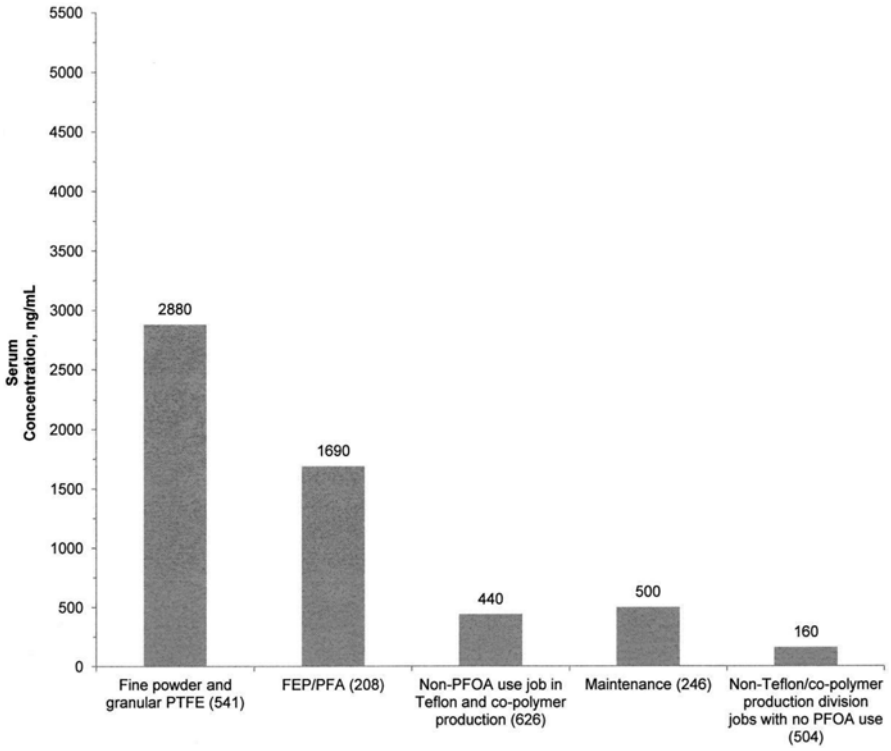

Fig. 4.4 DuPont Washington Works plant, median serum PFOA concentrations, (2,125 Samples) by five major job classifications, 1979–2004

serum PFOA concentrations from the samples for the five major job groups described above.

Covariates considered in the linear mixed models included workers' cumulative years worked, historical production of APFO used or emitted by the plant (Fig. 4.5) and the time where major process changes may have influenced workers' exposure. Predicted serum PFOA concentrations prior to 1979 were largely influenced by either the amount of PFOA used (direct or indirect exposure) or amount emitted (plant background exposure). From these linear mixed models, estimated weighted predicted annual median serum PFOA concentrations for all workers with potential exposure to PFOA reached the highest level of approximately 0.8 ppm (800 ng/mL) in the late 1980s (Fig. 4.6a). Among workers unexposed to PFOA, the highest predicted annual median concentration was in the 0.2 ppm (200 ng/mL) range (Fig. 4.6b). Data from these annual prediction serum PFOA models were used in an epidemiologic cohort mortality analysis of this plant population (Steenland and Woskie 2012).

The modeled estimated median serum PFOA levels, by year, are shown for workers in job groups with direct exposure (Fig. 4.7). [Note: Figs. 4.7 and 4.8 are

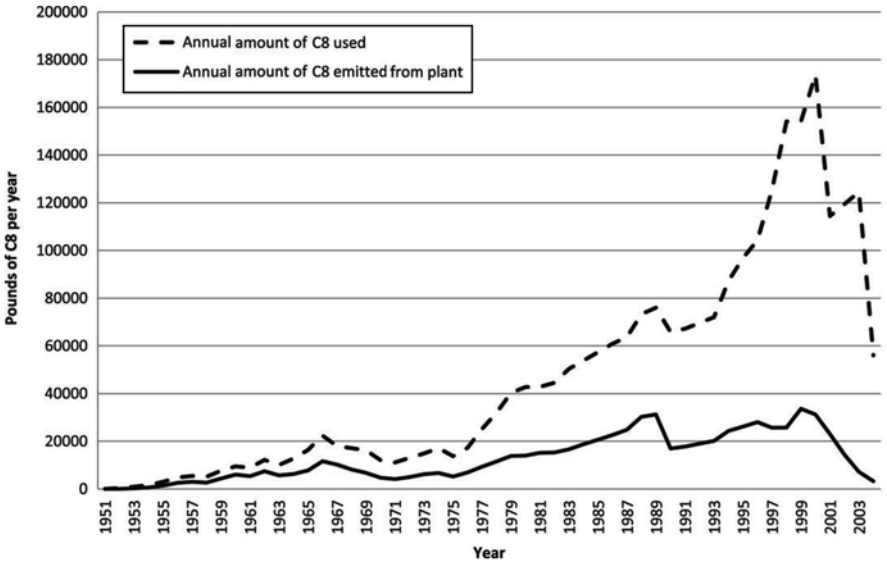

Fig. 4.5 Annual amount of PFOA used at the DuPont plant (lbs/year) and the estimated annual PFOA emissions from the plant (Reprinted from Woskie et al. 2012, by permission of Oxford University Press)

adapted from Woskie et al. (2012) who presented the data in ppm (μg/mL) units. [Note: Multiply by 1,000 to derive ppb (ng/mL) levels.] The increase in serum PFOA concentrations until 1980 among workers with direct exposure reflected the increase in annual PFOA use (Fig. 4.5). Although PFOA use increased substantially after 1980, there was a decline in estimated median PFOA concentrations from these models among the chemical and finish operators in the Fine Powder/Granular PTFE category. This was the consequence of the implementation of several exposure controls including the replacement of weighing powdered PFOA with premixed liquid PFOA, a dryer scrubber, and use of personal protective equipment. Estimated median serum concentrations of the FEP/PFA operator were also influenced by operational changes over time. Annual production use also influenced predicted median PFOA concentrations among job groups with intermittent direct or plant background PFOA exposure (Fig. 4.8).

4.2.3 Other APFO and Fluoropolymer Manufacturers

Besides 3M and DuPont plants discussed above, few other APFO manufacturing, fluoropolymer, and/or fluorotelomer manufacturing companies have published employee PFAS biomonitoring data in the scientific literature. This does not necessarily infer that biomonitoring analyses of these company workers have not been

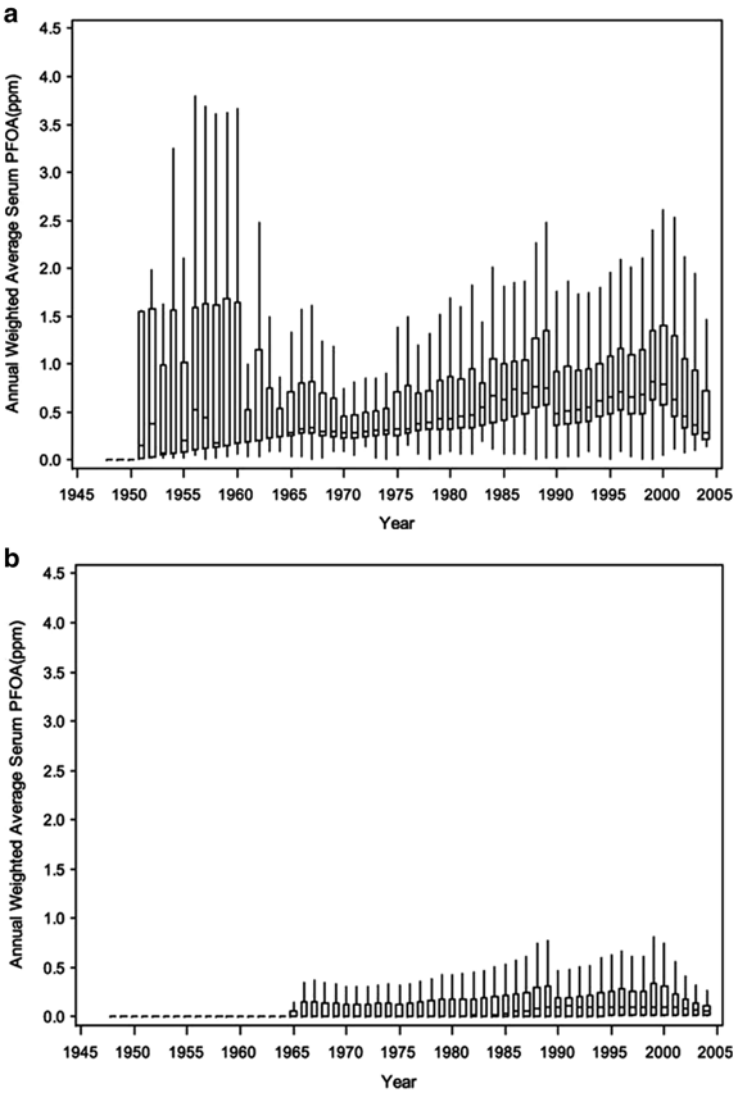

Fig. 4.6 Stem and leaf plots of the model estimated weighted annual median serum PFOA levels (ppm) for the full cohort of DuPont workers for those in job groups (see text) with potential PFOA exposure during the calendar year (**a**) and without potential (**b**). *Box plots* show the minimum, maximum, 25th and 75th percentiles and median (Reprinted from Woskie et al. 2012, by permission of Oxford University Press)

performed – just that nothing was found available in the scientific literature. The US EPA's 2010/2015 PFOA Stewardship Program (US EPA 2006) identified eight major fluoropolymer and telomer manufacturers: Arkema, Asahi, BASF (formerly Ciba), Clariant, Daiken, 3M/Dyneon, DuPont, and Solvay Solexis.

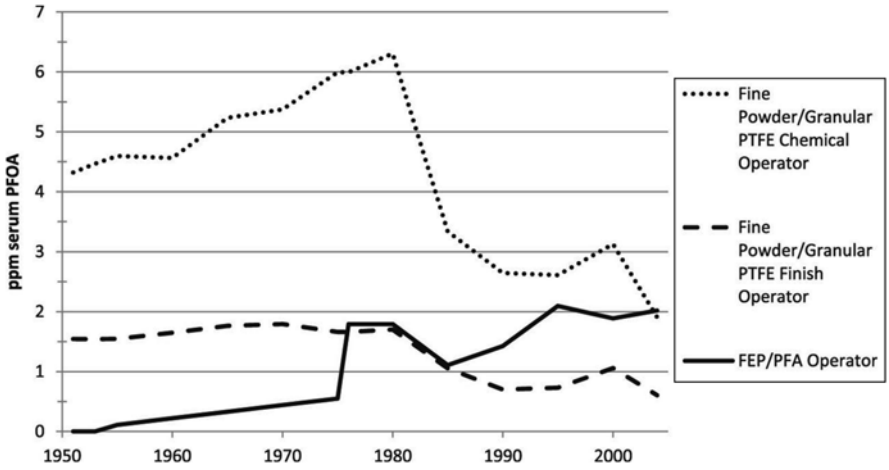

Fig. 4.7 Median serum levels estimated from models for workers in job groups with direct exposure to PFOA during the year (Reprinted from Woskie et al. 2012, by permission of Oxford University Press)

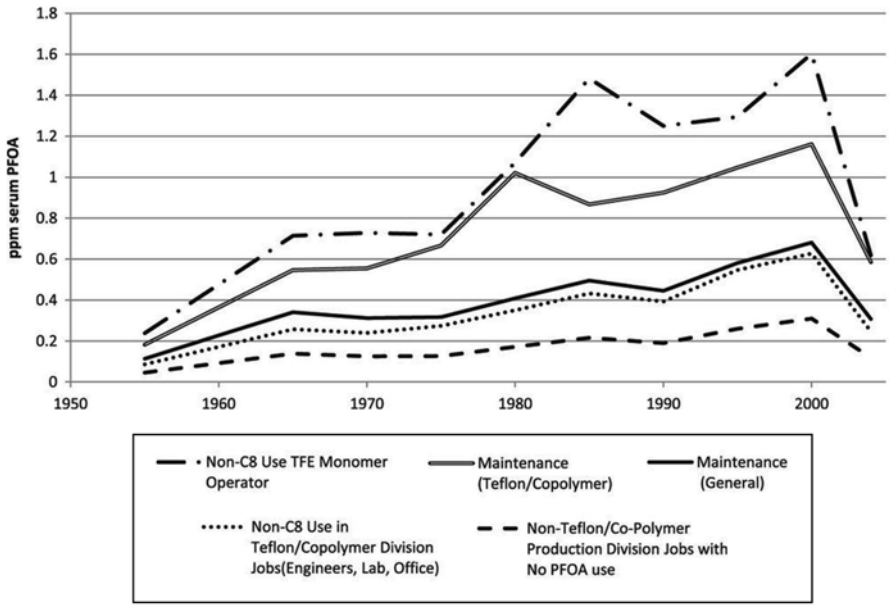

Fig. 4.8 Median serum levels estimated from models for workers in job groups with intermittent direct or plant background PFOA exposure to PFOA during that year (Reprinted from Woskie et al. 2012, by permission of Oxford University Press)

After the 3 M phase-out of PFOS-related materials, it appears many small scale POSF-based Chinese manufacturers expanded their production capabilities. Several PFOS-based companies have been identified to operate in Hubei and Fujian provinces.

Besides PFOS, APFO, fluoropolymer and telomer manufacturers, there are 'downstream' users of PFAS-related materials that need to be considered for biomonitoring of their workforce (Butenhoff et al. 2006). These 'downstream' users include the carpet, textile, mill, paper (food-protectant applications), semiconductor, and metal plating industries.

4.2.3.1 Polytetrafluoroethylene (PTFE) Plants (DuPont, Dyneon, Asahi, Solvay Solexis)

Consonni et al. (2013) reported a cohort study of PTFE production workers from four companies consisting of six manufacturing sites: Dyneon (Gendorf, Germany); Solvay Solexis (Spinetta Marengo, Italy); Asahi (Hillouse UK; and Bayone, NJ, USA); and DuPont (Dordrecht, Netherlands and the Washington Works plant located near Parkersburg, WV, USA). A total of 5,879 workers were in this cohort which included 2,379 from the DuPont Washington Works plant discussed above (this was approximately 40 % of the DuPont Washington Works overall cohort reported by Steenland and Woskie 2012). Consonni et al. developed a job exposure matrix with yearly semi-quantitative estimates (in arbitrary units) of both TFE and APFO exposure at each of the six plant sites. These semi-quantitative arbitrary units of TFE and APFO exposure were highly correlated ($r^2 = 0.72$, $p < 0.0001$).

The PTFE production processes are closed systems because of TFE's explosive nature. The potential for TFE exposure, however, could still occur through opening autoclaves in the polymerization area or decomposition of PTFE. Consonni et al. (2012) estimated historic TFE exposure in this cohort could have been up to a few parts per million. Overall findings of this multi-plant cohort included modestly elevated standardized mortality ratios (SMRs) for cancer of the liver and kidney, and leukemia (see reviews in Chap. 14 and Chang et al. 2014). [Note: the International Agency for Research on Cancer (IARC) recently evaluated PFOA as a group 2B (possible) human carcinogen. They evaluated TFE as a group 2A (probable) human carcinogen (Benbrahim-Tallaa et al. 2014).] Consonni et al. stated that these effects could not be disentangled between the highly correlated TFE and APFO exposure based on their semi-quantitative arbitrary units of analysis.

This inability to disentangle the reported associations with APFO and TFE, however, differed from the conclusion by Steenland and Woskie (2012) who reported APFO exposure response trends for liver and kidney cancer and leukemia in the DuPont Washington Works cohort study. Steenland and Woskie discounted the potential for TFE exposure in their DuPont Washington Works cohort study because they believed appreciable exposures to TFE were unlikely during normal operations because of its explosive nature. As a point of clarification, it should be noted that the lower explosion limit for TFE is 110,000 ppm (ACGIH 1997). The

8 h time-weighted average (TWA) for TFE is 2 ppm. Therefore, it is likely that low level TFE exposures could have occurred given the disparity between exposure levels between the TWA and the lower explosion limit. It should also be noted that the 3M Cottage Grove plant (discussed above) that manufactured APFO was not a PTFE production plant and therefore the exposure at this 3M plant was done in near isolation of any TFE exposure (Raleigh et al. 2014).

4.2.3.2 Miteni Plant (Trissino, Italy)

PFOA had been produced by ECF since 1968 at the Miteni plant in Trissino, Italy (Costa et al. 2009). It was not stated whether ECF production of POSF occurred at this facility. Worker biomonitoring for PFOA began in 2000 and continued annually through 2007 (Costa et al. 2009). For the 25–50 PFOA production workers who had serum measurements evaluated between 2000 and 2007, their geometric mean serum concentrations were 11,700 ng/mL, 10,200 ng/mL, 9,300 ng/mL, 6,900 ng/mL, 6,500 ng/mL, 5,800 ng/mL and 5,400 ng/mL, respectively. Maximum serum PFOA concentrations measured were >45,500 ng/mL (upper limit of quantitation), >45,500 ng/mL (upper limit of quantitation), 91,900 ng/mL, 74,700 ng/mL, 46.300 ng/mL, 41,900 ng/mL, and 47,000 ng/mL, respectively. Declining concentrations of PFOA were observed after 2002 following several workplace exposure reduction activities. PFOA is no longer manufactured at this facility.

4.2.3.3 Arkema Plant (Pennsylvania)

A series of cross-sectional 1976, 1989, 1995, 1998, 2001) medical surveillance analyses were conducted of workers (number ranging between 163 and 323 per year) from a manufacturing facility that used perfluorononanoic acid (PFNA or C9) blend in the production of high-performance polymers (Mundt et al. 2007). Other fluorinated hydrocarbons in this blend were the perfluorocarboxylic C11 and C13 congeners. No specific biomonitoring measurements of PFNA were reported. PFNA serum elimination half-life data in humans is unknown but would be expected to be several years, similar to PFOA.

4.2.3.4 Manufacturers in China

Manufacturing of POSF-based materials increased in China after the announced phase-out by the 3M Company (Fig. 4.9) (Zhang et al. 2012). The trend in PFOS-related production declined slightly in 2008 after the European Union directive to not import textiles treated with POSF-related materials (Zhang et al. 2012; Xie et al. 2013). PFOS-based production has remained relatively steady since 2009. Three major PFOS-based applications exist in China: metal plating; fire fighting foams; and insecticides (sulfuramid).

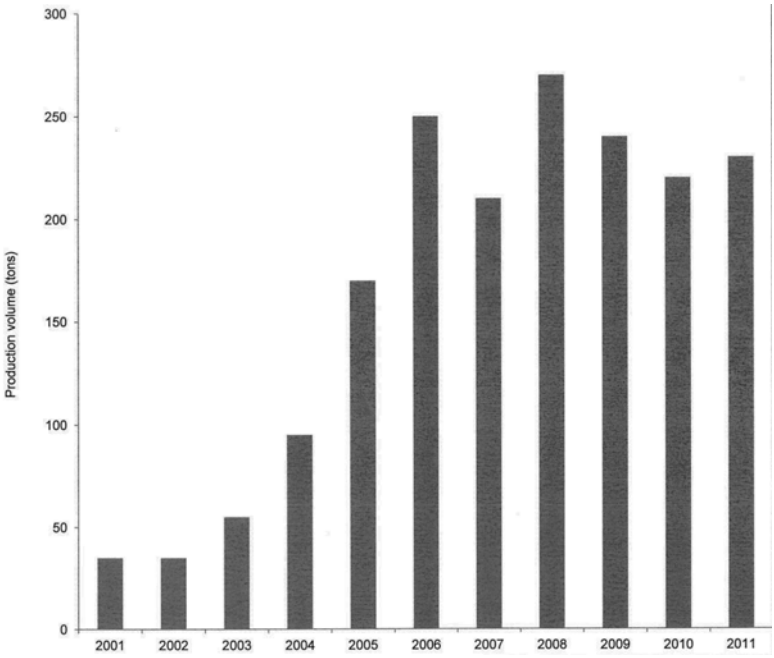

Fig. 4.9 Approximate annual production of PFOS (tons) in China, 2002–2008 according to Xie et al. (2013)

Twelve companies were identified as manufacturers of POSF-related materials that are located in Hubei and Fujian provinces (Table 4.2) but worker biomonitoring data were not presented (Huang et al. 2013). Wang et al. (2012) described an environmental assessment at a manufacturing facility near Wuhan, (Hubei Province) China. PFOS and PFHxS were found in dust, water, soil and chicken eggs. Concentrations were dependent on distance from the plant. Although dust was a major exposure, biomonitoring of the workers was also not reported. High serum concentrations of PFOS were reported among commercial fishermen in Tangxun Lake (Wuhan, China) that receives waste water treatment plant discharges originating from an industrial park that included a POSF-related manufacturing plant(s) (Zhou et al. 2014). See a detailed description of Tangxun Lake in the community studies section of this chapter. A fluorine chemical industrial zone was identified near Changshu City, in the Jiangsu province (Wang et al. 2012). A total of 27 fluorochemical plants were located in this industrial zone but Wang et al. did not identify company names or products manufactured were not identified. At one of these fluorochemical plants a biomonitoring study was performed on 55 male workers and 132 nearby residents (Wang et al. 2012). Results showed both occupational as well as residential exposure to PFOA compared to other general population levels reported in China (Wang et al. 2012). PFOA values differed between workers

Table 4.2 POSF- related chemical manufacturers (China)

Hubei Province (n = 9)
1. Hubei Hengxin Chemical Co., Ltd
2. Wuhan Chemical Industry Institute Co., Ltd.
3. Changjiang Fluorochemical Co., Ltd
4. Yingcheng Sanwei Chemical Co. Ltd
5. Hubei Xiaochang Xiangshun Chemical Co., Ltd.
6. Wuhan Jinfu Economic Development Co., Ltd
7. Wuhan Jiangrun Fine Chemical Co., Ltd.
8. Hubei Kaie Printing Ink Manufacture Co., Ltd
9. Wuhan Defu Economic Development Co., Ltd
Fujian Province
1. Shaowu Huaxin Chemical Co., Ltd
2. Shaowu Jintang Anshengqi Chemical Co., Ltd
3. Jianyang Tianfu Chemical Co., Ltd

Presentation given by Jun Huang[a], Gang Yu[a], and Shengfang Mei[b], at the 5th International Workshop on Per- and Polyfluorinated Alkyl Substances. Helsingör, Denmark. October 2013

[a]School of Environment, Tsinghua University, China

[b]China Association of Fluorine and Silicone Industry (CAFSI)

and residents: [workers 1,636 ng/mL (range 95–7,737 ng/mL); residents [378 ng/mL (range 10–2,427 ng/mL)]. Unlike PFOA, the other PFASs measured, including PFHpA, PFNA, PFDA, PFDoA, PFBS, PFHxS, and PFOS were not substantively different between workers and nearby residents.

4.2.3.5 'Downstream' PFAS Production

Specific PFASs applications occur in the carpet, textile, and leather industries, paper mills, the semiconductor industry, and metal plating. Although environmental exposure data was reported related to emissions from various industrial settings, biomonitoring data were not available related to the workers at these 'downstream' PFAS user facilities. Although PFAS biomonitoring data were not found in the scientific literature, it is possible such analyses could have been conducted but never published. For example, at Dalton, Georgia, known as the "carpet capital of the world," Konwick et al. (2008) conducted an environmental assessment of PFASs in surface water and reported high concentrations at a location in the Conasuga river near a wastewater land application site. A US EPA assessment of the drinking water in the area did not find PFOA or PFOS concentrations exceeding the Agency's provisional guidelines (US EPA 2009).

Similar to the above investigation at Dalton, Georgia, perfluorinated chemical analyses occurred in a river near the location of major Taiwanese semiconductor and electronics industries (Lin et al. 2009) as well as near the largest science park in

Taiwan (Lin et al. 2014). However, there was no indication that PFAS biomonitoring occurred among employees or residents living near these industries.

4.3 Biomonitoring in Communities Affected by Environmental Exposures of PFASs

Several communities have been affected by environmental releases of PFASs that reached surface and/or groundwater sources for drinking water. Depending on location, environmental releases were from three major types of sources: (1) industrial emissions (air, water) from nearby PFAS manufacturing plants; (2) landfill leachate where PFAS materials had been legally deposited with subsequent finding into aquifers; and (3) run-off into water ways (creeks, rivers, lakes) from agricultural fields where treated sewage sludge had been applied as soil conditioner.

Biomonitoring for PFAS in each affected community demonstrated concentrations above levels reported in the referent general population. The largest population (approximately 69,000) studied in a series of epidemiologic investigations, to date, resided in a mid-Ohio River valley community encompassing six water districts in either Ohio or West Virginia. In another community, increased serum PFAS concentrations were associated with fish consumption resulting in the highest serum PFOS serum concentration ever reported in the literature.

Brief reviews of six affected community studies are provided below.

4.3.1 United States

4.3.1.1 Minnesota ("East Metro" Study of Minneapolis-St. Paul)

The Minnesota Department of Health (MDH) (2008, 2012a), under cooperative agreement with the U.S. Agency for Toxic Substances and Disease Registry (ATSDR), issued public health assessments regarding emissions of PFASs from the 3M Cottage Grove manufacturing facility as well as several local landfills where the plant had legally disposed of wastes in the 1950s, 1960s, and 1970s. Several PFASs were detected in public and private wells in east metro communities of the Minneapolis-St. Paul metropolitan area. Exposure was attributed to landfill leachate with PFOA entering the aquifer. PFASs levels in the drinking water in some of these wells were above the state's health risk limits of 0.3 μg/L for PFOA and/or PFOS (see Chap. 17). Remediation efforts included installing granular activated charcoal filtration systems in municipal water systems, connecting residential users of affected private wells to municipal water systems, and placement of whole-house activated carbon filters in other rural residences. In addition remediation efforts at the affected landfills occurred to mitigate further leachate mediated PFOA entry into the groundwater.

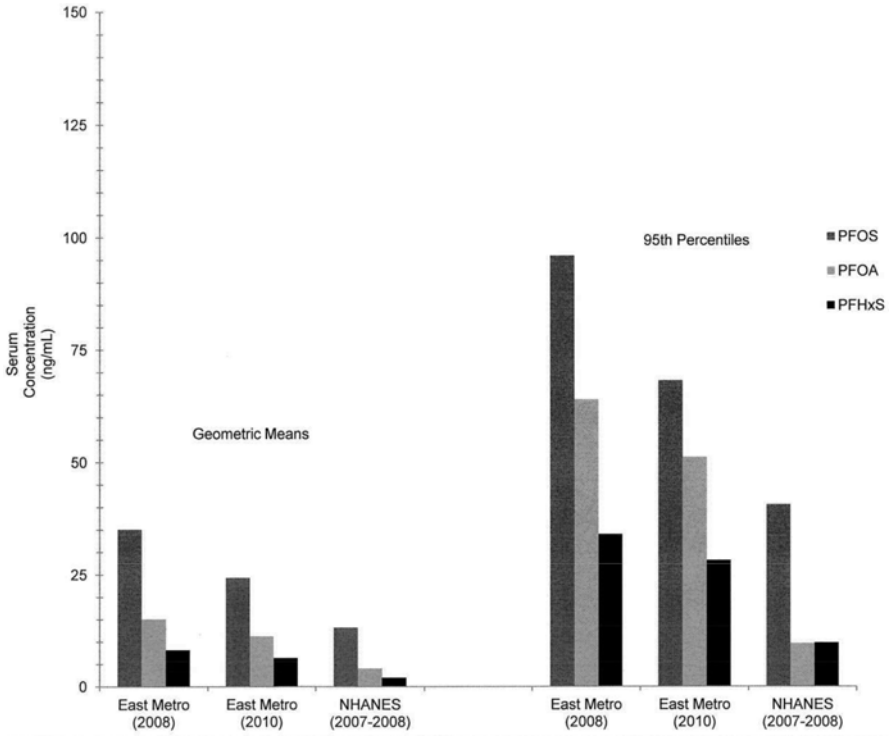

Fig. 4.10 Geometric mean and 95th percentile serum PFOS and PFOA concentrations in east metro residents of Minneapolis St-Paul, compared to NHANES

As part of the MDH's effort to assess citizens' exposure, a random sample of east metro citizens was contacted who lived in affected areas (MDH 2012b, c). In 2008 the geometric mean serum concentrations for PFOS (35. 1 ng/mL), PFOA (15.1 ng/mL), and PFHxS (8.2 ng/mL) were approximately three to four times higher than the 2007–2008 NHANES data (Fig. 4.10). In a resampling of this population 2 years later, the geometric mean serum concentrations for the East Metro area were 24.3 ng/mL, 11.3 ng/mL, and 6.4 ng/mL, respectively. This represented 2-year percentage declines of 26 %, 21 %, and 13 %, respectively. These percentage reductions approximate what might be the expected serum elimination half-lives that have been reported for these three PFASs (Olsen et al. 2007). Based on these percentage declines, the MDH concluded the exposure reduction efforts appeared to be working but continued biomonitoring was warranted (MDH 2012c). A third biomonitoring sampling of this population is being conducted in 2014.

4.3.1.2 Alabama (in the Vicinity of Decatur, AL and Morgan, Lawrence, and Limestone Counties)

Between 1996 and 2008, the Decatur, Alabama waste water treatment plant (Decatur Utilities) processed permitted wastewater effluent from local industries involved in the manufacture and/or use of PFASs (Lindstrom et al. 2011). It was estimated 34,000 tons of impacted biosolids from the wastewater treatment plant were applied as treated sludge to approximately 5,000 acres of agricultural fields in Lawrence, Morgan, and Limestone Counties. In 2007 the U.S. EPA was notified by a PFAS manufacturer, Daiken Corporation, in Decatur, Alabama that it had unknowingly discharged large amounts of perfluorocarboxylic acids into the Decatur Utilities wastewater treatment plant (Lindstrom et al. 2011; Decatur Daily 2009). The US EPA conducted a series of investigations sampling biosolids, surface water, ground water, drinking water, and soils in the area around these agricultural fields to determine PFAS concentrations. PFOA was detected (57 %) in surface waters near these fields and 4 (22 %) of 19 private wells had PFOA concentrations above the EPA's Provisional Guideline of 0.4 μg/L.

As reviewed by the US Agency for Toxic Substances and Disease Registry (ATSDR 2013), between 2008 and 2011 the US EPA conducted a series of municipal water testing involving five other public water distribution systems in the area (ATSDR 2013). One of the five municipal public drinking water systems, West Morgan/East Lawrence (WM/EL), had detectable PFOA and PFOS concentrations but both were below the EPA's Provisional Health Advisory levels. The WM/EL obtained its water from the Tennessee River 13 miles downstream from an industrial area with PFAS manufacturing and use that was located in the Decatur area. Studies of PFAS concentrations in the river had been previously reported (Hanson et al. 2002; Weston 2012).

The ATSDR (2013) subsequently conducted a human exposure investigation that resulted in letters sent to 519 eligible households. A total of 85 households (16 %) participated (153 people volunteered from these households). A primary objective was to measure PFASs in these participants' serum that lived and worked in the affected WM/EL public water system. Figure 4.11 provides the geometric mean serum concentrations for PFOS, PFOA, and PFHxS for the three different water sources reported by the ATSDR (2013): WM/EL public water system; water sources without detectable PFAS levels; and private drinking wells with detectable PFAS levels. NHANES general population data are also presented for comparison purposes. Geometric means serum PFAS concentrations were approximately two to five times higher in individuals residing within the WM/EL or having an affected private well than those individuals living in residences without detectable water levels (Fig. 4.11). The range of serum PFOS concentrations for these three water categorizations were (in parentheses): (5.6–248 ng/mL), (38.6–472 ng/mL), and (5.4–201 ng/mL), respectively. The range of serum PFOA concentrations were (in parentheses): (2.2–78.8 ng/mL), (7.6–144 ng/mL), and (2.8–50.4 ng/mL),

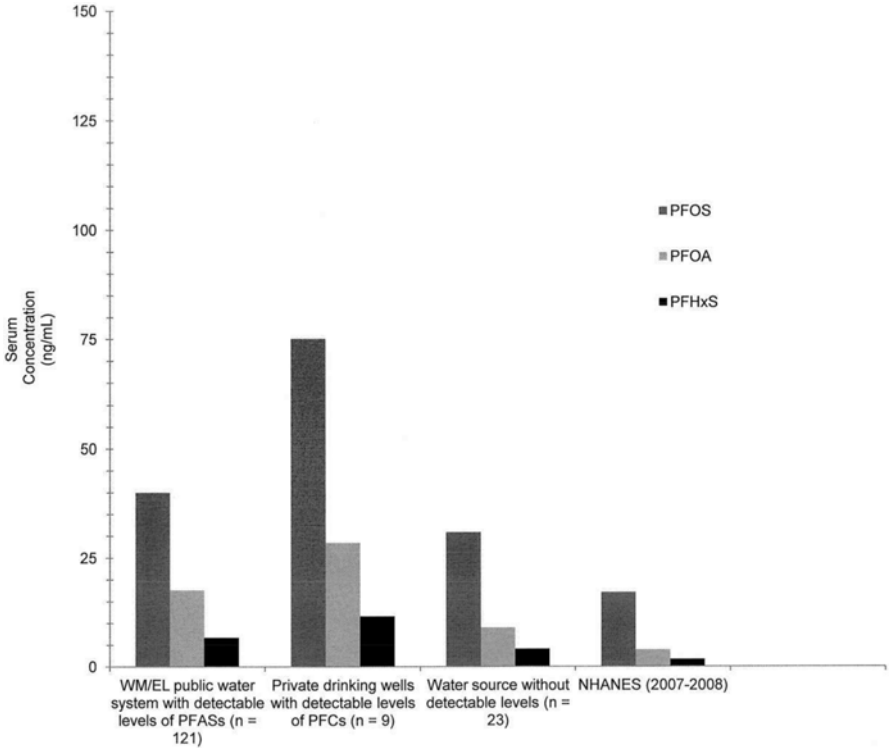

Fig. 4.11 Geometric serum PFOS, PFOA, and PFHxS concentrations in residents of affected communities through drinking water exposure near Decatur, AL compared to NHANES

respectively. The range of PFHxS concentrations for these three water sources were (in parentheses): (0.6–32.3 ng/mL), (6.1–59.1 ng/mL), and (1.2–24.8 ng/mL), respectively. Additional epidemiologic analyses and interpretation is included in this ATSDR Health Consultation (2013) (See Chap. 14).

4.3.1.3 Mid-Ohio River Valley (West Virginia/Ohio)

As discussed above, APFO (ammonium salt of PFOA) was used as an emulsifier in the polymerization of TFE to polytetrafluoroethylene (PTFE) at the DuPont Washington Works plant (near Parkersburg, West Virginia). Cumulative evidence demonstrated PFOA entered water supplies along this mid-Ohio River Valley area which led to a certified class action between plaintiffs (the 'Class') and DuPont (Frisbee et al. 2009). The PFOA water exposure was attributed to industrial emissions of APFO from the nearby DuPont Washington Works plant (Paustenbach et al. 2007; Shin et al. 2011a, b, 2012, 2014). A pretrial settlement between the Class and DuPont provided: (1) funds for health and education projects (subsequently known as the C8 Health Project); (2) provisions by the company to remove PFOA

from the water supply of six affected water districts; and (3) establishment of an independent panel of three scientific experts (the C8 Science Panel) to determine the presence or absence of "probable links" defined as the weight of the available scientific evidence that it is more likely than not there is a link between exposure to PFOA and a particular human disease among the Class. To arrive at these conclusions the C8 Science Panel initiated 12 epidemiologic investigations of 55 diseases and reached 6 probable link conclusions (Steenland et al. 2014). These 'probable links' are reviewed in Chap. 14.

Several papers provide insight into the chronology of some of the exposure research activities that were conducted in this community.

Emmett et al. (2006) initially described the highest PFOA drinking water concentrations were from the Little Hocking Water District (LHWD). The average PFOA concentration in the LHWD from January 2002 until May 2005 was 3.55 μg/L (range 1.5–7.2 μg/L). This is approximately tenfold higher than the current US EPA Provisional Advisory for PFOA (0.4 μg/L). Emmett et al. suggested residential water, and not air, was the likely pathway of exposure of PFOA among 161 households that participated in their study. Self-reported number of glasses of water consumed per day was associated with increased serum PFOA concentrations. The median serum PFOA concentrations for 0, 1–2, 3–4, 5–8, and >8 glasses of tap water drinks per day were 301 ng/mL, 265 ng/mL, 370 ng/mL, 373 ng/mL, and 486 ng/mL, respectively (trend $p < 0.0001$). Households that used bottled water had significantly lower serum PFOA concentrations. Also, residents who used household carbon water filters had lower serum PFOA levels (318 ng/mL) than those who did not (421 ng/mL) ($p = 0.008$).

Published a few years later were the Class findings from the settlement's large cross-sectional health survey and exposure study (i.e., the C8 Health Project) (Frisbee et al. 2009). Under the court settlement, an independent company, Brookmar, Inc., designed and implemented the C8 Health Project. The Class eligibility was defined by exposure to contaminated water, a combination of geographic, and concentration criteria and exposure duration (Frisbee et al. 2009). The final C8 Health Project enrollment was 69,030 individuals who were individually compensated for their study participation per terms of the settlement (Frisbee et al. 2009). Both clinical laboratory tests and measurement of serum PFASs were included in the study. Serum PFASs included the perfluorocarboxylate homologue series C5 to C12 (PFPeA, PFHxA, PFHpA, PFOA, PFNA, PFDA, PFUnA, and PFDoA) and the perfluorosulfonates PFHxS and PFOS. Individual blood samples were collected over a 13 month time period (August 2005–August 2006).

The overall geometric mean serum PFOA concentration was 32.9 ng/mL (mean = 82.9 ng/mL; SD = 240.8) compared to 3.9 ng/mL for NHANES (2003–2004) (Frisbee et al. 2009). The range of concentrations in each of these water districts was not reported by Frisbee et al. Figure 4.12 provides the age- and sex-adjusted mean serum PFOA and PFOS concentrations for the six water districts and private well users (West Virginia and Ohio) of the C8 Health Project cross-sectional study. The adjusted mean PFOA concentrations ranged from fourfold higher (Pomeroy, Mason County) to >50-fold higher (Little Hocking Water Association) than comparable NHANES data. The age- and sex-adjusted mean for the Little

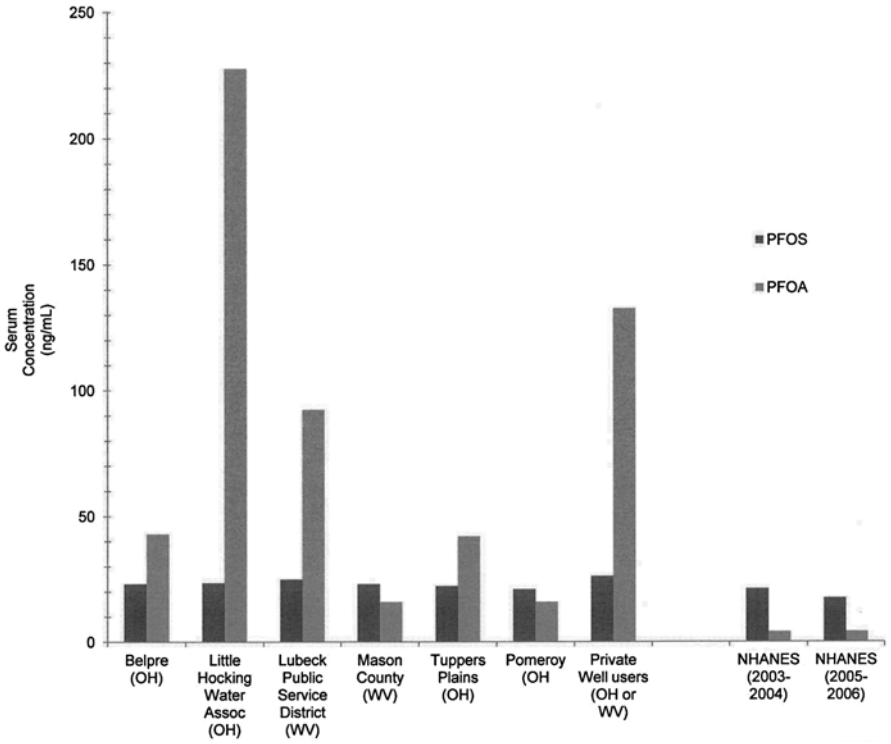

Fig. 4.12 Age-, sex- adjusted mean serum PFOS and PFOA concentrations for the C8 health project by six water districts and comparison with NHANES data

Hocking Water Association was 227.6 ng/mL for PFOA. The next highest adjusted mean PFOA concentration was for private well users (132.6 ng/mL). The overall mean serum PFOS concentration in this mid-Ohio river community (19.2 ng/mL) and was similar to NHANES data for 2003–2004 (20.7 ng/mL). This is to be expected as occupational exposure to PFOS was not present at this DuPont plant.

The Little Hocking Water Association residents studied by Emmett et al. had a 40 % higher average serum PFOA than those shown for this group in the C8 Health Project (in Fig. 4.11). This difference has been attributed to the fact that by 2005–2006 Little Hocking Water Association households had already reduced their exposure to PFOA because bottled drinking water had been supplied to their residences as part of the Class settlement (Frisbee et al. 2009). Subsequent to the 2005–2006 C8 Health Project, serum PFOA concentrations declined 26 % in a subset of residents from the Little Hocking and Lubeck water districts during the first year after charcoal activated filters were installed resulting in a serum elimination half-life of 2.3 years (Bartell et al. 2010).

Serum PFOA concentrations were higher among males than females in the C8 Health Project cross-sectional data (Fig. 4.13). The overall geometric mean for males (39.4 ng/mL) was higher than females (27.9 ng/mL) (means 98.2 vs. 68.8 ng/mL,

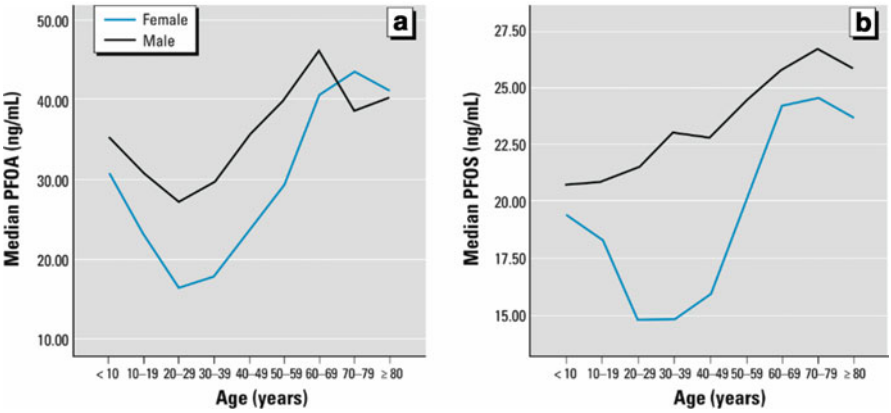

Fig. 4.13 Geometric mean PFOA and PFOS serum concentrations by age and sex, C8 health project, 2005–2006 (From Frisbee et al. 2009)

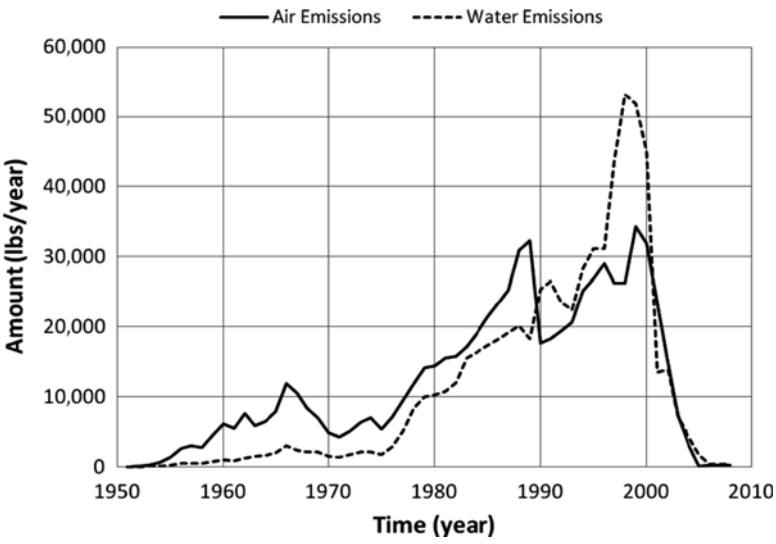

Fig. 4.14 Estimated historical PFOA releases into C8 health project area (Reprinted with permission from Shin et al. 2011a. Copyright 2011, American Chemical Society)

respectively). Several pharmacokinetic factors could explain, at least partially, these sex-related differences as PFOA is bound to serum protein. These factors may include pregnancy (Kato et al. 2014), parity (Berg et al. 2014; Brantsæter et al. 2013), lactation (Brantsæter et al. 2013; Fei et al. 2010; Sundström et al. 2011); and menstruation (Taylor et al. 2014).

Historic air and water emissions data were modeled by Shin et al. (2011a) (Fig. 4.14). These data, along with absorption, distribution, metabolism, and excretion (ADME) modeling, were used to predict annual serum PFOA exposures

(1951–2008) for the C8 Health Project participants based on their individual residential histories and water sources (municipal, well) (Shin et al. 2011b). For the six water districts' combined populations, the predicted median serum PFOA concentrations were within 0.5 orders of magnitude of the observed median concentrations measured in 2005/2006 during the course of the C8 Health Project. For example, for the C8 Health Project participants who had the same residence and workplace in one of the six water districts from 2001 to 2005 and assumed water consumption had a predicted median serum PFOA concentration in 2005–2006 of 32.2 ng/mL compared to 40.0 ng/mL observed. Predictions were less reliable for bottled water drinkers (10.5 ng/mL predicted versus 27.5 ng/mL observed) and those individuals not having had residences and workplace in one of the water districts from 2001 to 2005 (5.7 ng/mL predicted versus 15.3 ng/mL observed).

For the purpose of exposure reconstruction of PFOA in the C8 Science Panel's series of epidemiologic studies of a combined cohort of community participants and DuPont workers Winquist et al. (2013) were able to target 40,145 community members from the 54,457 C8 Health Project participants aged 20 years of age and older and 3,713 DuPont workers from the original 6,026 DuPont cohort. Of these 3,713 DuPont workers, 1,890 were also in the community cohort resulting in a total cohort of 30,431 participants that were contacted during the course of their epidemiologic studies. This combined cohort's historic annual estimated serum PFOA concentrations between 1951 and 2011 are presented in Fig. 4.15. Among only the community cohort, their median and interquartile ranges were 24.2 ng/mL and 12.3–58.9 ng/mL, respectively. Among the DuPont workers in the community cohort, their respective serum concentrations were 109.8 ng/mL and 55.9–256.2 ng/mL. The combined cohort's trend in serum PFOA concentrations (Fig. 4.15) mirrored the plant air and water emissions (Fig. 4.14).

Bartell et al. (2010) sampled the blood (up to six samples) of 200 residents of the Little Hocking and Lubeck water districts over an 18 month time frame. Their initial sampling serum PFOA concentration was 54.5 ng/mL. After water filtration was implemented, these investigators estimated the average serum PFOA decline was 26 % per year resulting in a median serum PFOA half-life of 2.3 years. This estimate was minimally biased from background exposures (Bartell et al. 2012).

4.3.1.4 Paulsboro, New Jersey

PFNA was detected at approximately 150 pg/mL (parts per trillion) in drinking water from the Paulsboro water department municipal well (New Jersey Health Department 2014). A potential source of exposure may be a nearby Solvay polymer plant that used to manufacture PFNA until 2009. No serum concentrations of area residents have been reported, to date.

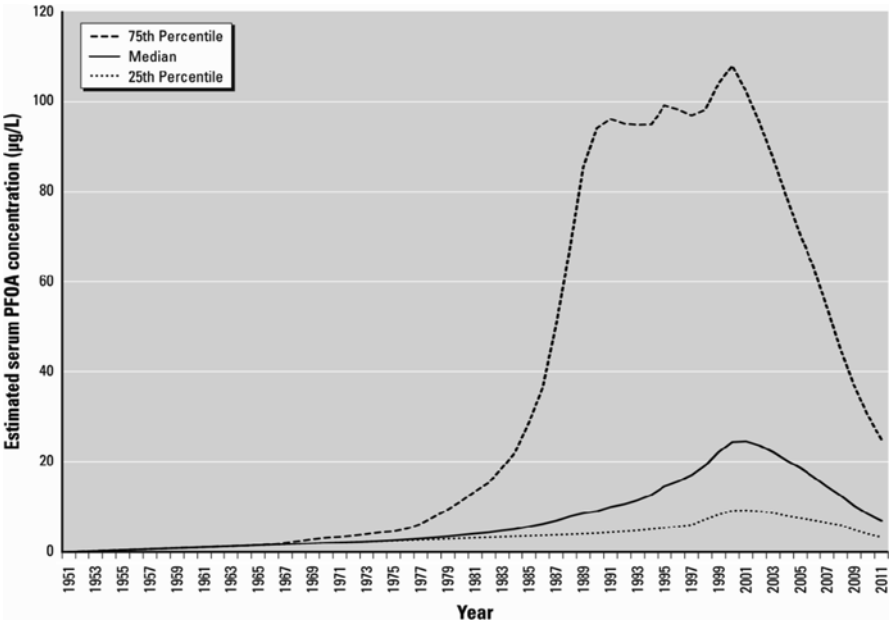

Fig. 4.15 Estimated historical serum PFOA concentrations by year for the community worker cohort study (From Winquist et al. 2013)

4.3.2 Germany

4.3.2.1 Arnsberg, Germany (Möhne Lake, Möhne River, Tributary of Ruhr River, Sauerland North Rhine-Westphalia Region)

A large environmental sampling study was conducted of surface and drinking water samples taken from multiple sites of the Rhine river and its main tributaries (Skutlarek et al. 2006). Sampling activity showed the summed PFAS concentrations in the water below 0.1 µg/L and that PFOA represented approximately 10 % of this total of PFAS. One tributary of the Rhine river, the Ruhr river located in northwest Germany, had at its mouth (near the city of Duisburg), a summed concentration of 0.94 µg/L with PFOA surprisingly representing 50 % of this amount. Investigators sampled further upstream on the Ruhr river focusing on one of its tributaries, the Möhne river. In a reservoir on this tributary, Lake Möhne, the summed PFAS concentrations reached 0.82 µg/L (PFOA = 0.65 µg/L). Upriver from this lake, the summed PFAS concentrations on the Möhne river reached 4.39 µg/L at Heidberg (PFOA = 3.64 µg/L). Investigations localized the main source of contamination between two parallel creeks where at the mouths of these creeks the summed PFAS concentrations reached 8.3 µg/L and 43.4 µg/L. PFOA represented more than 75 % of this amount at each mouth. Other perfluoroalkyls measured included PFBS, PFOS, PFBA, PFPeA, PFHxA, and PFHpA.

The investigators determined that between these creeks in a 10 ha-wide area (near Brilon-Scharfenberg) soil improvers were applied to the fields that had incorporated industrial wastes impregnated with high PFAS concentrations by a recycling company. Upon discovery of this affected area, installation of special drainage and water treatment was applied to reduce exposure to the upper Möhne river as well as charcoal filters installed in the Möhnebogen water works with frequent monitoring and change-out (Wilhelm et al. 2008).

Concentrations between the PFAS levels in the Möhne river and public drinking water were comparable for four boroughs of the city of Arnsberg which is situated near the mouth of the Möhne river. The majority of PFAS concentrations measured in the drinking water (total PFAS 0.60 μg/L) was due to PFOA (0.52 μg/L).

A biomonitoring study was conducted of a sample of residents from this Arnsberg population (men and mothers/children) with referent populations selected from the city of Brilon (men from the upper reaches of Möhne river before contamination site) and mothers and children in the Siegen area (not located on the Ruhr river or its tributaries) (Hölzer et al. 2008). Baseline blood samples were taken in 2006 and repeated in 2007 (Hölzer et al. 2008) and 2008 (Hölzer et al. 2009).

Provided in Fig. 4.16 are the results for the participants in the 2006 and 2008 surveys (Brede et al. 2010). In the baseline year (2006), the geometric mean and range of PFOA plasma concentrations (in parentheses) were: children (23.4 ng/mL, 95 % CI 19.2–28.5); mothers (23.6 ng/mL, 95 % CI 19.2–29.0); and men (30.3 ng/mL, 95 % CI 25.3–36.3). The 95th percentiles were 45.7 ng/mL, 53.5 ng/mL, and 49.2 ng/mL, respectively. These geometric mean and 95th percentile concentrations were approximately fivefold higher than the referent populations. Two years later after the remediation efforts, the geometric mean PFOA plasma levels declined by 39 % (children and mothers) and 26 % (men) in the Arnsberg population compared to 13–15 % in the reference groups (Fig. 4.16). The higher percentage declines among mothers and children were considered likely due to this population undergoing a greater initiative to reduce their drinking tap water consumption upon discovery of this environmental issue. The small decline of PFAS concentrations in the reference populations likely reflected the similar decreases observed in the general population. Geometric means of PFOS and PFHxS plasma concentrations were similar between the Arnsberg and referent populations.

Based on this 2 year study, Brede et al. calculated an estimated serum elimination geometric mean half-life of PFOA at 3.3 years assuming only background exposure. However, due to the fact this background exposure (approximately 4 ng/mL) approached the Arnsberg exposure data, Bartel (2012) calculated this 3.3 year half-life estimate was biased upwards by 26 %. Similarly, Russell et al. (2014) adjusted for background exposure in the Arnsberg database and estimated the PFOA geometric mean intrinsic half-life of 2.5 years (95 % CI 2.4–2.7) instead of the apparent half-life calculation of 3.3 years.

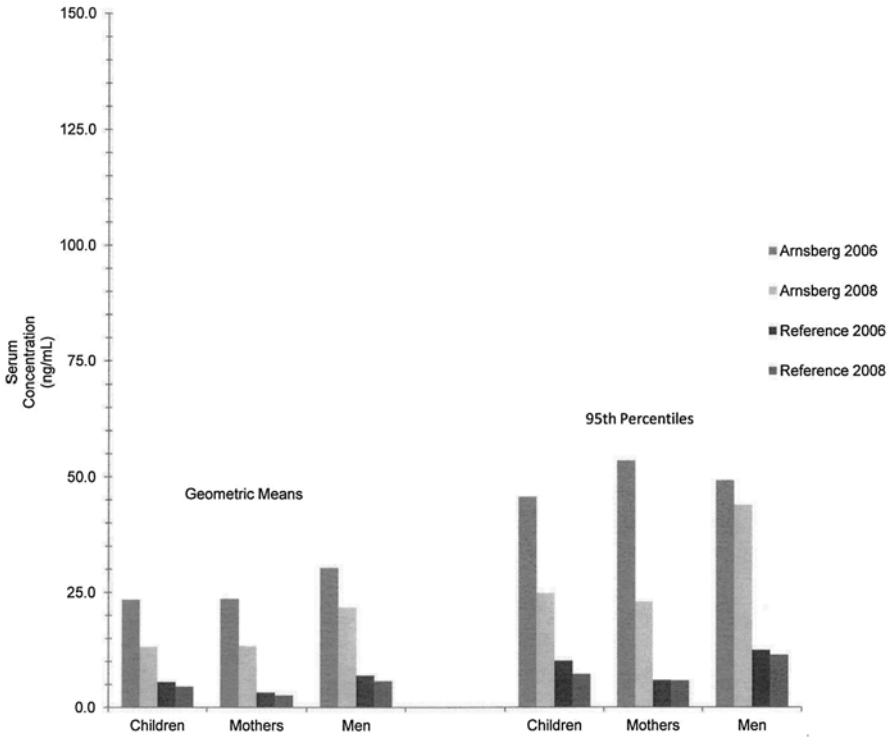

Fig. 4.16 Geometric mean and 95th percentile serum concentrations (ng/mL) of PFOA among children, women, and men from the City of Arnsberg, Germany and referent populations (Brilon, Siegen), 2006 and 2008

4.3.3 China

4.3.3.1 Tangxun Lake, Wuhan, China

Tangxun Lake is a relatively shallow body of water 36 km^2 area wide located in Wuhan, China (population ten million). Tangxun Lake water drains to the nearby Yangtze river. Elevated serum concentrations of PFASs were reported in the surface water and sediments of Tangxun Lake, its aquatic biota samples, and serum from commercial fishermen on the lake (Zhou et al. 2013, 2014). Fluorochemical manufacturing plants were identified in an industrial park upstream from the wastewater treatment plant situated on the upper reaches of the lake. As previously mentioned, Wang et al. (2010) described an environmental assessment at a manufacturing facility near Wuhan, (Hubei Province) China. The main products produced by ECF were perfluoroalkyl sulfonic acid, perfluorocarboxylic acids, and perfluorotertiary amines and their derivatives. Whether this plant is part of this industrial park is uncertain.

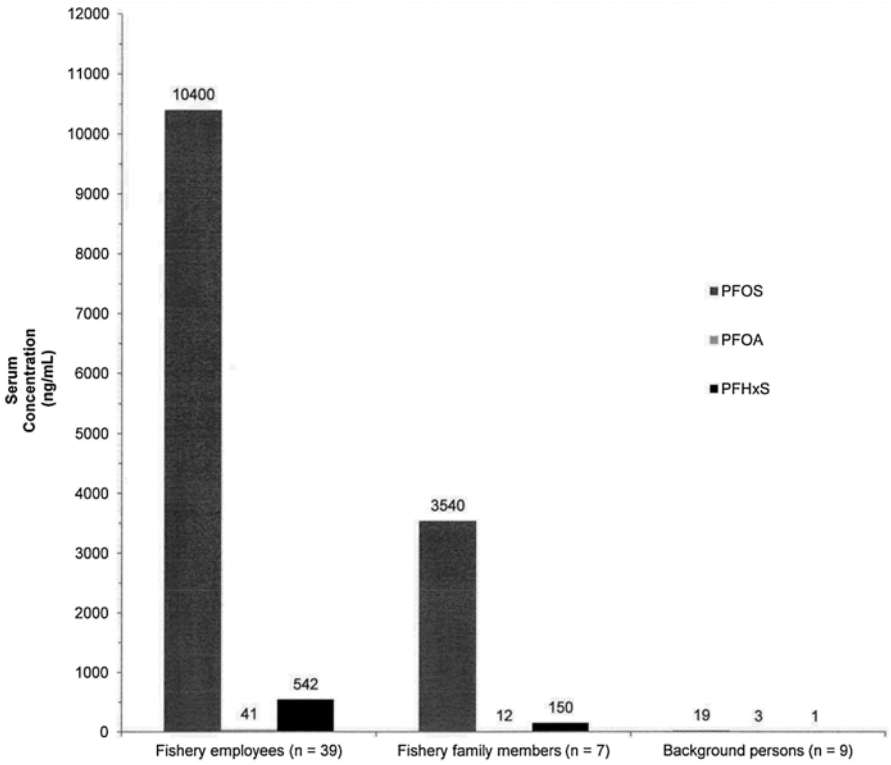

Fig. 4.17 Median serum PFOS and PFOA concentrations (ng/mL) among fishery employees and their family members, Tangxun Lake, Wuhan, China

Upstream from this Tangxun Lake wastewater treatment plant were water samples that had the following concentrations measured: PFBA 47.8 μg/L; PFOA 2.6 μg/L; PFBS 15.3 μg/L; PFHxS 0.49 μg/L; and PFOS 2.14 μg/L. Effluent from the wastewater treatment plant had similar mean concentrations of PFOS and PFOA but mean concentrations of PFBA and PFBS declined to 6 μg/L and 5 μg/L, respectively. Surface lake water concentrations of PFOA and PFOS ranged between 0.1 and 0.3 μg/L. For PFBA and PFBS, the average surface lake water concentrations were 4.8 μg/L and 3.7 μg/L, respectively. For perspective, the US EPA Provisional Advisory for Water for PFOS and PFOA are 0.2 μg/L and 0.4 μg/L (See Chap. 17 for other advisory values from other states and countries.)

Figure 4.17 presents the median PFAS serum concentrations for 37 Tangxun Lake fishermen, 7 family members, and 9 reference individuals. The median PFOS concentrations were 10,400 ng/mL, 3,540 ng/mL, and 19 ng/mL, respectively. The linear/branch PFOS ratio was 3.6:1 which approximates the ratio to be expected with the ECF manufacture of POSF. The highest serum PFOS concentration measured was 31,400 ng/mL in a commercial fisherman. This concentration is threefold higher than the next highest value ever reported – a worker engaged in

POSF production workers at the 3M Decatur plant (Olsen et al. 2003b). PFHxS concentrations were also considerably higher in the commercial fishermen (median 542 ng/mL) but lower for PFOA (41 ng/mL) (Fig. 4.16). Several species of Tangxun lake carp, shrimp and snail had PFOS concentrations ranging between 200 and 600 ng/g/ww (Zhou et al. 2013). Exposures to commercial fishermen on Tangxun Lake were considered likely due to their fish consumption (Zhou et al. 2014). Zhou et al. concluded the population identified around Tangxun Lake may offer an excellent research opportunity to resolve controversial PFAS findings in the published epidemiologic studies.

4.4 Other Biomonitoring Data (Medical, Occupational, and Consumer)

4.4.1 Phase I Clinical Trial of Cancer Patients

APFO has been shown to cause endoplasmic reticulum stress, inhibit PIM kinases, and exhibit anti-cancer activity in multiple xenograft models (MacPherson et al. 2010, 2011). The tolerability, safety and pharmacokinetics of APFO were reported in an update of a phase I clinical trial in 41 human patients with advanced (solid) cancer (MacPherson et al. 2010). Sequential cohorts of three patients were enrolled in this dose escalation trial that followed a standard 3+3 design until dose-limiting toxicity was observed in two or more of six patients at a given dose. The protocol-defined maximum tolerated dose was not reached. The recommended Phase 2 dose was 1,000 mg weekly based on the common cumulative drug-related toxicity of fatigue, nausea, vomiting, and diarrhea at weekly 1,200 mg doses. Based on a poster presentation (McPherson et al. 2010), highest plasma level of PFOA achieved in a patient approached 1250 μM (approximately 515,000 ng/mL). To date, this would be the highest PFOA concentration known to have been reported in a human.

4.4.2 Professional Ski Waxers

In a series of papers, Nilsson et al. (2010a, b, 2013) investigated PFAS exposures among professional ski waxers. Two types of ski wax are used depending on the race: grip and glide, but only the latter contains fluorinated additives. Glide ski waxes are applied using a petroleum based product that contains various linear hydrocarbons with the formula $(CH_3(CH_2)_nCH_3$ [where n is between 10 and 80 carbon atoms] and semifluoroalkanes with the formula $(CH_3(CH_2)_m(CF_2)_nCF_3$ [where m varies from 14 to 20 and n from 2 to 16]. Specific formulas are usually not disclosed by the manufacturers.

Nilsson et al. (2010a) conducted a seasonal biomonitoring trend study of eight professional ski waxers employed by the Swedish and US national cross-country ski teams. During the professional racing season, these technicians applied fluorinated ski wax approximately 30 h per week. A total of 57 blood samples were examined before, during, and after the International Federation Ski (FIS) World Cup season in 2007–2008. Nilsson et al. compared the ski wax technicians' blood levels to unexposed men of similar age. Among the professional ski waxers, their median PFOA whole blood concentration was 112 ng/mL compared to the unexposed group's 2.7 ng/mL level. Their PFNA levels (range 10.1–163 ng/mL) were between 15 and 270 times that of the referent group. Other perfluorocarboxylate concentrations reported higher than expected concentrations included perfluorohexanoate (PFHxA), perfluoroheptanoate (PFHpA), perfluorodecanoate (PFDA), and perfluoroundecanoate (PFUnDA). The sulfonated PFASs were not above background levels because these compounds are not incorporated in ski waxes.

Nilsson et al. (2010b) examined inhalation exposure to fluorotelomer alcohols as application of the ski waxes frequently occurs in small cabins. Air monitoring of perfluorocarboxylates, perfluorosulfonates, and fluorotelomers (6:2FTOH, 8:2 FTOH, and 10:2 FTOH) were analyzed. The 8:2 FTOH (range 830–250,000 ng/m^3) was the highest measured and ranged 8–32 times higher than PFHxA (57–14,000 ng/m^3) and 10–800 times higher than PFOA (80–4,900 ng/m^3). The average concentration of telomer alcohols 6:2 FTOH, 8:2 FTOH, and 10:2 FTOH were 240 ng/m^3, 92,800 ng/m^3, and 370 ng/m^3 in the air, respectively. Mean levels of PFOA and PFNA were 1,200 ng/m^3 and 30 ng/m^3 compared to 4,900 ng/m^3 for PFHxA. Air monitoring data were not correlated to serum concentrations due to the long serum elimination half-life of PFOA.

Nilsson et al. (2013) studied whether the PFOA measured in these professional ski wax technicians came from direct exposure to PFOA in the air or from biotransformation of the 8:2 FTOH. Their data indicated metabolism of FTOHs to PFOA and PFNA was the likely biotransformation pathway because 5:3 fluorotelomer carboxylic acid (5:3 FTCA) and 7:3 FTCA metabolites were also measured in the whole blood of these ski wax technicians (median concentrations 1.7 ng/mL and 0.92 ng/mL), respectively.

Freberg et al. (2010) examined PFAS blood concentrations and air samples among 13 professional ski waxers from the Norwegian ski team. They monitored serum concentrations after one season (March 2008), obtained a second sample just before the next season (November 2008), and collected final samples obtained after the second season (March 2009). At the end of the second season, median serum PFOA (57 ng/mL, range 20–162), perfluorononanoate (PFNA) (6.8 ng/mL, range 2.3–27), and PFDA (0.9 ng/mL, range 0.2–3.3) concentrations were approximately 25-fold, tenfold and tenfold higher, respectively, than the Norwegian general population. Serum PFOA, PFNA, and PFDA concentrations were correlated with the number of years exposed to ski waxes. C4–C14 chain lengths were determined in the air monitoring data; with PFOA (C8), PFDA (C10), and PFDoDA (C12), and perfluorotetradecanoate (PFTrDA) (C14) having the highest concentrations.

4.4.3 *Firefighters*

Because of their surface-tension properties, aqueous film-forming foams (AFFF) are chemical mixtures developed to extinguish and prevent re-ignition of hydrocarbon fuel-based fires. AFFFs were formulated with proprietary fluorinated surfactants (D'Agostino and Mabury 2014). AFFF differed by their multiple manufacturers and year of production (Houtz et al. 2013). In general, AFFFs contained fluorosurfactants, hydrocarbon surfactants, cosolvents and solvents (Weiner et al. 2013). PFOS was a commonly used fluorosurfactant in AFFFs (before phase-out) with 6:2 fluorotelomer chain length products subsequently becoming a dominant source in AFFFs with 6:2 fluorotelomermercaptoalkylamido sulfonate (FTAS) and 6:2 fluorotelomersulfonamide alkylbetaine (FTAB) as common components. D'Agostino and Mabury (2014) recently identified 12 novel and 10 infrequently reported PFAS classes in AFFFs with fluorinated chain lengths ranging from C3 to C15 that represented 103 total compounds. Investigations have examined AFFF training locations, including airport fire fighting training facilities whether they were military or civilian operations. Several of these sites have now been characterized for soil, ground water and other environmental assessments of PFASs and the reader is directed elsewhere for such analyses as findings are site-specific (Awad et al. 2011; Place and Field 2012; Weiss et al. 2012; Weiner et al. 2013).

Studies were not identified that reported biomonitoring data obtained from individuals who were trained with AFFF formulations that were applied to specific hydrocarbon fuel-based fires, whether actual or ignited for training based purposes. In Cologne, Germany ten nearby community residents were sampled via biomonitoring whose private drinking wells contained PFASs likely from a nearby fire training area (Weiss et al. 2012). For well "A", plasma concentrations for five of the individuals ranged for PFOS from 19.4 to 295 ng/mL, for PFOA from 4.0 to 18.0 ng/mL, and for PFHxS from 18.9 to 205 ng/mL. Serum concentrations were somewhat lower for individuals who belonged to well "B".

Large scale perfluoroalkyl-related biomonitoring studies of fire fighters have not been published. A subset of 36 individuals from the mid-Ohio River valley C8 Health Project cross-sectional study conducted in 2005–2006 (see community exposure) self-identified their single employment category as firefighters (Jin et al. 2011). These individuals' median PFHxS concentration was 4.6 ng/mL compared to those who reported other employment (3.6 ng/mL) or no job reported (3.5 ng/mL). Likewise, the median PFOS serum concentrations were 27.9 ng/mL, 23.0 ng/mL, and 20.9 ng/mL, respectively. Although Jin et al. suggested the PFHxS difference was likely the result of exposure to fire-suppression foam and/or fire conditions in households with stain resistant carpet applications, their small sample size, the absolute difference (1 ng/mL), and the lack of detailed occupational history suggests the authors' inference was rather speculative.

4.4.4 Fishermen

As reported in several northern European countries, diet, particularly that of fish, is considered an important source to the PFOS serum concentrations measured in Scandinavian general populations (Falandysz et al. 2006; Haug et al. 2010; Rylander et al. 2010), although this association has not been consistently observed in these countries (Eriksen et al. 2011). A sample of 196 Greenlandic Inuits, whose traditional diet consists of consumption of fish and marine mammals, had a mean PFOS concentration of 51.9 ng/mL in 2002–2003 (Lindh et al. 2012). This was approximately 50 % higher than NHANES data (Kato et al. 2011). Among these Inuits, higher concentrations were reported for those who lived in more isolated regions than those residing in Nuuk, the capital of Greenland, where purchased foods were a greater source of PFASs.

In other parts of Europe, geometric mean serum PFOS and PFOA concentrations of 478 freshwater fish anglers from six regions in France were comparable to U.S. and Canadian general population levels (Denys et al. 2014). This finding may be the result of the relatively low frequency of fresh water fishing in this population. However, the top 10th percentile of these anglers fished at least ten times during the year. At the 95th percentile of these fresh water anglers, their geometric mean concentration was 56.7 ng/mL for PFOS compared to 40.4 ng/mL in NHANES suggesting fresh water fish consumption contributes to PFOS concentrations among those who fish often.

It should therefore not be unexpected that fishermen may have higher serum concentrations of PFASs when consuming fish from lakes affected with higher PFAS concentrations as a consequence of industrial PFAS releases (e.g., Tangxun Lake, Wuhan, China) or from agricultural run-off into rivers where soil conditioner containing perfluoroalkyl compounds had been applied to the land (Lake Möhne, Germany). Commercial fishermen on Tangxun Lake, as well as their family members, had serum PFOS concentrations in the higher ranges of occupational manufacturing workers (Fig. 4.17). The highest serum PFOS concentration (31,400 ng/mL) reported, to date, in the scientific literature, was measured in one of these Tangxun Lake commercial fishermen (Zhou et al. 2014). At Lake Möhne (discussed above) near Arnsberg, Germany, Hölzer et al. (2011) reported two to threefold higher serum PFOS concentrations among individuals consuming at least three fish per month than those who did not consume fish (Fig. 4.18).

4.4.5 Post-market Consumers

Because diet was considered to represent a much larger source contribution, Trudel et al. (2008) estimated exposure to consumer products would result in minor exposures to PFOS and PFOA. For example, consumer-related exposures may occur through treated carpets and coated food contact material but exposures could change over time based on different formulations (Liu et al. 2014).

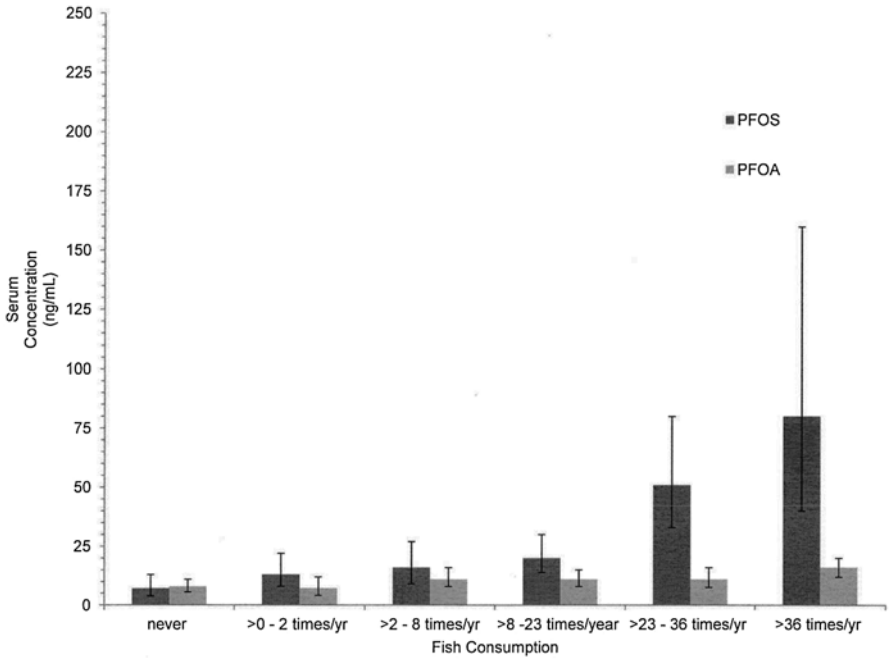

Fig. 4.18 Geometric mean PFOS and PFOA plasma concentrations (95 % confidence intervals) by fish consumption in 105 Anglers, Lake Möhne, Germany

Although human exposure to treated products is considered low, subgroups of the general population could obtain higher exposures (Herzke et al. 2012). In this regard, Beeson et al. (2012) reported unusually high serum perfluorohexanesulfonate (PFHxS) concentrations (range 27.5–423 ng/mL) in a family whose carpets had been commercially cleaned eight times over 15 years. As a reference, PFHxS concentrations in the Canadian general population ranged between 1 and 3 ng/mL. Measurement of vacuum dust in the home found high concentrations of PFHxS (2,780 ng/g) and PFOS (1,090 ng/g). In this particular family's case, their Edmonton residence had an in-floor radiant heating system. Wall-to-wall carpeting had been installed on top of these heated floors. Beeson et al. believed the high PFHxS to PFOS ratio reflected two historical 3M Scotchgard™ products that might have been commercially applied to provide such an exposure ratio. For reasons yet understood, the shorter chain PFHxS has been reported to have a longer serum elimination half-life in humans (approximately 7–8 years) than the longer chain PFOS (approximately 4 years) (Olsen et al. 2007) or the shorter chain PFBS (approximate half-life of 30 days) (Olsen et al. 2009). This is unlike the C4 (PFBA), C6 (PFHxA), and C8 (PFOA) perfluorocarboxylates whose human serum half-lives have been approximately 3 days (Chang et al. 2008), 32 days (Russell et al. 2013), and 2.3–3.5 years (Bartell 2012; Olsen et al. 2007), respectively.

Although general population serum concentrations of PFHxS in the United States and Canada generally range between 1 and 3 ng/mL, Olsen et al. (2004a) observed PFHxS concentrations were slightly higher among subsets of 598 children and hypothesized it may be due to their activity exposure patterns (e.g., related to playing more on carpets) (Olsen et al. 2004a). They reported 95 % of the adult (Olsen et al. 2003d) and elderly (Olsen et al. 2004b) populations had serum PFHxS concentrations less than 10 ng/mL but this percentage was 73 % in children. Furthermore, only 1 of 645 adults and 1 of 238 elderly individuals had measured serum PFHxS concentrations greater than 30 ng/mL compared to 11 % (N=67) of the 598 children samples. Similar distributions were observed for N-methyl perfluorooctanesulfonamidoacetate, found in PFOS-based products used primarily in surface treatment applications (e.g., carpets, upholstery, textiles), and therefore considered a possible marker for consumer-related exposure. Subsequent NHANES data reported by Kato et al. (2009) supported such a hypothesis in pooled analyses of children's serum. In addition, other sampling exposure regimens continued to show household dust as a source for PFASs, including PFHxS and fluorotelomer alcohols (Strynar and Lindstrom 2008; Haug et al. 2011) It should also be noted that N-methyl perfluorooctanesulfonamidoacetate (N-MeFOSA-AcOH) has declined in NHANES data between 1999 and 2000 when the geometric mean serum concentration was 0.97 ng/mL (95 % CI 0.84–1.11) and 2007–2008 (geometric mean 0.35 ng/mL, 95 % CI 0.32–0.38).

4.5 Summary

Provided in Fig. 4.19 (PFOS), Fig. 4.20 (PFOA), and Fig. 4.21 (PFHxS) are comparative analyses of the magnitude of concentrations measured across the three types of higher exposed populations that were reviewed in this chapter: (1) PFAS manufacturing and 'downstream' production workers; (2) communities affected by specific identifiable sources of PFAS exposure (above background levels) that have affected municipal and/or private water sources; and (3) medically-, occupationally- and consumer-related.

Until recently, the highest serum PFOS, PFOA, and PFHxS concentrations measured involved PFAS manufacturing workers. While this remains true for average concentrations, this is not the situation on an individual basis. A commercial fisherman in Tangxun Lake (Wuhan, China) has the highest concentration reported, to date, for PFOS (31,400 ng/mL). This is approximately threefold greater than the highest PFOS measured in a manufacturing worker and 2,500 times larger than the average in the general population. As for PFOA, again from a population standpoint, the highest exposed populations with PFOA concentrations are in the occupational setting (3M, DuPont, and Miteni). However, the highest serum PFOA concentration ever reported was from a cancer patient enrolled in a phase I clinical trial of APFO. This patient's serum PFOA concentration exceeded 515,000 ng/mL. This is fivefold greater than the highest PFOA concentration measured in a

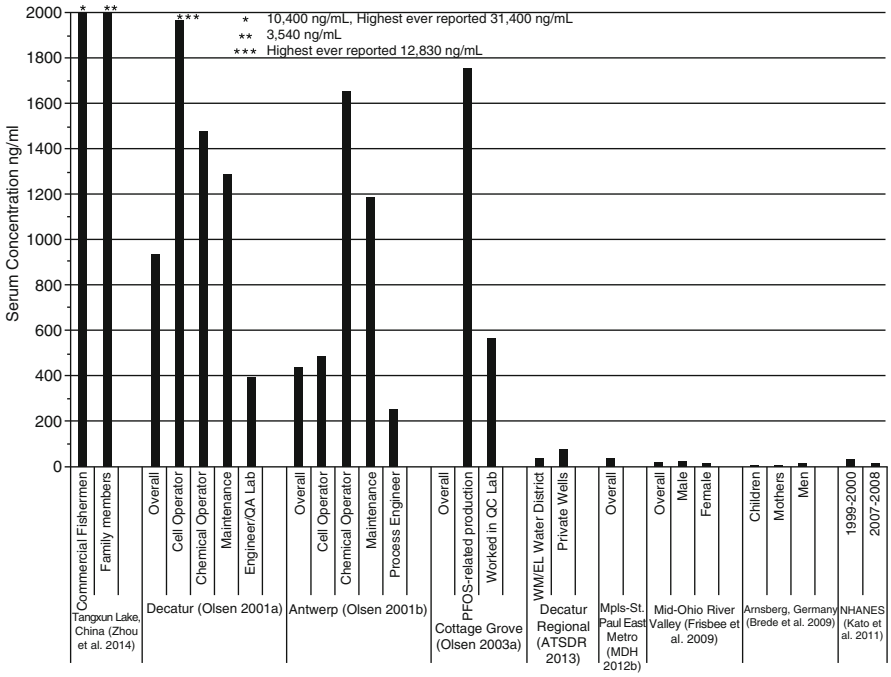

Fig. 4.19 Geometric mean (or median) serum PFOS concentrations in higher exposed populations. See text for descriptions of studies

manufacturing worker and 100,000 times higher than the average person in the general population.

Although affected communities are sometimes referred to as 'highly exposed', such terminology is always relevant to a baseline. Although individuals in these communities' populations may have concentrations comparable to manufacturing workers, as shown in Figs. 4.19, 4.20, and 4.21, the higher average exposed populations remain those in PFAS manufacturing and application jobs. The higher exposed former manufacturing populations have PFOS, PFOA, and PFHxS average serum concentrations 2–3 orders higher than the NHANES general population (Figs. 4.19, 4.20, and 4.21). Events unfolding with the very high PFOS concentrations being measured among commercial fishermen in Tangxun Lake, Wuhan, China may provide further opportunities for understanding PFAS concentrations in higher exposed populations (Zhou et al. 2014).

There are several areas of investigation among higher exposed populations that may be of interest to PFAS biomonitoring researchers. First, have the PFAS concentrations declined among the former manufacturing industrial workers? Have their PFAS blood concentrations declined at a rate to be expected? Unlike several biomonitoring trend studies of the general population where PFOS concentrations have declined by approximately two-thirds since 2000, such trends have not been reported among manufacturing workers. Second, have affected communities who had PFAS

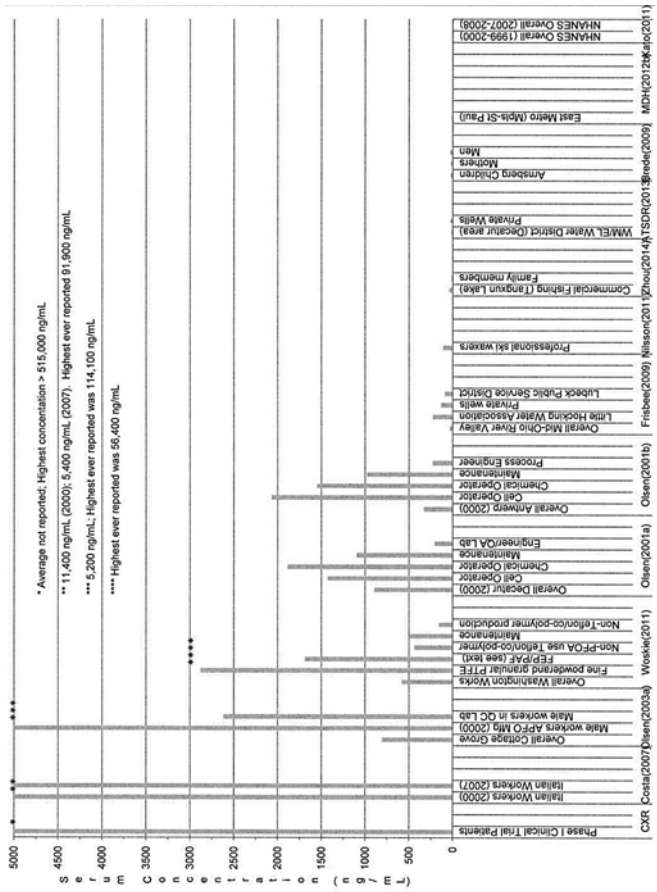

Fig. 4.20 Geometric mean (or median) serum PFOA concentrations in higher exposed populations. See text for descriptions of studies

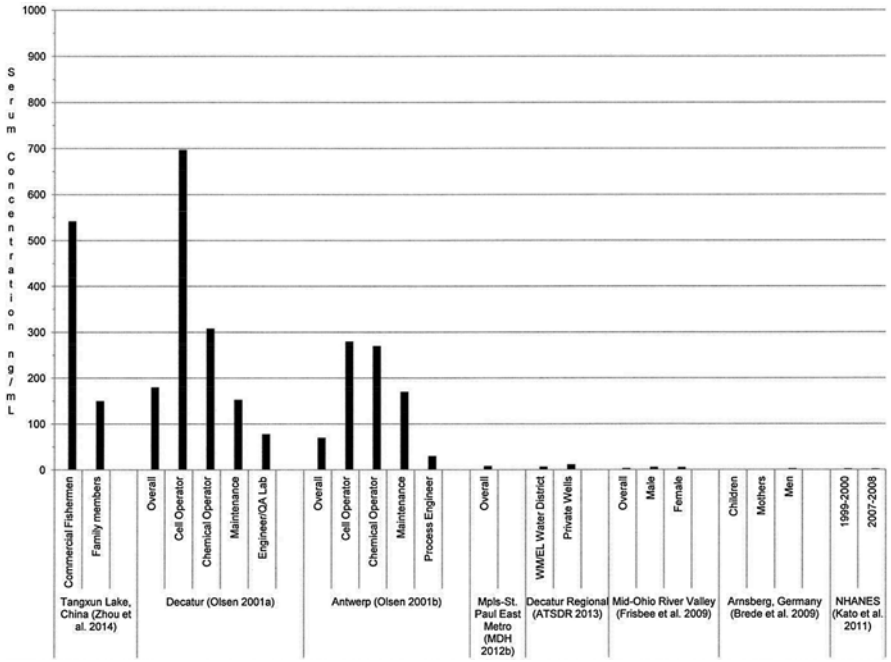

Fig. 4.21 Geometric mean (or median) serum PFHxS concentrations in higher exposed populations. See text for descriptions of studies

mitigation activities applied to their water supplies, continued to experience declining PFAS concentrations? Third, research should be directed at measuring and reporting PFAS concentrations in workers in the burgeoning Chinese perfluorochemical industry. Although concentrations in the Chinese general population appear to have increased (Jin et al. 2007), there is a virtual absence of reporting of biomonitoring data in these manufacturing workers. Fourth, although the study population was small, epidemiologic analyses of the clinical chemistry data of the patients in the Phase 1 clinical trial of APFO could answer critically important epidemiologic questions. These answers may provide substantial insight into the various epidemiologic associations reported about PFOA that have been inconsistently reported at much lower concentrations, often reported at general population levels (see Chap. 14). Finally, this chapter primarily focused on PFOS and PFOA. The replacement chemistry for the higher chain PFASs are shorter chain perfluorosulfonate and perfluorocarboxylate compounds that have considerably faster serum elimination rates in humans. Whereas there have been some biomonitoring data reported on the short-chain PFASs in the general population (Kato et al. 2011; Olsen et al. 2012a), understanding higher exposed populations to these shorter chain compounds in the occupational setting will provide additional perspectives.

References

ACGIH (1997) Tetrafluoroethylene. CAS number 116-14-3. TLV-TWA documentation. American Conference Governmental Industrial Hygienists, Cincinnati

ATSDR (Agency for Toxic Substances and Disease Registry) (2013) Health consultation. Exposure investigation report. Perfluorochemical serum sampling in the vicinity of Decatur, Alabama, Morgan, Lawrence, and Limestone counties. U.S. Department of Health and Human Services, Atlanta. Available at http://www.atsdr.cdc.gov/HAC/pha/Decatur/Perfluorochemical_Serum%20Sampling.pdf. Accessed 18 July 2014

Awad E, Zhang X, Bhavsar S et al (2011) Long-term environmental fate of perfluorinated compounds after accidental release at Toronto airport. Environ Sci Technol 45:8081–8089

Bartell SM (2012) Bias in half-life estimates using log concentration regression in the presence of background exposures, and potential solutions. J Expo Sci Environ Epidemiol 22:299–303

Bartell SM, Calafat AM, Lyu C et al (2010) Rate of decline in serum PFOA concentrations after granular activated carbon filtration at two public water systems in Ohio and West Virginia. Environ Health Perspect 118:222–228

Beesoon S, Genius SJ, Benskin JP et al (2012) Exceptionally high serum concentrations of perfluorohexanesulfonate in a Canadian family are linked to home carpet treatment applications. Environ Sci Technol 46:12960–12967

Benbrahim-Tallaa L, Lauby-Secretan B, Loomis D et al (2014) Carcinogenicity of perfluorooctanoic acid, tetrafluoroethylene, dichloromethane, 1,2-dichloropropane, and 1,3-propane sultone. Lancet Oncol 15:924–925

Berg V, Nøst TH, Huber S et al (2014) Maternal serum concentrations of per- and polyfluoroalkyl substances and their predictors in years with reduced production and use. Environ Int 69:58–66

Branstæter AL, Whitworth KW, Ydersbond TA et al (2013) Determinants of plasma concentrations of perfluoroalkyl substances in pregnant Norwegian women. Environ Int 54:74–84

Brede E, Wilhelm M, Göen T et al (2010) Two-year follow-up biomonitoring pilot study of residents' and controls' PFC plasma levels after PFOA reduction in public water system in Arnsberg, Germany. Int J Hyg Environ Health 213:217–223

Buck RC, Franklin J, Berger U et al (2011) Perfluoroalkyl and polyfluoroalkyl substances in the environment: terminology, classification, and origins. Integr Environ Assess Manag 7:513–541

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

Chang SC, Das K, Ehresman DJ et al (2008) Comparative pharmacokinetics of perfluorobutyrate in rats, mice, monkeys, and humans and relevance to human exposure via drinking water. Toxicol Sci 104:40–53

Chang E, Adami HO, Boffetta P et al (2014) A critical review of perfluorooctanoate and perfluorooctanesulfonate exposure and cancer risk in humans. Crit Rev Toxicol 44(S1):1–81

Consonni D, Straif K, Symons JM et al (2013) Cancer risk among tetrafluoroethylene synthesis and polymerization workers. Am J Epidemiol 178:350–358

Costa G, Sartori S, Consonni D (2009) Thirty years of medical surveillance in perfluorooctanoic acid production workers. J Occup Environ Med 51:364–372

D'Agostino LA, Mabury SA (2014) Identification of novel fluorinated surfactants in aqueous film forming foams and commercial surfactant concentrates. Environ Sci Technol 48:121–129

D'eon JC, Mabury SA (2011) Is indirect exposure a significant contributor to the burden of perfluorinated acids observed in humans? Environ Sci Technol 45:7974–7984

D'eon JC, Hurley MD, Wallington TJ et al (2006) Atmospheric chemistry of N-methyl perfluorobutane sulfonamidoethanol $C_4F_9SO_2N(CH_3)CH_2CH_2OH$: kinetics and mechanism of reaction with OH. Environ Sci Technol 40:1862–1868

Decatur Daily (2009) Feds to test 200 for DU toxic waste: officials say levels in Lawrence wells, beef safe, but health advisory planned. The Decatur Daily, Decatur, December 2, 2009
Denys S, Fraize-Frontier S, Moussa O et al (2014) Is fresh water fish consumption a significant determinant of the internal exposure to perfluoroalkylated substances (PFAS)? Toxicol Lett 231:233–238
Domingo JL (2012) Health risks of dietary exposure to perfluorinated compounds. Environ Int 40:187–195
Emmett EA, Shofer FS, Zhang H et al (2006) Community exposure to perfluorooctanoate: relationship between serum concentration and exposure sources. J Occup Environ Health 48:759–770
Environment Canada (2010) Environmental performance agreement ("agreement") respecting perfluorinated carboxylic acids (PFCAs) and their precursors in perfluorochemical products sold in Canada. Available from: http://ec.gc.ca/epe-epa/default.asp?lang-En&n=81AE80CE-1. Accessed 14 July 2014
Eriksen KT, Sørensen M, McLaughlin JK et al (2011) Determinants of plasma PFOA and PFOS levels among 652 Danish men. Environ Sci Technol 45:8137–8143
European Parliament (2006) Directive 2006/122/EC of the European Parliament and of the Council of 12 December 2006. Off J EU, 27 December 2006, L372/32-L372/34
Falandysz J, Taniyasu S, Gulkowska A et al (2006) Is fish a major source of fluorinated surfactants and repellents in humans living on the Baltic coast? Environ Sci Technol 40:748–751
Fasono WJ, Carpenter SC, Gannon SA et al (2006) Absorption, distribution, metabolism, and elimination of 8-2 fluorotelomer alcohol in the rat. Toxicol Sci 91:341–355
Fasono WJ, Sweeney LM, Mawn MP et al (2009) Kinetics of 8-2 fluorotelomer alcohol and its metabolites, and liver glutathione status following daily oral dosing for 45 days in male and female rats. Chem Biol Interact 180:281–295
Fei C, McLaughlin J, Lipworth L et al (2010) Maternal concentrations of perfluorooctanesulfonate (PFOS) and perfluorooctanoate (PFOA) and duration of breastfeeding. Scand J Work Environ Health 36:413–421
Freberg BI, Haug LS, Olsen R et al (2010) Occupational exposure to airborne perfluorinated compounds during professional ski waxing. Environ Sci Technol 44:7723–7728
Frisbee S, Brooks AP, Maher A et al (2009) The C8 Health Project: design methods, and participants. Environ Health Perspect 117:1873–1882
Fromme H, Tittlemier SA, Völkel W et al (2009) Perfluorinated compounds – exposure assessment for the general population in western countries. Int J Hyg Environ Health 212:239–270
Gilliland FD, Mandel JS (1996) Serum perfluorooctanoic acid and hepatic enzymes, lipoproteins, and cholesterol: a study of occupationally exposed men. Am J Ind Med 29:560–568
Glynn A, Berger U, Bignert A (2012) Perfluorinated alkyl acids in blood serum from primiparous women in Sweden: serial sampling during pregnancy and nursing, and temporal trends 1996–2010. Environ Sci Technol 46:9071–9079
Hanson KJ, Johnson EO, Eldridge JS et al (2002) Quantitative characterization of trace levels of PFOA and PFOS in the Tennessee River. Environ Sci Technol 36:1681–1685
Haug LS, Thomsen C, Brantsæter AL et al (2010) Diet and particularly seafood are major sources of perfluorinated compounds in humans. Environ Int 36:772–778
Haug LS, Humber S, Schlabach M et al (2011) Investigation on per- and polyfluorinated compounds in paired samples of house dust and indoor air from Norwegian homes. Environ Sci Technol 45:7991–7998
Herzke D, Olsson E, Posner S (2012) Perfluoroalkyl and polyfluoroalkyl substances (PFASs) in consumer products in Norway. A pilot study. Chemosphere 88:980–987
Hölzer J, Midasch O, Rauchfuss K et al (2008) Biomonitoring of perfluorinated compounds in children and adults exposed to perfluorooctanoate-contaminated drinking water. Environ Health Perspect 116:651–657
Hölzer J, Göen T, Rauchfuss K et al (2009) One-year follow-up of perfluorinated compounds in plasma of German residents from Arnsberg formerly exposed to PFOA_contaminated drinking water. Int J Hyg Environ Health 212:499–504

Hölzer J, Göen T, Just P et al (2011) Perfluorinated compounds in fish and blood of anglers at Lake Möhne, Sauerland area, Germany. Environ Sci Technol 45:8046–8052
Houtz EF, Higgins CF, Field JA et al (2013) Persistence of perfluoroalkyl precursors in AFFF-impacted groundwater and soil. Environ Sci Technol 47:8187–8195
Huang H, Yu G, Mei S (2013) PFOS production in China: production, application, and alternatives. Presentation given at 5th international conference on perfluoroalkyls. Helsingör, Denmark (Power point presentation. Available on request from chapter author) October 2013
Jin Y, Saito N, Harada KH et al (2007) Historical trends in human serum levels of perfluorooctanoate and perfluorooctane sulfonate in Shenyang, China. Tohoku J Exp Med 212:63–70
Jin C, Sun YH, Islam A et al (2011) Perfluoroalkyl acids including perfluorooctane sulfonate and perfluorohexane sulfonate in firefighters. J Occup Environ Med 53:324–328
Kato K, Calafat AM, Wong LY et al (2009) Polyfluoroalkyl compound in pooled sera from children participating in the National Health and Nutrition Examination Survey 2001–2002. Environ Sci Technol 43:2641–2647
Kato K, Wong LY, Jia LT et al (2011) Trends in exposure to polyfluoroalkyl chemicals in the U.S. population: 1999–2008. Environ Sci Technol 45:8037–8045
Kato K, Wong LY, Chen A et al (2014) Changes in serum concentrations of maternal poly- and perfluoroalkyl substances over the course of pregnancy and predictors of exposure in a multi-ethnic cohort of Cincinnati Ohio pregnant women during 2003–2006. Environ Sci Technol 48:9600–9608
Konwick BJ, Tomy GT, Ismail N et al (2008) Concentrations and patterns of perfluoroalkyl acids in Georgia, USA surface waters near and distant to a major use source. Environ Toxicol Chem 27:2911–2018
Kreckmann KH, Sakr CJ, Leonard RC et al (2009) Estimation and validation of biomarker-based exposures for historical ammonium perfluorooctanoate. J Occup Environ Hyg 6:511–516
Lau C. (2014) Perfluorinated compounds: An overview. Toxicity of Perfluoroalkyls and Perfluoroalkyl Substances. Chapter One. (ed) Dewitt J. Springer International Publishing
Lin AY, Panchangam SR, Lo CC (2009) The impact of semiconductor, electronics and optoelectronic industries on downstream perfluorinated chemical contamination in Taiwanese rivers. Environ Pollut 157:1365–1372
Lin AY, Panchangam SC, Tsai YT et al (2014) Occurrence of perfluorinated compounds in the aquatic environment as found in science park effluent, river water, rainwater, sediments, and biotissues. Environ Monit Assess 186:3265–3275
Lindh CH, Rylander L, Toft G et al (2012) Blood serum concentrations of perfluorinated compounds in men from Greenlandic Inuit and European populations. Chemosphere 88:1269–1275
Lindstrom AB, Strynar MJ, Delinsky AD et al (2011) Application of WWTP biosolids and resulting perfluorinated compound contamination of surface and well water in Decatur, Alabama, USA. Environ Sci Technol 45:8015–8021
Liu X, Gui Z, Krebs KA et al (2014) Concentrations and trends of perfluorinated chemicals in potential indoor sources from 2007 through 2011 in the US. Chemosphere 98:51–57
MacPherson IR, Bissett D, Petty B et al (2011) A first-in human phase I clinical trial of CXR1002 in patients with advanced cancer. J Clin Oncol 29:(suppl) abstract 3063
MacPherson IR, Bissett D, Tait B et al (2010) A phase I clinical trial of CXR1002 in patients with advanced cancer. Poster presentation. 22nd EORTC-NCI-AACR symposium on "Molecular targets and cancer therapeutics." Berlin, Germany
Minnesota Department of Health (2008) Perfluorochemical contamination in Lake Elmo and Oakdale, Washington county, Minnesota. US DHHS ATSDR, Atlanta. http://www.health.state.mn.us/divs/eh/hazardous/sites/washington/lakeelmo/phaelmooakdale.pdf. Accessed 27 June 2014
Minnesota Department of Health (2012a) Perfluorochemical contamination in southern Washington county, northern Dakota county, and southeastern Ramsey county, Minnesota. US DHHS ATSDR, Atlanta. Available at http://www.health.state.mn.us/divs/eh/hazardous/topics/pfcs/pha/woodbury/pha3m0112.pdf. Accessed 27 June 2014

Minnesota Department of Health (2012b) East Metro PFC biomonitoring project. Minnesota Department of Health, Minneapolis. Available at http://www.health.state.mn.us/divs/hpcd/tracking/biomonitoring/projects/eastmetropfc.html. Accessed 27 June 2014

Minnesota Department of Health (2012c) East Metro PFC biomonitoring project May 2013 report to the community survey analysis: how are participants exposed to PFCs? Minnesota Department of Health, Minneapolis. http://www.health.state.mn.us/divs/hpcd/tracking/biomonitoring/projects/CommunityReport-May2013.pdf Accessed 27 June 2014

Mundt DJ, Mundt KA, Luippold RS et al (2007) Clinical epidemiological study of employees exposed to surfactant blend containing perfluorononanoic acid. Occup Environ Med 64:589–594

New Jersey Department of Health (2014) Perfluorinated chemicals in the Paulsboro public drinking water system. Available at http://www.state.nj.us/health/eohs/documents/factsheet/paulsboro_pfc_factsheet.pdf. Accessed 27 June 2014

Nilsson H, Kärman A, Westberg H et al (2010a) A time trend study of significantly elevated perfluorocarboxylate levels in humans after using fluorinated ski wax. Environ Sci Technol 44:2150–2155

Nilsson H, Kärrman A, Rotander A et al (2010b) Inhalation exposure to fluorotelomer alcohols yield perfluorocarboxylates in human blood? Environ Sci Technol 44:7717–7722

Nilsson H, Kärrman A, Rotander A et al (2013) Biotransformation of fluorotelomer compound to perfluorocarboxylates in humans. Environ Int 51:8–12

Nøst TH, Vestergren R, Berg V et al (2014) Repeated measurements of per- and polyfluoroalkyl substances (PFAs) from 1979 to 2007 in males from northern Norway: assessing time trends, compound correlations and relations to age/birth cohort. Environ Int 67:43–53

Olsen GW, Gilliland FD, Burlew MM (1998) An epidemiologic investigation of reproductive hormones in men with occupational exposure to perfluorooctanoic acid. J Occup Environ Health 40:614–622

Olsen GW, Zobel LR (2007) Assessment of lipid, hepatic, and thyroid parameters with serum perfluorooctanoate (PFOA) concentrations in fluorochemical production workers. Int Arch Occup Environ Health 81:231–246

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

Olsen GW, Logan PW, Simpson CA et al (1999b) Fluorochemical exposure assessment of Decatur chemical and film plant employees. 3M Company, St Paul. U.S. EPA docket AR-226-0950

Olsen GW, Burris JM, Burlew MM et al (2000) Plasma cholecystokinin and hepatic enzymes, cholesterol and lipoproteins in ammonium perfluorooctanoate production workers. Drug Chem Toxicol 23:603–620

Olsen GW, Schmickler MN, Tierens J et al (2001a) Descriptive summary of serum fluorochemical levels among employee participants of the year 2000 Decatur fluorochemical medical surveillance program. 3M Company, St Paul. U.S. EPA docket AR-226-1030a020a

Olsen GW, Schmickler MN, Tierens J et al (2001b) Descriptive summary of serum fluorochemical levels among employee participants of the year 2000 Antwerp fluorochemical medical surveillance program. 3M Company, St Paul. U.S. EPA docket AR-226-1030a020b

Olsen GW, Butenhoff JL, Mandel JH et al (2003a) Assessment of lipid, hepatic and thyroid function in relation to an occupational biologic limit value for perfluorooctanoate. 3M Company, St. Paul. U.S. EPA docket AR-226-1351

Olsen GW, Logan PW, Hansen KJ, Simpson CA et al (2003b) An occupational exposure assessment of a perfluorooctanesulfonyl fluoride production site: biomonitoring. Am Ind Hyg Assoc J 64:651–659

Olsen GW, Burris JM, Burlew MM et al (2003c) Epidemiologic assessment of worker serum perfluorooctanesulfonate (PFOS) and perfluorooctanoate (PFOA) concentrations and medical surveillance examinations. J Occup Environ Med 45:260–270

Olsen GW, Church TR, Miller JP et al (2003d) Perfluorooctanesulfonate and other fluorochemicals in the serum of American Red Cross adult blood donors. Environ Health Perspect 111:1892–1901

Olsen GW, Church TR, Hansen KJ et al (2004a) Quantitative evaluation of perfluorooctanesulfonate (PFOS) and other fluorochemicals in the serum of children. J Child Health 2:53–76

Olsen GW, Church TR, Larson EB et al (2004b) Serum concentrations of perfluorooctanesulfonate and other fluorochemicals in an elderly population from Seattle, Washington. Chemosphere 54:1599–1611
Olsen GW, Burris JM, Ehresman DJ et al (2007) Half-life of serum elimination of perfluorooctanesulfonate, perfluorohexanesulfonate, and perfluorooctanoate in retired fluorochemical production workers. Environ Health Perspect 115:1298–1305
Olsen GW, Chang SC, Noker PE et al (2009) A comparison of the pharmacokinetics of perfluorobutanesulfonate (PFBS) in rats, monkeys, and humans. Toxicology 256:65–74
Olsen GW, Lange CC, Ellefson ME et al (2012a) Temporal trends of perfluoroalkyl concentrations in American Red Cross adult blood donors, 2000–2010. Environ Sci Technol 46:6330–6338
Olsen GW, Ehresman DJ, Buehrer BD et al (2012b) Longitudinal assessment of lipid and hepatic clinical parameters in workers involved with the demolition of perfluoroalkyl manufacturing facilities. J Occup Environ Med 54:974–983
Paustenbach DJ, Panko JM, Scott PK et al (2007) A methodology for estimating human exposure to perfluorooctanoic acid (PFOA): a retrospective exposure assessment of a community (1951–2003). J Toxicol Environ Health 70:28–57
Place BF, Field JA (2012) Identification of novel fluorochemicals used in aqueous film-forming foams used by the US military. Environ Sci Technol 46:7120–7127
Raleigh KK, Alexander BH, Olsen GW et al (2014) Mortality and cancer incidence in ammonium perfluorooctanoate production workers. Occup Environ Med 71:500–506
Russell MH, Nilsson H, Buck RC (2013) Elimination kinetics of perfluorohexanoic acid in humans and comparison with mouse, rat and monkey. Chemosphere 93:2419–2425
Russell MH, Waqterland RL, Wong F (2014) Calculation of chemical elimination half-life from blood with an ongoing exposure source: the example of perfluorooctanoic acid (PFOA). Chemosphere. http://dx.doi.org/10.1016/j.chemosphere.2014.07.061
Rylander C, Sandanger TM, Frøyland L et al (2010) Dietary patterns and plasma concentrations of perfluorinated compounds in 315 Norwegian women: the NOWAC postgenome study. Environ Sci Technol 44:5225–5232
Shin HM, Vieira VM, Ryan PB et al (2011a) Environmental fate and transport modeling for perfluorooctanoic acid emitted from the Washington Works facility in West Virginia. Environ Sci Technol 45:1435–1445
Shin HM, Vieira VM, Ryan B et al (2011b) Retrospective exposure estimation and predicted versus observed serum perfluorooctanoic acid concentrations of participants in the C8 Health Project. Environ Health Perspect 119:1760–1765
Shin HM, Ryan PB, Vieira VM et al (2012) Modeling the air-soil transport pathway of perfluorooctanoic acid in the mid-Ohio valley using linked air dispersion and vadose zone models. Atmosph Environ 51:67–74
Shin HM, Steenland K, Ryan PB et al (2014) Biomarker-based calibration of retrospective exposure predictions of perfluorooctanoic acid. Environ Sci Technol 48:5636–5642
Skutlarek D, Exner M, Färber H (2006) Perfluorinated surfactants in surface drinking waters. Environ Sci Pollut Res 13:299–307
Steenland K, Woske S (2012) Cohort mortality study of workers exposed to perfluorooctanoic acid. Am J Epidemiol 176:909–917
Steenland K, Savitz DA, Fletcher T (2014) Class action lawsuits. Can they advance epidemiologic research? Epidemiology 25:167–169
Strynar MJ, Lindstrom AB (2008) Perfluorinated compounds in house dust from Ohio and North Carolina, USA. Environ Sci Technol 42:3751–3756
Sundström M, Ehresman DJ, Bignert A et al (2011) A temporal trend study (1972–2008) of perfluorooctanesulfonate, perfluorohexanesulfonate, and perfluorooctanoate in pooled human milk samples from Stockholm, Sweden. Environ Int 37:178–183
Taylor KW, Hoffman K, Thayer KA et al (2014) Polyfluoroalkyl chemicals and menopause among women 20–65 years of age (NHANES). Environ Health Perspect 122:145–150
Toms LML, Thompson J, Rotander A et al (2014) Decline in perfluorooctane sulfonate and perfluorooctanoate serum concentrations in an Australian population from 2002 to 2011. Environ Int 71:74–80

Trudel D, Horowitz L, Wormuth M et al (2008) Estimating consumer exposure to PFOS and PFOA. Risk Anal 28:251–269

U.S. EPA (2006) 2010/2015 PFOA Stewardship Program. Available at http://www.epa.gov/oppt/pfoa/pubs/stewardship/. Accessed 14 July 2014

U.S. EPA (2009) Q&As: Perfluorochemical (PFC) Contamination in Dalton, GA. U.S. EPA. Available at http://www.pharosproject.net/uploads/files/sources/1459/doc_i_qa_pfc_daltonga.pdf. Accessed 2 July 2014

UN Environment Programme (UNEP) (2009) The new POPs under the Stockholm Convention. Available at http://chm.pops.int/Implementation/NewPOPs/TheNewPOPs/tabid/672/Default.aspx. Accessed 16 July 2014

Wang Y, Fu J, Wang T et al (2010) Distribution of perfluorooctane sulfonate and other perfluorochemicals in the ambient environment around a manufacturing facility in China. Environ Sci Technol 44:8062–8067

Wang J, Zhang Y, Zhang W et al (2012) Association of perfluorooctanoic acid with HDL cholesterol and circulating miR-26b and miR-199-ep in workers of a fluorochemical plant and nearby residents. Environ Sci Technol 46:9274–9281

Weiner B, Yeung LWY, Marchington EB et al (2013) Organic fluorine content in aqueous film forming foams (AFFs) and biodegradation of the foam component 6:2 fluorotelomermercaptoalkylamido sulfonate (6:2 FTSAS). Environ Chem 10:486–493

Weiss O, Wiesmüller GA, Bunte A et al (2012) Perfluorinated compounds in the vicinity of a fire training area – human biomonitoring among 10 persons drinking water from contaminated private wells in Cologne, Germany. Int J Hyg Environ Health 215:212–215

Weston Solutions, Inc. Perfluorooctanoic Acid (PFOA) Site related environmental assessment program, 3M Decatur, Alabama Site. Quarterly Status Report, April 1, 2012 to June 30, 2012. Prepared for 3M Company by Weston Solutions, Inc

Wilhelm M, Kraft M, Rauchfuss K et al (2008) Assessment and management of the first German case of a contamination with perfluorinated compounds (PFC) in the region Sauerland, North Rhine-Westphalia. J Toxicol Environ Health 71:725–733

Winquist A, Lally C, Shin HM et al (2013) Design, methods, and population for a study of PFOA health effects among highly exposed mid-Ohio valley community residents and workers. Environ Health Perspect 121:893–899

Woskie SR, Gore R, Steenland K (2012) Retrospective exposure assessment of perfluorooctanoic acid serum concentrations at a fluoropolymer manufacturing plant. Ann Occup Hyg 56:1025–1037

Xie S, Wang T, Liu S et al (2013) Industrial source identification and emission estimation of perfluorooctane sulfonate in China. Environ Int 52:1–8

Xu L, Krenitsky DM, Seacat AM et al (2004) Biotransformation of N-ethyl-N(2-hydroxyethyl) perfluoroctanesulfonamide by rat liver microsomes, cytosol, and slices and by expressed rat and human cytochromes P450. Chem Res Toxicol 17:767–775

Xu L, Krenistky DM, Seacat AM et al (2006) N-glucuronidation of perfluorooctanesulfonamide by human, rat, dog, and monkey liver microsomes and by expressed rat and human UDP-glucuronosyltransferases. Drug Metab Dispos 34:1406–1410

Yeung LWY, Robinson SJ, Koschorreck J et al (2013a) Part I. A temporal study of PFCAs and their precursors in human plasma from two German cities 1982–2009. Environ Sci Technol 47:3865–3874

Yeung LWY, Robinson SJ, Koschorreck J et al (2013b) Part II. A temporal study of PFOS and its precursors in human plasma from two German cities 1982–2009. Environ Sci Technol 47:3875–3882

Zhang L, Liu J, Hu J et al (2012) The inventory of sources, environmental releases and risk assessment for perfluorooctane sulfonate in China. Environ Pollut 165:193–198

Zhou Z, Liang Y, Shi Y et al (2013) Occurrence and transport of perfluoroalkyl acids (PFAAs), including short-chain PFAAs in Tangxun Lake, China. Environ Sci Technol 47:9249–9257

Zhou Z, Shi Y, Vestergren et al (2014) Highly elevated serum concentrations of perfluoroalkyl substances in fishery employees from Tangxun Lake, China. Environ Sci Technol 48:3864–3874