

## Perfluorochemicals (PFCs)

Perfluorochemicals (PFCs) are a group of synthetic chemicals that have been used in many consumer products.<sup>1</sup> The structure of these chemicals makes them very stable, hydrophobic (water-repelling), and oleophobic (oil-repelling). These unique properties have led to extensive use of PFCs in surface coating and protectant formulations for paper and cardboard packaging products; carpets; leather products; and textiles that repel water, grease, and soil. PFCs have also been used in fire-fighting foams and in the production of nonstick coatings on cookware and some waterproof clothes.<sup>1</sup> Due in part to their chemical properties, some PFCs can remain in the environment and bioconcentrate in animals.<sup>2-8</sup> Data from human studies suggest that some PFCs can take years to be cleared from the body.<sup>9-13</sup>

The PFCs with the highest production volumes in the United States have been perfluorooctane sulfonic acid (PFOS) and perfluorooctanoic acid (PFOA).<sup>1</sup> PFOS and PFOA are also two of the most frequently detected PFCs in humans.<sup>14</sup> Other PFCs include perfluorohexane sulfonic acid (PFHxS), which is a member of the same chemical category as PFOS; and perfluorononanoic acid (PFNA), which is a member of the same chemical category as PFOA.<sup>15</sup> Chemicals within a given PFC chemical category share similar chemical structures and uses. Although some studies have addressed PFHxS and PFNA specifically, the majority of scientific research has focused on PFOS and PFOA.<sup>15</sup>

In 2000, one of the principal perfluorochemical manufacturers, 3M, began phasing out the production of PFOA, PFOS, and PFOS-related compounds. The 3M phaseout of PFOS and PFHxS was completed in 2002, and its phaseout of PFOA was completed in 2008.<sup>16</sup> In 2006, to address PFOA production by other manufacturers, EPA launched the 2010/15 PFOA Stewardship Program, with eight companies voluntarily agreeing to reduce emissions and product content of PFOA, PFNA, and related chemicals by 95% no later than 2010. The industry participants also committed to work toward eliminating emissions and product content of these chemicals by 2015.<sup>17</sup> However, the fact that some of these chemicals may be persistent in the environment and have a long half-life in humans means that they may continue to persist in the environment and in people for many years, despite reductions in emissions.<sup>2-13</sup> EPA is currently evaluating the potential need for regulation of PFCs using the authorities of the Toxic Substances Control Act.<sup>15</sup>

The major sources of human exposure to PFCs are poorly understood, but may include food, water, indoor and outdoor air, breast milk, and dust.<sup>4</sup> Two recent studies pointed to food consumption as the primary pathway of exposure to PFOS and PFOA for Americans and Europeans.<sup>18,19</sup> PFC-treated food-contact packaging, such as microwave popcorn bags,<sup>i</sup> has been a

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<sup>i</sup> The U.S. Food and Drug Administration recently worked with several manufacturers to remove grease-proofing agents containing C8 perfluorinated compounds from the marketplace. These manufacturers volunteered to stop distributing products containing these compounds in interstate commerce for food-contact purposes as of October 1, 2011. For more information, see <http://www.fda.gov/Food/FoodIngredientsPackaging/FoodContactSubstancesFCS/ucm308462.htm>.

source of PFC exposure.<sup>20</sup> Meat and dairy products may also be contaminated with PFCs due to exposure of source animals to air, water, and feed contaminated with PFCs,<sup>21-23</sup> although a recent study reported that PFCs were undetected in nearly all milk samples tested in the United States.<sup>24</sup> In some areas, such as those near industrial facilities that either make or use PFCs, these contaminants have been found at high levels in drinking water, groundwater, and/or surface water.<sup>25-31</sup> PFCs have been detected in human breast milk.<sup>32-36</sup> PFCs have been measured in house dust as well, with some perfluorochemicals, such as PFOS, PFOA, PFHxS, perfluorobutane sulfonic acid (PFBS), and perfluorohexanoic acid (PFHxA), found to be present in the majority of dust samples examined.<sup>37-40</sup> Infants and small children may be more highly exposed to the PFCs present in house dust than adults are, due to their frequent and extensive contact with floors, carpets, and other surfaces where dust gathers, as well as their frequent hand-to-mouth activity.<sup>18,19,41,42</sup> Children could have increased exposure to PFCs in carpet and carpet protectants, due to the amount of time they spend lying, crawling, and playing on carpet.<sup>15,41</sup> Limited available data on levels of PFCs in children's blood suggest that the blood serum levels of most PFCs are higher in children ages 3 to 11 years compared with other age groups.<sup>43,44</sup>

Some PFCs have been widely detected in pregnant women and in umbilical cord blood, suggesting that the developing fetus can be exposed to PFCs while in the womb. However, findings between studies vary. For example, PFOS and PFOA were detected in 99–100% of blood samples collected from both pregnant and non-pregnant women in 2003–2004.<sup>45</sup> Additionally, PFOS and PFOA were detected in 99% and 100% of umbilical cord blood samples, respectively, collected from newborns in Baltimore.<sup>46</sup> In another study conducted in Japan, the level of PFOS circulating in a pregnant woman's blood was highly correlated with the level in cord blood. However, PFOA was detected in maternal samples but was not detected in umbilical cord samples in the Japanese study.<sup>47</sup> Even though studies suggest that the correlation between maternal and fetal exposure may vary, the ubiquitous presence of PFOS, PFOA, and other PFCs in blood of women of child-bearing age and in umbilical cord blood may indicate that fetal exposure to these chemicals is widespread.<sup>45,46,48</sup>

Some human health studies have found associations between prenatal exposure to PFOS or PFOA and a range of adverse birth outcomes, such as low birth weight, decreased head circumference, reduced birth length, and smaller abdominal circumference.<sup>49-52</sup> However, there are inconsistencies in the results of these studies, and two other studies did not find an association between prenatal PFC exposure and birth weight.<sup>53,54</sup> The participants in all of these studies had PFC blood serum levels comparable to levels in the general population. Animal studies echo these findings, though typically at levels much higher than what humans are normally exposed to. Developmental and reproductive effects, including reduced birth weight, decreased gestational length, structural defects, delays in postnatal growth and development, increased neonatal mortality, and pregnancy loss have all been associated with prenatal rodent exposure to PFOS and PFOA.<sup>55-65</sup>

Findings from a limited number of studies suggest that exposure to PFOS or PFOA may have negative impacts on human thyroid function. However, there are inconsistencies in the findings between these studies. Some studies have found that PFC exposures are associated with

alterations in thyroid hormone levels, as well as an increased risk of thyroid disease in the general public and in workers with occupational exposures.<sup>66-68</sup> However, a recent study of pregnant women with exposures comparable to those in the general population found that increasing levels of PFOS, PFOA, and PFHxS were not associated with differences in thyroid hormone levels.<sup>69</sup> The results from animal studies have been more consistent. Multiple animal studies have found that thyroid hormone levels are altered in animals exposed to PFOS.<sup>57,62,63,65,70-74</sup> One of these studies also found that PFOA-treated rats have altered thyroid hormone levels.<sup>71</sup> The health risks associated with maternal thyroid hormone disruption during pregnancy may make this a cause for concern. Moderate deficits in maternal thyroid hormone levels during early pregnancy have been linked to reduced childhood IQ scores and other neurodevelopmental effects, as well as unsuccessful or complicated pregnancies.<sup>75</sup>

Both animal and some human studies have found an association between PFCs exposure and cholesterol and/or triglyceride levels, although physiological differences between humans and experimental animals may cause lipid levels to vary in opposite directions.<sup>76</sup> Structurally, PFCs resemble fatty acids and can bind to receptors that play key roles in lipid metabolism and fat production.<sup>77</sup> In animal studies involving various species, PFCs are associated with decreased serum levels of these lipids,<sup>64,65,73</sup> in contrast some human studies show an increase in blood lipid levels with increased presence of PFCs, including PFOS, PFOA, PFHxS, and PFNA, while other human studies show no change in lipid levels with PFC exposure.<sup>77-84</sup> This could be a potential concern for children, because the mother's body provides a source of cholesterol and triglycerides to the developing fetus. Cholesterol and fatty acids support cellular growth, differentiation, and adipose accumulation during fetal development.<sup>49,85</sup> Finally, although human studies have not looked at the associations between PFC exposure and the immune system, animal studies have found an association between PFOS and PFNA exposure (in utero and in adulthood) and immune suppression, including alterations in function and production of immune cells and decreased lymphoid organ weights.<sup>86-88</sup>

The indicator that follows uses the best nationally representative data currently available on blood serum levels of perfluorochemicals over time for women of child-bearing age. Indicator B6 presents median blood serum levels of PFOS, PFOA, PFHxS, and PFNA for women ages 16 to 49 years.

## Indicator B6: Perfluorochemicals in women ages 16 to 49 years: Median concentrations in blood serum, 1999–2016

**About the Indicator:** Indicator B6 presents concentrations of perfluorochemicals (PFCs) in blood serum of U.S. women ages 16 to 49 years. The data are from a national survey that collects blood specimens from a representative sample of the population every two years, and then measures the concentration of PFCs in the blood serum. The indicator presents concentrations of PFCs in blood serum over time. The focus on women of child-bearing age is based on concern for potential adverse effects in children born to women who have been exposed to PFCs.

### NHANES

The National Health and Nutrition Examination Survey (NHANES) provides nationally representative biomonitoring data for PFCs. NHANES is designed to assess the health and nutritional status of the civilian noninstitutionalized U.S. population and is conducted by the National Center for Health Statistics, part of the Centers for Disease Control and Prevention (CDC). Interviews and physical examinations are conducted with approximately 10,000 people in each two-year survey cycle. CDC's National Center for Environmental Health measures concentrations of environmental chemicals in blood and urine samples collected from NHANES participants. Summaries of the measured values for more than 200 chemicals are provided in the *Fourth National Report on Human Exposure to Environmental Chemicals*.<sup>2</sup>

### Perfluorinated Compounds

Indicator B6 presents blood serum levels of four important PFCs: perfluorooctane sulfonic acid (PFOS), perfluorooctanoic acid (PFOA), perfluorohexane sulfonic acid (PFHxS), and perfluorononanoic acid (PFNA). These four PFCs were chosen because they are commonly detected in humans, and the bulk of PFCs health effects research in both humans and laboratory animals has focused on these contaminants—especially PFOS and PFOA.

PFCs bind to proteins in the serum of blood. Because PFCs remain in the human body for years, blood serum levels of PFCs are reflective of long-term exposures to these contaminants. Serum accounts for about half the weight of whole blood, so the blood serum concentration of PFCs is about twice the concentration of PFCs in whole blood.<sup>89</sup> The blood serum PFC levels for this indicator are given in nanograms of PFC per milliliter of blood serum (ng/mL).<sup>ii</sup>

Concentrations of 12 different PFCs, including PFOS, PFOA, PFHxS, and PFNA, have been measured in blood serum from a representative subset of NHANES participants ages 12 years

<sup>ii</sup> Most persistent organic pollutants (POPs) are lipophilic, meaning that they accumulate in fatty tissues; however, this is not the case for PFCs, which are both hydrophobic (water-repelling), and oleophobic (oil-repelling). They instead bind to proteins in the serum of blood. While blood levels of lipophilic POPs are commonly lipid-adjusted, the PFC measurements in blood are not.

and older beginning with the 1999–2000 survey cycle, although PFCs were not measured in the 2001–2002 cycle.

In 2015–2016, NHANES collected PFCs biomonitoring data for 1,993 individuals ages 12 years and older, including 534 women ages 16 to 49 years. The PFCs PFOS, PFNA, and PFHxS were detected in 99% to 100% of the individuals sampled in NHANES 2015–2016. PFOA was detected in 1% of the individuals sampled in 2015–2016. The median and 95<sup>th</sup> percentile of blood serum PFC levels for all NHANES participants in 2015–2016 were 5 ng/mL and 18 ng/mL, respectively, for PFOS; 2 ng/mL and 4 ng/mL, respectively, for PFOA; 1 ng/mL and 5 ng/mL, respectively, for PFHxS; 1 ng/mL and 2 ng/mL, respectively, for PFNA.

### Birth Rate Adjustment

Indicator B6 uses measurements of PFCs in blood serum of women ages 16 to 49 years to represent the distribution of PFC exposures to women who are pregnant or may become pregnant. However, women of different ages have a different likelihood of giving birth. For example, in 2003–2004, women aged 27 years had a 12% annual probability of giving birth, and women aged 37 years had a 4% annual probability of giving birth.<sup>90</sup> A birth rate-adjusted distribution of women’s PFC levels is used in calculating this indicator,<sup>iii</sup> meaning that the data are weighted using the age-specific probability of a woman giving birth.<sup>91</sup>

### Data Presented in the Indicator

Indicator B6 presents median concentrations of PFOS, PFOA, PFHxS, and PFNA in blood serum over time for women ages 16 to 49 years, using NHANES data from 1999–2016 (excluding the years 2001–2002).

Additional information on the 95<sup>th</sup> percentile blood serum levels of PFOS, PFOA, PFHxS, and PFNA for women ages 16 to 49 years is presented in the supplemental data tables for this indicator, along with information showing how median and 95<sup>th</sup> percentile blood serum levels of PFCs in women of child-bearing age vary by race/ethnicity and family income.

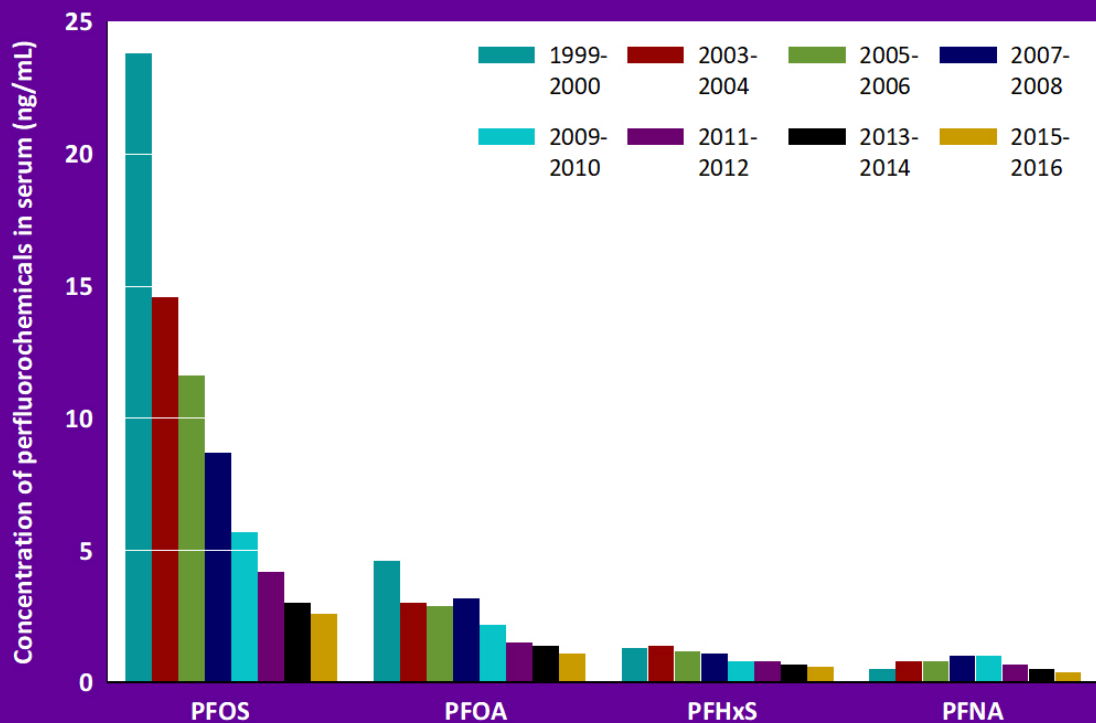
Please see the Introduction to the Biomonitoring section for an explanation of the terms “median” and “95<sup>th</sup> percentile,” a description of the race/ethnicity and income groups used in the ACE3 biomonitoring indicators, and information on the statistical significance testing applied to these indicators.

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<sup>iii</sup> There may be multiple ways to implement an adjustment to the data that accounts for birth rates by age. The National Center for Health Statistics has not fully evaluated the method used in ACE, or any other method intended to accomplish the same purpose, and has not used any such method in its publications. NCHS and EPA are working together to further evaluate the birth rate adjustment method used in ACE and alternative methods.

## Indicator B6

## Perfluorochemicals in women ages 16 to 49 years: Median concentrations in blood serum, 1999-2016



Data: Centers for Disease Control and Prevention, National Center for Health Statistics and National Center for Environmental Health, National Health and Nutrition Examination Survey

Note: To reflect exposures to women who are pregnant or may become pregnant, the estimates are adjusted for the probability (by age and race/ethnicity) that a woman gives birth.

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#### Data characterization

- Data for this indicator are obtained from an ongoing continuous survey conducted by the National Center for Health Statistics.
- Survey data are representative of the U.S. civilian noninstitutionalized population.
- PFCs are measured in blood samples obtained from individual survey participants.

- Between 1999–2000 and 2015–2016, median blood serum levels of PFOS in women of child-bearing age declined from 24 ng/mL in 1999–2000 to 3 ng/mL in 2015–2016. Median blood serum levels of PFOA in women of child-bearing age declined from 5 ng/mL in 1999–2000 to 1 ng/mL in 2015–2016. These decreasing trends were statistically significant.
- The median blood serum levels of PFHxS and PFNA were lower than those of PFOS and PFOA in women of child-bearing age. Median levels of PFHxS decreased from 1.3 ng/mL in 1999–2000 and 1.4 ng/mL in 2003–2004 to 0.6 ng/mL in 2015–2016. Between 1999–2000 and

2009–2010, median blood serum levels of PFNA showed an increasing trend, from 0.5 ng/mL in 1999–2000 to 1.0 ng/mL in 2009–2010 but then decreased to 0.4 ng/mL in 2015–2016.

- The decreasing trend in median PFHxS levels was statistically significant.
- The concentration of PFOS in blood serum at the 95<sup>th</sup> percentile in women of child-bearing age showed a decreasing trend from 50 ng/mL in 1999–2000 to 8 ng/mL in 2015–2016. The concentration of PFOA in blood serum at the 95<sup>th</sup> percentile in women of child-bearing age showed a decreasing trend from 8 ng/mL in 1999–2000 to 3 ng/mL in 2015–2016. The 95<sup>th</sup> percentile levels of PFHxS decreased from 4.9 ng/mL in 1999–2000 and 7.1 ng/mL in 2003–2004 to 2.5 ng/mL in 2015–2016. (See Table B6a.)
  - The decreasing trends in 95<sup>th</sup> percentile PFOS and PFOA levels were statistically significant.
- For the years 2013–2016, women of child-bearing age living at or above poverty level had higher median but lower 95<sup>th</sup> percentile concentrations of PFOS in their blood serum compared with women living below poverty level. (See Tables B6b and B6c.)
  - The differences between income groups were statistically significant after adjustment for differences in race/ethnicity and age.
- For the years 2013–2016, women of child-bearing age living at or above poverty level had higher median and higher 95<sup>th</sup> percentile concentrations of PFOA in their blood serum compared with women living below poverty level. (See Tables B6b and B6c.)
  - The differences between income groups were statistically significant after adjustment for differences in race/ethnicity and age.
- For the years 2013–2016, median concentrations of PFOA were higher in White non-Hispanic women of child-bearing age (1.4 ng/mL) compared with Black non-Hispanic women (0.9 ng/mL), Mexican-American women (0.9 ng/mL), and women of “All Other Races/Ethnicities” (1.3 ng/mL). (See Table B6b.)
  - The differences in median PFOA concentrations by race/ethnicity were statistically significant after accounting for other demographic characteristics (differences in age and income).
- In 2013–2016, median and 95<sup>th</sup> percentile concentrations of PFOS were lower in Mexican-American women of child-bearing age at 2.0 ng/mL and 5.4 ng/mL, respectively, compared with White non-Hispanic women at 3.0 ng/mL and 8.4 ng/mL, respectively, Black non-Hispanic women at 2.8 ng/mL and 9.7 ng/mL, respectively, and women of “All Other Races/Ethnicities” at 2.8 ng/mL and 15.7 ng/mL, respectively. (See Tables B6b and B6c.)
  - These differences were statistically significant both with and without adjustment for other demographic characteristics, with the following exception: the difference between Mexican-American and Black non-Hispanic women was not statistically significant at the 95<sup>th</sup> percentile.

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