

Sources of Exposure

Toxicokinetics and Normal Human Levels

Biomarkers/Environmental Levels

ToxGuide™ for Perfluoroalkyls

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www.atsdr.cdc.gov

Contact Information:
Division of Toxicology
and Human Health Sciences
Environmental Toxicology Branch

1600 Clifton Road NE, F-57
Atlanta, GA 30329-4027
1-800-CDC-INFO
1-800-232-4636

www.atsdr.cdc.gov/toxpro2.html



General Populations

- The major sources of exposure to perfluoroalkyls, especially PFOA and PFOS, are contaminated food and drinking water.
- Industrial releases of perfluoroalkyls into ambient air or surface water may also be a source of exposure for the general population.
- The general population may also be exposed to PFOS from carpets that have been mill treated to resist stains and to PFOA from migration from paper packaging and wrapping into food and inhalation from impregnated clothes.

Occupational Populations

- The production of perfluoroalkyl and use of perfluoroalkyl containing products are sources of occupational exposure.

Toxicokinetics

- Limited data indicate that perfluoroalkyls are absorbed from the respiratory tract. Studies in animals suggest that many perfluoroalkyls (including PFOA and PFOS) are almost completely absorbed from the gastrointestinal tract.
- The available data suggest that perfluoroalkyls are not metabolized nor do they undergo chemical reactions in the body.
- Perfluoroalkyls are primarily excreted in the urine.
- There are substantial differences in the elimination half-lives across perfluoroalkyl compounds and animal species. The estimated elimination half-lives in humans are 2.1-8.5 years for PFOA, 3.1-7.4 years for PFOS, 4.7-15.5 years for PFHxS, 2.5-4.3 years for PFNA, 665 hours for PFBuS, and 72-81 hours for PFBA. Much shorter half-lives have been estimated in experimental animals.

Normal Human Levels

- Perfluoroalkyls appear to be ubiquitous in human blood based on the widespread detection of these substances in human serum samples.
- Geometric mean serum levels of PFOA, PFOS, PFHxS, and PFNA in the U.S. population (≥ 12 years of age) were 1.94, 4.99, 1.35, and 0.675 ng/mL, respectively, and other perfluoroalkyls were generally < 1 ng/mL.

Biomarkers

- Measurement of serum or whole blood perfluoroalkyl concentrations is the standard accepted biomarkers of exposure to perfluoroalkyls.

Environmental Levels

Air

- Mean PFOA levels ranged from 1.54-15.2 pg/m^3 in urban air samples in the U.S., Norway, and Japan. PFOS levels in ambient air are generally $< 5 \text{ pg}/\text{m}^3$ and levels of other perfluoroalkyls are generally $< 1 \text{ pg}/\text{m}^3$.

Water

- Perfluoroalkyl levels in surface water samples are generally below 50 ng/L .

Soil

- Background levels of perfluoroalkyls in soil and sediment have not been located.

Reference

Agency for Toxic Substances and Disease Registry (ATSDR). 2018. Toxicological Profile for Perfluoroalkyls (Draft for Public Comment). Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service.

Chemical and Physical Information

Perfluoroalkyls are Solids or Liquids

- Perfluoroalkyls are a class of anthropogenic chemicals. There are a large number of perfluoroalkyl compounds; the toxicological profile discusses 14 of these compounds
- Perfluoroalkyls repel oil, grease, and water and have been used in surface protection products such as carpet and clothing treatments, coating for paper and cardboard packaging, and fire-fighting foams.
- Companies have stopped production of some perfluoroalkyls or have begun changing manufacturing practices to reduce releases and the amounts of these chemicals in their products.

Selected Perfluoroalkyl Abbreviations

- PFBA = perfluorobutyric acid
- PFBuS = perfluorobutane sulfonic acid
- PFDeA = perfluorodecanoic acid
- PFDoA = perfluorododecanoic acid
- PFHpA = perfluoroheptanoic acid
- PFHxS = perfluorohexane sulfonic acid
- PFNA = perfluorononanoic acid
- PFOA = perfluorooctanoic acid
- PFOS = perfluorooctane sulfonic acid
- PFUA = perfluoroundecanoic acid

Routes of Exposure

- Inhalation** – Most likely route of occupational exposure. Minor route of exposure for the general population.
- Oral** – Most likely route of exposure for the general population; food is expected to be the primary source.
- Dermal** – Potential route of exposure particularly among workers who handle perfluoroalkyl-treated products.

Perfluoroalkyls in the Environment

- Perfluoroalkyls are very stable in the environment and are resistant to biodegradation, direct photolysis, atmospheric photooxidation, and hydrolysis.
- Perfluoroalkyls are persistent in water and soil. They are mobile in soil and leach into groundwater.
- Perfluoroalkyls biomagnify in the food web and the highest concentrations are found in apex predators. The bioaccumulation potential of perfluoroalkyls appears to increase with increasing chain length.

Relevance to Public Health (Health Effects)

Health effects are determined by the dose (how much), the duration (how long), and the route of exposure.

Minimal Risk Levels (MRLs)

Inhalation

- No acute-, intermediate-, or chronic-duration inhalation MRLs were derived for perfluoroalkyls.

Oral

- No acute-duration oral MRLs were derived for perfluoroalkyls.
- Intermediate-duration (15-365 days) provisional oral MRLs were derived for
 - PFOA: 3×10^{-6} mg/kg/day
 - PFOS: 2×10^{-6} mg/kg/day
 - PFHxS: 2×10^{-5} mg/kg/day
 - PFNA: 3×10^{-6} mg/kg/day
- No chronic-duration oral MRLs were derived for perfluoroalkyls.

Health Effects

- A large number of studies have examined the possible relationship between levels of perfluoroalkyls in blood and adverse health effects in workers, highly exposed residents, and the general population. Although statistically significant associations have been found, the studies do not establish causality.

- The weight of evidence suggests links between perfluoroalkyl exposure and several health outcomes in humans: increases in serum lipids (PFOA, PFOS, PFNA, PFDeA), pregnancy-induced hypertension and/or pre-eclampsia (PFOA, PFOS), thyroid disease (PFOA, PFOS), decreased antibody response to vaccines (PFOA, PFOS, PFHxS, PFDeA), decreased fertility (PFOA, PFOS), and small decreases in birth weight (PFOA, PFOS).
- The primary effects observed in animals include liver toxicity (PFOA, PFOS, PFHxS, PFNA, PFDeA, PFUA, PFBA, PFBuS, PFDoA, PFHpA), developmental toxicity (PFOA, PFOS, PFHxS, PFNA, PFDeA, PFUA, PFBA) and immune toxicity (PFOA, PFOS). There are profound differences in the toxicokinetics and mode of action of perfluoroalkyls between humans and experimental animals. Many of the observed effects in animals result through the activation of peroxisome proliferator-activated receptor α (PPAR- α). Humans are much less responsive to PPAR- α than rodents and thus may not be as susceptible to these types of effects. However, some adverse effects of perfluoroalkyls occur through PPAR- α -independent mechanisms.

Children's Health

- Children exposed to perfluoroalkyls would be expected to experience effects similar to those expected in adults.