

## Toxicological Effects of Per- and Polyfluoroalkyl Substances (PFASs) and their Regulatory Impact

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**Background/Objectives.** Per- and polyfluoroalkyl substances (PFASs) are used to make products resistant to stains, grease, and water. They are used in a broad range of industrial applications and commercial products to make products resistant to stains, grease, and water. Hence, they are used in fire-fighting foams, paints and lacquers, hydraulic oils, textiles, and food packaging and have been found in food. Besides production of PFAS, PFAS are primarily released to the environment through the use fire-fighting foams, including aqueous film forming foam (AFFF), fluoroprotein (FP), and film forming fluoroprotein foam (FFFP). PFASs are used in these fire-fighting products because of their ability to wet the surface of spilled fuels and rapidly spread across the fuel. The carbon-fluoride bonds make the PFASs stable to metabolic and environmental degradation, rendering the compounds persistent, bioaccumulative, and toxic.

**Approach/Activities.** A scientific literature review indicates that PFAS toxicity data is prevalent for perfluorooctane sulfonic acid (PFOS) and perfluorooctanoic acid (PFOA); much less toxicity data is available for other PFAS. PFAS are resistant to biodegradation. Hence, PFOS and PFOA, two of the most abundant PFAS, are ubiquitous in the environment and could biomagnify. Their ubiquity and biomagnification properties suggest that they could significantly impact human health and the environment. Human exposure to PFAS is primarily through ingestion of food or water. The half-lives of PFOS and PFOA in humans are in terms of years whereas in rodents they are in terms of months, making extrapolation of animal studies to humans difficult.

**Results/Lessons Learned.** Toxicological data indicate that short-term and subchronic exposures of animals to PFOS and PFOA result in developmental and reproductive effects, liver toxicity, and kidney toxicity. PFOS is more toxic than PFOA. Longer-chain PFAS are more toxic than shorter-chain PFAS. Human epidemiological studies report associations between PFOS and PFOA exposures and high cholesterol, thyroid disease, and immunosuppression. Epidemiological studies also suggest an association with cancers, but the literature has been inconsistent. Nonetheless, the United States Environmental Protection Agency (USEPA), Agency for Toxic Substances and Disease Registry (ATSDR), and the International Agency for Research on Cancer (IARC) have classified PFOS and PFOA as “suggestive carcinogens” or “possibly carcinogenic to humans.”

In May 2016, USEPA issued a Lifetime Drinking Water Health Advisory for combined concentrations of PFOS and PFOA of 0.07 micrograms per liter ( $\mu\text{g/L}$ ) based on a reference dose developed from a developmental toxicity study in rats. However, this is not a legally enforceable limit. A limited number of states have set their own regulatory limits for drinking water or groundwater for PFOS and PFOA ranging from 0.011 to 0.56  $\mu\text{g/L}$ . The European Union (EU) is also proposing restrictions for higher-chain PFAS. Provisional drinking water standards developed by EU member states for PFOS range between 0.1 to 0.5  $\mu\text{g/L}$ . These values are 3 orders of magnitude higher than the EU Annual Average Environmental Quality Standard (AA-EQS) of 0.00065  $\mu\text{g/L}$  for surface freshwater, which is lower than background levels and limits of quantitation typically achieved by commercial laboratories.