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2019 SOT Conference  
Poster: Risk Assessment I  
Tuesday March 12, 2019  
9:15AM-4:30PM

## Considerations for Grouping Different PFAS Together to Develop Guidance Values

Regulatory agencies worldwide have taken an interest in developing acceptable levels of per- and polyfluoroalkyl substances (PFAS) in drinking water. Because there are so many different PFAS, it is challenging to generate values that are based on toxicokinetic and toxicological studies of each individual chemical. Some agencies have approached this challenge by grouping PFAS together and setting one limit for the combined concentrations of the chemicals. For example, US EPA set a combined drinking water health advisory of 70 parts per trillion (ppt) for the sum of perfluorooctanoate (PFOA) and perfluorooctane sulfonate (PFOS). For PFOA, PFOS, perfluorohexane sulfonate (PFHxS), perfluorononanoic acid (PFNA), and perfluoroheptanoic acid (PFHpA) combined, the Massachusetts Department of Environmental Protection set a drinking water value of 70 ppt, while the Vermont Agency of Natural Resources set a combined value of 20 ppt. We conducted an analysis of the toxicological and kinetic data for six perfluorinated chemicals, including perfluorobutanoic acid (PFBA), perfluorobutane sulfonic acid (PFBS), PFHxS, PFNA, PFOA, and PFOS, with the aim of determining whether grouping of any of these PFAS for regulatory purposes is scientifically sound according to standard US EPA methodology. Both the critical toxicological effects identified by regulatory agencies and the kinetics differ among the PFAS, which limits the utility of grouping them together for regulatory purposes. For PFOA, PFOS, and PFNA, the endpoints are developmental. Agency-identified critical effects for PFHxS are decreased body weight and serum lipid levels, and increase in prothrombin time. Decreased cholesterol has been identified as the critical effect for PFBA, and kidney histopathology and blood changes for PFBS. Regarding toxicokinetics, shorter-chain PFAS such as PFBA and PFBS have substantially shorter half-lives in the human body than the longer-chain PFAS. Based on our analysis, we concluded that PFAS should only be grouped together for the setting of regulatory guidelines if the compounds have both similar endpoints for toxicity and similar half-lives. According to US EPA methodology, PFOA, PFOS, and PFNA are appropriately grouped together based on similar critical effects and half-lives but PFBA, PFBS, and PFHxS should not be grouped with PFOA, PFOS, and PFNA or with each other. Our analysis provides guidance for setting science-based regulatory levels for PFAS in drinking water.