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A Comparison of PFAS Serum Concentrations in the General Population to Points of Departure Used in Regulatory Guidance

Per- and polyfluoroalkyl substances (PFAS) are a group of chemicals of growing concern to regulatory agencies. In deriving guidance values for PFAS in drinking water, agencies typically use a rodent serum PFAS concentration associated with a key toxicological effect as the point of departure (POD) to estimate a human-equivalent dose. A comparison of agency PODs with serum concentrations in the general population would provide perspective on the toxicological significance of the exposures of the general population to PFAS. We first conducted an analysis of the serum concentration PODs from both national and state agencies with finalized drinking water health-based values for perfluorooctanoate (PFOA), perfluorooctane sulfonate (PFOS), perfluorononanoic acid (PFNA), perfluorohexane sulfonate (PFHxS), perfluorodecanoic acid (PFDA), and perfluorobutane sulfonic acid (PFBS). Using PFAS serum concentrations measured in the most recent NHANES, we then conducted a margin of exposure (MOE) analysis to compare POD serum concentrations with those of both the geometric mean and 95th percentile of adults and children in the general US population. Agencies' PODs varied greatly for any given PFAS, and this was due to differences in selection of key studies, key toxicological effects, and model assumptions. For example, US EPA and the Minnesota Department of Environmental Protection estimated the highest POD as 38,000 ng/mL PFOA, whereas the New Jersey Department of Environmental Protection and New Hampshire Department of Environmental Sciences estimated the lowest POD as 4,351 ng/mL PFOA. MOE values also varied greatly depending on the agency and PFAS. For example, MOEs for the general population with PFOA serum concentrations at the 95th percentile (4.17 ng/mL) and geometric mean (1.56 ng/mL) ranged from 1,000-9,100 and 2,800-24,000, respectively. Similarly, MOEs for children aged 3-11 years in the general population with PFOA serum concentrations at the 95th percentile (4.19 ng/mL) and geometric mean (1.92 ng/mL) ranged from 1,000-9,100 and 2,300-20,000, respectively. Our analysis underscores the uncertainties in evaluations of PFAS toxicity. It further shows that current serum levels in the general population are well below any exposures that could potentially be associated with health effects.