Dietary Pathways and Routes of Human Exposure to PFAS

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Per- and polyfluoroalkyl substances (PFAS) are a manmade class of environmentally-persistent organofluorine chemicals widely used across various industries over the past seventy years. Toxicological evidence suggests that certain PFAS compounds can pose a human health risk, particularly long-chain varieties. Most regulatory and scientific focus has concerned the drinking water ingestion pathway of human exposure to PFAS compounds and not dietary. This is attributed, in part, due to analytical constraints in foods and an evolution in the understanding of potential risks posed by PFAS. Proportionally less focus has been put on ingestion exposure pathways through the consumption of food items, despite evidence suggesting that diet is the primary pathway of human exposure to PFAS for most populations. Here we review a conceptual exposure model for PFAS that describes sources, transport processes, and exposure to human receptors. Particular attention will be focused on food and beverages as exposure media to PFAS. More research is needed to fully understand where and in what magnitudes PFAS enters the food supply, but multiple government initiatives are underway to fill in these data gaps.

USDA FSIS Recent Developments related to PFAS: analytical approaches, surveillance testing, and incident responses

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As part of the National Residue Program (NRP), the USDA Food Safety and Inspection Service samples meat, poultry, and egg products and tests them for a wide range of veterinary drugs, pesticides, and contaminants. This ensures that the food supply does not contain unsafe chemical residues and also supports the regulatory efforts of our partner agencies such as the Food and Drug Administration and the Environmental Protection Agency. In the past couple years, USDA has augmented its contaminant testing program by developing an analytical method to detect 16 per- and polyfluoroalkyl substances (PFAS) in USDA-regulated meat and poultry products. Using this method, USDA has begun collecting data on the presence of these PFAS in the U.S. meat and poultry supply. At the same time, the Agency has been working with Federal and State partners to manage instances where the presence of PFAS has been identified in food-producing animals. This presentation will give an overview of USDA work related to PFAS in meat, poultry, and egg products.

Characterizing Biopersistence Potential of the Metabolite 5:3 Fluorotelomer Carboxylic Acid After Repeated Oral Exposure to the 6:2 Fluorotelomer Alcohol

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Our previous report on pharmacokinetic (PK) evaluation of 6:2 fluorotelomer alcohol (6:2 FTOH) examined the biopersistence potential of its metabolites based on data published from single inhalation and occupational 6:2 FTOH exposure studies (Kabadi et al 2018, *Food Chem Toxicol*). We calculated internal exposure estimates of three key metabolites of 6:2 FTOH, of which 5:3 fluorotelomer carboxylic acid (5:3 acid) had the highest internal exposure and the slowest clearance. No oral repeated 6:2 FTOH exposure data were available at the time to fully characterize the biopersistence potential of the metabolite 5:3 acid. We received additional data on 6:2 FTOH and 5:3 acid, which included a 90-day toxicokinetic study report on repeated oral 6:2 FTOH exposure to rats. We reviewed the study and analyzed the reported 5:3 acid concentrations in plasma, liver, and fat using one-compartment PK modeling and calculated elimination rate constants (k_{el}), elimination half-lives ($t_{1/2}$) and times to steady state (t_{ss}) of 5:3 acid at three 6:2 FTOH doses (Kabadi et al 2020, *Toxicol Appl Pharmacol*). Our results showed that t_{ss} of 5:3 acid in plasma and evaluated tissues were approximately close to one year, such that the majority of highest values were observed at the lowest 6:2 FTOH dose, indicating its association with the biopersistence of 6:2 FTOH. The results of our PK analysis are the first to characterize biopersistence potential of the 5:3 acid after repeated oral exposure to the parent compound 6:2 FTOH based on steady state PK parameters, and therefore, may have an impact on future study designs when conducting toxicity assays for such compounds.

Comparative analysis of the potential human health effects of 6:2 fluorotelomer alcohol (6:2 FTOH) versus perfluorohexanoic acid (PFHxA)

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The 6:2 fluorotelomer alcohol (6:2 FTOH) is a short-chain polyfluoroalkyl substance (PFAS) present in many polymeric PFAS-based substances. The general population may be exposed to 6:2 FTOH through various routes, including ingestion of food packaged in materials containing these types of short-chain polymeric PFAS. Some published risk assessments have assumed that the more extensive toxicity database for perfluorohexanoic acid (PFHxA), a metabolite of 6:2 FTOH, is adequate to characterize the human health effects of 6:2 FTOH. Recently identified studies conducted with 6:2 FTOH and its metabolite, 5:3 acid, have provided additional information that enables comparison of the toxicological profiles of PFHxA and 6:2 FTOH. This presentation summarizes a comparative analysis of the apical effects and dose-response profiles of PFHxA and 6:2 FTOH in animal models to determine whether the data for PFHxA could describe the potential hazards of 6:2 FTOH exposure.