# Workshop registrant input as of 10/21

## Exposure

- Perfluoropolyethers (PFPEs) are used in a wide range of consumer products, including food packaging. Yet little is known about related exposures and adverse impacts. What are the physicochemical properties and environmental fate of PFPEs? What impurities do they tend to contain? What are the environmental degradation, metabolism, and combustion products of PFPEs and how might exposures occur? What happens to the PFPEs when food packaging treated with PFPEs is composted? What exposures may result from consuming food grown in soils amended with such compost?
- In-utero and early life exposures via breast milk in humans. Animal studies - more cross foster studies.
- Understand totality of exposure to PFAS using total organic fluoride measurements and untargeted analyses
- Biomarkers are needed that might indicate extent of exposure to PFAS such as GenX that are not currently measurable in the blood but which communities were exposed to for potentially decades.
- Potential to generate vapors from underground/groundwater contamination which can get inside buildings via vapor intrusion
- Lake Sediments
- Bioaccumulation, food webs
- PFAS - protein interactions
- Quantifying extent of exposure to "legacy" PFAS replacements (e.g., GenX) and reasons for low detection in current studies.
- What is considered PFAS content in food producing animals and wildlife species (deer) for safe consumption?
- Relative external doses to internal serum concentrations for risk assessment (toxicokinetic assumptions).
- Legacy PFAS and GenX
- As we find novel PFAS in environmental media it is important to rapidly follow with bio-monitoring studies to determine if human exposure is resulting in a body burden of novel PFAS. As this work requires robust methods and native and isotope labeled standards time passes to get adequate methods in place. A data gap is a rapid response is needed for nontargeted analysis of human serum/blood that parallels environmental media efforts.
- PFAS incineration: what are the exposures in residential areas near the incinerators - are any new compounds formed? What are the mixtures?
- AFFF inhalation exposure
- Short chain and replacement highly-fluorinated compounds (e.g. GenX)

- Dermal absorption for the replacement PFAS is virtually unknown - a definite gap that needs to be filled.
- Coexposure with other persistent organic pollutants
- Do PFAS volatilize readily, and if so under what conditions? Would shower steam present a potential route of inhalation exposure?
- I'm interested in in learning more about mixture methods for analysis PFAS exposure mixtures.
- Huge data gap on PFAS as toxic air emissions, given how many sites have been contaminated by industry with no regulations at all on this issue as of yet.
- Exposure measurement and questionnaire data concordant with biomonitoring data for PFAS chemicals in study populations to provide understanding of the important sources and pathways related to personal exposures to PFAS chemicals and inform assessment of relative source contributions.
- Ambient air and indoor air exposure; exposure from food: fish, organ meat, plants, dairy
- EPA should not approve any PFAS unless meeting the conditions outlined in my "cross-cutting" response. Thousands of PFAS are approved that state regulators have no way to analyze to know where they are in the environment or people. This is not good policy or science.
- Need to better understand relative contributions of inhalation, ingestion, and dermal exposures to overall body burdens. -- Mark Johnson, US Army Public Health Center
- Best characterization of co-exposures to environmental pollutants including PFAS
- The use of PFAS in medical applications is an underappreciated source of human exposure and environmental contamination. For example, perfluorooctane for ophthalmic applications, including surgery; and perfluorobutane use as a medical imaging agent, halothane use an anesthetic was associated with hepatic necrosis, sevoflurane (anesthetic) is under review for potential neurotoxicity.
- Survey of exposures through food and other non-water sources.
- I think we need more information regarding how mixtures of different PFAs chemicals can impact human health. Most of the tox studies have focused on individual chemicals, when most exposures (especially with AFFF) are mixtures.
- PFAS Volatilization in the subsurface with potential for vapor intrusion into buildings for PFAS compounds with applicable molecular weights and Henry's Law Constants.
- Sound information about vapor-phase concentrations in the environment would help address (erroneous) presumptions that all PFAS are essentially nonvolatile. Sites where PFAS-containing products and wastes were discharged to the ground/subsurface could be identified, where vapor concentrations in soil gas and overlying ambient and indoor air could be measured.
- Methods to measure total exposure to organic fluorines. Exposure methods for newer generation PFAS, including non-targeted methods
- Quantitative Structure-Activity Relationship (QSAR) Modeling to Predict the Transfer of Chemicals across the Placenta

- Dermal, inhalation, ingestion of microplastics, PFAS, additional toxins and carcinogens found in synthetic turf. These plastic grass carpets are being used in daycare centers, schools, parks, residences, commercial properties as well as massive coverings for landfills and superfund sites. They are made from the same resin pellets and at many of the same plants that household and other carpets are being made at. They are unregulated, not recyclable and are frequently discarded illegally, contaminating soils and waterways.
- Methods of evaluating human exposure to thousands of PFAS through biomonitoring, which only captures ~10-15 PFAS. How does the lens we are limited to influence what we find?
- **Data gap:** most PFAS compounds other than C8, PFNA, PFHxS and major others are not known in terms of exposure. **Research priority:** activity based exposure assessment that allows multiple related PFAS compounds to be considered simultaneously
- How much PFAS are we actually measuring - in environmental samples or in people - when we do targeted monitoring?
- How much exposure in developing countries? Any wildlife exposure? Aquatic exposure?
- Choose a location (more than one would be preferable) to function as an initial test site to more fully: 1) characterize compounds and identify compounds whose bioavailability is certain and uncertain in terms of toxic endpoints and exposure variables so that 2) ability to conduct an adequate exposure assessment and risk analysis can be made
- The EPA states that PFAS exposure occurs primarily through eating contaminated food grown or collected from contaminated sources like soil and water as well as eating contaminated meat, like from fish which is one of the reasons the Washington State Department of Health (WADOH) is interested in testing PFAS compounds in different shellfish species. There are clinical evaluations and concerns as well as environmental ones which Washington State needs more information about since there are not enough significant data points to fully understand the contamination levels of PFAS in our State and the effects of these levels on our population.
- A high-priority research need is the sharing of chemical structure and detection/measurement information between industry and research entities (academic, state, federal, nonprofit, etc). The responsibility of aiding environmental scientists and chemists in evaluating novel PFAS should fall on the industries responsible for their use and release. Internal standards and other methodological knowledge/support should be freely shared so that environmental and human exposure monitoring can be conducted that will be able to measure and report all PFAS (rather than only compounds with known structures).
- Need assessment for exposure sources and amounts in food, soil, compost, biosolids, agricultural products, dairy, eggs, meats, fish/shellfish, game, air, rain, surface and groundwater, and blood.
- The focus from the Human Health has been on a handful of these chemicals with PFOS & PFOA being the two main compounds. With regards to Air Force & Naval Bases- uses across the country any PFAS residual would likely be from the use of the AFFF. Additionally, PFOS and PFOA have a very long half-lives in the body. The main health concern which has ben raised from most of these uses has been through ingestion of groundwater contaminated with the residual PFAS in the AFFF.

- Fundamental information on site sampling condition and media being sampled: Climate zone and geomorphology, Identification of water type /Cation and anion results and balance , Field sampling of PH/TDS/EC/ORP/S.G/Salinity/Temperature and similar measurement for soils/sediments to put sampling in context of what is being sampled under what conditions
- How to interpret human biomonitoring data on PFAS, what do those levels mean in a population and in individual blood samples.

## Toxicology

- What are the toxicological hazard traits of PFPEs and of their impurities and degradation/metabolism/reaction products?
- Understand effects of mixtures of PFAS
- Descriptions of pharmacokinetic behavior/systemic exposure metrics at environmental/occupational exposure levels beyond PFOA
- Scientists need access to the PFAS that are on the market, in our food, and polluting drinking water so that we can test for adverse health effects. If a company makes or puts the PFAS into a waste stream, they need to make it available for purchase for testing. They also need to report PFAS by-product waste.
- Develop a class approach to assess risk (e.g., toxicity equivalents)
- Research needed s a function of chain length of PFAS and mixtures. Cumulative effects
- What is the human exposure characterization of residents living near incinerators?
- Effects of shorter chain and replacement highly-fluorinated compounds (e.g. GenX)
- NAMs for PFAS are critical - these will not take the place of in vivo testing, but certainly can inform better hazard assessment.
- Interactions in PFAS mixtures- are they additive? synergistic? antagonistic? More needs to be done in this arena; Mechanisms of toxicity- we need a better understanding of the molecular interactions by which PFAS exert their effects on health.
- Inhalation toxicity values for PFAS; oral toxicity values (RfDs, CSFs) for additional PFAS; methods for aggregate exposure risk assessment for PFAS when no in vivo tox studies available for some components of the mixture
- Many PFAS have no or limited publicly available toxicity data to use in risk assessments. And toxicity information alone should not be the basis anyways for restricting production/use of "forever" chemicals.

- Need to better understand mechanisms of effect (to more accurately evaluate effects in animal models).
- Mixtures risk assessment methods
- The use of PFAS in medical applications is an underappreciated source of human exposure. Systematic evaluation of the reported health effects observed in medical applications provide insights into common targets of toxicity as well as shared mechanisms of action. For example, perfluorooctane for ophthalmic applications, including surgery; and perfluorobutane use as a medical imaging agent, halothane use an anesthetic was associated with hepatic necrosis, sevoflurane (anesthetic) is under review for potential neurotoxicity...to name a few.
- More animal studies on PFNA and PFHxS -- Ali Hamade, Oregon Health Authority
- Appropriate data sets and descriptors that would strengthen predictions of effect thresholds (e.g., LOAEL/NOAEL vs LD50) via machine learning
- Research is needed to address the connection between early life-stage exposure and adult-stage immune compromise/diseases
- Do high-quality and sufficient data already exist in the peer-reviewed literature to support an evaluation of the toxicity of this broad class of compounds via inhalation (including derivation of reliable toxicity values for human health risk assessment purposes)?
- PFOA has been shown to impact the developing mammary gland and low levels. It would be helpful to know if other PFAS also have similar impacts on the mammary gland.
- Integrating modern toxicity methods (in-silico, in-vitro) to regulate data-poor chemicals
- Placenta dataset
- "I will send my research questions separately to the organizers. Topics: saturation of binding capacity for albumin, OAT; placenta effects and prenatal development
- Mechanisms of action for health effects associations observed in epidemiological studies that could provide insights to the latency and persistence of excess risk after serum PFAS concentrations return to general population levels following cessation of exposure.
- To understand or characterize dose or Response-based additivity of combined exposure to multiple PFAS compounds
- Need studies on complex mixtures
- In what range of toxicity are PFAS? LD50s? LC50?
- Need toxicity information on more PFAS compounds besides PFOA and PFOS; need toxicity information for pathways other than ingestion such as dermal exposure
- There are massive data gaps in nearly all aspects of toxicology for the majority of PFAS. Only a small handful have been extensively studied, and even among those compounds much of the toxicological risks are not well characterized. A pressing research need and data gap is the extent to which PFAS exposure during early development (particularly in utero and other sensitive periods) sets the stage for a lifetime of increased disease susceptibility, including adult health outcomes already associated with PFAS exposure.
- Need much more work on toxicology of PFAS mixtures. Nobody gets exposed to just one!

- Considering that specific human health toxicity is still somewhat a moving target, it is difficult to make a direct comparisons of health issues with some specific PFAS compounds and concentrations.  It is my belief that Epi Studies will likely going to be used for this type of Toxicology investigation, how will the results be used? And will the study confirm the science that will be able to tell us exactly what is going on with these chemicals.
- Emulsions  Toxicology

## Health Human Effects

- There remains a gap in understanding the health effects of postnatal exposures in mothers and adolescents.
- What are the human health effects of exposure to consumer products containing PFPEs, such as food packaging?
- Plethora of responses in vulnerable populations
- Develop a means of removing  bio-accumulative PFAS from the blood of people/communities that have been exposed;
- Better understanding of the effects on both the mother and the newborn following PFAS gestational exposures - particularly the involvement of thyroid hormone effects on infant development, learning, behavior, and weight trajectory.
- Mixture effects
- What are the human health dose dependant to negative health consequences?
- Guidance and education for clinicians, medical community and public with respect to blood testing.
- Role in response to vaccination
- The link between diabetes and PFAS exposures is somewhat conflicted in the literature, this needs to be addressed and clarified.
- Besides the direct toxicity of some studied PFAS to people, especially in communities with contaminated drinking water, EPA doesn't fully acknowledge or study the health impacts to

people from the stress and anxiety of finding out they and their families--sometimes for multiple generations--have been exposed to these or other toxic chemicals. Acute and chronic stress has multiple impacts to people's health. So given that additional aspect of drinking water contamination, it is completely accurate to say people have been harmed by PFAS.

- Developmental, immune and hepatic effects
- We need a better understanding of the long-term implications of gestational exposure on children's health. A few, but not most, PFAS have been studied in this framework.
- The use of PFAS in medical applications is an underappreciated source of human exposure. Systematic evaluation of the reported health effects observed in medical applications provide insights into common targets of toxicity as well as shared mechanisms of action. For example, perfluorooctane for ophthalmic applications, including surgery; and perfluorobutane use as a medical imaging agent, halothane use an anesthetic was associated with hepatic necrosis, sevoflurane (anesthetic) is under review for potential neurotoxicity...to name a few.
- Synthesis of epidemiology findings available for different PFAS. Then, identifying studies to help fill the gap.
- Immunotoxicity including reduced vaccine responses in adults and children
- Need more research on the effects of PFAS on immune function
- Research is needed to address the connection between early life-stage exposure and adult-stage immune compromise/diseases
- Exposure to mixtures, exposures in-utero, additive effects in people impacted by chronic diseases or other persistent pollutants
- Modeling to Predict the Transfer
- Clarification of the mechanisms of immunological effects
- Gynecologic health.
- Long-term outcomes of chronic low dose exposure including thyroid hormone disruption related consequences including neurobehavioral effects
- Need more information on cancer and non-cancer health effects related to PFAS compounds
- Health concerns for PFAS are based on adverse outcomes observed in laboratory animals including developmental toxicity, liver toxicity, immune toxicity, testicular and thyroid toxicity, endocrine disruption (especially altered testosterone and thyroid hormones) and increased tumors in liver and other organs. There is some supporting evidence from epidemiological studies that a few PFAS may contribute to altered growth and development, reduced immune function, altered serum cholesterol and liver enzymes in human populations with elevated exposure. It is still unclear whether any PFAS pose a cancer risk to humans.
- A pressing need is the recognition that PFAS are not "model contaminants" in that they (as a group) do not consistently induce the same exact health effect(s) across populations, unlike

other environmental contaminants. While this makes studying their effects on human health a unique challenge, it does not mean the compounds can be assumed as safe due to the lack of consistency across the epidemiologic literature, especially when there are scientifically sound explanations for these heterogeneous reported findings. This argument is a red herring and must be addressed by the scientific and regulatory communities.

- All known exposed communities need biomonitoring and medical monitoring for effects from PFAS exposure.
- Current some studies have linked PFAS to "Decreased Immune System Response" and some cancers. How will the study results be used? Will this study, focus on Exposure Disease Relationships? Latency or passage of time can make it difficult to link cancer to past exposure because of cancer long latency- But we are hoping that you will consider Cancer in this study.
- Physician education and medical monitoring guidelines for impacted communities

## Cross Cutting Issues

- One thing missing is a point-of-use device that can be used to look at the amount of PFAS in source water.
- Research examining the health effects of simultaneous exposure to multiple PFAS using contemporary epidemiological and statistical methods is needed.
- Aquatic criteria are being developed for the protection of fish consumption. As sufficient data are not available, except for a few widely studied PFAS (e.g., PFOA and PFOA), various assumptions and extrapolations are being considered. Two main uncertainties remain: how to deal with the combined effects of PFAS mixtures encountered in the environment and how to estimate toxicity of PFAS compounds lacking sufficient data. More work is needed on methods for estimating/predicting PFAS toxicity such as application of Quantitative Structure Activity Relationships (QSARs) and machine learning approaches to PFAS and the regulatory acceptability of their outcome.
- What is the state of the art for mapping PFAS using geographic information systems (GIS)? What Federal or publically available PFAS GIS are there? Is there a portal or list of State and Federal PFAS occurrence data sets? Thank you! Drew Pilant
- Appropriate model systems for high throughput testing - binding to serum proteins is an issue even in culture for some PFAS. We cannot move forward in vitro until stability and solubility of compounds in diluent (DMSO, methanol, water), serum binding, and bioavailability are better understood.
- Portable sensing device for large-scale PFASs screening or detection on site or in field
- Bioaccumulation, ecotoxicology
- What are the current used mitigation techniques commonly used to separate PFAS like products from the water stream?
- Relation to other contaminants (e.g. PCBs, PBDEs) and discerning issues in epidemiology interpretation.
- How will community level exposure in high risk populations influence response to SARS COV-2 vaccines (as well as flu and other vaccines)
- Fate and transport of precursors to PFAAs. Biodegradation of precursors to PFAAs in different environmental conditions. Technologies for effective removal of the precursors.
- Detoxification and mitigation drug targets. More needs to be done on ways to increase detoxification of PFAS, and identify other mitigating agents that would reduce the impact on human health.
- Ensure that the TSCA reforms and risk assessments are accurately preventing production/use of PFAS. Allowing chemicals to get into our environment and bodies that can never be broken down or completely removed, even if not proven to have health effects at those levels, should only happen if there is absolutely a personal health benefit to people to have that chemical in some minimal application. No economic benefits should be used to justify approval of these chemicals. And if approved by EPA, EPA needs to partner

with the producers/users to monitor these chemicals to determine if they are exposing workers or other people that are not supposed to be exposed based on the initial information. These are my personal statements based on years of reviewing PFAS studies.

- Risk assessment approaches. Basics on calculations and models being used and how they correspond with the tox, exposure, and epi studies. Rationale behind endpoints being used for regulatory level setting, and what additional sensitive endpoints have been identified in toxicology studies. Areas of knowledge and data gaps in inter species sensitivity differences. Use of a class approach- with discussions of which PFAS currently have sufficient data to begin using this approach and additional work needed to assess potencies and mechanisms to add other PFAS to the class approach.
- Quantifying redox conditions in aquifer systems during conversion of PFAS precursors to PFAS alkyl acids (carboxylic and sulfonic acids) and rigorous evaluation of physicochemical processes controlling fate and transport in the subsurface required for risk analysis. -- Patrick Longmire, New Mexico Environment Department
- Laboratory methods for PFAS in air.
- There is strong interest in the wastewater industry about how public utilities may be affected by the presence of PFAS in treatment plant effluent, residuals, and biosolids. As recipients of household and industrial wastewater discharge, the industry promotes the reduction and regulation of PFAS at their sources in homes and industrial facilities in order to reduce loading to treatment plants.
- Do available chemodynamic models yield sufficiently accurate estimates of environmental partitioning parameters (e.g., water-to-air partitioning) for PFAS? Are specialized methods needed to measure environmental partitioning parameters for PFAS; if so, which methods are recommended?
- PFAS disposal, new technologies, methods to safely destroy fluorochemicals
- Not enough dataset
- Comparative evaluation of observed risks for human health indicators (shift in clinical laboratory values, symptoms and incidence of ICD-classified diseases)
- Disparities in exposure.
- How to best communicate about risk when there is so much uncertainty and differences in policies across states?
- Relative potency factor approach to multiple PFAS exposure
- Working on the risk assessment associated with the various routes of exposure that firefighters face - possible inhalation and dermal exposures. Understanding whether the PFAS finishes on the gear transfer from the fabric to the skin and be can they be absorbed.
- Stakeholder and regulator input on quantitative, weighted perspectives regarding risk-informed decision making and risk communication, commonly used for probability risk assessments.
- State regulatory numbers not consistent with EPA health advisory.

- Who is most adversely impacted by exposure to PFAS? A pressing, cross-cutting issue is the injustice of which populations are most adversely affected by industrial activity.
- If PFAS exposure affects the ability of immune systems to create antibodies, then understanding the human health effects of PFAS on our immune systems could not possibly be more important!
- Identify possible knowledge gaps, in our understanding of the current extent of human exposures to PFAS on the basis of PFAS Production, use, and human exposure data.