## **Exploring PFAS Inhalation Exposures and Toxicity**

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**Background/Objectives.** Much of the initial discourse on per- and polyfluoroalkyl substances (PFAS) focused on their impacts to drinking water supplies nationwide. Then, attention spread to source areas, such as airports, landfills, military installations, and other facilities where impacts to soil and/or groundwater may have occurred. Because of the high toxicity of some PFAS, the U.S. Environmental Protection Agency (USEPA) and many states began establishing PFAS guideline or regulatory limits for these media. Most recently, questions are being raised about potential PFAS inhalation exposures and toxicity.

**Approach/Activities.** Three types of air exposures will be described: outdoor ambient, indoor ambient, and vapor intrusion. PFAS in outdoor ambient air may come from stack emissions, waste management facilities or use of PFAS-containing materials outdoors. Indoor ambient air can be impacted by PFAS-containing materials, such as flame-retardant fabrics or stain-resistant carpeting. Vapor intrusion may be an emerging consideration as volatile PFAS, such as fluorotelomer alcohols (FTOH), are identified. The scientific literature will be researched and findings presented that point to these types of PFAS air exposures.

The toxicity criteria available for just a handful of PFAS are based on ingestion exposures. By using route-to-route extrapolation from ingestion toxicity to represent inhalation toxicity, a few states have already published numerical criteria for some PFAS in air. Alternatively, USEPA has been funding research into new approach methods (NAMs) for deriving chemical toxicity information without animal testing. A critical review of route-to-route extrapolation and NAMs for determining PFAS inhalation toxicity will be conducted.

**Results/Lessons Learned.** Examples of studies that support the potential significance of PFAS air inhalation exposures include the following (will be updated):

- Leary et al. (2020) analyzed blood serum concentrations of firefighters and found elevated concentrations in this population compared to the general public.
- Heydebreck et al. (2016) reported FTOH concentrations at five orders of magnitude above background at a manufacturing plant of high-performance textiles.
- Yao et al. (2018) measured PFAS in indoor air and dust and from these data calculated PFAS daily intake, which demonstrated that intake from air inhalation was greater than from ingestion.
- Abusallout et al. (2022) measured Henry's Law constants for 15 PFAS and found them to be within USEPA's definition of volatility.

There are limitations in extrapolating ingestion toxicity to inhalation toxicity, but a study published in October 2022 (Monnot et al.) concluded that available toxicity and toxicokinetic data for PFOA and PFOS supported route-to-route extrapolation. Meanwhile, none of the USEPA list of approved test guidelines for human health effects target the lung or inhalation effects, although other NAMs in development (e.g., computational toxicology tools) may prove useful.