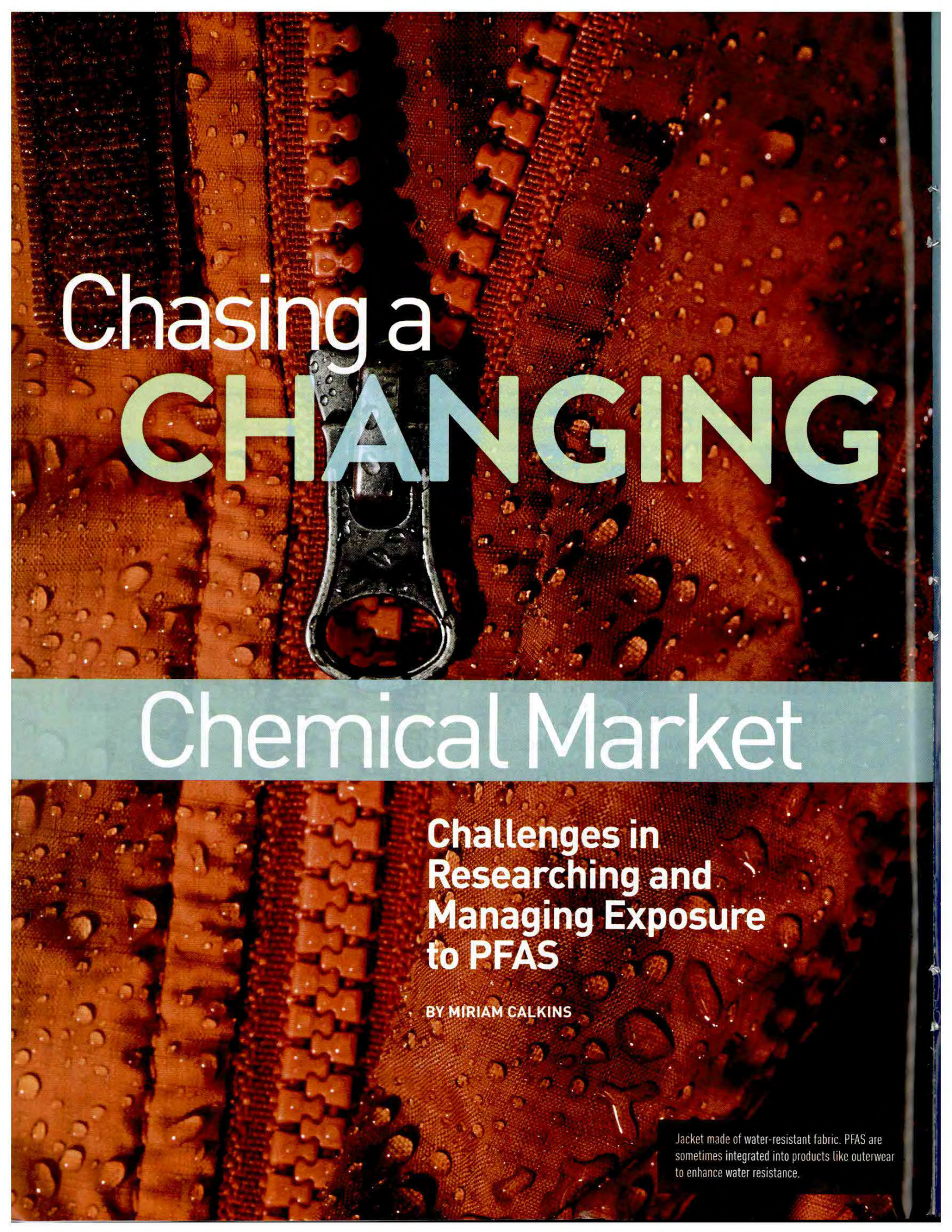




Chasing a **CHANGING**

Chemical Market

**Challenges in
Researching and
Managing Exposure
to PFAS**

BY MIRIAM CALKINS

Jacket made of water-resistant fabric. PFAS are sometimes integrated into products like outerwear to enhance water resistance.

Industrial hygienists and occupational and environmental health and safety professionals are challenged every day with protecting workers from exposures to known hazards in the workplace.

This task is noticeably more difficult when sufficient information exists about an emerging hazard to warrant concern, but occupational exposure limits have yet to be developed and the available data are insufficient to advance appropriate worker protection programs. Furthermore, for poorly characterized or understood workplace hazards, the research necessary to support the development of worker protection recommendations and OELs may be lacking. This is the dilemma for workers exposed to per- and polyfluoroalkyl substances (PFAS) in thousands of work sites across the U.S., where PFAS exposures fall into both challenging categories due to the complexity of potential exposures.

More than two decades ago, some of the better known PFAS—like the eight-carbon chain PFAS perfluorooctanoic acid (PFOA), also known as “C8,” and perfluorooctane sulfonic acid (PFOS)—were in the spotlight. The focus on exposures to PFAS has recently been renewed, driven by concerns over widespread environmental contamination of these “forever chemicals,” ongoing human exposure, and growing evidence of associations with adverse health effects. However, the focus is no longer on a select few PFAS, but on PFAS as a class of chemicals that includes as many as 9,000 individual compounds, many of which have never been tested in a toxicological setting, let alone included in an occupational exposure assessment or epidemiologic study. (A master list of PFAS substances can be found on EPA’s CompTox Chemicals Dashboard at bit.ly/pfasmaster.) While research programs and priorities across government, academic, and private sectors are rapidly expanding, substantial gaps complicate research prioritization and implementation of recommendations to reduce exposures to PFAS and protect worker health.

A BRIEF HISTORY OF PFAS

Developed nearly a century ago, PFAS comprise a group of synthetic chemicals that have been widely incorporated

into consumer and commercial products as well as used in industrial settings as a processing aid. They consist of one or more carbon atoms on which all the hydrogen atoms have been replaced by fluorine atoms, with a functional group or “tail” end. They are known to have highly desirable properties, such as being hydrophobic, oleophobic, and resistant to heat. PFAS were first used in the 1940s as a nonstick coating. By the 1960s, they were used to create class B firefighting foams known as aqueous film forming foam (AFFF) and integrated into products as a protective coating and to enhance stain and water resistance. Currently, PFAS are commonly used as a coating in the manufacturing of wires, paper products, textiles, and leather; as a coating, wetting agent, or etchant in the semiconductor industry; as a surfactant and mist suppressant in metal plating operations; in AFFF and firefighter turnout gear; and in the production of rubber and plastics. PFAS can also be present in products such as medical devices, cosmetics, construction materials, and ski wax. Additionally, a growing number of reports describe PFAS detected in waste products, drinking water, fish, wildlife, and people.

The prominent use of PFAS in thousands of products and across industry sectors suggests some degree of occupational exposure may be present in a wide range

of work environments as well as general population exposures in community settings. With limited prior research, concerns over possible human exposure and health effects surfaced around the turn of the century. Following an announcement in 2000 from a leading PFAS manufacturer regarding their voluntary phaseout of PFOS production globally, researchers analyzed serum samples collected in 1999–2000 and 2003–2004 as part of the National Health and Nutrition Examination Survey (NHANES), a nationally representative study administered by CDC, for 11 PFAS. According to a paper published in 2007 in *Environmental Health Perspectives*, five of the 11 PFAS were detected in 98 percent of samples collected between 2003 and 2004, with overall lower concentrations detected in the 2003–2004 samples compared with those collected in 1999–2000.

By 2005, a class-action settlement was approved by the West Virginia Circuit Court in a lawsuit involv-

Without guidance for how to interpret PFAS concentrations measured in the work environment, exposure monitoring can be difficult to interpret.

ing the release of PFOA from a West Virginia DuPont manufacturing facility (learn more in *Environmental Health Perspectives* at bit.ly/ehpc8). Later that year, the C8 Science Panel, a panel of epidemiologists chosen by the parties to the settlement, initiated exposure and epidemiologic studies of the surrounding communities. Results from these studies, which are summarized at c8sciencepanel.org, concluded there was a probable link between PFOA and a number of health outcomes, including testicular and kidney cancer, high cholesterol, ulcerative colitis, thyroid disease, and pregnancy-induced hypertension. These findings have been supported by animal toxicology studies. According to the toxicological profile for perfluoroalkyls published by the Agency for Toxic Substances and Disease Registry (ATSDR) in 2021, studies now strongly suggest PFAS may adversely affect reproductive, endocrine, immune, and cardiovascular systems. Additional research published in recent years (see the papers published in *Environmental Pollution* and *Environmental Science & Technology* in the “Resources” section on page 25) shows that PFAS can also cross the placental barrier and have been reported in breastmilk. In 2016, the International Agency for Research on Cancer listed PFOA as a class 2B carcinogen (possibly carcinogenic to humans), and little is known about how mixtures of various PFAS affect health.

Concurrent with the activities in West Virginia, EPA

took action on PFAS. In 2002, the agency published a significant new use rule requiring notification of future manufacturing and importing of 75 PFAS. In 2006, EPA launched its 2010/2015 PFOA Stewardship Program and invited eight of the leading PFAS manufacturing companies to participate in a voluntary phaseout of PFOA. However, a functional need for PFAS in manufacturing processes and consumer products remained. With the discontinued use of some commonly used long-alkyl chain PFAS, the focus of the manufacturing industry, as well as scientific and public communities, expanded to other PFAS, such as short-alkyl chain PFAS (including PFAS termed “C6”) and other alternatives. These substitutes were anticipated to be less hazardous due to anticipated shorter elimination half-lives in the human body and the inverse relationship between the solubility and carbon-chain length that is typically observed in chemicals. But ongoing toxicology studies suggest these short-chain compounds may still be problematic as they have exhibited similar health effects in *in vivo* and *in vitro* settings to their longer-chain counterparts and are comparably persistent in the environment (see the 2018 paper on short-chain PFAS from *Environmental Sciences Europe* under “Resources”). For workers, it is not clear how this transition to alternatives may affect exposure and subsequent health risk.

With this mounting knowledge base and a long history of use, why are there still so many challenges for research?

THE ANSWER: IT'S COMPLICATED

Research on PFAS is growing at a rapid rate, with the number of publications increasing from fewer than 50 per year prior to 2002 to over 800 per year by 2020. As the body of research expands, so does the scope of research necessary to understand and properly evaluate PFAS. The increased focus on specific compounds, health effects, and exposure routes of concern for the general public means that less research has examined settings directly applicable to workers despite the continued use of PFAS in these settings. As a result, three challenges have emerged for PFAS research and practice in work environments.

1. Challenges derived from limitations of the available analytical methods and scientific approach to evaluating a class of chemicals and chemical mixtures.

PFAS are a chemical group with thousands of possible chemical formulations. The majority of PFAS exposure assessments for occupational and community populations have used blood (or serum) to assess PFAS exposure. Serum is the preferred biological matrix to provide information on the exposure for an individual. Many of the long-alkyl chain PFAS have a relatively long half-life in the body, making blood (or serum) a good matrix to assess an individual's recent or past exposure. Other biological matrices, such as urine, have been analyzed for PFAS, but results are mixed. It is possible that urine may prove to be valuable for the detection of some PFAS, such as those with shorter half-lives in individuals with

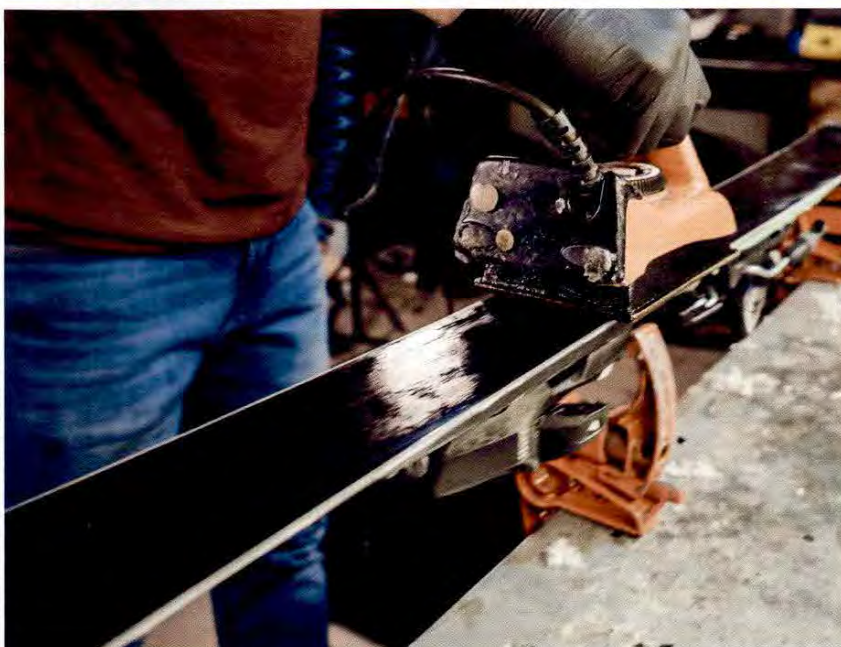
very recent exposure, but data from NHANES demonstrate infrequent detection of PFAS in urine from the general population. However, biomonitoring provides limited information on the sources of PFAS exposure (environmental vs. occupational), can be invasive, does not answer questions on the timing of the exposure, and requires an understanding of toxicokinetics to correctly time the collection of samples.

Currently, limited guidance exists to conduct appropriate industrial hygiene monitoring for PFAS. Analytical methods have been developed for water, air (passive and active), cosmetics, food, animal tissue, dust, and other materials (textiles and paper, for example), but there are limited studies of PFAS in the work environment. Previous occupational studies have contributed valuable information on concentrations in workplace air and dust, including quantification of PFAS in both particle and vapor phases. Methods for collecting these samples generally include wipe and vacuum methods for dust and active sampling with sorbent and filter media for air. (A 2021 paper on PFAS in fire station dust in the *Journal of Exposure Science & Environmental Epidemiology* and a 2013 paper on professional ski waxers' exposure to PFAS in air in *Environmental Science: Processes & Impacts* discuss these methods further.) Because PFAS are present in products that may come in contact with a sample, such as laboratory equipment or the technician's personal care products, sampling guidance is starting to include extensive consideration for cross-contamination of samples during the collection and analysis phase. For example, the Michigan Department of Environmental Quality's PFAS sampling guidance (PDF, bit.ly/mipfas) provides recommendations to decrease the possibility of cross-contamination.

Traditional chemical analysis for PFAS relies on the quantification of a targeted panel using liquid chromatography-tandem mass spectrometry. Although considered the gold standard, this method is limited in the number of PFAS it can detect. Historically, these panels have been restricted to a select number of PFAS, including PFOA and PFOS, that are either frequently detected in samples or for which a known exposure has occurred. Even with the recent advent and increased availability of expanded panels, a targeted analytical approach is likely to miss some of the many possible PFAS that may be present in a biological or environmental sample, including precursor compounds that are known to transform into other PFAS in the environment, body, or both. To complement the targeted approach, research and commercial laboratories are exploring the application of non-targeted analyses, such as the total oxidative precursor (TOP) assay, particle-induced gamma ray emission (PIGE) spectroscopy, or the total organic fluorine (TOF) method. However, these approaches are not widely used due to their high cost and because these methods only provide a summary measure of PFAS in the sample without differentiating between species. Given that most toxicological and epidemiological studies evaluate the health risks of specific PFAS,



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Top: Firefighter turnout gear hangs in a fire station. Bottom: Worker applies ski wax to a ski using an iron. PFAS are commonly used in firefighter turnout gear and can also be present in products such as ski wax.

these non-targeted methods do not provide enough detailed information to serve as anything more than a screening tool at this time. Using a combined approach, where samples undergo both targeted and non-targeted analyses, may provide a complementary solution to address some of the shortcomings of each method.

2. Limited understanding of current exposures to PFAS in occupational environments.

The widespread reliance on PFAS in products and production as well as the growing understanding of the extent of environmental contamination and anticipated remediation and waste removal needs suggest workers may be exposed in uncharacterized occupational environments. Firefighters and workers in chemical manufacturing have been the focus of the majority of published PFAS exposure data, but these workers

represent a small fraction of the overall uses of PFAS. Data from these populations show a wide range of serum concentrations in workers, with PFOA and PFOS serum concentrations in chemical manufacturing workers elevated as much as 100 times that of the general population. (Several studies focused on occupational exposure to PFAS are listed under “Resources” on page 25.) Data from other occupations and work environments provide some insight into potential exposures, but substantial gaps exist in characterizing many other work environments not currently represented in the published literature.

The focus on occupational exposure has lagged behind characterization of community exposures. Serum concentrations reported in NHANES have declined in recent years; however, community-level exposure in areas with local contamination has been known to contribute to serum levels that are similar to some occupational groups with lower-level exposures. This variability in non-occupational sources creates challenges in identifying the extent to which an individual is exposed from their work. Additionally, exposures experienced by workers may consist of a different set of PFAS than have been documented in the general public (for example, in NHANES) and thus there is no available comparison or reference populations for those compounds. In these cases, researchers need to build in appropriate comparison populations or stratify by work factors, such as tasks.

3. Limited data to develop health-based thresholds and recommendations.

Without guidance for how to interpret PFAS concentrations measured in the work environment, exposure monitoring can be difficult to interpret. Occupational exposure limits and recommendations are often instrumental in identifying whether an exposure is too high and warrants intervention. In addition to thresholds, guidance for personal protective equipment and other appropriate interventions is necessary.

ACGIH has established Threshold Limit Values for three PFAS in air, including AFPO (a form of PFOA), perfluoroisobutylene, and perfluorobutyl ethylene, but beyond those recommendations and guidance for drinking water from federal and state agencies, threshold-based guidance for PFAS is limited. Development of these thresholds requires health-based studies where the PFAS concentration and mixtures are known, health endpoints or indicators are well defined, and other risk factors are controlled for—requirements that are already strained based on the previously mentioned challenges. In the absence of specific thresholds for additional PFAS, IH and OEHS professionals may decide to introduce interventions based on an understanding of how workplace PFAS concentrations compare to data from non-occupational settings, differ when stratifying by task or other groups within a place of work, or change over time. However, there is a risk that these interventions will be over- or under-protective, especially for exposures in the

lower range, and guidance for appropriate interventions may be challenging to find. When in doubt, IH and OEHS professionals may consider adopting the precautionary principle (as described in *Injury Prevention* at bit.ly/precautionary) until additional exposure and health data are available.

THE PATH FORWARD

The response from the research community to understand exposure to and health risks associated with PFAS has been strong and collaborative. There is a sense of urgency and a need to identify, prioritize, and address research gaps. Guidance for clinicians treating patients with concern about PFAS is available from ATSDR and additional guidance for physicians on PFAS serum testing is forthcoming from the National Academies of Sciences, Engineering, and Medicine (see bit.ly/academiespfas). Congressionally funded studies at CDC and ATSDR are beginning to produce results on community exposure and health risk for PFAS, and these agencies are working to set research priorities that address gaps in the literature. The *American Journal of Industrial Medicine* is also working on a special issue for occupational PFAS research that should be available soon.

At NIOSH, research on PFAS began approximately 15 years ago with *in vivo* studies of dermal absorption. NIOSH research has since evolved to include more expansive *in vivo* and *in vitro* toxicological assessments, studies of PFAS in firefighter PPE, air sampling method development, and exposure and health assessments of occupational populations, including firefighters and workers from other industry sectors (see bit.ly/nioshpfas). NIOSH researchers are also coordinating with other federal agencies studying PFAS, including ATSDR, CDC's National Center for Environmental Health, the National Institute of Standards and Technology, and the Department of Defense, as well as collaborating academic partners.

The voluntary removal of some PFAS from production processes, growing regulations governing PFAS-containing products and environmental contamination standards, and pressure from consumers and purchasing managers are signs that some PFAS are being phased out or may be phased out in the near future. In many cases, PFAS serve an essential function, including reducing exposure to other known occupational hazards such as the hazard of a liquid fuel fire that is not extinguished quickly and efficiently. Thus, this transition will not occur overnight and may result in a shift in the occupationally exposed populations from those in production to those in other workplaces, such as remediation settings. Researchers are working to address critical gaps in the understanding of potential exposures to and health effects associated with PFAS as well as appropriate methods for disposal and remediation of PFAS-containing media. While this work is ongoing, other research is emerging to inform a responsible transition to other products when appropriate, guided by essential use principles and caution to avoid

introducing regrettable substitutions or increasing other exposures from a change in the use of PFAS. 9

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Disclaimer: The findings and conclusions in this article are those of the author and do not necessarily represent the official position of the National Institute for Occupational Safety and Health, Centers for Disease Control and Prevention.

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