

Medical News & Perspectives

EPA Takes Action Against Harmful “Forever Chemicals” in the US Water Supply

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In the early 2000s, more than 70 000 people from Ohio and West Virginia filed a [class-action lawsuit](#) against DuPont de Nemours for contaminating local drinking water with the chemical compound perfluorooctanoic acid (PFOA), then used to make the company's Teflon nonstick coating. A lawsuit settlement included provisions for many of the plaintiffs to receive medical monitoring—if an independent panel of epidemiologists could determine that exposure to PFOA was associated with human disease. The panel ultimately concluded that there were “[probable links](#)” between PFOA exposure and high cholesterol, kidney cancer, testicular cancer, thyroid disease, ulcerative colitis, and pregnancy-induced hypertension. The lawsuit was among the first well-documented cases of PFOA contamination in community water.

PFOA is just 1 of an estimated [more than 12 000](#) perfluoroalkyl and polyfluoroalkyl substances, a class of synthetic chemical compounds known as PFAS. Although US manufacturers have mostly phased out PFOA and another PFAS called perfluorooctanesulfonic acid (PFOS), decades of widespread use have left these so-called forever chemicals ubiquitous in the environment and in human bodies.

PFAS have remained largely unregulated by the US Environmental Protection Agency (EPA), but that could be changing. In 2021, the EPA released a [road map](#) to address harmful PFAS. The listed strategies provide ways to remediate, restrict, and research the substances. Among the key action items are drinking water regulations—the EPA has yet to establish “national drinking water regulations for any PFAS,” the road map noted. The goal is to finalize a water regulation proposal later this year. In the meantime, the EPA has released health advisories and toxicity assessments—including reassessments—of some PFAS.



“Current scientific research suggests that exposure to high levels of certain PFAS may lead to adverse health outcomes,” Betsy Behl, a director in the EPA's Office of Water, wrote in an email to *JAMA*. “However, research is still ongoing to determine how different levels of exposure to different PFAS can lead to a variety of health effects.”

The EPA recently reassessed what constitutes health-protective levels of PFOA and PFOS in drinking water. In [2016](#), the threshold was set at 70 parts per trillion; this [June](#), it changed to 0.004 parts per trillion for PFOA and 0.02 for PFOS—indicating there are essentially no safe levels of detectable traces.

“That's a stunningly low number,” Will Dichtel, PhD, a chemistry professor at Northwestern University, said of the PFOA threshold in an interview with *JAMA*. “What it means is that you shouldn't have any PFOA in your water.”

“The updated advisory levels, which are based on new science and consider lifetime exposure, indicate that some negative health

effects may occur with concentrations of PFOA or PFOS in water that are near zero,” Behl explained.

The advisories employ the latest data from epidemiological studies of different populations exposed to PFOA and PFOS. The EPA's [website](#) lists several health concerns, including cancer, low birth weight, and issues related to the cardiovascular and immune systems. However, “[t]he most sensitive non-cancer effect and the basis for the interim updated health advisories for PFOA and PFOS is suppression of vaccine response (decreased serum antibody concentrations) in children,” the website indicates.

Mitigating PFAS exposure and related health effects isn't the only challenge; scientists are also searching for ways to make these forever chemicals less permanent in the environment.

Forever Chemicals

PFAS are found in [air, soil, fish, and water sources](#)—including [rainwater](#)—across the

globe. Exposure is pervasive: researchers at the Centers for Disease Control and Prevention (CDC) have detected PFAS in [serum](#) samples of almost everyone tested since 1999 and consider the substances a [public health concern](#).

The chemicals have been used in various products since the [1940s](#). “They’re attractive because they repel oil, they repel water, they resist heat, and they reduce friction,” Ned Calonge, MD, MPH, the associate dean for public health practice and an associate professor of epidemiology at the Colorado School of Public Health, said in an interview with *JAMA*.

Today the substances commonly coat nonstick cookware as well as waterrepellent and stain-resistant fabrics; they’re also found in a broad range of other [everyday items](#), from cosmetics and dental floss to cleaning products and food packaging. Outside household goods, [fire-extinguishing foam](#) is a [major source](#) of PFAS in the environment.

PFAS earned the nickname forever chemicals because of their environmental persistence. They’re particularly problematic as they don’t degrade easily, they accumulate in animals, and they can negatively affect human health. Researchers have identified links between high serum levels of various PFAS (chiefly PFOA or PFOS) and increased risk of [high cholesterol](#), [breast cancer](#), [kidney cancer](#), and [thyroid disease](#)—to name a just few medical conditions. But many unknowns remain; there are thousands of PFAS with unique properties and [potentially different](#) toxicity levels and health effects.

“The toxicity of the chemicals varies, and people may be exposed to each chemical in different ways, in varying amounts, and/or with different mixtures,” Behl said. “Research is also underway to better understand the health effects associated with low levels of exposure to PFAS over long periods of time, especially in children.”

In response to public concern about PFAS contamination, US companies voluntarily began phasing out certain PFAS, including [PFOA](#) and [PFOS](#), in the early 2000s. They often replaced PFOA with hexafluoropropylene oxide dimer acid and its ammonium salt, referred to as [GenX chemicals](#). Perfluorobutanesulfonic acid (PFBS) and its potassium salt were also introduced as a PFOS alternative. But based on findings in nonhuman animal [toxicity studies](#), the EPA issued drinking water [health](#)

[advisories](#) for both GenX chemicals and PFBS this June.

The human health effects of GenX chemicals [are yet to be determined](#). Since [2017](#), the [GenX Exposure Study](#), funded by the National Institute of Environmental Health Sciences (NIEHS) and the North Carolina Policy Collaboratory, has investigated human exposure to GenX chemicals and other PFAS throughout the Cape Fear River Basin in North Carolina. For more than 35 years, a chemical manufacturing plant initially run by DuPont de Nemours and later its corporate spinoff Chemours discharged [PFAS-contaminated wastewater](#) into the river. In [2020](#), the GenX Exposure Study detected legacy PFAS, including PFOA and PFOS, in about 97% of 344 serum samples from Wilmington, NC, residents. The median serum concentration for PFOA among participants exceeded the 95th percentile for the US population.

The study also is looking at the potential effects of PFAS exposure on COVID-19 vaccine response because [the chemicals may affect antibody production](#). “Antibody response to vaccines is supposed to be the most sensitive end point for PFAS,” principal investigator Jane Hoppin, ScD, director of the Center for Human Health and the Environment at North Carolina State University, wrote in an email to *JAMA*.

Although Hoppin noted that her team is just beginning to analyze the data, there may be clues in prior research. According to the CDC and the Agency for Toxic Substances and Disease Registry (ATSDR), children exposed to high levels of certain PFAS may have a [decreased response to vaccines](#); the authors of a [2018 perspective](#) in the *Journal of Exposure Science & Environmental Epidemiology* concluded that epidemiological and toxicological studies “provide strong evidence that humans exposed to PFOA and PFOS are at risk for immunosuppression.”

Last year, researchers in [Sweden](#) determined that people living in areas with PFAS-contaminated drinking water had a higher risk of COVID-19 infection than those in areas without the contamination. Another group found that in the Veneto Region of [Italy](#), COVID-19 mortality risk was greater in areas with high exposure to PFAS in drinking water than in other parts of the region. However, it’s unclear whether the links are causal.

Increasing Accountability

The EPA’s health advisories for PFOA and PFOS will remain in place until the agency finishes developing a proposed [National Primary Drinking Water Regulation](#) for the chemicals, which Behl said is scheduled for release by the end of this year, consistent with the road map timeline.

To further abide by the road map, the aim is to “set enforceable limits for PFOA and PFOS in drinking water, require monitoring of public water supplies, and evaluate additional PFAS and groups of PFAS for regulation,” the EPA wrote in an emailed response to *JAMA*.

“The agency is also evaluating additional PFAS and considering regulatory actions to address groups of PFAS,” Behl added, noting that the EPA expects to finalize the rule by the end of 2023.

This August, the EPA [proposed](#) designating PFOA and PFOS as hazardous substances under the Comprehensive Environmental Response, Compensation, and Liability Act, also known as Superfund. If the designation is finalized, it could increase polluter accountability.

“A designation also would allow the government to recover PFOA and PFOS cleanup costs from potentially responsible parties to facilitate having polluters, rather than taxpayers, pay for these cleanups,” the EPA wrote in its email. “Whether the federal government chooses to exercise these authorities depends upon the site-specific facts of each situation.”

Simply removing harmful PFAS from contaminated environments won’t be enough; they also must be broken down. Various attempts thus far have had mixed results. Several cities in New York ceased incinerating PFAS-based fire-extinguishing foam when the method was [banned](#) in 2020 due to [concerns](#) about the safety of the process. But using high temperatures is a reliable way to break down the molecules. For example, PFAS can be destroyed using supercritical water oxidation, which involves subjection to temperatures higher than 374 °C, according to a [study](#) in the *Journal of Environmental Engineering*.

Dichtel and collaborators published [research](#) in *Science* this summer outlining how to mineralize carboxylic acid-containing PFAS—including PFOA and GenX chemicals—using a concoction of the solvent dimethyl sulfoxide and lye heated up to 120 °C. The technique degrades the

substances' signature carbon-fluorine bonds within 1 day, leaving behind fluoride ions and carbon-containing byproducts often found in nature. But there's a caveat: the method is ineffective at degrading sulfonate-containing PFAS, a category that includes PFOS.

Translating the laboratory results into practice presents another major hurdle.

"The entire world is polluted with PFAS, and there are so many different contexts that you can't just apply this method to all of them," Dichtel explained. "And we're not going to pour dimethyl sulfoxide all over the place."

New Clinical Guidance

While it remains to be seen whether PFAS can be eradicated from the environment, there's new guidance on expanding testing for exposure. This June, the National Academies of Sciences, Engineering, and Medicine (NASEM) published a [report](#) recommending that patients with a history of high exposure to PFAS should be tested for the substances. Depending on the results, they should also be monitored and screened regularly.

When it comes to PFAS, "there's so much of it, so many people are exposed, and it's linked to so many different conditions that it ends up being different than other environmental exposures," said Calonge, who chaired the NASEM's Committee on the Guidance on PFAS Testing and Health Outcomes. "If there's a chance that a person has elevated exposure, you should consider offering them testing, and a byproduct of more testing will be more information."

The report, which was funded by the CDC/ATSDR and the NIEHS, also provides specific advice for physicians with patients who may be at risk of exposure to high PFAS levels. A serum PFAS concentration of less than 2 ng/mL is considered low, so no additional testing or monitoring is required for

people with those levels. Patients with serum levels between 2 ng/mL and less than 20 ng/mL—the midrange of PFAS exposure—should receive routine lipid panels and screening for breast cancer and hypertensive disorders of pregnancy.

Serum PFAS concentrations 20 ng/mL or greater are considered high. In such cases, the report says that physicians should try to identify the PFAS source during conversations with patients and encourage reduced exposure. Physicians should examine patients older than 2 years with these levels for dyslipidemia. Patients older than 15 years should be assessed for testicular cancer and ulcerative colitis. For those older than 18 years, physicians should conduct thyroid function testing and check serum thyrotropin levels. And patients older than 45 years should undergo a urinalysis while being assessed for kidney cancer.

More broadly, Calonge, who also chairs the CDC's Community Preventive Services Task Force, wants physicians to be better aware of environmental factors that contribute to health issues. "There's a long-standing divide between public health and clinical medicine...and there's not enough environmental health in both nursing and medical school curricula," he said. "PFAS is an area that has so many clinical health outcomes associated with it, and this is an opportunity to bring the 2 disciplines together, especially in the environmental health arena."

Avoiding PFAS

According to the NASEM report, PFAS exposure can occur through a variety of pathways. Aside from consuming the substances, exposure is often occupational and can happen while working in a fluorocarbon manufacturing facility "or where PFAS-containing products, such as textiles or food contact materials, are made." Occupa-

tions with high levels of PFAS exposure include electroplating and firefighting as well as carpet installation and treatment. Another area with potentially high exposure is the food and hospitality industry; [food packaging](#) for takeout orders often contains PFAS.

The NASEM report recommends that consumers filter their drinking water with activated carbon or reverse osmosis filters to mitigate PFAS consumption. It also encourages the public to buy PFAS-free furnishings and avoid purchasing products that may contain the chemicals, such as microwave popcorn, waterproofing sprays, and stain-resistant carpeting.

However, the report also acknowledges that "it is difficult to reduce exposure to PFAS through personal behavior modifications."

Dichtel emphasized that the onus shouldn't be placed entirely on the public. "This is not a consumer-choice problem," he said, adding that it can be difficult for people with limited resources to make certain changes. "You can say, 'buy whole foods and cook every meal at home, and you might be able to reduce some of your exposure,' but that's not the reality we're all living in."

He also pointed out that efforts to remove PFAS from the environment and mitigate exposure aren't enough to fix the problem. "Cleaning up and destroying PFAS are like bandages," he said. "There's no replacement for phasing this stuff out." ■

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Conflict of Interest Disclosures: Dr Dichtel reported being a cofounder and equity holder of Cyclopure, a company that develops commercialized technologies related to PFAS detection and remediation. Dr Hoppin reported serving on the NASEM's Committee on the Guidance on PFAS Testing and Health Outcomes and receiving funding from the NIEHS to conduct research on the human health effects of PFAS. No other disclosures were reported.

Note: Source references are available through embedded hyperlinks in the article text online.