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Scientific Basis for Managing PFAS as a Chemical Class

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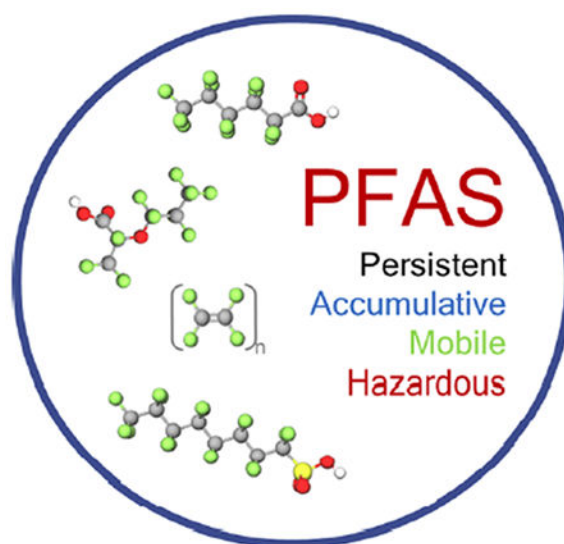
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Abstract

This commentary presents a scientific basis for managing as one chemical class the thousands of chemicals known as PFAS (per- and polyfluoroalkyl substances). The class includes perfluoroalkyl acids, perfluoroalkylether acids, and their precursors; fluoropolymers and perfluoropolyethers; and other PFAS. The basis for the class approach is presented in relation to their physicochemical, environmental, and toxicological properties. Specifically, the high persistence, accumulation potential, and/or hazards (known and potential) of PFAS studied to date warrant treating all PFAS as a single class. Examples are provided of how some PFAS are being regulated and how some businesses are avoiding all PFAS in their products and purchasing decisions. We conclude with options for how governments and industry can apply the class-based approach, emphasizing the importance of eliminating non-essential uses of PFAS, and further developing safer alternatives and methods to remove existing PFAS from the environment.

Graphical Abstract



INTRODUCTION

When chemicals have similar molecular structures, environmental properties, and/or biological hazards, managing them as a class can be an effective means of reducing adverse effects on human and ecological health.¹⁻⁴ While a class-based approach to chemical management can pose challenges to the traditional paradigm of individual chemical risk assessment, the extreme persistence and potential for harm from thousands of PFAS (per- and polyfluoroalkyl substances)^{5,6} demand a more efficient and effective approach. Examples of cases in which substances with common chemical characteristics are currently managed as a class include organophosphate pesticides, organochlorine pesticides, and organohalogen flame retardants.^{1,7} Thus, a class-based approach not only is feasible but also has already been implemented by regulatory agencies globally.

Here we provide scientific justification for why a class-based approach is appropriate and necessary for all PFAS, defined as chemicals with at least one aliphatic perfluorocarbon moiety (e.g., $-C_nF_{2n-}$).^{5,6} We discuss the following major subclasses of PFAS in detail: perfluoroalkyl acids and perfluoroalkylether acids (together termed PFAA) and their precursors, fluoropolymers and perfluoropolyethers, and other (primarily less reactive) PFAS (see Figure 1 for examples). PFAA are nonpolymer PFAS with at least one perfluorocarbon moiety (e.g., $-CF_2-$, $>CF-$) directly linked to an acid functional group. The most well-known are perfluorooctanesulfonic acid (PFOS) and perfluorooctanoic acid (PFOA). Many other PFAS may transform and yield PFAA in the environment and biota and are thus regarded as precursors to PFAA. Examples are PFAS derived from fluorotelomers and perfluoroalkane-sulfonyl fluorides, including so-called side-chain-fluorinated polymers (i.e., polymers with nonfluorinated backbones and fluorinated side chains). Fluoropolymers and perfluoropolyethers include polymers with backbones being per- or polyfluorinated. Other PFAS in the class include primarily nonpolymeric PFAS with limited chemical reactivity, such as linear and cyclic perfluoroalkanes, perfluoroalkylethers, and perfluoroalkyl amines.

PFAS function in many capacities, including as surfactants, friction reducers, and repellents of water, dirt, and oil. As such, they are used in a wide variety of consumer products to confer nonstick (waterproof, greaseproof, and stainproof) and low-friction properties. Examples of products that contain or are coated with PFAS include carpets, glass, paper, clothing and other textiles, plastic articles, cookware, food packaging, electronics, and personal care products. PFAS are also used directly or as technical aids (dispersants and emulsifiers) in many industrial applications, such as in metal coatings, lubricants for machinery, membranes, and firefighting foams. PFAS are used in the synthesis of or as adjuvants in pesticides, in medical procedures and products, and in many other applications.

The most consistent feature within the class of PFAS is that their perfluorocarbon moieties do not break down, or do so very slowly under natural conditions, which is why PFAS are often termed “forever chemicals”.⁹ Because PFAS are persistent, they accumulate or concentrate in the environment, including water, air, sediment, soil, and plants.¹⁰ Elevated levels of PFAS and their widespread presence in environmental media and drinking water stem from industrial sites that produce or use PFAS (or have done so in the past), airports, military bases (fire-training and response areas), landfills, wastewater treatment plants, and the spreading of PFAS-contaminated biosolids.^{11–13} Some PFAS are highly mobile in either air or water, allowing them to travel long distances from their source.

Environmental and human exposure to PFAS can occur throughout the life cycles of these chemicals and products containing them, including during chemical production, product manufacturing, distribution, use, disposal, and recycling. Many PFAS, particularly PFAA, have been detected globally and are in the bodies of nearly all people living in the United States (US), Europe, and other countries worldwide.^{14,15} Major sources of human exposure to PFAS are from contaminated food, water, air, and other media such as consumer products and house dust.^{16,17} Limited testing of primarily large public water sources in the US found PFAS in the water supplies serving an estimated 16.5 million people, including 6 million with a combined PFOS and PFOA concentration over the US EPA’s lifetime health advisory of 70 ng/L.¹¹ More recent testing of 25 public water systems in the US identified PFAS in every one, with an average of nearly 10 different PFAS at a combined concentration near 20 ng/L.¹⁸ Such testing is lacking in many other parts of the world, including many European countries. PFAS are also found in a variety of foods.^{19,20} The highest levels are found in fish and shellfish, but meat, eggs, and milk may also contain PFAS if animals have consumed contaminated feed or water. Fruits and vegetables have been shown to contain PFAS taken up from the soil and water used to grow them.²¹ Food contact materials are another source of exposure,^{22,23} as are consumer products and house dust.^{24–28}

Exposure to PFAS occurs in complex mixtures of multiple PFAS, yet at present, fewer than 50 individual PFAS (often fewer than 10) are commonly measured in environmental media.^{29,30} New analytical methods allow for more comprehensive screening such as measuring total fluorine or extractable/adsorbable organofluorine in the environment,^{31–33} products,^{22,23,34,35} dust,²⁷ biota,³⁶ and humans.³⁷ These methods reveal evidence that humans and wildlife are exposed to more PFAS than previously estimated. For example, in one study of tap water in five US cities, less than half the total organic fluorine measured in treated

drinking water was accounted for by the sum of individually identified PFAS, indicating far more PFAS and other organofluorine compounds were present in the water than were identified with targeted analysis.³⁸

The most well-studied of these substances, PFOA and PFOS, have been linked to a variety of health problems. They are termed “long-chain” PFAS, a designation that includes perfluoroalkylcarboxylic acids (PFCA) with seven or more fluorinated carbons, perfluoroalkanesulfonic acids (PFSA) with six or more fluorinated carbons, and their precursors. When some major manufacturers phased out the production of long-chain PFAS, most industries turned to structurally similar replacements, including homologues with fewer fluorinated carbons (short-chain PFAS) or other less well known PFAS (e.g., per- and polyfluoroalkylether-based substances).^{39,40} These replacement PFAS were marketed by producers as safer alternatives because of their presumed lower toxicity and lower level of bioaccumulation in human blood.⁴¹ However, several lines of evidence suggest that short-chain PFAS are not safer alternatives. Research has demonstrated that short-chain PFAS can be equally environmentally persistent and are even more mobile in the environment and more difficult to remove from drinking water than long-chain PFAS.^{33,42,43} Bioaccumulation of some short-chain PFAS occurs in humans and animals,^{44–46} and research in fish suggests they can do so in excess of the long-chain compounds they aimed to replace.^{47,48} Short-chain PFAS also can be more effectively taken up by plants.^{49–51} Because short-chain PFAS have, to a large extent, replaced the long-chain PFAS in commerce, the levels of short-chain PFAS, such as perfluorobutanoic acid (PFBA), perfluorobutanesulfonic acid (PFBS), and perfluorohexanoic acid (PFHxA), have increased in environmental media.^{37,43,52,53} To date, relatively little is known about possible health effects of long-term exposure to short-chain PFAS. However, a growing body of evidence suggests they are associated with similar adverse toxicological effects as long-chain PFAS.^{54–57} The ongoing accumulation of persistent chemicals that are known or potentially hazardous increases risks to human and environmental health over an indefinite period of time.

Fluoropolymers consist of molecular segments (monomers) that are linked together, with up to hundreds of thousands of linked monomers in high-molecular weight polymers. While they are commonly regarded as PFAS,⁵⁸ fluorochemical producers now argue that fluoropolymers should be separated from other PFAS for hazard assessment or regulatory purposes.⁵⁹ However, the production of fluoropolymers and perfluoropolyethers is responsible for extensive environmental PFAS contamination, including releases of both intentionally added PFAA processing aids and unintentional PFAS by products.^{13,43,60–65} It is estimated that the vast majority (~80%) of PFCA in the environment is from fluoropolymer manufacture and use.⁶⁰ Below, we discuss reasons why fluoropolymers and perfluoropolyethers should be included in the class approach to managing PFAS.

To date, managing the risk of PFAS has focused primarily on one chemical at a time, or a small group of PFAS. This approach has not been effective at controlling widespread exposure to this large group of chemicals with known and potential hazards. Below, we present scientific justification for managing PFAS as a single chemical class, and we suggest ways in which government and industry can reduce PFAS-related risks. For example, a

class-based approach can be implemented to more effectively eliminate non-essential uses of PFAS, develop safer alternatives, and clean up highly contaminated areas. Ultimately, this will reduce and prevent further accumulation of these hazardous chemicals in people and the environment and avoid replacing them with other related and harmful substances.

HEALTH AND ENVIRONMENTAL HAZARDS

With regard to biological activity and the potential for human health impacts, PFAA, particularly PFOA and PFOS, are the most well studied PFAS. Data from toxicokinetic studies of PFAA indicate that they are generally well-absorbed after ingestion.⁶⁶ After absorption, they distribute from blood to organs and tissues that receive high blood flow, such as the liver, kidney, lung, heart, skin, testis, brain, bone, and spleen.^{46,66–70} Because PFAA can occupy sites on multiple receptors, proteins, and cell interfaces in the body, they can produce physiological effects across a range of tissues.⁶⁶ Toxicological (*in vitro* and *in vivo*) and epidemiological (in occupational, highly exposed, and general populations) studies have identified a broad range of adverse health outcomes associated with exposure to PFAA in people and animals. In studies of exposed humans, elevated blood levels of PFAA have been associated with kidney and testicular cancer, elevated cholesterol, liver disease, decreased fertility, thyroid problems, changes in hormone functioning, changes in the immune system, and adverse developmental effects.^{54,71,72} Studies of experimental animals provide biological support for associations seen in human epidemiological studies, and mechanistic studies increase confidence in a causal relationship between PFAA and health effects in humans.^{72,73} To understand the potential of every PFAS to adversely affect health would require testing across the entire range of different biological end points.

Effects on the immune system are some of the most well studied health effects of PFAA. Multiple lines of evidence support PFAA as immunotoxicants and, more specifically, immunosuppressants at small administered doses in rodents, and measured serum concentrations in humans. Findings of suppressed vaccine response in humans and T cell-dependent antibody response in experimental animals led the US National Toxicology Program (NTP) to classify PFOA and PFOS as presumed immune hazards to humans.⁷² In a recent draft toxicological profile, the US Agency for Toxic Substances and Disease Registry (ATSDR) extended this finding to PFHxS and perfluorodecanoic acid (PFDeA), identifying all four compounds as suppressants of antibody response in humans.⁵⁴ These reviews provide strong evidence for immunotoxicity, especially when seen across multiple compounds, species, and studies. Notably, suppressed vaccine response in children indicates the period of early life as an exposure window of specific concern.^{74,75} As such, developmental toxicity has been used as the basis for managing PFAS in drinking water and food contact materials.^{76–80} Although the immune system, particularly during development, appears to be sensitive to these chemicals, few PFAS have been studied for such effects.

To date, a majority of human epidemiological studies have focused on long-chain PFAA. In experimental animal models, however, short-chain PFAA have shown effects similar to those of long-chain PFAA. For example, exposure to GenX has been associated with hepatic and renal effects^{81,82} and suppressed immune function in mice.⁸³ A study of PFBA in rats indicated changes to liver weight, serum cholesterol, and thyroid hormones,⁸⁴ and a two-

generation study of PFBS in rats demonstrated increased liver weight and pathological changes in kidneys.⁸⁵ Recent reports by NTP found that both PFBS and PFHxA had numerous adverse effects, including decreased thyroid hormones in male and female rats.^{55,56} Effects on kidneys⁸⁶ and on reproduction and development⁸⁷ also have been reported for PFHxA. Notably, effects observed with other PFAA may occur at larger administered doses compared to the long-chain PFAA. However, humans are exposed to multiple PFAS at once, and there is little research to date on the effects of combined exposures. To account for such effects, an additive model for PFAS toxicity is used by the US EPA for two PFAS and in several US states for five to six PFAS. In Europe, an additive model is used by the European Food Safety Authority (EFSA) for four PFAS,⁸⁸ by the EU drinking water directive listing 20 PFAS, and by individual European countries, including Sweden and Denmark.

Some manufacturers have proposed that fluoropolymers should not be grouped with other PFAS for regulatory purposes, arguing that they are biologically inert because of their high molecular weight.⁵⁹ However, these chemicals can release low-molecular weight PFAS and other hazardous substances to the environment throughout their life cycle. Thus, we argue for the inclusion of fluoropolymers and perfluoropolyethers in the overall class approach for PFAS, specifically for the following reasons.

(1) During production of fluoropolymers and perfluoropolyethers, low-molecular weight PFAS used as raw materials, processing agents, or additives, or generated as intermediates, can be released into different waste streams (air and water) and current emission filters do not completely capture them, nor is there an effective means of disposing of captured PFAS.^{13,89–91} For example, it was the production of fluoropolymers and the associated use and release of PFOA that led to the widespread contamination of the US mid-Ohio river valley and its residents.⁹² In addition, potent greenhouse gases such as HFC-23 [trifluoromethane (CHF₃)] can be formed during fluoropolymer production, and emissions to the atmosphere have been reported.^{93,94}

(2) During use, low-molecular weight PFAS may be released, for example, PFCA in personal care products that contain PTFE.⁹⁵

(3) During disposal, PFAA and other hazardous byproducts may be generated and released, such as when they are incinerated at an insufficiently high temperature for insufficient time.^{96–100} For example, when PTFE is heated above 350–400 °C, it decomposes and releases various gases that cause the so-called “Teflon fever” in workers.¹⁰¹

Other important considerations are that (1) some perfluoropolyethers (e.g., Krytox 157FS¹⁰²) are mixtures of PFAA with molecular weights of only several thousand grams per mole and thus potentially biologically active; (2) in the EU and many other countries, substances registered as polymers can consist of fewer than 10 monomers, which are likely to be small and bioavailable molecules;¹⁰³ (3) fluorine is 19 times heavier than hydrogen, and therefore high-molecular weight PFAS can be relatively small molecules, compared to hydrocarbon molecules of the same weight; and (4) fluoropolymer microplastics contribute

to global plastic and microplastics debris,^{104,105} thus adding to ongoing environmental plastic and PFAS pollution.

Similar to fluoropolymers, other PFAS such as perfluoroalkanes and perfluoroalkylamines are generally inert,¹⁰⁶ but they can be very potent greenhouse gases, up to 3 orders of magnitude more potent than CO₂.^{107–113}

In sum, scientific evidence supports the possibility that adverse effects of PFAS can occur in several bodily systems, with the developing immune system being particularly sensitive. Health effects have been demonstrated for several PFAS, including long- and short-chain PFAA, and chemicals associated with polymers. However, <1% of all PFAS have been tested for their hazardous effects. Proceeding with the approach of testing one chemical at a time will cause substantial delays in the effort to protect health and the environment from this large class of potentially hazardous chemicals.

ENVIRONMENTAL EXPOSURE: PERSISTENCE, ACCUMULATION, AND MOBILITY

An overarching property of all PFAS is that they have highly stable perfluorocarbon moieties in their molecular structure. Thus, all PFAS either are extremely persistent in the environment and biota or partially transform into extremely persistent PFAS.^{114–117} Studies have estimated that PFAS such as perfluoroalkanes have lifetimes in the thousands of years.^{113,118} Thus, PFAS will be present in the environment for centuries or longer, even if environmental releases cease immediately.

The high persistence of PFAS results in long-term accumulation in the environment and living organisms, which increases the risk of harm. A key concern in recent years is that some replacement PFAS, such as PFBA, PFBS, and GenX, have been widely detected in surface water and groundwater.^{43,65,119} PFAS can concentrate in plants, including food crops, when grown in contaminated soil or irrigated with contaminated water.^{20,120–122} Bioaccumulation occurs through the food chain, with top predators (e.g., whales, bald eagles, and humans) having the highest levels.^{123–127} Most concerning is that when PFAS accumulate, they can reach concentrations where hazardous effects are observed in humans and ecosystems, particularly when the effects of combined exposure to multiple PFAS are considered.^{128,129}

The high mobility of many PFAS further exacerbates the concern.¹³⁰ Many PFAS can travel long distances from their sources. PFAA, particularly short-chain types, are very water-soluble, being distributed readily in groundwater, surface waters, and the oceans.^{53,131,132} They can be difficult, costly, and sometimes even impossible to remove from water with conventional and even advanced treatment processes.^{13,43,133,134} Many other PFAS may be highly mobile in air, including the volatile perfluoroalkanes, fluorotelomer alcohols (FTOH), and many other (semi)volatile PFAA precursors.¹¹⁶

The extreme persistence of the fluorocarbon chain, combined with the propensity for accumulation and mobility of many PFAS, has resulted in PFAS being ubiquitous globally,

even in remote regions like the Arctic.^{36,53,135,136} The continued use of PFAS will result in increasing concentrations of PFAS, increasing numbers of exposed organisms,¹³⁷ and increasing probabilities of harm. Once adverse effects are identified, it will take decades, centuries, or even longer to reverse contamination and reduce the harm to our health and the environment.

MANAGING RISK

Risk management consists of various actions to minimize the chance of harm. Chemical risk management can be carried out by governments and businesses and includes the cessation or restriction of production and use of the chemicals, and efforts to clean up contamination.

Regulatory Approaches.

Many different regulatory frameworks are used for managing the risk of exposure to hazardous chemicals. While traditionally PFAS have been regulated one chemical at a time, subgroups of PFAS have also been regulated, with a focus on PFAA and their precursors.^{79,138–142} An advantage of targeting chemical subgroups is that the toxicological end points are often assumed to be similar, which allows for extrapolation from well-studied chemicals to those less studied. However, assessing only small subgroups systematically ignores the majority of PFAS and underestimates the overall risk, particularly when many of the chemicals are unknown. For example, the EU drinking water directive, which addresses a relatively large subgroup, covers only 20 PFAS.¹⁴³

Governments are increasingly using broader management approaches to control PFAS exposure, such as targeting all PFAS within certain use categories. For example, the US states of Maine and Washington banned all PFAS in food contact materials^{144,145} and Denmark banned PFAS from paper and paperboard food packaging.^{146,147} South Australia and Washington state (and other US states) enacted bans on PFAS in firefighting foam.^{148,149} California has proposed to regulate any PFAS used in carpets and rugs.¹⁵⁰ In the case of drinking water, a “PFAS - Total” limit was recently adopted by the European Commission.¹⁴³ Regulatory agencies in Europe and the US are working to advance, validate, and standardize currently available methods to measure total PFAS in certain media.

A more comprehensive risk management approach that has been gaining traction is to limit the uses of hazardous chemicals to only those considered “essential”, while fostering development of safer alternatives. In 1987, the Montreal Protocol defined essentiality (in the case of ozone-depleting chlorofluorocarbons) as being necessary for health or safety, or critical for the functioning of society, and without technically and economically feasible alternatives or substitutes that are acceptable from the standpoint of environment and health.¹⁵¹ In the 2015 “Madrid Statement”, more than 200 scientists advocated using a similar approach for PFAS, i.e., limiting the production and use of the entire class of PFAS, including polymers, to essential uses.¹⁵² A more recent publication applied the essentiality concept to specific PFAS use categories and described examples of current PFAS-free alternatives, as well as uses where alternatives still need to be developed.¹⁵³ In 2019, several European countries committed to phasing out all non-essential uses of PFAS by 2030.¹⁵⁴

Limiting PFAS to essential uses would incentivize further development of alternatives that do not require fluorinated chemicals. Focusing on pollution prevention is critical because remediation of PFAS-impacted media, such as polluted groundwater aquifers, is costly, is energy-intensive, and cannot fully reverse the damage.

Managing PFAS as a class has additional benefits. It reduces the likelihood of replacing well-studied hazardous chemicals with poorly studied but structurally similar PFAS that have the potential to be similarly hazardous (i.e., “regrettable substitution”). It can be simpler and less expensive to implement: for example, for premarket regulation of uses for the entire class, for setting procurement standards, for testing for compliance and communicating test results through the supply chain, and for authorities monitoring the extent of PFAS contamination of humans, products, food, water, and the environment. Simpler, cheaper, class-based methods also typically result in more frequent testing, which improves compliance and detection of emerging risks. Methods to screen for fluorine already exist, for example, extractable organic fluorine methods coupled to combustion ion chromatography (EOF-CIC) and particle-induced γ -ray emission (PIGE).^{23,155,156} Hence, focusing on risk management tools that address PFAS as a class has the potential not only to prevent pollution by known PFAS but also to prevent regrettable substitution, to improve the efficiency and effectiveness of chemical management, and to encourage the selection of treatment approaches that effectively reduce total PFAS exposure when remediating PFAS-contaminated sites.

Marketplace Approaches.

Compared to governments, retailers and manufacturers can make more rapid changes to reduce their use of chemical classes of concern. For instance, home retailer IKEA committed to a complete phase-out of all PFAS in its textile products and reported achieving this goal as of 2016.¹⁵⁷ Recently, H&M, Danish COOP, and ChemSec’s corporate initiative called to end the use of PFAS in products and the supply chain.¹⁵⁸ Numerous factors are encouraging companies to stop using the entire class of PFAS. Increasing demand for products containing fewer harmful chemicals is one driver. For example, demand from retailers for food contact materials, from textile brands for sportswear, or from large purchasers and green builders for carpets has resulted in safer PFAS-free products on the market. Pressure from environmental groups is another driver. One prominent campaign contributed to the decision of many apparel companies to eliminate PFAS in their textile treatments.¹⁵⁹ Companies’ values can also play a role, such as when member-owned retailer COOP Denmark announced a phase-out of all PFAS-containing cosmetics “on the basis of a precautionary principle”.¹⁶⁰ Similarly, Kaiser Permanente, Levi Strauss & Co., and Crate and Barrel are phasing out all PFAS based on the companies’ environmental and health values.³

New international, national, state, and local regulations focusing on PFAS in certain products are additional influences,¹⁵⁰ as are threats of future litigation and liability.¹⁶¹ While some companies may find it challenging to eliminate all PFAS from their products, others view it as important for mitigating business risks, or as a business opportunity. For example, treating PFAS as a class can help companies avoid multiple cycles of reformulations due to regrettable substitutions. Regulatory action addressing the class of PFAS will encourage

further preventive actions from companies and help “level the playing field” by reducing the financial disadvantage of industry front-runners developing safer alternatives while incentivizing even further innovation toward safer alternatives.

OPTIONS MOVING FORWARD

Thousands of PFAS have already been documented across multiple industries and business sectors, and the list is growing.^{5,6} Managing PFAS one by one is neither feasible nor cost-efficient. More comprehensive solutions are needed, given that traditional approaches have failed to control widespread exposures to PFAS and resulted in inadequate public health protection. For Europe alone, the annual health costs linked to exposure to just a few PFAS are estimated at 52–84 billion Euros, and environmental remediation costs at roughly 17 billion Euros.¹⁶² Here we suggest class-based options to more comprehensively and efficiently reduce PFAS exposure.

Government policy makers have already begun limiting PFAS through bans in certain product categories. However, to more effectively manage PFAS, governments can apply the essential uses framework. Examples of essential and non-essential uses of PFAS have already begun to be described.¹⁵³ To make the criteria fully operational for inclusion in legislation, a more precise set of decision criteria is needed to guide the categorization. Such decisions involve both scientific and ethical considerations and thus require input from a broad set of scientists, civil society, industry, and policymakers.

Limiting the entire class of PFAS, including fluorinated polymers, to essential uses is critical, given that currently, remediating PFAS, once released to the environment, is at best extremely costly and, in some cases, impossible.^{114,163} Governments can take a class-based approach to cleanup efforts, for example, by prioritizing research and development funding for treatment and disposal/destruction methods that are effective for the entire class of PFAS. Such an approach would ensure that treatment strategies remove all PFAS from all impacted environmental media (water, air, and soil) and that treatment residuals (for example, spent activated carbon and reverse osmosis concentrate) are managed such that the entire PFAS class is destroyed and its degradation products (or minerals) captured, so that unknown fluorinated reaction intermediates and harmful levels of organofluorines and hydrogen fluoride are not reintroduced into the environment. A class approach can also be used in developing cleanup standards, so that responsible industries are held accountable for remediation of all PFAS, not just a few. Additionally, governments can hold responsible parties accountable for exposure and health monitoring in heavily exposed populations, in order to promote effective and lasting solutions.

Regulatory agencies can also adopt class-based strategies to reduce exposure and minimize health risk. For example, they may extrapolate risk from well-understood PFAS when limiting uses of PFAS in commerce or setting protective cleanup levels. They can also assess combined exposures to PFAS (e.g., in drinking water, food, air, consumer products, and waste) as a basis to set regulatory limits and treatment standards. Establishing limits to the class rather than doing so on a chemical-by-chemical basis would result in lower exposure values that better protect vulnerable populations such as pregnant women, children, and

workers. In addition, systems that can track historic, current, and future uses of all PFAS, and releases to the environment, could help to guide and prioritize monitoring, for instance, for emerging risk detection and compliance/enforcement testing. The further development, use, and interlaboratory standardization of analytical methods to measure total PFAS would complement this effort, improving the accuracy, speed, and cost of screening for PFAS in the environment, consumer products, and people. Collaboration within and across national and international policy and regulatory bodies to foster class-based strategies would be beneficial. Such concerted efforts could help prevent shifting burdens from one geographical location to another and may evolve into “de facto” industry standards as international actors attempt to minimize costs of complying with multiple different regulations.

Solutions are also available in the marketplace. Chemical manufacturers can move quickly to develop safer non-fluorinated alternatives for PFAS with current essential uses. They can also work with product manufacturers and businesses to rapidly replace all PFAS uses that have technically and economically feasible alternatives that are acceptable from the standpoint of environment and health. Chemical and product manufacturers can be transparent about the use of any PFAS chemistries in the supply chain and monitor and strictly control releases of all PFAS into the environment until their use can be phased out. In addition, PFAS manufacturers can assist in developing better methods to detect, remove, and destroy PFAS, although regulatory incentives or pressures may be needed.

The more we study PFAS, the more we learn about the harm they can do to our health and the environment. However, it is not possible to thoroughly assess every individual PFAS, or combination of PFAS, for their full range of effects in a reasonable time frame. Without effective risk management action around the entire class of PFAS, these chemicals will continue to accumulate and cause harm to human health and ecosystems for generations to come. As demonstrated above, managing PFAS as a class is scientifically sound, will provide business innovation opportunities, and will help protect our health and environment now and in the future.

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Box Key Messages

1. Per- and polyfluoroalkyl substances (PFAS) make up a class of extremely persistent chemicals, numbering in the thousands, that accumulate in the environment and living organisms and can be highly mobile, leading to global contamination.
2. The use of PFAS in numerous consumer and industrial applications has led to widespread human and environmental exposure from, for example, drinking water, food, and consumer products.
3. Toxicological and epidemiological studies have identified a broad range of adverse health outcomes associated with exposure to PFAS in people and animals.
4. We suggest a class-based approach to managing the human and environmental risks associated with all PFAS, including polymers.
5. We provide options for how governments and industry can apply the class-based approach, emphasizing the importance of eliminating non-essential uses of PFAS, and further developing safer alternatives and methods to remove all existing PFAS from the environment.

Per- and Polyfluoroalkyl Substances (PFAS)

Perfluoroalkyl acids and perfluoroalkylether acids (PFAA), e.g.

perfluoroalkyl carboxylic acids (PFCA), $C_nF_{2n+1}-COOH$, e.g. PFOA

perfluoroalkane sulfonic acids (PFSA), $C_nF_{2n+1}-SO_3H$, e.g. PFOS

perfluoroalkyl phosphonic acids (PFPA), $C_nF_{2n+1}-PO_3H_2$

perfluoroalkyl phosphinic acids (PFPIA), $(C_nF_{2n+1})(C_mF_{2m+1})-PO_2H$

perfluoroalkylether carboxylic acids (PFCECA), e.g. $C_2F_5OC_2F_4OCF_2COOH$

perfluoroalkylether sulfonic acids (PFESA), e.g. $C_6F_{13}OCF_2CF_2SO_3H$

Precursors to PFAA, e.g.

perfluoroalkane sulfonyl fluorides (PASF)

perfluoroalkanoyl fluorides (PAF) and their derivatives, $C_nF_{2n+1}SO_2-R / C_nF_{2n+1}CO_2-R$

n:2 fluorotelomer-based substances $C_nF_{2n+1}CH_2CH_2-R$

per- and polyfluoroalkylether-based substances e.g. $C_nF_{2n+1}OC_mF_{2m+1}-R$

some hydrofluorocarbons (HFCs, e.g. $C_nF_{2n+1}-C_mH_{2m+1}$), hydrofluoroethers (HFEs,

e.g. $C_nF_{2n+1}OC_mH_{2m+1}$) and hydrofluoroolefins (HFOs, e.g. $C_nF_{2n+1}-CH=CH_2$);

perfluoroalkyl ($C_nF_{2n+1}C(O)C_mF_{2m+1}$) and semi-fluorinated ($C_nF_{2n+1}C(O)C_mH_{2m+1}$) ketones;

perfluoroalkyl alcohols ($C_nF_{2n+1}OH$)

side-chain fluorinated polymers e.g. (meth)acrylate, urethane, or oxetane polymers with non-fluorinated backbones and fluorinated side-chains

non-polymers R = NH, $NHCH_2CH_2OH$, etc.

Fluoropolymers, e.g.

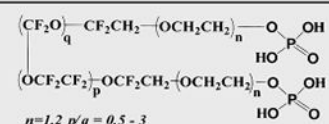
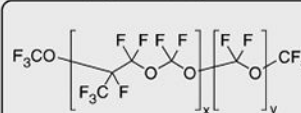
polytetrafluoroethylene (PTFE), $-(CF_2CF_2)_n-$

polychlorotrifluoroethylene (PCTFE), $-(CF_2CFCl)_n-$

polyvinylidene fluoride (PVDF), $-(CF_2CH_2)_n-$

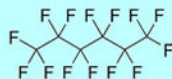
fluorinated ethylene propylene (FEP), $-(CF_2CF_2)_n-(CF_2C(CF_3)F)_m-$

Perfluoropolyethers, e.g.

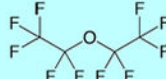


Other PFAS*, e.g.

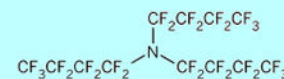
perfluoroalkanes, e.g.



perfluoroalkylethers, e.g.



perfluoroalkylamines, e.g.



* These PFAS have been less discussed in the public domain, but they meet the definition of PFAS as recommended in Buck et al. (2011) and OECD (2018). They are primarily PFAS with limited chemical reactivity.

Figure 1.

Examples of PFAS chemistries. *These PFAS have been less discussed in the public domain, but they meet the definition of PFAS as recommended in refs 58 and 5. They are primarily PFAS with limited chemical reactivity.