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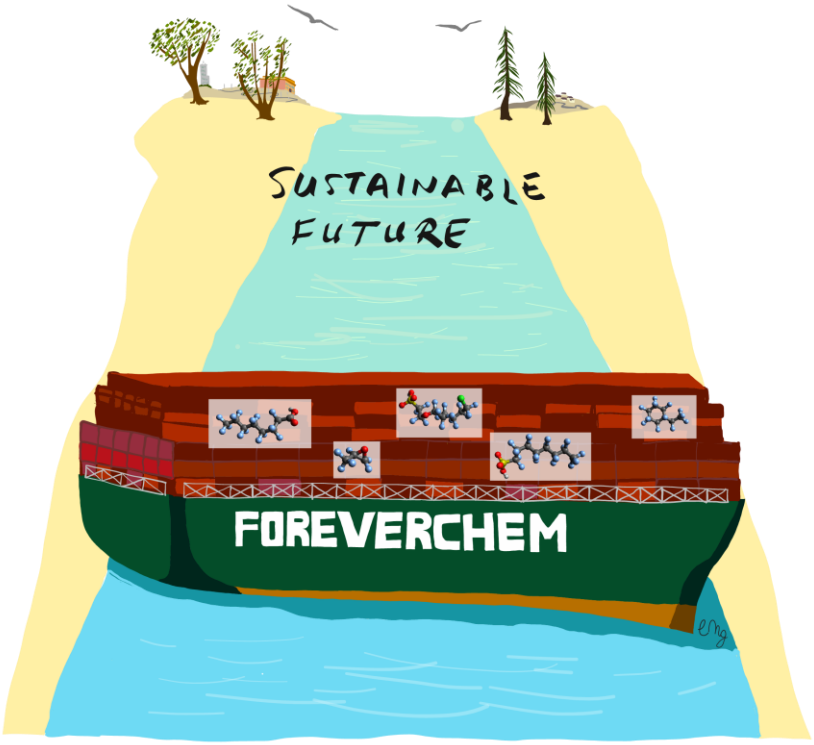


Abstract

Despite decades of research on per- and polyfluoroalkyl substances (PFAS), fundamental obstacles remain to addressing worldwide contamination by these chemicals and their associated impacts on environmental quality and health. Here we propose six urgent questions relevant to science, technology, and policy that must be tackled in order to address the "PFAS problem": (1) What are the global production volumes of PFAS, and where are PFAS used? (2) Where are the unknown PFAS hotspots in the environment? (3) How can we make the measurement of PFAS globally accessible? (4) How can we safely manage PFAS-containing waste? (5) How do we understand and describe the health effects of PFAS exposure? And (6) Who pays the costs of PFAS contamination? The importance of each question and barriers to progress are briefly described, and several potential paths forward are proposed. Given the diversity of PFAS and their uses, the extreme persistence of most PFAS, the striking ongoing lack of fundamental information, and the inequity of the health and environmental impacts from PFAS

contamination, there is a need for scientific and regulatory communities to work together, with cooperation from PFAS-related industries, to fill in critical data gaps and protect human health and the environment.

Synopsis: This article discusses key gaps in data, understanding, and technology to address the problem of global PFAS contamination, identifies persistent barriers, and suggests useful paths forward.

Introduction

Per- and polyfluoroalkyl substances (PFAS) are a class of thousands of chemicals[1–3] with perfluorinated carbon moieties that impart physical stability, chemical resistance, and, for most PFAS, extreme environmental persistence[4]. For decades, PFAS have been incorporated into a vast array of products and applications,[5] and as a result, are pervasive environmental contaminants[6,7]. The beginning of the 21st Century saw increasing detection of long-chain perfluoroalkyl acids (PFAAs) in the environment and organisms on a global scale. Recognition that some of these chemicals are globally transported, bioaccumulate, and exert multiple adverse effects in biological systems led to regulation and phase-out of several PFAS[8–11]. In response, an array of other PFAS have been used as substitutes and are increasingly detected in the environment, in wildlife, and in humans[12–16].

Despite two decades of research on fate and transport, biological effects, and environmental emissions, critical gaps remain in our knowledge, preventing researchers and society from finding effective solutions to the "PFAS problem". This is due to the diversity of chemicals in the PFAS class, to ongoing analytical challenges in detecting, characterizing, and quantifying different PFAS, and to a continued lack of transparency on the part of industry concerning which PFAS are produced, where they are used, and in what quantities. As society grapples with how PFAS may best be regulated and how to prioritize efforts to minimize environmental and human exposure, major challenges remain. Here, we identify a set of six urgent questions that must be addressed for the effective global management and eventual phase-out of

PFAS (Figure 1), building on the Zurich Statement on Future Actions on PFAS[17]. We also highlight major barriers that impede progress in answering these questions, and provide potential paths forward from the perspectives of science, technology, and policy.

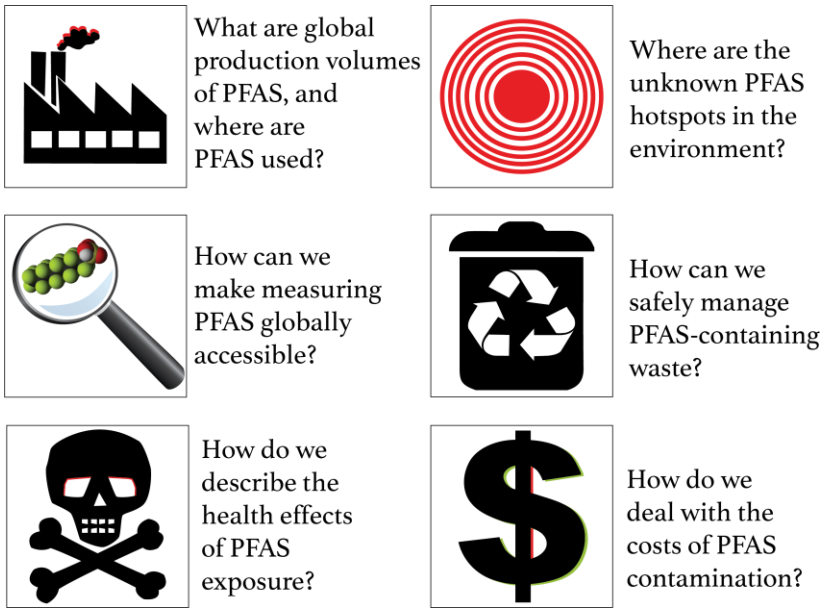


Figure 1: *Six urgent questions relevant to science, technology, and policy that must be tackled in order to address the "PFAS problem".*

1. What are the global production volumes of PFAS, and where are PFAS used?

Importance: This deceptively simple question highlights a fundamental gap in society's knowledge about nearly all PFAS. Despite painstaking emission estimates for the best-characterized sub-classes of PFAS[18,19], there is a lack of information on historical and ongoing production volumes of most PFAS, including even their identities[1,20,21]. This information is needed to build reliable emissions inventories, investigate environmental fate and transport, and assess associated exposures and health risks. While this is a general problem for most chemicals in commerce[22], the multitude of uses for PFAS and the transformation of various precursors into the same PFAS end-products make tracking the sources of PFAS exposure to

production and use particularly difficult. Without these data, society will fail to protect its members from unknown exposures until or even after harmful and irreversible effects are discovered.

Barriers: Regulatory bodies in many countries have developed registries of chemicals produced or used in their jurisdictions[18,19,22–24], but much of the collected information is confidential. In addition, many newer uses of PFAS remain poorly documented in the technical literature. The Kirk-Othmer Encyclopedia of Chemical Technology (2004)[25] and Kissa (2001)[26] are considered authoritative reference sources for industrial applications of PFAS. However, most of the PFAS-relevant content in both were written before the EPA's Stewardship Program (2006)[8], the addition of perfluorooctanesulfonic acid (PFOS; 2009), perfluorooctanoic acid (PFOA; 2019) and their precursors to the Stockholm Convention,[11] and a number of PFAS restrictions under the European Union REACH legislation[27]. The EPA's Toxics Release Inventory (TRI), designed to inform the public of releases of toxic chemicals in their communities, can shed light on some larger sources of PFAS releases. However, it often falls short of the level of detail needed to characterize environmental contamination because it requires only self-reporting and contains extensive exemptions for many industry sectors (e.g., oil and gas), small businesses, facility cleaning and maintenance applications, and trade secret claims, among others. A recently proposed new rule under the Toxic Substances Control Act (TSCA) could overcome some of these key limitations for PFAS, as discussed in the "Paths Forward" section that follows.

As a further complication, emissions and exposures vary depending on the properties, production, use patterns and end-of-life treatments of the product and the PFAS applied. A recent broad overview of PFAS uses[5] in different consumer and industrial applications revealed a large number of little known uses such as in ammunition, climbing ropes, guitar strings, artificial turf, and soil remediation. For other areas (e.g., cosmetics, paints), PFAS use is known, but it is often less clear which specific PFAS have been employed and at what quantities. Such lack of knowledge about PFAS in industrial processes and products also impacts retailers and consumers. Public pressure to phase out hazardous chemicals has led

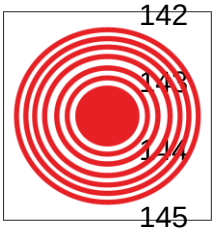
major retailers to remove certain PFAS from food packaging, clothing, and household furnishings[28,29]. However, retailers and product manufacturers often run into issues wherein PFAS are used somewhere along the supply chain but the exact use, PFAS type, and concentration are unknown. Proprietary information is used by industry as a justification for withholding the identity and concentration of chemicals in commercial products, with Confidential Business Information (CBI) claims used to protect details of formulas and manufacturing processes that confer an advantage over a company's competitors. This means that often little is publicly known about the identity and quantity of specific chemical structures present within a substance, formulation, or product.

Potential Paths Forward: Chemical identities, production and consumption volumes, use locations and emikssions, including of byproducts and impurities, need to be reported by industry, and such information needs to be made publicly accessible. Retailers and product manufacturers need to know and publish where PFAS are present in their supply chains to foster greater transparency and confidence in the composition and safety of end products. This will require public pressure, rules, and regulations. In June 2021, the US EPA published a proposed update to the reporting requirements for PFAS under TSCA[30] that could facilitate this type of reporting. The new rule potentially applies to a larger number of PFAS and no longer exempts small-scale businesses that manufacture PFAS from reporting requirements, an acknowledgment of the particular concern raised by these chemicals. However, this rule is still limited to producers, and as such will not resolve the supply chain issues of identifying PFAS in and emissions from downstream products. In addition, confidentiality of production and import volumes and chemical identity are still supported under the proposed rule, thus continuing to limit public access to these critical data under CBI claims. Another potentially useful mechanism is greater use of product registries, such as are maintained by the Scandinavian countries[31–33]. These require manufacturers and importers to declare chemical substances and products (excluding food, cosmetics, and medicinal products) in excess of 100 kg per year per company. Finally, a researcher-led approach to identifying PFAS occurrence in products and environmental emissions could entail greater use of coordination networks like NORMAN[34]. Such a

network can serve as a central touchpoint to harmonize analytical methods and share information on occurrence and effects of PFAS, but is limited to detecting pollution after it has occurred.

2. Where are the unknown PFAS hotspots in the environment?

Importance: The ability to identify geographic areas, environmental media, and populations with high



PFAS concentrations is crucial to manage exposures and for the development of models to predict PFAS transfer across environmental media, geographic borders, and food webs. The scientific community is well aware of certain contaminated sites such as airports and military facilities,[35–37] pulp and paper mills[38] and fluoropolymer manufacturing facilities[39–43], but others have only recently come to light[44]. Certain activities can lead to decade-long local releases that are poorly documented, because the respective PFAS amount is not substantial on a regional or global scale, and therefore difficult to identify without local knowledge.

Barriers: Region- or country-specific uses exist that may constitute important but primarily local contamination hot-spots. For example, high volumes of PFOS have been emitted in South America through the use of Sulfluramid, an insecticide containing the PFOS-precursor N-ethyl perfluorooctane sulfonamide used to control leaf-cutting ants[45,46] Moreover, small-scale manufacturers in both developed and developing countries have very different control practices in place, leading to PFAS emissions that are poorly understood in light of the current knowledge of a few large industries, mostly in the developed world. In developing countries, a general lack of access to the equipment, supplies, and infrastructure needed to perform PFAS analyses can hinder identification of hotspots, a particularly critical barrier discussed in detail under Question 3.

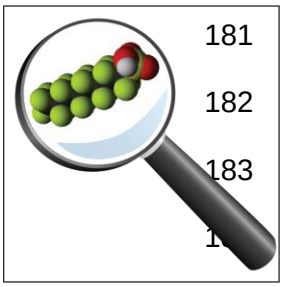
Potential Paths Forward: A systematic inventory of all PFAS industries is needed to identify current and former sites of emissions on a global scale. This requires international collaboration to integrate knowledge about locally important industries and practices. These inventories of industrial activities can

then be connected to known PFAS uses, enabling a systematic population of maps of potential PFAS contamination on a global scale, and bringing into focus areas that have been historically neglected in monitoring campaigns and/or research. This type of approach, for example using geographic information systems (GIS) to share and distribute data, is a means to organize knowledge and plan sampling campaigns on a global scale.

At the same time, funding from multiple sources (industries, governments, foundations) for monitoring campaigns that screen diverse media (e.g. air, water, soils, sediments) for PFAS can identify geographical hot spots not connected to a known or suspected PFAS-associated activity. Data on emissions and environmental occurrence could be integrated and evaluated through the use of environmental fate and transport models[47,48]. Mismatches between model predictions and measurements can provide clues to missing emissions sources or hot spots. The data generated through these concerted efforts will be key to raising awareness at the governmental level on the urgency and scale of PFAS pollution, with the intent to motivate sufficient funding for monitoring and remediation activities on a large scale, as well as stopping ongoing emissions of identified local sources.

3. How can we make measuring PFAS globally accessible?

Importance: Overcoming uncertainties in global and local PFAS distribution and exposure, and closing



critical geographical and biological data gaps as discussed above also requires, fundamentally, the ability to actually detect and measure a wide range of PFAS compounds in myriad locations and in diverse environmental and biological media. Analytical methods are needed for environmental media, drinking water, sewage sludge, foods, blood, fat, and various kinds of products and technical mixtures for monitoring and enforcement of current and upcoming regulations. Giving more researchers, communities, health-care providers, utilities, and businesses the ability to accurately detect PFAS will facilitate efforts to minimize exposure, protect vulnerable populations of humans and wildlife, and evaluate the effectiveness of

interventions. Making resources available to scientists in developing countries and developing rapid and cost-effective analytical approaches that are reliable and accessible will greatly improve the understanding of PFAS sources, fate and transport in areas where relatively little is currently known, such as Africa, Central America and parts of Asia.

Barriers: Until now the ability to measure and monitor PFAS has largely been restricted to well-resourced groups and countries with access to equipment, standards, infrastructure, and expertise. Well-established methods that can achieve high sensitivity with robust quality control require sophisticated analytical equipment (e.g. liquid chromatography tandem mass spectrometry, LC-MS/MS) that is expensive to acquire and requires specialized expertise to operate and maintain. In the past, the analysis of PFAS has been particularly challenging due to the presence of PFAS in certain laboratory and sampling materials and equipment, requiring control and monitoring of contamination, though measures have been developed to overcome this challenge[49,50].

Reliable and well-documented protocols are still limited to a narrow range of PFAS, and high-quality analytical reference standards that enable targeted analysis with reliable quantification are expensive, and still unavailable for many PFAS. Commercial standard providers[51,52] cover only about 80 different PFAS, plus variations (i.e., branched isomers or mass-labeled compounds). Without the availability of analytical standards, non-targeted analysis methods with expensive equipment and expertise are needed to identify unknown PFAS[53,54]. Recent actions by a PFAS producer may set a worrisome precedent. According to a letter sent by Wellington Laboratories to its customers in January 2021, the PFAS manufacturer Solvay has threatened to sue Wellington for patent infringement for their sale of a standard for a novel PFOA-replacement in Solvay's fluoropolymer production (CAS 1190931-41-9)[55]. This raises the potential for industry to monopolize access, maintain secrecy, and delay progress in establishing occurrence and toxicity data for these substances.

Potential Paths Forward: While the low (part per trillion) limit levels instituted for PFAS in drinking water in many jurisdictions [9,56] require high sensitivity methods and rely on the availability of standards, for purposes such as screening of sites or products, simpler lower-cost methods may suffice. There are several Total Fluorine (TF) methods to detect the presence of fluorine or fluorinated compounds (e.g. CIC[57], PIGE[58], and XPS[83]), which can be combined with sample preparation methods such as extractable organic fluorine (EOF[59]) to provide rapid screening of both abiotic and biotic matrices. Much research is ongoing to develop additional methods, such as versatile and low-cost PFAS sensors[60–62]. Whatever their technical approach, methods should be validated across laboratories and ideally standardized. Positive steps in this direction were recently illustrated for EOF measurements in water compared to total targeted PFAS in a Swedish interlaboratory comparison study[63].

Capacity building efforts can support a pipeline for training and technology transfer from better resourced countries and institutions. Some programs already exist for instrument donation, such as the Seeding Labs program on Instrumental Access that donates equipment to promote research and education in developing countries[64]. Such programs are important, but represent only a small part of the solution to this enormous challenge. In addition to equipment, access to supplies (e.g. standards, solvents) and reliable infrastructure (electricity, water, gases) is crucial and often unavailable. To make these efforts accessible and sustainable, traineeships could be established for scientists in under-resourced regions to learn PFAS analysis at host laboratories. This would provide the opportunity for scientists in regions without adequate infrastructure to collect local samples to be analyzed at the host institution, while retaining ownership of the data and authorship in resulting publications.

4. How can we safely manage PFAS-containing wastes?

Importance: As PFAS are phased out of specific products and uses, safe disposal of existing stockpiles becomes an urgent need. There are many diffuse sources of PFAS, such as textiles, food contact materials, personal care products, and household furnishings, that eventually enter landfills and wastewater, and are later re-emitted to the environment through the air, landfill leachate, or into soil from biosolids application[65–67]. Within recycling streams, separation and safe disposal of PFAS contained within complex matrices become extremely challenging, given knowledge gaps on which types of PFAS are present, and at which levels, in various types of waste. Knowledge on how to deal with PFAS-containing waste is also critical for legislation related to regulations such as EU REACH and the Stockholm and Basel Conventions and ongoing PFAS restrictions.

Barriers: Multiple technologies are being developed to remove PFAS from contaminated soil and water, some of which have proven effective, but high long-term cost and energy use remain major challenges. For example, sorptive or membrane-based processes result in contaminated wastewater streams (spent sorbent, membrane rejectate) that must be disposed of. Most desirable are in-situ clean-up methods (not "pump and treat") but, so far, such a remediation solution has not been found. Large-scale water treatment facilities can be equipped with advanced treatment technologies (e.g. reverse osmosis) to remove persistent and mobile (water-soluble) chemicals like PFAS, but these are prohibitively costly to install and maintain for small systems[68–72] and also generate PFAS-containing waste.

High-temperature incineration has been proposed for some concentrated stocks (e.g. aqueous film-forming foams), but given the high stability of the carbon-fluorine bond, there are concerns whether incineration is consistently operated under conditions that ensure the full mineralization of PFAS. In Europe, flue gases from municipal waste incinerators are meant to run at a temperature of 850 °C for at least two seconds[73], but studies show that complete combustion of PFAS such as PFOA and PFOS requires temperatures of at least 1000 °C[74]. Limited work is underway to monitor incineration plants for

emissions of PFAS, but few data from full-scale studies are yet available[75]. While intensive research is ongoing to identify and optimize routes of PFAS biodegradation[76–78] as a potentially less energy- and cost-intensive solution, none are currently effective at complete mineralization under reasonable time-scales.

Potential Paths Forward: Given the difficulties and costs associated with the disposal of PFAS, an upstream solution (i.e. avoiding PFAS except for cases of essential uses) is the most effective means of dealing with future PFAS-waste. The production of PFAS for essential uses should also be carefully controlled to result in close-to-zero emissions, because the few options available for safe disposal will always be costly based on currently available and foreseeable technologies. Recovery of PFAS from such uses is another important measure to ensure the need for energy-intensive destruction is avoided. Product labeling can be effective in reducing use and emissions of hazardous chemicals including PFAS, but trace PFAS contamination within recycling streams may prevent recycled materials from being incorporated into goods labeled PFAS-free. Given existing background levels, it may be necessary for PFAS-free labeling to include an allowance for trace, non-functional levels of PFAS for industry partners trying to move away from fluorinated chemicals.

Even when an "ideal" future can be achieved where only essential uses of PFAS occur and PFAS from these uses are recovered and not released, there are still the problems of legacy PFAS contamination and ongoing PFAS emissions. To address existing and ongoing waste issues, funding and research should be targeted towards technologies that can destroy PFAS with reasonable cost and environmental performance. Hybrid technologies that combine sorption and mineralization ("concentrate and destroy") approaches may be particularly helpful in dealing with initially complex and dilute waste streams. Whatever the approach, the re-emission and shifting of contamination across environmental media (e.g. from soil to air) must be prevented. This also argues against testing of destruction technologies at scale until proven strategies are in place to prevent re-emission. Until these technologies can be better

developed, confined disposal facilities that store PFAS wastes while preventing emissions via air and leachate may be a best imperfect choice.

5. How can we understand and describe the health effects of PFAS exposure?

Importance: Toxicological assessment of each of the thousands of PFAS is not required to decide that

further environmental contamination by PFAS and subsequent exposure should be avoided. However, pressing questions remain about how to deal with historical and ongoing PFAS pollution and associated health effects. To address the potential effects of existing exposures, and to prevent the extensive use of similarly bioavailable and toxic substances in the future, it is important to understand how to link measured exposures (e.g., levels of specific PFAS in blood) to current or anticipated health effects. It is also critical to link those health effects to specific physical-chemical properties and modes or mechanisms of toxicological action of PFAS, for example through adverse outcome pathways, AOPs. Concerns about their bioaccumulation and toxicity led to the global phase-out of a number of PFAAs. Yet advances in non-targeted analysis have facilitated discovery of many other structurally similar compounds in the environment, wildlife, and humans[16,42,80,81]. Some of the newly detected compounds are attracting increasing attention as they replace phased-out PFAAs in processes and products[41,82,83], although they have in fact been released for decades in certain industries[84–86] but were under the radar of the scientific and regulatory communities. The tissue distributions and bioaccumulation potentials are still not well understood[79,80], but laboratory studies suggest that several replacement PFAS bioaccumulate and/or exert toxic effects similar to the compounds they have replaced, as well as other distinct toxic effects[44,81–84].

Barriers: One of the most difficult questions scientists working on PFAS face is that of causality: is a health condition suffered by a community member the result of their exposure to PFAS, or does a blood test indicating the presence of PFAS mean that they will become sick in the future? Communities with

316 contaminated water supplies face challenges in court to having their health and remediation costs covered
317 by the parties thought responsible for the contamination. To make the link between exposure and effect,
318 clear lines of evidence are needed to both document the exposure and explain how it leads to an observed
319 adverse health impact[87]. A striking feature of PFAS toxicity is the diversity of biological pathways that
320 are affected[88], especially given that most of the toxicological data currently available for PFAS are for a
321 few single PFAAs. Understudied groups of PFAS (e.g. neutral, cationic, zwitterionic, cyclic) may have
322 substantially different biological behavior that could be missed by established sampling approaches. For
323 example, if their tissue distributions vary from those of anionic PFAAs, focusing on only serum or liver
324 concentrations could miss critical accumulation sites for these PFAS (e.g. in lipids[89]). The structural
325 diversity of PFAS and the fact that exposures are nearly always to mixtures rather than single substances
326 complicates the search for mechanisms and structure-activity relationships.
327
328 ***Potential Paths Forward:*** The use of class-based methods to evaluate PFAS can work as a
329 precautionary approach in the face of continuing uncertainty, particularly with respect to curtailing new or
330 continuing uses of PFAS[90]. For existing exposures, additional, appropriately funded epidemiological
331 studies that target large populations with a diversity of primary exposure routes can help to develop better
332 links between exposure and effect, especially for less-studied PFAS and exposure routes. Analyses in
333 these studies should include not only blood but also other matrices (urine, breast milk, hair, lipid tissues)
334 to capture a wider diversity of PFAS physicochemical properties, half-lives of elimination, and potential
335 internal storage sites. When occurrence data in populations are combined with PFAS identities and
336 concentrations in products and environmental matrices, as discussed under questions 1 and 2, scientists
337 can begin to develop "signatures" for exposures to PFAS from specific sources. Such information would
338 be highly useful in the design of effective interventions to minimize exposures. Strategic and periodically
339 implemented human biomonitoring studies combined with environmental exposure assessments can also
340 evaluate effectiveness of regulatory initiatives[91,92].
341

Better integration of mechanistic and observational studies can reveal how PFAS induce adverse health outcomes in humans and wildlife. Computational and in-vitro approaches (e.g. toxicokinetic models[93,94], food-web bioaccumulation models[95–97], protein and phospholipid interaction models and in-vitro studies[98–103]) can provide insight into expected exposures and effects in diverse species. However, these newer approaches still face substantial barriers to inform policy, as regulatory approaches still often require that risk assessment used to support regulatory standards be based on human epidemiology data or in vivo animal toxicology data. These data are largely lacking for many of the PFAS now widely detected in the environment. Strategies to incorporate in vitro and computational data into regulatory framework would allow for more rapid expansion of risk assessment to emerging PFAS. Such studies could be further strengthened by systematic reviews of existing data to confirm or refute linkages between exposures and outcomes. To avoid regrettable substitution with existing PFAS and non-PFAS alternatives, information revealed about modes or mechanism of toxic could also be used to inform future chemical design. Chemists should incorporate principles of hazard assessment, including structure-activity relationships, early in the molecular design phase to aid in the development of chemicals that are less persistent, bioavailable and toxic.

6. Who pays for the impacts of PFAS contamination?

Importance: A 2019 study for the Nordic Council of Ministers estimated the costs for Europe of water

treatment and soil remediation due to contamination of a sub-set of PFAS at between EUR 10-20 billion over a 20-year period[104]. Testing of publicly supplied drinking water sources indicates that as many as 80 million US residents may be receiving water with PFAS levels exceeding limits recommended by regulatory agencies and toxicologists.[9,105–107] These communities may face costs ranging from purchase of replacement (bottled) water to major capital expenditures and long-term maintenance of water treatment technologies by their water utilities, which are transferred to consumers through their water bills[108–111]. Removal and disposal of contaminated soil or treatment of groundwater (e.g., pump and treat) is particularly expensive[112], and is

therefore rarely undertaken. Indirect costs can include loss of property value or closure of a business if contamination is found. Examples include an organic farm in Colorado that had to stop growing crops because its water supply had been contaminated by PFAS from fire-fighting foam[113], and a dairy farm in Maine that had to cull its herd because the milk had levels of PFAS 60 to 150 times higher than health advisory levels, due to applications of contaminated paper mill sludge to pastures as fertilizer[114].

Moreover, projected health-related costs due to effects of PFAS exposure are many times higher than the costs of environmental remediation. The Nordic study estimated the costs of human-health impacts from exposure to PFAS to be a minimum of EUR 54-82 billion *each year* in Europe. Direct costs will include medical treatment for PFAS-related health impacts such as cancer, high blood pressure, obesity and low birth weight. Indirect costs range from lost years of life and/or lost quality of life, impacts on family or on mental health because of anxiety about PFAS exposure, and ongoing health monitoring.

Barriers: Costs of environmental and health impacts from PFAS exposure, like most environmental damages, continue to be treated as negative externalities – costs not borne by the polluter carrying out the activity causing the exposure, but by society at large. The major barrier to covering these enormous costs is lack of political agreement concerning who is responsible for this contamination and exposure, and who should pay. While the "Polluter Pays Principle" was first defined and championed by the OECD in 1972, it has rarely been implemented[115]. When local, regional, or national governments step in to finance clean-up of drinking water and other remediation processes, the costs are ultimately passed on to the taxpayer.

The costs of health impacts from PFAS exposure are often borne directly by the individuals who have developed the disease and by healthcare systems, because of complexities associated with establishing direct causal links between pollution and the health impact. The relationship between exposure and disease can be particularly difficult to verify when impacts of exposure do not arise until many years later (e.g., cancer). In the US, a few legal actions for compensation have been successful, e.g., a class action

suit against Dupont/Chemours on behalf of 70,000 persons exposed to industrial discharges in West Virginia settled for $670 million and a State of Minnesota lawsuit against 3M for water contamination settled for $800 million. However, the PFAS released by these companies remain in the environment and will likely remain a source of exposure for generations, not covered by these lawsuits.

Potential Paths Forward: The extreme persistence of nearly all PFAS highlights the absurdity of continuing to treat environmental damage—including damage to public health—as a negative externality that can be ignored or even denied by the emitter. Such long-lived environmental contamination does not simply shift a burden but rather extends it, indefinitely, to future generations and all species. This is not a transaction that can be supported in a sustainable society for the sake of preserving a specific market or manufacturer. Mechanisms already exist that could be activated to shift cost burdens away from communities and taxpayers, such as the aforementioned Polluter Pays Principle. The Superfund program under the Comprehensive Environmental Response, Compensation, and Liability Act of 1980 (CERCLA) in the United States[116] can hold polluters retroactively liable, but requires that the chemical to be remediated is first designated as a hazardous substance. The designation of PFAS as hazardous substances in the US is still under debate[117], but would mark an important step forward in assigning liability.

However, liability might justifiably lie with different parties under different circumstances. Should the polluter be defined as the company that released the PFAS-containing material into the environment or the company that manufactured the material in the first place? Was the product that contained PFAS properly used? Was it properly disposed of? Was the user sufficiently informed about the risks of release? How should that liability be treated when companies merge, split, and otherwise change their structure and identities, such as when Dupont spun off Chemours in 2015 and offloaded much of their PFAS-related liability[118]? A number of cost recovery mechanisms have been suggested under the Strategic Approach to International Chemicals Management[119] that could help countries to address these issues, by funding assessment, remediation, and health care costs. These include collecting fees from companies

who wish to register chemicals for use, charging environmental protection taxes, and charging for permits.

Conclusions: Answering Urgent Questions to Address the PFAS Problem

While these urgent questions highlight critical gaps in current understanding of the PFAS problem, enough is already known to take action. Costs associated with environmental cleanup and ongoing health effects of chemicals are magnified for extremely persistent environmental contaminants[4,120], adding urgency to efforts to phase out current non-essential uses of PFAS[121]. Beyond these well-founded precautionary actions, the most important step is to improve the transparency about where and in what quantity PFAS are used. This will aid in identifying and phasing out all non-essential uses of PFAS and provide opportunities to identify less hazardous substitutes for PFAS. Production of safer chemicals and products must be seen as a competitive advantage and as a driver for innovation and the opening of new markets.

Consumers are increasingly demanding that the products they use minimize their own health risks as well as risks to environmental health. These consumer-driven initiatives place pressure on major retailers to remove known problematic chemicals—e.g., bisphenol A (BPA)[122], polybrominated diphenyl ethers (PBDEs)[123], and, now, PFAS—from their products, and have proven enormously effective. However, this is not a perfect system, as illustrated by the case of BPA, where consumer pressure led to its replacement by bisphenol S (BPS), which has turned out to be just as harmful as BPA[124]. Thus, while consumers can demand that known harmful chemicals be removed from their products, it is up to industry under the purview of scientific and regulatory communities to ensure that regrettable substitutions do not occur. A first step would be to move towards household goods, cosmetics, food-packaging materials, and personal care products with a smaller total number of ingredients, simplifying the assessment of a particular formulation.

While consumers have direct purchasing power, their ability to use this to avoid hazardous substances is impeded by the lack of transparency in product ingredients and increasing cases of 'greenwashing'. Major retailers and institutions in charge of public procurement, on the other hand, can wield much more concentrated power as well as knowledge about product supply chains. When large multinational corporations demand that their product lines remove certain hazardous chemicals, it helps in the voluntary restriction of those chemicals and also serves as a driver for innovation in the search for less hazardous alternatives. One particularly effective means for public agencies and retailers is through the use of lists of prohibited chemicals, such as the "Substitute it Now" (SIN) list,[31] which can serve as a scientifically-vetted 'manual' of chemicals to avoid. Compilation and curation of such lists, as well as their counterparts—lists of preferred less hazardous chemicals and products such as US EPA's Safer Choice[125]—can help to prevent the chemical whack-a-mole game of regrettable substitutions.

The environmental health impacts of a chemical used in a product are often not borne by the same population who benefits from the sale and use of these products. Production of PFAS has shifted to China, India, Brazil, and other countries where there is little awareness of the public health risks from PFAS and almost no environmental or human health monitoring. Extremely high exposures are already occurring, as was recently documented near a production facility in China[44]. A key component of the solutions we propose here is to ensure that PFAS research and monitoring is supported in more countries, with the goal to alleviate the impacts of "off-shoring" the negative repercussions of emissions associated with the production and end-of-life of PFAS and PFAS-containing products. In answering urgent questions for the sustainable management of PFAS, technological and policy interventions cannot be effective without also addressing environmental equity.

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