The concept of essential use for determining when uses of PFASs can be phased out

Ian T. Cousins,[1*] Gretta Goldenman,[2] Dorte Herzke,[3] Rainer Lohmann,[4] Mark Miller,[5] Carla A. Ng,[6] Sharyle Patton,[7] Martin Scheringer,[8] Xenia Trier,[9] Lena Vierke,[10] Zhanyun Wang,[8] Jamie C. DeWitt[11]

[1]Stockholm University, Sweden. [2]Milieu, Brussels, Belgium. [3]NILU in Fram Centre, Tromsø, Norway. [4]University of Rhode Island, USA. [5]National Institute of Environmental Health Sciences & U.S. Public Health Service, Research Triangle Park, NC, USA. [6]University of Pittsburgh, PA, USA. [7]Health and Environment Program Commonweal, CA, USA. [8]ETH Zurich, Switzerland. [9]European Environment Agency, Copenhagen, Denmark. [10]German Environment Agency (UBA), Dessau-Roßlau, Germany. [11]East Carolina University, Greenville, NC, USA.

E-mail contact: ian.cousins@aces.su.se

Statement of author contribution:

The concept of essential use was developed during two 2-day meetings of the Global PFAS Science Panel attended by all coauthors. Following these meetings, Ian Cousins took the lead in making the plan for the paper in collaboration with all coauthors The plan was to write the paper as a team effort because the idea had been developed through joint discussion. The writing tasks were as follows: Gretta Goldenman and Martin Scheringer developed the criteria for essential use, Ian Cousins worked on the *Personal care products and cosmetics, Fire-fighting foams*, *Ski waxes* and *Durable water and stain repellency in textiles* case studies, Dorte Herzke and Xenia Trier worked on the *Food contact materials* case study, Rainer Lohmann and Xenia Trier worked on the *Laboratory supplies, equipment and instrumentation materials* case study, Jamie DeWitt worked on the *Pharmaceuticals* and *Medical devices* case studies, Mark Miller wrote the section in the discussion on chemical alternative assessments, Sharyle Patton wrote the section in the discussion on standards, Lena Vierke provided input on regulation of PFAS, and Carla Ng and Zhanyun Wang have provided critical comments and edits throughout the writing process. Carla Ng also double-checked all references and added them using a reference manager.

Abstract

Because of the extreme persistence of per- and polyfluoroalkyl substances (PFASs) and their associated risks, the Madrid Statement argues for stopping their use where they are deemed not essential or when safer alternatives exist. To determine when uses of PFASs have an essential function in modern society, and when they do not, is not an easy task. Here, we: 1) develop the concept of "essential use" based on an existing approach described in the Montreal Protocol, 2) apply the concept to various uses of PFASs to determine the feasibility of elimination or substitution of PFASs in each use category, and 3) outline the challenges for phasing out uses of PFASs in society. In brief, we developed three distinct categories to describe the different levels of essentiality of individual uses. A phase-out of many uses of PFASs can be implemented because they are not necessary for the betterment of society in terms of health and safety, or because functional alternatives are currently available that can be substituted into these products or applications. Some specific uses of PFASs would be considered essential because they provide for vital functions and are currently without established alternatives. However, this essentiality should not be considered as permanent; rather, constant efforts are needed to search for alternatives. We provide a detailed description of several ongoing uses of PFASs and discuss whether these uses are essential or non-essential according to the three essentiality categories. We suggest applying this concept of essential uses to all uses of PFASs, and considering its use also for other chemicals of concern.

Introduction

Per- and polyfluoroalkyl substances (PFASs) are a group of more than 4700 substances[1] that have been produced since the 1940s and used in a broad range of consumer products and industrial applications[2]. The multiple uses of PFASs have been well-illustrated by the FluoroCouncil[3]. PFASs can be broadly divided into low molecular weight and high molecular weight (polymeric) substances. The polymeric PFASs can be further subdivided into side-chain fluorinated polymers, fluoropolymers and perfluoropolyethers[2]. The review of Buck et al.[2] and the FluoroCouncil website[3] should be consulted for a detailed description of the structures, classes and uses of low and high molecular weight PFASs as that background will not be provided here.

Since 2000 there have been a number of voluntary industry phase-outs and regulatory actions to cease the manufacture and use of long-chain PFAAs (defined as including perfluoroalkane sulfonic acids (PFSAs) with perfluoroalkyl chains containing 6 carbons or more, and perfluoroalkyl carboxylic acids (PFCAs) with perfluoroalkyl chains containing 7 carbons or more) and their precursors, which can transform in the environment or within organisms to long-chain PFAAs. The most common replacements for the above defined long-chain PFAS chemistries are shorter-chain PFASs, e.g. PFAAs with fewer fluorinated carbons than long-chain PFAAs, and perfluoroether-based substances (PFASs with perfluoroalkyl segments joined by ether linkages)[4]. Although some of these replacement PFASs are less bioaccumulative, they are all similarly highly persistent in the environment as their predecessors[5,6]. PFAAs which are considered short-chain and non-bioaccumulative may also lead to high internal concentrations if people are continuously exposed to high levels. Moreover, short-chain PFAAs, such as perfluorobutanoic acid (PFBA) and PFHxA, tend to be highly mobile and to move readily into ground and surface waters once released to the environment where they can reside for decades to centuries[7–10] As a result of their high environmental persistence, widespread use and release of any PFAS, even polymeric PFASs[11], will lead to irreversible global contamination and exposure of wildlife and humans, with currently unknown consequences[12–14].

Based on concerns regarding the high persistence of PFASs and the lack of knowledge on chemical structures, properties, uses, and toxicological profiles of most PFASs currently in use, it has been argued by more than 200 scientists in the Madrid Statement that the production and use of PFASs should be limited[12]. Indeed, in the textile sector, some brand names and retailers have recognized the problems associated with PFASs and have already taken significant steps to phase out *all* uses of PFASs in their consumer products[15–18].

It is neither practical nor reasonable to ban all uses of PFASs in one step. Some specific applications may serve a critical role for which alternatives currently do not exist. However, if some uses of PFASs are found not to be essential to health, safety or the functioning of today's society, they could be eliminated without having to first find functional alternatives providing an adequate function. Elimination of non-essential uses of PFASs could form a starting point for a process that leads to a global phase-out (e.g. through the Stockholm Convention on Persistent Organic Pollutants). To critically evaluate the idea that PFASs are essential in modern society, the essentiality of PFASs should be carefully tested against the available evidence for each of their uses. Given the thousands of PFASs on the market and their many uses, this is a formidable but necessary task. Before proceeding in this task, a definition of essentiality, or essential use, is needed. If PFASs are considered non-essential in a given use, then a phase-out of PFASs from that use can be implemented. The aims and structure of this paper are therefore to: 1) define the concept of essential use or essentiality, 2) apply the concept of essentiality to various use categories of PFASs to determine the feasibility of limiting use, and 3) outline the remaining challenges for phasing out use of PFASs in society and provide recommendations for further work.

The concept of 'essential use'

This approach is based on the example of the Montreal Protocol, which phased out the use of ozone-depleting chlorofluorocarbons except for certain 'essential' uses, and which defined the concept of 'essential use' in Decision IV/25[19]. The two elements of an essential use are that a use is "necessary for health or safety or for the functioning of society" *and* that "there are no available technically and economically feasible alternatives". To identify uses of PFASs that are non-essential, we combine the definition of essentiality with several categories of PFAS uses. Overall, this leads to the three categories summarized in Table 1.

For uses in Category 1, a phase-out via a ban or restriction of PFASs can be prepared because these uses are not necessary for the betterment of society in terms of health, safety and functioning. The technical function of the PFAS (if it has one) in the use case could be considered "nice to have" (e.g. non-stick frying pans) but it is not essential. In many cases the "nice to have" function can be fulfilled through substitution with fluorine-free alternatives. Even where there are no alternatives to PFAS for providing the "nice to have" function, the use case can be banned or phased out because it is not essential.

Uses in Category 2 fulfill important functions but are assessed to be non-essential because there are functional alternatives available that can be substituted into these products or applications. It may be needed to make the alternatives more well-known and more easily available, but there is no fundamental obstacle to removing PFASs from these uses. Upon increased market uptake, the costs can be expected to decrease[20,21].

Uses in Category 3 are considered necessary and currently have no established alternatives to PFASs. Innovative research and development may be needed to identify chemical or engineering alternatives and to make them technically and economically feasible. By identifying these opportunities, strong market incentives will be created for industry to develop such alternatives. In support of this approach research and innovation funding could be made available specifically for this purpose, and to support start-up companies that intend to develop and market new alternatives.

Table 1. Three essentiality categories to aid the phase out of non-essential uses of chemicals of concern, exemplified with PFAS uses.

Category	Definition	PFAS examples
1	Uses that are not essential for health and safety, and the functioning of society. The use of substances is driven primarily by market opportunity.	Dental floss, water repellent surfer shorts, ski waxes
2	Uses that have come to be regarded as essential by society because they perform important functions, but where alternatives to the substances have now been developed that have equivalent functionality, which makes those uses of the substances no longer essential.	Most uses of AFFFs, certain water-resistant textiles.
3	Uses considered essential by society because they are necessary for health or safety or other highly important purposes *and* for which alternatives are not yet established.*	Certain medical devices, occupational protective clothing.

* This essentiality should not be considered permanent; rather, a constant pressure is needed to search for alternatives in order to move these uses into Category 2 above.

Implementation of this conceptual framework could give rise to 'grey zones' where it may not be straightforward to assign a use to a particular category. For example, a grey zone might appear between categories 1 and 2 because some uses of PFASs may be considered as nice-to-have by some (stain-proof and waterproof outdoor jacket for everyday use) and as necessary by others. Similarly, a grey zone could turn up between categories 2 and 3 because the availability and performance of alternatives is being debated (e.g. AFFFs used by the military for extinguishing fuel fires). In order to avoid/minimize such ‘grey zones’ in the implementation of this conceptual framework, clear criteria and relevant processes need to be pre-defined. This would require follow up work that is beyond the scope of the present paper.

Technical standards may play a role in defining whether the use of PFASs is or is not considered “essential” in certain cases. Technical standards are detailed specifications concerning how a product should perform in certain circumstances and are often voluntary. However, they may be used to define whether a product is of sufficient quality to be placed on the market or to be purchased through public procurement. For example, some European Union product-related legislation sets so-called “essential requirements” for certain products and then delegates the task of defining how to meet those requirements to European standard-setting bodies, such as the European Committee for Standardization (CEN). The International Standardisation Organization (ISO) and national bodies such as the German Technischer Überwachungsverein (TÜV) may also set certification requirements that may be important in the design of the product performance, and how to demonstrate it. The case studies below provide several examples of how technical standards may affect whether a use of PFASs is “essential” or not.

Case studies of uses of PFASs

Below we provide descriptions of several ongoing uses of PFASs. We discuss whether the uses of PFASs are essential or non-essential based on the categorization in Table 1.

Personal care products and cosmetics: PFASs have been found in a range of different cosmetics and personal care products including hair products, powders, sunblocks, skin creams[22]. The use of PFASs in these products can cause direct human exposure and potential health effects following dermal or oral uptake. It is not clear whether any technical function provided by the PFASs is truly necessary. After a recent campaign by a Swedish NGO publicizing the presence of PFASs in certain cosmetics, it was relatively easy for several major retailers and brands of cosmetics to quickly announce phase outs of PFASs, for example, L’Oréal, H&M, Lumene, The Body Shop, Isadora and Kicks[23]. If PFASs in these products were needed for their technical function (possibly water repellency) then drop-in alternatives appear to have been readily available given the rapid phase out by retailers. The use of PFASs in personal care products falls under Category 1 in Table 1.

Ski waxes: Whereas most skiers use hydrocarbon-based glide waxes, fluorinated glide waxes are also available, though much more expensive. The fluorinated waxes are favored by competitive skiers because they are highly water repellent and result in better glide compared to hydrocarbon-based waxes. The PFASs used in fluorinated ski waxes are diblock semifluorinated n-alkanes (SFAs) mixed with normal paraffins[2]. PFCAs, including perfluorooctanoic acid (PFOA), have also been found in fluorinated ski waxes provided as solids or in powder form[24]. The presence of SFAs in snow and soil samples from a ski area in Sweden was recently demonstrated[25] and professional ski wax technicians working for the Swedish national cross-country ski team were shown to be highly exposed to PFCAs[26].

From July 2020 onwards, PFOA and related substances (e.g. substances which might form PFOA in the environment) will be banned in all products sold in the EU, including ski waxes, due to its recent addition to the REACH Annex XVII list of restricted substances (entry 68). No essential use of PFAS in ski waxes was found in the restriction process and this use category is therefore clearly non-essential. Functioning hydrocarbon-based ski waxes were in use before the fluorinated waxes were introduced. The development of fluorinated waxes was driven by market opportunity. Fluorinated waxes provide a “nice to have” function that is not essential, and therefore this use case falls under Category 1 in Table 1. However, European ski teams are continuing to use fluorinated waxes. The exception is Norway which in Oct 2018 announced that it has banned the use of fluorinated ski waxes in U16 categories[27].

Fire-fighting foams: Class B firefighting foams are formulated to extinguish fires of flammable liquids, such as liquid hydrocarbon fuels. Those currently available are either; (i) aqueous film-forming foams (AFFF), fluoroprotein foams (FP), or film-forming fluoroprotein foams (FFFP), all of which contain fluorosurfactants (i.e. they contain PFASs) and (ii) fluorine-free Class B foams (F3) using proprietary mixtures of hydrocarbon or silicone surfactants[28]. PFAS-containing AFFFs historically contained long-chain PFAAs (and their precursors)[29], but since 2015[30] the foam manufacturers have eliminated long-chain PFAAs (and their precursors) from their products. Current fluorotelomer-based AFFF formulations contain fluorosurfactants that may transform to short-chain PFAAs (primarily PFHxA and shorter-chain PFAAs) in the environment, which are thought to be less bioaccumulative and less toxic than their longer-chain predecessors. However, short-chain PFAAs are extremely persistent and mobile, and if clean-up of soil or water is later needed, it will be extremely expensive and time-consuming, if at all possible[13,31].

Fluorine-free class B foams were first developed in the early 2000s by the 3M Company and since then many other companies have marketed fluorine-free class B foams[28]. Many of the currently available fluorine-free foams meet the standard firefighting performance certifications applicable to PFAS-containing AFFF and related foams[28].

Though some debate continues concerning whether PFAS-containing foams remain necessary for certain scenarios, e.g., fires at refineries or involving very large fuel tanks, in recent years, a number of commercial airports, chemical industry facilities, oil and gas platforms, fire brigades and some national defense forces around the world have switched to using fluorine-free foams based on demonstrated operational performance in extinguishing fuel fires. However, US military forces are currently prevented from switching to fluorine-free foams because the applicable technical standard MIL-F-24385F(SH) – though revised in 2017 to reduce PFOA and PFOS in AFFFs – still requires fluorinated chemistry in addition to setting a performance-based requirement. Note that in October 2018, the US Congress enacted a bill[32] permitting civilian airports across the US to use non-fluorinated alternatives. Hydrocarbon-based foams have been shown to be biodegradable with only localized, short-term problems associated with their release during extinguishing fires or spillages. The silicone-based foams may contain low residual amounts of cyclic siloxanes (e.g. decamethylcyclopentasiloxane or D5), which have been judged to be persistent and bioaccumulative.[33] Both D5 and D4 (octamethylcyclotetrasiloxane) are listed as Substances of Very High Concern under REACH, primarily because of their vPvB (very persistent, very bioaccumulative) properties[34].

In summary, the fluorine-free foams that have been developed and improved since the early 2000s are promising from an operational perspective[35–37] and also from an environmental and human health perspective. Some military maintain that only PFAS-containing AFFF can provide the necessary performance requirements, particularly in the case of large fuel fires. Because of ongoing debate, this use category therefore currently falls under Category 2 or 3 in Table 1.

Durable water and stain repellency in textiles: Liquid repellency in textile products can range from an optional “nice-to-have” property in leisure jeans to an essential protection needed in occupational protective clothing[38]. The textile sector often refers to these chemistries as durable water repellents (DWRs), but the leading market technology repels more than just water. Since their introduction in the 1950s, the highest level of repellency for both oil/stain and water has been achieved with side-chain fluorinated polymers. Substitution to ‘short-chain’ side-chain fluorinated polymers (typically C6 or C4 perfluoroalkyl chains) has taken place in recent years. However, there is concern regarding the extreme persistence and lack of human health data for short-chain PFAAs.

A variety of new non-fluorinated DWR alternatives has been developed to create repellent textile surfaces, with a variety of polymer architectures, including linear polyurethanes, hyper-branched polymers and nanoparticles[38]. The functional moieties in terms of liquid repellency consist of either saturated alkyl chains (i.e. hydrocarbons) or polydimethylsiloxane (PDMS) chemistry (i.e. silicone polymers)[38]. Although hazards associated with non-fluorinated DWRs are not yet fully understood, the development of biodegradable alternatives is an important step. Similar to the silicone-based surfactants used in fire-fighting foams, the silicone-based DWRs may contain residual amounts of persistent cyclic siloxanes (e.g. D4 and D5).

Non-fluorinated DWRs have been shown to provide high water repellency equal to short-chain fluorinated polymers and are suitable substitutes for consumer outdoor clothing.[39] Indeed, a number of leading brands already provide water-repellent outdoor jackets marketed as e.g. “fluorine-free”.

However, in the case of both non-polar and polar liquids with very low surface tension (such as olive oil or gastric fluid), so far only short-chain fluorinated polymers have been shown to provide effective protection[40]. Such protection may be important in certain occupational settings where a specified level of performance is required.

Medical textiles are an example of where technical standards to protect human lives require a certain performance that may be difficult to meet without the use of PFASs. The European standard EN 13795 defines how the essential requirements set forth in the EU Medical Devices Directive (93/42/EEC)[41] should be met with respect to surgical gowns, drapes and clean air suits. Along with setting performance requirements aimed at preventing the transmission of infectious agents between patients and medical staff, EN 13795 also stipulates the test methods for evaluating whether the performance requirement is met. Test method EN 20811[42] – resistance to liquid penetration -- measures the pressure at which water will penetrate the fabric and is used to determine whether the fabric will provide sufficient protection against contamination from penetration by e.g. bodily fluids. Current non-fluorinated DWRs may not provide sufficient liquid repellency for non-polar bodily fluids with low surface tension. An alternative is to use surgical gowns coated with a plastic laminate, which offer sufficient protection against biological fluids containing potentially harmful viruses and bacteria but may not be sufficiently breathable for longer operations.

Similarly, performance standards set by the US National Fire Prevention Association for protective clothing for firefighters and other emergency responders for water repellency, oil/stain repellency and breathability are currently not possible to meet without fluorinated chemistry. Other types of occupational clothing, e.g. in the oil and gas sector, may require a similar combination of water and oil/stain repellency as well as breathability. At least for now, these uses of PFASs may be considered essential and in Category 3, until effective and safer alternatives are available.

In summary, non-fluorinated DWRs are available that provide good water repellency (and certain stain repellency) meeting consumer requirements and expectations for most outdoor apparel, casual wear, and business attire (Category 2). In some cases, the use of fluorinated DWRs in textiles is “nice to have” (e.g. water repellent surfer shorts), but is non-essential and falls under Category 1. Only a few uses of PFAS in textiles, e.g. the occupational protective clothing market, where repellency of a wider range of liquids as well as breathability are necessary, fall under Category 3 in Table 1. In those cases, innovative solutions are needed to provide non-fluorinated alternatives.

Food contact materials: Food contact materials (FCMs) cover a range of materials, which at some stage come into contact with food. This includes (industrial) food production equipment and machinery, food packaging, and kitchen utensils like non-stick forms and pans. Growing consumer concern over environmental and health impacts of plastic packaging has led to an increasing market pressure for alternative packaging, including paper[43]. This may result in increasing exposures to PFAS-containing paper-based materials.

The types of fluorochemistry used to protect paper and board have changed over time[44]. The most studied use of PFASs in FCMs are the longer-chain perfluoroalkyl moieties[44] in paper and board used in food contact materials, which were phased out by major manufacturers in the 2000s. Current fluorinated paper and board products are largely based on “short-chain” fluorotelomer-based polymeric products, which are side-chain fluorinated polymers containing perfluoroalkyl side chains, typically with six perfluorinated carbons[44], and poly- and perfluoropolyethers[45–48].

Despite reassurances by the chemical manufacturing industry that short-chain fluorinated products are safe, there is concern that PFASs will migrate into food and cause harm to human health[44]. Non-fluorinated alternatives have subsequently entered the market in recent years. For example, COOP Denmark A/S, a Danish consumer goods retailer, has succeeded in completely removing PFAS from all its products since September 2014[49].

Although the current polymer chemistry used in paper and board in food contact materials is similar to that used in textiles, paper and board are often made for single use, whereas textiles (e.g. outdoor jackets) need to be durable over the lifetime of a garment. However, some paper and board products need to provide repellency to oil for weeks to months (e.g. butter wrappers), whereas others (e.g. fast food wrappers) only require oil repellency for a matter of minutes. The substitution strategies for paper and board are therefore different than for DWRs in textiles given the difference in materials and performance requirements, and may even be different among food contact applications.

There are generally two types of barriers against grease or fat for paper and board, a physical or a chemical barrier[44]. A physical barrier preventing penetration of a liquid into the paper may be sufficient in certain types of single use applications. The chemical barrier, which is the approach used in fluorinated products, repels the grease in the food due to the decreased surface energy of the paper surface. Two of the most common types of paper that provide a physical barrier against grease are Natural Greaseproof paper[50] and vegetable parchment[51], providing a dense cellulose structure that prevents the grease from soaking into the paper. There are also various non-fluorinated chemical barriers that can provide similar repellency to grease as fluorinated repellents, including hydrocarbon- and silicone-based alternatives[52]. A third alternative is to add aluminum or plastic coatings to the paper to provide protection[53].

In food production, PFASs are mainly used as non-stick fluoropolymer (e.g. PTFE) coatings of (metal) surfaces to lower friction (which protects the equipment from abrasion), to minimize adhesion (which allows better cleaning of surfaces), as non-stick/heat/acid resistant fluoroelastomer membranes on conveyor belts, and as lubricant oils and greases in machinery[54–57]. Many of the same uses exist in household kitchen utensils and appliances. These uses are described in industry patents and commercial materials[54], but the levels and types of PFASs have been studied only to a limited extent[58,59].

Non-stick kitchenware is normally produced by either spraying or rolling layers of PTFE onto the surface of the kitchenware. One could argue that the non-stick is a “nice to have” function rather than an essential function given that it is possible to cook food without the non-stick functionality. If the non-stick coating is considered an essential function in a modern society, then other possible non-stick coatings are available, including: enamelled iron-, ceramic-, and anodized aluminium coatings[60].

In summary, non-fluorinated alternatives have been historically available for all applications of paper and board food packaging and the use of fluorinated protective coatings has never been essential (Category 1). For example, COOP, a major grocery retailer in Denmark, has found alternatives for all products that previously used PFAS[49,61]. For non-stick cookware there are also non-fluorinated non-stick alternatives which work well in households and this is also not an essential function (Category 1). In the food production industry non-fluorinated conveyor belts, lubricants and greases exist, but it is not clear currently whether functional alternatives to fluoropolymer protection against abrasion exist (Categories 2 or 3).

Medical devices: Another use of fluoropolymers is as coatings in catheters, stents and needles to reduce friction and improve clot resistance and to provide protein-resistance in filters, tubing, o-rings, seals, and gaskets used in kidney dialysis machines and immunodiagnostic instruments[3,54,62]. The safety evaluation of these devices for use in humans was discussed by Henry et al. (2018).[63] After review, multiple regulatory agencies have concluded that the use of PFASs in these products, including on devices implanted into patients' bodies, does not pose an appreciable risk because the fluoropolymers are not bioavailable[63–65]. It is however unclear whether impurities of fluoropolymer processing aids such as PFOA and HFPO-DA were included in the regulatory reviews.

In summary, the inclusion of fluoropolymers into medical devices confers several benefits and does not appear to pose substantial health risks to those who are exposed to these devices through procedures or who have received implants. However, the production and disposal of these devices will continue to lead to the release of PFASs into the environment unless steps are taken to eliminate environmental releases. The use of PFASs in medical devices falls under Categories 1–3 in Table 1 (depending on specific use). However, due to limited information in the public domain, it is currently unclear if all medical devices need fluoropolymers or only certain types of medical devices need fluoropolymers

Pharmaceuticals: There are a wide range of fluorine-containing pharmaceuticals[66]. Since the first fluorine-containing drug was approved by the U.S. Food and Drug Administration (FDA) in 1955, nearly 150 fluorinated drugs have reached the market and about 30% of newly approved drugs contain fluorine constituents including fluoroalkyl groups (a smaller subset can be defined as PFASs). According to Zhou et al. (2016)[66], fluorinated drugs encompass all therapeutic areas, are structurally diverse, and are among the most-prescribed and/or profitable in the U.S. pharmaceutical market.

Fluorination of pharmacological agents is often used to enhance their pharmacological effectiveness, increase their biological half-life, and improve their bioabsorption[66]. Some agents are analogous to the long-chain PFASs, such as several types of artificial blood formulations and drugs for the lungs of prematurely born children (for example: perfluorooctyl bromide, an eight-carbon bromine-substituted PFAS[67]). However, most fluorine-containing pharmaceuticals have only one or two fluorine atoms. A smaller number of drugs contain one or two trifluoromethyl groups (-CF_3), or the perfluoroalkyl moiety C_nF_{2n+1} as defined by Buck et al. (2011)[2]. As these agents become more widely produced, prescribed, and used, disposal of these fluorinated drugs (e.g. through municipal wastewaters) is likely to lead to increasing environmental releases of various PFAS. A transformation product of nearly all of the anesthetics is trifluoroacetic acid (TFA or CF_3COOH), which can arise from several metabolic or atmospheric degradation pathways[68] and has been a cause of environmental concern.[69–71]

In summary, the addition of 1-3 fluorine atoms or trifluoromethyl groups to various pharmaceutical agents has improved their efficacy, half-lives, and bioabsorption and does not appear to pose substantial health risks to those who take them, relative to analogous non-fluorinated drugs. However, their production and disposal will continue to lead to the release of PFASs into the environment unless steps are taken to eliminate environmental releases. Releases of human metabolic excretion products may pose an additional environmental concern (contamination of water and greenhouse gases) as these drugs become more widely used. The uses of –CR_2F, -CRF_2, and -CF_3 groups in pharmaceuticals should not be evaluated for essentiality as a single group, as specific applications will likely fall under either Categories 2 or 3 in Table 1; there are functional non-PFAS alternatives for some pharmaceutical applications, whereas for other uses the pharmaceuticals have essential life-saving functions.

Laboratory supplies, equipment and instrumentation: PFAS-containing products, in particular fluoropolymers, are also ubiquitous in laboratories, laboratory supplies and analytical instrumentation. Initially this caused major concerns regarding PFAS contamination of environmental and biological samples during PFAS analysis and maintaining quality control in PFAS analysis[72,73]. The PFASs are used because they have high resistance to chemicals and heat, low surface energy and permeability, which prevents chemicals/analytes from being adsorbed to the surface and absorbed into the material.

In the laboratory, there are easily identifiable fluoropolymer (e.g. PTFE) and fluoroelastomer-based products (e.g. Viton). Examples include the use of fluoropolymer-based vials, caps and tape, and fluoropolymers in the solvent degassers of liquid chromatography (LC) instruments. Non-PFAS replacements may be available, depending on the purpose. Personal protective equipment can also contain PFASs, including protective gloves and protective mist/anti-fog coatings of glass (e.g. PFPE). These applications can in general be substituted without major loss of functionality; recommendations for PFAS-free alternatives are often provided as part of guidance to prevent cross-contamination when sampling or analyzing environmental matrices for PFAS.[74–76]

As part of field or laboratory collection of particles of different sizes, some filters are made of or are coated with PFASs to minimize sorption of compounds to the filter itself, such as glass fiber filters, or ultrafiltration filters. As an alternative plastic filters/vials with a low solid surface energy can be used (e.g. polypropylene (PP), polytetramethylene oxide (PTME) and polyamide (nylon))[46,77].

More difficult to identify are fluoropolymer and fluoroelastomer seals (o-rings), and fluoropolymer-based tape within internal components of existing instrumentation. As a result of advances in analytical instrumentation, in particular ultra high-pressure liquid chromatography (UHPLC), the use of fluoroelastomers is widespread as seals and membranes and PTFE as inert surfaces inside analytical instruments and in some cases as tubings. The tubing can be replaced by polyetheretherketone (PEEK) or stainless steel tubing without a loss of performance in most applications. Some applications rely on fluorinated solvents (e.g., trifluoroethanol) and acids (trifluoroacetic acid, pentafluorobutanoic acids etc.) added to reversed phase LC-MS solvents, and specialty LC-columns are based on fluorinated materials. Non-fluorinated alternatives exist for both these uses.

Perfluorpolyether-based lubricants are also used as oils and greases in pumps and equipment; this can cause laboratory background contamination. Oil-free pumps exist and are reducing the laboratory background contamination, which is beneficial for both the analyses and workers' health. To address concerns related to instrument contamination by PFASs, manufacturers offer a delay column to keep the instrument-borne PFASs from eluting with target analytes during the same time window.

For the vast majority of laboratory applications, PFAS alternatives have been used historically or have been newly developed. Therefore, most applications fall within Categories 1-2 in Table

1, i.e., they are non-essential and replaceable. A small number of current laboratory applications may fall within Category 3 as being essential and without appropriate alternatives, and thus further innovation for effective substitution is required.

Perfluorosulfonic membranes: These are fluoroelastomers that exist in many forms and are used in a wide range of chemical synthesis and separation operations and in analytical instrumentation. These membranes are often used in processes that displace less efficient historical methods that use more energy and/or generate hazardous materials and byproducts[78,79]. Nafion® (CAS Number 66796-30-3) is the brand name for a perfluorosulfonic acid membrane from Chemours (formerly DuPont) that consists of a perfluorosulfonic acid copolymer with pendant sulfonic acid groups. It is stable in strongly oxidizing conditions and high temperatures. The density of sulfonic acid groups can be controlled during synthesis to select for variable ion exchange capacity, electrical conductivity, and various mechanical properties.

One of the earliest principal uses of Nafion was as a membrane in the chlor-alkali process, which is the large-scale industrial process that uses brine and electricity to produce the common chemical feedstocks, chlorine gas and sodium hydroxide[80]. Historically these high-volume chemical commodities were prepared with brine in either asbestos diaphragm cells or mercury electrode cells. Both methods generate substantial quantities of hazardous wastes through either the mining and the fabrication of suitable asbestos membranes or the release of aqueous and volatile mercury wastes. Use of Nafion copolymer as a membrane in the electrochemical cell allows for excellent conductance of ions necessary for the process, while maintaining separation of the two parts of the cell under highly caustic conditions.

Perfluorosulfonic acid membranes are also used in high-efficiency fuel cells where, in one example, hydrogen and oxygen are pumped into different chambers within a cell that are separated by the membrane, giving rise to a continuous supply of electricity for various specialty applications. Perfluorosulfonic acid membranes are also used as an acid catalyst in a wide range of chemical conversions leading to decreased energy inputs and higher purity products.

While it can be argued that perfluorosulfonic acid membranes have made many chemical preparation processes more efficient and cleaner, it is also important to acknowledge that the impacts from their production and use are still poorly understood. Research at one fluorochemical production site in Bladen County, North Carolina has documented that Nafion-related wastes have been released into the nearby Cape Fear River since at least 2012.[81] Moreover, the relatively advanced drinking water treatment plant in the city of Wilmington, North Carolina, has been unable to remove these Nafion-related wastes[82,83] giving rise to a situation where approximately 99% of the residents of Wilmington now have measurable concentrations of Nafion Byproduct 2 in their blood[84]. No human health data are currently available for Nafion Byproduct 2, and the human half-life of this material is likely to be on the order of months to years[83]. The production of perfluorosulfonic acid membranes has provided great utility by improving the efficiency of large-scale chemical syntheses while also reducing the emissions of other known hazardous byproducts (asbestos and mercury), but the current production process leads to the release of at least one persistent byproduct with near universal exposure in a downstream community.

The use of perfluorosulfonic acid membranes is currently judged to be Category 3 (essential) in the chlor-alkali process. Before the use of Nafion, there were concerns for worker safety and the environment associated with mercury and asbestos. The use of Nafion as an alternative was the direct result of the chlor-alkali industry addressing these concerns. In the case of the use as a proton exchange membrane (PEM) in fuel cells, there are alternatives to perfluorosulfonic acid membranes[85], but these are under development and not used as commonly as Nafion (Category 2). Although there is a lack of functional alternatives for certain applications, it is reasonable to insist that emissions of persistent and potentially toxic wastes from the production and use of perfluorosulfonic acid membranes be quantitatively determined and minimized as much as possible.

Discussion

The Montreal Protocol has provided a successful blueprint to assess the essentiality of a class of widely used persistent chemicals found to have significant human and environmental health risks. Because of their extreme environmental persistence, and increasing data on their adverse effects including human health-related endpoints, PFASs are a prime opportunity for applying a similar approach to protect human health and the environment through the removal of these chemicals from non-essential uses. Our review of several key uses of PFASs demonstrates that currently a global phase-out of PFASs will be complicated, but it also indicates a number of starting points. In particular, different phase-out strategies will be required for each essentiality category. The essentiality of PFASs in the different use categories, based on our three categories in Table 1, is summarized in Table 2. Within a few of the larger use categories (e.g. textiles) certain uses of PFASs appear to be easier to phase out (e.g. leisure rain jackets) than others (occupational protective clothing) due to different technical performance requirements.

Table 2: Essentiality of PFASs in selected use categories.

Use	Table 1 Category*
Personal care products including cosmetics	1
Ski waxes	1
Fire-fighting foams (commercial airports)	2
Fire-fighting foams (military)	2 or 3
Apparel (medical: long operations)	3
Apparel (protective clothing oil and gas industry)	3
Apparel (medical: short operations, everyday)	2
Apparel (military: occupational protection)	2 or 3
Waterproof jacket (general use)	2
Easy care clothing	1
Food contact materials	1, 2 or 3
Non-stick kitchenware (fluoropolymers)	1 or 2
Medical devices (fluoropolymers)	1, 2 or 3
Pharmaceuticals	2 or 3
Laboratory supplies, equipment and instrumentation	1, 2 or 3
Perfluorosulfonic membranes in fuel cells	2
Perfluorosulfonic membranes in chlor-alkali process	3

*Note that the categories in the above table represent the current evaluation and may change in the future.

Alternatives assessment. Even if PFASs are assessed, according to the criteria in Table 1, to be non-essential in a particular use, and functional alternatives are available, this is only a first step to phase out and responsibly substitute PFASs. It cannot be generally assumed that non-fluorinated alternatives will be less harmful to human health and the environment than the PFASs they are replacing. The scientific discipline of alternatives assessment has established processes and best practices for identifying, evaluating, comparing, and selecting safer alternatives to chemicals of concern based on hazards, performance, and economic viability[86–88]. This process can be applied to PFASs used in material components, finished goods, manufacturing processes, or technologies. Not all substitutions require direct replacements of a fluorinated compound with a non-fluorinated alternative (i.e. chemical alternative); a technological or engineering innovation (i.e. functional alternative) can be equally successful[4] and should always be encouraged/prioritized over chemical alternatives. Multiple alternatives should be assessed for a given PFAS until an acceptable substitution is found. Often, once an alternative is found for one use case, it may be easily adapted for other use cases of that chemical as well. In the assessment, once possible non-hazardous alternatives are identified, it is also important to consider multiple endpoints [89] such as energy use, material use (incl. food waste, water use, packaging/machinery use and durability), and land-use (e.g. paper vs. plastic vs. glass), to avoid burden-shifting between different environmental and human impacts.

When considering chemical alternatives for PFASs, the focus should be on the service the product should deliver. The compound should therefore be evaluated for performance using the specifications required for the product, as opposed to comparing directly to the PFAS being replaced. Additionally, the potential for health hazard and potential for exposure – combined, these elements establish the health risks associated with the alternative – must be considered for the general public and vulnerable populations. Finally, additional considerations such as product longevity, persistence in the environment, and sustainability may be considered. Currently there are several established frameworks and evaluation metrics available for conducting alternative assessments[86,90]. In the absence of a thorough evaluation, regrettable substitutions can occur.

Challenges and opportunities in chemical regulation. The Madrid Statement[12] recommends limiting the use of PFASs in society. Although all PFASs are highly persistent (or lead to highly persistent transformation products), many of them do not comply with the usual concerns considered in international chemical regulation. It can be argued that their extremely high persistence alone should be cause for regulation and substitution[13,14], but the practical regulatory tools to implement this approach are currently lacking.

Within the context of the EU REACH Regulation, it has been argued[91] that the most effective way of regulating short-chain PFASs (as with the regulation of long-chain PFASs) is to identify them as Substances of Very High Concern under REACH Article 57, followed by a REACH Annex XVII restriction. Indeed, the EU has considered (e.g. in the case of the restriction of PFOA and its related chemicals), and is continuously considering ways to group PFASs in recognition of the impossibility of regulating more than 4700 PFASs individually.

Another relevant regulatory framework is the UN Stockholm Convention on Persistent Organic Pollutants. , which are similar to the essential-use exemptions under the Montreal Protocol. Under the Convention, the Conference of the Parties (COP) considers listing new persistent organic pollutants for elimination (Annex A), or restriction (Annex B), and/or involuntary production (Annex C) based on a recommendation from the Convention's Persistent Organic Pollutants Review Committee (POPRC). The Convention requires that the Conference, "taking due account of the recommendations of the Committee, including any scientific uncertainty, shall decide, in a *precautionary* manner, whether to list the chemical, and specify its related control measures, in Annexes A, B and/or C" (Art. 8, Para. 9). As part of its deliberation of whether to list a chemical, the COP also considers whether to allow for any "specific exemptions" and/or "acceptable purposes""Specific exemptions" is time-limited with one period of five years with the possibility of one extension for another five years, whereas the time period for the applicability "acceptable purposes" is more open-ended.

Currently, there is no clear defined criteria for identifying "specific exemptions" and "acceptable purposes" set in the text of the Stockholm Convention. Such "essential use-like" exemptions are primarily identified through the work of POPRC on a case-by-case basis. However, the COP has subsequently adopted detailed criteria for consideration of requests to extend specific exemptions. For production exemptions, the requesting party must have submitted a justification for the continuing need for the exemption that establishes that the extension is necessary for health or safety, or is critical for the functioning of society; included a strategy in its national implementation plan aimed at phasing out the production for which the extension is requested as soon as is feasible; taken all feasible measures to minimize the production of the chemical and to prevent illegal production, human exposure and release into the environment; and the chemical must be unavailable in sufficient quantity and quality from existing stockpiles. Finally, in the case of a party with an economy in transition, the party must have requested technical or financial assistance pursuant to the Convention, in order to phase out as soon as feasible the production for which the extension is requested (see COP Decision SC-2/3, "Review process for entries in the Register of Specific Exemptions"[92]).

We are convinced that having clear legal guidelines for what constitutes an essential use (a process started in this present work) will benefit the Stockholm Convention and other regulatory frameworks by supporting clear guidelines for determining how to apply the essential use-like exemptions, i.e., by balancing costs versus the societal benefits of the use of a substance or product. A clear definition of essential use ensures that only those applications that are necessary for health or safety (or other purposes highly important to society as a whole) and for which non-fluorinated alternatives are not yet available could receive exemptions when chemicals are listed under the Convention. Further, this approach would protect those uses that are legitimately deemed essential until appropriate substitutions can be identified.

The way forward. Innovation in the development of alternatives to PFASs is ongoing and many functional alternatives have been developed and put into practice for some use categories. However, in other use categories little innovation is under way, due to lack of financial or regulatory drivers to change methods/production, significant technical challenges, lack of awareness of the market opportunities, or the small size of the market. Innovation is being encouraged in countries like Denmark (e.g. substitution of PFASs in textiles) and in Sweden through the availability of government funding for industry-academic partnerships (e.g. the POPFREE project[93] to encourage small companies to develop non-fluorinated alternatives to PFASs). Furthermore, one of the four key areas in ECHA's 2018 strategy on substitution[94] is to 'Develop coordination and collaboration networks' between all stakeholders, ranging from institutions, member states, industry, academia and civil society.

In some cases, the PFASs in a product or use will be determined as the only compound capable of delivering the required level of performance for that application. In these cases, it is recognized that immediate phase out will not be feasible. But this assessment is only based on current technologies. With clear legislative incentives, new technologies will typically be developed, and consequently PFASs in Category 3 should continue to be reviewed for potential removal or replacement by new entrants to the market. In fact, use cases identified as Category 3 should be the targets of industry and academic programs to develop innovations that may succeed in removing or replacing the PFAS with more sustainable functional alternatives. This system creates a market pressure to be the first to develop new technologies.

Chemical regulation on the other hand progresses slowly compared to product innovation, and assessment of individual PFASs is not feasible for protecting public health. It is simply unlikely that society and industry will spend the money and time to generate adequate data to risk assess >4700 PFAS. Therefore, we strongly recommend a grouping approach be employed, and for PFASs to be regulated as a group. Since regulation of the many thousands of PFASs by authorities is likely to be time consuming, it is important for industry (in particular product designers and manufacturers) to take voluntary measures that will contribute substantially in reducing the emissions of PFASs and their presence in products. There have already been several examples of retailers who through private procurement have phased out PFASs from their supply chains (e.g. IKEA, Lindex, and H&M in Sweden[15,17,95], COOP in Denmark[61], Vaude in Germany[96], L'Oreal in France[97]), which in turn puts pressure on chemical manufacturers to find safer alternatives.

We are convinced that our criteria on essential use can inform and encourage other retailers to consider phasing out and substituting PFASs in their products. These types of voluntary measures will in turn help regulators by demonstrating that functional alternatives exist. When policy makers face stakeholder groups from both sides, they can use data-driven essentiality assessments to support their decision making, e.g., to show why certain uses are not necessary and therefore can be restricted. This will speed up regulatory actions in support of phasing out non-essential uses of PFASs, without risk to health or safety applications.

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