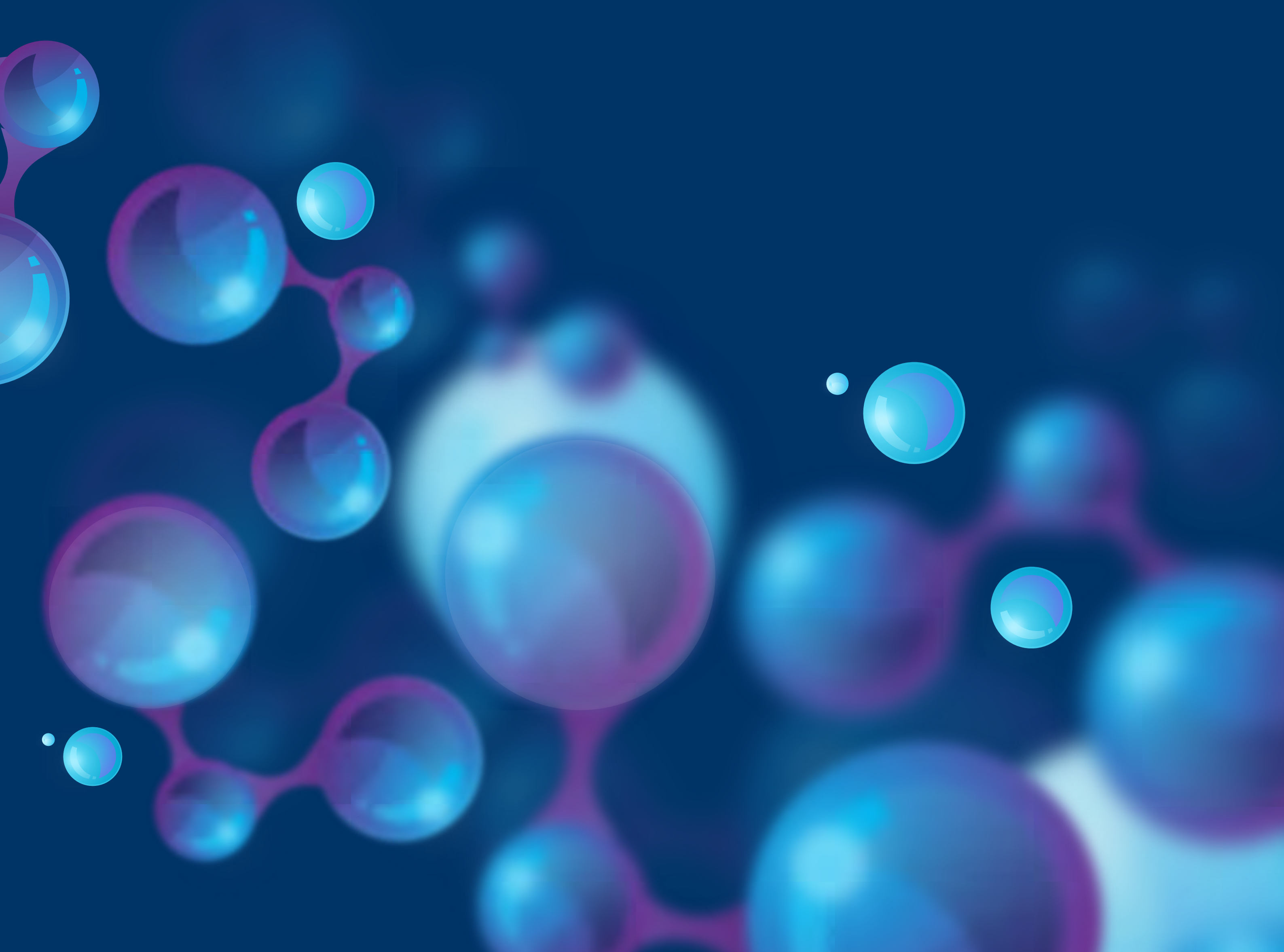
PRESCOUTER

The importance of a data-driven dissection of fluoropolymers based on safety and functionality

A PLEDGE FOR PTFE IN LIFE-SAVING MEDICAL AND DIAGNOSTIC APPLICATIONS



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With increasingly stringent regulatory policies surrounding materials in general, investigations about fluoropolymers and their safety have risen as well. Looking at why these compounds are deemed more of a necessity than hazardous will help to understand why the future of fluoropolymers should exist beyond these investigations.

Fluoropolymers are not all the same

Fluoropolymers comprise a subset of over 9,000 chemicals (EPA, 2021)[1] known as per- and polyfluoroalkyl substances (PFAS). It is a chemical group that contains carbon and fluorine, whose widely varying chemical and physical properties are highly important from an industrial and commercial perspective, such as hydrophobicity, a larger contact angle with liquids, as well as heat and chemical resistance (OECD, 2018)[2]. Some PFAS substances have been a general concern regarding their potential persistence in the environment and bioaccumulation, for this reason, they are known as “forever chemicals” (Wang et al., 2017)[3]. Currently, low molecular weight PFAS compounds have been found in water, air, fish, and soil at locations across the globe and have been linked to health problems such as low birth weight or kidney problems (ATSDR, 2021)[4].

While PFAS are typically referred to as a group, some individual members of this group of molecules are much more harmful than others. Perfluoroalkyl acids (PFAAs) and their precursors have increased mobility and toxicity, characteristics directly correlated to their reduced molecular weight (MW) and stability. As a result, perfluoroalkyl carboxylic acids (PFCAs), such as perfluorooctanoic acid (PFOA) and perfluorononanoic acid (PFNA), and fluorotelomer-based compounds, such as fluorotelomer alcohol (FTOH) and polyfluoroalkyl phosphate (e.g., diPAP), face some level of regulatory restriction according to the Organization for Economic Co-operation and Development (OECD) (Figure 1 highlights such substances in red).

However, not all members of the PFAS family are harmful. In particular, fluoropolymers’ electronic structure, arising from their stable carbon-fluorine covalent bonding, reflects the unique interactions responsible for their distinct composition and set of properties that make them irreplaceable for industrial applications (Teng, 2012)[5] and safe for humans and the environment (Henry et al., 2018)[6].

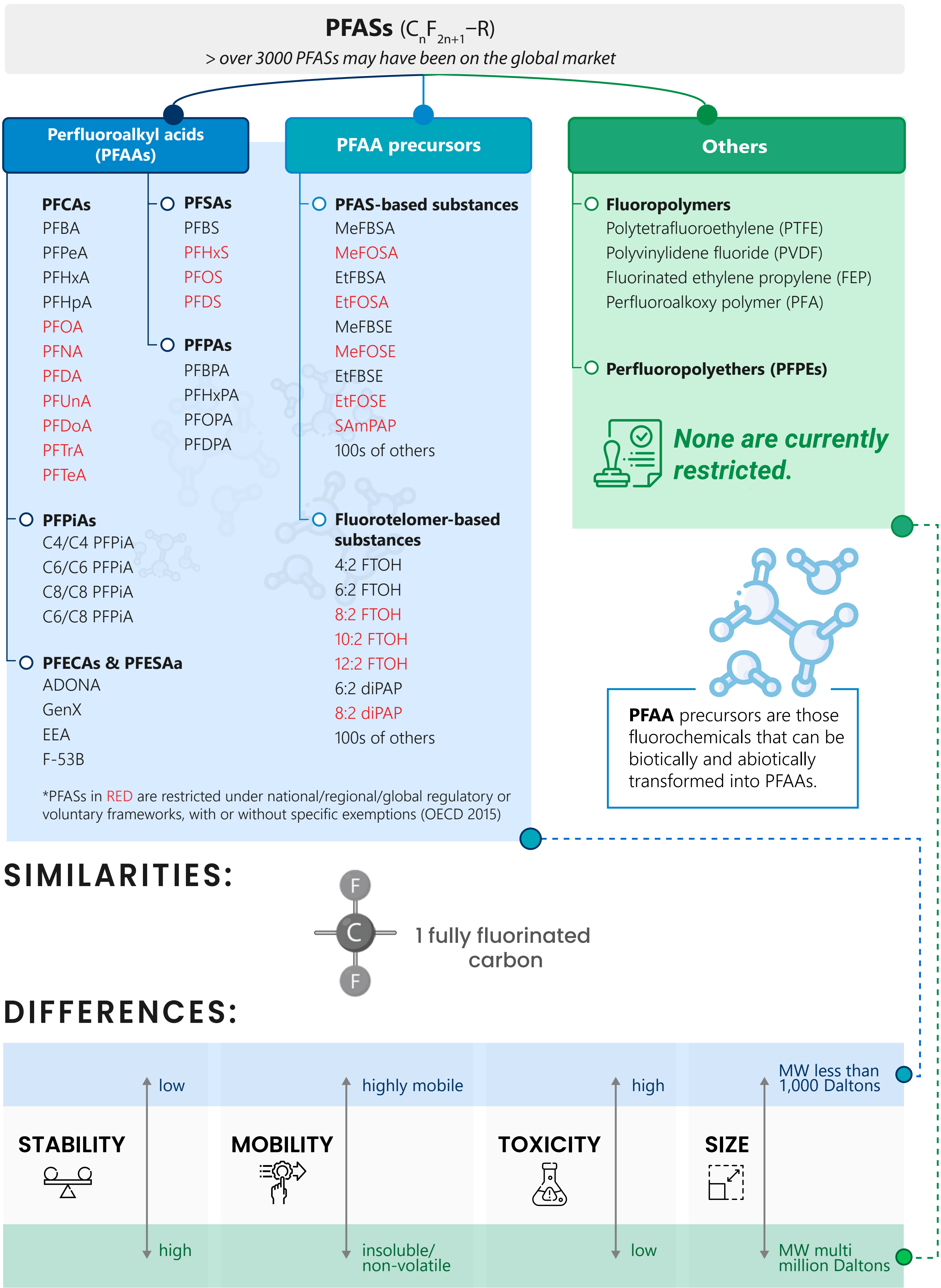


Figure 1. The overall structure of PFAS and fluoropolymers, particularly highlighting their large and heterologous composition, as well as key features differentiating safe (e.g., PTFE) from hazardous compounds (e.g., PFOA).

PFAS regulatory state of play and current bottlenecks

Over the last 10-15 years, there has been a rising concern about the impact of PFAS on human health and the environment, which triggered regulatory agencies across the world to study measures to ban these compounds from industries in general. However, several theoretical and practical bottlenecks prevent such regulation from being established under a well-balanced socio-economic implementation (Table 1).

Table 1. Key bottlenecks on PFAS regulatory banning for policymakers.

1	No harmonized classification system to group chemicals according to specific safety features
2	No established correlation between individual chemicals and hazard levels
3	No clear exposure limits or hazard effects are measured across different industrial applications (e.g., food and beverage versus healthcare applications)
4	Lack of diagnostic methods for low-level detection of chemicals (e.g., ppm or ppb)
5	Lack of specific rules differentiating essential from non-essential uses (e.g., packaging versus diagnostics)

Currently, no global system for PFAS classification exists, which directly interferes with an acknowledgment of which classes of PFAS require management action. Unfortunately, a compound-by-compound assessment of harmfulness is immensely challenging and would require years of toxicological studies. Therefore, most regulatory bodies refer to PFAS as a single entity and are steering toward a blanket ban on these substances. Blanket banning would not only limit the use of hazardous chemicals, but also impact the use of safe fluoropolymers in essential, and sometimes life-saving applications.

Besides the lack of compound-specific analysis and data, there is a poor understanding of the correlation between individual PFAS compounds and their hazard level or toxicity. Given that there is no current regulation or definition for acceptable levels of leaching fluoropolymers in place, nor any certified analytical method to measure these levels at scale, it will be nearly impossible for regulatory agencies to dissect the safety profiles of PFAS compounds in the next few years.

The EU regulations

In the European Union (EU), the first time PFAS were formally targeted for regulatory action was in June 2019 when the European Commission (EC)[7] developed an action plan to eliminate all non-essential uses of PFAS by releasing a series of measures in its 2020 Chemical Strategy for Sustainability Towards a Toxic-Free Environment. According to the Montreal Protocol (IV/25)[8], an essential use is defined as necessary for health, safety, or critical functions in society, where no other technical or economically feasible alternatives are available.

The US regulations

In the US, discussion about PFAS restrictions has been going on for the last 15 years. Until now, the only instance in the US where the phase-out of a particular PFAS impacted fluoropolymer production was the Environmental Protection Agency (EPA) PFOA Stewardship Program[9] (2010/2015). The industry, led by the private sector, voluntarily committed to this program, which converged into the elimination of perfluorooctanoic acids (PFOA) in manufacturing. The latest US regulation about PFAS has been so far focused on water quality, sustainable products, food, industrial emissions, and waste, targeting specific families of PFAS rather than all compounds.

Challenges with establishing limits and standards

The Third Meeting of the OECD Experts on Polymers (held in April 1993)[10] indicated that fluoropolymers have well-established safety profiles and are not hazardous as other PFAS substances. Over the coming years, the EPA plans to create a list of categories based on structural, physicochemical, and toxicity data. Contrary to many PFAS compounds, fluoropolymers are large, stable, inert polymeric molecules. Not all fluoropolymers are created the same and polymeric, high MW fluoropolymers are too large to cross biological membranes and therefore pose little potential for human or environmental exposure. More importantly, these compounds are neither part of the PFOA or perfluorooctane sulfonic acid (PFOS) family, nor can they transform into those substances in the environment.

Another key bottleneck that is currently being investigated by both the European Chemicals Agency (ECHA) and the EPA is how to accurately establish standard limits of detection for multiple PFAS chemistries. A clearer understanding of PFAS in the environment and an assessment of their properties would be able to determine which classes of PFAS require management action. The International Electrotechnical Commission, which has been debating the ban of fluoropolymers from electronics[11] since 2017, also makes this key identification.

> "Based on current investigations and the expected scrutiny when implementing standard detection limits across different compounds and end-applications, it could take up to a decade before regulations are implemented throughout the whole European continent."
>
> *Polymer expert from a global materials engineering company.*

The case for PTFE

One example of a PFAS chemical of low concern that would suffer greatly from a blanket ban is Polytetrafluoroethylene (PTFE). Although best known for its chemical & thermal inertness, PTFE is a highly versatile material with a wide range of applications and is both processed as a coating or a venting membrane.

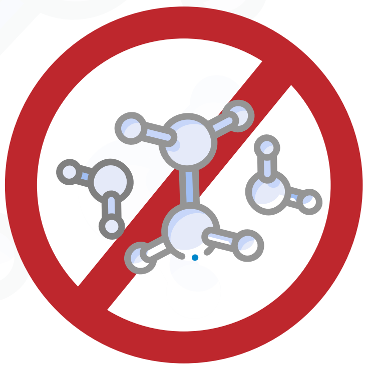
An instance of the detection limit difficulties that regulatory agencies would face is PTFE's fine powder which is labeled as a "very low" concern polymer (extremely low solubility 1x10-5 mg/L of water)[12,6], and is very different from highly soluble and mobile compounds (e.g., 10-10000 mg/L posing potential health issues according to OECD, 2009)[13]. Such detection definitions also lack a standardized methodology to view the level of leachables in individual fluoropolymer substances, as even the production and treatment processes directly interfere with the data.

Previous exceptions paving the way

A blanket ban on fluoropolymers of low concern poses a major issue for both the private sector and government agencies, as its impact would force their manufacturers to look for materials that do not exist to date, and in the case of PTFE, may never exist. To circumvent the ban on essential chemicals, previous blanket bans have been supplemented with exception regulatory modules that allow certain chemistries to be used for specific industrial applications.

For example, in 2014, ECHA[14] made it possible for the aviation sector to use substances of very high concern (e.g, potassium dichromate)[15] through an authorization process. This decision was made due to the supply chain complexity and lack of alternative chemicals, a similar case to what is currently being debated for PTFE.

> "Exceptions have been made within previous banning regulations given the regulatory context in which critical applications operate and where no suitable alternatives are available is particularly apparent, such as medical and diagnostic applications."
>
> *Chemical regulatory manager from a global chemical company*



PTFE in life-saving diagnostics

Adding to their safe and inert profile, some fluoropolymers (such as PVDF and PTFE) are used for a variety of critical purposes in chemical industries, power generation, electronics, wire insulation, coatings, and textiles due to their special properties. These properties were reviewed in a recent study by Henry et al., (2018)[6] and include resistance to abrasion, heat, chemical degradation, and low friction characteristics (Figure 2).

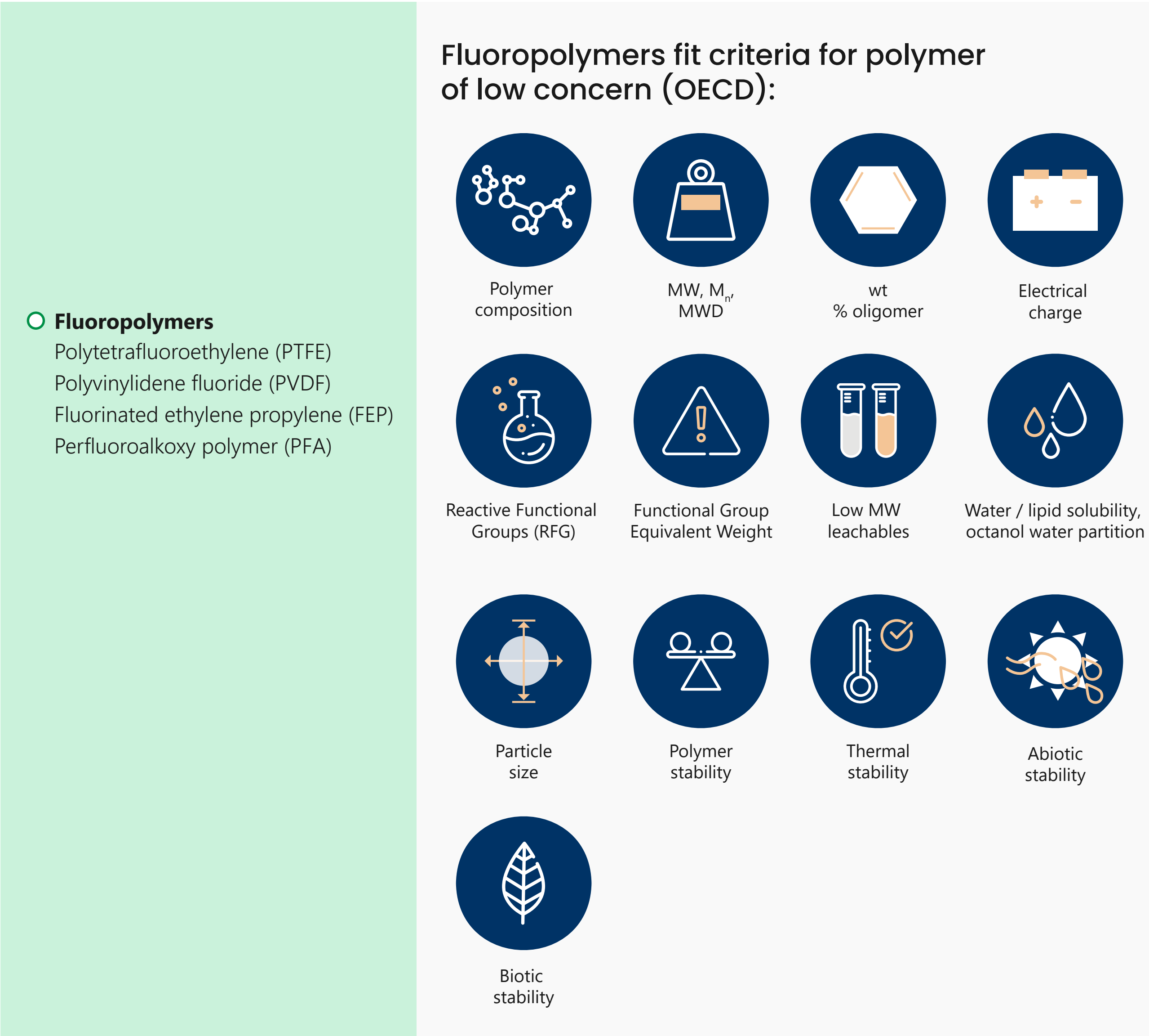


Figure 2. Fluoropolymers criteria for a polymer of low concern (PLC). PTFE, in particular, fits all features essential for its characterization as a PLC, with particularly critical applications throughout medical (e.g., surgical guidewires and implantable devices) and diagnostic devices (e.g., Point of Care or microfluidics).

PTFE makes up more than half of the fluoropolymer market and is used as a cost-effective solution for industries ranging from life sciences, oil and gas, chemical processing, industrial, electrical/electronic, and construction sectors, among others. While PTFE is not considered essential in all these applications, it is known to be included as an essential component in critical medical and diagnostic devices such as Point of Care (PoC), microfluidic, or lab-on-chip devices for the detection of SARS-CoV-2 or monitoring blood glucose levels in diabetic patients (Roina et al., 2021)[16]. In these devices, PTFE is used to allow for an inert fluid flow, mitigate bacterial/viral contaminants, and remove bubbles to ensure proper device functioning.

In addition to diagnostics, PTFE is commonly used as a coating for surgical instruments like guidewires, as well as a membrane material used in implantable devices. In 2021, for example, the US Food & Drug Administration (FDA) provided complete research on PTFE-made implantable devices[17], considering PTFE-based catheters, vascular and endovascular grafts, stents, and prosthetic materials as safe for use. In particular, the report states that PTFE implantables "provide better patency rates than percutaneous transluminal angioplasty" as reported in nearly all human studies conducted on this subject, thus reinforcing the non-hazardous characteristic of PTFE based on its application even within the human body.

> "Molecular PoC diagnostics use harsh reagents (e.g., acidic nitrile, ethanol and other alcohols, acetone) that require membranes with high stability. PTFE membranes offer unique and excellent stability. PTFE is a key part of these diagnostic systems."
>
> *Senior R&D engineer at a US-based microfluidics company*

PTFE's outstanding stability and safeness

Besides its outstanding resistances, the uniqueness of PTFE relies on its non-toxic and safe use, as to break down into a different substance, the compound would have to be exposed to temperatures above 440 ˚C (824 ˚F). Moreover, PTFE can be safely used under a continuous temperature at or below 260 ˚C (500 ˚F), as stated by Teng (2012)[5].

> "PTFE is an appealing material for the development of medical and diagnostic devices because it is hydrophobic, inert, and stable to different chemicals and temperatures."
>
> *Research engineer at a Maryland-HQ molecular diagnostics developer*

In addition, PTFE is practically insoluble in water and is non-bioavailable, as evidenced by a wide range of toxicology studies including acute and subchronic toxicity, irritation, sensitization, cytotoxicity, genotoxicity, hemolysis, and thrombogenicity (Henry et al., 2018)[6]. Table 2 depicts a more in-depth description of PTFE's features compared with hazardous PFAS compounds. Taking PTFE's distinguished characteristics and safety profile into account, there is no current one-to-one substitute for this chemical that could be implemented for critical applications such as medical and diagnostic devices.

Table 2. A comparison between PTFE and PFOA (an example of perfluoroalkyl acid) structural, chemical, and stability features.

Feature	PTFE (Fluorpolymer)	PFOA (Perfluoroalkyl acid)
Particle Size	100-500 μm [6]	≤0.14 μm [18]
Molecular Weight	MW > 1,000 Daltons [6]	MW < 1,000 Daltons, potentially penetrating cell membranes [6]
Ionic Characteristic	Neutral [6]	Anionic pollutants, associated with human and environmental toxicity [19]
Solubility	Practically insoluble in water and organic solvents (1x10-5 mg/L) [6]	9,500 mg/L (water solubility) [20]
Thermal Stability (i.e., melting point)	Maximum 440 °C (824 °F), continuous temperature ≤260 °C (500 °F) [5]	50-60 °C (122-140 °F) [20]
Chemical Stability	Stable to hydrolysis, light, oxidation, and biodegradation [6]	Persistent, bioaccumulative, and toxic substance [21]

[6]Henry et al., 2018; [5]Teng, 2012; [18]Dreyet et al., 2014; [19]Xiao et al., 2018; [20]USEPA 2016; [21]ECHA, 2015

The safeness and irreplaceable use of PTFE are strongly corroborated by science and the industry, with both the FDA and the European Food Safety Authority reinforcing the safety and reliability of this compound throughout their manufacturing life cycle (PlasticsEurope, 2021)[22]. It is undeniable that using this compound is more beneficial than harmful to human health and the environment, providing that the material is manufactured and used according to the industrial guidance established by regulatory bodies (Teng, 2012)[5].

> "The data presented demonstrate that the fluoropolymer class of PFAS is well defined, meets PLC criteria, and should be considered as distinctly different from other classes of PFAS. The grouping of all PFAS together is not supported by scientific data."
>
> **Henry et al. 2018**

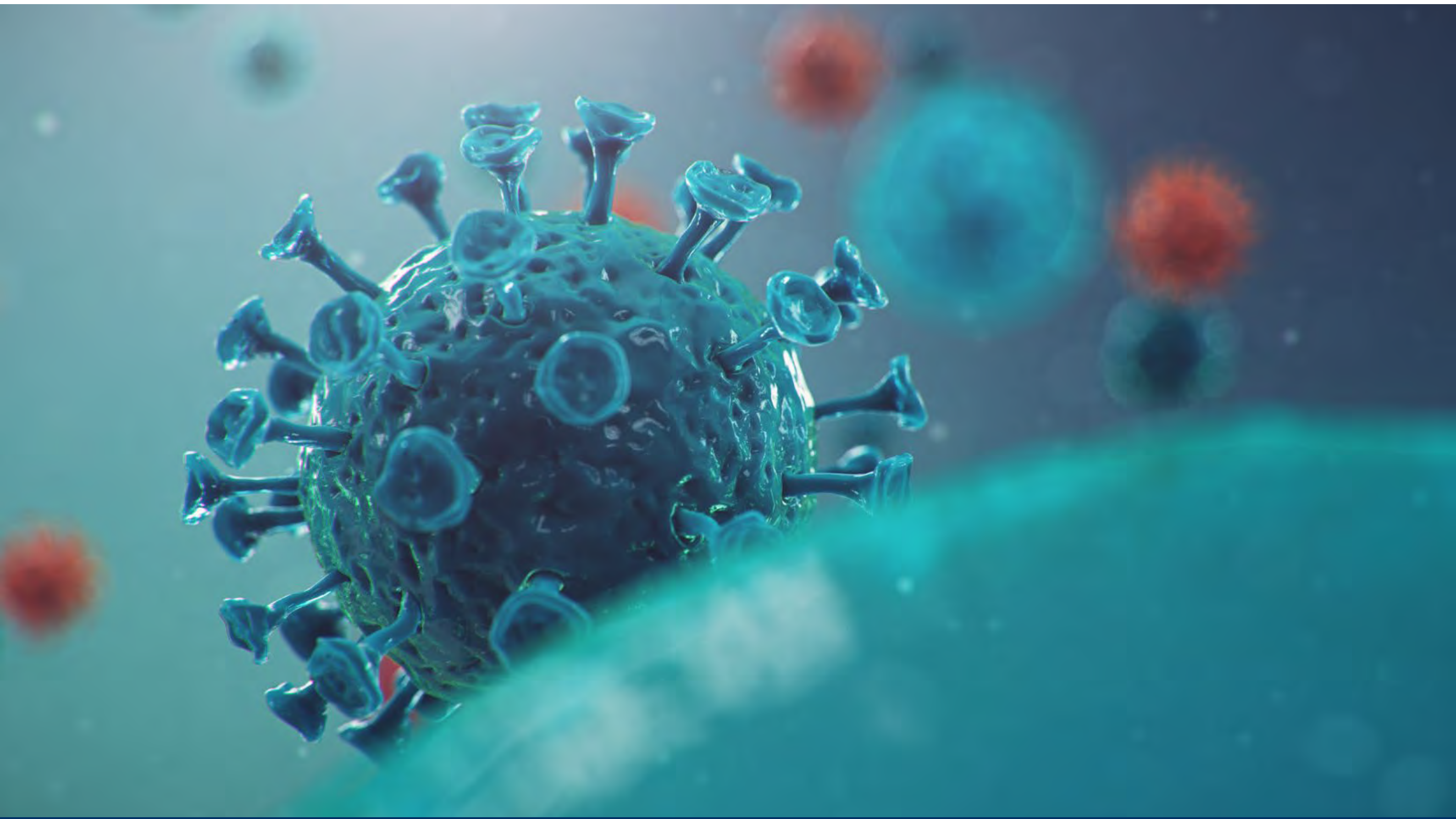
The critical use of PTFE during the SARS-CoV-2 pandemic

Such importance is even more immeasurable when it comes to the use of PTFE membranes during critical times such as the recent SARS-CoV-2 pandemic for diagnostic test devices. These membranes act as a physical barrier and are used to seal diagnostic devices from outside contaminants, ensuring the sensitivity of tests. Particularly impacted by the increased demand for molecular diagnostics during the SARS-CoV-2 pandemic, the use of PTFE membranes has almost doubled over the last 3 years. Moreover, PTFE is also used in other healthcare products, such as facemasks, surgical gowns, and personal protective equipment, where it helps in filtering viruses and other microorganisms from the environment.

"The use of PTFE membranes has increased between 50-100% over the last 3 years, particularly impacted by SARS-CoV-2 and the consequent increased demand for molecular diagnostic devices."

R&D engineering manager at a California-HQ molecular diagnostics developer

PTFE alone has made billions of lives safer, having more expressive numbers in the medical and diagnostic sectors, as well as ten other fields of application.



Towards a sustainable use of PTFE within essential applications: Current trends and future directions

While scientific research findings suggest that some fluoropolymers pose a threat to human health, other compounds of the family of molecules are supporting human health as part of essential medical devices or diagnostic workflows. PTFE is a proven reliable compound that is present in a myriad of products in modern times. More importantly, the medical sector has an undeniable advantage in using PTFE membranes, from personal protective equipment to the diagnosis of potentially lethal diseases such as SARS-CoV-2. Without a proper and efficient-like technology or chemistry to replace PTFE, banning it from manufacturing and industrial production can have serious negative repercussions for the medical industry and billions of human lives.

It is clear why government agencies and regulators should be investing in researching and acknowledging the differences between hazardous and non-hazardous PFAS chemicals. Leaders in supply chain and manufacturing are working to learn more and call for scientific data to support identifying the level of incidence that is considered hazardous so we might all walk in the same direction for the benefit of human health and safety; whether by regulating bans, continuing to supply life-saving devices, or diagnosing quickly. Great devices and products already in use are helping in critical medical procedures, as well as preventing diseases and saving patients' lives daily.

PTFE's capabilities as a remarkable human ally are more evident nowadays, after the most frightening challenge of the last century, the SARS-CoV-2 pandemic. Assessing fluoropolymers individually is the key point to alienating from unnecessary supply chain and product performance disruptions. The market, public, and government must collaborate to correctly address fluoropolymers and continue to reap the benefits of this important and safe chemical.

Moreover, research and monitoring programs are continuously in place not only to build or discover safe alternatives that could fill the remaining gaps left by PFOA and PFASs, but also to seek effective ways to control and remediate damage through cutting-edge technologies. An example of a recently developed remediation technology was that of Rice University. This newly developed approach uses a catalyst, based on a composite of boron nitride and titanium dioxide to destroy 99% of PFOA within only a few hours of ultraviolet light exposure (Duan et al., 2022)[23]. This technology greatly highlights how science can be used to pave the way for the safer and more sustainable application of PFAS compounds.

For device manufacturers, the regulatory teams must review previous bans on essential use chemicals and weigh risks versus benefits related to manufacturing medical devices with safeness and quality for both human health and the environment, considering the costs to develop new compounds while ensuring the quality and properties are comparable to PTFE. Scientific studies have historically been proven to be the best path for safety and overall human benefit. The same will remain for certain fluoropolymers like PTFE.

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