# Position of Hamilton Bonaduz AG, Business Unit Process Analytics on the draft for a restriction of PFASs

**Content**



12. September 2023


Author:
Peter Pianegonda, Senior Quality Manager, Hamilton Bonaduz AG

## 1 Summary

The European Chemical Agency (ECHA) has opened a comprehensive restriction procedure for per- and polyfluorinated alkyl substances, or PFAS. PFAS are extremely stable compounds that do not degrade under natural conditions, accumulate in the environment and can enter the human body. Short-chain PFAS are classified as harmful to health; individual substances have already been banned in the EU under POP or REACH. The special properties have made long-chain PFAS important materials in various industries, the fluoropolymers and the fluoroelastomers. These include, for example, polytetrafluoroethylene, also known as Teflon®. Fluoropolymers are also used in water-repellent textiles, in fire-fighting foams, electronic equipment, in the automotive industry, in medical products - and in plants for the **production of active ingredients, medicines, vaccines or antibiotics, hereinafter referred to as PharmaTech**, e.g. seals for aggressive chemicals as well as sensors, valves, pumps, pipes, tubes etc., for PharmaTech plants, which must be autoclavable (SIP) or cleaned inside the plant with strong alkali lye (CIP). Furthermore, **fluoropolymers are used in equipment for sophisticated chemical analytics**, e.g. to determine the threshold of traces of unwanted substances in a formulation or in complex articles.

According to current knowledge, there are no alternative materials that could combine all the properties of **fluoropolymers or fluoroelastomers**. A ban would therefore have a significant impact on the production of vital medicines, vaccines and antibiotics, even with the largest possible time exemption. In addition, it is important to ensure the availability of fluoropolymers/fluoroelastomers in the required quality. The first manufacturers of fluoropolymers/fluoroelastomers are withdrawing, reducing production capacities or discontinuing them completely. This threatens new dependencies on manufacturers in China, India, etc., which may have lower standards in terms of environmental protection than within the EU.

This position paper of Hamilton Bonaduz AG discusses the chemistry and properties of fluoropolymers/fluoroelastomers, highlights their importance for pharmaceutical technology equipment and chemical analysis, and shows the consequences of a ban on these groups of substances for the supply of medicines, vaccines and antibiotics as well as for sophisticated chemical analytic equipment. The positions of Hamilton Bonaduz AG outline a more differentiated, risk-based approach to PFAS to take into account patient welfare and safety as well as environmental and health protection concerns. **This includes allowing the continued use of low risk PFASs such as fluoropolymers and fluoroelastomers**. This would also be welcome about other key European projects, as PFAS and fluoropolymers also play a decisive role in the manufacture of medical devices, semiconductors, hydrogen and battery, "green deal" technologies, among others.

## 2 Background

PFAS are organic compounds with carbon chains of different lengths in which hydrogen atoms are replaced by fluorine atoms: fully (perfluorinated) or partially (polyfluorinated). According to the OECD definition (OCED, 2021), this includes almost all substances that contain at least one fully fluorinated methyl group (-CF3) or methylene group (-CF2-) without further hydrogen, chlorine, bromine or iodine atoms. This group of substances comprises more than 10,000 compounds. The OECD distinguishes between long-chain and short-chain PFAS. Short-chain PFASs include, for example, perfluorinated carboxylic and sulfonic acids (and corresponding precursor compounds) with fewer than seven and six perfluorinated carbon atoms, respectively (Umelt Bundesamt DE, 2020). They are excreted more rapidly after absorption into the human and mammalian organism than those with longer carbon chains. In addition, numerous so-called precursors are in use, for example PFASs interrupted by ether bonds (Bundesinstitut für Risikobwertung, 2023). Among other things, these precursors can be converted into PFASs that are difficult to degrade. The best known and best studied are PFOS (perfluorooctane sulfonic acid or perfluorooctane sulfonates) and PFOA (perfluorooctanoic acid). The PFOS and PFOA are already banned under the POP resp REACH regulation and are not under discussion in this paper, .i.e. they are dangerous to humans and the environment and should remain banned.

The various PFAS have been used in many areas since about the 1950s. Among them are or were:

- Automotive industry
- Building Materials
- Chemical industry
- Electrical and semiconductor industry
- Energy industry
- Firefighting foams
- Household goods
- Laboratory and analysis technology
- Aerospace industry
- Medical technology
- Pesticides
- Pharmaceutical technology for the production of drugs, vaccines and antibiotics.
- Transportation of chemical and pharmaceutical bulk goods
- Textile impregnation
- Packaging
- Waxes/lubricants
- Detergents

The decisive factors are the special properties of PFAS: water-, grease- and dirt-repellent, chemically and thermally stable. The very strong bond between carbon and fluorine can only be broken with a very high energy input. Under natural environmental conditions, neither biotic processes (bacteria) nor abiotic processes (water, air, light) can contribute to the degradation of PFAS. Once the substances are

introduced into the environment, they disperse, for example, in water and sediment, but are not degraded (are persistent). Accordingly, they are referred to as "eternity chemicals." Some PFAS, especially long-chain PFAS, accumulate in organisms and along the food chain (bio-accumulative). Short-chain PFASs are excreted more rapidly but are highly mobile. They are not retained in the soil and therefore quickly reach groundwater. Due to their low adsorption potential, short-chain PFASs can hardly be removed from water during treatment. In addition, short-chain PFAS are taken up and stored by plants, thus entering the food cycle and ultimately the human body.

In humans, short-chain PFASs such as PFOA bind to proteins in the blood, liver and kidney. Decreased immune response to vaccinations and increased cholesterol levels are cited as health effects. In 2020, the European Food Safety Authority (EFSA) set a new threshold for the main PFASs that accumulate in the human body (EFSA Panel on Contaminants in the Food Chain, 2020). This is 4.4 nanograms per kilogram of body weight per week. It is known from animal studies that many PFASs damage the liver and have a developmental toxic effect. However, they do not directly alter the genetic material and in animal studies only have a carcinogenic effect at doses above those ingested by humans via food (Bundesinstitut für Risikobwertung, 2023). Particularly critical is the transfer from mother to child during pregnancy and lactation. However, only limited toxicological data are available on short-chain PFAS (Bundesinstitut für Risikobwertung, 2023).

## 3 Chronology of the restriction

### 3.1 PFOS

In October 2006, the European Parliament decided to restrict the use of PFOS to a few areas of application. The corresponding Directive 2006/122/EC regulates the *"approximation of the laws, regulations and administrative provisions of the Member States relating to restrictions on the marketing and use of certain dangerous substances and preparations (perfluorooctane sulfonates)"* (Europäische Union, 2006). On June 20, Regulation (EU) 2019/1021 on "persistent organic pollutants" entered into force in a new version, the so-called "POP Regulation" (EUR-Lex, 2019).

### 3.2 PFOA

Under the European Chemicals Regulation REACH, PFOA was identified as a so-called chemical of very high concern in 2013 and added to the REACH candidate list (Umwelt Bundesamt, 2017). Subsequently, the regulations were transferred to the POP Regulation[1]. Since July 2020, PFOA may no longer be manufactured and placed on the market. Delegated Regulation (EU) 2020/784 "concerning the intake of perfluorooctanoic acid (PFOA), its salts and PFOA precursors" sets the upper limit in substances, mixtures or articles at 0.025 mg/kg, for PFOA precursors at 1 mg/kg (EUR-Lex, 2020).

### 3.3 PFHxS

Perfluorohexane sulfonic acid (PFHxS) was included in the Candidate List of substances of very high concern for Authorisation (REACH) in 2017. PFHxS has been used, for example, in fire fighting foams, textile impregnation, cleaning agents and detergents, and in the manufacture of semiconductors (Persistent Organic Pollutants Review Committee., 2018). PFHxS is one of the most commonly detected PFAS in human blood and has a very long half-life in humans of 8.5 years (range 2.2 -27 years). Called effects on liver, serum lipids, cholesterol, thyroid hormones and nervous system development (Persistent Organic Pollutants Review Committee., 2018). 2022 are PFHxS has been included in Annex A of the Stockholm Convention. In Switzerland, the production, placing on the market and use has been banned since October 1, 2022.

In addition, the marketing, production and use of perfluorinated carboxylic acids with nine to fourteen carbon atoms (PFNA, PFDA, PFUnDA, PFDoDA, PFTrDA, PFTeDA) have been restricted since February 25, 2023. Several other PFAS, such as perfluorobutanesulfonic acid and "GenX" (ammonium 2,3,3,3-tetrafluoro-2-propanoate), have already been identified as Substances of Very High Concern (SVHC) under REACH and included on the associated SVHC list with the aim of substituting them as well (Bundesministerium für Umwelt, Naturschutz, nukleare Sicherheit und Verbraucherschutz, 2023).

### 3.4 PFAS

Whereas up to now mainly those PFAS were regulated that were detected in the environment in the highest concentrations and whose effects on the environment or human health could be justified, the planned procedure covers the entire group with about 10,000 substances (Bundesministerium für Umwelt, Naturschutz, nukleare Sicherheit und Verbraucherschutz, 2023).

In its "Chemicals Strategy for Sustainability - Towards a Pollutant-Free Environment" (European Commission, 2020), the EU Commission outlined in October 2020 that PFAS require "*special attention*" due to the high number of contaminations of soil and (drinking) water. Key initiatives therefore include "*phasing out the use of the most harmful substances, including (...) persistent substances such as per- and polyfluoroalkyl substances (PFAS), unless they are shown to be essential for the public good."*

Subsequently, the European Chemicals Agency (ECHA) has entered consultation on a possible restriction of PFAS under REACH. At the request of the European Commission, a Member State or ECHA can initiate the restriction process if there is concern that a particular substance may pose an unacceptable risk to human health or the environment. ECHA may also propose a restriction for articles containing substances included in the list of substances subject to authorization (Annex XIV) (European Chemicals Agency, 2023).

The date of intention was published on July 15, 2021. The reason given by ECHA for the restriction is:

*PFAS are persistent substances or eventually transform into such, leading to irreversible environmental exposure and accumulation. Due to their water solubility and mobility, contamination of surface water, groundwater, drinking water and soil has occurred in the EU and worldwide and will continue. It has proven very difficult and extremely costly to remove PFAS after their release into the environment. In addition, some PFAS have been shown to be toxic and/or bio accumulative, both with respect to human health and the environment. If no action is taken, their concentrations will continue to increase; the toxic and environmentally damaging effects will be difficult to reverse* (European Chemicals Agency, 2021).

On July 19, 2021, the "Call for Evidence" was launched. The proposal dossier contains background information such as substance identity and justifications for the restriction. It provides information on the identified risks and alternatives for the substances and the costs and environmental and human health benefits of the restriction (European Chemicals Agency, 2021). Interested parties were able to submit comments and formulate arguments for exemptions. The initial deadline for submission of the restriction dossier was mid-July 2022. In fact, authorities from Germany, Denmark, the Netherlands, Norway and Sweden did not submit the dossier until January 13, 2023. On March 22, the "Annex XV Restriction Report" was published. On this basis, the consultation procedure was initiated, which ends on September 25, 2023. Subsequently, the opinion of the ECHA Committees will be formed. It remains to be seen when the Commission will decide on the proposal and the restriction will enter into force.

## 4 PFAS in PharmaTech and Equipment of Sophisticated Chemical Analytics

For years, fluoropolymers and fluoroelastomers have been used in PharmaTech (PharmaTech refers to all equipment that meets substances in the manufacture of drugs, API, vaccines and antibiotics). Likewise, the fluoropolymers and fluoroelastomers are needed for the equipment for cutting edge chemical analysis to avoid any cross contamination with the substance to be analyzed. The special properties of the fluoropolymers and fluoroelastomers are decisive for the respective field of application (Banghard, 2023):

- Chemically inert: PTFE, FKM, FFKM (see below) shows no reaction with the substances used in drug, vaccine and antibiotic production, as well as with the chemicals commonly used for cleaning and reprocessing; extremely resistant to all bases, many acids, alcohols, ketones, benzines, and others.
- Thermally stable: The melting point of PTFE is 327°C and can therefore be autoclaved (SIP) or used for in-line cleaning (CIP) of equipment without any problems.
- Thermoplastic: Fluoropolymers and fluoroelastomers can be conformed or attached to complex geometries.
- Biocompatible: Fluoropolymers and fluoroelastomers pass biocompatibility testing according to the applicable test from the DIN EN ISO 10993 series
- Biostability: The material maintains its function over the entire period of use (production of drugs, vaccines and antibiotics) even in aggressive cleaning agents.

The following table shows typical fluoropolymers and fluoroelastomers used in PharmaTech and Chemical Analytics. The list does not claim to be complete:

| | | |
|---|---|---|
| **PVDF (Kynar®, Solef®); Polyvinylideifluorid** | Biocompatible polymer with piezo-, ferro- and pyroelectric properties. Due to the hydrophobic surface, the material has high media purity and no leaching behavior. This is an important requirement for the use of these materials as materials in PharmaTech and equipment for chemical analytics. High gamma radiation resistance, which is necessary for gamma sterilization. | |
| Application in PharmaTech and Equipment of Sophisticated Chemical Analytics | as coating: | - Packagings<br>- Hoses and tubes<br>- Seals<br>- Reaction vessels<br>- Transport and storage tanks<br>- Filtration plants<br>- Pumps<br>- Valves |
| | As design material: | - Membrane in sensors<br>- Luer locks and interfaces for tubing |

| | | |
|---|---|---|
| **PTFE/PFA (Teflon®) Perfluoralkoxy, Polytetrafluorethylen** | Biocompatible fluoropolymer with outstanding non-friction properties and chemical inertness. | |
| Application in PharmaTech and Equipment of Sophisticated Chemical Analytics | as coating: | - Antiadhesive coating<br>- inert coating of manufacturing vessels for Active Pharmaceutical Ingredients |
| | As design material: | - Seals (e.g. Luer-Lock)<br>- Heat shrinkable tubing<br>- Insulation of wires, cables and electronic components<br>- Filters, pumps, valves<br>- seals for transport containers of pharmaceutical precursors and substances<br>- high purity transport lines and containers<br>- lubricants |

| | | |
|---|---|---|
| **ECTFE (HALAR®); Ethylen-Chlortrifluorethylen** | Biocompatible polymer with high dielectric strength (high resistance combined with high application temperature). | |
| Application in PharmaTech and Equipment of Sophisticated Chemical Analytics | As design material: | - Heat shrinkable tubing<br>- Seals Insulation of wires, cables and electronic components<br>- Filters, pumps, valves |

| | | |
|---|---|---|
| **FEP or PFEP Tetrafluorethylen-Hexafluorpropylen-Copolymer** | | |
| Application in PharmaTech and Equipment of Sophisticated Chemical Analytics | As design material: | - Injection molded parts<br>- Low temperature applications<br>- Pipes<br>- Valves<br>- Pumps<br>- Filters<br>- Heat Exchangers |
| | As coating: | - Lining of reaction vessels<br>- Lining of transport vessels |

| | | |
|---|---|---|
| **PCTFE Polychlortrifluoreth-ylen** | | |
| Application in PharmaTech and Equipment of Sophisticated Chemical Analytics | As design material: | - Injection molded parts for<br>- cryogenic applications<br>- Pumps<br>- compressors<br>- Tubes<br>- Valves<br>- Filters<br>- Heat Exchangers |
| | as coating: | - Lining of reaction vessels<br>- Lining of transport vessels |

| | | |
|---|---|---|
| **FKM und FFKM Fluorkautschuk** | As an elastic co- or terpolymer, particularly resistant to mineral oils and lubricants; stable to temperature, chemicals and radiation. Many components exhibit a particularly high shrinkage rate. Application range from approx. -25 °C to 200 °C | |
| Application in PharmaTech and Equipment of Sophisticated Chemical Analytics | As design material: | - Pumps, Valves, Filters<br>- Metrology & Analytics Instruments<br>- Insulations<br>- Heat shrinkable hoses<br>- Drive Belts<br>- O-rings<br>- spacers<br>- gaskets<br>- washers/sealing tapes<br>- in mechanical seals and screw connections |

Furthermore, the following PFAS are used (Banghard, 2023; European Chemical Agency, 2023):

- PBSF (Perfluoro-1-Butansulfonylfluorid)
- PFA Perfloaroalkoxy
- MFA (Methyl-Fluoroacetat)
- mPTFE (modified PTFE)

Other applications for fluoropolymers/fluoroelastomers in PharmaTech and Equipment of Sophisticated Chemical Analytics include (European Chemical Agency, 2023):

- Hoses and containers for transport of ultrapure media
- Technical fluids for cleaning and heat conduction
- Gases (sterilization)

- packaging
- Coatings for optical sensors
- Particle filters

In addition, it should be noted that PFAS can be found not only in products, but also - across industries - in production processes and logistics processes. In particular, PFAS can be found in raw materials, auxiliary materials and operating supplies, as well as in lubricants, insulators, fixings, seals, molds, assembly aids or hoses. Those materials are essential for function in applications in PharmaTech and Equipment of Sophisticated Chemical Analytics.

## 5 Content of the draft Restriction

The dossier looks at a whole range of applications for PFAS. Among these are.

- Food contact materials and packaging
- metal coatings
- ski waxes
- medical devices
- fluorine-containing gases
- transport sector
- Electronics and semiconductors
- lubricants

**There are significant gaps in this list. Only the Use Sector "Transport (Annex E.2.10.)" is mentioned in Annex XV and a generic remark regarding “Fluoropolymer applications” in the Use sector “Petroleum and mining” (Annex E.2.15.), which in no ways considers the following missing applications:**

- PharmaTech equipment for the production of drugs, vaccines and antibiotics
- Laboratory technology and analytics, which in turn are used for the research of drugs, vaccines and antibiotics, etc.
- Equipment for sophisticated chemical analytics and for the development of analytical methods to prove compliance with threshold values, e.g. 25pbb for the 10,000 PFASs
- Transport and storage containers, pipe systems for substances for storage and transport of precursors for the production of drugs, vaccines and antibiotics
- Active pharmaceutical substances (biopharmaceuticals)

**All of these applications are at stake if fluoropolymers and fluoroelastomers are banned. The socio-economic impact cannot be quantified in the time available; it will be exceptionally enormous**:

- Shift of manufacturing of drugs, vaccines and antibiotics to countries with lower environmental standards.
- As a consequence, stronger dependencies even at normal times
- Sever bottlenecks in times of crisis or disrupted supply chains
- Relocation of innovative companies outside Europe
- Reinforcement of deindustrialization
- Loss of highly skilled work places. At Hamilton, appr. 3000 employees are at concerned.

If PharmaTech products are significantly modified - as is the case with the replacement of fluoropolymers and the fluoroelastomers - they must go through a new approval process with the Drug Administration in order to maintain GMP requirements. The dossier says nothing about their use in the pharma tech/biopharma industry. Drug manufacturing is highly regulated, so the entire process from identification of a possible alternative to an approved product could take decades, with the risk that at

the end of this process, approval for the manufacture of drugs, vaccines and antibiotics is no longer given (European Chemical Agency, 2023).

## 6 Full ban

After transition period (RO1) resp. The derogation time (RO2) a full ban is in force. This includes

- the production, use and import of PFAS as well as
- the placing on the market and the use of PFAS as a constituent of (another) substance, in mixtures or articles, if certain limit values are exceeded.

The dossier lists the proposed thresholds (European Chemical Agency, 2023):

- 25 ppb for all PFAS with targeted PFAS analysis (except polymeric PFAS),
- 250 ppb for the sum of PFAS with targeted PFAS analysis, with degradation of precursors where appropriate,
- 50 ppm for PFAS including polymeric PFAS. If the total fluorine content exceeds 50 mg/kg, the manufacturer, importer, or downstream user must provide evidence of measured fluorine as a PFAS or non-PFAS content to enforcement authorities upon request.

To detect such very low thresholds, new sophisticated chemical analytical methods using adequate laboratory equipment using materials with no cross-contamination, e.g. fluoropolymers and fluoroelastomers.

Therefore also Equipment of Sophisticated Chemical Analytics needs to be excepted by the PFAS ban.

## 7 Positions of Hamilton Bonaduz AG, Business Unit Process Analytics

PFASs exhibit unique properties. These include temperature resistance and dielectric strength, very good autoclavability, chemical resistance, sliding properties and excellent biocompatibility. The use of PFAS contributes significantly to the advanced and safe treatment of patients in various fields of application. Here - and in other industrial areas - the enormous stability of the substances has undeniable advantages. In nature, it causes problems when critical PFASs accumulate and enter the human body. On one side benefit, on the other risk. Until now, this weighing has been done on a case-by-case basis. Now an entire group of substances is to be restricted. This is understandable in that, in the past, banned substances were replaced without further ado by compounds that were no less dangerous but were not regulated, which ran counter to the actual objective. Therefore, reducing overall emissions and further regulating the handling of chemicals is undoubtedly to be welcomed. The concerns are not directed at the dossier. However, the current approach ensures that substances that can be used safely will also be subject to a ban. These points will be outlined below.

### 7.1 Role of PharmaTech and Sophisticated Laboratory Analytics in the Restriction Draft

In the dossier, an attempt has been made to identify as comprehensive an overview as possible of the various areas of application of PFAS and to relate the restriction in each case to, among other things, emission savings, alternatives and (follow-up) costs. After weighing the pros and cons, plant protection products, biocidal products and pharmaceuticals have been excluded from the further procedure.

But to manufacture pharmaceuticals, you need adequate PharmaTech equipment and sophisticated chemical analytics using special laboratory equipment to do so.

➔ **in comparison with crop protection products, biocidal products and pharmaceuticals, the role of Pharmatech equipment and chemical analytical equipment for people and society must be appreciated even more and distinguished more clearly from other industries.**

### 7.2 Abandonment of „essential use" and specific risk assessment

In the past, products and applications have been examined to establish "essential use." This covers products that are necessary for health or to maintain the safety and function of society or for which there are no technically and economically viable alternatives. The main objective of the approval procedure under REACH is to replace substances that have particularly concerning properties in the near term if it is technically feasible and economically viable to do so. Users of these substances may continue to use them over a certain period of time if they show that they can handle the substance without risk, or at least with a low level of risk, and there are no comparable alternatives (Bundesanstalt für Arbeitsschutz und Arbeitsmedizin, 2021). A general restriction on 10,000 substances represents a departure from this principle. What is more, the burden of proof as to why the use of PFASs is considered essential for society now lies with manufacturers and users.

The mention in REACH of "substances that have particularly concerning properties" above relates to ecological risk criteria (including endocrine substances) as well as effects on human health (including CMR substances). Previous restriction processes have targeted precisely these types of substance for removal from circulation or aimed to impose strict regulations on handling them, as has already been done with a number of PFASs. What is happening now, on the other hand, is that **restrictions are being imposed on substances even if their effects on humans and nature can be controlled and there are still no alternatives in sight**. No specific risk is being investigated.

➔ **Instead of a general restriction, PFASs should be evaluated using a risk-based approach and their "essential use" should be assessed.**

### 7.3 Fluoropolymere „of low concern"

There are different grades of PFASs. The properties of short-chain PFASs are different from those of long-chain fluoropolymers. Although they match the structural definition of a PFAS, they have very different physical, chemical, ecological and toxicological properties compared to other substances. Fluoropolymers make up their own family within the group of substances. The study by Henry et al. (Henry, et al., 2018), shows, among other things, that fluoropolymers are thermally, chemically, photochemically, hydrolytically, oxidatively and biologically stable. They contain practically no monomer and oligomer residues and have minimal or no leachable components. Fluoropolymers are practically insoluble in water and are not transported over long distances.

With a molecular weight of over 100,000 Da, fluoropolymers cannot penetrate the cell membrane. Fluoropolymers are not bio accumulative, as demonstrated by toxicological studies of PTFE (acute and sub chronic systemic toxicity, irritation, sensitization, local toxicity upon implantation, cytotoxicity, in vitro and in vivo genotoxicity, hemolysis, complement activation and thrombogenicity). Clinical studies on patients who have received permanently implanted cardiovascular medical devices containing PTFE show no chronic toxicity or carcinogenicity. The conclusion reached by Henry et al. (2018) is that fluoropolymers meet widely accepted assessment criteria for classification as "polymers of low concern" (PLCs) and that they are significantly different from other polymer and non-polymer PFASs and should therefore be considered separately for risk assessment or regulatory purposes. The OECD criteria for "fluoropolymers of low concern" (OECD Enviornment, 2008) include high molecular mass, low persistence, nonsignificant bioaccumulation, low toxicity and negligible exposure. The substances investigated in detail were PTFE, ETFE (ethylene tetrafluoroethylene), FEP (fluorinated ethylene propylene) and PFA (perfluoroalkoxy). Korzeniowski et al. (Korzeniowski, et al., 2022) have examined several fluoroplastics, fluoroelastomers and special fluoroplastics in more detail and have set out criteria for "polymers of low concern" in each case:

- Composition
- Molecular weight
- Ionic character
- Reactive functional groups
- Low-molecular-weight leachable components

- Particle size
- Structural composition
- Elemental composition
- Water and lipid solubility
- Stability
- Abiotic stability
- Biotic stability
- Thermal stability

All the substances that were examined met the requirements for classification as “polymers of low concern”. Including the four fluoropolymers from the previous study by Henry et al., a total of 18 fluoropolymers can thus be rated as "polymers of low concern."

- PTFE
- ETFE (ethylene tetrafluoroethylene)
- FEP (fluorinated ethylene propylene)
- PFA (perfluoroalkoxy)
- PVDF (polyvinylidene fluoride)
- PVDF-HFP copolymer (vinylidene fluoride hexafluoropropylene copolymer)
- ECTFE (ethylene chlorotrifluoroethylene copolymer)
- ECTFE (ethylene chlorotrifluoroethylene hexafluoroisobutylene terpolymer)
- PCTFE (polychlorotrifluoroethylene)
- FEVE (fluoroethylene vinyl ether copolymer)
- EFEP (1-propene, 1,1,2,3,3,3-hexafluoro-, polymer with ethylene and 1,1,2,2-tetrafluoroethylene)
- CPT (1,1,1,2,2,3,3-heptafluoro-3-[(trifluoroethenyl)oxy]propane polymer with chlorotrifluoroethylene and tetrafluoroethylene)
- THV (1-propene, 1,1,2,3,3,3-hexafluoro-, polymer with 1,1-difluoroethylene and tetrafluoroethylene)
- Perfluoro(alkenyl vinyl)ether polymer
- Sodium or potassium salts of perfluorosulfonic acid/TFE copolymer or perfluorocarboxylic acid/TFE copolymer
- FEPM (tetrafluoroethylene propylene polymer)
- FKM (1-propene, 1,1,2,3,3,3-hexafluoro-, polymer with 1,1-difluoroethylene copolymer and terpolymers)
- FFKM (tetrafluoroethylene trifluoromethyl trifluorovinyl ether copolymer)

These are **chemically stable, non-toxic, non-bioavailable, non-water-soluble and non-mobile materials** that do not have unwanted effects on the environment or human health. There is therefore an urgent need to proceed with the restriction process using scientifically based evidence and to remove families of substances that do not have the potential to pose risks to humans or the environment. PTFE

has been particularly well studied. It can be considered neither carcinogenic (Radulovic & Wojcinski, 2014) nor genotoxic (Radulovic & Wojcinski, 2014) or toxic for reproduction (Davis, Rothmann, Tan, & Thomas, 1993). Likewise, no effects on the immune system are known (Kim, et al., 2013). Skin exposure to PTFE has also been considered safe for a long time. This is evident, for example, in the use of PTFE needles for intravenous access (Smith, Bell, Fulton, Quine, & Morden, 1993). In attempts to use PTFE as a filler for dietary products, it was found that the material cannot be absorbed through the digestive tract (Naftalovich, Naftalovich, & Greenway, 2016). For particle sizes larger than 20 µm, the insoluble polymer cannot enter the bloodstream with reasonable certainty. It is therefore imperative that the restriction process be based on scientific evidence and exclude substance families that do not pose a risk to humans or the environment. These are substance families that have been used safely in PharmaTech and chemical analytics for decades.

➔ **Fluoropolymers "of low concern," which present no potential risk to humans or the environment and are essential for PharmaTech and chemical analytics, should be excluded from the restriction process.**

### 7.4 Missing alternatives

The restriction proposal considers the availability of technically and economically feasible alternatives to decide on exemptions. In the dossier, applications to PharmaTech and chemical analytics are not listed, and there are no comparable substitute materials for fluoropolymers and fluoroelastomers in prospect. And the likelihood is high that none will be found. This is explicitly confirmed in Anne XV, sector Petroleum and mining, "Fluoropolymer applications": *In light of the sufficiently strong evidence pointing to the* ***non-existence of technically and economically feasible alternatives*** *at EiF, a derogation is proposed for Fluoropolymer applications.*

The restriction dossier focuses in particular on persistence, or the long-lasting nature of PFASs. It should be assumed that any alternatives will share this property. This makes it even more unlikely that it will be possible to use them.

A broader view is needed in this context. A restriction will affect medical technology directly, but also indirectly. PFASs can be found in auxiliary materials and working materials (such as lubricants) or in production system components (such as seals and tubes). PFASs are used in the production of semiconductors, which in turn are used in active medical devices. In those areas too, fundamental changes are expected that will impact on companies: they will need to invest in new assets and systems, which they will then need to integrate and validate in compliance with the regulatory framework.

In view of the high degree of uncertainty as to whether alternative substances with comparable properties can be found at all, the use of non-critical, essential PFASs such as fluoropolymers must continue to be authorized beyond the 12-year period. Manufacturers of PharmaTech and equipment for chemical analytics urgently need legal certainty in this area.

### 7.5 Impact on PharmaTech and Equipment for Sophisticated Chemical Analytics

As there is neither reporting nor labelling obligation for PFAS materials in place, the industry as a downstream user needs to conduct complex investigation across the supply chain to identify the components impacted by the PFAS restriction to have a complete overview. The current proposal bans the use of PFAS in PharmaTech and other applications in pharmaceutical production processes where substitution has to be assessed individually. Without equipment containing fluoropolymers and fluoroelastomers, EU manufacturing plants cannot operate. Manufacturing processes are qualified and validated processes covered by sectorial legislations and global marketing authorizations. These are severely impacted by the restriction. The regulatory oversight over equipment and the validation for operation is necessary to assure a consistently manufactured product; one that had been proven to be safe and effective during clinical development. The manufacturing equipment must demonstrate that it will not introduce an unacceptable impurity into the product authorized for market. Concerns exist around the timeframe for identification, testing and validating alternatives for components that need to be replaced, in the rare case that alternatives are feasible and available. A ban of these substances or **even a time-limited derogation** will create a serious competitive disadvantage for the EU in global manufacturing. In practice, such a ban would impact all human and veterinary medicinal products including biopharmaceuticals, vaccines and antibiotics and would seriously affect medicines availability in the longer term.

This is another reason why an exemption for fluoropolymers and fluoroelastomers must be thought in a wider scope. Without supply chains that continue to function, socially relevant industries such as pharma tech will not be able to survive. Those PFASs that are absolutely necessary for the production of polymers (emulsifiers, etc.) must not be forgotten. To ban these and other starting materials would be tantamount to a de facto ban on the production of fluoropolymers. The example of Chemours shows that emissions-neutral production is possible: the company is investing 75 million euros in its plant in Dordrecht (Netherlands) to reduce PFAS emissions by 99 percent by 2030 compared to the 2017 fiscal year.

Above all, it is important to keep and strengthen these supply chains in the EU. In recent years, it has become painfully clear how dependent the European family of countries is on non-European suppliers. For example, the European Chips Act is a direct result of this realization. In 2023, the European Commission published a study on the extent to which key industries have unrestricted access to important raw materials. Fluoropolymers are among the processed materials mentioned, for example in energy technology, robotics and chip manufacturing. One conclusion is that the EU is heavily dependent on third countries, and China in particular, at various stages of the value chain. An allover PFAS ban runs counter to all well-intentioned efforts. Instead of bringing value creation back to Europe, dependence on non-European manufacturers is growing.

### 7.6 Emissions and emission prevention

The proposed restriction aims to reduce the discharge of PFASs into the environment to as close to zero as possible. To this end, it looks at manufacture, use and disposal. For medical technology, a 400% increase in emissions is expected between 2025 and 2050. The largest component in the dossier is fluorinated gases, followed by fluoropolymers and non-polymer PFASs (including precursors of perfluoroalkyl acids, PFAAs). In the case of polymer PFASs, it is assumed that 1% of the PFASs used are released. For fluorinated gases, discharge percentages of between 10% (gases used in industrial processes for medical applications) and 100% (e.g. propellants, anesthetics, contrast agents) are used.

It remains to be seen whether this forecast is completely accurate. However, it should be noted that significant contributions to emissions reductions are possible even at the manufacturing stage for PFASs. Medical technology, the PharmaTech and equipment for chemical analytics procures these materials, but does not manufacture them. With a uniform European standard, it would be possible to achieve the highest level of “containing” even at the manufacturing stage. Steps have already been taken to achieve this (in the Netherlands, for example).

Pharmatech and equipment for chemical analytics are intended for professional use by specialists in the respective industry and research. This also means that the products follow a tightly defined flow of goods (manufacturer - user - disposer) and that uncontrolled discharge of materials containing PFAS into the environment is virtually impossible. The requirements for the disposal of waste from pharmaceutical production are already strict, both from a hygienic point of view and for environmental reasons.

In the meantime, the disposal of fluoropolymers has also been scientifically investigated[38]. To show that PTFE can be converted almost completely and in order to establish the possible formation of low-molecular-weight PFASs, the incineration of PTFE was investigated under typical waste disposal conditions at the BRENDA pilot plant at the Karlsruhe Institute of Technology (KIT). Within the methodological limits, no statistically significant indications were found that any of the detected PFASs were produced in the incineration of PTFE. For this reason, the municipal incineration of PTFE using the best available technologies is not a significant source of the PFASs investigated and should be considered an acceptable form of waste treatment.

Raw and starting materials, intermediates, auxiliaries, equipment, and consumables required for manufacture of pharmaceuticals and medical devices should also be exempt, as these are handled under controlled conditions and without them, manufacturing of medicinal products and devices is impossible. Any emission of industrial manufacturing into environments is controlled and regulated via other existing EU legislation. Any risk posed by emissions of these substances can be further mitigated through waste management or circularity regulations.

Brand new research indicates novel approach to destroy PFAS based on kinetic mechanical forces (Gobindlal, Shields, Whitehill, Weber, & Sperry, 2023).

### 7.7 Assessments from outside the EU

The fact that PFAS emissions need to be reduced can be seen as a global consensus. However, countries outside the EU have different and in some areas much more nuanced processes, especially for fluoropolymers.

Australia

In 2017, an Expert Health Panel for PFASs was set up in Australia to advise the Australian government on the available knowledge, including important international reports and opinions from the public and other stakeholders. The panel concluded that although the scientific evidence is limited, the previous reviews and research have provided consistent reports of a connection with various health effects. The Environmental Health Standing Committee (enHealth) has published guidelines intended to help assess public health risks. As a precautionary measure, enHealth recommends that exposure to PFASs be minimized as far as possible while further investigations into the potential health effects are carried out[40].

The declarations contain information on the possible health effects of exposure to PFOS, PFOA and PFHxS. With regard to PTFE, it states that although the polymer is part of the PFAS family, it has a different structure and therefore different properties to PFOA, PFOS or PFHxS:

- PTFE is not water soluble – PFOA, PFOS and PFHxS are water soluble.
- PTFE is too large and too insoluble to be absorbed by organisms – PFOA, PFOS and PFHxS are easily absorbed by organisms.
- PTFE is not toxic to animals – PFOA, PFOS and PFHxS have a range of toxic effects in animals.

These differences mean that the regulatory authorities do not consider PTFE to be a chemical of concern for human health or the environment[41].

United Kingdom

In 2021, the UK government set the first restrictions to be introduced under the new chemicals regulation system, the UK REACH system42. A restriction is introduced when there is evidence of an unacceptable risk to human health and the environment. The review is carried out by the Health & Safety Executive (HSE) with the support of the Environment Agency (EA). Those bodies also examine the risk from PFASs. In the UK's most comprehensive analysis of these chemicals to date, HSE has identified the most common and harmful uses of PFASs and demonstrated what measures could be taken to control and deal with them. According to the Regulatory Management Option Analysis (RMOA), restrictions do not need to be applied to low hazard groups or low risk uses. The "low hazard groups" category includes fluoroplastics and fluoroelastomers. These could be highlighted as derogations from a proposed restriction (Health and Safety Executive, 2023).

USA

The U.S. Environmental Protection Agency (EPA) published an Advance Notice of Proposed Rulemaking (ANPRM) in April 2023. It focuses on the potential identification of hazardous material discharges of PFASs as part of the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA) (United States Enviromental Protection Agency, 2023). Dabei sollen die neuesten wissenschaftliche Erkenntnisse und Informationen zu PFAS gesammelt werden. Der Schritt folgt dem Regelungsvorschlag aus dem September 2022 zur Einstufung von PFOA und PFOS als gefährliche Stoffe.

aims to gather the latest scientific findings and information on PFASs. This step follows the regulatory proposal from September 2022 on classifying PFOA and PFOS as hazardous substances.

The EPA's roadmap sets out the concrete steps to be taken by 2024 (Unites States Enviormental Protection Agency, 2021). It defines three pillars: Research (investments in research and development and innovation to gain a better understanding of PFASs and their impact on health and the environment), restrict (comprehensive approach to proactively prevent PFASs from reaching quantities in the air, soil and water that are critical for humans and the environment) and remediate (expanded and accelerated remediation of PFAS contamination to protect human health and ecosystems). The production and processing of PFASs, metal finishing, airports, pulp and paper, landfill sites and the manufacture of textiles and carpets are all named as key industries with significant documented emissions.

Under "restrict," the objectives described are as follows:

- To use and harmonize all the available legal measures to control and prevent PFAS emissions and minimize the exposure of consumers and industry to PFASs.
- To entrench the responsibility of manufacturers, processors, dealers, importers, industry and other important users for limiting PFAS discharge and for dealing with risks.
- To set up programs to reduce PFAS use and discharge.
- To avoid or minimize PFAS discharges and emissions in all communities.

The EPA also plans to review past PFAS regulatory decisions. In this context, additional notification obligations may be imposed so that it can examine PFASs before they are used in a new, potentially questionable way.

➔ **Outside the EU, countries are taking a nuanced attitude and allowing the use of fluoropolymers and fluoroelastomers to continue in some areas. It would be wise to take this view in the proposed restriction.**

## 8 Literature reference

Aleksandrov , K., Gehrmann, H.-J., Hauser , M., Mätzing, H., Pigeon, D., Stapf, D., & Wexler, M. (2019). Waste incineration of Polytetrafluoroethylene (PTFE) to evaluate potential formation of per- and Poly-Fluorinated Alkyl Substances (PFAS) in flue gas. *Chemospere*, 898-906.

Banghard, M. (2023). *Lebensrettende Eigenschaften der Fluorpolymere.*

Bundesanstalt für Arbeitsschutz und Arbeitsmedizin. (2021). *Bundesanstalt für Arbeitsschutz und Arbeitsmedizin.* doi:10.21934/reach:info20201015

Bundesinstitut für Risikobwertung. (2023, Juni 16). *Bundesinstitut für Risikobwertung*. Retrieved from https://www.bfr.bund.de/de/fragen_und_antworten_zu_per__und_polyfluorierten_alkylsubstanzen__pfas_-242936.html

Bundesministerium für Umwelt, Naturschutz, nukleare Sicherheit und Verbraucherschutz. (2023, Januar 16). *Bundesministerium für Umwelt, Naturschutz, nukleare Sicherheit und Verbraucherschutz*. Retrieved from Bundesministerium für Umwelt, Naturschutz,nukleare Sicherheit und Verbraucherschutz

Davis, N. S., Rothmann, S. A., Tan, M., & Thomas, A. J. (1993). Effect of catheter composition on sperm quality. *J Androl*.

EFSA Panel on Contaminants in the Food Chain. (2020). Scientific Opinion on the risk to humanhealth related to the presence of perfluoroalkyl substances in food. *EFSA Journal 2020*, 391. doi:https://doi.org/10.2903/j.efsa.2020.6223

EUR-Lex. (2019, Juni 20). *EUR-Lex.* Retrieved from https://eur-lex.europa.eu/legal-content/DE/TXT/PDF/?uri=CELEX:32019R1021&from=DE

EUR-Lex. (2020, April 8). *EUR-Lex.* Retrieved from https://eur-lex.europa.eu/legal-content/DE/TXT/PDF/?uri=CELEX:32020R0784&from=DE

Europäische Union. (2006, Dezember 12). *EUR-Lex.* Retrieved from https://eur-lex.europa.eu/legal-content/DE/TXT/PDF/?uri=CELEX:32006L0122&from=DE

European Chemical Agency. (2023, März 22). *European Chemical Agendcy.* Retrieved from ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

European Chemicals Agency. (2021, Juli 15). *European Chemicals Agency*. Retrieved from https://echa.europa.eu/de/registry-of-restriction-intentions/-/dislist/details/0b0236e18663449b

European Chemicals Agency. (2023). *European Chemicals Agency*. Retrieved August 2023, from https://echa.europa.eu/de/regulations/reach/restrictions/restriction-procedure

European Commission. (2020, Oktober 14). Retrieved from https://environment.ec.europa.eu/strategy/chemicals-strategy_en

Gobindlal, K., Shields, E., Whitehill, A., Weber, C. C., & Sperry, J. (2023). Mechanochemical destruction of per- and polyfluoralkyl substances in aqueous film-forming foams and contaminated soil. *Enviormental Science Advances*, 982.

Health and Safety Executive. (2023, März). Retrieved from https://www.hse.gov.uk/REACH/assets/docs/pfas-rmoa.pdf

Henry, B. J., Carlin, J. P., Jon, H. A., Buck, R. C., Buxton, W. L., Fiedler, H., . . . Hernandez, O. (2018). A Critical Review of the Application of Polymer of Low Concern and Regulatory Criteria to Fluoropolymers. *Integrated Environmental Assessment and Management, 14*(3).

Kim, K. W., Kim, J. C., Moon, J. H., Koo, H., Kim, T. H., & Moon, N. J. (2013). Management of complicated multirecurrent pterygia using multimicroporous expanded polytetrafluoroethylene. *Br J Ophthanolmol*, 697-700.

Korzeniowski, S. H., Buck, Robert, C., Newkold, R. M., El Kassmi, A., Laganis, E., . . . Musio, S. (2022). A critical review of the application of polymer of low concern regulatory criteria to fluoropolymers II: Fluoroplastics and fluoroelastomers. *Integrated Environmental Assessment and Management*, 326-354.

Naftalovich, R., Naftalovich, D., & Greenway, F. L. (2016). Polytetrafluoroethylene Ingestion as a Way to Increase Food Volume and Hence Satiety Without Increasing Calorie Content. *Diabetes Sci Technol*, 971-6.

OCED. (2021). Reconciling Terminology of Universe of Per- and Polyflouroalkyl Substances. Recommandations and Practical Guidance. *OECD Series on Risk Management, 61*.

OECD Enviornment. (2008).

Persistent Organic Pollutants Review Committee. (2018). *Stockholm Convention on Persistent Organix Pollutants.*

Radulovic, L. L., & Wojcinski, Z. (2014). PTFE (Polytetrafluoroethylene; Teflon®). In *Encyclopedia of Toxicology* (pp. 1133-1136).

Smith, M. R., Bell, G. D., Fulton, B., Quine, M. A., & Morden, A. E. (1993). A comparison of winged steel needles and Teflon cannulas in maintaining intravenous access during gastrointestinal endoscopy. *Gastrointest Endosc*, 33-6. doi:10.1016/s0016-5107(93)70007-3.

Umelt Bundesamt DE. (2020, Januar). Retrieved from https://www.umweltbundesamt.de/sites/default/files/medien/2546/publikationen/uba_sp_pfas_web_0.pdf

Umwelt Bundesamt. (2017, Mai 09). *Umwelt Bundesamt*. Retrieved from https://www.umweltbundesamt.de/themen/eu-verbietet-pfoa

*Umweltbundes Amt*. (2023). Retrieved from https://www.umweltbundesamt.de/themen/chemikalien/chemikalien-reach/stoffgruppen/per-polyfluorierte-chemikalien-pfc#wo-komme-ich-mit-pfc-in-beruhrung

United States Enviromental Protection Agency. (2023, April 13). *United States Enviromental Protection Agency.* Retrieved from https://www.epa.gov/newsreleases/epa-takes-important-step-advance-pfas-strategic-roadmap-requests-public-input-and-data

Unites States Enviormental Protection Agency. (2021, Oktober). *Unites States Enviormental Protection Agency.* Retrieved from https://www.epa.gov/system/files/documents/2021-10/pfas-roadmap_final-508.pdf