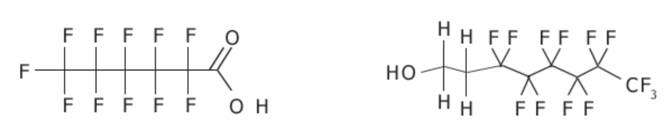
Per- and Polyfluoroalkyl Substances (PFASs) in primary packaging and the proposed restriction in the European Union

INJECTO
PHARMACEUTICAL PACKAGING

WHAT IS PFAS

Per- and polyfluoroalkyl substances (PFASs) are a large, complex group of synthetic chemicals that have been used in consumer products around the world since about the 1950s. They are ingredients in various everyday products. For example, PFASs are used to keep food from sticking to packaging or cookware, make clothes and carpets resistant to stains, and create more effective firefighting foam.

The Organisation for Economic Co-operation and Development (OECD) updated the definition of PFASs in 2021 to any substance that contains at least one fully fluorinated methyl (CF_3-) or methylene (-CF_2-) carbon atom without any H/Cl/Br/I attached to it.



The carbon-fluorine bond is incredibly strong, which makes the substances highly stable but also very persistent. This is why they do not degrade easily in the environment or by waste incineration and because of this extreme persistency the European Chemical Agency defines PFASs as:

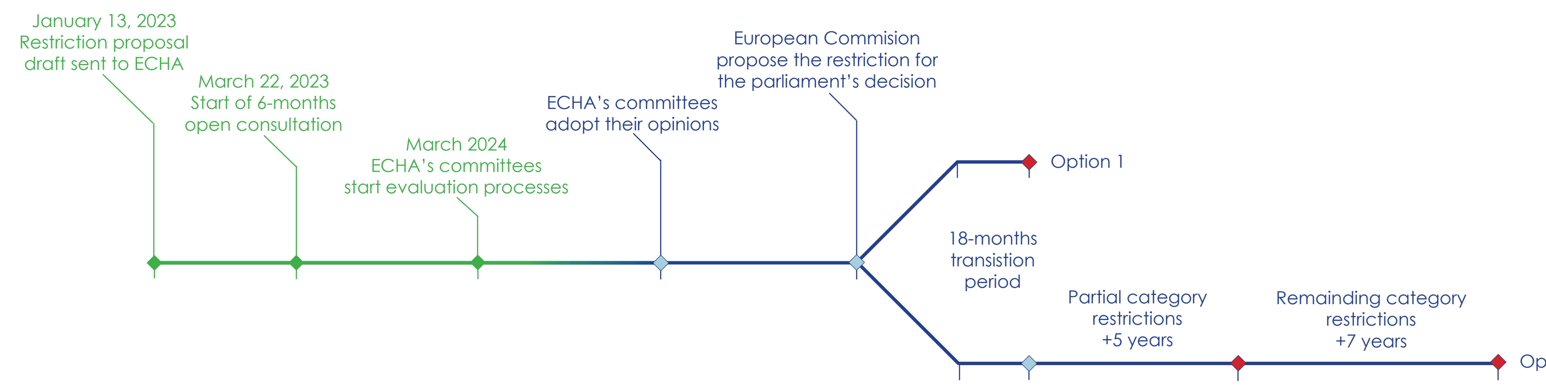
RESTRICTION PROPOSAL IN THE EUROPEAN UNION

In February 2023 five member countries submitted the broadest, most restrictive proposal that has ever been made in the European Union.

The restriction proposal was submitted to the European Chemical Agency (ECHA) under Annex XV of the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) proposing a substantial restriction for the manufacture, placing on the market and use of of all PFAS variants. The aim is to regulate PFASs in their entirety, including precursors.

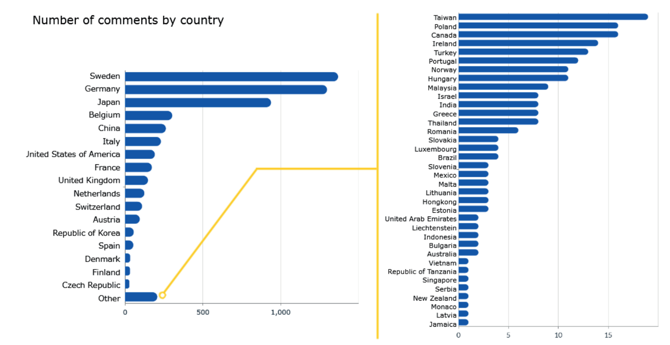
The submitted technical dossier is in alignment with the new OECD definition and thus include a significantly wider scope than the previous restrictions' approach of independently regulating single subgroups of PFASs. The proposal for restriction of PFASs contains a transition period of 18 months and two restriction options:

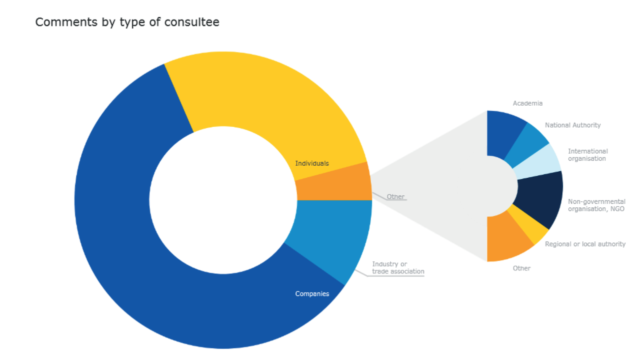
- **Option 1 – No derogation period after the transition period**
- **Option 2 – Either a 5-year or 12-year derogation period after the transition period**



OPINIONS AND COMMENTS

From March to September 2023 the ECHA opened consultation to receive comments to the restriction proposal from industry, organisations and individuals. The proposal received more than 5,600 comments (> 100,000 pages) originating from more than 50 countries, which, together with the proposed restriction, are being evaluated by ECHA's scientific committees for Risk Assessment (RAC) and for Socio-Economic Analysis (SEAC).





Independent of the open consultation, RAC had checked the restriction dossier for feasibility and in October 2023 RAC published their advices on the enforceability. Their report indicating that some parts of the dossier were unclear and they provided suggestions for improving the restriction proposal.

Ultimately ECHA will deliver the final opinions to the European Commission in the shortest possible timeframe, while ensuring proper scrutiny by the scientific committees. Once the committees adopt their opinions, they will be communicated to the public.

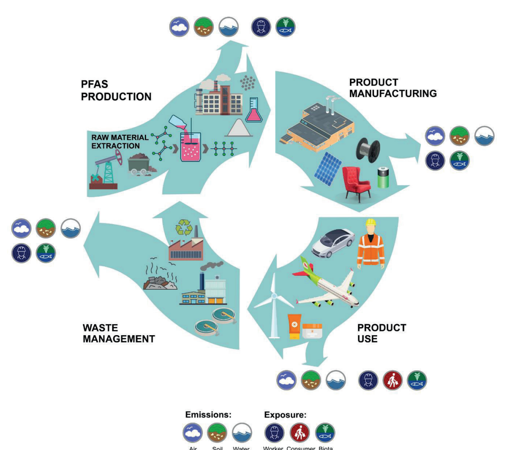
"Careful consideration of these comments and the information they contain is of great importance to ensure that any future regulation of PFAS is based on the best possible information."

PFAS IN THE ENVIRONMENT

PFASs are, or ultimately transform into, persistent substances, leading to irreversible environmental exposure and accumulation.

Due to their water solubility and mobility, contamination of surface, ground- and drinking water and soil has occurred in the EU as well as globally and will continue. It has been proven very difficult and extremely costly to remove PFASs from the environment.

Studies have shown that PFASs have already contaminated rainwater, groundwater, soil, sediment, biota, drinking water and food crops. Without taking action, their concentrations will continue to increase, and their toxic and polluting effects will be difficult to reverse.



The authorities estimate that around 4.4 million tonnes of PFASs would end up in the environment over the next 30 years unless action is taken.

PFAS IN PRIMARY PACKAGING

Stoppers and plungers used as closures for vials, cartridges and prefilled syringes are typically made of (halogenated) butyl rubber applied with a coating to minimize extractables and leachables and to assist the mechanical performance.

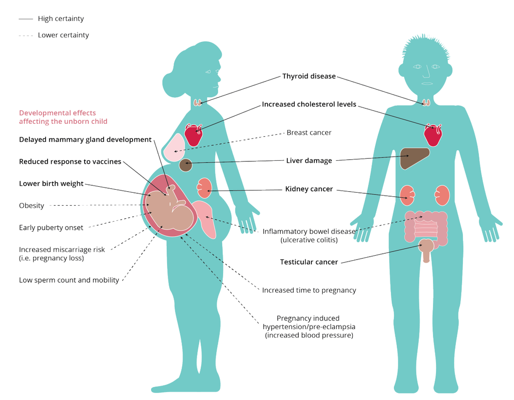
These coating are typically made of:

- PTFE - Poly(tetrafluoroethylene), $(CF_2 - CF_2)_n$
- ETFE - Poly(ethylene-co-tetrafluoroethylene), $(CH_2 - CH_2)_n$ ...$(CF_2 - CF_2)_m$
- PCTFE - Poly(chlorotrifluoroethylene), $(CF_2 - CClF)_n$

or similar fluoropolymer-based variations that contain -CF_2-or-CF_3 groups and hence are PFASs by definition.

Therefore, the restriction proposal may entail direct consequences for the use of PFASs in primary packaging and injection devices for pharmaceuticals, especially for coated container closure systems.

CONSEQUENCES OF PFAS



PFASs are bioaccumulative substances that in some cases have been documented as toxic due to their endocrine-disrupting behaviour, both with respect to human and animal health.

Consequently, they are considered a major health liability. PFASs are linked to a weakened immune system, elevated cholesterol levels, liver damage and various kinds of cancer.

The two cancer types with the most evidence linked to PFAS are kidney cancer and testicular cancer.

On a global scale it is estimated that 99% of people have PFAS in their blood.

In combination with environmental monitoring, future human biomonitoring will be essential to track long-term trends of both previously used and currently used chemicals like PFAS.

ALTERNATIVES

Finding alternative solutions for the many use cases of PFASs are highly important in all industries.

Currently there are suitable alternatives for the most commonly used applications of PFAS and even more solutions are being developed.

PFAS free plungers, stoppers and needle shields for vial and prefilled syringes are commercially avaible and more solutions are undoubtely to come.

Transitioning to PFAS-free alternatives requires careful evaluation of trade-offs as well as accounting for uncertainties to determine the most effective short- and long-term research and development strategies.

Thus, the two derogation periods suggested in the restriction proposal, are to ensure time to develop, test and implement PFAS free alternatives in cases where either alternative solutions do not exist or where the existing alternatives does not prevail.

CONSIDERATIONS

As the restrictions risk impacting the coating in primary packaging, e.g., on container–closure systems for prefilled syringes, cartridges and vials, businesses should aim to de-risk and seek alternatives to their use.

Clearly, the pharmaceutical industry should care about the use of PFASs and, in due time, prepare for the risk of a ban of PFASs. Furthermore, the pharmaceutical industry's continuing support of and contribution to the 17 sustainable development goals of the United Nations should be taken into account.

Most companies are putting considerable efforts into corporate environmental awareness, minimizing their environmental footprint, and implementing various sustainability programs. So why not also be proactive — de-risk and turn this challenge into a value proposition in the presentation and marketing of drug products in PFAS-free primary packaging?

Overall, the restriction proposal should raise some questions for consideration:

- **What can we do to prevent the use and spread of PFASs?**
- **Are PFAS-based coatings in primary packaging a necessity?**
- **Can we contribute to reduce the use of PFAS-based products?**

ABOUT

Injecto A/S is a Danish manufacture and supplier of PFAS Free, Silicone Oil Free components for prefilled syringes.

When we state that "***Everyone is entitled to safe medical treatment***", it is not only a commitment to provide optimum solutions for the pharmaceutical industry and the patients in need; it also necessitates that we consider the entire supply chain and how we contribute to the human, animal and environmental health.

Author and presenter: Taras Tim Bredel
Co-authors and reviewers: John Adamsen & Torben Helmer

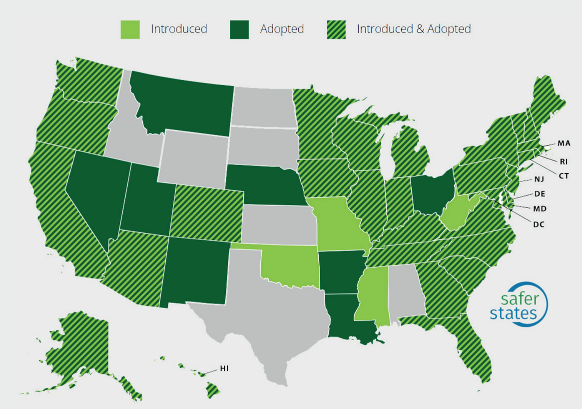
Visit: injecto.eu

SOURCES AND MORE INFORMATION

echa.europe.eu | oecd.org | eea.europe.eu | eeb.org | chemsec.org | epa.gov | hhs.gov | saferstates.org

PFAS IN USA

The U.S. Environmental Protection Agency (EPA) has gradually added different PFASs to the list as hazardous substances under the Comprehensive Environmental Response, Compensation, and Liability Act, also known as Superfund, however the concept of a nation wide regulating of the entire class of PFASs is being evaluation.



According to Safer States, a national alliance of environmental health organizations, in addition to the federal actions, 34 states have currently introduced 295 policies to protect people from toxic chemicals including PFASs. 153 state policies have already been adopted in 30 states.

As of April 2024, 30 US State Attorneys General (AGs) have initiated litigation against the manufacturers of PFAS chemicals for contaminating water supplies and other natural resources.

These AGs include AK, AZ, AR, CA, CT, CO, DE (settled), DC, HI, IL, IN, ME, MD, MA, MI (settled), MN (settled), NH, NJ (settled), NM, NY, NC, OH (settled), OR, PA, RI, SC, TN, VT, WA and WI.

In December 2022, 3M announced that they will exit PFAS manufacturing and discontinue the use of PFAS by the end of 2025.

"With these two actions, 3M is committing to innovate toward a world less dependent upon PFAS"