Contribution from the European Directorate for the Quality of Medicines and HealthCare (EDQM) of the Council of Europe (CoE)

Public Consultation from ECHA on universal restriction of PFAS – Annex XV restriction dossier

The European Directorate for the Quality of Medicines and HealthCare (EDQM) of the Council of Europe (CoE) welcomes the opportunity to provide its contribution to the public consultation on the proposed universal PFAS restriction published by the European Chemicals Agency (ECHA).
While the EDQM supports the restriction of per- and polyfluoroalkyl substances (PFAS) with a view to minimising their impact on the environment and on human and animal health, it would also like to stress that the proposed restriction – as currently formulated – could heavily disrupt access to medicines and health products in the EU and beyond which, in consequence, would also have a negative on public health.
Although an exemption for the manufacture/use/release on the market of PFAS as active substances in medicines is proposed, it should be noted that PFAS are largely used throughout the lifecycle of medicines as reagents, in consumables or in reference standards used by manufacturers to release medicines placed on the market. The EDQM is thus calling for commensurate and progressive measures that would not jeopardise the access to medicines and health products and for further clarification of the scope of the proposed restriction.

1. Background information

The European Directorate for the Quality of Medicines and HealthCare (EDQM) of the Council of Europe (CoE) is a leading international organisation in public health that ensures access to good quality and safe medicines and health products. It plays a central role in the European pharmaceutical regulatory system, as enshrined in the EU pharmaceutical legislation.
In the field of pharmaceuticals, the EDQM is responsible for:

- establishing and supplying documentary standards – the European Pharmacopoeia monographs and other texts – and physical reference standards used for the manufacture and quality control of medicines; the Ph. Eur. is legally binding in 39 countries (including the 27 Member States of the EU) that have signed the Convention on the elaboration of a European Pharmacopoeia;
- granting Certificates of Suitability (CEPs) confirming that the ingredients used in medicines comply with the European Pharmacopoeia standards and are suitably controlled by these standards, and for carrying out inspections of manufacturers of active substances; these CEPs replace the detailed information on the substances that is to be provided in marketing authorisation applications;
- co-ordinating the network of Official Medicines Control Laboratories (OMCL) that perform market surveillance studies and batch release testing to control the quality of medicines.

With its broad member- and observership, the outreach of the EDQM extends beyond the political and geographical boundaries of Europe.

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2. EDQM comments and recommendations

2.1. Impact of the proposed restriction on the European Pharmacopoeia (Ph. Eur.)

PFAS covered by a Ph. Eur. monograph (documentary standard)

A large number of PFAS are covered by a Ph. Eur. monograph. These include active substances and, to a lesser extent, excipients; they are also referred to in Ph. Eur. monographs as impurities.

As per the restriction proposal, active substances in human and veterinary medicinal products, would be exempted: it is therefore understood that the monographs concerned can remain in the Ph. Eur.

There are 39 Ph. Eur. active substance monographs for PFAS; more than 160 PFAS impurities are referred to in the Ph. Eur.

PFAS used as reagents in the European Pharmacopoeia

PFAS, particularly trifluoroacetic acid (TFA), are used as reagents in a wide range of analytical procedures, e.g. liquid chromatography-based procedures described in the Ph. Eur. Thus, the restriction could disrupt the supply chain for such substances which would again have an impact on both manufacturers and the Official Control Medicines Laboratories responsible for testing medicines. Users would then be unable to comply with the Ph. Eur. texts.

PFAS reagents are used in more than 170 texts (monographs and general chapters). Of these, 100 prescribe the use of TFA.

Recommendations:

The ECHA is asked to clarify whether the PFAS referred to as substances for pharmaceutical use (active substances or excipients), as impurities and as reagents in the Ph. Eur., would also be temporarily exempted from the restriction, given the huge impact this is liable to have.

Should this not be the case, the EDQM would like to suggest that efforts and discussions among stakeholders on this matter should be co-ordinated in order to define timelines for implementation that would allow alternative substances for pharmaceutical use and reagents to be developed.

Developing alternatives and/or revising monographs that are legally binding quality standards in 39 countries and beyond are complex processes that require resources and time. It is therefore crucial to take these factors into consideration, as well as the impact such decisions may have on the medicines supply chain, a priority issue at European level (among others).

2.2. Impact of the proposed restriction on the establishment of reference standards

PFAS for which a reference standard has been established

The EDQM produces reference standards whose use, when described in a Ph. Eur. monograph, becomes mandatory. The material used to produce reference standards can be an active substance, an excipient or an impurity. The restriction proposal may have an impact on the procurement of the PFAS used to produce reference standards, with a knock-on effect on users, i.e. manufacturers and Official Control Medicines Laboratories.

It is important to note that more than 70 chemical reference standards would be impacted.

Recommendations:

The ECHA is requested to clarify whether the exemptions foreseen in article 67 of the REACH regulation and/or in paragraph 5 (t) of the proposal apply to reference standards. Should this not be the case, the EDQM would like to suggest that the exemptions should be extended to include its reference standards.

PFAS used in articles – vial stoppers/septa used for reference standards

Polytetrafluoroethylene (PTFE) and derivatives are found in all vial stoppers/septa. PTFE is mostly used as a protective layer to avoid chemical reactions between closure components and contents and then prevent or limit both substance degradation. More than 90% of EDQM reference standards, i.e. more than 2500 reference standards, are supplied in glass vials with a PTFE (or derivative)-coated stopper or septum. Due to the recognised and validated properties of PTFE as protective layer, very few PTFE-free substitutes exist on the market and not all may be suitable for the EDQM's needs. The resulting lack of appropriate packaging materials could severely affect the production and availability of EDQM reference standards, with the supply chain consequences already described above.

Recommendations:
Given the huge impact of the restriction proposal, the ECHA is requested to consider an exemption for vial stoppers/septa for reference standards.