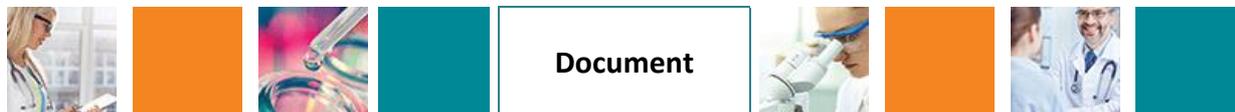


EFPIA position on the ECHA Microplastics restrictions

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Background

End of January 2019, ECHA published an Annex XV restriction proposal¹ with regard to intentionally added microplastic in consumer and professional products and its impact on the environment.

Restrictions are normally applied to limit or ban the manufacture, placing on the market (including imports) or use of a substance, and can impose additional requirements such as technical measures or specific labels.

ECHA's definition of microplastic is very broad. Plastic is not defined as such, and ECHA uses the definition of polymers (REACH Art 3.5). The use of synthetic polymers in medicinal products for human and veterinary use is derogated from ban, but intricate labelling and reporting is required.

With this paper, EFPIA would like to outline its position on ECHA's Annex XV proposed restriction of intentional use, reporting and labelling of microplastic and the implication it could have for the pharmaceutical industry.

Impact on the Pharmaceutical Industry and EFPIA's Position

ECHA's proposed definition of microplastic comprises all solid polymers at ambient conditions with a particle size smaller than 5 mm in all dimensions. Not subject to the restriction are naturally occurring, not chemically modified polymers, and (bio)degradable polymers according to interim criteria set out in the Annex XV dossier.

Use of Synthetic Polymers in Medicinal Products

ECHA's broad definition of microplastic puts a significant number of excipients used in the pharmaceutical industry and listed in the European Pharmacopoeia into scope of the restriction (e.g. cellulose acetate, hydroxypropylcellulose, polyvinylpyrrolidone, hydroxypropylmethylcellulose phthalate, polymethacrylates, polyethyleneglycol, and microcrystalline cellulose). Excipients are essential constituents in the formulation of medicinal products.

The European Pharmacopoeia includes an adopted list of excipients which are approved and safe for use in drug products; these are polymers in many cases. Excipients listed in pharmacopoeias show a good safety profile with regard to human or animal health and are comprehensively tested in accordance with the required safety studies for approval of drug products.

Furthermore, under European pharmaceutical law, the use of excipients depicted in monograph(s) of the pharmacopoeias, e.g., but not limited to, European Pharmacopoeia, is favoured. The requirements for the submission and approval of drug products are regulated in the EU guidelines and processes overseen by the European Medicines Agency (EMA) and health authorities of the EU member states which include proven safety and efficacy. Formulating a drug product is a complex task in which different factors like drug transport, drug release, uniformity (of content), hardness, and also shelf life have to be considered,

¹ [ECHA's restriction proposal Annex XV dossier](#)

as well as patient (human and animal) acceptance. The formulations of certain active pharmaceutical ingredients (API) need compensation of undesired physicochemical properties in order to improve the producibility, pharmacokinetic profile and the therapeutic effect. The use of polymers is very broad in medicinal products as they provide solutions to various API specific properties. There are limited alternatives to exchange polymers as excipients in medicinal products and the alternatives are not suitable for most formulations due to their inability to mimic the specific and necessary properties as outlined above. Therefore, the vast majority of solid oral dosage forms contain polymers.

Thus, changing the composition and formulation of a drug product once approved is an extremely involved process, in many cases substituting may not be possible due to changes in bioavailability &/or efficacy of the API. However, where changes may be viable extensive studies would be necessary which would take years to perform and may include bioequivalence studies, in addition to approval of variation of one or multiple authorities responsible for drug product approval in respective markets.

To conclude, EFPIA would like to stress that a restriction on the use of polymers will affect most solid form drug products for human or veterinary use, and potentially other dosage forms. This would have severe impact on the availability of drugs in Europe, and patients' safety. As such, EFPIA welcomes the derogation of medicinal products for human and veterinary use from the restriction of intentionally added microplastics.

Reporting

ECHA's draft restriction proposal requests reporting of the used excipients, which are considered as microplastics under the ECHA definition. Such reporting is required to be performed on an annual basis and includes: the identity, the use and quantity of the polymer, and the estimated quantity released to the environment. In EFPIA's point of view, this raises a high bureaucratic burden for the pharmaceutical sector without any benefit to the patient or environment. Volumes of polymeric excipients are expected to remain the same over time due to their importance for e.g. oral dosage forms. Polymers have been essential to the formulation technology of medicinal products for decades. New excipients on the market for tablets are limited and any additions will most likely only have minor structural edits by cross linking of existing polymers or differently modified cellulose backbones but all fall under the broad definition used for microplastics.

Labelling

According to the EU pharmaceutical law, the package leaflet contains a note on disposal of unused medicinal product. This information covers the labelling needs described in ECHA's restriction proposal. EFPIA therefore concludes that no revised package leaflet or any other additional labelling of medicinal products is needed.

Conclusion

The Pharmaceutical sector uses a variety of synthetic polymers e.g. derivatized celluloses, which would fall under the current very broad definition of microplastics by ECHA. These excipients, which are proven safe and would be difficult to replace, are critical to ensuring the uninterrupted supply of high quality and efficacious medicines of importance to patients.

We consider it inaccurate to define every polymer with a size < 5 mm as a microplastic. This definition would even include oligonucleotides, polysaccharides and peptides, when being chemically treated during manufacture. Even microcrystalline cellulose, as being chemically treated during the manufacturing process and commonly used in galenics, would fall under the definition of microplastic, while chemically untreated cellulose, also used in galenics, would not fall under this definition.

The key points and requests EFPIA would like to make to ECHA are:

- We strongly support the derogation of medicinal products from the REACH restriction.

- We believe the definition of microplastics, whereby it includes common polymeric excipients, would benefit from a refinement of the scope/definition.
- The requirements for reporting and labelling of medicinal products will entail a high bureaucratic burden for companies without a beneficial impact on society or the environment. To this point we ask that you support our proposal whereby current medicinal product labelling regulations are adequate to meet the requirements of ECHA's restriction proposal and the medicinal product derogation should extend to reporting requirements.