Extractable elements in plastic materials for pharmaceutical use (2.4.35.)

Supporting Information

I With the implementation of the ICH Q3D guideline on elemental impurities, the control of elemental impurities is undergoing a shift in paradigm, moving away from pure substance-based testing towards a holistic control strategy in the finished product¹. Parts of the Scope and the Introduction sections of the Q3D guideline are reproduced in the European Pharmacopoeia (Ph. Eur.) in general chapter *5.20. Elemental impurities*, which is rendered legally binding by a cross-reference in the general monograph on *Pharmaceutical preparations* (2619) for example. Plastic containers for pharmaceutical preparations and closures are covered by this general monograph.

These changes have made it necessary to review and adapt the actual testing of elements in plastic materials, containers and closures, based on whether the ICH Q3D guideline applies to these different categories.

The fishbone diagram given in the Q3D guideline indicates container/closure systems as potential sources of elemental impurities. Ph. Eur. General chapter 5.20 is thus also applicable to Ph. Eur. general chapters 3.2.2. Plastic containers and closures for pharmaceutical use, 3.2.2.1. Plastic containers for aqueous solutions for infusion, and 3.2.9. Rubber closures for containers for aqueous parenteral preparations, for powders and for freeze-dried powders.

Even if plastic materials for the manufacture of containers for pharmaceutical preparations (3.1 and subsections) are not directly in the scope of the guideline, their quality still influences that of the containers manufactured from them, as they are used earlier in the container manufacturing process. It is thus proposed that the long-established individual tests for specific elements are maintained in the general chapters on plastic materials.

With a view of updating the specifications for these elements, their contents were determined in extraction solutions of various plastic materials currently available on the European market and described in the Ph. Eur. The experimental results confirmed that each material had a unique elemental impurity profile, depending on the formulation and manufacturing process. Batch data also showed the ubiquitous presence of further 10 elements which were not intentionally added. The control of these 10 elements is considered useful and is proposed in this general chapter.

It is foreseen that a cross-reference to this new general chapter is made in each existing Ph. Eur. text on plastic materials in the future. As a start, a cross-reference is included in the new

¹ See EDQM press release: https://www.edqm.eu/sites/default/files/press_release_pheur_policy_on_elemental_impurities_update_january_2017.pdf

general chapters on COP (3.1.16) and COC (3.1.17), which are also published in Pharmeuropa (32.2 and 32.3).

Further, it is envisaged to revise all the existing Ph. Eur. general chapters on plastic materials to delete the heavy metals test and to perform the tests on target elements according to this general chapter (2.4.35).