

<661> PLASTIC PACKAGING SYSTEMS AND THEIR MATERIALS OF CONSTRUCTION

INTRODUCTION

Systems are used to package therapeutic products (pharmaceuticals, biologics, dietary supplements and devices). Such systems and their associated materials and components of construction are considered and defined in *Packaging and Storage Requirements* <659>. Such systems may be constructed from plastic materials and components. The plastics used in packaging systems are composed of homologous polymers with a range of molecular weights and contain additives such as antioxidants, stabilizers, lubricants, plasticizers, colorants, and others. The nature and amount of additives in the plastics used for packaging systems are dictated by the type of polymer, the polymer's use, and the process used to convert the polymer into components, containers, or packaging systems.

Therapeutic products come into direct contact with packaging systems and their plastic materials of construction as the product is manufactured, stored, and administered. Such contact may result in an interaction between the therapeutic products and the packaging systems and its materials or components of construction. These interactions must be such that the suitability for use (including its safety and efficacy) of the therapeutic product and the packaging systems is not adversely affected by the interaction. Although suitability for use includes several quality aspects of the packaged drug product and its performance, the suitability for use aspect addressed in this chapter is patient safety. Obtaining such a necessary and desirable outcome is facilitated by the use of well-characterized plastic materials of construction in components, containers, and packaging systems and by the appropriate testing of packaging systems.

SCOPE

Establishing the suitability of plastic packaging systems for therapeutic products involves multiple tests and testing procedures, as briefly outlined below:

- **Material screening:** Characterization of a packaging system's materials of construction to evaluate ingredients as probable extractables and potential leachables. Such a characterization facilitates the identification of materials that are suitable for use in packaging systems.
- **Controlled extraction (simulation) study:** Worst-case controlled extraction (simulation) study to determine the extent to which extractables may become probable leachables (for additional information, see *Assessment of Extractables Associated with Pharmaceutical Packaging/Delivery Systems* <1663>).
- **Product assessment:** Actual-case measurement of confirmed leachables in the therapeutic product in the pharmaceutical packaging/delivery system intended for the commercial market (for additional information, see *Assessment of Drug Product Leachables Associated with Pharmaceutical Packaging/Delivery Systems* <1664>).

Additionally, information provided by the vendor(s) of plastic packaging systems and their associated materials or components of construction can facilitate suitability assessments, as such information may be appropriate additions to or surrogates for the results obtained by performing the tests noted previously.

The process of manufacturing a packaged therapeutic product is complex. Considering the packaging system specifically, packaging systems typically consist of components that are individually manufactured from plastic materials of construction. These individual plastic materials of construction are initially generated from reagents that are reacted to produce a base polymer, which is then compounded with various additives to produce a base resin. Individual base resins either are materials of construction themselves or may be combined with additional additives and processing aids to form a plastic material of construction. Testing of these plastic materials of construction to establish that they are well characterized and suitable for use, specifically considering safety, in packaging systems is within the scope of this series of chapters and is addressed in *Plastic Materials of Construction* <661.1>.

Individual plastic materials of construction are combined to form components of the packaging system. The packaging system is completed by assembling its various components into its final form. Testing of packaging systems to establish that they are suited for their intended uses, specifically considering safety, is within the scope of this series of chapters and is addressed in *Plastic Packaging Systems for Pharmaceutical Use* <661.2>.

Assembled packaging systems are filled to contain the therapeutic product by various means and at various points in the packaging system manufacturing process, thereby generating the packaged therapeutic product. Testing of packaged therapeutic products to establish that they are suited for their intended uses is addressed in compendial monographs relevant to the specific therapeutic product and falls outside of the scope of this series of chapters.

For more information on the scope of, applicability of, and other topics related to the <661> suite of general chapters, see *Evaluation of Plastic Packaging Systems and Their Materials of Construction with Respect to Their User Safety Impact* <1661>.