Drug development

Navigating updates to USP testing guidelines for plastic labware

Introduction

Plastic labware offers many advantages in scientific laboratory work, from single-use applications to being less breakable than glass. Laboratory plastics are also available in many distinct types, from polystyrene to polypropylene to fluorinated polymers and more, making it easy to find a product for a particular application with the necessary characteristics, such as chemical resistance. Plastics are made by converting the appropriate monomers to polymers. This process can sometimes involve using catalysts (which may contain metal ions) or other additives, such as clarifiers, antioxidants, or stabilizers, that impart necessary functions to the plastic. These additives may potentially be released from the plastic, depending on environmental and use conditions. Extractables, compounds that are released under extreme or harsh conditions, demonstrate the worst case of chemicals that might emerge from the plastic, while leachables are chemicals that migrate from the plastic during regular use. In the pharmaceutical field, monitoring extractables and leachables (E&Ls) in plastic containers is of particular importance because these substances may impact the effectiveness or efficiency of manufacturing a drug product, and potentially adversely affect its quality and safety.

Revisions to USP testing guidelines for plastics

The United States Pharmacopeia (USP) has developed guidelines to ensure that plastics do not affect the safety or effectiveness of pharmaceutical products. For example, plastic packaging could include a leachable that interacts with a drug product.

The USP has developed several chapters outlining guidelines for how to best characterize the plastic used in a drug's manufacturing and storage. Understanding the needs of the pharmaceutical field, Thermo Fisher Scientific has worked to incorporate some of these characterizations of our plastic products and to provide the results to our customers.

Originally, USP chapter <661> provided guidelines to evaluate the identity of the plastic and presence of heavy metals and nonvolatile residue (NVR) as potential E&Ls. These guidelines were recently revised, and USP chapter <661> is being replaced with USP chapters <661.1> and <661.2>. Anticipated to be implemented in December 2025, these updates outline a risk-based approach to classifying plastic materials to ensure minimal influence on downstream processes of drug manufacturing.

Testing of plastic materials

Process overview

The guidelines in USP chapters <661.1> and <661.2> can be viewed as a funnel-shaped process that pharmaceutical companies can follow to verify that the plastic packaging does not impact the drug product (Figure 1). At the top of the funnel is USP chapter <661.1>, Plastic Materials of Construction, which focuses on characterization of the plastic resin (the simplest component). At the middle and more narrow part of the funnel is USP chapter <661.2>, Plastic Packaging Systems for Pharmaceutical Use, which describes the procedure for assessing the plastic material both as the packaging system and to ensure it does not interact negatively with the drug product. To further evaluate the plastics used in drug product manufacturing, there is also USP chapter <665>, Plastic Components and Systems Used to Manufacture Pharmaceutical Drug Products and Biopharmaceutical Drug Substances and Products. This chapter is at the bottom part of the funnel because it extends upon the risk assessment from USP chapters <661.1> and <661.2>, focusing on risk-based E&L analysis of the finished good product as it relates to the drug manufacturing process.

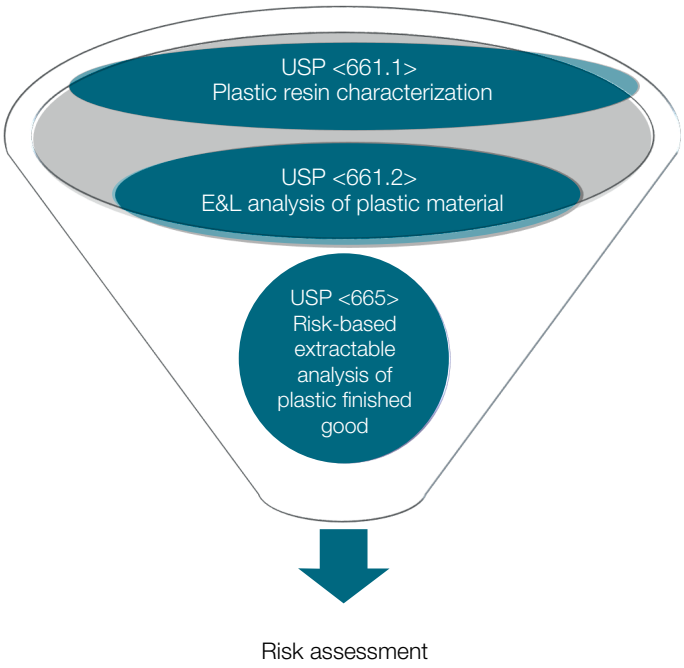

Figure 1. Multistage process outlined by USP guidelines for characterizing and assessing the safety of using plastic materials in the manufacturing and storage of pharmaceutical drugs.

USP chapters <661.1> and <661.2>

USP chapter <661.1> describes the procedure and specifications for evaluating plastic materials used for drug packaging systems. The screening tests outlined in USP chapter <661.1> are used to ensure that the plastic resin is an appropriate candidate for its intended use as a construction material. The chapter specifically names eight classes of resins; many of these resins were described in the original <661> chapter, though there are new additions to <661.1> such as cyclic olefins. The goals of the tests are to (1) obtain conclusive identity of the resin, (2) quantify general physicochemical properties, and (3) quantify the presence of 12 plastic additives. Additional testing for extractable elements (USP chapter <233>) or biological reactivity (USP chapter <87>) might be applicable depending on the dosage form or as deemed so by the end user. The results from <661.1> testing serve as one way for end users to make informed decisions on which material is appropriate in the intended application. More information about USP chapter <661.1> can be found on the USP website [1]. Further information can be found in USP chapter <1661> or from articles published by Smithers describing these new requirements [2]. USP chapter <661.2> details tests that can facilitate understanding of the packaging system's general physicochemical properties and its biocompatibility and chemical compatibility with the drug product. These tests involve studying the E&Ls and performing a toxicological assessment of the results. Depending on the application and drug product, the assessment of the extractables can vary. Although we cannot perform the testing outlined in chapter <661.2> as it requires knowledge of the drug product, we have undertaken those assessments outlined in chapter <661.1> for many of our plastic labware products and can assist customers by sharing those results.

USP chapter <665>

Scheduled to be enforced in 2026, this chapter outlines a risk-based approach to evaluating the chemical suitability of manufacturing components for their intended use by means of chemical testing and interpretation of the results based on suitability of use (such as toxicological evaluation). These manufacturing components may include items such as connectors, containers (like bottles or storage plates), filters, closures, and tubing. USP chapter <665> provides testing procedures to evaluate the extractable profile from the plastic manufacturing component, specifically from the finished good.

If there are later steps in the drug manufacturing processes that remove the extractable(s), the risk of using the item may be insignificant. However, the testing on the finished good is still important because knowing the extractable profile can help identify the risk in the event changes in the drug manufacturing process are implemented (e.g., eliminating the step that removes the extractable).

Based on the risk level, different solvents and testing procedures are recommended in evaluating the plastic manufacturing component. At the highest risk, components are recommended to be incubated with an acidic, basic, and organic solution. The time frame for each incubation varies depending on how the plastic component is utilized in the workflow, with the longest incubation time being 21 days. The incubation solutions are then analyzed for NVR, UV absorbance, and organic extractables. If deemed necessary, USP chapters <232> and <233> can be used for analyzing elemental extractables.

The goal of obtaining results from these procedures is to evaluate the risk and suitability of using the plastic component for an intended use within drug manufacturing. While results from assessments outlined in USP chapter <665> alone may not be enough to determine the suitability of a plastic product, the data can be used to reduce risk when choosing a product for the workflow. The results can be used as a gauge for which product could be best for use under the specific manufacturing conditions. More information about USP chapter <665> can be found on the USP website [1]. Further information can be found in USP chapter <1665> or from other organizations such as Smithers [3].

Supporting customers in pharmaceutical manufacturing

As part of our commitment to helping customers deliver the best science through quality products and to identify products best suited for the intended application, we have already adopted these guidelines and validated our USP <661.1> and <665> procedures. For our USP <665> procedure, we picked the highest-risk conditions for testing, even though we recognize that the actual application might put the plastic finished goods in a lower-risk category. Therefore, our USP <665> test summaries report the worst-case scenario. As a result of our early adoption, we can provide customers upon request with USP <661.1> test summaries for the resin, and USP <665> test summaries for selected products. Requests may be submitted to ROCRegSupport@thermo.com.

References

1. United States Pharmacopeia (USP). usp.org
2. Smithers (2021) USP <661> compared with USP <661.1> and USP <661.2>. smithers.com/resources/2021/august/usp-661-compared-with-usp-661-1-and-usp-661-2
3. Smithers (2021) USP <665>, USP <1665>, and BPOG extractables protocol—reviewing single-use technology (SUT) extractables and leachables (E&L) testing. smithers.com/resources/2023/june/reviewing-single-use-technology-(sut)-extractables

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