Material Matters:

New USP Requirements for Plastics and Elastomers

USP <382>, <661.1>, and <661.2>

White Paper

solvias

Introduction

Pharmaceutical packaging systems are essential to preserving the quality, efficacy, and safety of drug products throughout their lifecycle, from manufacturing and storage to transport, distribution, and administration. These systems do far more than simply contain the product; they act as a protective barrier against environmental factors and potential contamination, ensuring that patients receive medications as intended.

Many modern packaging systems, particularly those used for parenteral drugs, rely heavily on plastic materials. Commonly used polymers include polyethylene (PE), polypropylene (PP), polyvinyl chloride (PVC), and polyethylene terephthalate (PET), which are found in components such as bottles, caps, closures, and containers. In addition to plastics, elastomeric components are widely used, especially in injectable drugs.

However, the use of these materials introduces potential risks. Packaging components can interact with drug products over time, especially when exposed to stressors like temperature shifts, light exposure, humidity, and pressure. These interactions may lead to the leaching of substances into the drug product or, conversely, to the absorption or degradation of the drug by the packaging material. For this reason, pharmaceutical developers must perform thorough assessments of chemical, mechanical, and environmental compatibility to ensure the packaging does not compromise the product.

To support these evaluations, the United States Pharmacopeia (USP) has introduced a series of chapters that define the standards and testing requirements for plastic and elastomeric packaging materials. Three of these chapters — USP <661.1>, USP <661.2>, and USP <382> — are particularly critical and are **scheduled to become officially effective on December 1, 2025:**

USP <661.1>: Plastic Materials of Construction

USP <661.2>: Plastic Packaging Systems for Pharmaceutical Use

USP <382>: Elastomeric Closure Functionality in Injectable Pharmaceutical Packaging/Delivery Systems

With the implementation date quickly approaching, it is essential for pharmaceutical companies and their partners to fully understand the scope and requirements of these chapters. Preparing now, by reviewing current packaging systems, identifying gaps, and aligning testing protocols, will be key to maintaining compliance and avoiding costly disruptions in development, manufacturing, or regulatory approval.

The following sections of this white paper will delve deeper into the changes introduced by these USP chapters, their implications, and how to effectively implement them to ensure both regulatory adherence and product safety.

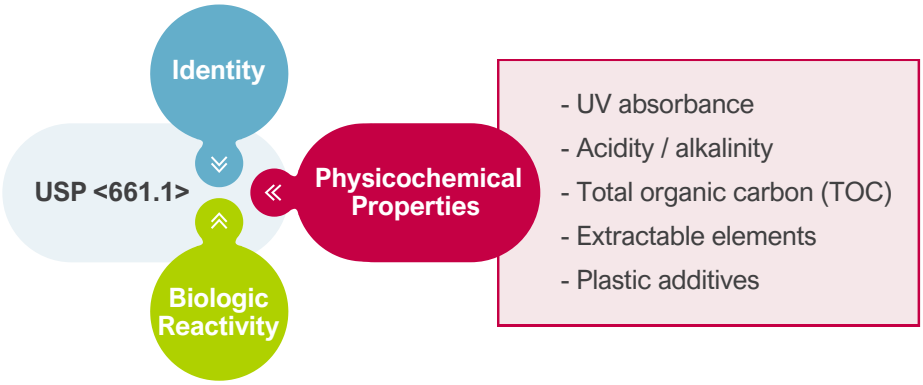
USP <661.1> & <661.2>

USP <661.1>: Plastic Materials of Construction

This chapter addresses the characterization of plastic materials before they are formed into packaging components. It contains tests, methods, and acceptance criteria for:

- Cyclic olefins
- Polyamide 6
- Polycarbonate
- Polyethylene
- polyethylene terephthalate (PET)
- Polyethylene terephthalate G (PET-G)
- Poly(ethylene-vinyl acetate)
- Polypropylene
- Polyvinyl chloride (PVC)
- Polyvinyl chloride (PVC) plasticized

Plastic materials not listed above are referred to as unaddressed materials.
For the purposes of this chapter, a plastic material of construction is considered to be well characterized for its intended use if the following characteristics have been adequately established:



USP <661.2>: Plastic Packaging Systems for Pharmaceutical Use

While <661.1> evaluates raw materials, <661.2> is focused on the final packaging system, outlining the criteria and methodologies for confirming that the packaging system is chemically and biologically suitable for its intended use. A packaging component or system is considered suitable under USP <661.2> if:

- Its general physicochemical properties have been established;
- Its biological reactivity has been appropriately established;
- It has been established to be suitable by means of the appropriate chemical suitability for use assessment.

Plastic materials are considered characterized and appropriate for use if they meet the requirements of USP <661.1> or are used in a packaging system that meets the requirements of USP <661.2>.

USP <382>:

Elastomeric Closure Functionality in Injectable Pharmaceutical Packaging/Delivery Systems

Elastomeric closures are designed to protect and contain the contents of a package while allowing safe and effective access at the time of use. USP <382> aims to assess their functional performance within the context of the final, assembled packaging system (rather than as standalone components) by considering factors such as the drug formulation, route of administration, delivery method, and overall product risk profile. The goal is to ensure that these closures are fit for real-world use and maintain product integrity throughout the lifecycle.

Packaging and delivery systems that incorporate elastomeric components include:

- Bottle and vial stoppers designed to be accessed with a needle or spike
- Plungers, needle shields, and tip caps used in prefilled syringes and cartridges
- Components for pen, jet, and related injector systems
- Lined caps for blow-fill-seal (BFS) plastic containers
- Access ports on plastic bags or blow-molded infusion containers

The specific function of an elastomeric component depends on the design and purpose of the packaging or delivery system in which it is used. However, regardless of the application, all elastomeric components serve as a seal protecting the drug product.

As such, all packaging systems for injectable products that are closed with elastomeric components must demonstrate their ability to prevent microbiological ingress, product leakage, and ingress of external liquid or solid matter, preserving the drug's physicochemical properties and maintain sterility.

Beyond these, additional functional expectations arise depending on how the packaging system is used.

In plunger-based delivery systems, such as prefilled syringes and cartridges, the elastomeric plunger must move smoothly to allow dose delivery on demand. Key performance attributes include:

Plunger break force:
The force required to initiate the movement of the plunger of a prefilled syringe or cartridge.

Plunger glide force:
The force required to sustain the movement of the plunger to expel the content of the syringe or cartridge.

Plunger seal integrity:
The ability of the plunger to maintain a fluid seal while under pressure.

Other elastomeric components are designed to be pierced, once or repeatedly, by a needle or spike. Additional relevant tests for these systems include:

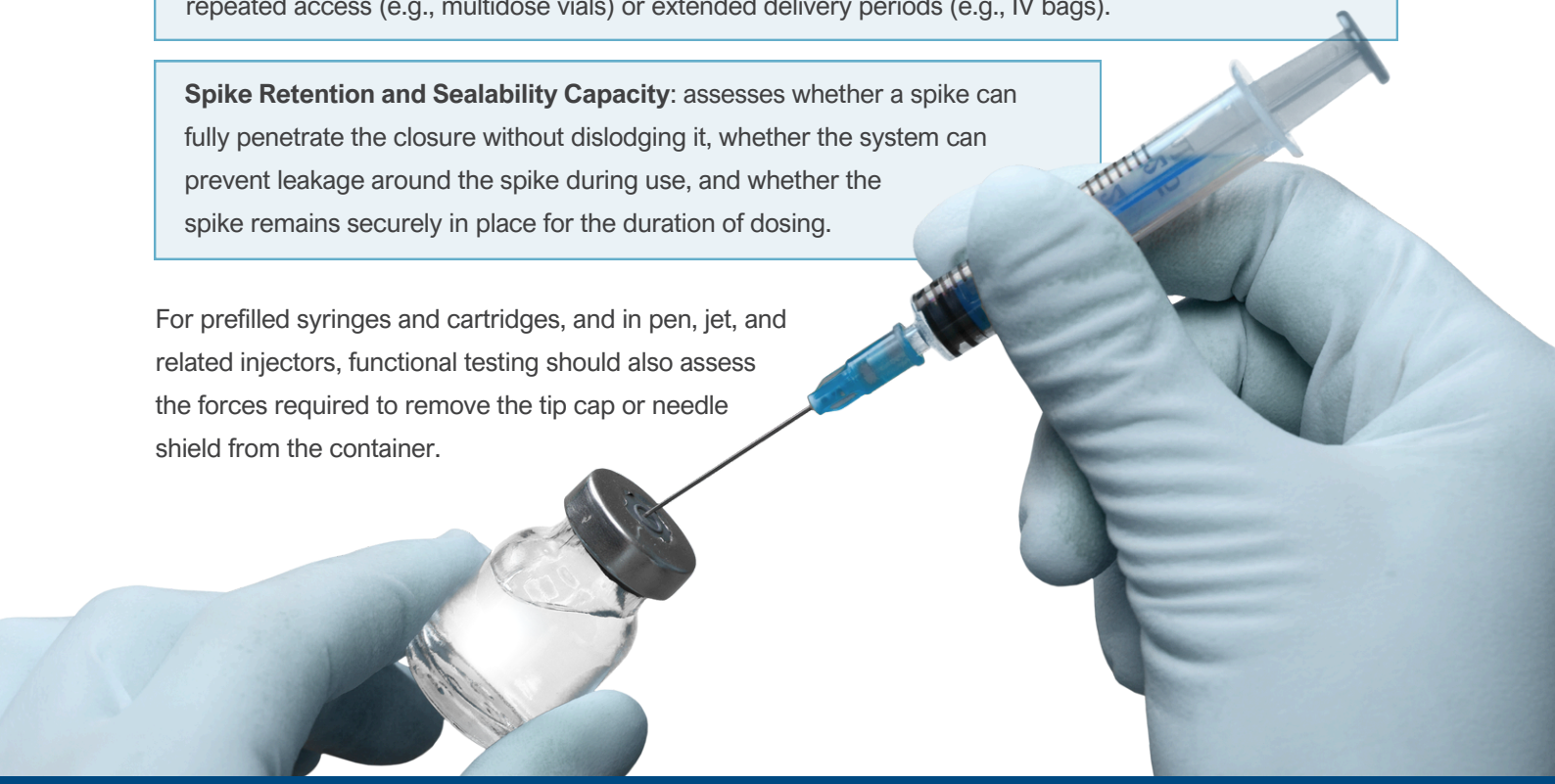
Fragmentation (also known as coring): a measure of the package's tendency to fragment or core when pierced by a spike or hypodermic needle. Any resulting particles could be injected into the patient, posing a safety risk.

Penetration Force (also known as penetrability): the maximum force necessary to penetrate the closure using a spike or hypodermic needle.

Self-Sealing Capacity (also known as reseal capacity or in-use leakage testing): the closure's ability to maintain some degree of integrity after piercing, which is particularly important for systems that allow repeated access (e.g., multidose vials) or extended delivery periods (e.g., IV bags).

Spike Retention and Sealability Capacity: assesses whether a spike can fully penetrate the closure without dislodging it, whether the system can prevent leakage around the spike during use, and whether the spike remains securely in place for the duration of dosing.

For prefilled syringes and cartridges, and in pen, jet, and related injectors, functional testing should also assess the forces required to remove the tip cap or needle shield from the container.



Beyond USP <661> and <382>

While this white paper focuses on the requirements introduced by USP <661.1>, <661.2>, and <382>, a complete qualification strategy for pharmaceutical packaging systems must also account for additional USP chapters. These chapters provide critical guidance on chemical safety, material compatibility, and the integrity of packaging systems, including in the context of parenteral and sterile products. Here are four key USP chapters that every developer should be familiar with:

USP <665>: Plastic Components and Systems Used to Manufacture Pharmaceutical Drug Products and Biopharmaceutical Drug Substances and Products

USP <665> applies to polymeric components used in single-use systems, such as bioreactor bags, tubing, connectors, and filters, many of which share materials with packaging components. This chapter defines requirements for material characterization, including extractables profiling and toxicological risk assessments. To better understand how USP <665> applies to both manufacturing systems and packaging development, explore our white paper.

Access the White Paper

USP <1207>: Package Integrity Evaluation for Sterile Products

Container closure integrity (CCI) is essential for maintaining sterility and product quality. USP <1207> provides an overview of probabilistic and deterministic methods for package integrity testing, such as dye ingress, helium leak detection, and vacuum decay. This chapter helps guide the selection and validation of appropriate CCI methods for both routine QC and product development. For more on how to implement robust container closure integrity testing strategies, including method selection and regulatory considerations, read our white paper:

Access the White Paper

USP <1663>: Assessment of Extractables Associated with Pharmaceutical Packaging/Delivery Systems

This chapter outlines a scientific framework for identifying and characterizing *extractables*, which are substances that can be generated in a laboratory by extraction from containers, closures, or other packaging by means of solvents or through stressed conditions.

USP <1664>: Assessment of Drug Product Leachables Associated with Pharmaceutical Packaging/Delivery Systems

Building on the findings from USP <1663>, this chapter focuses on *leachables*, which are chemical compounds that leach into the drug product from the containers, closures, or other packaging because of direct or indirect contact with the formulation. For a deeper dive into best practices, common pitfalls, and the financial risks of inadequate extractables and leachables (E&L) testing, see our white paper.

Access the White Paper

BONUS: Critical Testing Strategies for Autoinjector Drug Products

As demand for self-administered therapies accelerates, autoinjectors, formally known as automated needle-based injection systems (NIS-AUTO), are playing an increasingly central role in modern medicine. However, their dual role as both drug and device introduces a unique set of regulatory and performance challenges that must be addressed from early development through to commercialization.

This white paper outlines best practices and evolving regulatory expectations across four critical domains: functional testing, extractables and leachables (E&L), container closure integrity testing (CCIT), and stability testing.

Access the White Paper

Your Trusted Partner

The performance of your packaging system can make or break the quality of your drug product. At Solvias, we understand how critical it is to get this right. That's why we offer a comprehensive range of analytical and functional testing services specifically designed for plastic and elastomeric components used in pharmaceutical packaging.

Our teams bring together deep scientific expertise and hands-on experience with USP <661.1>, <661.2>, <382>, and related chapters. Whether you're evaluating raw materials, qualifying a new container-closure system, or troubleshooting an issue in development, we tailor our support to meet your goals and help you stay aligned with evolving regulatory expectations.

Analytical Testing for Packaging Materials

Solvias provides end-to-end analytical support for compatibility assessments, including:

- Spectroscopic Techniques: FTIR, UV, and NIR for material identification
- Thermal Analysis: DSC, TGA, TG-FTIR, DVS
- Chromatographic Techniques: HPLC, GC, GC/MS, HPLC-MS/MS, TLC
- Elemental Analysis: ICP-OES, ICP-MS
- Leak Testing: Container Closure Integrity Testing (CCIT), with both probabilistic and deterministic methods
- Silicone-Specific Methods: For evaluating siliconized components

We support full extractables and leachables studies, from study design to complete identification of unknowns.

Method Development and Validation

Our experts develop and validate routine ID tests and advanced custom methods, including:

- Release testing for standard packaging
- Support for non-conventional packaging formats
- GMP method validation for regulatory submissions
- Troubleshooting of packaging-related issues in development

Functionality Testing

We offer comprehensive mechanical and functional testing, including:

- Penetrability, fragmentation, and self-sealability
- Compression and puncture resistance
- Customized testing protocols for unique container-closure designs

Conclusion

Plastic and elastomeric packaging components are indispensable to modern pharmaceutical products. However, their safety and performance must be proven through rigorous testing guided by USP standards. Recent updates, such as USP <661.1>, <661.2>, <382>, and <665>, reflect the increasing complexity of pharmaceutical packaging systems and regulatory expectations. These changes underscore the responsibility of the manufacturer to ensure that packaging materials do not compromise the drug product's integrity, safety, or effectiveness.

Solvias stands ready to assist clients in navigating these evolving requirements. With deep scientific expertise, flexible testing capabilities, and a proven track record in regulatory support, we help ensure your packaging materials meet both compliance standards and business objectives.

For further information and details about these analytical testing services, or to get in touch with an expert, contact us at info@solvias.com.

Acknowledgements

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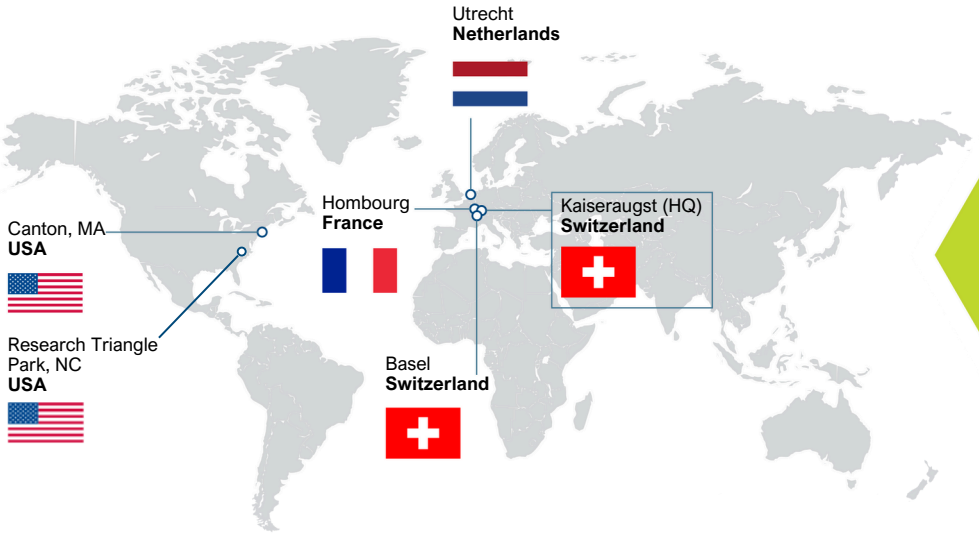

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