

The Importance of Understanding the Requirements for Pharmaceutical Elastomers

Selecting the appropriate primary packaging components for parenteral drugs is a key element for new product success. Many product attributes, such as stability, potency, safety and container closure integrity, could be negatively affected by an incompatible combination of drug product and primary packaging materials. This could hold up the drug development cycle, resulting in a delayed market entry.

To avoid such situations, pharmaceutical manufacturers should make sure that the primary packaging materials are compatible with one another and with the packaged drug. By working closely with the component manufacturer early in the drug development process, pharmaceutical companies can avoid costly packaging errors.

Requirements for pharmaceutical elastomeric closures can be found in various sources.

Pharmacopoeias

The leading pharmacopoeias define the requirements for pharmaceutical elastomers:

- a) Ph. Eur. 5.0
Section 3.2.9 "Rubber Closures for Containers for Aqueous Parenteral Preparations, for Powders and Freeze Drying Powders"

- b) USP 29
Section 381 "Elastomeric Closures for Injection"
Section 87 "Biological Reactivity Tests, in Vitro"
Section 88 "Biological Reactivity Tests, in Vivo"
- c) JP 14
Section 59 "Test for Rubber Closures for Aqueous Infusion"

DIN/ISO Standards

EN/ISO 8871 part 1-3

Regulatory Guidances

- a) "Guidance for Industry – Container Closure Systems for Packaging Human Drugs and Biologics" – United States Food and Drug Administration, May 1999
- b) "Guidance for Industry – Sterile Drug Products Produced by Aseptic Processing – Current Good Manufacturing Practice" – United States Food and Drug Administration, September 2004
- c) "Guideline on Plastic Primary Packaging Materials" – EMEA/CVMP/205/04, May 2005

In general, pharmaceutical elastomers must meet the compendial requirements, which are mostly limited to biological and chemical properties; the Ph. Eur. also describes physical testing. The DIN/ISO standards, in addition, address dimensional and functional properties.

Elastomeric pharmaceutical closures may be processed as ready-to-sterilize (RS)

or ready-to-use (RU) products. With RS and RU products, the component manufacturer performs some of the steps required to prepare stoppers for introduction into filling lines. The component manufacturer's processing must meet appropriate regulatory and cGMP requirements. In addition, qualification and validation of the washing/siliconization and, for RU products, the sterilization process is necessary. By selecting RS and RU components, pharmaceutical manufacturers benefit because they can eliminate some of the stopper preparation steps from their facilities.

Regulatory guidances for primary packaging materials also reference the occurrence of leachables that could migrate from the container closure system components into the packaged drug.

- a) "Guidance for Industry—Container Closure Systems for Packaging Human Drugs and Biologics" (Container Closure Guidance) – United States Food and Drug Administration, May 1999
- b) "Guideline on Plastic Immediate Packaging Materials" – EMEA, May 2005

Depending on the route of administration, drug product formulation, container closure system and if the material or construction is described in a monograph, extensive leachable migration studies should be performed. Examples of potential leachables include polymer stabilizers and residuals of the vulcanization system.

Lab Testing Can Help Speed Products to Market

More-stringent regulatory demands, in conjunction with decreasing time lines for drug development, are challenging companies' resources. To avoid costly delays and to manage resources effectively, drug manufacturers can turn to a contract laboratory for extractables and leachables testing, pharmaceutical stability studies and medical device analysis.

West Monarch Analytical Laboratories offers three testing packages: PakProfile®, PakScreen® and PakTox®.

PakProfile

A PakProfile study is the most extensive of the three offerings, as it includes a long-term extractables and leachables study over the shelf life of a biopharmaceutical product. The data collected help reveal the possible interactions between the primary packaging and the drug product. One such risk is aggregation or drug degradation caused by extracted materials from the packaging system interacting with the active ingredient, stabilizers or other auxiliaries used for drug production.

For setting up a specific test series for an application system, West Monarch would:

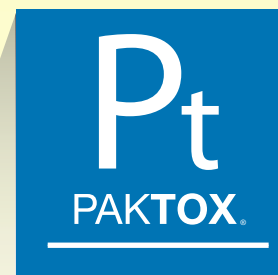


- Develop a quantitative test method for each extractable to be tested.
- Validate the test method in accordance with USP and ICH guidelines.
- Conduct tests on stability samples.
- Write a protocol approved by West Monarch Analytical Laboratories and the client before a study begins.

The testing begins after these steps have been approved by the customer. Progress reports are issued regularly.

PakScreen

A PakScreen study provides data to select appropriate primary packaging components for new or unique biopharmaceutical applications. It is an investigational screening and gross compatibility study recommended for drug products in Phase I clinical trials or prior to finalizing packaging options.



The customer provides bulk product for the study. The product is filled in the recommended package options which are stored under accelerated conditions to evaluate which package would be best for the customer's specific application. The testing takes about eight weeks.

PakTox

The PakTox service provides existing baseline toxicity profiles of potential extractables from elastomers that may leach into drug products, and provides profiles and risk assessment services for leachables detected in drug products. The PakTox packages provided by West are developed and reviewed by board-certified toxicologists and include a reliable resource of toxicology information. PakTox package helps biopharmaceutical companies to meet regulatory requirements easily.

West Monarch – An Experienced Analytical Laboratory

With its in-depth knowledge of the interaction and compatibility of drug products with elastomers, glass and plastic components and its state-of-the-art analytical techniques, West Monarch has the resources to conduct tests cost—effectively and efficiently.

By relying on West Monarch's analytical expertise, biopharmaceutical companies can focus their resources on what they do best – discovering and developing new drugs – and do not have to expend valuable resources to establish their own methods for extractables/leachables testing.

West Monarch is qualified to provide services in accordance with applicable cGMPs. The laboratories are FDA—registered, are approved to handle DEA Schedule I-V controlled substances and are equipped to handle most cytotoxic drugs.

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