

## Choosing a Prefillable System

### *The World of Prefillables*

The use of prefillable syringes for injectable drugs is increasing rapidly. Most in the industry expect continued growth, especially for biopharmaceuticals.

In this issue of *The Source*, we will take a look at the components that make up a prefillable syringe system. We'll also discuss testing issues unique to prefillable systems.

From October 23 to 25, West will participate in the Parenteral Drug Association's forum, *The Universe of Pre-Filled Syringes and Injection Devices*, in Bethesda, Md. West's technical experts will be available at Table 13 to answer your questions.

Fran DeGrazio, Vice President, Marketing and Strategic Business Development, will present at the conference on the topic "Unique Packaging Solutions for Prefillable Syringe Systems," October 23 at 2:15 p.m.

Also, Jennifer Riter, Manager of Technical Customer Support, will present a poster, "The Effects of Ozone and Various Sterilization Techniques on Elastomeric Needle Shields and Tip Caps."

We hope to see you there.

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Many drug manufacturers are marketing their new products in prefillable syringes. Prefillable syringes are convenient for health care professionals and others who administer injectables. They can help avoid misidentification of drugs, dosage errors and contamination. For the pharmaceutical manufacturer, prefillable syringes may eliminate the need for overfilling that is common with vials.

System components include a syringe barrel and a rod tipped with an elastomeric plunger. Some systems come with an attached needle that has a protective component, known as a needle shield. Others have a Luer lock connection that is protected by a tip cap.

Syringe barrels are manufactured from glass or a plastic, such as Resin CZ®, a cyclic polyolefin. Cyclic polyolefins are the preferred material for biopharmaceuticals, oncologic and toxic drugs where glass breakage is a concern. Resin CZ syringes, manufactured in Japan by Daikyo Seiko, Ltd., pass all major compendia including the physicochemical and biological tests of the USP and JP. Resin CZ also meets the Ph.Eur. physicochemical tests for polyolefins.

Further, Resin CZ syringes do not require siliconization to provide lubricity. Silicone can be a source of incompatibility and contamination to the packaged drug.

Plungers provide container closure integrity (CCI) for the packaged drug and create the impetus that forces the drug out of the syringe. They must be manufactured from a material that can maintain its chemical and physical properties for up to two years to help preserve the purity of the packaged drug throughout its shelf life.

Because the plunger contacts the drug, stability and efficacy can be adversely affected if the plunger is not compatible with the drug product. A plunger must minimize the drug's interaction with the component. One way to address this issue is a fluoropolymer barrier film that can reduce the risk of drug contamination. The film also provides lubricity, which may lead to lower amounts of silicone needed for functionality.

Needle shields and tip caps should be molded from an elastomer that resists cracking caused by exposure to ozone and is less susceptible to frosting or hazing. Cracked needle shields and tip caps cause unacceptable risks for patients and health care administrators and can result in costly product recalls. Cracks can cause leaks, resulting in a loss of drug potency.

Tip caps, like plungers, contact the packaged drug, so selection criteria should include an examination of the potential extractables and leachables in the component. Barrier films can be applied to the drug contact surface to minimize the risk.

To discuss the most appropriate prefillable syringe system for your drug product, contact Brian Brucker at 610-594-3334 ([brian.brucker@westpharma.com](mailto:brian.brucker@westpharma.com)) or Adrienne Williams at 610-594-3160 ([adrienne.williams@westpharma.com](mailto:adrienne.williams@westpharma.com)).



# Testing Components for Prefillable Syringes

Syringe plungers and tip caps are considered primary pharmaceutical closures because they contact the packaged drug. As such, these components should be subjected to extractables/leachables testing. In addition, most pharmaceutical manufacturers perform functional testing unique to plungers to make sure they perform adequately for the end user.

Plungers and tip caps help maintain the integrity of the packaged drug. The FDA has specified considerations for determining appropriate components in its guidance "Container Closure Systems Used for the Packaging of Human Drugs and Biologics" (May 1999), which discusses the possibility of interaction between the drug and the container and components. Testing components in early product development stages can reduce the risk of incompatibility of the drug and the packaging later in the development process.

## Extractables and Leachables Testing

Extractables are chemical species that migrate from packaging components or other components in an appropriate solvent under exaggerated temperature and time conditions. The data generated by extractables testing during initial package selection and compatibility studies can be used to help select appropriate syringe plungers and tips caps for a prefillable system.

Leachables are chemical species that migrate from packaging or other components under normal conditions or use, during the shelf life of the drug product, or during stability testing of the drug product. It is important to test for leachables because they may:

- Interfere with drug product assays
- Interfere with medical diagnostic tests
- Increase the total impurities to unacceptable levels
- React with other drug products, vehicles or excipients
- Increase the toxicity of the drug product

A program should test for the presence of residual tungsten, which may be the result of the process used to manufacture glass syringe barrels. Tungsten contamination is pertinent to protein-based drugs.

## Functional Testing

Container closure integrity and functional testing of syringe plungers should be conducted as complementary studies.

- Container closure integrity is evaluated by methylene blue dye ingress and egress testing of the seal between the syringe barrel and the elastomeric plunger. The seal between the plunger and syringe should contain the drug and keep environmental contamination from entering the syringe.
- Breakloose testing measures the force required to engage the plunger rod and start it moving down the syringe barrel. The initial movement should be smooth and not require undue pressure.
- Extrusion testing evaluates the travel of the plunger rod down the barrel during drug administration. The plunger should glide smoothly and should require consistent pressure as the drug is administered. The plunger generally requires a method of lubricity to achieve a consistent extrusion force.

Extractables/leachables studies and functional testing for prefillable syringe components will require time and a budget

that must be built into the early stages of product development. Planning for and performing this testing minimizes risk and contributes to a successful product launch.

Contact Brian Brucker at 610-594-3334 (brian.brucker@westpharma.com) or Adrienne Williams at 610-594-3160 (adrienne.williams@westpharma.com) for more information.

## Visit West at AAPS

The American Association of Pharmaceutical Scientists (AAPS) Annual Meeting and Exposition is a premiere event for biopharmaceutical professionals. This year's meeting runs from October 29 through November 3 in San Antonio.

As always, West will have a strong presence at the AAPS meeting. West's technical experts will be available in the exhibit hall at booth 227 to answer questions and demonstrate West's innovative products.

West's exhibit will feature:

- Reconstitution and Transfer Systems – easy-to-use product differentiation
- West FluroTec® barrier film – risk mitigation for packaged injectable drugs
- Westar® RU Ready-to-Use Components – sterile stoppers
- Resin CZ syringes – silicone-free, break-resistant systems for biopharmaceutical drugs
- West Monarch Analytical Laboratories – extractables/leachables, compendial and functional testing
- The Tech Group – manufacturing solutions for drug delivery systems

**To learn more, contact [adrienne.williams@westpharma.com](mailto:adrienne.williams@westpharma.com) (610-594-3160) or [brian.brucker@westpharma.com](mailto:brian.brucker@westpharma.com) (610-594-3334)**

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