

Optimizing Stopper Preparation

Because of their sensitivity and often poor solubility, many biopharmaceutical drug products are brought to market in lyophilized, or freeze-dried, form. Lyophilization extends the shelf-life of the drug, which may be unstable as a liquid.

In this issue of *The Source*, we will examine the effect of residual moisture in the elastomeric stopper on a packaged lyophilized drug and the impact of the stopper drying cycle after steam sterilization.

Because lyophilization is a costly and complicated process, selecting the appropriate vial and stopper is essential to market success. The packaging components must assure seal integrity and should maintain the purity of the packaged drug product.

We are pleased to share results from an ongoing study of elastomeric stoppers that is testing their effectiveness in protecting a lyophilized drug product from moisture absorption.

Previous issues of *The Source* are posted at westthesource.com. Call us or send an email and we will add you to the mailing list.



Protecting Against Moisture Absorption

Residual moisture in elastomeric closures can cause degradation of a lyophilized drug product. Pharmaceutical manufacturers typically wash, steam sterilize and dry the closures. This process drives moisture into the closure. If the drying conditions for the closure are not optimized, residual moisture can transfer into the lyophilized drug product over time.

Moisture can be introduced into a lyophilized cake from the elastomeric stopper and from the atmospheric headspace. Further, moisture can permeate through the stopper, a process known as moisture vapor transmission.

West Pharmaceutical Services is conducting a study of butyl and bromobutyl stoppers to determine their effectiveness in protecting a lyophilized drug product from moisture absorption. The study uses vials filled with lyophilized lactose, a compound chosen because of its hygroscopic properties.

Stoppers were autoclaved and then dried at three durations. The study will monitor the moisture content of the stoppers after initial sterilization and drying and at each time point over a three-year period. West will also evaluate the moisture levels in the lactose over the same time.

Test Observations

The study has shown that the residual water content of an elastomer is specific to that formulation. The longest drying time (8 hours) leads to the lowest stopper residual moisture content and provides the lowest cake moisture increase. Additional studies have shown that longer drying times do not affect the residual moisture content.

The study also shows that the dryness of a stopper may not limit the impact on the moisture content of the lyo cake. While butyl shows much lower residual moisture content after drying compared to bromobutyl, this is not reflected in the respective cake residual moisture content. After three months, cake moisture content is even higher for vials closed with a butyl stopper. An explanation for this is found in looking at the different moisture vapor transmission rates for both elastomer formulations.

For all samples, the study shows that moisture will migrate from the environment to the closure and consequently to the lyophilized cake over time. While it is important to optimize the drying time of closures to reduce residual moisture, it is also important to choose a closure formulation that will reduce the transfer of retained moisture to the lyophilized cake.

To receive a copy of this technical report or to discuss stopper options for your lyophilized drug product, contact Brian Brucker at 610-594-3334 (brian.brucker@westpharma.com) or Adrienne Williams at 610-594-3160 (adrienne.williams@westpharma.com).



Lab Adds New Instruments, Adopts New Name

West's laboratory has added instrumentation that provides clients with new, high-performance testing capabilities.

The laboratory has added a Lighthouse Instruments headspace pressure/moisture analyzer to measure and monitor moisture and pressure in parenteral containers that have been stoppered and sealed. The benefit of this system is fast, accurate, non-destructive testing that provides true stability analysis. The instrument is recommended for leak detection, measurement of moisture, container closure integrity testing, moisture permeability testing, stability testing (real

time and accelerated), and vacuum integrity testing.

The addition of a Waters Acuity Ultra-Performance Liquid Chromatography® instrument provides more sensitive testing to identify small amounts of extractables in elastomeric components. The instrument requires small quantities of compounds for sampling and a much shorter testing time compared to other LC/MS instruments.

The laboratory also recently adopted the name, West Analytical Services. The business unit had been known as West Monarch Analytical Laboratories since the acquisition

of Monarch Analytical Laboratory in 2005. West Analytical Services maintains laboratories in Lionville, Pa. and Maumee, Ohio.

"As the market changes and new technologies develop, we will change so we can continue to help our pharmaceutical customers manage their risk through development and commercialization as it relates to their packaging, delivery systems and devices," said Jennifer Riter, Associate Director, Analytical and Technical Services.

Free Tech Seminar Offered at AAPS

The American Association of Pharmaceutical Scientists (AAPS) Annual Meeting is a premier event for biopharmaceutical professionals. The 2007 meeting runs from November 12 through 15 in San Diego.

This year, West will present a free technical seminar, "Innovative Solutions for Injectable Drug Administration." The seminar will be presented on Tuesday, November 13, from 10:00 a.m. to noon. Topics include Solutions for Elastomeric Closure Control of Extractables; Technical Considerations for Plunger Placement into Syringes; and Characterization of Prefillable Syringe Systems for Biopharmaceutical Drug Delivery.

To register, go to westpharma.com/register.asp.

West will also have a strong presence at the AAPS exhibition. West's technical experts will be available in the exhibit

hall at Booth 908 to answer questions and demonstrate how West's innovative products can provide solutions to your product development challenges. West's exhibit will feature:

- VeriSure™ - components certified for extractables
- Safety and Administration Systems – needle-free reconstitution and transfer systems
- West FluroTec® barrier film – risk mitigation for packaged injectable drugs
- Westar® RU Ready-to-Use Components – sterile stoppers appropriate for direct entry into isolators
- Daikyo Crystal Zenith® syringes – silicone-free, break-resistant systems for biopharmaceutical drugs
- West Analytical Services – laboratory expertise for extractables/leachables, compendial and functional testing
- West Spectra™ seals – technologies for enhanced product safety

New Product is Certified for Extractables

West will introduce VeriSure components at the PDA Extractables/Leachables Forum, November 6 through 8, in Bethesda, Md.

VeriSure is a product and service offering that is certified for extractables, which allows manufacturers to eliminate costly, time-consuming testing upon product receipt. VeriSure components support the quality-by-design process because West assures that appropriate controls are in place throughout component manufacturing. To help minimize risk, customers can specify VeriSure stoppers with FluroTec barrier film and Westar ready-to-use or ready-to-sterilize processing.



VeriSure™

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

Visit West at westthesource.com



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