

PharmaED's

Register by  
July 1<sup>st</sup> and  
receive a \$300  
Discount!

# Container Closure Systems

*Strategies for Selection, Compliance and Mitigation  
of Extractables and Leachables Challenges*

SEPTEMBER 15-16, 2008, RADISSON-PLAZA WARWICK, PHILADELPHIA, PA

**Featuring Case Studies and Lessons Learned from Industry Experts!**

- Understand Current USP Standards for Container Closure Systems and Recent Changes
- Strategies for Evaluating, Selecting and Qualifying Materials for Container Closure Systems
- Examine Suitability for Use Considerations Associated with Extractables and Leachables
- New Methods for Determining Moisture in Container Closures
- Strategies for Integrity Testing of Container Closure Systems
- Examine Challenges and Case Studies in Container Closure Systems

**Plus In-Depth Pre-Conference Workshop:**

**Guidances, Regulations, and Requirements for Extractables and Leachables in Pharmaceutical Packaging and Devices**

**Featuring Representation From:**

United States Pharmacopoeia  
Baxter Healthcare Corporation  
Packaging Consulting and Training  
CardinalHealth  
Linda A Walker Consulting, LLC  
West Pharmaceutical Services

Eli Lilly & Company  
Bayer Health Care LLC  
NAMSA  
Ciba Expert Services  
Phase Technologies, Inc.



**PharmaED**  
RESOURCES, Inc.

Monday, September 15, 2008

8:45 *Chairperson's Welcome and Opening Remarks*

## IN-DEPTH PRE-CONFERENCE WORKSHOP

9:00 **Guidances, Regulations, and Requirements for Extractables and Leachables in Pharmaceutical Packaging and Devices**

Recently, the FDA and Health Canada have been increasingly asking for more information on extractables from packaging components and drug delivery devices and on leachables in drug products. This trend is being seen for both NDA's and ANDA's alike. The FDA Guidance, Container Closure System for Packaging Human Drugs and Biologics, is dedicated totally to packaging requirements. The FDA Guidance on Container Closure Systems (May 1999) specifies the extractables/leachables information that should be submitted for various types of drug products but does not clearly outline the steps necessary to obtain the information. This presentation will explore aspects of this guidance in relation to extractables and leachables and discuss the various ways the marketplace is addressing this area of evaluation. Overall guidance is given on the general approach industry is taking on this subject and what industry groups like PQRI are working on to get agreement from industry and regulatory agencies on what should be done.

- Understand how people in industry are interpreting the regulations and the demands of the government agencies for more information
- Learn what people in industry are currently doing to address this issue
- Clarify the differences between extractables and leachables, and why each is important to a regulatory submission
- Review case studies that brought the industry to this crossroads
- Practical points of consideration are given for different dosage forms
- Pulmonary and Nasal
- Injectables and Ophthalmics
- Open and candid question and answer session to talk about specific issues attendees are facing

### *About your workshop leader:*

Andrea Straka is a Technical Account Specialist for West Analytical Services. She helps her global customers develop solutions for their testing needs and helps them traverse the complex issues surrounding extractables and leachables. Andrea joined West in 2003, and prior to that worked in the pharmaceutical industry as an analytical chemist in Quality Control. Andrea holds a B.S. in Biology/Chemistry from Lock Haven University.

12:00 *Luncheon*

## USP UPDATE

1:30 **Current USP Standards for Container Closure Systems**

*Dr. Desmond G. Hunt, Scientist, Department of Standards Development (DSD), United States Pharmacopoeia*

In the past year, there have been several revisions to these chapters and there are more revision planned for the upcoming year. Thus, the speaker will outline some of the changes to date and talk about revision to be expected in the near future. He will also discuss USP's current standards that are used to qualify containers used to store pharmaceutical products.

- Current USP's standards for glass and plastic container
- Current standard for elastomeric closures
- Future revisions

## MATERIALS QUALIFICATION

2:15 **Strategies for Qualifying Materials for Container Closure Systems**

*David E. Albert, M.S., DPM, Ph.D, Senior Scientist II, NAMSA, Ohio Division*

An important step in the process of qualifying container closure systems is that of characterizing the materials and the chemicals that can migrate or extract. Which tests to use to establish initial qualification of materials will be discussed, as well as ongoing tests to monitor and evaluate consistency. Specific points to be discussed are:

- How to establish suitability of material
- What quality control tests to use on an ongoing basis

- How to deal with changes to materials
- Role of toxicological evaluation for the safety of extractables

3:00 *Refreshment Break*

## 3:15 **Evaluating and Selecting Polymeric Materials for Container Closure Systems**

**Michael A. Ruberto, President,  
Ciba Expert Services**

Plastics and elastomers are commonly used in the fabrication of components for container closure systems. The chemistries associated with these polymers can be quite varied and the inherent stability of these materials can differ depending on the type of substrate. In the presence of light, heat, oxygen, and other external environmental factors, polymers can degrade, leading to premature failure of the components. These degradation products can be sources of extractables and leachables. Additives and stabilizers are commonly added to these polymer systems to minimize this degradation as well as to impart other desired effects to the polymers such as improved processing characteristics, antistatic or antimicrobial properties, and color. However, if not compatible with the polymer, these additives can also be sources of extractables and leachables. Secondary packaging including the inks, curing agents, paper, and adhesives used in labels are very complex entities often with proprietary formulations of chemicals and solvents that must be carefully scrutinized when being used in medical packaging applications. This presentation will provide a brief overview of the issues associated with the use of plastics and elastomers for container closure systems and recommend some best practices for evaluating the needs of the pharmaceutical product and selecting the most suitable materials.

Topics covered will include:

- Selecting the best polymers, stabilizers, and colorants to meet the packaging requirements
- Techniques for evaluating the safety of these raw materials
- The merits of utilizing compounds that are already approved for food contact applications in the US and European Union

- Considerations for minimizing the risk of materials selection and streamlining the testing required for container closure systems made from these sources

## 4:00 **Container Closure Systems and Products Lifecycle**

**Dr. Mihaela Simianu, Manufacturing Science  
and Technology, Eli Lilly & Company**

This presentation will present a general overview of the qualification/validation activities for parenteral container closure systems over product life cycle. The container closure system is an intrinsic part of the parenteral product and essential to delivery and handling of the pharmaceutical product. It defines the closure, protection and functionality of a container while it ensures the safety and quality of the drug product over the product shelf life. Changes to components and materials, suppliers and processing flow are also part of product lifecycle. This presentation will discuss general aspects related to the parenteral container closure systems qualification & validation for their intended use. Case studies for implementation of the change to components and modernization of container closure systems for marketed products will be presented.

The implementation of change and the continuous improvement of primary packaging components are an important source of projects and activities to be appropriately managed at a manufacturing site. The presentation will provide case studies and models, which may be used to effectively introduce local and global changes to the container closure components in contact with parenteral products. The models can be applied to improve the materials process, update definition of components quality with suppliers, update components specifications and control strategies as needed to maintain product quality and the validation state of the container closure systems.

The models and case studies presented can be applied to improve the materials process, update definition of components quality with suppliers, update components specifications and control strategies for container closure systems.

4:45 *Close of Day One*

Tuesday, September 16, 2008

8:45 **Leachables from Container-Closure Systems: How to Detect, Measure, Assess, Reduce, and Manage**

*Edward J. Smith, Ph.D., Packaging Science Resources, Packaging Consulting and Training*

The management of Extractables & Leachables (E&L) from container-closure systems (CCS) has become a necessary part of the development and marketing of any new drug product. Although the primary goal of any E&L management program is to mitigate risk to the patient, the currently available guidelines are not always specific regarding the precise steps to take in this regard.

The first and most direct step in managing E&L is reduction via the choice of best available packaging components (i.e. CCS) and packaging conditions. This presentation will discuss the available guidelines and regulations and the work of the Product Quality Research Institute (PQRI) to quantify and specify the qualification process. Examples will also be presented to demonstrate how E&L issues can be mitigated through CCS choices and packaging conditions.

10:15 *Refreshment break*

10:30 **Suitability for Use Considerations Associated with Extractables and Leachables from Container Closure Systems**

*Dennis Jenke, Senior Baxter Research Scientist, Baxter Healthcare Corporation*

The general performance expectations for manufacturing, packaging and delivery systems used with pharmaceutical agents and products revolve around the concept of suitability for use. While the intrinsic safety of substances leached from such systems, as reflected in their ability to produce a toxic effect, is an important and widely studied aspect of suitability for use, there are additional considerations that must be addressed in order to establish that leached substances do not adversely affect the quality of a pharmaceutical agent or product. This presentation will:

- Delineate what these additional considerations are
- Review documented examples of these considerations

- Suggest methods by which these considerations can be identified and addressed
- Consider the practical aspects of using safety thresholds in extractables/leachables assessments

## DETERMINING MOISTURE

11:15 **A New Rapid and Nondestructive Method for Determining the Moisture in Closures**

*T.A. Jennings, Phase Technologies, Inc., K. Lomartire, CardinalHealth*

This presentation will describe a new rapid nondestructive method for determining the residual moisture in elastomer closures used to manufacture lyophilized products. The means for correlating the moisture content determined by the Karl Fischer method to the dielectric properties will be shown.

Moisture data in the form of a histogram and frequency distribution will be shown for a large number of closures as they are received from the closure manufacturer, after sterilization and after drying in an oven. The results of a study of the absorption of moisture by the closures at a given temperature and relative humidity as a function of time will be presented. Those attending this presentation will learn the following key points:

- That determination of the residual moisture in elastomer closures no longer needs to be destructive and a time consuming task.
- No longer are the number of closures limited to perhaps just three but the moisture in hundreds of closures can be determined in the time it now takes to determine the moisture in just one closure by the Karl Fischer method
- Use of a histogram allows one to develop an optimum closure drying process that will ensure that the moisture in all of the closures is within the specified limits.
- Closure moisture in terms of a frequency distribution allows one to assess the risk of having closures with excess moisture being used in the manufacture of a lyophilized product and is vital in meeting PAT guidelines.

- Understanding how long a sterilized dry closure can be exposed to the manufacturing environment before it is no longer viable to be used as a seal will be an important consideration in the manufacturing of lyophilized products.

12:00 Luncheon

## INTEGRITY CONSIDERATIONS

1:30 **The Effects of Temperature and Other Environmental Factors on Closure Integrity**

*Linda Walker, President,  
Linda A Walker Consulting, LLC*

The integrity of a container closure system is impacted in many ways by a variety of shipping and distribution hazards – vibration, top load, temperature, gas permeation, partial pressures and others factors. Dispensing systems, child-resistance, torque, and gas expansion can all be affected by various distribution and storage conditions, alone or in combination. This presentation will take a look at a few real life examples, as well as some ways to model these hazards in the laboratory. By creating a test matrix in the early stages of a new product or package launch you can assure the package will perform through its useful life.

2:15 **Understanding the Impact of Process Variation on the Integrity of the Container-Closure System**

*Myles Striebich, Manager – Packaging Technology, Bayer Health Care LLC*

- Identify and understand the process variables in the manufacture, converting, and packaging of container-closure systems with associate packaging components
- Establish limits on critical to function features and parameters based on design and process capability
- Develop meaningful specifications and controls that will ensure the suitability of the container–closure system for the intended drug product
- Establish a base line for container-closure system qualifications.
- Mitigate risk of out of specification (OOS)
- Optimize production efficiencies

3:00 *Refreshment Break*

## EVALUATING MATERIALS

3:15 **Evaluating and Selecting Materials for Container Closure Systems**

*Jeff Smythe, Manager, Technical Customer Support, West Pharmaceutical Services*

A great deal of time, effort and research go into the formulation and preparation of drug products. Often, the selection of packaging materials is considered late in the development cycle.

The processing and selection of packaging materials, in particular, the elastomeric closures play a critical role in preserving the drug product over the intended shelf life. Factors to consider include the materials of construction, leachables / extractables, physical properties required films and coatings and others.

Different elastomeric closure formulations and configurations possess different chemical, physical and functional characteristics. Choosing the right closure for your product is critical. During the presentation, we will review rubber formulations and ingredients, recommended configurations, films and coatings, processing parameters, and trends in closures and closure manufacturing.

Careful selection of appropriate closures and optimization of processing cycles can help reduce product development time and yield more robust packaging solutions.

## PANEL DISCUSSION

4:00 **Challenges and Case Studies in Container Closure Systems**

In this session, attendees will have the opportunity to pose scenarios and questions to conference faculty. Bring your container closure challenges with you to discuss during this interactive session.

4:45 *Close of Conference*



**About your conference destination:**

The Radisson-Plaza Warwick is located in the heart of downtown Philadelphia, and adjacent to beautiful Rittenhouse Square. From the conference venue, you can access many points of interest in Philadelphia including Independence Hall, the Kimmel Center and the Avenue of the Arts and numerous shops, hotels and excellent restaurants!



**REGISTRATION INFORMATION**

Register for the conference using one of four options:

Online: [www.pharmaedresources.com](http://www.pharmaedresources.com) Phone: (217) 355-7322 Fax: (847) 589-0708

Mail: 2810 Robeson Park Drive, Champaign, IL 61822

**PLEASE COMPLETE THE FOLLOWING:**

FIRST NAME: \_\_\_\_\_

LAST NAME: \_\_\_\_\_

TITLE: \_\_\_\_\_

COMPANY: \_\_\_\_\_

ADDRESS: \_\_\_\_\_

ADDRESS: \_\_\_\_\_

CITY: \_\_\_\_\_ STATE: \_\_\_\_\_

ZIP: \_\_\_\_\_ COUNTRY CODE: \_\_\_\_\_

OFFICE PHONE: \_\_\_\_\_

MOBILE PHONE: \_\_\_\_\_

FAX: \_\_\_\_\_

E-MAIL: \_\_\_\_\_

*Please register me for:*

**CONTAINER CLOSURE SYSTEMS:**

**Strategies for Selection, Compliance and Mitigation of Extractables and Leachables Challenges**  
*September 15-16, 2008, Radisson-Plaza Warwick, Philadelphia, PA*  
**\$1,895 USD**

**REGISTER BY JULY 1<sup>ST</sup> AND TAKE \$300 OFF**

**PAYMENT METHOD**

CREDIT CARD REGISTRATION:

CREDIT CARD  VISA  MASTERCARD  AMEX

NAME: \_\_\_\_\_

CARD #: \_\_\_\_\_

EXPIRATION: \_\_\_\_ / \_\_\_\_

SIGNATURE: \_\_\_\_\_

BILLING ADDRESS: \_\_\_\_\_

CHECK REGISTRATION:

To pay by check, please provide a purchase order below. Please note that all payments must be received five (5) days prior to the conference to ensure space. Attendees will not be admitted to the conference without full payment.

PURCHASE ORDER #: \_\_\_\_\_

**PLEASE NOTE:**

PharmaEd Resources does not offer refunds. However, if you cannot attend after registering, we are happy to apply your registration fee to another PharmaEd Resources event, or transfer your registration to a colleague. Notice of cancellation must be received at least 5 days prior to the event.

**VENUE INFORMATION:**

**Dates:** September 15-16, 2008  
**Hotel:** Radisson Warwick Plaza Hotel  
**Hotel Address:** 1701 Locust Street  
Philadelphia, PA 19103  
**Reservations:** (888) 201-1718 US  
**Hotel Telephone:** (215) 735-6000  
**Fax:** (215) 789-6105  
**Email:** [rhi\\_plph@radisson.com](mailto:rhi_plph@radisson.com)