



**PDA 2010 Pharmaceutical Freeze Drying Workshop**  
**Current Science and Technology of Lyophilization**  
**November 17 - 18, 2010**  
**Sheraton San Diego Hotel and Marina | San Diego, CA**

**Wednesday, November 17, 2010**

➤ 7:00 a.m. – 5:30 p.m.

**Registration Open**

➤ 7:00 a.m. – 8:00 a.m.

**Continental Breakfast**

➤ 8:00 a.m. – 8:15 a.m.

**Welcome and Opening Remarks**

**Edward Trappler**, President, *Lyophilization Technology, Inc.* and Chair, 2010 Pharmaceutical Freeze Drying Program Planning Committee

8:15 a.m.-9:45 a.m.

**Session P1: Advances in Lyophilized Health Care Products: Past, Present and Future**

**Moderator: Edward Trappler**, President, *Lyophilization Technology, Inc.*

**Session Description:** Freeze drying processes for parenterals such as vaccines and other pharmaceuticals were developed on an empirical basis early as the 1930's to enhance product stability. The physico-chemical basis for understanding freeze-drying was developed since the 1950's to promote an understanding of the lyophilization methods and a growing number of potential products. In parallel, growth in the use of lyophilized clinical chemistry and diagnostic reagents provided means of evaluating the human condition and identify effective treatments. Greater understandings of the technology and the demand for new and ever expanding diversity of products, manufactured using robust processes were necessary. Increasing need for more efficient processing and GMP compliant manufacturing has spurred the development of the science and hardware required for contemporary approaches to developing and manufacturing lyophilized preparations.

These presentations will review the development of scientific principles, current industry trends and the horizons being created through recent developments. Recognizing where this unique sector of the industry has been and what lies ahead for the future is a meaningful reflection and precursor to understanding the future of lyophilized products.

8:15 a.m. - 8:45 a.m.

**Lyophilization of Diagnostic Products**

Industry Speaker Invited

8:45 a.m. - 9:15 a.m.

**Lyophilization of Parenterals**

**Edward Trappler**, President, *Lyophilization Technology, Inc.*

9:15 a.m. - 9:45 a.m.

**Q&A/Discussion**

➤ 9:45 a.m. – 10:10 a.m.

**Refreshment Break, Exhibits and Poster Presentations**

9:45 a.m. – 10:10 a.m.

**Poster Presentation**

\* *The following poster will be presented during Wednesday's refreshment breaks*

**Residual Moisture: Determining the Effect of Closure Composition and Drying Parameters on Lyophilized Product Moisture**

**Michael Gills**, Process Engineer, *West Pharmaceuticals*

10:10 a.m. - 11:40 a.m.

**Session P2: Product and Formulation Design**

**Moderator: Samir Sane, PhD**, Associate Director, Biologics Manufacturing Sciences and Technology, *Genentech, Inc.*

**Session Description:** Lyophilization continues to be a widely used method to preserve health care products or to convert them into a format that is more suitable for its intended use. It is often one of the final steps in the manufacture of a therapeutic or a diagnostic product. In fact, lyophilization is typically performed after the product has been dispensed in the final container that is presented to the end user. Thus, lyophilized product and formulation design involves many considerations of product stability and aspects related to its function, delivery, manufacturability and finished product attributes.

Advances in formulations and product presentations are introducing greater effectiveness and convenience for lyophilized preparations. The focus of these presentations is on the current trends in lyophilized product design and how these various considerations need to be balanced in order to deliver a commercially viable product that meets the needs of the final customer.

10:10 a.m. - 10:40 a.m.

**Unique Aspects of Diagnostic Formulation and Product Design**

Industry Speaker Invited

10:40 a.m. - 11:10 a.m.

**Parenteral Formulation for Oncology Products**

**Shanker Gupta, PhD**, Program Director, Pharmaceutical Resources Branch, NIC, *National Institute of Health*

11:10 a.m. - 11:40 a.m.

**Q&A/Discussion**

➤ 11:40 p.m. - 1:00 p.m.

**Lunch**

1:00 p.m.-2:30 p.m.

**Session P3: Aspects of Process Development**

**Moderator: Sidney Wolfe**, Principal, *DPD Consulting*

**Session Description:** Commercial production of a lyophilized product requires the development of a formulation and lyophilization process that produces an elegant dried product, sufficiently low moisture and readily reconstituted for routine manufacturing in an effective and efficient manner to achieve a maximum yield. The process to meet these requirements can be developed using the principles of Quality by Design (QbD). QbD as applied to the preparation of lyophilized drugs uses modern tools to understand critical properties of the drug formulation as well as the performance of the process equipment during development and production runs. Furthermore a lyophilization process developed using QbD determines, at a pilot scale, establishes the limits of lyophilization process control parameters necessary to maintain critical product temperatures. Even so, there are some product designs, such as formulations containing mannitol that present extraordinary challenges. Though not exclusively, mannitol based formulations are associated with a high incidence of vial breakage.

This session will provide a contrast between what could and should be accomplished during development and how the nature of a formulation often dictates the success achieved. The presentations will discuss how to analyze the thermal properties of formulations and use that information for development of a process and process limits for full scale implementation. Case studies will be presented for process development of the lyophilization process for formulations that require a detailed understanding of their glass and phase transition properties. Information will also be presented on how to modify formulations so that their thermal properties permit a wider range of processing conditions.

1:00 p.m. - 1:30 p.m.

**First Approach Applying QbD in a Scale-up of a Lyophilization Cycle for an Antiviral Product**

**Laura Noguera**, QA Manager, *Reig Jofre Group (Invited)*

1:30 p.m. - 2:00 p.m.

**Lyophilization Issues: Modification of Formulation and Process Parameters for Trouble-shooting**

**Enrico Corona**, Formulation and Process Development Manager, *Patheon Italia S.p.A.*

2:00 p.m. - 2:30 p.m.

**Q&A/Discussion**

➤ 2:30 p.m. - 3:00 p.m.

**Refreshment Break, Exhibits and Poster Presentations**

3:00 p.m. – 4:30 p.m.

**Session P4: Industrialization of Lyophilized Products**

**Moderator: Michael Radomsky, PhD, Director, Product and Process Development, Ben Venue Laboratories, Inc.**

**Session Description:** It is generally accepted that degree of supercooling, ice nucleation temperature and freezing rate impact ice crystal morphology, which in turn can affect drying rates during lyophilization operations. Several techniques that can provide insights into the relationship between nucleation temperature, drying rates and final product cake appearance have been studied, along with the development of a more systematic approach to lyophilization cycle development. A lyophilization process needs to be suitable robust to minimize the inherent heterogeneity within a batch and sufficient robustness in transferring a product from one lyophilizer or one manufacturing site to another.

As freezing is recognized as the most critical step of the process, and technology transfer is at times difficult at best, this session will explore these challenging aspects to control.

3:00 p.m. - 3:30 p.m.

**Techniques for Assessing the Effects of Ice Nucleation Temperature on Primary Drying Rate and Final Cake Morphology**

**Chris Heynes, Sr. Research Associate, Genentech Inc.**

3:30 p.m. - 4:00 p.m.

**Technology Transfer to an Alternate Manufacturing Site**

**Sidney Wolfe, Principal, DPD Consulting**

4:00 p.m. - 4:30 p.m.

**Q&A/Discussion**

- 4:30 p.m. – 6:00 p.m.  
**Networking Reception**

**Thursday, November 18, 2010**

- 7:00 a.m. – 10:00 a.m.  
**Registration Open**

- 7:00 a.m. – 8:00 a.m.  
**Continental Breakfast in Exhibit Area**

8:00 a.m. – 10:00 a.m.

**Session P5: Quality of Lyophilized Products**

**Moderator: Michael Radomsky, PhD, Director, Product and Process Development, Ben Venue Laboratories, Inc.**

**Session Description:** Quality aspects for lyophilized preparations of key interest are the residual moisture, physical appearance of the dried product along with assurance of the composition of the headspace and achieving container closure integrity. Residual moisture at the end of the process, along with maintaining the integrity of the container closure are two key considerations in maintaining proper product quality. Moisture is critical for long term stability of freeze dried materials. Headspace moisture can be used to gather information on the dynamics of water within a sealed vial containing freeze dried material. Discussions will also include an overview of available vacuum testing technologies for a better understanding of the application of NIR oxygen headspace technology for integrity testing of lyophilized vial.

The presentation includes the current knowledge base of water dynamics within the sealed vials. The role and dynamics of water could improve the current understanding which could assist in formulation design, process development and quality assurance. The session will also include experience in applying headspace analysis and the advantages and disadvantages of commercially available technologies for 100% inspection of lyophilized vials for vacuum maintenance.

8:00 a.m. - 8:30 a.m.

**Applications of Headspace Moisture Analysis for Investigating the Water Dynamics within a Sealed Vial Containing Freeze Dried Materials**

**Isobel Cook, Principal Research Scientist, Biopharma Technology Ltd**

8:30 a.m. - 9:00 a.m.

**The Use of Near Infrared Oxygen Headspace Technology to Assess Vacuum Maintenance in Lyophilized Vials**

**Fred Lim, PhD, Principal Engineer, Genentech Inc.**

9:00 a.m. - 9:30 a.m.

**Defining Physical Attributes of a Lyophilized Preparations**

**Wendy Sunderland, Associate Director, Technical Operations, Lyophilization Technology, Inc.**

9:30 a.m. – 10:00 a.m.

**Q&A/Discussion**

➤ 10:00 a.m. – 10:30 a.m.

**Refreshment Break and Exhibits**

10:30 a.m. – 12:00 p.m.

**Session P6: Current Regulatory Expectations**

**Moderator: Edward Trappler, President, Lyophilization Technology, Inc.**

**Session Description:** Industry initiatives are pushing for a greater level for knowledge and understanding of product characteristics and attributes gained during development, critical processing parameters in methods of manufacturing and critical quality attributes. Progressive innovators of new products are providing more and better quality data in submissions, indicative of their knowledge and understanding of their products and methods of manufacturing. As a consequence, more and better quality data passed on when a new product is integrated into manufacturing results in greater success in getting the new product to market. This can also be reflected in the observations noted by an independent assessment of the development, manufacturing and control in manufacturing a health care product.

An independent assessment is invaluable feedback in preparing to bring a new product to market and assuring that manufacturing operations are providing the highest quality product to the patient. Insight to critical considerations, along with a unique perspective and insight into the current status of the industry is the focus of this session. Hear from individuals knowing the level of development, science being applied and approaches for manufacturing as a benchmark to contemporary industry expectations.

10:30 a.m. - 11:00 a.m.

**FDA Perspective on Biologics Regulatory Submissions**

**David Doleski, Team Leader, CBER, DMPQ, FDA**

11:00 a.m. – 11:30 a.m.

**Inspection Trends: What You Should Know and Have In-place for Manufacturing**

**Sharon Thoma, National Expert Pharmaceutical Inspections, FDA**

11:30 a.m. – 12:00 p.m.

**Q&A/Discussion**

12:00 p.m. - 12:15 p.m.

**Closing Remarks and Adjournment**

**Edward Trappler, President, Lyophilization Technology, Inc. and Chair, 2010 Pharmaceutical Freeze Drying Program Planning Committee**