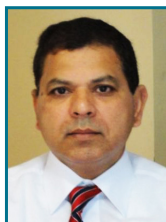


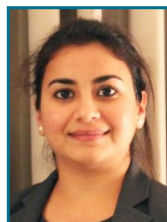
Lyophilization Forum 2017:

Formulation, Cycle Optimization,
& Emerging Freeze Drying Technologies
October 4–5, Racquet Club of Philadelphia, PA

Featured Speakers Include:



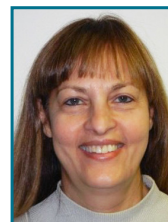
Padam Sharma
Senior Manager
Teva



Ekneet Sahni
Senior Scientist
Pfizer



Jamie Tsung
Assoc. Director
Alnylam Pharmaceuticals



Indu Javeri
President & CEO
CuriRx



Lokesh Kumar
Assoc. Scientist
Genentech

With Comprehensive Coverage On:

- Compliance and Regulatory Expectations for Lyophilized Products
- Process Validation for Lyophilized Drug Products: Developing a Program for Continued Process Verification
- Development of Lyophilization Cycle for Improving Stability of Liposome-based Nanoparticles
- Using Hydrogen Deuterium Exchange Mass Spectrometry (HDX-MS) for Lyophilized Protein Formulation and Process Optimization
- Biopharmaceutical Lyo Products: Scale-up from Development to Manufacturing
- Performance Of Conventional Borosilicate Glass Vials and Polymeric Vials for Lyophilization of Therapeutic Protein Formulations
- Considerations of Excipient Selection for Stable Lyophilized Product Development
- Tech Transfer & Scale Up in Lyophilized Vaccines
- Comparing and Contrasting Two Methods of Controlled Nucleation for use in Lyophilization: A Live Viral Vaccine (LVV) Perspective
- And Much More!

With the global lyophilization market expected to exceed \$2.6 billion in 2019, you cannot afford to miss this two-day intensive conference on the most recent innovations in pharmaceutical freeze-drying. At Lyophilization Forum 2017, you will hear the latest case studies in process optimization, scale-up and tech transfer, excipient selection, controlled nucleation, regulatory compliance, and much more.

With Representation From:



Wednesday, October 4, 2017

8:00 *Complimentary Breakfast & Chairperson's Welcome and Opening Remarks*

Spotlight on Regulatory Compliance

8:30 **Compliance and Regulatory Expectations for Lyophilized Products**
Karen Bossert, Ph.D., Pharma Consulting Services

The path from discovery to commercialization of a new drug product is a long, costly one that takes years of research and development. Innovator firms have a distinct challenge in deciding where to set the bar for regulatory compliance at each step along the development pathway, with quality requirements typically becoming more stringent as the product progresses in development through to commercialization. Along with regulatory guidance, the principles of Quality Risk Management can be applied to design and monitor appropriate quality systems to ensure product is suitable for its intended use in every phase of clinical development, and in commercial manufacture. This presentation provides an overview of compliance and regulatory considerations for lyophilized materials throughout the product lifecycle.

Technology Spotlight—Innovations in Freeze-Drying of Parenteral Products

9:30 **Lyophilization in Sterile Manufacturing of Injectables**
Padam N. Sharma, Ph.D., Sr. Manager, Injectables, Sterile manufacturing & Development, Third Party Operations, Teva Pharmaceuticals

Lyophilization (freeze-drying) plays a major role in the sterile manufacturing of injectable drugs, which are not stable in ready to use formulations and, therefore, have short shelf lives and expiry periods. The role of the lyophilization process in increasing the shelf life and expiry period of injectables while providing sterility assurance and container closure integrity will be discussed. This process is prominently used in the manufacturing of proteins, peptides and various biologics.

10:15 *Morning Coffee and Networking Break*

10:40 **The Latest Technology in Parenteral Product Filling and Freeze-Drying: Completely Enclosed Barrier Isolator Systems**
Jeff Schwegman, Ph.D., CEO, AB Bio Technologies

Traditional clean rooms for preparing parenteral drug products are quickly becoming a thing of the past. New technologies in modular clean rooms, barrier isolators,

and ready to use components are quickly becoming the norm for parenteral manufacturing facilities. The most recent advancements in barrier isolators removes human intervention completely by utilizing robots to aseptically facilitate vial/stopper handling, filling, stoppering, capping, and freeze-drying making the process cleaner and more efficient.

Scale-Up to Manufacturing: Challenges and Opportunities

11:25 **Tech Transfer & Scale-Up Challenges and Considerations for Lyophilized Products**
Adam Viverette, Associate Director, Manufacturing, Science & Technology, Melinta Therapeutics

This presentation will outline common challenges that are faced when executing technology transfer and scale-up projects for Lyophilized products as well as methods to mitigate and prevent these challenges. Several key considerations should be given during the project planning stage in order to complete a successful technology transfer and scale-up project. A successful technology transfer and scale-up project is achieved by the proper integration of the lyophilization process, sterile product and the Lyophilizer equipment. In addition, case studies and lessons learned from recent technology transfer and scale-up projects will be discussed. Key takeaways include:

- Common challenges faced when executing a tech transfer & scale-up project
- Considerations for a successful tech transfer & scale-up project
- Integrating Process, Product & Lyophilizer Equipment

12:10 *Complimentary Networking Lunch*

1:30 **Biopharmaceutical Lyo Products: Scale-up from Development to Manufacturing**
Lisa Hardwick, Research Scientist, Baxter Healthcare

This presentation will cover classic equipment and process related challenges during scale-up of a lyophilized product. Also discussed will be formulation and lyo cycle challenges that are unique to biopharmaceuticals

Critical Issues—Excipient Selection

2:15 **Considerations Of Excipient Selection For Stable Lyophilized Product Development**
Jamie Tsung, Ph.D., Associate Director, Alnylam Pharmaceuticals

Abstract Coming Soon

3:00 *Afternoon Coffee & Networking Break*



3:25

Use of Old and New Methods in Optimizing Freeze Drying Cycles

Paul Matejtschuk, Ph.D., Principal Scientist, NIBSC

New biological products make a continuing requirement for development and optimization of freeze drying cycles. While a number of technologies, both off-line and on-line already exist to help the lyophilization scientist, new and experimental methods are adding to our capabilities. I will describe two methods we have recently had experience with: an off-line dynamic mechanical analysis and an on-line impedance analysis and illustrate these with examples from our laboratory.

Research Spotlight—Controlled Nucleation Methods for Live Viral Vaccines

3:50

Comparing and Contrasting Two Methods of Controlled Nucleation for use in Lyophilization: A Live Viral Vaccine (LVV) Perspective



Morrissa Jones, Senior Scientist, Vaccine Product Development, Merck (Contributing authors: Ahkilesh Bhambhani, Daniel Roth, Robert Levin and Jeffery Blue).

One step in lyophilization that is important, but often overlooked, is the freezing process. Freezing is important because how the product freezes can directly effect how the product dries. By controlling the nucleation/freezing process, efficiencies in the lyophilization process can be observed, including shortened cycle times, improved cake appearance and consistency, and more homogeneous moisture levels.

Controlled nucleation, however, requires the product to be shelf frozen, thereby resulting in higher time in solution, which for certain vaccines may not be compatible. To determine the effect with a sensitive material like a LVV, two methods of controlled nucleation were evaluated: pressurization/depressurization technology (SP Scientific) and “ice fog” technology (Millrock Technology, Inc.). The technologies were evaluated first with placebos and then with two different LVVs: one with a low liquid stability requiring a flash freeze to maintain potency and a more stable vaccine that can be shelf frozen to determine if controlled nucleation can impart consistency while maintaining vaccine potency. Our results suggest that for a vaccine that has low liquid stability controlled nucleation is not a viable option due to the product taking a substantial potency loss during freezing. Additionally to be shared are the impact on cycle time, consistency, and moisture levels.

4:35

End of Day One

Thursday, October 5, 2017

8:00

Complimentary Breakfast

Critical Issues—Stabilizing Liposome Based Drug Delivery Systems

8:45

Development of Lyophilization Cycle for Improving Stability of Liposome Based Nanoparticles

Indu Javeri, Ph.D., President & CEO, CuriRx

This presentation is focused on utilizing lyophilization for stabilization of liposome based drug delivery systems. The major limitation in the widespread use of liposome drug delivery system is its instability. Lyophilization is a promising approach to ensure the long-term stability of liposomes. Freeze-drying of nanoparticles is a very complex process that requires extensive effort in developing the formulation and lyophilization process conditions. Many parameters of the formulation determine the success of freeze-drying due to the nanoparticle’s composition (type of polymer, type and concentration of surfactant, type and concentration of cryo and lyoprotectants, interaction between cryoprotectants and nanoparticles, surface modification of nanoparticles). Furthermore, the applied conditions of freeze-drying can impact the stabilization of nanoparticles during and after freeze-drying. Lyophilization overcomes poor stability by rendering labile nanoparticles in a solid form more tolerant of long-term product storage.

This presentation is designed as an introduction to a multifaceted program taking into account: a) the impact of varying freezing rates; b) physical dynamics of controlled temperature and pressure parameters for sublimation of water; c) the stability of the nanoparticle (physical and chemical), both drug and lipid (active and excipient composition); d) possible compromising of appropriate buffers, excipients and their chemical effect. Main take-aways from this talk include:

- Efforts required to develop a Lyophilized dosage form for liposomal nanoparticles
- Transfer, scale up and GMP manufacturing consideration during developing the lyophilized dosage formulation

Research Spotlight—Exploring Glass and Polymeric Vial Performance for Lyophilized Products

9:30

CASE STUDY

Performance Of Conventional Borosilicate Glass Vials And Polymeric Vials With Novel Silica-Coated Surfaces For Lyophilization Of Therapeutic Protein Formulations

Dr. Carly Fleagle Chisholm, Department of Chemical and Biological Engineering, University of Colorado, Boulder (Co-authors: Christopher M. Weikart, Theodore W. Randolph)

A common primary container for storage of parenteral drug products is the borosilicate glass vial. Disadvantages of borosilicate glass vials include delamination of glass particles and metal ion migration from the vials into drug formulations which may affect drug product stability and quality. Furthermore, high dimensional variability is characteristic of glass manufacturing techniques. In this study, we investigated the performance of a new generation of primary containers for lyophilization of therapeutic protein formulations. These novel containers are composed of cyclic olefin polymer (COP) whose inner surfaces are plasma-coated with a nanoscopic layer of silica and compared to conventional borosilicate glass vials. A high frequency of vial breakage was observed during lyophilization of borosilicate glass vials containing a high fill volume of a mannitol formulation, whereas all silica-coated COP vials remained intact. Particle concentrations in formulations contained in borosilicate glass vials that remained intact after lyophilization were significantly higher than those in formulations contained in silica-coated COP vials. Additionally, vial heat transfer coefficients (KV) were determined in order to design lyophilization cycles for pharmaceutically-relevant formulations in silica-coated COP vials. KV values for silica-coated COP vials were lower than those for borosilicate glass vials, but silica-coated COP vials had smaller standard deviations in KV. Minimal changes in the lyophilization cycle were needed to produce lyophilized formulations in silica-coated COP vials with similar residual moisture content to those in borosilicate glass vials. After lyophilization and reconstitution in silica-coated COP vials, no soluble aggregates were generated and particle concentrations in the micron-size range remained the same before and after lyophilization, whereas particle concentrations increased after lyophilization and reconstitution in borosilicate glass vials.

10:15

Morning Coffee & Networking Break

10:40

CASE STUDY

Determining and Using Kv for Transfer and Scale Up

T.N. Thompson, President, Millrock Technology

Transferring freeze-drying protocols between freeze dryers can be difficult due to differences in heat transfer characteristics. One successful method of transfer between freeze dryers is using the vial heat transfer

11:25

CASE STUDY

Elucidating Vial Breakage Mechanisms During Lyo Cycle Optimization Using Strain Gauges

Ekneet Sahni, Ph.D., Sr. Process Development Scientist, Pfizer

Abstract Coming Soon

12:10

Complimentary Networking Lunch

Technology Spotlight—Using HDX-MS in the Lyophilization Process

1:30

CASE STUDY

Using Hydrogen Deuterium Exchange Mass Spectrometry (HDX-MS) for Lyophilized Protein Formulation and Process Optimization

Lokesh Kumar, Ph.D., Associate Scientist, Genentech

This presentation will cover the following areas:

- Basics of Hydrogen Deuterium Exchange Mass Spectrometry (HDX-MS) to evaluate solid state protein formulation will be discussed.
- Use of HDX-MS to optimize the protein formulation will be demonstrated.
- Use of HDX-MS to optimize the lyophilization process would be shown. Special emphasis would be given to the correlation of the HDX-MS trend with the impact of controlled ice nucleation (vs uncontrolled ice nucleation) on stress stability of low protein lyophilized formulations.
- Applicability of HDX-MS technique to different protein formats will be demonstrated.

2:15

Innovative Container Closures Solutions for Lyophilized Drugs

Andrea Straka, Senior Specialist, Scientific Communications, West Pharmaceutical Services

Closure systems for lyophilized vials of drug products have not changed much in the last half century. The aluminum crimp seal has been a trusted secondary closure for much of that time. Recently, innovation in design has brought new options for in-chamber sealing immediately following the freeze-drying process delivering clear benefits to lyophilized drugs and the fill-finish process to:

- Preserve and protect sensitive drugs, safeguard vacuum and headspace by sealing vials before leaving the lyo chamber
- Secure the stopper in the vial to avoid raised or “pop-up” stoppers, and provide a buffer between the stopper and chamber shelves to prevent stopper sticking
- Simplify sealing by combining the lyophilization and capping processes into one step, reducing human intervention and product handling

This talk will review common issues in Lyophilization fill finish and alternatives that look to solve these challenges.

3:00 *Afternoon Networking Break*

3:15 **Process Validation for Lyophilized Drug Products: Developing a Program for Continued Process Verification**

Karen Bossert, Ph.D., Pharma Consulting Services

The product lifecycle concept described in the 2011 DA Guidance for Industry, "Process Validation: General Principles and Practices", poses the challenge of providing ongoing assurance that the process remains in a state of control during commercial manufacture. The Critical Quality Attributes (CQAs) for lyophilized drug products can be trended and evaluated over time using well-established techniques.

Ongoing batch-to-batch evaluation of Critical Process Parameters (CPPs) continues to receive greater attention. Independent process parameters of shelf temperature, chamber temperature, and time, with acceptable ranges for each CPP, are defined and challenged during development. This presentation compares methods to evaluate variability in process performance, using data from multiple product lots, with potential applications of long-term monitoring for routine manufacture.

4:00 *Close of Program*

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