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Lyophilization

*Optimizing the Lyophilization Cycle through
Strategic Application, Processes and Technologies*

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

***Featuring Case Studies and Lessons Learned from Industry Experts from
Multiple Scale-Up and Cycle Development Projects!***

- Examine Current Freeze Drying Technologies and Qualification Requirements
- Critical Factors in the Design and Optimization of Lyophilization Processes
- Developing a Lyophilization Cycle for a Range of Clinical Doses
- Considerations in Process Design and Validation for Lyophilized Drug Products
- Examining Container & Closure Needs for Lyophilized Drug Products

Plus an In-Depth Pre-Conference Workshop:

Global Regulatory and Compliance Requirements for Lyophilized Products

Douglas Stockdale, Ph.D., President, Stockdale Associates, Inc.



Featuring Representation from Leading Companies:

Baxter BioPharma Solutions
GEA Lyophil North America
Kiang Consultant Services
Millennium Pharmaceuticals Inc.
West Pharmaceutical Services

BIOCORP Inc.
Hollister-Stier
Lyophilization Technology, Inc.
SCHOTT Pharmaceutical Systems



PharmaED
RESOURCES, Inc.

Monday, September 15, 2008

In-Depth Pre-Conference Workshop:

9:00

Global Regulatory and Compliance Requirements for Lyophilized Products

This half-day workshop will encompass the global regulatory requirements for the sterile lyophilization of drugs, including both FDA and EU. Due to the critical nature of an aseptically filled and sterile lyophilized product, it is one of most heavily regulated manufacturing processes with extensive compliance requirements.

The regulatory pathway from pre-clinical development through product registration and commercialization is complex, and a pathway that should be well understood for any business organization.

This program will enable you to visualize your validated and fully compliant lyophilization process to meet your global distribution requirements. This will include the regulatory requirements for both clinical and commercial distribution sterile lyophilized products.

During the discussion of the validation of the lyophilization equipment and methods, the presenter will also review best practices for aseptic validation of lyophilized products.

- Lyophilization regulatory overview
- FDA requirements for aseptically filled and lyophilized drugs
- Annex 1 requirements for aseptically filled and lyophilized drugs
- Introduction to lyophilization equipment validation: FAT, Site Acceptance, IQ, OQ, PQ
- Basics of lyophilized process validation; media & registration batches

This workshop is extremely beneficial to those in Quality, Regulatory, Clinical, Research and Operations.

About your workshop leader:

Douglas Stockdale, Ph.D. is the President of Stockdale Associates, Inc., which provides extensive Aseptic Fill/Finish and Sterile Barrier System Consulting services to the Life Sciences Industry. He had twenty years of operational experience with Baxter Healthcare prior to founding Stockdale Associates. He is an internationally known consultant, speaker, and writer about the issues of Aseptic Fill/Finish, including Sterile Lyophilization, and Sterile Barrier Systems.

During his tenure with Baxter, he was an Operations Manager for the world's largest aseptic fill-finish operation for International distributed LVP and SVP protein solutions and lyophilized protein products. Subsequently as the Director of Global Distribution for a Baxter Biotech business unit, he had global manufacturing and distribution responsibilities for a novel family of aseptically manufactured MAb proteins for NHL and other disease conditions.

12:00

Luncheon

EXAMINE CURRENT TECHNOLOGIES

1:30

Examining Current Freeze Drying Technologies and Qualification Requirements

**Heikki Hyttinen, Manager,
GEA Lyophil North America**

Lyophilization is a process that requires a complex set of integrated, automated process equipment. Although commonly fairly well understood the complexity of lyophilizers require a comprehensive qualification program. The success of qualification of lyophilizers is best served by good understanding of the user requirements and their implication on the design of the equipment. Furthermore, a comprehensive review and understanding of the design and transparency in the delivery and testing of the equipment are vital to ensure validatability of the lyophilizer.

This presentation will address the design, specification and qualification of lyophilizers. The presentation shall include an overview of current process technologies and standards and, certain innovative technologies available today that increase the process efficiency and reliability. The qualification of lyophilizers shall be discussed as a case study that describes the fast track delivery of a lyophilizer from the design to SAT and completion IQ/OQ.

DESIGN CONSIDERATIONS

2:15

Critical Factors in the Design and Optimization of Lyophilization Processes

Lisa M. Hardwick, Associate Research Scientist, Baxter BioPharma Solutions

Development of a freeze-dried drug is a long and multi-faceted process, starting in the development laboratory and ending in the production facility that supplies a commercial product to the marketplace. Because efficacy is the early driver that allows a drug to advance from laboratory to clinical trial, often processes that are "good enough" to deliver the desired dose are quickly developed for early trials, and then often never optimized

for commercial production. Although existing processes are adequately validated to fulfill regulatory requirements, normal variations that are likely to occur are not planned for or built into acceptable conditions for production of the product. Because the processes were not fully characterized or understood from the beginning, a design space that allows for deviations within the validated parameters does not exist. With planning and forethought, steps can be taken in early development that will ultimately streamline the process and produce a more robust regulatory submission. Topics covered will include:

- Dryer characterization
- Formulation and cycle development
- Scale-up
- Strategies for product validations

3:15 *Refreshment Break*

LYOPHILIZATION CYCLE DEVELOPMENT

3:30 **Developing a Lyophilization Cycle for a Range of Clinical Doses**

Willow R. DiLuzio, Ph.D, Sterile Products Formulation Sciences Group, Millennium Pharmaceuticals Inc.

Developing a lyophilization cycle that can be used for a range of clinical doses accelerates the drug development process and allows clinical trial material to be made as soon as the clinical doses are known. In order to design a lyophilization cycle for a wide range of clinical doses, the effect of vial size and fill volume on the lyophilization process must be well understood. To gain this understanding, experiments can be performed that examine the following relationships: the effect of fill volume on drying time; the effect of fill volume on residual moisture in the product; and the effect of vial dimensions (width and thickness) on the required drying conditions. By performing a few key lyophilization experiments, a cycle can be developed that can be applied to a wide range of vial sizes and fill volumes.

- Learn techniques for developing a lyophilization cycle that can be applied to a range of vial sizes and fill volumes
- Understand how vial dimensions and fill volume affect the lyophilization process

4:15 *Close of Day One*

Tuesday, September 16, 2008

PROCESS DESIGN AND VALIDATION

8:30 **Clinical vs. Commercial Manufacturing: Considerations in Process Design and Validation for Lyophilized Drug Products**

Karen A. Bossert, Ph.D., R.Ph., Lyophilization Technology, Inc.

Lyophilized drug products are sterile, solid dosage forms which are manufactured using unique processing technology. As drug products evolve from initial design through early phase clinical manufacturing, to late phase clinical manufacturing, final scale-up and commercialization, many aspects of the dosage form may also change. This talk examines various aspects of lyophilized drug products, including cycle definition, interpretation of cycle data, process design and validation, sampling and testing, and scale, and their impact on acceptability of finished product. Also included are case studies which highlight potential issues with site and scale changes.

Benefits - participants can gain a practical understanding of the following:

- How lyophilization cycles are developed and the scientific data required to provide sound rationale for cycle design.
- The difference between lyophilization processes for clinical products and those used in commercial manufacturing.
- The impact of scale or site changes and line extensions on the lyophilization process.
- Design of process validation studies and establishing appropriate design space for the lyophilization process.

10:00 *Refreshment Break*

10:15 **Validation Requirements for Lyophilized Products in a Parenteral Manufacturing Facility: Focus on Aseptic Processing, Clinical Trial, and Commercial Scale Lyophilization**
Barbara Berglund, Hollister-Stier

Manufacturing lyophilized products in a contract manufacturing facility must take into consideration the need for specialized equipment validation. For an aseptic operation, it is necessary to demonstrate environmental monitoring while the equipment is in use and normal aseptic interventions are in occurrence. Further, the size of the lyophilizer and the final use, such as development batch, clinical trial or commercial production, dictates the requirements of the equipment. The pumps must be capable of evacuating the chamber for VHT, the condenser

must be capable of handling full chamber water loads, the materials of construct must be sterilizable, and the product contact and non-contact equipment must be inert. In some cases, aseptic thermal probing can be obtained, and this requires additional validation and monitoring considerations. Loading and unloading systems must also be validated for this processing environment. A summary of the requirements and needs for scale-up will be addressed.

FREEZE-DRY-SEAL TECHNOLOGIES

11:15 Freeze-Dry-Seal Technologies: Meeting Class A Crimping Regulation and Reduction of Operational Burden

Philippe LeGall, Director, BIOCORP Inc.

Freeze-dry-seal technologies allow to crimp vial inside the freeze dryer and to meet the new regulation requiring class A crimping. Most importantly, crimping into the freeze dryer eliminates common issues and burden associated with lyophilization of injectable drug products, whether associated with downloading, transferring or crimping lyophilized products.

The technology is evaluated in terms of container integrity benefits, impact on existing production lines, validation and overall benefits vs. cost.

- Learn about the freeze-dry-seal technologies
- List operational and container integrity issues associated with Lyophilization
- Evaluate cost elements in a production set up
- Evaluate validation approaches pertaining to container closure integrity

12:00 Luncheon

CONTAINER CLOSURE CONSIDERATIONS

1:15 Strategies for Selection of Appropriate Closures and Optimization of Processing Cycles **Lynn Lundy, 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.

2:00 Examining Container & Closure Needs for Lyophilized Drug Products

Patty Kiang, PhD, Kiang Consultant Services

Container / Closure systems play a critical role in Lyophilized Drug Products. Many companies experienced drug stability failures due to the excessive moisture content which is attributed to the improper container/closure system.

The successful container /closure system depends on:

1. Proper material composition
2. Suitable design
3. Optimal process / treatment: washing, siliconing, sterilization and drying cycle etc.

Several case studies will be discussed to demonstrate the impact of the container & closure system on the productivity and stability of the Lyophilized Drug Products.

3:00 Refreshment Break

3:15 Container Considerations in the Lyophilization Process

Christian Helbig, SCHOTT Pharmaceutical Systems

The lyophilization process is the ultimate challenge for glass made containers. The conditions under which Lyophilization takes place are pushing glass made containers to their limits. Glass is by far the best material for pharmaceutical containers due to its very low interaction potential combined with its extraordinary barrier functions. On the other hand it stiff and ridged structure makes it very sensitive to negative temperature gradients. Optimized design and improved cosmetic quality are crucial for best Lyophilization performance and crack investigations help to improve processes. The blowback figure is very important part of the container closure system. Only a stopper with the corresponding blowback design will allow safe and competitive Lyophilization, but which design is the best? In order to make the best selection, stopper-vial fit analysis can be applied. Beyond the design, modifying the vial surface properties can further improve the result of the lyophilization process.

4:00 Close of Conference



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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!



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VENUE INFORMATION:

Dates: September 15-16, 2008
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