PharmaED's

Disposable & Single-Use Biopharmaceutical Manufacturing Systems

Understanding the Advantages, Costs, Regulatory and Process Considerations in the Usage of Disposables and Single-Use Systems

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SEPTEMBER 27-28, 2010, RADISSON-PLAZA WARWICK, PHILADELPHIA, PA

Key Learning Objectives:

- Understand the Advantages and Benefits of Disposable and Single-Use Systems
- Explore and Quantify the Cost Outcomes Managing the Risks Associated with Materials Utilized to Fabricate Single-Use Bio-Processing Equipment
- Using Single-use Assemblies for Final Fill and Finish Application
- Implement a Risk-based Approach to Single Use Systems Implementation
- Understand Facility Design and Equipment Considerations
- Risk-based Assessment of Extractables & Leachables in Single-use Systems
- Implement Containment Solutions Under Time & Budget Constraints Using Disposable Technologies

Featuring Representation From:

Pall Life Sciences
Robert Bosch Packaging Technology, Inc.
Hecht Technologies
Millipore Corporation
Vivalis, France
ProBioGen
Packaging Science Resources
AMEC
Biopharm Services Ltd.
Hyde Engineering + Consulting, Inc.
Material Needs Consulting, LLC
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Monday, September 27, 2010

8:00 *Registration and Coffee*

8:30 *Chairperson's Welcome and Opening Remarks*

BEST PRACTICE GUIDELINES

8:45 **Development of Best Practice Guides for Single Use Manufacturing**

Jerold Martin, Senior Vice President, Pall Life Sciences

Implementation of single use systems in biopharmaceutical manufacturing has evolved from disposable capsules and biocontainers to bioreactors and complex storage and filling systems. Several professional scientific organizations and trade groups, including BPSA, PDA, ASME-BPE and ISPE, have introduced "standard" best practice guides for single use disposable manufacturing to assist the industry in implementation in GMP environments. This presentation will review the guides that have been published and discuss regulatory responses.

- Learn about consensus practices
- Discover opportunities to contribute to a dynamic new industry trend
- Find resources for networking and resolving application challenges

COST CONSIDERATIONS

9:30 **Cost Considerations in the Use of Disposables and Single Use Systems**

John Finch and Mackenzie Miller, AMEC

The cost advantages/disadvantages of Single Use Systems (SUS) versus traditional stainless steel (SS) are a function of several factors. We will explore and quantify the cost outcomes of SUS systems over a range of applications from development/clinical pilot plants, through manufacturing plants, and green field versus retrofit projects. "Cost" considerations will not be limited to dollars but will also include relative operational risks of SUS versus SS systems. We will develop the framework for the listener to make a rational selection of SUS versus SS systems based upon economics, probability of operational success, and engineering and scientific principles.

10:15 *Networking Refreshment Break*

10:30 **Considerations in Implementing Single Use Filling Systems**

Jeff Jackson, Director, Robert Bosch Packaging Technology, Inc.

The objective of this presentation is to create awareness and understanding of the many factors involved in implementing single use product path technology into final filling operations.

- Understand options in single use filling
- Be aware of factors involved in implementation
- Presentation contents
- Review of current dosing technologies
- Advantages of single use filling systems
- Overview of single use systems
- Identify critical points for implementing single use systems
- Comparison of single use dosing systems

11:15 **Cost Impact of Single Use Technologies - As a Function of Scale and Technology**

Andrew Sinclair, Managing Director, Biopharm Services Ltd.

The objectives of this presentation are to investigate the impact of single use technologies on manufacturing operations looking at issues such as the overall impact on facilities in terms of materials, consumables, materials etc and the influence on cost, questions the speaker will address:

- How single use technologies reduce costs
- Understanding the impact of different technologies on cost
- How sensitive are overall savings to technology pricing?
- Understand the impact of individual new processing technologies

12:00 *Luncheon*

RISK-BASED APPROACHES

1:30 **Materials Utilized to Fabricate Single-Use Bio-Processing Equipment: Managing the Risks**

Michael Ruberto, Ph.D., President, Material Needs Consulting, LLC

Many of the single-use systems utilized in bio-processing are fabricated from polymers such as plastics and elastomers (rubber). Plastic components are lightweight, flexible, and often more durable than traditional metal or glass and can be modified by the addition of polymer additives to have many of the desirable properties of these conventional materials such as strength and

clarity. Plastic and rubber are also disposable, so issues associated with cleaning and its validation are often avoidable. Although polymers are becoming the material of choice for single-use systems and have many advantages over metal and glass, they are not without shortcomings of their own. In the presence of light, heat, oxygen, and other environmental factors, polymers will degrade. This degradation can manifest itself as cracking, discoloration, or surface blooming / exudation and can severely impact the mechanical properties of the polymers. Additives, such as stabilizers, are incorporated into the polymers to prevent this degradation. However this results in a much more complex formulation than typical metal and glass, and makes materials such as plastic and rubber much more prone to leaching unwanted chemicals into the drug product formulation when they are used in applications such as manufacturing or packaging. This does not in any way mean that these materials should not be used in these applications. In fact, their benefit greatly outweighs their risk. However, the risk must be managed. The goal of this presentation is to discuss the issues associated with using polymers for pharmaceutical manufacturing equipment and provide some ideas or "best practices" for managing the risks. Topics covered will include:

- Materials commonly used in single-use bioprocessing applications
- Potential extractables from processing equipment
- An overview of the polymer supply chain
- Best practices for managing the supply chain for raw materials
- Material selection
- Industry recommended testing programs
- Partnering with vendor

2:15

Case Study: A Risk-based Approach to Single Use Systems Implementation

Dr. Stephen Brown, Chief Technical Officer, Vivalis, France

The presentation will review how SingleUse Systems (SUS) have been implemented at Vivalis for the manufac ture of clinicalphase I/II IMP drug substance. A risk management approach has been applied tothe project implementation for the choice of equipment for the integration of process knowledge and manufacturing facility with the preparation of user requ irements, the application of a technology survey, risk assessment,materials management (supply and quality agreements, waste disposal) and HSEissues. Two different biomanufacturing processes for API have been developed ,one for live virus manufacturing (poxvirus vaccines) and one for recombinanttherapeutic proteins. For the virus process, the main equipments used areclassical Multiple Use Systems (MUS - bioreactors, cell breakage, filtrationand chromatography) integrated together with modular SUS components. The MABs process is almost entirely SUS based. These two case histories will be reviewedand set in the context of the Vivalis requirements.

3:00 ***Networking Refreshment Break***

FILL AND FINISH APPLICATION

3:15

Using Single-use Assemblies for Final Fill and Finish Application

Ernie Jenness, Millipore Corporation

Single-use technology has been predominantly adopted in the area of handling and storing of buffer, media and other process intermediates. However, as the technology has evolved and gained wider acceptance, customers are showing strong interest in using disposable assemblies to handle the 'final product.' This presentation will focus on the suitability of single-use assemblies to fill the need at final fill and finish, with emphasis on the following areas:

- System design
- System validation including sterility, shelf life, pack age integrity, and device integrity
- Extension of the Grade A sterile filling environment into the Grade C space via isolator systems

4:00

Cost Considerations in the Usage of Disposable and Single-Use

Susan Dexter, Principal Consultant Biopharm Services, Inc.

Use of disposables in the bio-manufacturing process continues at a rapid pace. Manufacturing with disposables affords speed flexibility and improved capital and operating costs. This talk will review the cost modeling of the integration of disposables into the manufacturing process and the effect of operating costs and the . The model identifies the major areas of cost and the scale at which disposable's costs (not to be confused with 'value'), compare to stainless alternatives. We'll review other factors that influence the value and cost of using disposables and discuss the optimal combination of technologies for low cost, efficient manufacturing.

4:45 ***Panel Discussion***

5:30 ***Close of Day One***

Tuesday, September 28, 2010

8:30 **Usage of Disposables in Protein and Vaccine Production in a Pilot Plant**

Rene Brecht, VP Process Science & Manufacturing, ProBioGen

The biotech industry is challenged by finding solutions for flexible, cost efficient and scalable bio-manufacturing. Regarding the life cycle of new biological drugs, it can be distinguished between pilot and commercial plant activities. Modern pilot plant concepts need to consider the complexities of biopharmaceutical processes, cost of goods and safety issues, as well as low probability of success of such products. The presentation highlights some of our experience in designing, constructing and operating our flexible pilot manufacturing plant. Different case studies using disposables in the bio-manufacturing of proteins, antibodies and viruses are illustrated. Additionally, the advantages and limits of disposables are shown.

9:15 **Particle and Endotoxin Testing of Disposable Tubing Manifolds for Formulation and Filling**

Jerold Martin, Senior Vice President, Pall Life Sciences

Sterile formulation and filling is increasingly being conducted with disposable plastic tubing manifolds. As these manifolds are typically not pre-cleaned like stainless steel filling manifolds, they may provide a potential source of particles and endotoxins that could contaminant final filled product. Tests were conducted to determine particulate matter and endotoxin content in radiation-sterilized disposable tubing manifold systems and monitor levels over multiple manufacturing lots. Design rationale and support data is provided for a master surrogate tubing system incorporating multiple connection points to simulate a complex manifold requiring the most handling during manufacturing and assembly.

- Learn about particle and endotoxin method development and analysis from single-use systems
- Develop a rationale for application of Master System concepts based on ISO standards
- Establish criteria for quality audit programs for particles and endotoxin in single-use systems

10:00 ***Networking Refreshment Break***

FACILITY DESIGN & EQUIPMENT CONSIDERATIONS

10:15 **Facility Design and Equipment Considerations**

Geoff Hodge, Xcellerex

Single use components are available in increasingly larger scales and applications and have become a standard consideration for new biomanufacturing facilities. This talk will examine a novel facility design which maximizes the benefits of single use systems, including decreased capital cost, increased operating efficiency and improved flexibility compared to other single use facility designs. Examples covering a variety of biotherapeutic products and vaccines produced in this type of facility will be presented and economic and strategic considerations will be reviewed.

11:00 **Flexible Manufacturing Facilities for the Future**

Peter K. Watler, Ph.D., Principal Consultant and CTO, Hyde Engineering + Consulting, Inc.

The 21st century has brought a wide range of disposable technologies that are seeing widespread implementation in GMP facilities. Higher titers, more competitive therapies, the emergence of biosimilars, and heightened vaccine demand are driving the need for smaller, more flexible facilities. This case study will review a new disposable-based approach that enabled design and construction of a GMP facility in just 12 months and for under $20 million. A 'hybrid' approach of integrating disposable systems with conventional systems reduced construction costs, time and complexity. Disposable technologies were leveraged to reduce capital outlay, equipment lead times, and simplify startup. Disposables further enhanced GMP operations by offering exceptional control of endotoxins, bioburden and product purity. This presentation will review trends in design and operation for bioprocess facilities:

- Lean design techniques
- Flexible facility design for multi-product operation
- Innovative technologies such as disposables to reduce costs and delivery time
- Lean compliance engineering to eliminate non-value added activities

12:00 ***Luncheon***

EXTRACTABLES & LEACHABLES

1:15

Risk-based Assessment of Extractables & Leachables in Single-use Systems

Vikas Gupta, Millipore Corporation

New or early adopters of single-use technology often do so with a high level of trepidation. One of the biggest concerns is the risk posed by extractables and leachables from single-use components. The concern often results in seemingly endless and exhaustive analytical studies of extractables. The pursuit entails spending countless hours and expensive manpower, as well as conducting largely avoidable, extensive animal studies. The presentation will briefly discuss existing guidelines used by the biopharmaceutical industry to assess the toxicological impact of extractables and leachables from single-use systems.

The main focus will be to share pragmatic approaches to conduct risk-based assessment of E/Ls from single-use systems. One of the most useful approaches is called Threshold of Toxicological Concern (TTC). It states that chemicals when present below a certain threshold in a patient dose, do not present any substantial risk to the patient's health. The presentation will also cover other safety factors that can be incorporated in a risk-based evaluation.

These approaches will be discussed in detail using two case studies: a buffer storage manifold assembly representing upstream use and a final drug product storage assembly representing downstream use in a typical biomanufacturing process. The case studies will calculate total leachables ending up in a patient dose per day for two commercially available drugs, and demonstrate the use of various safety factors to reduce the toxicological concern from the leachables.

2:00

E &L for Disposables and Process Components

Edward J. Smith, Ph.D., Principal Consultant, Packaging Science Resources

Like packaging materials and components used for the marketing of pharmaceutical products, an extractables/leachables (E&L) evaluation is necessary to qualify disposables and process components that are in contact with drugs or drug products. There are unique differences in the methods of assessing E&L for these components versus packaging components including contact time, area, and temperature and range and number of materials. These and other variables will be discussed supported by case studies that illustrate approaches that have been successfully utilized.

2:45

Networking Refreshment Break

3:00

Strategies to Implement Containment Solutions Under Time & Budget Constraints Using Disposable Technologies

Hari Floura, President, Floura LLC

Pharmaceutical and biotech companies of all sizes are increasingly required to handle high risk and potent compounds in the laboratory during drug discovery, through final product packaging and quality testing. In addition, the biopharma industry is additionally faced with the challenge of increasingly tight budgets and schedules during execution of capital projects. This session will discuss practical measures for safely handling, containing and minimizing exposure risk. The speaker will demonstrate, via case studies and practical examples, how single and multiple use disposable containment solutions can be applied where traditional containment methods may not be practical or economically feasible. During the session, we will discuss and describe:

- The use of disposable systems to provide operator protection and maintain cGMP conditions
- The implementation of disposable engineering controls to contain new and old process equipment
- Disposable single and multi-use contained transfer systems
- Advantages and disadvantages as related to the technologies discussed

3:45

Unique Considerations for Processing of Traditional and Potent Lyophilized Compounds

Harry Lindenmuth, Lyophilization Technology, Inc.

For many drug compounds, the process of lyophilization provides distinct benefits and is a necessity for maintaining suitable long-term product stability. The technology and equipment used during the lyophilization process is well established within the biopharmaceutical industry. However, the coupling of this technology with that needed to effectively and safely process potent compounds is not well established. When processing such materials, one of the significant challenges arises with coupling the principles of traditional aseptic processing and lyophilization with those necessary for effective containment operations. The use of disposable technologies throughout the entire product pathway can prove useful/beneficial/effective in such situations. A sample strategy and process flow for the use of disposable technology during processing of lyophilized drug products is discussed, including points to consider when designing manufacturing processes for lyophilized materials.

4:30

Close of Conference

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DISPOSABLES & SINGLE-USE BIOPHARMACEUTICAL MANUFACTURING SYSTEMS:

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