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

Register by June 10th and receive a $300 Discount!

JULY 30-31, 2012, THE RACQUET CLUB OF PHILADELPHIA, 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:

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Monday, July 30, 2012

9:00 *Chairperson's Welcome and Opening Remarks*

9:15 **A Case Study of Process Scale-up and Transfer from a Non-Disposable to a Fully Disposable System**

Sigma S. Mostafa, Ph.D. Director, Process Development, Upstream, KBI Biopharma, Inc.

This case study describes our procedure for scale-up and transfer of processes developed in non-disposable glass and stainless steel bioreactors into disposable bioreactors. Disposable bioreactor production data for key CHO platforms including CHO-GS, CHO-DG44, and CHO-S, will be presented. This presentation will also describe our disposable harvest procedure. Three separate cases will be presented in which the process development or initial production runs were done in non-disposable bioreactors. In each case the unique attribute of the process was considered in deciding the sparger type, agitation, gas flow rate etc . for the disposable bioreactor process. These attributes included high peak cell density (> 20 million cells/mL), high oxygen uptake rate per cell, sensitivity to high dissolved CO2 etc. The large scale (200 and 2000L) production runs were conducted without any shakedown or demonstration runs. Detailed mixing studies were conducted in the bioreactors prior to the production runs. Along with agitation, sparge rate, and working volume, the type of sparger (2 um to 1 mm) was also evaluated. The results from these studies and key learning points will be presented.
We used disposable harvest technology up to 2000L scale. Small scale harvest studies were conducted using cell culture material from lab scale bioreactors. Two depth filters of different constructions were put in series followed by a 0.2 micron polishing filter. Throughput and final turbidity were used as criteria for choosing the combination of filters. This type of filterability testing is done prior to each new project. This presentation will describe the lab scale harvest filterability study and compare in to large scale harvest data. We will also present harvest data from an alternate disposable harvest technology called kSep. In summary this presentation will discuss the common challenges in transferring processes to a disposable system and the solutions we developed for successful large scale disposable bioreactor runs.

10:45 *Mid-Morning Break*

11:00 **Case study-Development of Best Practice Guides For Single-Use Manufacturing**

Jerold Martin, Sr. V.P., Global Scientific Affairs, Biopharmaceuticals, Pall Life Sciences (div. Pall Corp.)

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

12:00 *Luncheon*

1:00 **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. 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 will review other factors that influence the value and cost of using disposables and discuss the optimal combination of technologies for low cost, efficient manufacturing.

2:00 **Extractables and Leachables Considerations and Strategies for Testing Parenterals and Process Components**

Edward J. Smith, Ph.D., Packaging Science Resources, LLC

The demand for extractables and leachables (E&L) data by health authorities has mushroomed since the release of the FDA's 1999 Guidance on Packaging. The main focus of the Guidance document is the final or market container closure systems (CCS) for drug products but there are small sections of the document which discuss for single-use systems containers for both bulk drug substances and bulk drug products. Currently there is particular interest the management of E&L studies for injectable drug products and and devices (aka disposables) used for biopharmaceutical manufacturing. Both areas lack specific guidance on protocols and limits. The PQRI (Product Quality Research Institute) has formed a working group to develop recommendations and best practices for parenteral and ophthalmic products using an approach similar to that used previously for inhalation products; these recommendations are not yet finalized. In 2010, the Bio-Process Systems Alliance (BPSA) released

recommendations for managing the E&L of components that are used in the processing or manufacturing of drug products. A recent survey revealed that 71.4% of respondents cited the need for E&L data as holding up the use of disposables. Current best E&L practices for parenterals and disposables will be compared.

3:00 *Afternoon Break*

3:15 **Pharmaceutical Manufacturer's Approach to Qualification of Sing-Use System Use Systems Implementation**

Ken M. Wong, Merck & Co. Center for Extractables and Leachables (CEL) ACDS - Specialty Analytical

As single-use systems (SUS) technology matures many biopharmaceutical companies are embracing the new technology in the competitive market place. However, the regulatory guidance on qualification and validation of SUS is murky which can inhibit adaptation of SUS. Here is one approach Merck & Co. is taking to qualify SUS. The approach is a combination of risk assessment of the SUS in accordance to ICH Q9 to determine the amount of in-house qualification data required to complement supplier's qualification data. Both sets of supplier and in-house qualification data are required to demonstrate suitability of SUS for its intended use.

Take home benefits:

For biopharma companies, representatives can take home an approach to qualify SUS specifically what to request from supplier to speed up qualification of SUS and its associates risk assessment concept.

For SUS suppliers, representatives will gain understanding the important of their roles in providing what validation information and what it takes for their customer to fully qualify a SUS for a given process.

Presentation Objectives:

To share best practices and promote discussions among biopharma participants and regulators on what are the acceptable routes to qualify SUS. Similarly, promote collaboration among suppliers and biopharma customers and allow suppliers to understand what they can do to help their customers by leveraging the existing data from suppliers in qualifying their SUS quickly.

4:15 **Factors to consider when selecting polymeric tubing and tubing assemblies for use in Single Use Disposable Systems**

John Stover, Director of New Business Development and Product Technical Director, NewAge Industries-AdvantaPure.

Single Use Disposable Systems are quickly emerging as a preferred method of fluid handling in the processes used by the manufacturers of pharmaceuticals. Additionally, other industries such as the manufacturing of fragrances, cosmetics, and food products are beginning to examine the benefits of implementing disposable systems. The major benefits of the use of these disposable systems are well documented and include significant cost savings by greatly reducing validated in-line cleaning and sterilization that is needed for permanently piped systems, the significant lowering of risk of cross-contamination, and smaller manufacturing line footprints. Flexible polymeric tubing is part of the backbone of these disposable systems. There are many factors to consider when selecting the proper tubing and pathway construction. Material regulatory testing, Extractables and Leachables consideration, integrity of the fluid path, sterilization method impact on the materials of construction, and design of fluid path circuit are all examples that the user of these systems must consider when selecting the proper tubing.

Session Objective

Session attendees will be given an overview that will include the different types of tubing and molded parts most commonly used; a discussion on manufacturing capabilities and conditions and how they can impact the final product; assembly methods used to put together tubing sets and how they can impact final product; Extractables & Leachables considerations; regulatory testing considerations; the use of tubing with different container types and container closures; and a general discussion on sterilization techniques used for these assemblies.

Audience Take Home Benefits

Attendees will have a better understanding of the types of tubing and assemblies currently available and factors to consider when choosing the best suited tubing and assembly styles and vendors for their application.

5:00 *Close of Day One*

Tuesday, July 31, 2012

9:00 **Case Study: Single-Use Components Enable Rapid Multi-Product Biomanufacturing**

Geoffrey Hodge, Vice President, Manufacturing Services, Xcellerex, Inc.

The use of single-use components, coupled with facility design and operational strategies, enabled the rapid multi-product biomanufacturing of four molecules within a single manufacturing suite. In order to meet an aggressive clinical timeline, four separate molecules (produced

by the same parental cell line and destined for the same multi-component formulation) were produced in a single manufacturing suite, in an overlapping multi-product campaign. Four batches, one for each molecule, were produced from cell bank thaw to bulk drug substance filtration in less than three months. This case study will outline the strategy employed to minimize the risk of cross contamination during concurrent manufacturing and assure segregation of operations according to the Q7A guidance. Topics included: Maximal use of single-use components, coupled with select product-dedicated equipment, to eliminate the risk of cross contamination from product-contact surfaces, chronological staging of activities and use of portable clean micro-environments to minimize the risk of contamination from the environment, and procedural and documentation controls to maintain segregation of equipment and materials.

10:15 **Critical Quality Systems for Single Use / Disposable Processes**

George Kuniholm, Principal, ACT Professional Services

Nothing impacts a company more than a GMP inspection that goes awry. The secret to prevention is the establishment of a closed loop Quality System that responds to the critical aspects of operations. With the proliferation of single use and disposable technologies, it is particularly important that the Quality Systems consider the new challenges posed by the deployment of such technology. No longer is the focus on the Commissioning and Qualification of stainless steel production trains, but on creating strong process validation and clear instructions for the set-up and operation of disposable production trains. The purpose of this session is to present how Quality Systems such as Documentation, Change Control, Deviation, CAPA, Quality Risk Assessment, MRB, and Supplier Compliance need to be tightly linked to the Critical control points of single use / disposable technologies.

Attendees will learn how to create linkages between single use / disposable production technology and controlling Quality Systems and how the organization can continually improve and enhance the quality of their product and processes. The application of Risk Management is applied throughout the overview and the approach is harmonious with the Pharmaceutical Quality System described in ICH Q10.

11:00 *Mid-Morning Break*

11:15 **Defining the Next Generation Manufacturing of Biological Products**

Jeff Odum, IPS – Integrated Project Services, Inc.

This presentation addresses significant challenges in designing, constructing and operating biopharmaceutical facilities. This presentation offers an in-depth look at the next generation of design options where the implementation new technologies will provide a higher level of flexibility, utilization and operational excellence.

12:15 *Luncheon and Exhibit Viewing*

1:15 **Considerations in Implementing Single Use Filling Systems**

Jessica Frantz Product Manager, Single-Use Dosing Systems, Bosch Packaging Technology

From Media Prep to Product Formulation, Single-Use (SU) technology has made its way into the Pharmaceutical Manufacturing arena. The acceptance of SU options in these upstream processes has producers of liquid formulations wanting to carry the SU concept through the final step: Fill and Finish.

Dosing System Options, Product Path Design, Supply Chain Management, Process Control & Validation are all items that need to be considered when bringing SU technology into the Fill/Finish area. This presentation will create awareness and understanding of the many factors involved in implementing single-use product path technology into final filling operations.

Session Objectives:

- Understand options in single use filling
- Be aware of the advantages in using SU technology
- Recognize Factors in Implementation (Supply Chain, Process Control and Validation)

Presentation Contents:

- Dosing Technology Review
- Overview of Single-Use Systems
- Trends in Aseptic/Parenteral Filling
- How single-Use Systems address challenges in Filling Trends
- Considerations for Implementation of SU Filling systems

2:15 **Accelerated Process Development and Scale Up of Downstream Purification for MAbs: A Case Study**

Sue Walker, Senior Applications Engineer, Biomanufacturing Sciences Network, EMD Millipore

With over 500 monoclonal antibodies (MAbs) in Preclinical and Phase I stages, speed to clinic continues

purification process for a MAb is developed with to be a critical factor for commercial success. While the use of template processes, at least to some degree are commonly used today for MAbs, opportunities exist for further streamlining process development activities and scaling up the developed processes using off-the-shelf single use technologies. In this case study, a downstream the specific intent of minimizing effort and understanding cost to subsequently produce clinical scale quantities. The devices and certain operational parameters are fixed for each unit operation resulting in reduced process development activities. The resultant process is successfully scaled to purify 100g of MAb using standard, off-the-shelf single-use systems and assemblies.

Benefit Points:

- Pragmatic approach leveraging the use of a template process coupled with single use technology
- Assist in delivering process and cost efficiencies at both PD and Clinical scale implementation
- Process will successfully scale using standard off the shelf assemblies and equipment

3:00 *Afternoon Break*

3:15 **Performing Containment Verification Assessments of Flexible Containment Systems following the revised 2012 ISPE Good Practice Guide "Assessing the Particulate Containment Performance of Pharmaceutical Equipment (APCPPE)"**

George S. Petroka, CIH, CSP, RBP, Principal, IES Engineers

Flexible and disposable containment systems can be effective in providing operator protection and maintaining cGMP conditions during the handling of potent pharmaceutical compounds.

Prior to the actual use of the flexible or disposable containment system, containment verification or the containment system should be performed to verify it contains to the Containment Protection Target (CPT) it was designed to. The APCPPE Good Practice Guide provides technical guidance and consistent methodologies for evaluating the particulate containment performance (particulate emissions) of Pharmaceutical equipment and systems including flexible containment systems. This session will review the Guide, application of the guide in performing containment verification assessments for flexible and disposable containment systems. Actual case studies and examples of containment verification assessments utilizing the guide for flexible and disposable containment systems will be presented.

4:00 **New protection technologies make adoption and use of single use bags**

Tuna Sava, UFP Technologies, Manager, Sterile Process Products

Single use bags have been gaining acceptance across the industry. Their advantages are clear yet they come with the risk of damage. Storage, handling and shipping – especially for frozen bags, are areas of serious concern and sometimes reasons that prevent adopting. There are numerous products and solutions focused on safety of single use bags. Most of them successfully protect the liquid holding bags. Protecting frozen product have been a challenge for both bag makers and end users.
BioShell is an excellent option that can eliminate the hesitation to switch to bags or protect bags that are already in use. With its unique suspension technology, BioShell surpasses all ISTA and ASTM protection requirements. It can be used for both liquid and frozen product holding bags – down to -90C.
Suspension technology holds the bag in air between two films. It prevents the load to make contact with the top, bottom or the sides of the container during accidental drops or bumps. Key points are:

- Exceptional protection from significant drop heights – 32" drop protection for a 20L bag at -70C
- Versatility
  - Can handle all bags from all manufacturers with any port/tube combination at any fill level
  - Can be configured to hold multiple small bags within a larger unit
  - Works for both liquid and frozen product holding bags
- Rapid freeze/thaw cycles
- Works with industry standard upright or walk-in freezers
- Space savings
  - Stackable
  - Nestable
- High purity construction that adhere to USP Class VI classification
- Visibility – allows for viewing of the bag and its components from outside
- Customizable – for specific freezers, storage or shipping environments
- Reusable – durable shell for many cycles
- Recyclable – each component is fully recyclable

New protection technologies make adoption and use of single use bags.

5:00 *Close of Conference*

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DISPOSABLES & SINGLE-USE BIOPHARMACEUTICAL MANUFACTURING SYSTEMS:

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