PharmaED RESOURCES, Inc.

Process Validation 2018 Summit

May 17–18, 2018, Racquet Club of Philadelphia, PA

Featured Speakers Include:

Kashappa Goud Desai
Investigator, Biopharmaceutical Product Sciences,
GlaxoSmithKline

Dushyant B. Varshney
Head of Manufacturing Science & Technology,
Pfizer

Carmen Medina
Vice President, Technical,
PAREXEL

Pritish Patel
Supervisor, Technical Services—Validation,
Bayer

Anita Michael
FDA ORA Pharmaceutical Specialist,
FDA

Robert Luo
Manager, Downstream Process Development,
GlaxoSmithKline

Alan Golden
Senior Quality,
Abbott

Elizabeth Rivera
Technical Services Manager,
Steris

With Comprehensive Coverage On:

- FDA Process Validation and Risk Management Approaches
- Lifecycle Approach to Process Validation
- Global Technololgy Transfer and Process Validation
- Scientific and Practical Considerations of Small Scale Model Qualification and Related Statistical Analysis for Biopharmaceutical Manufacturing Processes
- Legacy Products—From Retrospective to Prospective Process Validation
- Validation Sampling Plans and Statistical Process Control
- Cost-effective Process Validation Lifecycle Management
- Implementing a Comprehensive Strategy for Process Validation: Stage 3, Continued Process Verification
- Assessing the Practical Significance of Statistical Study Results
- Revalidation of Biopharmaceutical Drug Product Manufacturing Process
- How to Integrate Quality by Design (QbD) and ASTM E2900 to Maximize Impact on Validation Stage 1
- And Much More

Are you compliant with FDA requirements for process validation? Today's regulators are applying more fine-grained specifications and demanding more sophisticated procedures for planning, executing, and documenting your processes throughout a drug product's lifecycle. This two-day intensive summit brings together industry leaders to help you exceed regulatory thresholds and avoid costly FDA inspection findings.

With Representation From:

Abbott · Bayer · FDA · Pfizer · gsk · Stat4ward · SynoloStats · PAREXEL · pharmatech associates · QPharma · STERIS · Snee Associates LLC · Wiley Rein LLP · CTI Compliance Team Inc · Tunnell · Validation Edge

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Thursday, May 17, 2018

8:15 *Complimentary Breakfast & Chairperson's Welcome and Opening Remarks*

Regulatory Considerations

8:30 **FDA Process Validation and Risk Management Approaches**

Anita R. Michael, FDA ORA Pharmaceutical Specialist, FDA

This presentation will focus on FDA Regulations, cGMP's current practices and inspections for Validation. The presentation will address inspectional approaches for cGMP's, Process Validation, Stage 3 Continuous Process Verification and Life Cycle Approaches. Data Integrity Inspections and relevant cGMP's Regulations will be discussed. Pre-Approval Inspections, Post-Approval inspections and cGMP Inspections as well as the application of the regulations will be reviewed. The presentation and discussions will address commercial manufacturing and 21 CFR Part 210 and 211 Current Good Manufacturing Practice (CGMP's) and inspectional readiness.

9:15 **Stage 3 of Process Validation: Continued Process Verification—Implementation, Strategies and Lessons Learned**

Pritish Patel, Supervisor, Technical Services—Validation, BAYER

This presentation will examine a high-level idea of FDA's new Process Validation guidance for Pharmaceutical Manufacturing. The presentation focuses on Stage 3 of Process Validation: Continued Process Verification, its implementation strategy, lesson learned and must do for out of trends. Further, the presentation will detail the documentation requirements and strategy for the selection of various parameters or attributes for the Continued Process Verification. The Stage-3 process verification implementation of already manufactured products as well as for the future products is also included in the presentation. Looking at the future, the presentation will also address the upcoming approaches to make the Continued Process Verification more robust.

10:00 *Networking Break*

10:15 **Scientific and Practical Considerations of Small Scale Model Qualification and Related Statistical Analyses for Biopharmaceutical Manufacturing Processes**

CASE STUDY

Robert G. Luo, Diana Ritz, Kathleen Van Manen-Brush, Rachel DuVilla, Philip McGoff, GSK

The qualification of small scale models for biopharmaceutical manufacturing processes is an important task that supports process validation and is required by regulatory authorities. However, carrying out small scale model qualification studies can be challenging due to the lack of clear guidance on the best practices for design, execution, and data analysis. For example, common questions asked by scientists and engineers tasked with conducting qualification studies include:

- How many large-scale runs do I need to qualify the model?" "How many small-scale runs do I need to carry out in the lab?" "If the manufacturing scale or site changes, do we need to qualify the model again?"
- What statistical methods should I use to analyze the data?"

In this presentation, we will evaluate these questions based on experiences with qualification of small scale models. In addition, we will discuss proposed answers to the questions based on scientific, statistical, and practical considerations.

11:00 **Validation Sampling Plans and Statistical Process Controls**

Alan Golden, Senior Quality, Abbott

A. Expectations for validation sampling
   a. Regulatory requirements
   b. Product needs

B. What is required
   a. Concept of acceptable quality limit/reject quality limit
   b. Setting appropriate limits for your product or process
   c. What type of data do you have?
      i. Variables or Attributes

C. How many, how many times
   a. Selecting the best sampling plans for your product or process needs
   b. Step by step process of selection of a sampling plan

D. Keeping your process in control
   a. Statistical Process Controls

12:00 *Complimentary Lunch*

Spotlight on PV Metrics

1:00 **Master Your PV Metrics**

Carmen Medina, MPH, Ph.D, Vice President, Technical, PAREXEL International

Ensure sustainable commercialization and a competitive edge through the establishment of a quality-centric, efficient, and comprehensive platform for process validation. Learn how to design the most exacting approach for risk assessment at each critical phase, coupled with a in-depth validation master plan resulting in a meaningful continuous verification scheme. Lifecycle Process Validation provides the perfect starting point for the installment of an enterprise-wide Quality Metrics Initiative that will proactively compile, analyze and monitor metrics related to an array of operational quality indicators; such as, manufacturing deviations, out-of-specification data, complaints; and most importantly, production and

process controls. This opening session will highlight the components needed to integrate PV metrics to an enterprise-wide analytics platform. Presentation will demonstrate a comprehensive approach for quality by design during early stage process design, tools for successful process qualification, and a method to ensure PV outputs will contribute to a 360º feedback-loop of metrics aimed at fostering predictability, rapid accountability, targeted risk mitigation and continuous improvement. We will also discuss today's regulatory landscape for PV at each critical milestone, and which quality metrics, data and applied statistics should be part of any ongoing process validation program.

I. The Preliminary Platform Design

II. Regulatory Overview

III. Multi-phase Risk Assessment Plan: Methodology and Required Outputs

IV. Select Parameters for QbD

V. Establish Quality Target Product Profile

VI. Monitor for Competitive Edge

VII. Integrate PV Outputs for Enterprise-wide Quality Metrics and Sustainable Commercialization

3:15 *Afternoon Networking Break*

3:30 **Launching a Continued Process Verification Program for Legacy Products**

Mark Mitchell, Principal Engineer, Pharmatech Associates, Inc.

The FDA Process Validation Guidance (2011) adds a post-process qualification stage called Continued Process Verification (CPV), which requires ongoing trending of new and legacy products. For pharmaceutical companies with a large number of products, a risk-based strategy needs to be employed for a staged approach to launching this program. In this case study, initially a Pugh matrix is used to set the priority for legacy products. For each product, a CPV plan is developed using risk assessment and historical data to determine the frequency of review of critical parameters, material attributes, and quality attributes. A comparison of different statistical tools is evaluated including control charts, normality, and capability. Finally, solutions to common program challenges such as CPV meeting structure, interpretation of "out-of-control", and the quality response to statistical events are discussed.

4:15 **Assessing the Practical Significance of Statistical Study Results**

Ronald D. Snee. PHD, President Snee Associates, LLC

Data collection and statistical analysis has long been an integral part of process validation studies and continues to grow in importance. One of the lingering questions is how one should interpret and take action on a statistically significant result. The p-value is less than 0.05, now what do I do? What action should I take? Curiously this issue is discussed very little in statistics textbooks and is a source of confusion for many analysts and users of statistical methods. It is argued that one should be most concerned about practical significance of results. Statistical significance is the criteria that determines whether it is appropriate to consider whether an effect or difference is practically significant and action is needed. This presentation provides guidance on how to determine the practical significance of results. Examples from Pharma and Biotech studies are included to illustrate the proposed analysis and decision making processes.

5:00 **Revalidation of Biopharmaceutical Drug Product Manufacturing Process**

Kashappa Goud Desai, Biopharmaceutical Product Sciences, Investigator, GlaxoSmithKline

Lifecycle-based process validation involves 3 stages (stage 1: process design, stage 2: process performance qualification/PPQ, and stage 3: continued process verification) over the lifecycle of the biopharmaceutical drug product manufacturing process. Revalidation of Stage 2 may be performed to ensure that changes in the process do not adversely affect process characteristics and product quality. The revalidation may be performed after process change(s) occur that have a risk of impacting product quality and/or the established control strategy. This presentation provides an overview of different types of validation, current regulatory expectations with regard to the revalidation, revalidation of legacy products, common questions and answers, and issues and strategies.

5:45 *End of Day One*

Friday, May 18, 2018

7:45 *Complimentary Breakfast & Chairperson's Remarks*

8:00 **Process Validation Lifecycle: A Risk Based Approach**

Ned Wyman, Principal Scientist, MS&T, AstraZeneca Biologics

Over the past several years, validation philosophies have been altered. The requirements in general, and for process validation in particular, have significantly changed and changed for the better. Most of the process validation changes are related to handling any learnings over the product lifecycle.

Additional validation updates are related to taking a risk based approach. As per ICH Q9, Quality Risk Management is to be used to identify the scope and extent of verification, qualification, and validation activities (e.g., analytical methods, processes, equipment, and cleaning methods).

Putting these two improvements together, various aspects of risk based approach should be employed over the course of the process validation lifecycle. As such, this interactive session will provide a risk based approach for:

- classifying process parameters (PV Stage 1)
- determining the minimum number of lots for each PV study (PV Stage 2)
- taking the family approach in PV (PV Stage 2)
- selecting which PV parameters to monitor during CPV (PV Stage 3)

8:45 **Stage 1: Process Understanding, Define Process Control and Success for Continuous Improvement**

Elizabeth Rivera, Technical Services Manager, STERIS Corporation | Life Sciences Formulated Chemistries

The presentation will discuss the different GMP requirements regarding "stage 1" process validation. The presentation will also detail and explain the changes of recently effective process validation EMA guideline on process validation. Following that, the presentation will share a systematic method to a science and a risk-based approach for product and process development linked with the production and patient need. The following concept will be discussed during the presentation quality target product profile, determination of the critical quality attribute, the design of space. These concepts are crucial to implementing effective control strategy and robust process and product lifecycle. During the presentation, different tools, case studies and lessons learned will be shared to demonstrate the benefit of a robust stage 1 to control process variability and failure during stage 2 and stage 3. Finally, the pre-requisite before starting the stage 2 will be discussed.

In-Depth Coverage on Statistical Approaches

9:30 **The New Streamlined Approach to Validation Stage 1—New Implications for ASTM E2900**

Regina Fullin, Senior Compliance Consultant, Compliance Team, Inc.

ASTM E2900 was introduced to the pharmaceutical industry more than ten years ago. Conventional wisdom suggests that with a standard so old, pharmaceutical companies must already be leveraging it to greatest advantage, but this is not the case. Poor communication of user requirements, often created through organizational silos between Process Development (R&D), Manufacturing/Production, and Engineering groups frequently result in equipment that meets specified requirements, but may not be suitable for the intended use. This results in a streamlined equipment qualification, but adds delays later in the process development lifecycle. This presentation will provide strategies to obtain a streamlined approach without imposing last-minute delays. thus ensuring a smooth technology transfer.

Attendees will learn:

- How to integrate Quality by Design (QbD) and ASTM E2900 to maximize impact on Validation Stage 1.
- A variety of strategies for facilitating a smooth transition from Stage 1 to Stage 2 validation, from pilot phase to technology transfer.
- How to build user requirements that result in functional specifications that truly address end-user concerns.
- Through a series of examples and case studies, how to structure a project so that all stakeholders have a common understanding of the desired project outcome.

10:15 *Mid-Morning Coffee Break*

10:30 **Avoiding Statistical Blunders in Process Validation**

Tara Scherder, Partner, SynoloStats

Applying statistical analyses without a thorough examination of the data structure for both expected and unexpected features can make those statistical analyses not only less accurate, but actually counter-productive, potentially resulting in wasted effort and poor decisions from those data. This talk will show why this is true, and ways to avoid these blunders via case studies of scenarios frequently encountered in process validation and manufacturing.

Critical Issues—Tech Transfer—Pfizer Case Study

11:15 **Global Tech Transfers and Process Validation Approaches**

Dushyant B. Varshney, Ph. D, Head of Manufacturing Science & Technology, Pfizer Inc.

Biologicals (e.g., therapeutic proteins, mAbs, ADCs, biosimilars), oncolytic and vaccines are developed as sterile injectable dosage form by small and large biopharmaceutical companies. Development of such biologics is quite expensive and many companies lack in-house setup and capability to develop at commercial scale. On the contrary, companies engaged in core or non-core business, have realized cost-saving by utilizing contract manufacturing organizations and improved productivity trends, as compared to investing in setting up and maintaining own facilities with required expert staff and regular updates. In such industry trends, technology transfer and validation of manufacturing process is becoming increasingly important to deliver safe and quality products. Moreover, challenges unique to each modality warrant special attention to manufacturing process and analytical method transfer during the entire product lifecycle in accordance with cGMP.

The talk will focus on the current challenges and solutions during global technology transfer and process validation approaches. Specifically, process validation roadmap for manufacturing of sterile liquid and lyophilized biologics & vaccines products will be discussed.

12:00 *Complimentary Lunch*

1:05 **How to Set the QC Limits and Do the Statistical Process Control (SPC)**

Shuguang Huang, Chief Scientific Officer, Stat4ward LLC

Shewhart Control charts are commonly used in monitoring the quality of a process. It includes two components: (1) setting the QC limits, and (2) implementing a decision algorithm—e.g. Westgard's rule—to determine process failures and warnings. The first component, setting the QC limits, may seem very simple. Many people use formula "Mean +/- 3*SD". Yet a thoughtful person may ask: why Mean? Why 3? Why SD? Why are the upper and lower limits symmetric around the mean? And what N should be required to do this calculation? For the second component, there are different empirical ones (e.g. Westgard rule) and mathematical ones (e.g. CUSUM, EWMA). How do we understand the relationship between the decision algorithm (e.g. some sensitizing rules) and the impact (e.g. false positive rate, false negative rate, average run length)? This presentation focuses on the statistical aspect of these basic questions.

1:50 **Business Perspectives On Process Validation**

Parveen Bhandola, President, Validation Edge, LLC

Process Validation being a regulatory requirement is imperative for the life sciences industry even to exist in business. Though most companies understand the necessity of Process Validation from regulatory compliance standpoint, they often tend to overlook the business benefits of performing Process Validation effectively and efficiently. Effective and efficient Process Validation can tremendously help in minimizing the business losses associated with the poor quality of the products resulting from process failures. The science-and-risk based lifecycle approach emphasized in the FDA's Process Validation Guidance (2011) is clearly aimed at improving the product quality and enhancing the process reliability. This is achieved by minimizing the process variability through improved understanding, control and monitoring of the manufacturing processes. Obviously, the improved product quality and reduced process failures directly lead to the higher business benefits.

This presentation will summarize key aspects of the Process Validation Guidance (2011) that are directly aimed at improving the product quality and reducing the process failures. Significance of these aspects of PV Guidance will be discussed from the perspective of enhancing the business benefits.

The presentation will also include three or four case studies illustrating the business losses directly related to performing the Process Validation ineffectively.

2:35 **Validation Master Plan**

Scott Collins, Director of Laboratory Operations and Compliance, QPharma, Inc.

Validation Master Plans (VMP) are a company's way to communicate a clear strategy for performing validation within the company. These documents are useful to external parties such as inspectors and auditors, but also to new personnel just joining the company. There may be one VMP with many sections, or multiple VMPs addressing different topics or areas of concern. This talk will provide logical rationale why a VMP should be developed, then point to several regulatory requirements for a VMP. We will define what a VMP is; review the contents of a typical VMP; demonstrate the difference between a VMP and a Validation Project Plan, and discuss the benefits of a VMP. Finally the presenter will share his experience working with the Agile Development Methodology and provide some direction on how this can be included in a VMP. This will be an interactive discussion, so please feel free to participate!

I. What is a Validation Master Plan?
- Definition and purpose of a VMP
- Regulatory and other rationale for having a VMP
- Scope and Types of VMPs
- VMP vs. VP

II. VMP Documentation Design
- General format recommendations
- Content and template

III. VMP Do's and Don'ts
- Pitfalls of poor designs
- Supplements and Attachments vs. direct content
- Improvements and Gap Analysis
- Maintaining a Validated State
- Document Maintenance

IV. Benefits and Strategies

V. Working Within the Agile Development Process
- Designing an Agile VMP
- Documentation List

3:20 *Afternoon Networking Break*

3:30 **Control Strategy for Cell and Gene Therapy Products**

CASE STUDY

Julia O'Neill, Principal, Tunnell Consulting

2017 was a milestone year for cell and gene therapy development, with several first-in-class FDA approvals granted. Often these products serve patients with few other options, and commercialization proceeds on an accelerated timeline. Moving these products quickly to market, while ensuring patient safety and product efficacy, requires us to challenge paradigms and develop new streamlined approaches. This session will provide an inside look at ways to define process control strategy, building on lessons from earlier biopharmaceutical technologies and a platform approach for cell and gene therapy manufacturing controls. Examples of challenging experiences and solutions will be presented.

4:15 **Review of FDA's Guidance on Quality Agreements and Best Practices to Ensure Your Supply Chain is Secure**

Sonali P. Gunawardhana, Counsel, Wiley Rein LLP

As companies continue to shift manufacturing operations and procurement overseas, knowing your supply chain and having comprehensive quality agreements becomes increasingly important. In addition, there are substantive differences between foreign inspections and domestic inspections, in terms of notice and agency responsibility, and more subtle differences, in terms of cultural differences, language barriers. This session will discuss how FDA's Guidance on Quality Agreements and will outline what your responsibilities are in terms of ensuring your supply chain is secure.

5:00 ***Close of Program***

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