PharmaED RESOURCES, Inc.

Cleaning Validation Virtual Summit, 2021

February 10–11, Online, EST

Featuring Lessons Learned and Case Studies From Industry Experts

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Hyde Consulting, Inc.

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Cleaning Validation Solutions

Michael Moussourakis
Senior Director
Alconox, Inc.

Walid El Azab
Senior Manager
Steris Corp.

Stephen Spiegelberg
President & Co-founder
Cambridge Polymer Group

David Vincent
CEO
VTI Life Sciences

And Comprehensive Coverage On:

- Lifecycle Management of Analytical Methods for Cleaning Verification Support
- Advances in Biopharmaceutical Cleaning Validation
- Best Practices for Regulatory Audits of Cleaning and Cleaning Validation
- Exploring ASTM Standards in Medical Device CV
- Exploring Manual Cleaning: Methods & Validation
- Maintaining Stainless Steel Equipment: Common Issues and Problems
- Cleaning Validation: Visual Inspection Practices
- And Much More!

Featuring Representation From:

STERIS · Bristol-Myers Squibb · novo nordisk® · ALCONOX CRITICAL CLEANING EXPERTS · Cleaning Validation Solutions

Hyde ENGINEERING +CONSULTING · Cambridge Polymer Group · VTI LIFE SCIENCES · NOVATEK INTERNATIONAL

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Wednesday, February 10, 2021

9:15

Chairperson Beth Kroeger's Welcome and Opening Remarks

Critical Issues—Lifecycle Management for Cleaning Validation

9:30

Common Issues with Cleaning and Maintaining Stainless Steel Equipment

Beth Kroeger, Technical Services Senior Manager, STERIS Life Sciences

Stainless steel equipment is ubiquitous in the Pharmaceutical manufacturing environment. How well it is maintained or not can impact the manufacturing schedule, the product, or the piece of equipment itself. Stainless steel has the unique ability to maintain a chemically resistant, chromium enriched, passive layer when exposed to oxygen. Acids such as nitric, phosphoric, citric as well as proprietary acid blends are commonly used to enhance the rate of formation of this passive layer. When the passive layer is exposed to adverse conditions there can be damage to the passive layer is exposed to adverse conditions there can be damage to the passive layer resulting in surface non-uniformities. This presentation will review standard recipes to enhance the passive layer formation as well as common test methods to evaluate the passive layer for predictive maintenance rather than reactive. The presentation will also include laboratory studies that investigate cleaning, passive layer monitoring, and preventative maintenance approaches to prevent surface non-uniformities and costly un-scheduled equipment downtime of process equipment, vessels, and piping.

10:15

Advances in Biopharmaceutical Cleaning Validation: A Decade of Transformation

Rizwan Sharnez, PhD., Founder and President, Cleaning Validation Solutions

In this session, we will discuss recent advances in our understanding of protein inactivation during cleaning. We will then leverage these advances to identify the elements of a robust cleaning validation program for bio-pharmaceuticals. We will also see how each element is systematically developed and integrated to ensure successful implementation. Current regulatory expectations, science-based methodologies for bench-scale cleaning characterization, CIP cycle development, and the lifecycle approach to cleaning validation and monitoring will also be discussed.

We will also cover the following advanced topics:

- Unique cleaning challenges for multiproduct bioprocess equipment.
- Effective strategies for addressing these challenges through planned bench-scale studies.
- Protein degradation studies and how they can be used to set achievable and meaningful acceptance limits for degraded human therapeutic proteins.
- Cleaning tenacious residues in bioreactors and media tanks.
- The use of master soils to streamline and provide flexibility for scheduling cleaning validation activities.

11:00

Manual Cleaning: Methods and Validation

Michael Moussourakis, Senior Director, Strategic Affairs, Alconox Inc.

A brief introduction will be presented reinforcing general cleaning concepts, chemistry and detergency. Aqueous detergent cleaning methods will be reviewed with a detailed focus on manual cleaning methods, associated pros and cons, and equipment. The necessary pre-and post-cleaning steps, vital to any cleaning application are presented as a lifestyle approach. Their goal being to facilitate cleaning validation programs. This includes needs for focus on set up and procedures before cleaning steps are introduced, during the cleaning process itself, and methods for good practice in post cleaning—long after the final rinse has been completed. Finally, a recent manual cleaning validation of a pharmaceutical product is presented as a case study and reviewed. The requirements, results and procedure followed. The residue detection methods chosen for both residual product and detergent will be discussed.

11:45

Lunch Hour.

12:45

Cleaning Validation Lifecycle—Applications, Methods, and Controls

David W. Vincent, CEO, MPH, Ph.D., VTI Life Sciences

Participants will benefit from surveying a hands-on approach to support the life science industry in the development and establishment of compliant cleaning programs that meet or exceed regulatory expectations. Key topics to be covered include:

- Current Regulatory Expectations
- How to Gain Process Understanding
- CIP and Automated Systems Design and Qualification of Equipment
- Cleaning Cycle Development and Validation
- Continued/Ongoing Cleaning Process Verification
- Tools That Enable Effective and Efficient Validation
- Change Management/Process Monitoring Stage

1:30 **Making Sense of Cleaning Limits**

Fred Ohsiek, Senior Specialist, Novo Nordisk

Determining cleaning validation limits can be very confusing and stressful, especially with all the recent changes. This presentation will cover:

- A brief history of cleaning limits
- Deciphering the HBEL paradigm shift for setting safety limits
- Acceptable ways to calculate active residue and cleaning agent safety limits
- Different methods for calculating limits for biotech
- Bioburden and endotoxin limits
- Methods for assessing non-accessible areas (i.e., pipes)
- Different approaches to calculating rinse grab sample limits
- Available analytical methods—when and where to apply
- Dedicated facilities/areas cleaning limits
- Any questions you have about limits

2:15 **Designing to Optimize Swab Recovery**

Brook Meadows, Senior Technical Service Associate, STERIS Life Sciences

Validation of cleaning processes is an FDA requirement to guard the purity and safety of pharmaceuticals and therapeutics. Cleaning of manufacturing equipment is critical to ensure that residues from products and cleaning agents do not carry over into subsequent product batches. Evidence of cleanliness depends heavily on the effectiveness of swab sampling of equipment surfaces.

Attendees will be guided through considerations (and their implications) when designing a swab sampling procedure. Low recoveries, interferences, contamination, analyte loss, and unexpected results are just some of the challenges that may be encountered when swab sampling. This presentation will cover effective swab sampling approaches to avoid issues and optimize swab recovery results.

3:00 ***End of Day 1***

Thursday, February 11, 2021

Regulatory Spotlight

9:25 **ASTM Standards in Medical Device Cleaning Validation**

Stephen Spiegelberg, President and Co-founder of Cambridge Polymer Group, Inc.

ASTM has been active in developing standards for medical device cleaning activities for the past two decades. These standards are being used for single use devices (permanent implants, disposable devices) as well as re-usable devices (surgical tools, patient assist devices, personal protective equipment), to help companies design, test, and validate their cleaning processes. These ASTM Standards are also referenced in the standards of allied organizations, including AAMI and ISO documents and guidance documents authored by the U.S. FDA. This presentation summarizes the current and pending standards that are available to assist in matters involving cleaning processes for the medical industry, along with how the standards are being used in the industry.

10:15 **Current Best Preparatory Practices for Regulatory Audits of Cleaning and Cleaning Validation Practices**

John M. Hyde, Chairman and Founder, Hyde Engineering & Consulting, Inc.

The cleaning of processing equipment and interconnecting piping systems is an essential process in pharmaceutical and biopharmaceutical manufacturing facilities. Cleaning is used to remove post production and cleaning agent residues to acceptable levels prior to the production of the next batch or product. Cleaning process efficacy and its validation are often the subject of regulatory audits because of concerns for drug substance and/or drug product adulteration. The materials presented in this session will address best practices for regulatory audit preparations for both pre-approval inspections (PAIs) and periodic GMP inspections for critical aspects of process equipment cleaning and cleaning validation activities.

The session will specifically address:

- Country specific and global cleaning validation requirements and expectations including 21 CFR 211, Eurdralex Vol. 4 Annex 15, ICH Q7, US FDA Cleaning Validation Guidance, Health Canada Cleaning Validation Guidelines, PIC/S PI 006-3 and others
- GAP analysis methodologies for audit preparation
- Best practices for cleaning validation program design and documentation
- Effective organization and presentation of cleaning validation testing methodologies and data to regulatory auditors
- Strategies for response to cleaning related questions from auditors both in real-time during an inspection and follow-up responses to regulatory observations

Critical Issues—Software Validation for Manufacturing Execution Systems

11:00 **Those Boring CV Documents Made Exciting**

Fred Ohsiek, Senior Specialist, Novo Nordisk

Documenting your cleaning validation activities is a regulatory requirement. There are so very different ways to do this. It is not just about having the information, but also how and where it is housed. This presentation will cover how to organize your legacy facility

or how to create a new program from the ground up. Topics for discussion are:

- List and discussion of all required documents and some nice-to-have documents
- Significance and advantages of stage 1 documents
- The "be all" cleaning validation risk assessment
- Organizing and storing legacy data
- Different approaches to cycle development and how to properly close them out
- Cleaning related SOPs
- Skinning up those CV protocols
- Using only normal operating systems (i.e., LIMS, MES) to document execution of CV
- CV failures and how to handle them
- Routine monitoring frequency using a risk-based approach

Fred Ohsiek is the Sr Cleaning Validation Specialist for Novo Nordisk in Clayton, NC. He earned his Bachelor in Chemistry from University of South Florida. His professional work experience includes 7 years of R&D performing enzymatic digestion, ultrafiltration and fermentation on citrus peel while working for the USDA and over 20 years of cleaning validation while working for Catalent Pharma Solutions, Amylin Pharmaceuticals, Ben Venue Laboratories, Teva Pharmaceutical Industries, Astellas Pharma Technologies Bayer (biotech division), and Novo Nordisk.

His cleaning validation experience includes risk assessments, cleaning development, validation, and monitoring cleaning processes for equipment used to manufacture small molecule [oral dose (solid and liquid) and parenteral], peptide hormone encased (parenteral), and large molecule (biotech) pharmaceutical, OTC, and nutritional products. The scope of his work involved drug substance and drug product manufacturing start-up, remediation, legacy justification, and increasing manufacturing capability. He has created lean CV strategies for document structure/flow and execution in every aspect of the cleaning validation process.

He was one of the authors on the new ISPE Guide: *Cleaning Validation Lifecycle—Applications, Methods, and Controls* and the cleaning validation acceptance criteria chapter lead.

11:45 *Lunch break.*

12:45

Lifecycle Management of Analytical Methods for Cleaning Verification Support

Mariann Neverovitch, Research Scientist, Bristol-Myers Squibb

Equipment Cleaning is a critical GMP element of the Manufacturing Process. It ensures quality and safety of the future batch. Cleaning Validation/verification is a measurement of the effectiveness of the cleaning process

In this presentation we will go over advantages and challenges of specific and non-specific analytical methods based on risk assessment of the residual product. Case studies, training and qualification programs will also be discussed.

1:30

Cleaning Validation: Visual Inspection Practices

El Azab Walid, Manager Senior Technical Services Steris Corp

The presentation goal is to compare the current practices for visual inspection amongst several pharmaceutical manufacturers. The presentation discusses the manufacturer practices against the current regulatory requirements for cleaning validation (EU Annex 15, ICHQ7, US FDA guideline on cleaning validation, EMA HBEL guideline, etc.). In this regard, a survey performed on various manufacturers around the world will be shared. The goal is to discuss the survey results, compare practices and share the minimum requirement for visual inspection procedure. Through a case study, the presentation shares factors that could alter visual inspection of cleaned equipment.

Key take away:

1. Understand the current benchmark regarding visual inspection of clean process equipment.
2. Understand the regulatory requirements for cleaning inspection.
3. Share lessons learned and understand the minimum requirement for visual inspection training

2:15

Implementing a Risk-Based, Data Integrity Compliant Cleaning Validation Management System

Sheba Zaman, Head of Product Specialists, Novatek International

In pharmaceutical manufacturing, risk of contamination is from a broad range of factors such as cross contamination (other pharmaceutical active ingredients), cleaning agents and micro-organisms.

Additionally, the risk of contamination may in some cases be from a calculation error which results in choosing the wrong Maximum Carry-Over Limit (MAC). For example, can you consider the number of calculations required for an equipment train, with twenty (20) sample points, having different surface areas (swab sample area), different sampling types (swab/rinse), five (5) products manufactured on the equipment train, and each product has ten (10) production stages, and two (2) different cleaning agents are used. There is a huge risk associate with calculating the Maximum Carry-Over Limit (MAC) manually.

Automation has played a key role in decreasing risks associated with various processes. Data integrity is an important component of industry's responsibility to ensure the safety, efficacy, and quality of pharmaceutical products.

3:00

Readily Rinse Residues

Seth Robinson, Technical Service Associate, STERIS Life Sciences

Validation of cleaning processes is an FDA requirement to guard the purity and safety of pharmaceuticals and therapeutics. Cleaning of manufacturing equipment is critical to ensure that residues from products and cleaning agents do not carry over into subsequent product batches. Evidence of cleanliness depends heavily on the effectiveness of sampling of equipment surfaces. Discussion will involve what factors to be considered when designing rinse studies aimed at the removal of material from surfaces as an alternative to swabbing. An example of how a rinse study could be performed will be discussed, giving details on each step of the process. Data obtained from a rinse study could fulfill the requirements or improve upon a cleaning validation.

3:45

Close of Conference

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In the Age of COVID, the Show Must Go Online

In response to overwhelming audience and speaker feedback, and in view of the current health and safety concerns involving the novel coronavirus COVID-19, we're taking our events online (at least for the foreseeable future; we do hope to see you again soon in person when all this is over!) **Cleaning Validation Virtual Summit, 2021** is an entirely online event, complete with insightful presentations from leading researchers, 1:1 networking opportunities, live question & answer sessions, and sponsored informational presentations that highlight how vendors are tackling some of the key issues facing the Microneedle market today. Just sit back and enjoy this online learning experience from the safety and comfort of your home or office. Missed a session or two? No worries—the full program will be archived and available for post-conference viewing and download.

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