PharmaED RESOURCES, Inc.

Cleaning Validation Summit 2017

October 2–3, 2017, Racquet Club of Philadelphia, PA

Featured Speakers Include:

Keynote Speaker
David G. Dolan, Ph.D., DABT
Occupational, Environmental & Quality Toxicology Expert at Amgen Inc.

Robert Jernigan
Validation Group Leader QA Validation Oversight at GSK Zebulon

Stephen Spiegelberg
President Cambridge Polymer Group, Inc.

Mariann Neverovitch
Research Scientist at Bristol-Myers Squibb

Fred Ohsiek
Sr. Manager Cleaning Validation at Bayer

Joe Cagnassola
Principal Validation Engineer Alcon, a Novartis company

Andrew Walsh
President at Center for Pharmaceutical Cleaning Innovation

With Comprehensive Coverage On:

- Ensuring your Cleaning Program is FDA Audit Ready
- Cleaning Validation and Continued Process Verification
- Risk-Based Approach
- Cleaning Limits and Visual Inspection from the Analytical Perspectives
- Determine Cleanability and its Applications in Cleaning Validation
- Process Validation & Cleaning Strategies during Technology Transfer of Sterile Injectables
- EU GMP Changes and Its Impact on Cleaning Validation
- Quality by Design for Effective Cleaning Procedure
- Writing Cleaning Validation SOPs
- And Much More

Are you compliant with FDA requirements for cleaning 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:

Cambridge Polymer Group · MedImmune, A member of the AstraZeneca Group · Bristol-Myers Squibb · Alcon, a Novartis company · TOXIKON, Advancing Your Innovation · chematic, formulated detergents · Bayer · ECOLAB, Everywhere It Matters · ValSource · CPCI · Hospira · Dartmouth College · G&W Laboratories, Helping People Realize Their Potential · Akorn · Amgen · Dober · Sandoz, a Novartis company · STERIS · GlaxoSmithKline · Columbia University

PharmaEd Resources, Inc. • 2810 Robeson Park Drive • Champaign, IL 61822
tel. 217.721.5774 • *web.* www.pharmaedresources.com

Monday, October 2, 2017

7:30 *Complimentary Breakfast & Chairperson's Remarks*

7:50 *Welcome and opening remarks by Chairperson: Edward (Ned) Wymann, Principal Scientist Validation, MedImmune*

8:00

The Toxicological and Risk Assessment Basis of Establishing ADEs/PDEs for Risk-Based Cleaning

David G. Dolan, Ph.D., DABT, Occupational, Environmental, & Quality Toxicology Expert, Amgen Inc.

This presentation will address the toxicological and risk assessment basis for establishing Health-Based Exposure Limits (HBELs, i.e., ADEs/PDEs), in support of cleaning validation programs, and the rationale for use of HBELs over the traditional, non-risk-based methods.

8:45

Using the ADE/PDE Concept for Implementing a Science and Risk-based Cleaning Program

Andrew Walsh, President, Center for Pharmaceutical Cleaning Innovation, (CPCI)

This presentation will discuss how cleaning limits based 0.001 dose / 10ppm should be replaced by the ADE/PDE which are truly "science-based" and provide for appropriate assessments of Risk which can allow for greatly simplified cleaning validation programs, reducing the effort, formality and documentation necessary for cleaning validation, allowing the use of much easier and faster methods and simplifying new product introductions.

9:30

Standard Operating Procedure for Cleaning Validation Methods Including Method Transfer Activities in an Analytical Lab

Salvador Lopez, Sr. Analytical Scientist, R&D, Akorn Pharmaceuticals

The key elements of a robust cleaning method validation that should be included in a standard operating procedure (SOP) will be discussed. A cleaning verification program in an R&D analytical laboratory setting should also incorporate and include the Method Transfer activities to a receiving laboratory. There must be a high level of confidence in the analytical results in order to verify the absence of residues at the prescribed limits on the various equipment surfaces. Typically the most common surfaces to be discussed will be SS316, Teflon, Red Rubber and Silicone.

This talk will also discuss the validation parameters to be performed during a cleaning method validation. Details on some key factors to consider during the cleaning verification in the Analytical Laboratory will be provided, while highlighting many common mistakes to avoid.

10:15 *Networking Coffee Break*

10:45

Development of a Modified SDS-PAGE for Quantifying Protein Degradation to Support Cleaning Validation

CASE STUDY

Dylan Wang, Dartmouth College

This Case Study will present an analytical method to quantify the degradation of biopharmaceutical protein products during cleaning processes. The degradation of proteins, in this way, can be accurately measured and proven instead of assumed. Based on the existing SDS-Page method, we have developed a highly accurate, low cost and time saving technique to analyze protein degradation. The time of exposure, cleaning agent concentration and temperature are controlled to mimic cleaning procedures. Using Design of Experiments(DOE) results can be analyzed to statistically evaluate the importance of each cleaning factor as well as their interactions, providing additional information to help manufacturers optimize their cleaning processes.

11:30

Analytical Approach for Implementation of Visual Inspection

Mariann Neverovitch, Cleaning Validation SME, Analytical Strategic Operations, Analytical & Bioanalytical Operations, Bristol-Myers Squibb

Visual inspection following equipment cleaning is a mandatory step in the cleaning verification workflow for pharmaceutical equipment. Equipment must pass visual inspection before swab sampling for analysis can be performed. However, since a significant number of low risk compounds are visible well below established safety levels, it is possible to justify equipment as "visually clean" without performing swabbing analysis. Internal studies performed at BMS showed that over 90% of participants could identify residual product at a level of ~2 ppm without preliminary training. The implementation of a robust visual inspection qualification program and clear "Visually Clean" inspection parameters can enable visual inspection to be used to qualify equipment in lieu of swab analysis for low risk products.

12:15 *Complimentary Lunch*

1:15

Three-Legged Stool Approach to Stage 1 for Cleaning

Edward (Ned) Wymann, Principal Scientist Validation, MedImmune

In this presentation, we will review the three main aspects of Stage 1 (Process Design) Cleaning Validation:

- Product Characteristics (Active Ingredient and other raw materials):
  - Bio/chemical Properties
  - Tox info
  - Denaturation studies
- Small-Scale Studies:
  - Recovery studies
  - Cleanability studies vs. worst-case materials

- The Commercial-Scale Validation/Verifications requirements are based upon above
  - Hardest-to-clean: Full Blown Validation
  - Not harder-to-clean: Commercial-Scale Verification
  - Easier-to-clean: Minimal Sampling

2:00 **Determining TOC Surface Swab Location(s) during Cleaning Validation**

Danielle Gabrish, Associate Scientist II, AstraZeneca Biologics, (MedImmune)

In this presentation, we will review the methodology of determining TOC surface swab locations during Cleaning Validation:

- Sampling (Rinse Sampling and TOC Surface Swabbing)
  - Pre-determined acceptance criteria
  - Illustrate removal of carbon from representative surface area via recovery
- Development for TOC Surface Swabbing:
  - Post-OQ results during riboflavin for "hardest" spray coverage, if applicable
  - Visual Inspection Program
- Justification:
  - Design and Construction
  - Material of Construction
  - Define worst case raised/sample ports
  - Agitators
  - Filter housings
  - Hard-piped transfer lines
- Process Contact Surfaces
  - Worst case locations based on shadowing from the sprayball, if applicable
  - Representative locations for largest surface area

2:45 *Afternoon Networking Break*

3:00 **Use of Statistics For Cleaning Validation**

Igor Gorsky, Senior Consultant at ConcordiaValSource, LLC

Use of Statistics in Cleaning Validation Lifecycle proposes a number of statistical tools that help in evaluation of data attained in three stages of Cleaning Validation efforts – Stage 1: Process Design, Stage 2: Process Qualification and Stage3, Continued Process Verification. In a light of upcoming ASTM Standard Guide for Science-Based and Risk-Based Cleaning Process Development and Validation this information should be valuable to Cleaning Validation professionals, as it provides practical methods for data analysis and interpretation. The key learning objective of this presentation is to show that data gotten during Cleaning Validation lifecycle is not just measured on "pass" and "fail" merits but can be understood on a more granular level which in turn should help in understanding of the cleaning processes which in turn should help in optimization of the latter to improve consistency thus reducing risk due to cleaning for product's manufacturing and protection of patient's safety.

3:45 **Cleaning Validation Protocols and Contents**

Fred Ohsiek, Sr Manager of Cleaning Validation and Site Cleaning Validation SME for Bayer U.S. LLC

The presentation will discuss the different types of cleaning validation protocols (i.e. verification, cycle development, validation, clean hold time, and campaigning). It will cover the progression and timing of the protocol types. Protocol sections will be discussed in detail: Purpose; Scope, Rationale; Acceptance Criteria; and Equipment and Product Release. Finally, the presentation will discuss issues during protocol execution (i.e. visual, swab, and cleaning procedure failures).

4:30 **Designing an Effective Cleaning Process**

Beth Kroeger, Technical Services Manager, STERIS Life Sciences

An effective and robust cleaning program can reduce equipment downtime and minimize the risk of cross contamination in multi-product facilities. Building an effective cleaning program from the onset is important and should consider equipment design aspects, residue selection and conditions and establish adequate cycle parameters. Part of this process is establishing correct limits within process capability to avoid excessive cleaning equipment changeover. This discussion will cover cleaning design issues, development of cleaning cycles, how to establish limits and culminate it tying it all together with lessons learned from a process capability cleaning issue demonstrating the need for process understanding to improve your current cleaning validation program.

5:15 *End of Day One*

Tuesday, October 3, 2017

7:30 *Complimentary Breakfast & Chairperson's Remarks*

7:50 *Welcome and opening remarks by Chairperson: Edward (Ned) Wymann, Principal Scientist Validation, MedImmune*

8:00 **Cleaning Process Development from Lab Bench to Full Scale—A Lean Six Sigma Case Study**

CASE STUDY

Sophie Song, Process Development Scientist, Center for Pharmaceutical Cleaning Innovation, (CPCI)

This Case Study will show how improvements in laboratory techniques for Cleaning Process Development incorporating Design of Experiments were used to optimize and simplify cleaning processes at a Semi-Solid Dosage Manufacturer resulting in significant time, energy and resource savings while executing a compliance remediation project. This presentation will also showcase new technologies that have been developed for use in bench scale analysis.

8:45 **ASTM Activities in Cleaning Validation**

Stephen Spiegelberg, President, Cambridge Polymer Group, Inc.

The improvements in medical device design and surgical procedures in the past several years have resulted in a higher standard of clinical success for medical devices. As fewer complications arise from previous issues of material failure, product design, or surgical technique, emphasis is now being placed on the cleanliness of medical devices. Ideally, manufacturers would like to produce parts with no contaminants. Practically, this goal is not achievable, and manufacturing costs increase dramatically as manufacturers attempt to reduce the levels of contamination. Two key questions that most quality assurance engineers are asking these days are "how clean is clean enough?" and "how does one assess cleanliness?".

The FDA has provided guidance for cleaning validation of processing equipment for pharmaceutical compounds since 1993, but there has been little guidance for medical devices. Past product recalls relating to device cleanliness have helped to spur activities within ASTM, as well as inclusion in ISO and USP standards. Working with medical device manufacturers, analytical laboratories, NIST, the FDA, and medical device consultants, an ASTM task force has been working for the past 16 years to address issues of cleanliness in biomedical components. Standards have been developed to determine the level of manufacturing residues on medical devices, formulations for test soils to develop and verify cleaning procedures for re-usable devices, and guides for validating cleaning lines. This presentation summarizes the current and pending standards that are available to assist in matters involving cleaning processes for the medical industry.

9:30 ***Networking and Coffee Break***

10:00 **The Science of Cleaning to Achieve Optimal Equipment Efficiency**

Dan Dobrez, Executive VP, Formulated Detergents, Dober

If you are a manufacturer of regulated products, with challenging residues in your process equipment and a need to increase productivity by reducing cleaning time, it's important to develop a robust cleaning process.

We will share the science behind effective equipment cleaning and the variables involved in determining the best cleaning process for your specific residues, equipment, energy resources and manufacturing environment. The critical cleaning parameters to know and understand begin with T.A.C.T. (Time, Action, Chemistry and Temperature). It is also important to understand that effective cleaning is a combination of both physical and chemical processes.

An optimized cleaning process will improve manufacturing throughput and turnaround time to meet market demands.

Learning Points:

- Effective and efficient cleaning can maximize your assets by minimizing equipment downtime, reducing labor costs, maintaining turnaround time and ensuring regulatory compliance.
- Understanding the science of cleaning and the nature of the residue will help identify opportunities to improve your current process or be a starting point on how effective cleaning could improve operational efficiencies.
  - The science of cleaning is best understood through a discussion of T.A.C.T (Time, Action, Chemistry and Temperature), as well as understanding that effective cleaning is a combination of both physical and chemical processes.

10:45 **Manual Cleaning . . . Why Validate?**

Maria Ramirez-Marrero, Sr. Scientist II, Technical Services, G&W Laboratories, Inc.

The presentation will discuss the importance of validating the manual cleaning process of the GMP equipment used in the pharmaceutical industry. It will include definitions, FDA guidelines, the cleaning parameters to consider when performing a manual cleaning validation, effective cleaning instructions, situations to avoid that could compromise the repeatability of the process, how to implement the successful results into an effective manual cleaning procedure, and how to verify the effectiveness of the validated procedure.

11:30 **Analytical Methods for Residual Analysis: Is it Clean? What am I Looking for Anyway?**

Dr. Stephen A. Doherty, Director of Analytical Chemistry, Toxikon

During manufacture and processing an implantable device can be exposed to a variety of processing agents, lubricants, oils, polishing agents and cleaning agents. During its product lifetime, a reusable medical device (RMD) may go through multiple cycles of use and cleaning, which require confirmation that the soiled device is ready for use. When evaluating cleaning procedures an important consideration is how to access that the component is clean. One method of accomplishing this is to analytically evaluate the component for the presence of material(s) of interest. An understanding of the composition of the materials of interest allows for the selection of the appropriate analytical instrumentation. Common methods of analysis are by Total Organic Carbon (TOC), Gas Chromatography, Liquid Chromatography and Ultra-Violet Visible (UV/Vi). Strategies for analysis including method selection, the use of marker components and validation requirements and common challenges will be discussed.

12:15 ***Complimentary Lunch***

1:15

Do What You Say, Say What You Do, Ensuring Cleaning Procedures Match Actual Practice

Joe Cagnassola, Principal Validation Engineer at Alcon, A Novartis Company

In today's heightened regulatory scrutiny, customers demand for faster turnaround times and ever changing production priorities the difficulty is establishing a robust repeatable cleaning program is easier said than done. The foundation of the cleaning program is based on concise and repeatable procedures that include design, regulatory and personnel considerations. The cleaning scope includes but is not limited to legacy and new installations automated and manual cleaning processes, personnel training and continued verification.

The cleaning procedures should be based on the actual process steps, but as many individuals have encountered not all cleaning procedures are specific or detailed enough to dictate that the cleaning process is followed as expected. This gap is what auditors are looking at when reviewing a firms cleaning approach. To ensure that the hard work that is applied to cleaning process is value added, cleaning procedures need to meet and or exceed the required regulatory, customer expectations but provide reasonable turnaround times that rapid pace manufacturing facilities require. To accomplish this we will review the development of a Cleaning SOP, form, protocol and report that will provide guidance for how to document the cleaning program that anyone from the new employee to the site SME will be able to understand and defend.

Examples of Cleaning Problems

Written procedures for cleaning and maintenance fail to include description in sufficient detail of methods, equipment and materials used.

The deviation indicates that the most probable cause was human error in that the SOP cleaning instructions were not properly executed.

2:00

Cleaning Protocol Development and Program Maintenance

Robert Jernigan,Validation Group Leader, QA Validation Oversight, GSK Zebulon

Cleaning validation protocols should describe the equipment to be cleaned and state the cleaning methods to be used. Protocols should describe the extent of the cleaning and list any critical parameters to be monitored and/or controlled. Protocols should provide analytical methods used for sample analysis. Cleaning Protocols should also state method of sample collection i.e. swabbing vs rinses and how samples will be collected and labeled. Protocols should also clearly indicate areas where samples will be taken. Finally, residue limits should be stated and limits should be practical and verifiable. Limits should be based on minimum known pharmacological or physiological activity of the API. Also, cleaning procedures should be periodically examined to ensure procedures are robust and remain effective.

2:45

CASE STUDY

Work Smart: Risk Based Approach for Cleaning Validation

Walid El Azab, Technical Service Manager STERIS N.V. / S.A., A Subsidiary of STERIS Corporation

The presentation will explain the impact of the changes in EU and EMA guidelines regarding cleaning validation. Following that, the presentation will deep dive on risk-based approach to be used to ensure compliance with the international cleaning regulatory. Finally, through a case study (used as an example) the presentation will present rational to develop risk based cleaning validation limit and program: (1) assess and prioritize the toxicological value, (2) assess the safe threshold value versus the cleaning process capability, (3) understand the influence of the recovery rate, LOQ/LOD of the analytical methods on setting cleaning limit, (4) when visual residue limit could be used only. The risk assessment objective is to rationalize the numbers of validations run, prioritize the workload and demonstrate effective the cleaning process in place. Finally, we will share different approaches implemented by manufacturers around the globe.

3:30 *Afternoon Networking Break*

3:45

CASE STUDY

Detergent Requirements for the Pharma Industry

Grant Lindh, Senior Chemist, Global Life Sciences, RD&E, Ecolab

Cleaning and cleaning validation have been hot topics in the pharma industry for decades. Even today, there is a focus on cleaning per the latest guidelines where terminologies like cleanability and effective cleaning agents are outlined. This talk will focus on requirements for cleaning agents in terms of composition, substances that should not be present in detergents, and what kind of documentation is needed. Questions like using the LD50 or PDE values for limit calculations will be discussed. Finally, you will get to know what level of information is required for a cleaning agent to have on file to do a proper cleaning validation.

4:30

At-Line PAT Using TOC— A Lean Six Sigma Case Study

Andrew Walsh, President Center for Pharmaceutical Cleaning Innovation, (CPCI)

The Case Study will discuss how Total Organic Carbon Analysis can be implemented as an "At-Line" Process Analytical Technology (PAT) application replacing HPLC and greatly reducing the time and resources needed to release manufacturing equipment back into production through an example at a Solid Oral Dosage Form manufacturer.

5:15 *Close of Program*

Cleaning Validation Forum is Sponsored By

CPCI

ECOLAB
Everywhere It Matters.

chematic
formulated detergents

TOXIKON
ADVANCING YOUR INNOVATION

STERIS

BECKMAN COULTER
Life Sciences

PharmaED RESOURCES, Inc.

PharmaEd Resources, Inc. • 2810 Robeson Park Drive • Champaign, IL 61822

About your conference destination:

The Racquet Club of Philadelphia is located in the heart of downtown Philadelphia, adjacent to beautiful Rittenhouse Square. From the conference venue, you can access many points of interest in Philadelphia including Independence Hall, the Kimmel Center, the Avenue of the Arts, numerous shops, and excellent restaurants!

Registration Information

Register for the conference using one of three options:
Online: www.pharmaedresources.com **Phone:** (217) 721-5774
Mail: 2810 Robeson Park Drive, Champaign, IL 61822

Please Complete the Following

FIRST NAME: _____

LAST NAME: _____

TITLE: _____

COMPANY: _____

ADDRESS: _____

ADDRESS: _____

CITY: _____ STATE: _____

ZIP: _____ COUNTRY CODE: _____

OFFICE PHONE: _____

MOBILE PHONE: _____

FAX: _____

E-MAIL: _____

VENUE INFORMATION:

Dates:	October 2–3, 2017
Venue:	The Racquet Club of Philadelphia
Venue Address:	215 South 16th Street Philadelphia, PA 19102
Venue Phone:	(215) 735-1525
Hotel Room Block:	Radisson Blu Warwick
Hotel Address:	220 South 17th Street Philadelphia, PA 19103
Reservations:	(800) 967-9033
Hotel Telephone:	(215) 735-6000

Please register me for:

Cleaning Validation Summit 2017

Standard Registration: $1,595
Early Bird Special: Register by July 15th and save $200!
Call for government or academic discount

PAYMENT METHOD

CREDIT CARD REGISTRATION:

☐ CREDIT CARD ☐ VISA ☐ MASTERCARD ☐ AMEX

NAME: _____

CARD #: _____

EXPIRATION: ____ / ____

SIGNATURE: _____

BILLING ADDRESS: _____

CHECK REGISTRATION:

To pay by check, please provide a purchase order below. Please note that all payments must be received five (5) days prior to the conference to ensure space. Attendees will not be admitted to the conference without full payment.

PURCHASE ORDER #:

PLEASE NOTE:

PharmaEd Resources does not offer refunds. Howerver, if you cannot attend after registering, we are happy to apply your registration fee to another PharmaEd Resources event, or transfer your registration to a colleague. Notice of cancellation must be received at least 5 days prior to the event.