Cleaning Validation Summit 2018
September 12–13, 2018, Philadelphia, PA
Pharma-Ed Exclusive: The new ASTM Cleaning Standard for Drugs and Devices
—Hear From All of the Authors—

Featured Speakers Include:

Mohammed Ovais
Amgen

Andrew Walsh
CPCI

Jessica Graham
BMS

Robert Kowal
Johnson & Johnson

Stephen Spiegelberg
Cambridge Polymer Group

Fred Ohsiek
Bayer

Beth Kroeger
Steris Corporation

Thomas Altmann
Ecolab

Are you up to speed on the new Science, Risk and Statistics based approaches for Cleaning Validation? Today’s regulators are now asking for, and expecting, ADE Monographs and Risk Assessments of Cleaning Validation Programs. This two-day intensive summit brings together industry leaders on science, risk and statistics-based cleaning validation to get you started in implementing these 21st Century approaches. These new approaches can reduce the level of effort, formality and documentation of cleaning validation based on risk, streamline the validation work and accelerate the introduction of new products.

The entire team that wrote the new ASTM Standard Guide for Science Based and Risk Based Cleaning Process Development and Validation will be there and presenting!

With Comprehensive Coverage On:

- ASTM Standard on Science and Risk-Based Cleaning Process Development and Validation
- Case Study for Low-Risk Manufacturing
- ASTM Standard on Derivation of Health Based Exposure Limits (ADEs/PDEs)
- How to use ADEs/PDEs for Setting Cleaning Acceptance Limits
- ASTM Standard for Validating Cleaning Processes Used During the Manufacture of Medical Devices
- Upcoming ASTM Cleaning Standards Covering Both Drugs and Devices
- Automation for Rapid Cleaning Process Development
- Application of Risk Assessments to Cleaning Processes
- Risk-based Selection of Analytical methods
- Risk-based Implementation of Total Organic Carbon Analysis (TOC)
- Application and Qualification of Visual Inspection
- Identification of Unknown Residues Found in Cleaning Validations
- Statistical Evaluation of Cleaning Validation Data
- Application of Bayesian Statistics to Cleaning

With Representation From:

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Wednesday, September 12, 2018

Complimentary Breakfast & Chairperson’s Remarks
7:30

Welcome and opening remarks by Chairperson, Joe Cagnassola, Principal Validation Engineer, Alcon, a Novartis Company
7:50

FDA Standards Specific to Cleaning/Medical Devices
8:00

How the FDA Uses Standards in General, and Specifically to Cleaning Activities in Medical Devices – The CDRH Voluntary Consensus Standards Program

Sharon Lappalainen, AStd Deputy Director, FDA| CDRH|OCD|Standards and Conformity Assessment

FDA will present an overview of the US Standards Strategy and specific legislative activities related to the Center for Devices and Radiological Health recognition authority for medical device standards and how they are used in premarket submissions. Included in this discussion is the recognition process and requests for recognition. The talk will then turn to reprocessing (including cleaning, disinfection, and sterilization) of reusable and single use medical devices with examples given with regards to research on cleaning residuals for cardiac electrophysiology catheters and GI biopsy forceps. The presentation will conclude with how to locate FDA guidance documents, recognized standards, and web resources.

New ASTM Cleaning Standards for Drugs and Devices
8:40

New ASTM Standard for HBELs and Calculation of Cleaning Limits

Jessica C. Graham, Ph.D., DABT, Senior Toxicologist, BMS, (ASTM, HBEL Team Member)

This presentation will describe the work of a team of experts in toxicology and cleaning validation who comprise the ASTM’s Health Based Exposure Limits Guideline Workgroup. Limit-setting to establish acceptable levels of unintended human exposure to active pharmaceutical ingredients (APIs) and other molecules related to the pharmaceutical manufacturing process (e.g. synthesis intermediates, cleaning agents) are necessary to comply with various global regulations as part of international cGMP quality requirements, needed as good product stewardship, and are considered the industry standard. ASTM is actively developing a standard for the derivation of Health Based Exposure Limits (HBELs) to assist industry in the derivation and documentation of HBELs. These limits can then be further utilized to calculate cleaning residuals limits used in quality risk assessment for the manufacture of pharmaceuticals. This standard will provide a scientifically justified, data driven, consistent approach to deriving safe limits for unintended exposures to individual substances. This presentation will focus on the key components of this standard (1) Hazard characterization, (2) Identification of the critical effect(s) including dose-response assessment, (3) Determination of one or several Points of Departure (PoD)s for the calculation of HBELs, (4) Application of PoD-specific Adjustment Factors (AFs), and (5) Calculation of HBELs including justification for the preference given to a particular derivation rationale if more than one was developed.

Introduction to the New ASTM Cleaning Standard — Case Study For Low-Risk Products

Andrew Walsh, President, Cleaning Validation SME, CPCI, (ASTM Cleaning Team Member)

The presentation will be explore the structure of the new ASTM E3106 Standard and its foundation in ICH Q9 and the FDA’s Guidance on Process Validation. The importance of using HBELs will be discussed in combination with Cleaning Process Development, Analytical Method Development and the statistical evaluation of cleaning data. A case study showing how the implementation of E3106 for a low risk pharmaceutical manufacturing facility provided improvements to the cleaning process (reduce temperature, cleaning time and water usage) while simplifying and streamlining the cleaning validation. The presentation will also include a discussion and analysis on the updated EMA Q&A on Setting Health Based Exposure Limits and its applicability to the E3106 Standard.

Mid-Morning Networking Break
10:05

ASTM Standards in Medical Device Cleaning Validation

Stephen Spiegelberg, Ph.D President, Cambridge Polymer Group, Inc., (ASTM Device Cleaning Team Member)

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 and disposable devices), as well as re-usable devices, (surgical tools and patient assist devices), to help companies design, test, and validate their cleaning processes. 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.

Practical Implementation of the ASTM E3107 in the Pharmaceutical Industry

Thomas Altmann, Global CIP/COP Technical Manager, Ecolab Life Sciences, (ASTM Cleaning Team Member)

In 2011, the FDA published general principles for process validation following a life cycle approach. The pharmaceutical industry has begun to apply these principles to cleaning process validation; however, to fully implement life cycle practices into cleaning process development and validation, the industry’s challenge is to translate the 2011 guidance to a structured, practical, risk-based approach. The ASTM guide E3107 provides the framework and structure for science- and risk-based approaches. This presen-
Risk Assessment in Cleaning of Pharmaceutical Products
Robert Kowal, Cleaning Validation SME, Johnson & Johnson, (retired), (ASTM Cleaning Team Member)

This presentation will discuss the concept and measurement of risk as it applies to the cleaning of pharmaceutical products. Attendees will learn how to apply risk tools to science based data to assist in measuring and assessing the risk associated with cleaning process failures as well as how these tools can be applied to develop a cleaning risk dashboard.

Developing and Writing Cleaning Procedures
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 firm’s cleaning approach. To ensure that the hard work that is applied to the 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.

Evaluation of Cleaning Data: More Than Just Pass/Fail
Mohammad Ovais, Cleaning/Process Validation SME, Amgen, (ASTM Cleaning Team Member)

How clean is clean? Should the cleaning validation results be averaged? What should one do if any of the results are outside acceptance limits? These are some of the questions that one might have heard from scientists involved in validation of cleaning procedures. But there seem to be no definitive answers. This presentation will be an attempt to address these concerns.

This presentation will discuss some of the regulatory expectations related to cleaning validation, and current approaches to cleaning data evaluation and their limitations. It will then discuss how statistical thinking can be used for understanding of cleaning processes and associated variability. The highlight of the presentation will be a novel approach for estimating probability of exceeding cleaning limits. Using real-world examples, the presentation will demonstrate the application of the proposed approach.

Automation of Cleaning Process Development
Sophie (Ruijin) Song, Cleaning Process Development Scientist, CPCI

Newly developed automated, high throughput technologies will be presented that can be used to rapidly determine the Cleanability of Pharmaceutical, Biological, Cosmetic, etc. products as described in E3106. These devices can also rapidly determine the best cleaning agents, and rapidly determine optimal cleaning parameters for a cleaning process using Design of Experiments and other statistical techniques. Why bench-scale determination is the only legitimate means of selecting “hardest-to-clean” products will be presented. One of the automated, high throughput devices will be on hand for demonstration.

Targeted Cleaning for the Pharma Industry
Chad Rhodes, Business Development Manager, North America, Dober

With growing competition and market demand, the pharmaceutical industry needs to constantly upgrade itself in order to be efficient and get the most of its assets. Therefore, cleaning of pharmaceutical equipment has come to the forefront, as this is one of the factors that limit increases in productivity. Correct cleaning chemistry and knowledge of parameters impacting the cleaning would be helpful in reducing equipment downtime and increasing capacity along with conforming to regulatory requirements.

- Why is knowledge of cleaning important?
- What is knowledge to R&D?
- What is cleaning to production?
- Understand and discover hidden residues when cleaning
- Define effective cleaning processes
- Delve into the science of cleaning
- Implementing an effective cleaning process
- Review cleaning case studies
Designing an Effective Cleaning Process
Beth Kroeger, Technical Services Manager, Steris Corporation

An important aspect of any Cleaning Validation program is selection of the cleaning agent. Selection is based on many factors such as equipment design, residue selection, soil conditions, and cleaning parameters available. Most importantly, cleaning agents should meet the requirements of a cGMP regulated industry. Appropriately selecting a cleaning agent that considers the factors influencing cleaning and is validatable could simplify Cleaning Validation activities for a new process and the lifetime of the product.

1. Identifying Risk
   1. Components of cleaning chemistry – What is clean? From FDA guidance
   2. How to design cleaning process, what to consider?
      1. Materials of construction impact
      2. Design
      3. Process?
      4. Understanding your soils – residue selection
   3. What “problem” areas to look for
2. cGMP validatable attributes
   1. Quality – change control, raw materials, supply
   2. Determining limits for cleaning agents
   3. Analysis – detection - degradation
   4. Compatibility
3. Performing a Lab Scale cleaning study
   1. Advantages of a lab study
   2. Understanding the interdependent parameters
   3. Acceptance criteria

Swab Sampling
Beth Kroeger, Technical Services Manager, Steris Corporation

Swab sampling is designed to maximize recovery of surface residues, especially on difficult to clean areas and is used, in conjunction with rinse sampling to verify that the surface of the equipment is in fact, clean. This would account for residues that might adhere to the surface post-cleaning process, thus not detected in the rinse water. Swab sampling involves the removal of residue from a target surface after the final rinse with a fibrous material (swab tip). The residue is then extracted from the swab tip with an appropriate solvent and the extract analyzed for residue content. It’s advantageous in that it allows for physical removal of your target residue, however, swabbing can be extremely technique dependent. This demonstration is intended to discuss best practices in swab qualification.

Complimentary Happy Hour Sponsored by Steris Corporation
Mid-Morning Networking Break

Analytical Approach for Implementation of Visual Inspection
Mariann Neverovich, Cleaning Validation SME, BMS, (ASTM Cleaning Team Member)

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.

Cleaning Program Development

Knowledge and Risk-Based Optimization of Cleaning Validation Programs
Sunil Patel, Senior Global Technical Manager, Ecolab Life Sciences

It is a large undertaking for pharmaceutical manufacturers to change decades-old legacy cleaning validation programs. Without known cleaning issues or historical regulatory inspection findings, there is little impetus to change current practice. In most cases, legacy cleaning procedures were developed based on excessive cleaning strategies rather than characterization by scientific data and correlation between critical cleaning performance parameters (CCPP) and their impact on cleaning performance. This presentation will examine a scientific and risk-based cleaning validation program optimization based on ICH Q9 principles and the newly published ASTM E3106 standards. It will outline how scientific data and performance of risk assessments throughout the cleaning validation life cycle can be leveraged to optimize and deliver a compliant and efficient cleaning validation program. Case studies will be shared to demonstrate the time, water, chemistry or energy savings achieved utilizing this approach.

Cleaning Validation Protocols and Contents
Fred Ohsiek, Sr. Manager Cleaning Validation, 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.

Validation Master Planning
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; discuss the benefits of a VMP; demonstrate the difference between a VMP and a Validation Project Plan; and review the contents of a typical Cleaning 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
   Benefits of VMPs
   VMP vs. VP

II. VMP Do’s and Don’ts
   Pitfalls of poor designs
   Supplements and Attachments vs. Direct Content Improvements and Gap Analysis
   Document Maintenance

III. VMP Documentation Design
   General Format Recommendations
   Content and Template
   Process Description
   Detergent/Cleaner Determination
   Facility / Utility Requirements
   Equipment Design
   Cleaning Process Procedures

IV. Cleaning Validation Approach
   Rationale
   Limit Determination
   Bracket/Matrix?
   Sampling Methods
   Analytical Methods
   Maintaining a Validated State
Cleaning Development; Using a Quality by Design Approach to Stop Cleaning for Long Hours

Walid El Azab, Technical Service Manager, Steris Corporation

The presentation will share a systematic cleaning development method to a science and a risk-based approach for product residue cleaning. The following concept will be discussed during the presentation: determination of the cleaning critical parameter, critical quality attribute, the design of space, and cycle development. The understanding of this concept is crucial to implementing effective cleaning processes and avoiding complex cleaning processes.

Afternoon Networking Break

User Requirements & Implementation of a Risk Based, Compliant Cleaning Validation Management System Based on the Draft Guidance on DATA Integrity

Parsa Famili President & CEO, Novatek International

In the 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.

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 Stage 3, Continued Process Verification. In 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 obtained during cleaning validation lifecycle is not just measured on “pass” or “fail” merits, but can be understood on a more granular level. This should help to understand the cleaning processes which in turn should aid in optimization of the latter to improve consistency thus reducing risk due to cleaning for product’s manufacturing and protection of patient’s safety.
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