GMP Training Systems, Inc.

Creators of the GMP Ready-to-Use Training System™

Cleaning Validation Boot Camp

Learning Objectives

Upon completion of this workshop, participants will be able to:

- Understand the regulatory requirements as they pertain to cleaning the facilities, equipment and utensils used in the manufacture, packaging and storing of drug products.
- FDA, ICH, Health Canada, and GMP terms they are likely to encounter during cleaning and cleaning validation.
- Understand the intent of the GMP regulations as it pertains to validation.
- Understand the concept of the Cleaning Lifecycle and continuous improvement.
- Have a thorough understanding of what is needed to develop a successful cleaning program and complete a successful cleaning validation.
- Interpret all the standards associated with Cleaning Validation.
- Develop all of the documents needed to complete a successful cleaning validation including the Cleaning Standard Operation Procedures (SOPs), the Cleaning Validation Master Plan (CVMP), and cleaning validation Protocols.
- How to execute cleaning validation protocols and address deviations encountered during the execution.
- How to maintain the validated state through development and implementation of a Change Control/Management system, a CAPA program and monitoring the effectiveness of the cleaning procedures.

Who should attend

This workshop is designed to introduce technicians and professionals involved in the manufacture, packaging and storing of drug products to the fundamentals of cleaning and cleaning validation. The discussions would be beneficial to personnel who have just started their involvement with cleaning validation or manage groups that will be involved in cleaning validation. Professionals and technicians who should attend include:

- Technical Services
- Manufacturing and packaging
- Engineering
- Facilities Services and Maintenance
- Validation
- QA/QC

DAY ONE

Cleaning and Cleaning validation: The Regulatory Imperative

The drug, food and cosmetics act gives the FDA the authority to ensure that such products are safe for human consumption. The Code of Federal Regulations (CFR) clearly stipulate that manufacturers of healthcare products, namely pharmaceuticals, biologics and medical devices are to insure that their equipment, facility and personnel are cleaned and maintained in a clean state. To achieve such an objective the industry and the regulators expect that manufacturers of such products will develop appropriate methods to clean and that the methods will be validate these methods. In this segment, we will:

- Review GMP cleaning requirements for drug manufacture
- Review CFR requirements to validate cleaning
- Review of FDA and Health Canada Guidance on Validating the Cleaning Process
- Review ICH Q7 and Q9 requirements on Cleaning and Cleaning Validation
- Identify FDA's expectation as gleaned from 483 observations
- Applying the Risk Based Compliance approach to Cleaning and Cleaning Validation.

The Cleaning Lifecycle: A Holistic Approach to Compliance

The presentation will focus on advancing the principal of a cleaning and cleaning process validation lifecycle consisting of three phases. These are namely;

a. The development and planning phase
b. The execution phase
c. The implementation and continuous improvement phase.

In order to ensure that cleaning is compliant with the regulatory requirements, one must spend time on planning and developing the appropriate strategies of ensuring the equipment and facility can be cleaned through applying proper design strategies. The next step is to plan how to clean the equipment and facility and develop the cleaning procedures. The validation protocols are then developed and of course development of appropriate analytical methods as well as measuring techniques to be implemented as part of the validation and maintenance phases are identified.

The execution phase is where the cleaning procedure and techniques devised are tested and validated. This requires defining meaningful acceptance criteria and the appropriate approaches to address deviations from such criteria. Information gleaned from the execution phase is then fed back into the planning and development phase allowing for modification and continuous improvement.

Once the cleaning process is validated, then it is implemented according to plan. As time progresses, issues that arise are identified through implementation of a monitoring program and a robust CAPA program. The information resulting from both programs is also fed back into the planning and development phase to insure continuous improvement is achieved and that the knowledge is used for future development.

Master Planning for Cleaning Validation

The Cleaning Validation Master Planning (CVMP) is an essential part of the overall cleaning validation effort in the production of pharmaceuticals and/or biological therapeutic agents. It is a scope document aimed at defining the extent of the validation effort, defining the philosophy to be implemented, the general methodologies to be used, categorizing the major equipment and contaminants to be cleaned, and define the analytical methodology to address the objectives of the validation effort. The document also defines the resources, responsibilities and the time table required to implement the effort. During the presentation you will learn:

- To define major equipment and contaminants groupings
- The protocol requirements to complete the cleaning validation and meet the regulatory imperatives
- How to define acceptance criteria and how to address/resolve deviations encountered during cleaning validation
- How to prepare a CVMP which will be approved and continues to be useful once it is approved
- Define the schedule and priorities to insure successful validation effort
- How to obtain commitment from the various organizations and stakeholders within your company to assist on making the cleaning validation effort a success

The Cleaning Procedure: What it Looks Like

The cleaning procedure is a regulatory requirement and represents the basis for preventing contamination of the product. The procedure details the responsibilities for cleaning, the materials to be used in cleaning, how the equipment would be disassembled and re-assembled if necessary, how the various parts will be cleaned and what additional steps must be taken to ensure the item (whether equipment, facility, or container) is cleaned and would not cause contamination of the product. This session will focus on the contents that must be included in a successful cleaning procedure. This session will discuss the following:

- The purpose of the cleaning procedure
- How to define the frequency for cleaning
- Who is responsible for the cleaning
- How to define the procedure itself and ensure proper cleaning
- What and where to clean
- The documentation required for successful and compliant cleaning

Hands on Exercise

Attendees will be asked to prepare a Cleaning Standard Operating Procedure (SOP). A short introductory discussion will be moderated by the course instructor. Once attendees are familiar with SOPs, they will be given a defined assignment to prepare a specific Cleaning SOP following the guidelines presented. Upon completion of the assignment, an open discussion of the issues encountered by the attendees in the preparation of the document will ensue.

DAY TWO

Cleaning Validation Protocol: Development and Defining Acceptance Criteria

The current industry standard is to use a Cleaning Validation (CV) Protocol to validate the cleaning procedure. Since the procedure is regarded as a cleaning process, CV itself could be considered a process validation exercise. If cleaning or washing equipment is used to achieve the cleaning, then such equipment must be qualified prior to performing the cleaning validation itself. The Cleaning Validation (CV) protocol when successfully executed signifies the completion of the validation effort and the acceptability of the cleaning procedure for the intended use.

It is important to recognize that the CV protocol is designed to accomplish a specific objective, namely that the cleaning procedure achieves the required results. Choosing the appropriate acceptance criteria to ensure the protocol achieves its objective is the most important part of preparing such protocols. In this session you will learn:

- What the cleaning validation protocols is designed to accomplish
- How to prepare a flexible protocol that is easy to execute
- What are the appropriate acceptance criteria
- How to sample and test for cleanliness
- How to develop the appropriate test to ensure the cleaning procedure achieves the intended result
- What analytical methods to use in executing the protocols

Hands on exercise

In this session, the attendees will be given a description of a cleaning problem and an SOP to be validated. Attendees will be divided into groups to work together on developing the appropriate protocol for validating the cleaning procedure. At the end of the session the class will review and discuss the issues encountered while developing the protocol and attempt to identify hurdles to the execution of such protocol.

Execution Phase and Addressing Deviations

Once the protocol has been prepared and approved it must be executed. Execution has to be performed by trained personnel. Measurements and analysis have to take place using calibrated instruments, accepted sampling techniques and validated analytical methods. As the protocol is being executed, one will encounter many challenges associated with execution of the procedure. These have to be properly and effectively addressed prior to pronouncing the cleaning process validated. In this session you will learn:

- The appropriate methods to approach protocol execution.
- Who should perform the protocol execution
- The need to qualify cleaning equipment prior to validating the cleaning process.
- The importance of analytical methods validation and the use of calibrated instruments.
- Validating manual cleaning and how to ensure that it meets the regulatory requirements of consistency and effectiveness.
- How to effectively address deviations from pre-established acceptance criteria
- How to prepare summary reports for executed protocols that will be approved.

Implementation, Change Control, CAPA, Monitoring and Continuous Improvement

Once the cleaning procedure is validated, it is to be used consistently as intended. A logging mechanism to follow the history of the cleaning and provide a means to monitor the effectiveness of the procedure with time is used. Monitoring and Corrective Action Preventive Action (CAPA) programs are the basic tools ensuring continuous improvement of the cleaning procedure and its extension to new applications. Change Control is also used to ensure that any changes to the procedure are reviewed prior to implementation. It is also the means for ensuring that the procedure remains suitable for its intended use and continues to be in a validated state.

The concept of the validation life cycle will be discussed and ways of ensuring changes do not result in loss of control will be reviewed. In this session you will learn:

- The meaning of CAPA, Monitoring, and Change Control
- What could cause problems with the existing cleaning procedure
- How to establish alert and action levels and what to do when reached
- When and where would validation be affected by change
- When to use data collected from monitoring to plan your next cleaning procedure
- How CAPA plays a role in the continuous improvement of the cleaning process
- Why and when to revalidate - Is it revalidation or a new validation?
- How to defend your actions to the regulators