GMP Training Systems, Inc.

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

Validation Boot Camp

Validation Fundamentals:
Conducting a Successful Validation Project

Learning Objectives

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

- Understand FDA and GMP terms they are likely to encounter during validation.
- Understand the intent of the GMP regulations as it pertains to validation.
- Have a thorough understanding of what is needed to complete a successful validation.
- Interpret all the standards associated with Validation.
- Develop all of the documents needed to complete a successful validation including Standard Operation Procedures (SOPs), Validation Master Plan (VMP), and associated Protocols.
- How to execute 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

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 validation. The discussions would be beneficial to personnel who have just started their involvement with validation or manage groups that will be involved in validation. Professionals and technicians who should attend include:

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

DAY ONE

1. Introduction to GMP and Validation requirements

   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 they are producing quality products and that they build the quality into rather than measuring it in the final product. To achieve such an objective the industry and the regulators expect that processes to manufacture such products would be validated.
   a. Review the GMP requirements for drug manufacture
   b. Review of CFR requirements of validation and process consistency
   c. Review of ISPE Guide Base Line guide on commissioning and validation.
   d. FDA's expectation as gleaned from 483 observations
   e. What is validation and how to approach it

2. Process Validation: General Principles and Practice- FDA Guidance

   In this session we will discuss the FDA guidance on process validation issued in January 2011. The guidance promotes the implementation of a process-product life cycle approach to verification that the process is always in a validated state. The guidance defines three distinct stages to process validation. These are:

   Stage 1: Process Design
   Stage 2: Process Performance Qualification
   Stage 3: Continued Process Verification

   This is not a new concept, although the guidance may suggest it is. It was always important in the design and development of the process to consider GMP implications and keep validatability in mind. Process Performance Qualification or PPQ was always the necessary step confirming that the process is capable of consistently producing a

product that meets its predetermined specifications and quality attributes. As for continuous process verification, this has always been a needed activity and was always accomplished through process and product monitoring.

3. ASTM E2500 Consensus Standard: New Thinking on Validation

The presentation will focus on providing an overview of the contents of this important standard. The imputes for developing the standard was to reduce the cost of validation, reduce the amount of paperwork and simplify the effort.

The standard sets scientific risk assessment as the basis for defining systems which must be verified as to their suitability for the intended use. It does recommend that Subject Matter Experts (SME) be utilized extensively in any verification effort and suggests that it is a good strategy to leverage information from your supplier and not repeat the work. Both industry and the regulators are still reviewing it and assessing its potential impact.

We will explore:

- The details of the standard and how to apply them
- What is meant by Verification of suitability for intended use
- How to use a science- and risk-based approach to ensure the proper verification is conducted
- The importance of User Requirement Specifications (URS), Good Engineering Practice (GEP), Quality by Design (QbD), and SME in support of the validation effort
- How well the does the standard meet the requirements of the FDA Guidance on Process Validation.
- What's in store for the immediate future?

4. Master Planning for Qualification/Validation

   Qualification/Validation Master Planning is an essential part of the overall process validation effort for the production of pharmaceuticals and/or biological therapeutic agents. It is a scope document aimed at defining the extent of the qualification/validation effort and guiding it and the personnel involved with it. The plan defines which systems will be qualified, and how they will be qualified. In addition, the plan identifies the required resources to meet its objectives and the schedule to successfully implement the effort.

   During the presentation you will learn:

   a. How to use risk assessment to define critical systems requiring qualification and prioritizing the qualification effort.
   b. The protocol requirements to complete the qualification and meet the regulatory imperatives.
   c. How to define acceptance criteria and how to address/resolve deviations encountered during qualification.
   d. How to prepare a Q/VMP which will be approved and continue to be useful once it is approved.
   e. Define the schedule and priorities to insure successful qualification effort.
   f. How to obtain commitment from the various organizations and stakeholders within your company to assist on making the qualification effort a success.

5. Critical Documents Needed for Successful Validation

   Validation, which is confirmatory in nature, is a regulatory requirement. The regulation requires the preparation of many documents (VMP, Protocols, SOPs, etc.) in order to conduct the validation itself. Prior to preparing the required document you need to assemble, file and control certain documents associated with all of the equipment and each of the systems being validated. Collecting, filing and controlling of such documents is an integral and necessary part of any successful validation effort.

This session will discuss the following:

a. Which documents you need?
b. What are they needed for and how to use them?
c. Where are the document and how to obtain them?
d. How to file and control such documents

DAY TWO

6. Hands on Exercise

   Attendees will be asked to prepare a Standard Operating Procedure (SOP). A short introductory discussion will be moderated by the course instructors followed by a review of example SOPs. Once attendees are familiar with SOPs, they will be given a defined assignment to prepare a specific 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.

7. Validation protocol development and defining acceptance criteria

   The current industry standard is to use Installation Qualification (IQ), Operation Qualification (OQ), and Performance Qualification (PQ) protocols to qualify equipment and systems. The Process Performance Qualification (PPQ) protocol is the ultimate protocol, which when successfully executed signifies the completion of the process qualification effort. Protocols are a procedure to perform the appropriate tests to measure the performance of the system/equipment and represent a repository of all the data collected. It is important to recognize that each protocol is designed to accomplish specific objectives. 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:

a. What the various protocols are designed to accomplish?
b. How to prepare a flexible protocol that is easy to execute
c. What are the appropriate acceptance criteria?
d. How to develop the appropriate test to ensure the systems function as designed

8. Hands on exercise

In this session, the attendees will be given a description of a small system to be Qualify. Attendees will be divided into groups to work together on developing the appropriate protocols for qualifying the system.

9. Hands on exercise

In this session, the attendees will review and discuss the issues encountered while developing the protocols and attempt to identify hurdles to the execution of such protocols.

10. Protocol Execution and Addressing Deviations

Once the protocols have been prepared and approved they must be executed. Execution has to be performed by trained personnel. Measurements and analysis have to take place using calibrated instruments and validated analytical methods. As the protocols are being executed, one will encounter many challenges associated with the as built conditions, which have to be properly and effectively addressed prior to pronouncing the equipment or system qualified or the process itself validated.

In this session you will learn:

a. The appropriate methods to approach protocol execution.
b. Who should perform the protocol execution
c. The importance of analytical methods validation and the use of calibrated instruments.
d. How to effectively address deviations from pre-established acceptance criteria
e. How to prepare summary reports for executed protocols that will be approved.

11. Ensuring the Operation Stays in a Controlled and Validated State

Once the process and facility are validated it is important to ensure that they remain in validated state. Such an endeavor is achieved through monitoring, maintenance, and establishing a Change Control System. 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:

a. What is Change Control?
b. What are the various types of changes one may encounter?
c. When and where would validation be affected by change?
d. How to prepare a Change Control SOP?
e. When to apply change control in a simple manner?
f. What constitutes monitoring and how to monitor?
g. What is the difference between individual events and trends and its importance?
h. What are the other quality systems components that ensure the operation remains in the validated sate of control?