Validation Tutorial

This tutorial is designed to enhance knowledge of biotechnological/pharmaceutical processes. The topics covered within this tutorial will give preliminary explanations and conclusions. However, references for more in depth study will be provided. It is strongly suggested that you investigate these references.
Overview

- **What is Validation?**
  - This section will define validation and will put its meaning in terms pertinent for a chemical engineer.

- **Food and Drug Administration (FDA)**
  - This section will explain the role of the FDA in validation and the guidelines it sets forth.

- **Equipment Validation**
  - This section will explain what role unit operations equipment plays in validation and why that is important.

- **Process Validation**
  - This section will explain the implications of validation in the overall manufacturing process.

- **Applications to Facility Design**
  - This section will discuss considerations to facility design in light of validation.
What is Validation?

According to the Food and Drug Administration (FDA), the goal of validation is to:

“establish documented evidence which provides a high degree of assurance that a specific process will consistently produce a product meeting its predetermined specifications and quality attributes.” [1]
What is Validation?

What does this mean?

– An quantitative approach is needed to prove quality, functionality, and performance of a pharmaceutical/biotechnological manufacturing process.

– This approach will be applied to individual pieces of equipment as well as the manufacturing process as a whole.

– Guidelines for validation are set by the FDA, but the specifics of validation are determined by the pharmaceutical/biotech company.
What is Validation?

- Phases of Validation
  - Validation is broken down into three phases:
    - Installation Qualification (IQ)
    - Operational Qualification (OQ)
    - Performance Qualification (PQ)
  - These three protocols are used to define tests that will demonstrate that the process consistently and repeatedly produces the desired product.
What is Validation?

- **Installation Qualification (IQ)**
  - This is the first step in validation.
  - This protocol insures that the system/equipment and its components are installed correctly and to the original manufacturer’s specifications.
  - Calibration of major equipment, accessory equipment, and/or utilities should be performed in this step as well.
What is Validation?

Operational Qualification (OQ)
- This step proceeds after the IQ has been performed.

- In the OQ, tests are performed on the critical parameters of the system/process. These are usually the independent and/or manipulated variables associated with the system/equipment.

- All tests’ data and measurements must be documented in order to set a baseline for the system/equipment.
What is Validation?

- Performance Qualification (PQ)
  - This is the third and final phase of validation.
  - This phase tests the ability of the process to perform over long periods of time within tolerance deemed acceptable.
  - PQ is performed on the manufacturing process as a whole. Individual components of the system are not tested individually.
What is Validation?

An example validation protocol can be seen here: sample validation protocol.
The FDA is a federal science-based law enforcement agency mandated to protect public health.

The validation process is regulated by the guidelines and restrictions set forth by the FDA. However, the actual validation protocol, documentation, and execution is the responsibility of the manufacturer. More specifically, this is the responsibility of the engineer.
FDA

Code of Federal Regulations (CFR)

- This is the body of regulations, created by the US government, that sets forth the guidelines pertaining to food and drugs.

- 21 CFR Part 210 concerns current good manufacturing practice in manufacturing, processing, packing, or holding of drugs.

- 21 CFR Part 211 concerns current good manufacturing practice for finished pharmaceuticals.
FDA

- 21 CFR Part 600 pertains to the safe production of biological derived products.

- 21 CFR Part 610 pertains to the safe distribution of biologically derived products.
As mentioned earlier, each piece of must be validated in order to legally operate within the facility.

The goal is to produce consistent results with minimal variation without compromising the integrity of the product and the persons operating the equipment.

A plan of validation should be drafted and executed by engineers in order to satisfy guidelines. The validation plan generally consists of IQ and OQ sections.
Equipment Validation

- Any major equipment changes after the initial validation will result in the need for subsequent revalidation.

- In the end, equipment validation will create specification ranges and tolerances that will be applied to the normal operation of equipment.
Process Validation

- The manufacturing process, in addition to the individual equipment, must be validated.

- The goal is to create a robust manufacturing process that consistently produces a drug product with minimal variation that adheres to quality criteria of purity, identity, and potency.

- A validation plan for the manufacturing process should be drafted and executed by engineers in order to satisfy guidelines. The validation plan usually involves just a PQ section.
Process Validation

- Just as equipment validation, major changes after the initial validation will result in the need for subsequent revalidation.

- In the end, process validation will ensure a robust product that is highly reproducible over time.
Applications to Facility Design

- Facilities should be designed in order to facilitate any changes that may arise after initial validation.

- In the case of retrofitting, current facilities services (WFI, CIP, SIP, HVAC, etc.), equipment, and instrumentation should be assessed for revalidation. This assessment will be based on age of the individual system and the needs of the new process.
Resources

[1] [www.fda.gov](http://www.fda.gov)
- 21 CFR Part 210:
- 21 CFR Part 211:
- 21 CFR Part 600:
- 21 CFR Part 610:
Resources


