

A vertical strip on the left side of the slide contains a world map at the top, followed by three small images: a laboratory with glassware, a modern building interior with a curved walkway, and a conference room with a long table and chairs. At the bottom of this strip are several large, semi-transparent green pills.

Process Validation Update

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Regulatory Requirements

- Canada – Food and Drugs Act
- United States – Food, Drug and Cosmetic Act
- Both jurisdictions have corresponding GMP or cGMP requirements

Regulatory Authorities

have duty to ensure products are safe and effective

- **Integration of quality systems and risk management**
- **Not dependent on commodity**
- **Require objective evidence**
- **Risk assessments and validation**

Manufacturer's Responsibility

- Know and meet regulatory requirements
- Document and approve development and processes
- Validate systems and equipment
- Develop a continuous improvement philosophy

US Requirements

- The FDA defines process validation as follows:
Process validation is establishing documented evidence which provides a high degree of assurance that a specific process will consistently produce a product meeting its pre-determined specifications and quality characteristics.

Canadian Requirements

- Health Canada defines Validation as:
The action taken to demonstrate, and to provide documented evidence that a process will, with a high degree of assurance, consistently achieve the desired and intended results.

VALIDATION OBJECTIVES

- MEETS OR EXCEEDS SPECIFICATIONS
- PROPERLY INSTALLED, OPERATED AND MAINTAINED
- CONFORMS TO cGMP
- REGULATORY COMPLIANCE
- ACHIEVES QUALITY, SAFETY & PRODUCTIVITY

Canadian Guidance on Responsibilities for Cdn. fabricators, packagers/labellers or testors

- Validation master plan
- Cleaning validation
- Test method validation
- Qualification of utilities, support systems and equipment

Master Plan

The purpose of a Master Plan is:

- to serve as a liaison document to communicate to the Regulatory Body an understanding of company responsibilities concerning the validation of the facility
- plans to discharge that responsibility
- serves as a guide to those administering and performing validation activities
- is a road map to successful project completion.

The Master Plan may be used as an instrument to define areas of responsibility and accountability to validation team members

Master Validation Plan Contents

- Responsibilities of various departments
- Recognized validation approaches
- Conditions for using approach
- Compliance requirements for worst case and reproducibility
- Revalidation criteria
- Documentation format requirements
- Review and approval requirements
- Change control system

MASTER PLAN FOCUS

- cGMP PROGRAMS
- OPERATIONS PROGRAM
- RESOURCE REQUIREMENTS
- SCHEDULE

Life Cycle

- The life cycle concept of validation is a recurring theme throughout a Master Plan. Paramount is the establishment of the infrastructure to ensure that a facility will be supported by sufficient documentation throughout its conceptual and functional lifetime.
- The life cycle will encompass project inception, design, engineering, construction through testing, certification, maintenance, revalidation and change control. These programs are necessary to maintain the processes and equipment in the state at which they were originally validated.

Developing Validation Documentation Hierarchy

- Quality Systems - QA
Quality Manual
Quality Policy

Established and approved by top management and outlines the organization policy, objectives and commitments to quality. Top management is responsible of ensuring that the policy is understood, implemented and maintained at all levels of the organization.

Validation Program

Validation Program is a second level validation document. It is a detailed document and outlines the following as examples;

- Definitions
- Format for validation protocols and reports
- Protocols review and approval
- Protocol number assignment
- Procedures for initiation, execution and reporting validation activities
- Protocol Change Control

Validation Program (cont'd)

Impact Assessment on product quality

- System/Process Changes and its Impact Assessment on the validation status and the quality/efficacy of the product
- Methodology of handling non-conformance
- Revalidation
- Retention time, location and archiving of validation record and reports

Validation Program (cont'd)

- There can be more than one program (i.e. Cleaning Validation Program, Computer Validation Program.....etc.).



Components of Validation

- Facility Qualification
- Equipment Qualification
- Processing Equipment
- Utility Systems
- Testing Equipment
- Cleaning Validation
- Process Validation
- Computer Validation
- Methods Validation
- Revalidation

Validation SOP's


- A detailed step-by-step procedure required to be followed to accomplish a task (i.e. SOP for sampling, testing...etc)






Establishing Methodology for Impact Assessment and Validation Rational

- The Validation Program shall establish a methodology for validation rational based upon an impact assessment of systems and their components.



Establishing Methodology for Impact Assessment and Validation Rational (cont'd)

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- Direct Impact System/Process (Critical)
 - In-direct Impact System/Process
 - No impact System/Process (Non-critical)

Key elements for successful validation activities

- Timely planning and scheduling
- Impact assessment
- Validation/Qualification rational
- Good Documentation Practice
- Active participation of QA
- End-user participation and ownership
- Pre-determined acceptance criteria
- Additional checks, tests and verifications
- Methodology for handling non-conformance and changes

FACILITY CERTIFICATION (OVERALL SCHEDULE)

- MASTER PLAN PREPARATION
- PROTOCOL PREPARATION & APPROVAL
- DQ/IQ/OQ
- REGULATORY LIAISON
- CERTIFICATION
- FACILITY TURNOVER

Facility/Equipment/Utility Qualification

- **Design Qualification (Review)**

The following are some critical items to be considered for successful Design Qualification

- Compliance with cGMP and all regulatory requirements
- Satisfy User/Functional Requirements Specification (URS/FRS)
- Facility design layout, construction, air flow, differential pressure, process flow and personnel flow to minimize cross contamination

Facility/Equipment/Utility Qualification (cont'd)

- Material of construction and cleaning
- Capacity and Efficiency
- Accessibility for maintenance and cleaning
- Commissioning, start-up and shut-down process
- Safety and environmental requirements and regulations
- Supporting documentations

Factory Acceptance Testing (FAT)

- When appropriate, the equipment shall be tested/challenged at the supplier site by the user to simulate actual production conditions.
- FAT allows for early identification of any problems and troubleshooting prior to shipping and provides confidence that the system will meet the FRS and URS upon delivery.

Site Acceptance Test (SAT) and Commissioning

When appropriate, the equipment shall be tested/challenged on site prior to qualification by the user to simulate actual production conditions. SAT allows troubleshooting prior to qualification and provides confidence that the system will meet the FRS and URS.

SAT and Commissioning when performed according to Good Engineering Practice (GEP) and within the qualification requirements can significantly support the qualification activities and ensure successful qualification.

Installation Qualification

Installation qualification is a physical inspection/verification of the system and its components to meet the Detail Design Specification (DDS).

The IQ confirms that correct component has been properly installed according to the design documents and all supporting documentation is in place and instruments are calibrated. The Validation Program shall establish the general approach and pre-requisites for IQ activities.

Operational Qualification

Operational qualification testing confirms that the system and its components operates within the limits and tolerance defined in the Functional Requirement Specification (FRS).

The operating parameters are tested to confirm compliance with URS and the design documents (i.e temperature, pressure, flow....etc.).

The OQ also test for proper operation of components alarms and interlocks and its integrated operations.

The Validation Program shall establish the general approach and pre-requisites for OQ activities.

Performance Qualification

Performance Qualification combines the performance of the systems procedures, personnel and materials to deliver the desired output within the desired quality attributes.

The Validation Program shall establish the general approach and pre-requisites for PQ activities.

GENERAL PRINCIPLES

- VALIDATION STUDIES ARE CONDUCTED AS PER WRITTEN PROTOCOL
- ONE PROTOCOL PER EQUIPMENT, PROCESS OR SYSTEM
- EACH PROTOCOL WILL REFERENCE ALL INFORMATION NEEDED TO COMPLETE STUDY

GENERAL PRINCIPLES (Cont)

- ALL CRITICAL SYSTEMS, EQUIPMENT AND PROCESSES REQUIRE VALIDATION
“CRITICAL” – HAVING A POTENTIAL TO IMPACT PRODUCT CONFORMANCE TO QUALITY SPECIFICATIONS
- SOME SYSTEMS REQUIRE MULTIPLE VALIDATION STUDIES

MAINTAINING VALIDATED STATE OF THE SYSTEM

- CALIBRATION
 - CRITICAL INSTRUMENTS ARE CALIBRATED AS PER DETERMINED SCHEDULE
- TRAINING
 - TRAINING PROGRAM IS IN PLACE
 - TRAINING IS DOCUMENTED
- PM AND CHANGE CONTROL
 - NO EQUIPMENT MODIFICATION WITHOUT CHANGE CONTROL

Validation Schedule

- Establish target dates
- Strive to ensure that validation (DQ,IQ,OQ) is completed before any construction, regulatory authorizations etc.-allows for approvals
- Revalidations for changes (equipment, processes)– that affect product characteristics
- Assess the need for revalidation during APR's regardless of Change Controls



THANK YOU !

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