IMPLEMENT AN EFFECTIVE MASTER VALIDATION PLAN (MVP)

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MASTER VALIDATION PLANS

- Are you familiar with Master Validation Plans?
- How do you use it?
- What challenges have you encounter with the use of master validation plan or the lack of?
- What observations or finding have you received?

AGENDA

- Review some Regulatory Requirements
- Define the importance of Master Validation Plans
- Explore different types of Master Validation Plans
- How to prepare Master Validation Plans

REGULATIONS

- What are the regulatory requirements?

REGULATION REQUIREMENTS

[Code of Federal Regulations]
[Title 21, Volume 8]
[Revised as of April 1, 2017]
[CITE: 21CFR820.30]

TITLE 21--FOOD AND DRUGS
CHAPTER I--FOOD AND DRUG ADMINISTRATION
DEPARTMENT OF HEALTH AND HUMAN SERVICES
SUBCHAPTER H--MEDICAL DEVICES

PART 820 -- QUALITY SYSTEM REGULATION
Subpart C--Design Controls

Sec. 820.30 Design controls.

(f) Design verification. Each manufacturer shall establish and maintain procedures for verifying the device design. Design verification shall confirm that the design output meets the design input requirements. The results of the design verification, including identification of the design, method(s), the date, and the individual(s) performing the verification, shall be documented in the DHF.

(g) Design validation. Each manufacturer shall establish and maintain procedures for validating the device design. Design validation shall be performed under defined operating conditions on initial production units, lots, or batches, or their equivalents. Design validation shall ensure that devices conform to defined user needs and intended uses and shall include testing of production units under actual or simulated use conditions. Design validation shall include software validation and risk analysis, where appropriate. The results of the design validation, including identification of the design, method(s), the date, and the individual(s) performing the validation, shall be documented in the DHF.

REGULATION REQUIREMENTS

Sec. 820.30 Design controls.

(h) Design transfer. Each manufacturer shall establish and maintain procedures to ensure that the **device design is correctly translated into production specifications**.

(i) Design changes. Each manufacturer shall establish and maintain procedures for the identification, documentation, **validation or where appropriate verification, review, and approval of design changes before their implementation**.

DEFINITION

Sec. 820.70 Production and process controls.

(a) General. **Each manufacturer shall develop, conduct, control, and monitor production processes to ensure that a device conforms to its specifications.** Where deviations from device specifications could occur as a result of the manufacturing process, the manufacturer shall establish and maintain process control procedures that describe any process controls necessary to ensure conformance to specifications. **Where process controls are needed they shall include:**

(1) Documented instructions, standard operating procedures (SOP's), and methods that define and control the manner of production;

(2) Monitoring and control of process parameters and component and device characteristics during production;

DEFINITION

Sec. 820.70 Production and process controls.

(c) Environmental control. **Where environmental conditions could reasonably be expected to have an adverse effect on product quality, the manufacturer shall establish and maintain procedures to adequately control these environmental conditions**. Environmental control system(s) shall be periodically inspected to verify that the system, including necessary equipment, is adequate and functioning properly. These activities shall be documented and reviewed.

(g) Equipment. **Each manufacturer shall ensure that all equipment used in the manufacturing process meets specified requirements and is appropriately designed, constructed, placed, and installed to facilitate maintenance, adjustment, cleaning, and use.**

DEFINITION

Sec. 820.70 Production and process controls.

(i) Automated processes. **When computers or automated data processing systems are used as part of production or the quality system, the manufacturer shall validate computer software for its intended use** according to an established protocol. All software changes shall be validated before approval and issuance. These validation activities and results shall be documented.

DEFINITION

Sec. 820.72 Inspection, measuring, and test equipment.

(a) **Control of inspection, measuring, and test equipment. Each manufacturer shall ensure that all inspection, measuring, and test equipment, including mechanical, automated, or electronic inspection and test equipment, is suitable for its intended purposes and is capable of producing valid results**. Each manufacturer shall establish and maintain procedures to ensure that equipment is routinely calibrated, inspected, checked, and maintained. The procedures shall include provisions for handling, preservation, and storage of equipment, so that its accuracy and fitness for use are maintained. These activities shall be documented.

DEFINITION

Sec. 820.75 Process validation.

(a) **Where the results of a process cannot be fully verified by subsequent inspection and test, the process shall be validated** with a high degree of assurance and approved according to established procedures. The validation activities and results, including the date and signature of the individual(s) approving the validation and where appropriate the major equipment validated, shall be documented.

(b) **Each manufacturer shall establish and maintain procedures for monitoring and control of process parameters for validated processes** to ensure that the specified requirements continue to be met.

MASTER VALIDATION PLANS

- What does Master Validation Plans have to do with it?
  - Master Validation Plans are a systemic approach
  - It is summary of all validation activities
  - It helps in translating design requirements into production requirements
  - It help us to maintain control of the validations

MASTER VALIDATION PLANS

- Types of Master Validation Plans
  - Design Project Master Validation Plans
  - Design Transfer to Production Master Validation Plans
  - Site Master Validation Plans
  - Cleaning Master Validation Plans

- General definition for Master Validation Plans
  - Establish and document all validation related activities to achieve the validated state and, where applicable, maintain the validated state.

•DESIGN PROJECT MASTER VALIDATION PLANS

- Design Project Master Validation Plans
  - A documented plan containing validation evidence for Items utilized during product development, design verification and design validation activities for a project under Design Controls.
  - Basically it lists all the validation activities required to test the design requirements during design verification and design validation activates.

DESIGN PROJECT MASTER VALIDATION PLANS

- List all the requirements to be tested during design verification or design validation
  - These requirements are high level for a specific product or system.
    - They include but not limited to requirements that cannot be tested or are not intended to be tested in a production environment.

DESIGN PROJECT MASTER VALIDATION PLANS

For each requirement to be tested document the following:

- Test Method – how the requirement is going to be tested
- Equipment to be used in the test method
- IQ Report for each equipment
- Software Validation Report
- Test Method Validation Report

With the test method validated you are ready to execute the testing.

Once the testing is complete, document the validation/verification documents where the results are documented.

DESIGN PROJECT MASTER VALIDATION PLANS

- Sections to include:
  - Purpose and Scope
  - Overview
  - Validation Approach
  - Applicable Documents
  - Validation Plan and Results

Design Project
MVP Template

DESIGN TRANSFER TO PRODUCTION

- Master Validation Plans can also be used to translate design requirement into production/manufacturing requirements.
- How?
  - List all the requirements that can and will be tested in production.
    - Use mechanical drawings, product specifications, etc…

DESIGN REQUIREMENTS INTO PRODUCTION REQUIREMENTS

- Like for Design Project Master Validation Plans
  - For each design requirement list the following:
    - Manufacturing Test Method – how the requirement is going to be tested
    - How the requirements are controlled – 100% verification, process monitoring, etc.
    - Test Method Validation Reports

DESIGN REQUIREMENTS INTO PRODUCTION REQUIREMENTS

- List each manufacturing process.
  - For each manufacturing process list the following:
    - Equipment and tooling
    - IQ report for each equipment and tooling
    - Equipment Cleaning Validation Report
    - Equipment Software Validation
    - Process Software Validation
    - Process Characterization Report
    - Operational Qualification Reports
    - Performance Qualification Reports

Design to Production MVP

DESIGN TO PRODUCTION MASTER VALIDATION PLAN

- Is a living document that describes the validated state of a product/manufacturing line
- It also used to plan the validation activities when changes occur
- It is first drafted at the as early as the development stage of the process

EQUIPMENT CLEANING MASTER VALIDATION PLANS

Definition

- The inventory and plan for cleaning validation of equipment and tooling involved in the manufacture of product.

It's use

- It summarizes the validation activities relating to equipment and tooling cleaning processes.
- Cleaning validation demonstrates that the cleaning process removes residues of interest from the surfaces of equipment and tooling, used to manufacture product, to predetermined levels.
- Document the equipment cleaning processes that will be validated and those that will not be validated with justification.

Equipment Cleaning MVP

SITE MASTER VALIDATION PLANS

Definition

A a documented plan for the validation of all the areas that are in scope of validation and intended to be maintained in a validated state.

In other words,

It is a compilation of all the validation activities for each validation area of each site.

SITE MASTER VALIDATION PLANS

- Areas?
  - Facilities
  - Utilities
  - Equipment and Tooling
  - Equipment and tooling for Cleaning processes
  - Products
  - Products Manufactured
  - Software
  - Manufacturing Processes
  - Test Methods

SITE MASTER VALIDATION PLANS

- One way is creating an INVENTORY per area per site.

SITE MASTER VALIDATION PLANS

- What is an inventory?
  - Is a list of the items to be validated including those that are exempt or do not require validation with justification.

- Importance of an Inventory
  - Demonstrate that an item is validated (Inclusions)
  - Documents the Plan to validate an item
  - Document the rational for not validating an item (Exclusions)

CREATE INVENTORIES – DEFINE THE SCOPE

- Determine what must be included and excluded from the area inventory
  - For example:

Inventory Area	Inclusions	Exclusions
Equipment and Tooling	• **Development Equipment and Tooling** Equipment and tooling that will be used to support design, design validation and verification that are used on a regular basis and needs to be maintained. • **Post Design Control Equipment and Tooling** Equipment and tooling that will be used manufacturing activities that are used for design control.	• **Development Equipment and Tooling** Equipment and tooling that will be used to support design, design validation and verification which is **not** used on a regular basis and do not need to be maintained. • **Pre-Design Control Equipment and Tooling** Equipment and tooling that is used for feasibility activities; typically will not be used in Formal Design Control.

  - Establish the inclusions and exclusions for each inventory area.

CREATE INVENTORIES – WHAT TO INCLUDE

- Item number unique identifier
- Item description
- Manufacturing plant/facility where it is located
- Location within the manufacturing plan/facility
- If it requires validation or not. If not, provide justification
- Validation Report
- Date of last validation
- When it will it be revalidated (depending on the periodic assessment)

Inventory Template

INITIATE SVMP

- Sections to include in a SMVP
  - Purpose and Scope
  - Site Description
    - Manufacturing Site (its address)
    - Manufacturing areas (clean room environment areas (CEAs), sterilization, packaging, parts cleaning, passivation
    - Laboratories

INITIATE SVMP

- Sections to include in a SMVP
  - Supporting Utilities
    - What type of utilities are used in the manufacturing areas? (Compressed air, argon, de-ionized water, heating, ventilation, air conditioning, electrical, etc.)

INITIATE SVMP

- Sections to include in a SMVP
  - Production Flow Description
    - May Include:
      - A general flow stream map and a brief description of each process
      - The product manufactured at the manufacturing plant and a high level description
      - A description of the process(es) used to manufacture the product and a high level description

INITIATE SVMP

- Sections to include in a SMVP
  - Supporting Quality Systems
    - Examples:
      - Document Control System(s),
      - Equipment and Tooling Control System,
      - Manufacturing Execution System (MES)
      - CAPA
      - Product Life Cycle Management System
      - Learning Management System

INITIATE SVMP

- Sections to include in a SMVP
  - Definitions
    - Include terms and their definitions
  - Responsibilities
    - Define the roles and responsibilities for the maintenance of the SVMP

INITIATE SVMP

- Sections to include in a SMVP
  - Validation Methodology and Requirements
    - May Include a high level description of the validation disciplines program and its requirements
  - Validation Schedule
    - Based on the inventory schedules.

INITIATE SVMP

- Sections to include in a SMVP
  - Metrics
    - Define the metrics and how they are going to be measured
  - Inventory Maintenance
    - Describe the process of maintaining the inventories

INITIATE SVMP

- Sections to include in a SMVP
  - SVMP Update Requirements
    - Include what will trigger an update to the SVMP

INITIATE SVMP

- Sections to include in a SMVP
  - References
  - Inventories References
  - Attachments or Appendices List
  - Attachments or Appendices
  - History of changes

TAKEAWAYS

- Master validation plans help us to:
  - Show that we have validated the requirements
  - Think strategically
  - Summarize the validation activities
  - Find the validation evidence

QUESTIONS