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1. Philosophy of Validation

According to GMP definition 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 attributes."

Appropriate and complete documentation is recognised as being crucial to the validation effort. Standard Operating Procedures (SOPs), manufacturing formulae, detailed batch documentation, change control systems, investigational reporting systems, analytical documentation, development reports, validation protocols and reports are integral components of the validation philosophy. All validation documentation is prepared and maintained to be readily accessible to Operations personnel. The validation documentation provides a source of information for the ongoing operation of the facility and is a resource that is used in subsequent process development or modification activities.

All validation activities will incorporate a level of Impact Assessment to ensure that systems, services and products directly influenced by the testing have been identified. Additionally, an EHS Audit, incorporating risk assessment activities, are performed by the EHS management on all product lines to address the safety issues involved in the manufacturing process.

A revalidation programme will be implemented based on routine equipment revalidation requirements and on the Change Control Policy.

2. Responsibilities

It is the responsibility of the Project Manager to source appropriate resources, assign responsibility and obtain agreement to participate in the project.

Considerations should include:

- Skills needed
- Facilities needed
- Equipment and technology required
- Suppliers/contractors and materials
- Capital funds needed
- Special resources identified.

Project teams are assembled for a limited or fix duration to deal with new equipment, processes or systems. Team members can be drawn from single departments, cross-functional divisional areas and contractors. Skills, which do not exist inside the organisation, or for which there is insufficient capacity, will need to be sourced externally.

All Validation Plan and Reports are reviewed, approved and accepted, as applicable by members of the review team identified below as a minimum. It is the responsibility of the individual project teams to identify appropriate and/or additional reviewers as identified in the individual Validation Plan for that project:

- Quality Assurance Manager
- Validation Manager

2. A Validation Project Log Form (**Form-375**)
3. A Validation Plan
4. Installation Qualification Report/s
5. A series of Operational Qualification Test Protocols and Raw Data Results (as defined in the Validation Plan.
6. An Operational Qualification Report
7. EHS Report
8. Quality Audit Report (for new process lines)
9. A series of Performance Qualification Test Protocols and Raw Data Results (as defined in the Validation Plan and during the OQ phase).
10. A Validation Report
11. Discrepancy Forms
12. System SOPs (a list of SOP's relating to the process)
13. System Changes (Change Request Forms, see **SOP QMS-030**).

5.1.1. All Validation Documents are to be clearly identified with numbered pages, with clear units of measure stated, results/signatures recorded in black or blue pen, and signatures of persons performing tests and dates conducted are all to be captured.

5.1.2. The original copies of approved Validation documents are the responsibility of the Project Coordinator typically Validation Manager. During the Validation Project they are to be kept in a secure place and copies issued to members of the Validation Team as required, in a controlled manner, by the Project Coordinator. The original approved copies are to be included in the Validation File.

5.1.3. Raw Data relating to the execution of Operational and Performance Qualification tests can consist of result sheets, temperature recordings, etc. Raw Data is the real time recording of the results obtained and must always be signed and dated by the person performing the test and then included in the Validation file. Operational and Performance Qualification protocols and the Raw Data relating to them are to be filed in a separate section or volume of the Validation file. It is the responsibility of the person/s assigned responsibility for checking and approving the completed protocols to ensure that the data presented in the Reports is factual and truly represents the Validation effort. The Reports are then presented to the Validation Committee for their approval.

5.1.4. The composite Validation Files are to be appropriately numbered and indexed to allow for easy review of the Validation effort and are to include a section to record any changes that are hence made to the validated equipment/process/system, in accordance with **SOP QMS-030.**

5.2. **Numbering System of Validation Documents**

5.2.1. The Project Coordinator is responsible for registering the Validation Project with the Validation Dept by filling out a **Validation Project Log Form (Form-375)**.

5.2.2. The Validation Dept is responsible for allocating a unique Project No. to each Project. The same code number will be utilised for the numbering of associated documentation relating to that Validation file e.g. Validation plan, IQ, Qualification test protocols, Validation reports, and other associated documentation and will be used on all validation forms. Validation documentation will be numbered according to the following designated sequence:

- Supplier installation inspections
- Instrument data sheets.

Operating Documentation

- Supplier operating & maintenance manuals.

6.1.2. **Equipment & Instrument Lists**

- All process and ancillary equipment and instrumentation must be identified and clearly described as to vendor, model, serial number; instruments must be calibrated according to approved procedures and have calibration certificates issued. Motors, agitators and pumps must be identified as to vendor and model, electrical requirements, power and/or capacity output.
- Spare parts lists and preventative maintenance schedules must be obtained.

6.1.3. **Materials of Construction & Lubricants in Potential Product Contact**

- Materials of construction and lubricants in potential product contact must conform to design specifications and be suitable for the intended application.

6.1.4. **Utilities Verification**

- Utilities must be properly installed and available as specified by the manufacturer's design specifications and in-house requirements.

6.1.5. **SOP Verification**

- SOPs shall be listed and verified to be in place. SOPs should accurately describe the equipment setup and operation.
- SOPs must be available to support the satisfactory operation, maintenance, cleaning and change control of the equipment.
- Training records should be available for all personnel operating the machinery.

6.1.6. **Acceptance**

- All documentation identified as required in the approved protocol must be obtained and filed in the established Validation Filing System. See section 5.2
- Change control on all equipment and systems must be instituted in the facility from the start of IQ either using manufacturer's or in-house Change Control procedures. Any changes during OQ to system turnover must be made in accordance to the in-house Change Control Procedure.
- All discrepancies must be satisfactorily resolved prior to system acceptance.

6.2. **General Criteria for Operational Qualification**

The OQ must demonstrate that the system operates as intended throughout the specified design, operational or approved acceptance range of the equipment, as applicable.

Acceptance criteria for all OQ protocols will be based on the following requirements.

6.2.1. **Record of Test Instrumentation**

- Indicating and recording Instrumentation utilised to obtain test data required by the protocol must be calibrated according to approved procedures and traceable ISO, AS or British standards and have calibration certificates.

Approval of this report by the Validation Committee signified that a provisional approval (of a maximum of 6 months duration) has been granted to enable the equipment/system to be utilised for production use.

7.1.8. Performance Qualification (PQ) Test Protocols

The Performance Qualification phase consists of the conducting of tests defined in the Validation Plan and during the Operational Qualification phase to determine if the equipment/process/system continues to operate in a reliable manner required to attain a specified quality in the process output/product.

Materials used at performance qualification should be those actually used at the normal processing. Performance Qualification usually consists of the manufacture of three consecutive production runs that satisfy all of the acceptance criteria.

7.1.9. Validation Report

This document summarises all the tests that have been conducted as part of the Operational Qualification (OQ) and the Performance Qualification (PQ). It addresses the requirements for the Validation programme stipulated and the Validation Plan. Approval of this report by the Validation Committee signifies that full approval of the equipment/system for routine production use has been granted. The Validation Report will stipulate the required Revalidation programme.

7.1.10. Revalidation

The routine performance of tests to check that a validated subject or an element of a subject still does what it is expected to do.

7.2. Activities to be conducted during the Validation Programme

7.2.1. General Points

All Validation projects are to be logged with the Validation Department. The Validation Department is responsible for allocating a Project Number that is to be referenced on all validation documentation.

All DQ, IQ, OQ and PQ Protocols shall define the acceptance criteria with qualification procedures, be reviewed and approved by the persons identified in the Validation Plan prior to execution.

All checks and testing must be carried out using measuring instruments that are identified and calibrated according to established methods. All calibrations must be recorded.

Only validated test methods are to be used.

The different steps of the Validation Programme (IQ, OQ & PQ) should be followed as identified in the Validation Plan.

All qualification test results obtained during the testing must be recorded even those that did not meet the acceptance criteria.

The test results must be clearly written up and compared with the test acceptance criteria.

Results should be reviewed by the same members of the Project Team who approved the Test Protocol.

An effective change control procedure should be operational and encompass the whole project from the pre-planning stage through to the final acceptance of the process validation exercise.

7.2.2. Preparatory Work - The Validation Programme

