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Review Article

Brief Overview of Pharmaceutical Facility Validation

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Abstract

The validation of the facilities is assuring that the quality system is consistently producing the products that are suitable for their intended use. Validation of the facility plays major role whether it has contact directly with the product or not because adequate facility plays good role on getting quality product. Facility validation is the foundation for assuring success in further manufacturing process validation. Before you begin validating a manufacturing process, an acceptable facility, and the utilities and equipment to support manufacturing operations must be in place. Also in case of the renovated facility, maintaining the aseptic manufacturing and providing the quality attributes to the product manufactured at the location, facility validation becomes essential.

Keywords: Validation, Qualification, Validation Master Plan, Standard Operating Procedure.

1. Introduction[1,2,3]

For a new or upgraded facility, commissioning and facility validation is the foundation for assuring success in further manufacturing process validation. Before you begin validating a manufacturing process, an acceptable facility, and the utilities and equipment to support manufacturing operations must be in place. Good Validation Practices (GVPs) like Design Qualification (DQ), Installation Qualification (IQ), Operational Qualification (OQ) & Performance Qualification (PQ) thus play a crucial role in delivering operationally effective, safe, and efficient facilities, process air handling systems, utilities, equipment, and also provide the medium by which compliance is achieved, demonstrated, and retained. Facility validation provides the documentation necessary to demonstrate that facilities, utility systems, and process equipment are operationally effective, safe, and efficient. The important aspect to note in the facility validation is the interaction and interdependency of many of the engineering and validation activities. Such as:

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- DQ confirms the GMP facility design supporting utilities, and equipment. This can be conducted in parallel with development of Factory Acceptance Testing (FAT) methodology.
- Pre-Delivery Inspection of major system components can contribute to the IQ
- Factory acceptance operational tests can contribute to the OQ
- Commissioning activities can overlap with some IQ/OQ activities, and can confirm the User Requirement Specification (URS) for "indirect impact" systems
- IQ verifies construction and installation
- OQ verifies functional design
- PQ verifies the URS, and will challenge a collection of both "direct impact" and "indirect impact" systems working together

1.2 Validation Planning[4]

For significant validation efforts involving multiple equipment and utility systems, a Validation Master Plan (VMP) should be developed early in the project, as early as the conceptual engineering design

phase, to define the overall validation philosophy and methodology to be used throughout the project. This allows the validation team to plan resource and scheduling requirements, and ensures that design engineer specifications and detailed design are suitable for validation. The VMP should be a structured, detailed plan defining all the testing, acceptance criteria, and documentation required to satisfy the regulatory authorities and support the validation process. Based on an impact assessment, the plan also clearly defines the scope and extent of the qualification or validation process by listing the matrix of products, processes, equipment, or systems affected. The VMP also assigns responsibilities for developing and executing validation program activities, and gives a first look at an anticipated testing execution schedule. At the inception of projects, it is necessary, and in fact, essential, that the project team and project sponsor approve the VMP to enable the release of sufficient financial and staffing resources to support the entire project.

1.3 Qualifications[5,6,7]

A) Design Qualification (DQ)

"It is a documented verification that the proposed design is suitable for intended purpose." The process of ensuring and providing documentary evidence that the premises and equipment comply with the standards and design intentions that they comply with user and GMP requirements. The design qualification on the instruments and the manufacturing equipments both involve the same kind of documentation and objectives. But the design qualification of an analytical instrument is one in which the customer does not have much to demand for, as most of the analytical instruments are commercial off-the shelf and hence the design and functions are predetermined for each and every model of the instrument. On the contrary the manufacturing equipments are custom made and the customer could ask for the various features that need to be incorporated into the equipment.

Preparation and Approval of the DQ

DQ is to be prepared before purchasing the equipment and this should on the basis of purchasing equipment.

DQ is prepared jointly by the user and the representatives of the Engineering department and approved by the engineering and the quality assurance department.

B) Installation Qualification (IQ)

Documented verification that \the equipment or system as installed or modified comply with the approved design or user requirements.

The process of ensuring and providing documentary evidence, that the equipment and premises have been delivered and installed to the design specification. The basic principles are as follows:

- Equipment to be correctly installed in accordance with an installation plan.
- Requirements for calibration, maintenance and cleaning be covered in approved Standard Operating Procedures (SOP's).
- A test to be conducted to assure that equipment is operating correctly, under normal and "worst caste" conditions.
- Operator training requirements pertaining to new equipment be conducted and documented.

Methodology for IQ

The IQ for any equipment or instrument requires a formal and systematic check of all installed equipment against the equipment supplier's specifications and additional criteria identified by the user as part of the purchase specifications. These checks, .tests and challenges should be repeated a significant number of times to assure reliable and meaningful results. The IQ is carried in accordance to previously approved protocols.

An ideal IQ protocol shall document the following;

- Objective
- Equipment Description & identification
- Equipment master file
- Major components
- Material of construction

- safety features & alarms
- utilities
- identification of standard operating procedures/ departmental procedures/ preventive maintenance/ procedures/cleaning procedures
- installation verification
- acceptance criteria

C) Operational Qualification (OQ)

"It is a documented verification that the equipment or system installed or modified performs as intended throughout the anticipated operating ranges."

OQ establishes confidence that the equipment and ancillary system are able to consistently operate in accordance with the design specifications. Within scope of OQ, it is tested and verified that the equipment operates according to its specifications. For this purpose, the place in which the equipment is set up is tested according to metrological aspects. The execution of an operational qualification should be followed by an authorized person. The critical operating parameters for the equipment or the plant should be identified at the operational qualification stage. The plans for the operational should identify the studies to be undertaken on the critical variables, the sequence of those studies and measuring equipment to be used and the acceptance criteria to be met. Studies on the critical variables should incorporate specific details and test that have been developed from specialist knowledge of the process and how the equipment will work (defined in designed criteria and specifications). Wherever applicable, simulated products may be used to conduct the operational qualification. Studies on critical variables should include a condition or a set of conditions encompassing upper and lower processing or operating limits and circumstances; commonly referred to as "worst case" conditions. Such conditions should not necessarily induce product or process failure. The completion of a successful OQ should allow the finalization of operating procedures and operator instruction documentation for the equipment. This information should be used as the basis for training of operators in the requirements for the satisfactory operation of equipment.

Methodology for performing the OQ

The OQ is to be carried out in accordance to an approved protocol. The OQ involves testing and insuring that the IQ is appropriate. All the features identified are tested in OQ. The OQ is to be performed without any load. The satisfactory completion of OQ gives an assurance that the machine is satisfactory for use. Following are the contents that can be a part of OQ of an instrument or equipment:

- Objective
- Instrumentation calibration
- Control panel testing
- Safety features testing
- Verification of SOP's/ Departmental procedures /Preventive maintenance procedures
- Operational testing
- Acceptance criteria

The objective of the operational qualification clearly identifies and defines the scope of the protocol and also the various aspects that protocol shall encompass.

D) Performance Qualification (PQ)

"It is a documented verification that the equipment and ancillary systems as compared together can perform effectively and reproducibly based an approved method and specification." PQ is establishing confidence that the process is effective and reproducible, establishing confidence that a process in accordance with the design qualifications. Performance Qualification is documented proof that the equipment functions in your facilities exactly as intended. This is insured by verifying the suitability of the equipment under the actual operating conditions of the environment and according to its intended task (e.g., compliance with safety regulations for accident prevention, traceable data transmission). Performance Qualification reviews the critical parameters of the equipment using suitable test methods. These

procedures are documented in form of test specifications.

It is not mandatory to perform Performance Qualification on all equipments or instruments. However Performance Qualification is to be performed for all the process equipments and the equipments that are critical. The question on whether not to carry out Performance Qualification is generally done on a case-to-case basis.

Methodology for Performance Qualification

The methodology for performance qualification is similar to as proposed for OQ except for that the OQ is performed without the load but the PQ is performed with the load.

1.4 Change Control[8,9,10]

Written procedures should be in place to describe the actions to be taken if a change is proposed to a product component, process equipment, process environment, processing site, method of production or testing or any other change that may affect product quality or support system operations.

All changes must be formally requested, documented and accepted by the Validation Team. The likely impact / risk of the change on the product must be assessed and the need for the extent of re-validation should be determined.

Commitment of the company to control all changes to premises, supporting utilities, systems, materials, equipment and processes used in the fabrication/packaging of pharmaceutical dosage forms is essential to ensure a continued validation status of the systems concerned.

The change control system should ensure that all notified or requested changes are satisfactorily investigated, documented and authorized. Products made by processes subjected to changes should not be released for sale without full awareness and consideration of the change by the Validation Team. The Team should decide if a re-validation must be conducted prior to implementing the proposed change.

1.5 Periodic Review and Revalidation[11,12]

To verify compliance with procedures and policies, validated systems should be subjected to ongoing operational audits. Review of a previously validated system is recommended to identify possible trends in the system's performance.

This periodic review should be conducted according to an SOP, and in accordance with schedules established and documented in QA audit plans. The frequency of audits should be based on system importance relative to regulated operations. Upon completion of the evaluation, a report of the findings should be issued, including all actions recommended, and the corresponding supportive documentation. The result of this periodic review will then determine the need and degree of system revalidation, if necessary.

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