JETIR.ORG ISSN: 2349-5162 | ESTD Year : 2014 | Monthly Issue
JOURNAL OF EMERGING TECHNOLOGIES AND INNOVATIVE RESEARCH (JETIR)
An International Scholarly Open Access, Peer-reviewed, Refereed Journal

PHARMACEUTICAL VALIDATION: A REVIEW

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ABSTRACT:

The ability to effectively create and put into practice the specified procedures while using documentation is known as "validation." Process validation gives evidence that a certain method produces a product that also complies with specified requirements and quality criteria. Validation of the drug product's manufacturing method, from formulation development to the final commercial batch. Developing a method for the portion of the pharmacy industry that is interested in the finished product or process tests, going to prepare samples, and offering a practical method for estimating the selectivity, specificity, quantity limit detection, linearity, the accuracy of the range, precision, consistency of the recovery solution, robustness, and robustness of liquid chromatographic methods are all part of this process. Therefore, legality is a crucial part of pharmaceutical chemistry and quality control.

KEYWORDS: Standard Operating Procedures, Process Qualification, Operational Qualification, Limit of Quantification, Limit of Detection.

INTRODUCTION: [1, 5]

Validation is the procedure, process, or activity that is used in testing and then production must be validated in order to create documentary proof that it consistently maintains the desired level of compliance at all the stages.

Any pharmaceutical facility's main goal is to consistently produce goods with the required qualities and attributes at the lowest costs. Although validation studies have long been carried out in the pharmaceutical sector, In order to obtain such a quality, the pharmaceutical industry is today interested in a wide range of perspectives.

The term "validation" first appeared in the United States in 1978. The concept of validation has evolved over time to include a wide range of activities, from computerized systems for clinical trials, labeling, or process control to analytical methods used for the quality control of drug substances and drug products. Validation is founded on regulatory requirements but is not authorized by them, and is best viewed as a crucial and essential component of cGMP.

The 21 CFR parts 210 and 211 provide validation that is mostly based on FDA standards that describe current good manufacturing practice (cGMP) for finished pharmaceuticals.

According to the cGMP regulations, manufacturing procedures must be planned and monitored to ensure that raw materials used during production and the final product consistently meet predetermined quality standards.

HISTORY OF VALIDATION [6, 7]

In an effort to raise the quality of medications, Ted Byers and Bud Loftus, are two FDA officials, originally introduced the idea of validation in the middle of the 1970s. It was proposed in direct response to several problems in the sterility of large volume parenteral market. The primary validation efforts were focused on the production procedures for these items, but they quickly expanded to the related medicinal operations.

The FDA first suggested the current GMP requirements in 1976. Since then, they have undergone various revisions. GMP requirements are regarded as formal legislation in a number of significant nations, and noncompliance is punishable by law. Additional compliance policies, manuals, and directives are not binding on the law. However the pharmaceutical industry follows them as a part of good management and business practice

Although U.S.F.D.A. was the first to promote the idea of process validation, the term did not appear in any of the agency's material until 29th September, 1978. Process validation was not covered by any cGMP rules.

BENEFITS OF VALIDATION: [7, 8]

- Processes that are consistently in control need less process support and have less downtime.
- Only fewer batch failures and possibly more productive operations.
- Additionally, timely and adequate validation studies will demonstrate a dedication to product quality, which could speed up the marketing permission process and pre-approval inspection.
- Validation is a smart business move.
- Decrease in reworks and rejections
- Reduced testing time and final products.
- Faster and more precise process deviation analysis.

NEED OF PHARMACEUTICAL VALIDATION: [9, 10]

Since it involves systematically assessing systems, facilities, and processes to see whether they carry out their intended activities efficiently and consistently, validation is a crucial component of quality assurance. A validation method has been officially recognised because it has been demonstrated to offer a high level of assurance that uniform batches will be generated that meet the necessary criteria. Process improvement does not occur as a result of validation; rather, validation verifies that a process has been created correctly and is being controlled.

The pharmaceutical industry employs highly skilled personnel, pricey materials, and material removal facilities and technology.

SCOPE OF VALIDATION: [11, 12]

Finding the validation scope becomes a very challenging assignment because pharmaceutical validation is a vast area of work that covers almost every component of pharmaceutical manufacturing activities. But a careful review of the pharmaceutical processes will at least highlight the following areas for pharmaceutical validation.

- Analytical
- Instrument Calibration
- Process Utility services
- Raw materials
- Packaging materials
- Equipment
- Facilities
- Manufacturing operations
- Product Design
- Cleaning
- Operators

IMPORTANCE OF VALIDATION: [13,15]

- Lowering the cost of quality.
- Minimal batch failures, increased productivity, and efficiency.
- Decreased rejections.
- Avoiding investing on new equipment.
- Less complains regarding errors in the processes.
- Increased process knowledge among employees.
- Faster automation.
- New equipment starts up more quickly and consistently.
- Government regulation (Obtaining approval to manufacture and introduce new items requires compliance with validation standards).
- Tests on finished goods and processes are reduced.

TEAM AND RESPONSIBILITIES FOR VALIDATION: [16,17]

Department/Designation	Responsibility
Manager production	Accountable for batch production, as well as for reviewing reports and procedures.
manager QC	You are responsibility is sample analysis.
Executive QC	You are responsible for gathering and submitting the sample to QC.
Executive production	Responsible for batch manufacturing and protocol development.
Manager QA	My responsibilities include approving the procedure and producing the summary report.

TYPES OF VALIDATION:[18,19]

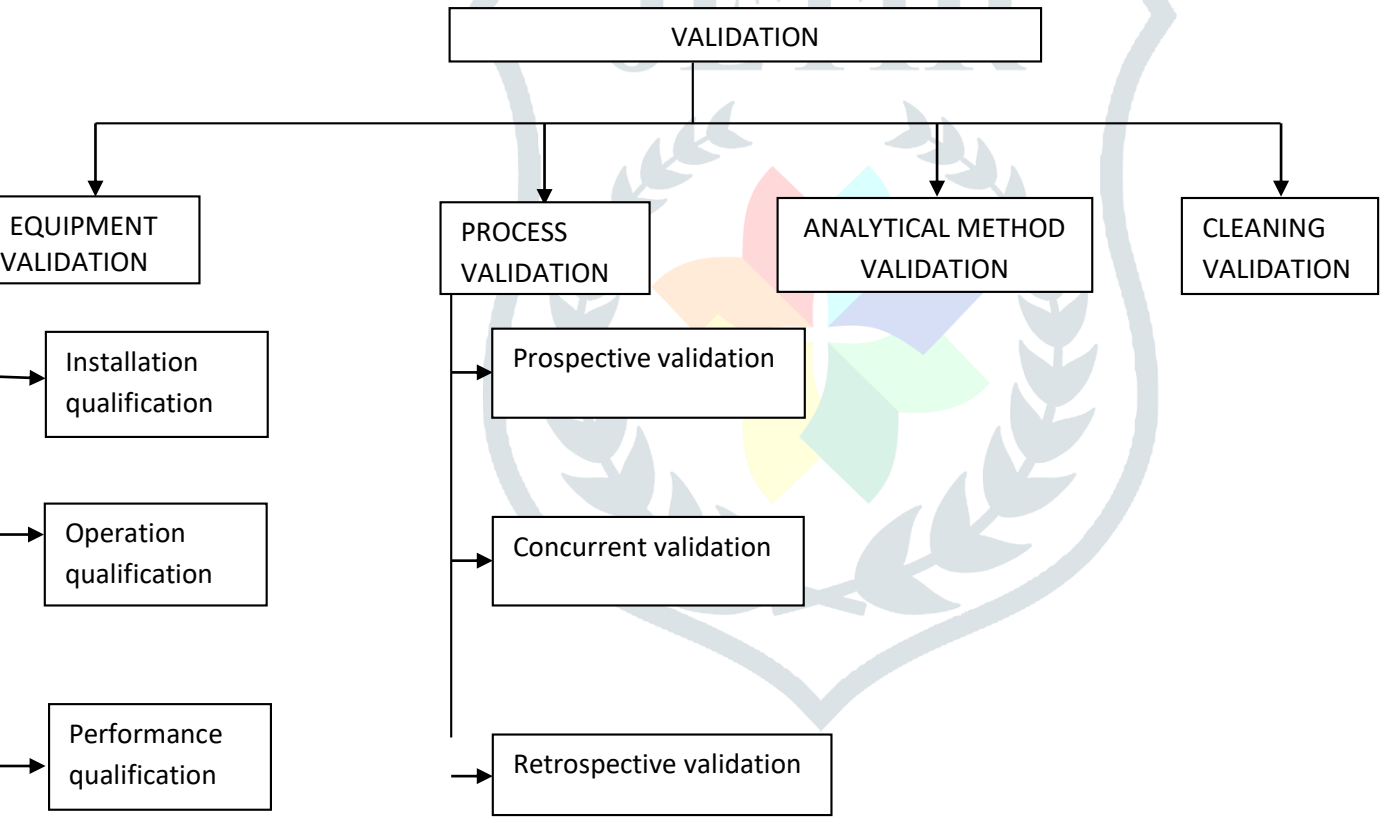

Figure 1: types of validation

EQUIPMENT VALIDATION: [20,26]

Equipment validation is a documented process that has been established to demonstrate that any equipment is functionally acceptable and produces results that can be trusted.

The principle behind equipment validation is that it must be built, maintained, and customised in order to carry out the tasks that need to be done.

There are four types of equipment validation mentioned below

- Installation qualification (IQ)
- Design qualification (DQ)
- Performance qualification (PQ)
- Operational qualification (OQ)

Design Qualification (DQ):

Verification in writing that the facilities, systems, and equipment suggested are appropriate for the intended use. Design compliance with GMP should be shown in this certification. The design principles used should be such that the equipment meets the GMP goals. It is important to look at the mechanical drawings and design elements that the equipment's manufacturer provided.

Installation Qualification (IQ):

Process equipment and related systems must operate consistently under a set of restrictions and tolerances for food and drug management (FDA). It is primarily recorded whether newly installed or updated appliances and equipment comply to the requirements and recommendations of the manufacturer. On new or updated facilities, systems, and equipment, installation qualification (IQ) should be carried out.

Operational qualification (OQ):

Operational qualification is a set of tests that evaluates the equipment's performance potential. Operational qualification places more of an emphasis on the equipment than it does on demonstrating performance capabilities related to manufacturing a particular good.

OQ considerations include:

- Limits of process control (time, temperature, pressure, line speed, and setup conditions).
- Software settings.
- Raw material requirements.
- Process operational guidelines.
- Needs for material handling.
- Control of process change.
- Education and training.

- The process's capabilities and short-term stability.

Performance qualification (PQ):

It is described as the procedure to ensure that the system can produce a quality product consistently. Or alternatively the method used to show that the instrument can meet the requirements stated in the design qualification.

PQ consideration includes:

- The OQ processes and actual product and process parameters.
- Acceptability of product.
- Confirmation of process capabilities according to OQ.
- Repeatability and long-term stability of the procedure.

Re- Qualification:

Revalidation provides evidence that modifications made to a process or its surroundings do not adversely alter its characteristics or the quality of its products. It is necessary whenever there is a change to any of the crucial process parameters, the formulation, the principal packaging elements, the manufacturer of the raw materials, the major equipment. Process revalidation would also be necessary in the event that batches of the product or process did not satisfy specifications. Application qualification must comply by evaluations and document approval that changes the scheme by changing standard policies.

PROCESS VALIDATION: [27,28]

Establishing written proof that a certain process will consistently result in a product meeting its predetermined specifications and quality of products is known as process validation.

Process validation is the collecting and assessment of data from the process design stage through production that creates scientific proof that a process is able to generate high-quality products consistently. the documented act of demonstrating that any action, process, tool, resource, activity, or system actually produces the desired result.

Phases in Process Validation:

There are three phases to the activities involved in validation studies.

Phase 1: Validation or Qualification Phase:

The pre-validation phase, also known as the qualification phase, is the term for all operations involved in product development: creating stability conditions, scaling-up research, transferring technology to commercial-size batches, formulation, storage, and handling of in-process and finished dosage forms, equipment qualification, installation qualification, master formula record, operational qualification, and process capability.

Phase 2: Process Validation Phase (Process Qualification phase):

This phase is used to ensure that even under the most extreme circumstances, it is still possible to generate products that are satisfactory.

Phase 3: Validation Maintenance Phase:

The validation and maintenance phases require regular examination of all process-related documentation, including validation audit reports, to ensure that there have been no adjustments to the production process and that all SOPs, including the change control processes, have been adhered to.

The Validation Team assures that no modifications or deviations that should have been required for requalification and revalidation have occurred at this stage.

TYPES OF PROCESS VALIDATION: [29,30]

Prospective validation:

It is defined as the established, written evidence that a system performs as it is intended to do in accordance with a predetermined protocol. This validation is usually done before a new product or one created using a modified manufacturing process is released. According to the processes being used commercially, the validation technique is carried out through prospective validation.

The production process should be divided into several steps during the product development phase. To determine the crucial factors that may have an impact on the final product's quality each step should be evaluated in terms of actual or theoretical considerations.

Concurrent Validation:

It is related to prospective with the exception that the operational firm will sell the product to the general public during the qualification runs at its market price, and it is also related to retrospective validation.

This validation includes product testing and in-process observation of crucial processing steps. This makes it easier to produce and document evidence that the production process is under control. This documentation of the critical processing validation in process is evidence that the production process is under control.

Retrospective validation:

In this case, historical data from records of manufacturing batches that have been completed is used to offer the documented evidence that the process has been in a controlled state before the request for such evidence.

Revalidation:

The validation process is being repeated. This is done when there is any modification or replacement to the formulation, the equipment plan or site, the location, the batch size, or when successive batches fail to fulfill the requirements of the product. It is also done at predetermined intervals when there are no modifications.

ANALYTICAL METHOD VALIDATION: [30]

Method validation is the process of verifying that the analytical testing technique used for a specific test is appropriate for its intended usage. Using laboratory tests, the analytical methodology is verified to see if its performance characteristics meet the specifications for the application in consideration.

Parameters of the Analytical Method Validation:

The analytical procedure's main goal must be understood clearly because it will determine the validation qualities that must be assessed. The following is a list of typical validation qualities that should be taken into account:

- Accuracy
- Precision
- Repeatability
- Intermediate Precision
- Specificity
- Detection Limit
- Quantitation Limit
- Linearity
- Range

CLEANING VALIDATION: [31]

The validation of cleaning ensures that the cleaning procedure properly reduces residues from production facilities to below a set level. In the pharmaceutical sector, cleaning validation is mostly used for process equipment cleaning. Cleaning validation analyses cleaning procedures or cycles. It should also explain how acceptability criteria, such as chemical and microbiological parameters, detection limits, and choice of sampling procedure, were developed.

Objective of Cleaning Validation:

- Reduction of solvents.
- Increased cleaning equipment and shorter cleaning times.
- Equipment utilization, equipment life extension, and multiproduct.
- Infrastructure, worker safety, and cost-effectiveness are few other objectives.

- The major goal of cleaning validation is to verify whether the technique involved in cleaning could reliably eliminate debris from the accessible product while staying within the Tolerances.

Benefits of Cleaning Validation:

- **Operator safety:** Validation enhances operator security. To reduce accidents and boost safety, equipment that has been properly calibrated and approved is used.
- **Better Customer Quality:** Proper validation helps to decrease market recalls, which leads to better customer service and product quality.

CONCLUSION:

Validation is an essential part of GMP. Validation ensures that the product will meet GMP standards for quality, safety, efficacy, purity, and effectiveness. Validation is frequently used in drug development, production, and final product specification. Validation helps in quality cost reduction, resulting in the highest possible product quality. When a product is produced in accordance with GMP guidelines, batch uniformity and integrity are absolutely assured due to pharmaceutical validation. Pharmaceutical validation is recognized as the most important and widely accepted prerequisite for cGMP in the current literature analysis. Pharmaceutical companies should establish a general validation policy that details how validation will be carried out. The validation of the production process, cleaning procedures, analytical techniques, and in-process control test procedures will be included in this. Overall, we can draw the conclusion that the goal of the validation is to demonstrate that steps like production, cleaning, and analytical testing are necessary for the research and manufacture of pharmaceuticals.

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