INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES
[ISSN: 0975-4725; CODEN(USA): IJPS00]
Journal Homepage: https://www.ijpsjournal.com

OPEN ACCESS

Review Article

Process Validation in Pharmaceutical Industry

Mahima Kanojia*, Neha Sodiyal, Shivanand Patil

Shree Dev Bhoomi Institute of Education Science and Technology, Uttarakhand.

ARTICLE INFO

Published: 31 May 2025
Keywords:
Validation, Verification ,current Good Manufacturing Practices , Process
DOI:
10.5281/zenodo.15557939

ABSTRACT

Validation is Essential & key steps towards fulfilling and maintaining the consistency of the finished product. If every step of the manufacturing operations is checked and analyzed , we can ensure that obtained end product is of highest quality and have appropriate effectiveness. Validation is technique which measures that have been planned alongside the documentation. Validation and quality assurance will jointly ensure the high quality of items. Process validation / verification emphasizes process design components and retains procedure management during monetization and communicates that it is in progress initiative and aligns process validation activities with the product life cycle. The objective of this review provide an introduction and a general overview of the process validation of pharmaceutical production with specific reference to the criteria lay down by the US FDA.

INTRODUCTION

Drug development process is a time consuming process which includes discovery of new drug molecule, laboratory testing of drug, studies on animals, clinical trials and regulatory registration. Drug product should fulfill the following conditions such as Quality, Safety and efficacy, in order to get the best quality and required therapeutic action of the drug. Best quality drugs can be obtained by checking or testing the Digital & Virtual performance & Self-contained and physical performance during the producing process and then validate it. After the Producing process, current Good Manufacturing Practices itself requires written procedures and documents for process performance can be monitored.

Validation

Validation of the process is described as the reorganization of recorded results & outputs which provide a elevated level of confidence that provided process can reliably deliver a product which meets the predetermined requirements and quality attributes.

***Corresponding Author:** Mahima Kanojia
Address: *Shree Dev Bhoomi Institute of Education Science and Technology, Uttarakhand*.
Email ✉: mahimakanojia22@gmail.com
Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

PV is a crucial factor which ensures that certain assumptions and objectives are met.

The Assumptions on which validation can be stated are:

1. Process equipment has the capacity to function comprised with necessary specifications.

2. The power, tracking and measuring equipment's and instruments are capable of working with specifications specified for the process equipment.

3. Track the validated procedure during routine operations. Re-qualify and re-certify the equipment as required.

Why Validation is done?

Validation of the process can be done for the following reasons:

1. To cross verify that our equipment's, system meets the User requirements ,manufacturer requirements and organization requirements .

2. To provide evidence that no mix ups and cross contamination was done during the whole activity .

3. The effective use of these tools is important to ensure the continued growth of the industry.

4. Costs of product defects, rejects, recalls, grievances are major parts of the total cost of production.

5. Analysis and monitoring of the production.

6. To show evidence that the crucial and critical steps and significant changes made to the process are verified .

Importance of Validation

Validation process conducted has the following importance in pharmaceutical industry:

1. Assurance of product quality.
2. Optimization of the process conducted.
3. Quality cost is reduced.
4. The number of rejection of the product due to errors or defects is reduced.
5. Market recall is prevented by proper validation, which results in improved customer service and product quality.

Elements of Validation

1. **Design Qualification**

- The design qualification defines the main features of the device intended to meet a specific supplier's consumer specifications, regulatory enforcement and selection rationale.
- When putting together a design qualification, care should be taken as it can have a direct effect on installation, service and efficiency qualification. The more design validation roles are defined, the more work needs to be included in the processes of implementation, operational and performance qualification.

2. **Installation Qualification**

Installation qualifications for new or updated facilities, systems and equipment should be carried out. In the Installation qualification, the following key points should be included:

- Checking the facilities installations.
- Set repair specifications of the supplier and their calibration criteria.
- Verification of the building materials.

- Sources and repair of spares.

3. Operational Qualification

Operational qualification is a series of tests which measure the equipment's performance capability. Instead of demonstrating performance skills relevant to manufacturing a specific product, the operational certification focuses on the equipment.

4. Performance Qualification

It is characterized as the method of verifying that a quality product is repeatable and consistently generated by the device or in other words, the process of demonstrating that the instrument can meet the requirements outlined in the design qualification.

Types of Validation

1. Analytical method Validation

AMV is the procedure used to ensures that the process used for specific test is appropriate and suitable for its intended use Outputs and end results comes from AMV can be used to determine the quality , efficacy and consistency of analytical results .AMV should be perform in accordance with Analytical method Validation protocol & with Analytical method Validation report . the protocol should consist of all procedures and steps and acceptance criteria for all tests .

2. Equipment Validation

Equipment Validation Comprises a series of qualifications such as Installation Qualification (IQ), Operational Qualification (OQ), Performance Qualification (PQ) and Design Qualification (DQ) that provided a assurance of consistent and expected functioning of the particular Equipment .

3. Cleaning validation

Cleaning validation ensures that the cleaning process or technique adequately and consistently removes the product residue and dirt or environmental contaminants from the cleaned equipment. Clean and dirty equipment hold time study also performed to check whether how long the equipment Remain clean after the cleaning MACO(Maximum Allowable Carry over) , NOEL(amount of drug in mg that does not have any effect on human health) and PDE Value (Permitted daily exposure) are some key terms used during Cleaning validation

4. HVAC System validation

The qualification of the HVAC system should be defined in Validation master plan. The HVAC System is basic requirement of a Pharmaceutical manufacturing facility heating , Ventilation and Air conditioning is a system that is used to control the air temperature by controlling the ai filtration and the moisture in the air . Basic Components of HVAC are : Fans , Supply air duct , return air duct , Outside air regulator , Air mixing chamber , Filter , Heat exchanger , Compressor , Chiller , Condenser , Control panel , de-humidifier .

5. Process Validation

Process validation is a documented programme that provides a high level of assurance that a specific process will consistently produce a product that meets its pre-determined specifications and quality attributes. Process Validation is divided into various categories as follows:

a) Prospective validation

It is characterized as the establishment of recorded proof that a system does what it supposes to do on the basis of a pre-planned protocol. This validation is typically conducted prior to the launch of new

drugs and their manufacturing process. This approach to validation is usually followed whenever a new formula, procedure or facility must be tested prior to the start of routine pharmaceutical formulations.

b) Retrospective validation

It is characterized as the establishment of recorded evidence that the system does what it intends to do on the basis of a study and analysis of historical data. This is done by analyzing historical data on production testing to demonstrate that the process has always been under control.

c) Concurrent validation

It is similar to prospective, except that the operating firm would sell the commodity to the public at its selling price during the certification period. This validation includes monitoring crucial processing steps and testing of the product. It is a replication of the validation process or a part of it. This shall be carried out when there is some adjustment or substitution in the formulation, equipment and position of the plant or site.

d) Revalidation

Periodic revalidations offers the opportunity to cross verify that the systems are still operating as originally validated and that no changes have affected the process system or piece of equipment's and the end results .

- Change in critical raw material (whether it is addition or deletion of another Raw material)
- Change or replacement of Equipment .
- Technology transfer or change in the facility.
- Change in Batch Size (Increase or decrease)

Major Phases in Validation

The activities relating to validation studies can be categorized in three parts:

Phase I- This is the pre-validation qualification phase, which includes all activities related to product research and development, development of pilot batch tests, scale-up testing, transfer of technology to commercial scale batches, establishing stability and storage conditions and handling of in-process and finished dosage forms, equipment qualification, master product.

Phase-II- This is the validation step of the process. It is intended to verify that all the defined limits of the critical process parameter are true and that satisfactory product can be generated even under the worst conditions.

Phase-III- Known as the Validation Maintenance step, It involves a regular review of all process relevant records, including the validation of audit reports, to ensure that no adjustments, irregularities, defects and improvements have been made to the production process and that all standard operating procedures and change control procedures have been followed. At this point, the validation team of individuals from all major departments also assures that there have been no changes or deviations that should have resulted in requalification and revalidation. Careful design and validation of systems and process controls will provide a high degree of trust that all lots or batches produced comply with their intended specifications. It is believed that during production and control, operations are carried out in compliance with the Good Manufacturing Practice concept, both in general and with a particular reference to sterile product manufacturing.

VALIDATION TEAM

A multidisciplinary team is primarily responsible for conducting and supervising validation studies. Personnel qualified by training and experience in

a relevant discipline may conduct such studies. The working party would usually include the following staff members such as;

- Head of quality assurance.
- Head of engineering.
- Validation manager.
- Production manager.
- Specialist validation discipline: all areas.

The validation team must be

Prepare the site validation master plan with the specific requirements as per the company policy.

- Meet regularly, In accordance with a defined schedule, to discuss the progress and compliance with the Validation plan and schedule.
- Determine the systems / equipment to be qualified / validated and the extent of validation to be carried out.
- Determine the frequency of validation.
- Prepare and evaluate the suitability of the protocols.
- Verify the adequacy of the tests used for proving that the objectives are achieved.
- Complied reports should be checked and approved by validation team members. Maintain records of validation studies and inform to the Corporate Quality Assurance of progress in terms of validation plan and schedule .

DOCUMENTATION

Documentation at each stage of the process validation lifecycle is essential for effective communication in complex, lengthy, and multidisciplinary projects.

Documentation is important so that knowledge gained about a product and process is accessible and comprehensible to others involved in each stage of the lifecycle. Information transparency and accessibility are fundamental tenets of the scientific method. They are also essential to enabling organizational units responsible and accountable for the process to make informed, science based decisions that ultimately support the release of a product to commerce.

VALIDATION LIFE CYCLE

Validation is a continuing and evolving process. The validation process which extends from the very basic to a very broad theological and methodical investigation if how the system and processes perform. Its scope encompasses documentation revision control, training and maintenance of the system and process. Evidence of validation should be seen at the corporate level, and be reflected in the management structure. Validation is a method for building and maintaining quality.

VALIDATION PROTOCOL

A written plan of actions stating how process validation will be conducted, it will specify who will conduct the various tasks and define testing parameters, sampling plans, testing methods and specifications, will specify product characteristics, and equipment to be used. It must be specify the minimum number of batches to be used for validation studies, it must specify the acceptance criteria and who will sign \ approve \ disapprove the conclusions derived from such a scientific study. The validation protocol should contain the following elements,

- Short description of the process.
- Summary of critical processing steps to be investigated.

• In process, finished product specification for release.

• Sampling plans.

• Departmental responsibility.

• Proposed timetable.

• Approval of protocol .

VALIDATION MASTER PLAN

The validation master plan should provide an overview of the entire validation operation, its organizational structure, its content and planning. The main elements of it being the list/inventory of the items to be validated and the planning schedule. All validation activities relating to critical technical operations, relevant to product and process controls within a firm should be included in the validation master plan. It should comprise all prospective, concurrent and retrospective validations as well as revalidation. The Validation Master Plan should be a summary document and should therefore be brief, concise and clear. It should not repeat information documented elsewhere but should refer to existing documents such as policy

The format and content should include:

• Introduction: validation policy, scope, location and schedule.

• Organizational structure: personnel responsibilities.

• Plant/process/product description: rational for inclusions or exclusions and extent of validation.

• Specific process considerations that are critical and those requiring extra attention.

• Key acceptance criteria.

• Documentation format.

• Reference to the required SOPs.

• Time plans of each validation project and sub-project.

• List of products/ processes/ systems to be validated, summarized in a matrix format, validation approach.

• Re-validation activities, actual status and future planning .

THE VALIDATION REPORT

A written report should be available after completion of the validation, if found acceptable it should be approved and authorized. The report should include at least the following

• Title and objective of study.

• Reference to protocol.

• Details of material.

• Equipment.

• Programes and cycles used.

• Details of procedures and test methods.

• Result. Recommendations on the limit and criteria to be applied on future basis.

IMPORTANCE OF PROCESS VALIDATION

Assurance of Quality : Validation is an extension of the concepts of quality assurance since close control of the process is necessary to assure product quality and it is not possible to control a process properly without thorough knowledge of the capabilities of that process without validated and controlled processes, it is impossible to produce quality products consistently. End product testing, in the absence of validation, gives little

assurance of quality for variety reasons, among which are.

1. Very limited sample size.

2. The limited number of tests performed on a sample. For example, it is impractical to test for all potential impurities or contaminants.

3. The limited sensitivity of the test.

Process Optimization : The optimization of a process for maximum efficiency, while maintaining quality standards, is a consequence of validation. Literal meaning of word to optimize is "To make as effective, perfect or useful as possible". The optimization of the facility, equipment, systems, and processes results in a product that meets quality requirements at the lowest cost.

Reduction of quality costs : Quality costs are divided in to four categories. They are:

a) Preventive costs.

b) Appraisal costs.

c) Internal failure costs.

d) External failure costs.

e.g. of internal failure costs: Any validated and controlled process will result in fewer internal failures like; Fewer rejects , Reworks , Re-tests & Re-inspection .

CONCLUSION

Process validation is a common term used in Pharmaceutical industry during Drug development , Manufacturing , Testing and Finish Product analysis . Process validation makes sure that validated procedure works in consistent manner and reliable to product high quality end products and medicines which are safe and efficient for patient use In the pharmaceutical Industry , Validation is a key part of Good manufacturing Practices.Comprehensive documentation should be available for the concept of help and document of the overall process of validation Pharmaceutical validation and procedure after the drug has been approved, control is important to ensure that the drug product meets pharmaceutical requirements for identification, strength, consistency, purity, stability and efficacy. Finally it can be concluded that process validation is a key element in the quality assurance of pharmaceutical product as the end product testing is not sufficient to assure the quality of finished product.

List of Abbreviations

cGMP : Current Good Manufacturing Practices

PV : Process Validation

DQ : Design Qualification

IQ : Installation Qualification

OQ : Operational Qualification

PQ : Performance Qualification.

REFERENCES

1. Singh Harshim ranjit, Industrial process validation of solid dosage forms- A review. International research journal of pharmacy 2012; 3(4): 63-70
2. Sharma Tejal, Process validation: An Essential in the Pharmaceutical Industry. International Journal of Pharmaceutical Research and Development 2011; 3(10): 133-142.
3. Gupta G D, Garg R, Aggarwal S, Guidelines on General principles of validation: solid liquid and sterile dosage forms, 2008, 28-33.
4. Chawla Nirmaljot Singh. An Overview of Process validation in tablets,International

research journal of pharmacy 2012; 3 (1): 114-116.
5. Sharma S., Khurana G., Gupta R., A review on pharmaceutical validation and its implications. Indian Journal of Pharmaceutical and Biological Research, 1(3): 100-104, (2013).
6. Current Good Manufacturing Practices (CGMP) Revision 1, Process Validation: General Principles and Practices, 2011 (Jan. 2011).
7. Murthy D. N., Chitra K., Review article on process validation as a quality assurance tool a theoretical approach.
8. Agalloco J. The validation life cycle. J ParenterSci Technol. 1993; 47(3):142-147.
9. Satyabratajena, Arjun G, Anil kumarravipati N V, SatishkumarD,Vinod K R, David banji . Industrial Process Validation of SolidDosage Forms–An Overview International Journal of Pharmaceutical Sciences reviw and rsearch. 2010, 4(2).
10. Guidelines for Process Validation of Pharmaceutical Dosage Form – Saudi Food & Drug Authority; Version 2; February, 1992.
11. Nash RA and Berry IR. Pharmaceutical Process Validation., second edition, Marcel Dekker inc., 167-188,200-202,205.
12. Good manufacturing practices for pharmaceutical products, WHO expert. Committee on specification for pharmaceutical prepration, 32andreport, WHO technical report series no.823, WHO, Geneva, 1992,14-96.
13. Patel VB, Rathwa MR, Patel K. Studies in prospective process validation ofcimetidine tablet dosage form. Int J Res Pharm Biomed Sci, 2011; 2(4): 1823-1836.
14. Kathiresan K, Moorthi C, Prathyusha Y, Gade B. R, Reddy B. K, Manavalan R, ; An overview of pharmaceutical validation; Research Journal of Pharmaceutical, Biological and Chemical Sciences; ISSN: 0975-8585; October – December 2010; RJPBCS 1(4); 1026.
15. Validation Master Plan Installation and Operational Qualification – Pharmaceutical Inspection Convention; Pharmaceutical Inspection Co-Operation Scheme; PI 006 – 2; July, 2004

HOW TO CITE: Mahima Kanojia*, Neha Sodiyal, Shivanand Patil, Process Validation in Pharmaceutical Industry, Int. J. of Pharm. Sci., 2025, Vol 3, Issue 5, 5049-5056. https://doi.org/10.5281/zenodo.15557939