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

OPEN ACCESS

Review Article

A Review on Process Validation of Pharmaceutical Tablet

Pratibha Thapliyal*, Neha Sodiyal, Shivanand Patil

Department of Pharmacy, Shree Dev Bhoomi Institute of Science & Technology, Dehradun, Uttarakhand.

ARTICLE INFO

Published: 26 May 2025
Keywords:
Introduction, Validation, its importance, Types of Validation, Process Validation, and Approaches of Process Validation
DOI:
10.5281/zenodo.15518879

ABSTRACT

This review aims to outline the effects of effective process validation in the pharmaceutical sector. Pharmaceutical tablets are the solid oral dosage form widely used for the prevention, diagnosis, and mitigation of disease. Process validation refers to the documented proof that a manufacturing process reliably yields a product that meets established specifications and quality attributes. The main objective of process validation is to guarantee that pharmaceutical products are consistently safe, effective, and of superior quality. This process focuses on enhancing the safety and quality of the dosage forms produced in the pharmaceutical industry.

INTRODUCTION

Process validation ensures that the manufacturing process consistently produces high-quality products that meet regulatory requirements and align with industry standards. It offers uniformity, weight, and dosage across batches, complies with quality benchmarks for attributes such as dissolution and hardness, and ensures regulatory adherence through documented evidence of reliability. In summary, process validation is essential for maintaining consistency, quality, and compliance in tablet manufacturing. Drug product development is a sophisticated process that involves drug discovery, laboratory testing, animal studies, clinical trials, and regulatory registration. Process controls include inspection of raw materials and packing materials, in-process controls, and targets for the final product. Process validation includes monitoring each process involved in the whole manufacturing process to produce high-quality, efficient, and safe products. Process validation is an integral part of CGMPs (Current Good Manufacturing Practices). The requirement of process validation appears as the regulatory agency's requirement to ensure that the product manufactured is consistent, safe, and reliable throughout its lifecycle.

Validation

***Corresponding Author:** Pratibha Thapliyal
Address: *Department of Pharmacy, Shree Dev Bhoomi Institute of Science & Technology, Dehradun, Uttarakhand.*
Email ✉: pratibhathapliyal01@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.

Validation is the documented act proving that any procedure, process, equipment, material, activity, or system leads to the expected result. Validation as defined in ICH Q7 - 'Establishing documented evidence which provides a high degree of assurance that a specific process will consistently produce a product meeting its predetermined specifications and quality attributes.' Validation defined in ICH Q8(R2)/Q11 - Continuous Process Verification is an alternative approach to process validation in which manufacturing process performance is continuously monitored and evaluated.

ISO definition - Validation is the confirmation by examination and the provision of objective evidence that the requirements for a specific intended use are fulfilled.

According to the Food and Drug Administration (FDA), the goal of validation is to:

Establish documented evidence that provides a high degree of assurance that a specific process will consistently produce a product meeting its predetermined specifications and quality attributes.

Importance of Validation

1. Process parameters and controls are determined during the validation of any process or system.
2. It helps to determine the worst case and risks that may arise during the manufacturing of the products.
3. It helps to investigate deviations caused during the process.
4. The risk of regulatory non-compliance is minimized after validation.
5. A validated process requires less process control and finished product testing.
6. Batch-to-batch variation is minimized due to the validation of processes, systems, and equipment.
7. Reduces the production cost of the product.
8. Increases the production of the manufacturing facility due to the minimized rework and rejection.

Types Of Validation

There are several different types of validation:

1. Process validation
2. Cleaning Validation
3. Equipment and Instrument Validation
4. Analytical Method Validation
5. Computer Software Validation

Process Validation

In pharmaceutical manufacturing, process validation refers to the documented evidence ensuring that the manufacturing process consistently produces a product that meets predetermined specifications and quality attributes. This process plays a critical role in meeting regulatory requirements set by agencies such as the FDA, EMA, and ICH (International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use).

Cleaning Validation

Cleaning validation is the documented evidence that assures that the cleaning process is effective in removing all residues of the product that was manufactured and cleaning agents that were used during the cleaning process, and preventing contamination.

Equipment and Instrument Validation

Equipment validation ensures that every piece of equipment used in the manufacturing process performs as expected, producing high-quality products.

Analytical Method Validation

According to ICH Q2 (R1), method validation can be defined as, ‘‘Establishing a documented proof, which provides a high degree of assurance that a specific process will consistently produce a desired result at its prearranged specifications and quality characteristics.”

Computer Software Validation

Computer Systems Validation (CSV) is a process used to test, validate, and formally document that a regulated computer-based system does exactly what it is designed to do consistently and accurately that is secure, reliable, and traceable in highly regulated sectors that impact public health and safety such as the pharmaceutical and medical device industries.

Process Validation

Process validation is a step-by-step procedure designed to ensure that a manufacturing process can consistently produce quality products. Generally, process validation is carried out before releasing a new product, or when applying any change to an existing product, and for periodically verifying the process.

History of Process Validation

This concept was first introduced in the mid-1970s for improving the quality of pharmaceuticals by two Food and Drug Administration (FDA) officers, Ted Byers and Bud Loftus [1] In 1987, the FDA released the first process validation guidance.[4] The fundamental approach was testing the process to ensure it worked, along with periodic retesting of the manufacturing process to ensure it was continuing to work. In the mid-2000s, regulatory agencies developed ICH Q8 – Pharmaceutical Development to provide foundational concepts required for companies to develop high-quality manufacturing processes. The final 2009 guidance provided several definitions intended to provide the basis for very important concepts for building processes [5]

The most important PV concepts begin with the following terms defined in ICH Q8 (R2):

- Critical Process Parameter (CPP)
- Critical Quality Attribute (CQA)
- Design Space (DS)
- Control Strategy (CS)
- Quality by Design (QbD)
- Real-Time Release Testing (RTRT)

In addition, acknowledging that developing and manufacturing pharmaceuticals was primarily a risk management and control exercise, regulatory agencies in 2006 developed and issued ICH Q9 – Quality Risk Management [6]

Types of Process Validation

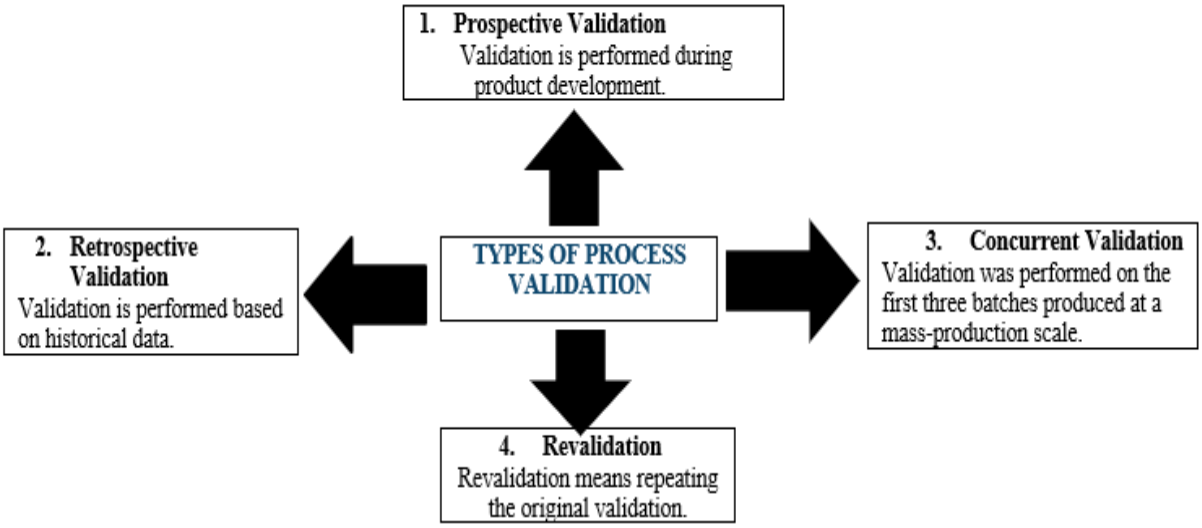

Figure 1: Types of Process Validation

Prospective process validation- also known as pre-market validation. Prospective process validation is executed after the completion of the R&D trial to produce the product for commercial purposes. This type of validation is generally connected with the introduction of new drug products into the market and involves studies of all their manufacturing processes.

Retrospective process validation- The Retrospective process validation establishes documented evidence that a system does what it is supposed to do based on a review and analysis of historical information. It is normally conducted on a product already being commercially distributed and is based on accumulated production, testing, and control data.

Concurrent process validation- Concurrent validation is a type of validation that occurs during the routine production of the product. It involves collecting and analyzing data from each batch or lot to verify that the process or system is operating within the specified limits and producing consistent results. Concurrent validation can also be used as an alternative to prospective validation in some cases, such as when there is a lack of historical data, when the product has a short shelf life, or when the product is urgently needed.

Revalidation process validation- Revalidation means repeating the original validation. Revalidation is performed if there is any sort of change in the batch size, or formulation or when the consecutive batches of the manufacturing unit don't meet specifications as stated in its product, when changes are made in the site location, equipment size, and capacity or new advance equipment are introduced for further processing or when new manufacturing methods and control are to be followed or changes are made in them.

Approaches in Process Validation

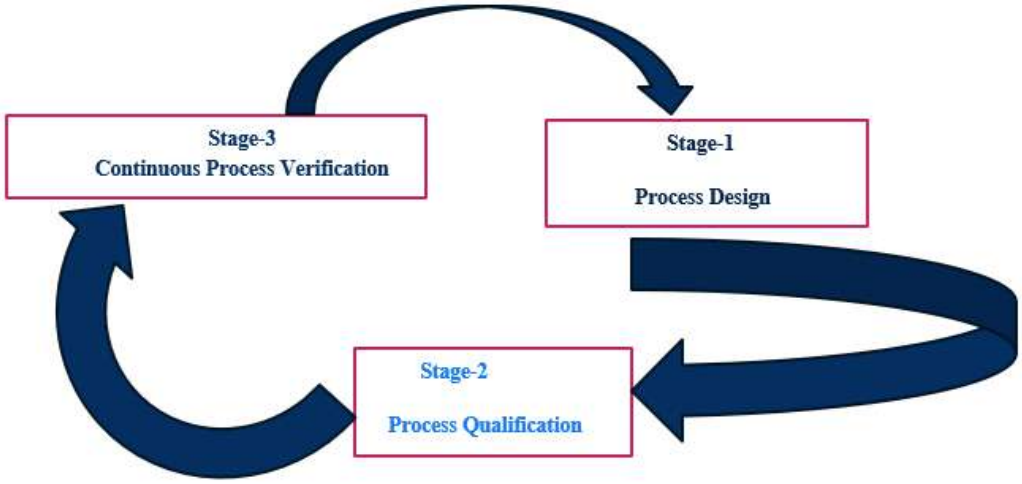

Figure 2: Approaches of Process Validation

Stage-1 Process Design:

The commercial manufacturing process is defined during this stage based on knowledge gained through development and scale-up activities.[7] This stage also involves process control and planning strategies to reduce input variation and/or adjust for it during manufacturing. The following are sources and methods to capture process information:

- Product development activities
- Functionality and limitations of production equipment
- Predicted contributions to variability
- Design of experiment (DOE) studies
- Risk analysis tools
- Experiments or demonstrations at laboratory or pilot scale
- Computer-based or virtual simulations

Stage-2 Process Performance:

During this stage, the process design is evaluated to determine if the process is capable of reproducible commercial manufacturing.[7] This stage has two elements:

a) Design of the facility and qualification of the equipment and utilities

b) Process Performance Qualification (PPQ)

a) Design of the facility and qualification of the equipment and utilities

Proper design of a manufacturing facility is required under part 211, subpart C, of the CGMP regulations on Buildings and Facilities. Activities performed to ensure proper facility design and commissioning must precede PPQ. Qualification of utilities and equipment generally includes the following activities:

- Selecting utilities and equipment construction materials, operating principles, and performance characteristics based on whether they are appropriate for their specific uses.

- Verifying that utility systems and equipment are built and installed in compliance with the design specifications (e.g., built as designed with proper materials, capacity, and functions, and properly connected and calibrated).

- Verifying that utility systems and equipment operate according to the process requirements

in all anticipated operating ranges. This should include challenging the equipment or system functions while underloading comparable to that expected during routine production.

b) Process Performance Qualification (PPQ) combines the actual facility, utilities, equipment (each now qualified), and trained personnel with the commercial manufacturing process, control procedures, and components to produce commercial batches. A successful PPQ will confirm the process design and demonstrate that the commercial manufacturing process performs as expected. Process performance qualifications should be executed through a protocol and documented in a report:

- The manufacturing conditions include operating parameters, processing limits, and component (raw material) inputs.
- The data to be collected and when, and how it will be evaluated.
- Tests to be performed (in-process, release, characterization) and acceptance criteria for each significant processing step.
- The sampling plan includes sampling points, the number of samples, and the frequency of sampling for each unit operation and attribute.
- Criteria and process performance indicators that allow for a science- and risk-based decision about the ability of the process to consistently produce quality products. The criteria should include:

— A description of the statistical methods to be used in analyzing all collected data (e.g., statistical metrics defining both intra-batch and inter-batch variability).

— Provision for addressing deviations from expected conditions and handling of nonconforming data. Data should not be excluded from further consideration in terms of PPQ without a documented, science-based justification.

- Design of facilities and the qualification of utilities and equipment, personnel training and qualification, and verification of material sources (components and container/closures), if not previously accomplished.

- Status of the validation of analytical methods used in measuring the process, in-process materials, and the product.

- Review and approval of the protocol by the appropriate departments and the quality unit.

Stage-3 Continuous Process Verification:

Ongoing assurance is gained during routine production that the process remains in a state of control. The goal of the third validation stage is to continually ensure that the process remains in a state of control (the validated state) during commercial manufacture should include:

- Adherence to the CGMP requirements, specifically, the collection and evaluation of information and data about the performance of the process, will allow the detection of undesired process variability. The data collected should include relevant process trends and the quality of incoming materials or components, in-process materials, and finished products. The data should be statistically trended and reviewed by trained personnel. The information collected should verify that the quality attributes are being appropriately controlled throughout the process.
- Variation can also be detected by the timely assessment of defect complaints, out-of-specification findings, process deviation reports, process yield variations, batch records,

incoming raw material records, and adverse event reports.

- Process variability should be periodically assessed, and monitoring adjusted accordingly.
- Procedures should describe how trending and calculations are to be performed and should guard against overreaction to individual events as well as against failure to detect unintended process variability.
- Good process design and development should anticipate significant sources of variability and establish appropriate detection, control, and/or mitigation strategies, as well as appropriate alert and action limits.
- Many tools and techniques, some statistical and others more qualitative, can be used to detect variation, characterize it, and determine the root cause, such as using quantitative and statistical methods whenever appropriate and feasible.
- Continuous monitoring and sampling, process parameters and quality attributes at the level established during the process qualification stage until sufficient data are available to generate significant variability estimates.
- Production line operators and quality unit staff should be encouraged to provide feedback on process performance**.** Data gathered during this stage might suggest ways to improve and/or optimize the process by altering some aspects of the process or product, such as the operating conditions (ranges and set points), process controls, components, or in-process material characteristics.
- The equipment and facility qualification data should be assessed periodically to determine whether re-qualification should be performed and the extent of that re-qualification. Maintenance and calibration frequency should be adjusted based on feedback from these activities.

Elements of Effective Validation

- **Awareness-** The most important element required for effective validation is a better understanding of what validation is all about.

- **Communication skills.** Good communication skills are essential for conducting effective validation, as it involves multiple departments. Anyone involved in the initiation of the validation process will be able to convey the same to the respective departments.

- **Data Collection**- A thorough data collection strategy would have been required for successful validation. This project uses mainly secondary data collection methods as a way of acquiring data in the form of already existing literature from reliable sources like peer-reviewed journals, government documents, business periodicals, and appropriate databases containing real-time information.

- **Blueprint -** A structured approach and strategy must be implemented for successful validation.

Validation Master Plan - A validation program must clearly outline essential elements in a validation master plan (VMP) or similar documents. The VMP specifies the scope and objectives of the validation. It comprises the following components:

a) The VMP should be a summary document, which is brief, concise, and clear.

b) The VMP should contain data on at least the following:

- Validation policy.
- Organizational structure of validation activities.
- Summary of facilities, systems, equipment, and processes to be validated.

- Documentation format: The format to be used for protocols and reports.
- Planning and scheduling.
- Change control.
- Reference to an existing document.
- In the case of large projects, it may be necessary to create separate validation master plans.

- **Experience-** Well-experienced and trained validation team is required to execute the validation process.

- **Standard Operating Procedures (SOPs)-** SOPs include information on how to execute the validation process; hence, they are to be followed by all the respective departments before execution.

- **Resources-** It involves extensive expenditure on time, manpower, and money.

- **Lab support-** A well-facilitated Quality Control lab is required to get results at the expected time.

- **Good Documentation Practices (GDP)-** GDP is to be followed as per ALCOA (Attributable, Legible, Contemporaneous, Original, and Accurate) for an effective process.

- **Change Control-** Validation is to be initiated with proper change control and completed within the timeline.

CONCLUSION

Validation is a dependable approach to ensure the creation of a safe, high-quality product. The study mentioned above indicates that Pharmaceutical Process Validation is a crucial regulatory requirement for agencies to achieve a high-quality, efficient, and safe product. Process validation involves a series of activities that occur throughout the lifecycle of the product and process.

REFERENCES

1. Salade Darshan A., Arote Kishor S., Patil P. H, Patil Vikas V., Pawar Amol R., A Brief Review on Pharmaceutical Validation, Asian Journal of Pharmaceutical Analysis; 12 (3); 211-17.
2. M. R. Patel, M. Patel, and K. P. Patel. "Pharmaceutical Process Validation: A Review." International Journal of Pharmaceutical Sciences Review and Research, 2012; 17 (1), 23-28.
3. FDA (CBER/CDRH) Guidance for Industry: Process Validation: General Principles and Practices. May 1987.
4. FDA (CBER/CDER) Guidance for Industry, Q8(R2): Pharmaceutical Development, Nov. 2009, ICH. Rev. 2.
5. FDA (CDER/CBER) – Guidance for industry: Q9 quality risk management. June 2006. ICH.
6. FDA (CDER/CBER) – Guidance for Industry: Process Validation: General Principles and Practices. January 2011. Rev. 1.
7. Witcher, M., A Functional History of Process Validation, Part-1, Week Foundation, Pharmaceutical Online, August 7, 2020, pp. 1.
8. Kakad SB, Kolhe MH, Dukre TP. A review on pharmaceutical validation. International Journal of Pharmaceutical Quality Assurance, 2020; 25, 11(3): 338-42.
9. Dr. Ahir B., Singh Khushboo D., Yadav Sushma P., Patel Hetal S., Poyahari Chetan B., Overview of Validation and Basic Concepts of Process Validation, Scholars Academic Journal of Pharmacy (SAJP) Sch. Acad. J. Pharm., 2014; 3(2): 178-190.
10. Kaur H, Singh G, Seth N. Pharmaceutical process validation: a review. Journal of Drug Delivery and Therapeutics, 2013; 14, 3(4): 189-94.

11. Patanjali Rishi R., Shrestha Saroj, Lamichane S., Pokrel Priyanka: a Review on Pharmaceutical Process Validation of solid dosage forms (Tablets). Journal of Drug Delivery and Therapeutics, 2015; 5 (6): 1-7.
12. Jain Kiranbala, Agarwal Princy, and Bharkatiya Meenakshi, A Review on Pharmaceutical Validation and its Implications, International Journal of Pharmacy and Biological Sciences, 2018;2, pp.117-24.
13. ICH Q7 Chapter 12 & 19.6: Process Validation, Parenteral Drug Association, September 2014, pp. 8-9.

HOW TO CITE: Pratibha Thapliyal*, Neha Sodiyal, Shivanand Patil, A Review on Process Validation of Pharmaceutical Tablet, Int. J. of Pharm. Sci., 2025, Vol 3, Issue 5, 4393-4401. https://doi.org/10.5281/zenodo.15518879