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Basic Concept and Review on Process Validation

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Abstract: Process-validation(pv) is a critical component in ensuring the quality, safety, and efficacy of products in industries such as pharmaceuticals, biotechnology, and food manufacturing. This review provides an overview of the principles and basic concepts involved in process validation. The main emphasis is on comprehending the function of validation in quality assurance and regulatory compliance, as well as the techniques used to show that a process reliably yields a product that satisfies predetermined standards. In addition to highlighting important regulatory criteria like those from the FDA and ICH, the review looks at the three steps of process validation: process design, process certification, and continuing process verification. It also explores the evolving trends in process validation, including the shift towards continuous and real-time validation methods, and the application of risk-based approaches to enhance the efficiency and reliability of the validation process. This review emphasizes the importance of risk management, data integrity, and robust documentation to provide a comprehensive understanding of process validation and its significance in maintaining product quality and regulatory compliance.

Keywords: *Validation, Process Validation, ICH, FDA.*

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I. INTRODUCTION

Validation is the process that gathering proof through documentation that is a method, procedure or undertaking used in production and testing keeps the required degree of compliance throughout [1]. By the FDA ensuring the quality of a product is achieved by paying meticulous and comprehensive attention to several crucial criteria, such as choosing the right quality method. Via testing of the final product and the process. Providing documentation to show that a method activity or process used in production and testing consistently maintains the appropriate degree of compliance. The idea of validation began to take shape in the United States in 1978[2]. Over time, the nation of validation has broadened to encompass an extensive array of endeavors from analytical techniques employed in the quality assurance of medicinal components and final product to be digitized process control system, labeling or clinical trials Although validation is based on, it is not mandated by legal specifications and is best understood as a crucial and essential component of cGMP. Process validation is the very much important parameter of cGMP. The quality system directed validation to become evident [3]. A quality system's goal is to consistently produce things that are appropriate for the uses for which they are intended. In order to guarantee that these rules and goals are met, process validation is crucial [3]. The required validation documents included in the marking submittal file authorization are uniform, and this serves as the verifying process. The guidelines on the general principles of process validation identified four different forms of validation:

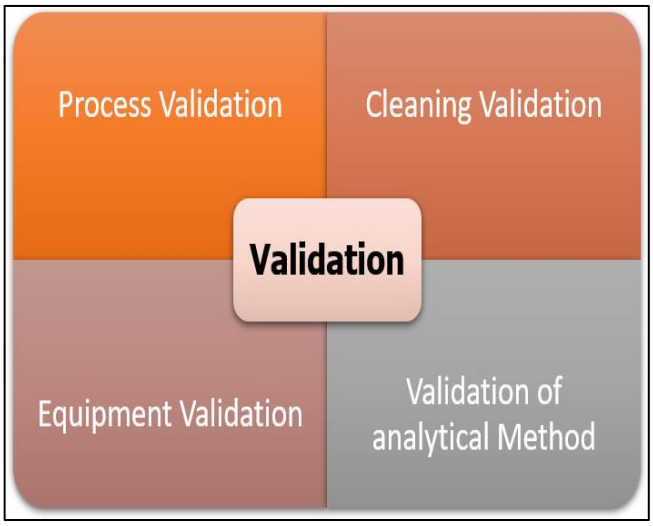

Fig 1 Different Forms of Validation

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➢ *Process Validation [4]: –*

USFDA Specifies the process of gathering and analyzing data from the process design phase to the production stage, which is known as process validation. It provides scientific proof that a process can reliably produce high-quality goods.

➢ *Types of Process Validation: -*

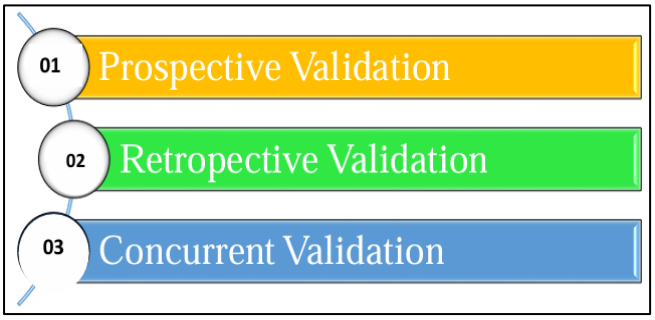

Fig 2 Types of Process Validation

➢ *Prospective Validation: -*

An important technique that shows that a manufacturing process can reliably produce a product that satisfies the specified product specification when run under specified standard conditions is validation.

➢ *Retrospective Validation [5]: -*

Under the presumption that composition, procedure, and equipment remain identical, retrospective validation entails reviewing previous production experience. The outcomes of in-process and final control tests are then assessed.

- Production failures and recorded difficulties are analyzed to find the process parameters' limit.

➢ *Concurrent Validation: -*

- Validation that is done in parallel with regular production is known as concurrent validation.
- Because the method is well understood, it is more acceptable to validate it during ordinary production.
- Vigorous testing and observation guarantee the product's required quality attributes with a high level of assurance.

➢ *Re-Validation [6]: -*

- It is required to make sure those modifications to the process its surroundings won't have a negative impact on the process's features or the quality of the final result.
- Two categories can be applied to revalidation: - Revalidation following any modifications that affect the caliber of the product.
- Periodic revalidation that happens on a prearranged timetable.

➢ *Analytical Validation [7]: –*

- The collection and evaluation of data from the process or methodology used in the production of a product, whether for commercial, experimental, or scientific reasons, is known as analytical validation.
- In the food, biotechnology, and pharmaceutical sectors, analytical method validation is an essential process to ensure the quality and safety of products.
- The aim of validation is to confirm that an analytical method is appropriate for its intended usage. Both the process and the intended use must be specified. This suggests that method validation cannot start until the method is fully developed and optimized.
- The validation process should be followed when doing the validation. All attributes should have procedures and acceptability criteria included in the protocol. The validation report has to provide a record of the outcomes.

➢ *Cleaning Validation –*

The term "cleaning validation" describes documented evidence that a system or piece of equipment can be routinely cleaned to predetermined and approved standards.

Table 1 Parameter of Cleaning Validation

Parameter	Definition
Accuracy	An assessment of the different between the measured value and the real value.
Precision	A measure of the agreement for multiple measurements on the same sample.
Specificity	The ability to assess the analyte when in the presence of other components.
Limits of detection and quantitation	The lowest amounts of analyte that can be detected/determined accurately, respectively.
Linearity and range	The proportionality of the measurement to the concentration of the analyte within a specified range.

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➢ *Equipment Validation [8] –*

As per the FDA May 1987, equipment qualification is the process of demonstrating that any piece of equipment functions as intended and produces the desired outcomes.

It is a multi-phase process that is not accomplished in a single step.

II. A HISTORIC OVERVIEW

A brief overview of the history developed by the regulatory outlook of process validation in the United State. The United States chosen as mention before the FDA is main regulatory activity of the pharmaceutical industry. After, The United States of American pharmaceutical marketed the drug product or the active pharmaceutical ingredients (APIs) is the biggest in the world.

To raise the caliber of medications, Ted Byers, and Bud Loftus, two Food and Drug Administration (FDA) officials, initially introduced the idea of validation in the United States in 1979. It was put up in direct reaction to several issues with the parenteral market's high-volume sterility. The U.S. Food and Drug Administration was the first to promote the idea of process validation; yet, before September 29, 1978, the term was not defined in any certain U.S.F.D.A. material does not contain any cGMP regulations discussed the topic of process validation [10].

The engineering procedures employed in the delivery of big equipment parts that would be produced, tested, delivered, and accepted in accordance with a contract where the idea of validation for equipment and processes originally originated.

➢ *Definitions –*

- *US FDA Definition: –*

✓ Validation (1991): "Act of proving by GMPs that Any....." procedure genuinely produces the desired outcomes.
✓ 2000: The official method of proving that a piece of machinery, a system, a material, an activity, or a procedure yields the intended result.

Establishing recorded proof that offers a high level of assurance that a given process will reliably yield a product is known as "process validation" fulfilling the predetermined requirements and standards of quality traits.

- *ICH Definition: –*

The process of verifying and supplying written proof that processes operating within their designated design parameters are able to consistently and dependably generating a final product of the necessary caliber.

- *WHO Definition: –*

The formal process of demonstrating that a system, equipment, process, material, activity, or procedure genuinely produces the desired outcome.

➢ *Need of Process Validation [11, 12] –*

Validation testing is a tool that development teams can use to ensure that the work satisfies the expectations of stakeholders. It also offers them one last opportunity to correct any errors or discrepancies in between the specification and the application. The program is more dependable and has a lower crash rate because a flaw wasn't found before a production release.

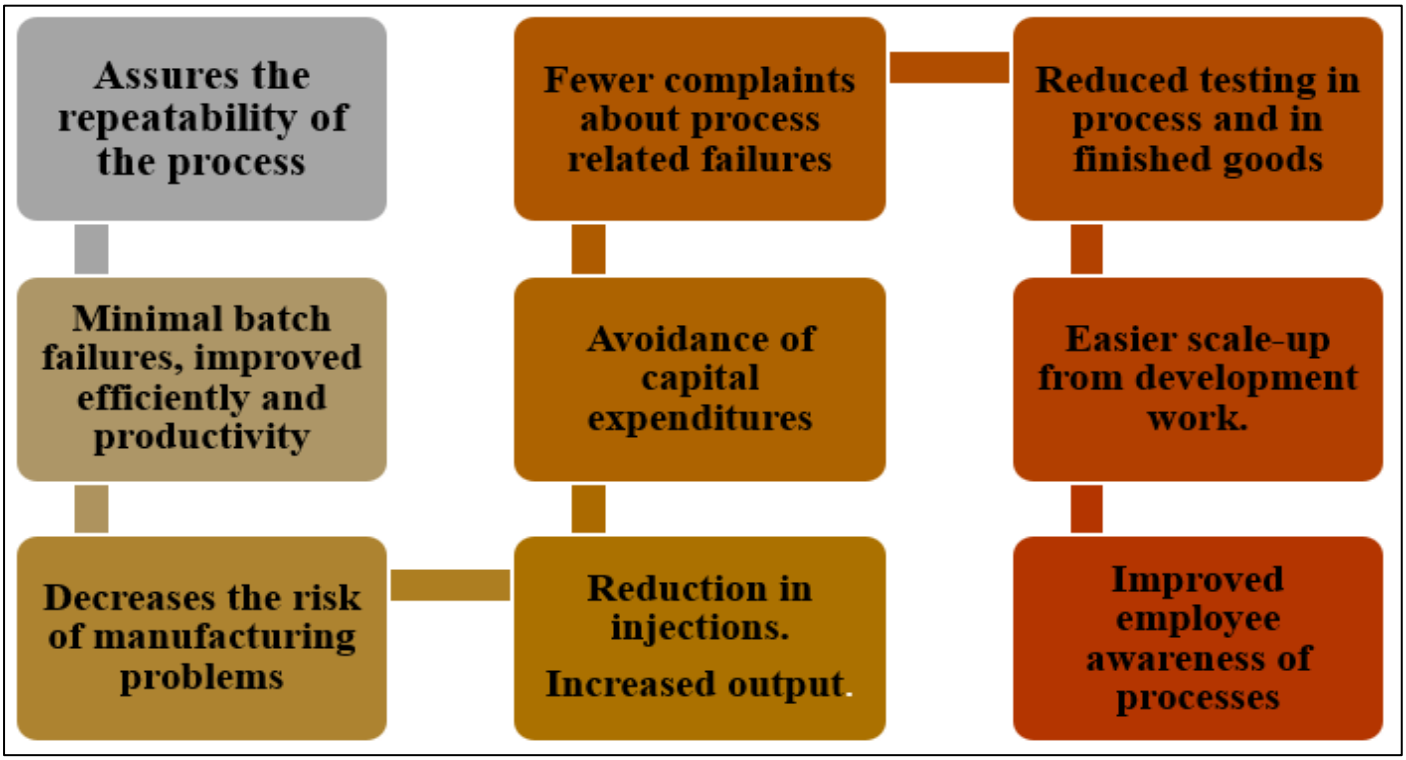

Fig 3 Needs of Process Validation

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In order to comply with legal requirements and guarantee that goods are efficient, safe, and live up to customer expectations, process validation is crucial. The FDA principle of quality Assurance highlights that rather than depending exclusively on testing and inspection, quality, safety, and efficacy should be incorporated into the product. this idea emphasizes how crucial it is to oversee every stage of the production process in order to guarantee that the finished product satisfies all design specification and quality standards.

III. VALIDATION AND RESPONSIBILITY OF DIFFERENT OFFICERS

Table 2 Different Departments and their Role/ Responsibility

Department	Designation	Responsibility
Research and development (R & D)	Executive/ Officer	To coordinate the entire validation process by scheduling and discussions with production, quality control and quality assurance. Preparation of preliminary validation protocol, master formula record, monitoring the process, compiling and analysing data and test results and preparing the final report. To review the preliminary validation documents.
Quality assurance	Officer	To coordinate the entire validation process by scheduling meetings and discussions with the team. Preparation of validation protocol, compiling and analysing data and test results and preparing the final report. To review of validation documents.
Production	Officer	To participate in performing the validation steps during manufacturing process. To assist in collection of data.
Quality control	officer	To test and report the test result.
Quality assurance	General manager Quality assurance	To approve the process validation protocol and report. To review of validation documents. To approve the process.

➢ *The 3 Stages of Process Validation: -*

Good manufacturing practices are necessary for the production of pharmaceutical goods that are both safe and high-quality. Ensuring pharmaceutical goods consistently fulfill quality requirements and expectations are the aim regarding process verification. The gathering and assessment of data that proves, by scientific evidence, that a person can reliably produce high-quality goods, based on the process architecture phase through industry wide manufacturing.

- *Process Validation*

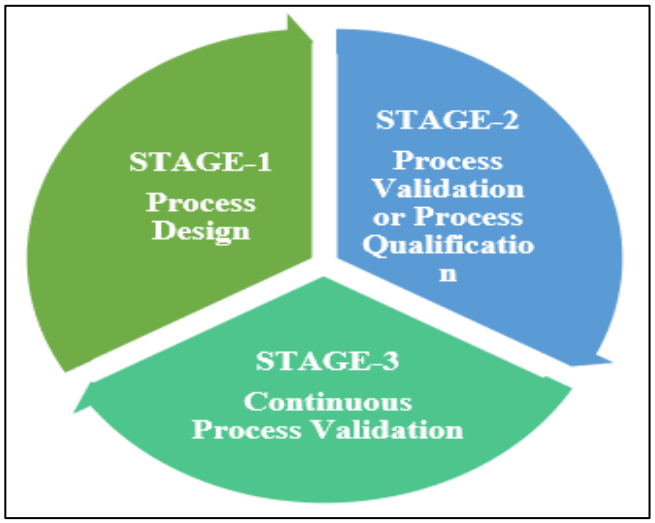

Fig 4 Different Stages of Process Validation

- *Stage 1: - Process Design*

✓ The main objective of process design is to determine the optimal method for a product's commercial manufacturing.
Although cGMP requirements are not necessary for early process design studies, they should nonetheless be conducted in line with sound scientific standards.
✓ Adherence to proper documentation practices is crucial. It is intended that studies leading to an improvement in process understanding would be documented in particular.
✓ The FDA typically does not anticipate continuous testing and retesting at this point unit process fails.

- *Stage 2: - Process Qualification [14]*

✓ Determining whether the process design is successful in commercialization is the primary objective of process qualification.
✓ cGMP regulations demand that the manufacturing facility be designing appropriately selection of equipment and utility systems that are constructed in compliance with the necessary design criteria.
✓ Process performance qualification brought together equipment, facilities and utilities with staff who had received the necessary training. When feasible the FDA strongly advises using objective measurements such statistical metrics.

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- *Stage 3: - Process Verification [15]*

✓ Maintaining the process in a verified state during verification of processes is primarily done for commercial manufacturing.
✓ cGMP protocols and guidelines must be adhered to in order to identify areas of variability that need to be looked into and corrected.
✓ The FDA recommends continuing observation and sampling at the level selected unit adequate data during the process qualification phase are obtained.
✓ Maintaining the building, services, and equipment is crucial.

IV. CONCLUSION

In conclusion, the validation process plays a critical role in ensuring the accuracy, reliability, and effectiveness of a system, product, or model. By systematically testing and verifying components against predefined criteria, we can identify any issues early, refine processes, and ensure that outcomes align with user expectations or regulatory standards. The process not only fosters confidence in the results but also ensures that the final output meets quality standards, reducing the risk of failure or defects in real-world applications. Through continuous feedback and refinement during validation, we enhance overall performance, user satisfaction, and trust in the system.

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