



Pharmaceutical Process Validation: A Review

¹Satyajit Samapatrao Patil, ²Dr. K.A. Wadkar.

^{1,2}Appasaheb Birnale Collage of Pharamcy, Sangli

ABSTRACT:

validation is most important step for achieving and maintaining the quality of final product. Identification, Measuring, evaluation and documentation of critical steps in manufacturing process done by the process validation that ensures quality of process. Process validation provides high degree of affirmation and evidence that process being carried out that gives Uniform result and that result meet required specification and quality characteristics. Various steps are Validated in the process of manufacturing of Pharmaceutical product is known as process validation. Validation does improvement in procedure and proper development of process for mitigation of risk factors. validation is fundamental piece of quality Assurance.

Keywords: process validation, prospective validation, documentation, consistent

INTRODUCTION:

The main objective of by pharmaceutical plant is manufacturing product with requisite attribute & quality a consistency at minimum cost. The concept of validation proposed by FDA officials, Ted byers & Bud loftus, for improving the quality of pharmaceutical product in 1970. quality of product derived from careful attention to the product.

The FDA, in "Guidelines on general principles of process validation defines process validation as, "establishing documented evidence which provide high degree of assurance that specific process will consistently produce a product meeting its predetermined specifications and quality characteristics. Process validation ensures the process within their specific criteria, therefore product will meet its predetermined specifications and quality attributes with constant result".

Validation base on the FDA regulations that describes current good manufacturing processes for finished products are covered in 21 CFR part 210 and 211. The cGMP regulation prescribe that designed and controlled processes ensure that inprocess material and finished product should meet predetermined quality requirement.

Process validation:

process validation is the action of proving effectiveness.

According to E MEA, " Process validation can be defined as documented evidence that process operated within established parameters, can perform effectively and reproducibility to produce product meeting its predetermined quality attributes. Process validation widely used by pharmaceutical, biotechnological medical device & herbal industries.

In manufacturing process validation, evaluation and monitoring of process performance takes place. process validation is ongoing Process that must be frequently adapted as manufacturing Feedback is gathered for determination of product quality. End-to-end validation of production process is essential because quality cannot always determined by finished product inspection.

WHO guidelines has stated validation as documented act which proves that any material, component system, machine or activity will essentially direct to estimation of result. Validation verify that process has been improved and confirms procedure have been developed, established within expected control. Validated status of process must be preserved, measures must be taken that will allow significant process changes to be addressed promptly. This change control can apply to SOP's, equipment, manufacturing processes, environmental conditions that has affect on its state of control and then state of validation.

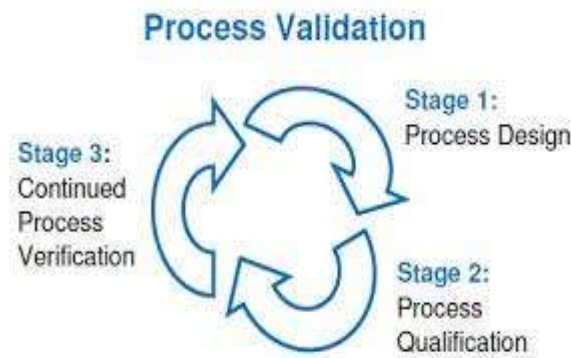
Why validation required?

- The pharmaceutical industry utilize expensive materials, worldly facilities and equipment and highly qualified personnel.

The usage of equipment would not be practical without knowing whether, it will produce favorable product or not.

- To achieve success of industry, the efficient use of sources is recommended.
- The cost of product failure, rejects reworks and recalls complaints are significant part of total production cost.
- For reduction in failure and productivity improvement detailed study and control of manufacturing process validation is necessary
- The pharmaceutical industry are concerned about validation because of following reasons
 - Affirmation of quality
 - Reduction in cost
 - Government regulation

Phases of validation



Process validation classified into three phases

- Process design
- Process qualification
- Continued process validation

1. Phase I.

- Product research and development, scale-up studies, Formulation pilot batch studies, establishing Stability condition & storage and handling of In-process & finished dosage forms relating all activities covered by pre-validation Qualification phase
- Equipment qualification, Installation qualification master formula Record, operational qualification in this pre validation step.

2. Phase II

- This step verify that, all established limits OF critical process parameters are valid & that Satisfactory product can be produced under critical condition
- This phase is process validation phase(process qualification phase)

1. Phase III

- Validation maintainace phase review all processes related documents , including audit reports to affirm that there have been no deviation or modification to production process.
- At this phase, validation team also assures that there have been no change that should have resulted in revalidation.

Validation documentation

1. Validation protocol -

- validation protocol is the written plan that States how validation will be conducted

- This validation protocol includes test parameter product characteristics, production & packaging equipment on what constitutes acceptable test results
- This protocol consist list of selected processes and control parameters, state the number of batches to be included in the study
- This provide synopsis of what hoped to be completed.

Validation protocol should contain as minimum the following information:

- Title
- Objective and scope
- Responsibility
- Product composition
- Process flow chart
- Protocol approval
- Review of packing material and material and raw material
- HSE requirement
- Sampling location
- Review of equipment
- Documentation
- Acceptance criteria

2. THE VALIDATION REPORT

A written report should be available of the validation after completion

If it is acceptable it must be authorized with sign and date. The report should include the following:

- Title and objective of study
- Details of material
- Equipment
- Programmes used
- Details of procedures and test methods performed
- Results (compared with specifications)
- Reference to protocol

3. validation master plan

A validation master plan includes entire philosophy and approaches that are going to be used in the manufacturing of the company

Validation master plan is written approved plan of objectives and action stated that how and when the manufacturing industry will achieve compliance with cGMP requirement

Types of process validation

1. Prospective process validation

- This validation is generally undertaken whenever a new formula developed
- Prospective validation includes those considerations that should be made before an entirely new product introduced and when there is change in manufacturing process which affect product quality.
- Prospective process validation where an experimental plan called validation protocol is executed before the process is put into commercial use

- Prospective validation require efforts in order to generate validation support data
- The key elements of prospective validation as equipment and process, equipment installation qualification, process performance qualification, product performance qualification to assure timely revalidation and documentation

2. Concurrent process validation

- Concurrent validation is used to ensure that establishing documented evidence that process do what they purport to do, based on the information generated during process
- the concurrent validation process is similar to that of prospective validation. The process starts with the development of a Validation Plan, followed by the DQ, Risk Assessment (RA), IQ, OQ and PQ phases after which process, computer, analytical and cleaning validations are performed, ending with a final report.
- And then, routine preventative maintenance, requalification and periodic review are performed.
- concurrent validation performed on batches for marketing prior to approval of batches of complete validation based on individual batch record

3. Retrospective process validation

- In this type validation of legacy product takes place
- Retrospective validation establishes documented evidence that a system does what it is purport to do based on a review and analysis of historic information
- It is conducted on already distributed product and is based on the accumulation of the product , testing and control data
- the approach needs to be evaluated and completed in a timely manner with significant data to support the process
- this type of validation in only acceptable for well established product or processes because the process control can takes place by historical data provide the necessary documentary evidence that the process is doing what it is believed to do

4. Revalidation process validation

- Revalidation helps to maintain the validated status of the equipment, plant, manufacturing process as well as the computer systems. This procedure is necessary for periodic checking of the validation results according to the revalidation period.

Possible reasons for starting the revalidation process include:

- The transfer of a product from one plant to another.
- The necessity of periodic checking of the validation results.
- Significant (usually order of magnitude) increase or decrease in batch size.
- Changes to the product, the plant, the manufacturing process, the cleaning process, or other changes that could affect product quality.
- Sequential batches that fail to meet product and process specifications.

Conclusion:

From the study it is concluded that pharmaceutical process validation is necessary and effective recognized parameter of cGMP. Process validation ensures that drug product will meet standards for quality,safety , efficacy,identity , strength,effectiveness. It is quality control tool for pharmaceutical industries Process validation and process control give a certain assurance of batch uniformity and integrity of the product manufactured. After the approval of drug, the pharmaceutical process validation affirms that each an every pre-determined standard will be acquired leading to precision of results. Not following the validation protocols cleaves our goal and entire process leads to defective product production and processing.

Reference

1. B.T. Lotus and R.A. Nash pharmaceutical process validation drugs and pharma science series vol.129
2. Guidance for Industry: Process Validation: General Principles and Practices. U.S. Department of Health and Human Services, Food and Drug Administration, Centre for Drug Evaluation and Research (CDER), Centre for Biologics Evaluation and Research (CBER), Centre for Veterinary Medicine (CVM), January 2011.

3. Quality Management System – Process Validation Guidance GHTF/SG3/N99-10:2004 (Edition 2).
4. Mohammed-Ziegler and I Medgyesi. Increased importance of the documented development stage in process validation. Saudi Pharmaceutical Journal. 20; 2012: 283-285.
5. Nandhakumar *et al.* An Overview of Pharmaceutical Validation: Quality Assurance View Point. International Journal of Research in Pharmacy and Chemistry. 1(4); 2011: 1003-1014
6. Validation Master Plan Installation and Operational Qualification –Pharmaceutical Inspection Convention; Pharmaceutical Inspection Co-Operation Scheme; PI 006 – 2; July,2004
7. Guidelines for Process Validation of Pharmaceutical Dosage Form – Saudi Food & Drug Authority; Version 2; February, 1992.
8. Validation of Compendia Methods. United States Pharmacopoeia and National Formulary XVIII, Rockville, MD: The United States Pharmacopoeia Convention, Inc., 1995, pp. 1612-710
9. Validation of Analysis Procedures. International Conference on Harmonization (ICH) of Technical
10. 8. Health Canada / Health Products and Food Branch Inspectorate Validation Guidelines for Pharmaceutical Dosage Forms (GUI – 0029) / December, 2009
11. Good Manufacturing Practices for Pharmaceutical Products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. 32nd Report, WHO Technical Report Series no. 823. Geneva: WHO, 1992: pp 14-96.
12. M.J. Green, Anal. Chem' Analytical Methods Validation', 1996,68;305
13. Nandhakumar L., Dharmamoorthy G., Rameshkumar S and Chandrasekaran S. "An Overview of Pharmaceutical Validation: Quality Assurance View Point" International journal of research in pharmacy and chemistry .2011,1(4);12.
14. U.S. Food and Drug Administration. *Guidelines on General Principles of Process Validation*. 1987
15. Sanjay Bajaj, Dinesh Singla and Neha Sakhuja' Stability Testing of Pharmaceutical Products' Journal of Applied Pharmaceutical Science 02 (03); 2012: 129-138.
16. Sharma Ajay , Sharma Rohit "Validation of analytical procedure :a comparison of ICH Vs pharmacopoeia" irjp.2012,3(6);39-42.