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

PROCESS VALIDATION OF TABLET: A REVIEW

Deerghayu Pant [1], Kashif Hussain [2], Praveen Kumar Ashok [3]

Gyani Inder Singh Institute of Professional Studies, Dehradun, Uttarakhand

ABSTRACT

The article provides an introduction and broad overview of the pharmaceutical tablet manufacturing process validation. Process validation is a crucial step in achieving and maintaining final product quality. The validation study determines the accuracy, sensitivity, specificity, and reproducibility of the manufacturer's established and published test techniques. As a result, validation is a crucial component of quality assurance. This review looks at the importance of pharmaceutical validation, as well as the many methodologies, processes, and steps that must be monitored during the tablet production process.

INTRODUCTION

The validation study determines the accuracy, sensitivity, specificity, and reproducibility of the manufacturer's established and published test techniques. As a result, validation is a crucial component of quality assurance. This review looks at the importance of pharmaceutical validation, as well as the many methodologies, processes, and steps that must be monitored during the tablet production process. The process validation is the standardisation of the validation documents that must be presented with the marketing permission submission file.The process validation is meant to help producers understand the quality management system (QMS) criteria for process validation, and it is applicable to any manufacturing process.

Fig. 1: TABLETS

SOME DEFINATIONS OF VALIDATION:

According to the FDA, assurance of product quality is generated from rigorous and systematic attention to a variety of critical criteria, such as quality process selection via in-process and end-product testing.

According to the US Food and Drug Administration in 1978, "a validation manufacturing process is one that has been proven to do what it purpose or is represented to do." The validation proof is obtained through data collection and evaluation, preferably beginning with the process development phase and continuing through the production phase. Validation must involve process qualification (the qualifying of materials, equipment, systems, buildings, and staff), but it also includes overall process control for repeated batches or runs."

Validation - "Act of verifying, in compliance with GMPs, that Any" procedure genuinely leads to desired results," **European Commission, 1991.**

Validation - "Documented evidence that the process, when operated within established parameters, can perform effectively and reproducibly to produce a medicinal product meeting its predetermined specifications and quality attributes," according to the European Commission in 2000.

According to WHO criteria, validation is defined as Validation is the documented act of demonstrating that a procedure, process, equipment, material, activity, or system produces the intended results. Validation is the act of demonstrating, in compliance with GMPs, that any process produces the intended results. Documented evidence that the procedure, when run within set parameters, can create a medical product that meets its predetermined standards and quality qualities in an effective and reproducible manner.

2.TYPES OF VALIDATION:

2.1 Analytical Validation: Analytical validation is the testing of product quality attributes to demonstrate that reliability is maintained throughout the product life cycle and that precision, accuracy, specificity, LOD, linearity, selectivity, strength, purity, and specification are not compromised. The analytical method specifies the specific processes required to conduct an analysis. This can include things like preparing samples, standards, and reagents, using apparatus, and using a formula to calculate, among other things.

2.2 Equipment Validation: Qualification refers to the process of validating equipment. Installation Qualification (IQ), Operational Qualification (OQ), and Performance Qualification (PQ) are the three levels of equipment validation. An IQ document specifies static attributes of a facility or item to demonstrate that the unit was appropriately installed and that the manufacturer's installation specifications were met. After installation, the device must supply the operational ranges specified in the purchase order. This is known as OQ.

2.3 Process Validation:

A documented method that offers a high level of assurance that a particular process will consistently generate a product that meets its set specifications and quality attributes is known as process validation. The various types of process validation are as follows:-

A) Prospective Validation: It is described as the creation of concrete proof that a system performs as intended in accordance with predetermined protocol. When a new formula, technique, or facility needs to be validated before commercial routine pharmaceutical formulation can begin, this approach to validation is typically used. The production process should be divided into several segments during the product development phase

B) Retrospective validation: It is described as the creation of recorded evidence that a system performs as intended based on a review and analysis of historical data. This is accomplished by reviewing previous manufacturing testing data to demonstrate that the process has always been under control. It is permitted to use data from a minimum of ten consecutive batches produced for the purposes of retrospective validation studies.

C) Concurrent validation: Concurrent validation is similar to prospective validation, except that the operational firm will sell the product to the public at its market price during the qualifying runs. This validation includes essential processing step process monitoring and product testing. It is the repetition of a validation

procedure or a portion of one. This is done whenever there is a change or replacement in the formulation, equipment, plant, or site location.

D) Re-validation:

Re-validation is typically done to confirm initial validation for a Periodic review. Re-validation provides evidence that modifications made to a process and/or the process environment have no negative impact on process characteristics or product quality.

2.4 Process/ Product Validation:

Process validation is the establishment of written evidence that gives a high level of assurance that a certain system will consistently deliver a product that meets its set standards and quality attributes.

2.5 Cleaning validation:

Cleaning validation is the methodology used to ensure that a cleaning process removes residues of the active pharmaceutical ingredient of the product manufactured in a piece of equipment, and that all residues are removed to predetermined levels (product contamination below the acceptable level) to ensure the quality of the next product to be manufactured.

- **Validation Protocol :**

The validation protocol should be numbered, signed, and dated, and it should include at the very least the following information:

- Title
- Objective and Scope
- Product Composition Protocol Approval Validation Team Product Composition
- Process Flow Diagram
- Equipment/Utilities Manufacturing Process Review
- Raw Materials and Packing Materials Evaluation
- Analytical and batch manufacturing records must be reviewed.
- Validation of Batch Quantities (Raw Materials & Packing Materials)
- Requirements of the HSE
- Analyse Process Parameters Acceptance of Validation Procedure Sampling Location Documentation Criteria
- Summary and conclusion.

- **Validation master plan:**

A validation master plan is a document that describes the organization's overall philosophy, goals, and methodologies for establishing performance sufficient. The Validation Master Plan must be approved by management. In general, validation needs preparation and meticulous planning of the process's many components. Furthermore, all work should be completed in conformity with formally authorised standard operating procedures. All observations must be documented, and true numerical findings must be presented if possible. The validation master plan should give a high-level overview of the validation operation's organisational structure, content, and planning.

- **Evaluation, selection, and validation of processes:**

1.Dispensing:

Prior to formulation, dispensing is performed. Ensure that the dispensing booth is clean and that queue clearance is issued in accordance with SOPs. Check that the balance is calibrated and that the expiry date of the product to be issued is later than the batch expiry date. Check and confirm that all materials are issued in

accordance with BMR. And all of the rooms, such as the granulation room, compression room, coating room, packaging room, and so on, are clean, with line clearance completed prior to processing.

2. Blending or mixing:

Ones having similar physical qualities will mix or blend more easily and will not segregate as readily as ones with major variations.

The following parameters must be considered:

Diffusion (tumble), convection (planetary or high intensity), or blending technique.

Mixing or blending speed: Determine the mixing or blending intensity (low/high shear) and/or speed (rpm). The medication and excipient will require more vigorous mixing than the lubricant in the final mixture.

Time for mixing or blending: The time for mixing or blending will be determined by the mixing or blending technique and speed.

3.Wet granulation:

The type of wet granulation technology utilised may result in granules with varying physical qualities and will necessitate monitoring of various processing parameters.

- **Binder concentration:**

The best binder concentration for the formulation must be determined. If the binder is to be sprayed, the binder solution must be dilute enough to pass through the spray nozzle. It should also be concentrated enough to produce granules without over-wetting the materials.

Addition rate of binder solution/granulating solvent.

It's time to start mixing.

- **Granulation end point:**

This is determined or regulated by granulation end point equipment (e.g., an ammeter) or by setting important processing parameters.

4.Drying:

The sort of drying process necessary for the formulation (e.g., tray, fluid bed, and microwave) must be determined and justified. The technique used may be determined by the qualities of the medicine or formulation as well as the availability of equipment. Changing dryer procedures may have an impact on tablet qualities such as hardness, disintegration, dissolving, and stability. It is necessary to identify the appropriate moisture level of the dried granulation. High moisture concentration can cause tablet picking or adhering to tablet punch surfaces, as well as poor chemical stability due to hydrolysis.

5. Milling:

Milling will lower the particle size of the dry granulation. The particle size distribution that results will have an impact on material qualities such as flow, compressibility, disintegration, and dissolution. It will be necessary to identify the appropriate particle size/size distribution for the formulation. Milling factors to consider include:

- Impact or screen milling.
- Screen size: The particle size is affected by the screen size. A smaller screen size results in a smaller
- particle size and a bigger amount of fines.
- Feed rate and mill speed.

6.Lubrication:

- The lubricant grade that was used.
- Compatibility with other substances.
- Time to mix:

The amount of lubricant used: Too much lubricant will produce a hydrophobic layer on the tablet, causing dissolving issues.

7.Compression:

Compression is an important stage in the manufacturing of a tablet dosage form. The materials being squeezed will require sufficient flow from the hopper to the feed frame and into the dies. Inadequate flow can cause "rat holing" in the hopper and/or mix segregation in the hopper/feed frame. This can lead to issues with tablet weight and consistency. Consider the following factors when compressing:

- **Tooling:** Based on the formulation qualities and commercial specifications, the shape, size, and concavity of the tooling should be assessed.
- **Compression speed**: The formulation should be compressed at a variety of compression speeds to determine the compressor's operational range.
- **Compression/ejection force**: The compression profile for the tablet formulation must be developed in order to identify the best compression force to achieve the specified tablet hardness.

During the compression stage, the following in-process tests should be performed:

- Hardness
- Thickness
- Tablet Weight
- Friability
- Disintegration Time
- Weight Uniformity

8.Tablet Coating:

Tablet coating can take several forms (sugar, film, or enteric), with film coating being the most prevalent. The following factors should be considered when coating tablets:

- Tablet qualities like as hardness and form are vital in obtaining a successful film-coated tablet.
- Type of equipment.
- The coating pan's rpm.
- Spray guns: Spray angle.
- Application/spray rate: The most effective spray rate should be determined. Spraying too quickly will cause the tablets to become overly wet, resulting in tablet clumping and possibly tablet surface breakdown. If you spray too slowly, the coating components will dry before adhering to the pills.
- Flow of tablets.
- Temperature and airflow at the inlet and outflow.
- Coating solution: The coating solution's concentration and viscosity must be calculated.
- To determine the shelf life of the coating solution, its stability should be examined.
- Coating weight: To ensure a uniform look, a minimum and maximum coating weight should be determined for the tablet.
- Residual solvent level: If solvents are used to coat tablets, the residual solvent level must be assessed.

9.In-process testing:

- Moisture content of "dried granules" Distribution of granulation
- particle size
- Disintegration Impurity profile Blend homogeneity
- Individual tablet/capsule weight
- Tablet hardness and thickness.

10. Finished product tests:

- Appearance
- Tablet mottling
- Picking of the monogram
- Tablet filming
- Assay.
- Uniformity of content Beginning, Middle, and End
- Tablet toughness
- Impurity profile Tablet friability

11. Labelling and packing:

Check and record the temperature of the heating and sealing rollers, as well as overprinting instructions on labels and boxes. Check and confirm that the price overprinted on the label and carton corresponds to the current price list. Check for the appropriateness of carton packing for tablets after confirming proper labelling.

- **Finished product analysis and release**:

Finished products must be analysed in accordance with in-house specifications, and products must be released only after meeting preset criteria and quality attributes.

In general, process validation testing is performed on the first three batches of product manufactured in production-size equipment. Revalidation testing is only performed when there has been a "significant" change.

- **The following are the reasons for selecting three consecutive batches for Validation:**

In general, it is assumed that obtaining the intended quality in the first batch is an accident, that the quality in the second batch is a regulator, and that the quality in the third batch is validation. When two batches are used as validation, the data is insufficient for evaluation and proving reproducibility since statistical evaluation cannot be done on two points; at least three points are required because two points always make a straight line. As a result, at least three consecutive batches are reviewed for manufacturing process validation. Validation can be performed in more than three batches, however this incurs additional costs and effort.

- **Report on the Final Process Validation:**

A final report should be prepared at the conclusion of validation activities. All protocols and outcomes should be summarised and referenced in this report. It should draw conclusions about the process's validation state and make any necessary recommendations for normal processes. The validation team and authorised management should examine and approve the final report.

Following batch execution, a validation report must be created to check protocol adherence.

The names of the ingredients, the quality of the ingredients used, and the product batch number, as well as the names of the equipments used at each processing stage, the equipment numbers, and the make/model/capacity of the equipments, must be checked against the formulation sequence.

The formulation order of the validation batch processing records shall be validated against the stage of process, details of process variables, and the appropriate observations and recommendations.

Any work done in addition to that specified in the protocol, as well as any divergence from the protocol, should be clearly documented and explained.

CONCLUSION:

It is concluded that process validation is a step in ensuring the identity, strength, purity, safety, and efficacy of pharmaceutical medication products, and it is the most commonly used term in drug development, production,

and completed product specification. For process efficiency, process validation is a crucial requirement of cGMPs regulation

Continued knowledge of validation criteria, as well as meticulous implementation of validation principles, will help to ensure that pharmaceutical products may be designed and produced with the quality and reproducibility required by regulatory bodies worldwide.

REFERENCES:

1. Aulton M.E, Pharmaceutics-The Science of Dosage Form Design. 2nd edition, Churchill Livingstone, Elsevier, 2006.
2. Oechslein C, Lazar M. S – Process Validation from view report of the FDA, Maas & Peither AG – GMP Publishing, Logfile No. 3/ February 2012
3. Quality Management System – Process Validation Guidance GHTF/SG3/N99-10:2004 (Edition 2
4. Nash R. A and Wachter A. H, Pharmaceutical Process Validation an International Third Edition. Revised and Expended, Marcel Dekkar, Inc., New York, 2003; 17 – 40
5. Patel R. C, Bhuva C. K, singh R. P, Dadhich A,Sharma A, Pharmaceutical Process Validation, Pharmatutor – ART – 1053.
6. Jatto, E., Okhamafe.O.A,.An overview of pharmaceutical validation and process controls in drug development. Tropical J pharm research. (2), 115-122. 2004
7. USA-FDA, Guidelines on General Principles of Process Validation, CEDR, FDA-USA, 1987.
8. Guidance for Industry, Process Validation General Principles and Practices (2011)
9. Guide to Inspections Validation of Cleaning Processes, US Food and Drug Administration, Washington Dc, 2005
10. . Guide to Inspections of Oral Solid Dosage Forms pre/post Approval Issue for Development and Validation; issue (1/94); January, 2010.
11. Note for Guidance on Process Validation The Europe Agency for Evaluation of MedicinalProducts;CPMP/QWP/848/96;EMEA/CVMP/598/9 9
12. Mayer RJ. Validation of Product and Process, PPMA. Seminar on Validation of solid Dosage form Processes. Atlanata May – 1980.
13. A. Ojha, M. Bharkatiya and S. Kitawat, Pharmaceutical Process Validation Of Solid Dosage Forms: A Review, World Journal Of Pharmacy And Pharmaceutical Sciences,Volume 3, Issue 6, 476-484.
14. 14. S. Jena, G. Arjun, N. V. Anil Kumar Ravipati, D.Satish kumar, Vinod.K.R, David Banji Industrial Process Validation Of Solid Dosage Forms – An Overview International Journal of Pharmaceutical Sciences Review and Research Vol 4, Issue 2, 2010; 145-154
15. 15. Bankar GS, Anderson NR Tablets: The Theory and practice of industrial pharmacy (3rd edn), Varghese publishing house, Mumbai, India, (1987).
16. 16. http://whoguideline.blogspot.com/2008/ importance-of-master manufacturing.
17. 17. Quality Management System – Process Validation Guidance GHTF/SG3/N99-10:2004 (2 nd Edition).