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A Review on Process Validation of Erythromycin Estolate Tablets IP 500 mg (Eltocin-DS)

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Abstract: -

Validation is an important part of cGMP. The meaning of validation is assessment of validity or proving action of effectiveness. It is an art of designing and practice the designed steps along with the documentation. Validation and Quality assurance will ensure the quality of product. Process validation is the important step in achieving and maintain the final product quality. This article include introduction, validation types, view product lifecycle, process validation phases, selection of CCP & CQA, Document required, VMP, process validation protocol, sampling planning study on Process validation by these mention parameters highlight the output quality of finish dosage form. The main aim and objective of this work is to establish scientific evidence by collection and evaluation of data from the manufacturing of product Erythromycin estolate tablet which establish document evidence that the process is capable of providing consistently quality product and meet the pre-defined process parameters, specification and quality characteristic.

Keywords: -

Process validation, manufacturing procedure, process validation protocol, Quality, Erythromycin, Regulatory guideline.

Introduction: -

The validation concept was first proposed bye FDA in 1970 for improving quality of pharmaceutical products. The simply meaning of word validation is assessment of validity and action of prove effectiveness. Quality, safety and efficacy are three principle. Validation is basically based on FDA guidelines or regulation which describe cGMP for finished products are given in 21 CFR part 210 and part 211. The cGMP regulation requires the manufacturing

process will designed and control to assure the in-process material and FG product meet with pre-determined quality specification consistently. USFDA states that validation is an establishing document evidence which provide high degree of assurance that specific process will consistently produce product meet its pre-determined specification and quality attributes. WHO defines validation is documented act of proving any procedure, process, eqp., material, activity, system actually leads to expected result.

Validation: -

Validation may be defined as the action of proving and documenting that any process, procedure and method consistently leads to expected results.

Scope of Validation: -

1. Analytical
2. Process utility services
3. Product design
4. Raw material
5. Packing material
6. Equipment's
7. Calibration of all instrument.
8. Manufacturing operations

Importance of validation: -

1. Process optimization
2. Quality affirmation
3. Quality cost reduction
4. Minimal batch fail
5. Improved efficiently and productivity
6. Expand output
7. Reduce in testing in process and finished goods

Process validation: -

Process validation is defined as the establishing documented evidence which provide a high degree of assurance that a specific process will give consistently produce product meet its pre-determined specification and quality characteristics or attributes. The FDA in new guideline make some changes in aspects of process validation and it may be defined as the collection and evaluation of data from the design stage throughout production which establish evidence that the process is capable of consistently delivering quality products.

Types of Process Validation: -

The types of Process Validation are mention below

1. Prospective validation (Pre-marketing validation)

2. Concurrent validation

3. Retrospective

4. Revalidation

Prospective validation: - Prospective validation is defined as the establishing document evidence, it is based on the pre-planned protocol. This process is carried out prior to introduction of new drug and manufacturing process. This validation is proceeding normally under taken when new formula introduce, process or facility is also validated before formulation commences. The main objective of prospective validation is to prove that the process will work according with VMP or protocol prepared for pilot product trials. Validation activity must be completed prior to distribution and sale of the product.

Concurrent validation: - It is similar to prospective validation except the firm will sell the product during the run of qualification to the public as market price. This validation involves in product testing and monitor critical processing steps. This will help to generate document evidence to show the production phase is in quality control.

Retrospective validation: - This validation is acceptable only for well establish process without any change in composition, operating process, equipment uses. The source of data includes Batch document, process chart, logbooks, process capability data, FG data, trend data, stability studies and data. The data generated for 10-30 batches should be examined to assess consistency.

Revalidation: - It is a repetition part of validation process. This will be carried only when any change and replacement in formula, formulation, equipment's change, site location change, batch size and in case when the sequent batch not meet with product specification**.**

Elements of process validation: -

It involves a series of activity taking place over the lifecycle of the product and process. All the activities of PV divided into Three stages as below: -

1. Process design

2. Process qualification

3. Continued process verification

Process design: - It is depending on commercial based development and scale up experience. It is focus exclusively on qualification efforts also understanding the manf. Process. It is based on knowledge gained through scale up activities and development. It involves two important phases

a) Capturing and building process knowledge

b) Establishing a strategy for controlling process.

It includes all activities related to product research and development, formulation, pilot plant studies, scale up study, establishing stability data, technology transfer, storage condition of in process and finished dosage products, qualification of equipment, installation qualification, operational qualification, master documentation.

Process qualification: - This process design confirming that it is accomplished of reproducible commercial manufacturing. It has two elements: -

a) Facility design and equipment and utilities qualification

b) PPQ (process performance qualification). It states that it is based on science and the manufacturer overall level of product and process understanding.

It confirms that the limits of CPP are valid and satisfactory product produced under worst case condition.

Continued process verification: - It confirmed that the process design is capable of reproducible commercial manufacturer, the manufacturer assure that the process remains a state of control throughout commercial manufacturer. The programme to collect and analyse process data and product is relate to quality product must be established. Quality aspect are appropriately regulated during the process. It should follow ICH Q8(R1), Q10, CPPs, cGMP and GDP. The main objective is to generate scientific evidence that process is capable of making product meet quality acceptance criteria. It ensures that the process will remain in state of control, complies with the MFR, cGMP.

Objectives of Process Validation: -

The main objective of Process Validation is as under: -

1. Process validation ensures that product is highly reproducible over time.

2. The validation plan should be drafted and executed by engineer.

3. Manufacturing process as well as individual equipment's must be validated.

4. The main goal is that process is consistently produces a drug product with minimal variation related to quality criteria, identity and potency.

Asset of Process Validation: -

1. Evaluate process performance and product variables by enhanced ability to statistically.
2. Expand real time monitoring and process.
3. It increased confidence about process reproducibility and quality.
4. It increase reporting capability

Phases of Process Validation: -

The goal of Process Validation is to follow in three steps or stages.

1. Pre-validation qualification stage.
2. Process validation phase.
3. Validation maintenance phase.

Pre-Validation qualification stage: - It cover all information related to pilot batch study, product research and product development, scale-up study, technology transfer, stability data, storage condition of finished goods and in-process dosage form, qualification of equipment's, installation qualification, Master documents, process capacity and operational qualification**.** It develops a relationship between material and process parameters and attributes of quality.

Process validation phase: - It is a process qualification phase designed to check that all limits for CCP are valid and products produced even under condition of worst case. Control procedures must be set to monitor the output and conform the manufacturing process may be responsible for causing variation in the virtue of in-process material and drug product.

Validation maintenance qualification phase: - It claim frequent review of all process referred to documents, audit reports, to ensure there has no changes, deviation, failure, modification in production parameters and SOPs involve change control procedure has follow.

Process validation protocol: - Validation protocol is a written procedure for actions starting how process will be conducted, it includes who will conduct the task and testing, various sampling plan, testing method and procedure. It must be identifying the number of batches to be used for validation. It must describe the acceptance criteria and who will signature/who will give approval the conclusion from the study. The validation protocol consists of the following elements: -

1. Objective and scope
2. Validation type
3. No. of batches.
4. Equipment use
5. Reference document
6. Approval sheet

7. Check points

8. Authority

9. Manufacturing process/procedure

10. Calibration status

11. CCP and CQA

12. Process variables and attributes

13. Process flow chart

14. Sampling plan

15. Specification

16. Summary

17. Conclusion.

Process validation parameters: -

There are various process validation parameters which are involved in manufacturing process as shown in below table

S.no.	Step process	Monitor control variables	Test measured responses
1	Pre-blending	RPM, blending time	Blend uniformity
2	Granulation	Granulation fluid amount, mixing speed	Particle size, drug distribution
3	Drying	Outlet and inlet temperature, drying temperature and time	LOD, assay
4	Milling	Milling speed, screen size	Particle size
5	Lubrication	Blend time and speed	Flow property, particle size
6	Tableting	Compression force, compression rate, pre-compression force	Weight variation, hardness, friability, moisture content, thickness, disintegration, assay, appearance
7	Coating	Pan speed, inlet temperature, pan load, spray rate	Thickness, weight gain, dissolution, assay, residual solvent

Sampling plan and acceptance criteria: -

Sampling plan for different location and acceptance criteria as mention in below table

Stage	Sampling plan	Test	Acceptance criteria
Drying	Three samples from three different locations	LOD	LOD specification
Final blend	Three samples from 10 different location and composite sample	Blend uniformity, density, appearance, flow property	RSD
Tableting	Layered sampling	Uniformity, in house specification	Inhouse specification
	Composite sample	Uniformity assay, friability, hardness, disintegration, dissolution, visual inspection	Uniformity as per inhouse specification
Coating	01 sample from coating pan	Assay, moisture content, residual solvent	Assay inhouse moisture solvent follow ICH guideline
Printing	Stratified sampling	Visual inspection	In house
Primary packing	Stratified sampling	Visual inspection, integrity test	In house
Environmental monitoring	During the manufacturing process	Temperature, RH	In house

Conclusion: - Process validation is an essential part of validation for equipment's, cleaning and vendor validation. It insures to identify, purity, safety, efficacy of product. The stability of validated process to produce a quality product is very important for industry. Process validation is most important parameter in cGMP.

Abbreviation: -

RH- Relative humidity

ICH- International council on harmonization

LOD- Loss on drying

RSD- Relative standard deviation

CCP- Critical check point

CQA-Critical quality attributes

SOP- Standard operating procedure

cGMP- Current good manufacturing practice

MFR- Master formula record

References: -

1. https://www.researchgate.net/profile/Abhijit-Jadhav-2/publication/281390016_An_Overview_of_Pharmaceutical_Process_Validation_of_Solid_Dosage_Form/links/55e51b7508aecb1a7ccb951a/An-Overview-of-Pharmaceutical-Process-Validation-of-Solid-Dosage-Form.pdf

2. https://saspublishers.com/media/articles/SAJP32-178-190.pdf

3. http://www.ijapbc.com/files/27-233.pdf

4. http://www.pharmasm.com/pdf_files/20150426231255_23_charvi.pdf

5. https://pubchem.ncbi.nlm.nih.gov/compound/Erythromycin-estolate

6. https://en.wikipedia.org/wiki/Erythromycin

7. Guidance for Industry. Process Validation: Principles and Practices, 2011, http://www.fda.gov/Drugs/GuidanceComp lianceRegulatoryInformation/Guidances/d efault.htm.

8. Kumar and Bharat, "Process Validation cGMP Concept", International Journal of Pharmaceutical Science, February 2013, pp. 13-20. 5. Nash RA. A

9. UK Orange Guide. Lead to Good Pharmaceutical Manufacturing Practices; United Kingdom, 1983;345-359.

10. Sharma A, Saini S; Process Validation of Solid Dosage Form: A Review. International Journal of Research in Pharmacy and Science, 2013; 3 (2): 12- 30.

11. GMP for Pharma Products, WHO/Pharm./93.562/Annex: Guidelines on Validation of Manufacturing Process. Geneva: WHO

12. Guidance for Industry, General Principles and Practices of Process Validation. U.S. Food and Drug administration FDA, Department of Health and Human Services, CBER, CDER, Centre for Veterinary Medicine (CVM), January 2011. 20. Oechslein C, Lazar MS; Process V

13. ICH Q7A Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients: 33.

14. https://en.wikipedia.org/wiki/Process_validation

15. http://www.pharmainfo.net/reviews/guidelines generalprinciplesforvalidation,solid,liquid and sterile dose form.