PROCESS VALIDATION: AN OVERVIEW

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ABSTRACT

The present article gives an introduction and general overview on process validation. Validation is one of the important steps in achieving and maintaining the quality of the product, each step of production process is validated we can assure that the final product is of best quality. Validation of the individual steps of the processes is called the process validation. Process validation is the key element in assurance of pharmaceutical product. It is the most important and recognized parameters of cGMP. Here this article concentrates on the reasons, advantages and objective of process validation, types, phases, validation protocol preparation and validation report.

KEYWORDS: Process validation, cGMP, Food and Drug Administration, WHO.

INTRODUCTION

Pharmaceutical Process Validation is the most important and recognized parameters of cGMPs. The concept of validation has expanded through the years to embrace a wide range of activities from analytical methods used for the quality control of drug substances and drug products to computerized system for clinical trials, labelling or process control. The concept of validation was first proposed by two Food and Drug Administration (FDA) officials, Ted Byers and Bud Loftus, in the mid 1970s in order to improve the quality of pharmaceuticals. Validation is an integral part of quality assurance; it involves the systematic study of systems, facilities and process aimed at whether they perform their intended functions adequately and consistently as specified. The process validation establishes the flexibility and constraints in the manufacturing process controls in the attainment of desirable attributes in the drug product while preventing undesirable properties. The principal objective of dosage form is to achieve a predictable therapeutic response to a drug included in a formulation which is capable of large scale manufacture with reproducible product quality.
To ensure product quality, numerous features are required, like chemical and physical stability, suitable preservation against microbial contamination if appropriate, uniformity of dose of drug, acceptability to users including prescriber and patient, as well as suitable packing, labeling and validation.

USFDA defined process validation as “establishing documented evidence which provides high degree of assurance that a specific process will consistently produce a product meeting its pre determined specification and quality characteristics”

Validation is a necessary part of a quality assurance program and is fundamental to an efficient production operation. This is an important concept, since it serves to support the underlying definition of validation, which is systematic approach documenting, and re-evaluating a series of critical steps in the manufacturing process that require control, ensure a reproducible final product.

REASON FOR PROCESS VALIDATION
The possible reason of performing process validation may include:
- New product or existing products as per SUPAC changes.
- Change in site of manufacturing.
- Change in batch size.
- Change in equipment.
- Change in process existing products.
- Change in composition or components.
- Change in the critical control parameters.
- Change in vendor of API or critical excipient.

ADVANTAGES AND OBJECTIVE

OBJECTIVE OF PROCESS VALIDATION
- To reduce variation between various batches.
- To provide a high degree of assurance of quality of the product.
- To decrease the risk of defect costs and regulatory noncompliance.
- To ensure the consistency of the manufacturing operation and reproducibility of the process.
- To demonstrate the robustness of the process.
A fully validated process may require less in-process controls and end product testing.

ADVANTAGES OF PROCESS VALIDATION
1. It is simple process and moisture sensitive and heat sensitive products can also be processed.
2. Expanded real time monitoring and adjustment of process.
3. Decreases the risk of preventing problems and thus assure the smooth running of the process.
4. Enhanced ability to statistically evaluate process performance and product variables e.g. individuals; mean; range; control limits.
5. Enhanced data and evaluation capabilities and increased confidence about process reproducibility and product quality.

Regulatory requirement for process validation-
The basic principles of quality assurance have as their goal the production of articles that are fit for intended use. These principles may be stated as follows:
- Quality, Safety and effectiveness must be designed and built in to the product.
- Quality can’t be inspected or tested in to finished product.
- Each step of the manufacturing process must be controlled to maximize the probability that the finished product meets all the quality and design specification.

Process validation defined by various regulatory agencies is given below
- The WHO CGMP’s (World Health Organization)- defines process validation as “Establishing documented evidence, which provides a high degree of assurance that a planned process will consistently perform according to the intended specified outcomes.”
- The European commission guide defines process validation as “Establishing documented evidence that the process operated with in established parameters can perform effectively and produce a medicinal product meeting its predetermined specifications and quality attributes.”

TYPES OF PROCESS VALIDATION
- Prospective Process Validation: It is defined as the established documented evidence that a system does what it purports to do based on a preplanned protocol. This validation usually carried out prior to distribution either of a new product or product made under a revised manufacturing process performed on at least three successive production-sizes.
Retrospective Process Validation: It is defined as the establishment of documented evidence that a system does what it purports to do on review and analysis of historical information. The sources of such data are production, QA and QC records.

Concurrent Process Validation: It is similar to prospective, except the operating firm will sell the product qualification runs, to the public as market price. This validation involves in process monitoring of critical processing steps and product testing.

Revalidation: It is the repetition of validation process or part of it. This is carried out when there is any change or replacement in formulation, equipment plan or site location.

PHASES OF PROCESS VALIDATION
The activities relating to validation studies may be classified into three

- Phase 1- This is Pre-validation Qualification Phase which covers all activities relating to product research and development, formulation pilot batch studies, scale-up studies, transfer of technology to commercial batches, equipment qualification, installation qualification

- Phase 2- This is the process validation phase. It is designed to verify that all established limits of the critical process parameter are valid that satisfactory. Products can be produced even under the worst condition.

- Phase 3- This is known as the validation maintenance Phase, it requires frequent review of all process related documents, including validation of audit reports, to assure that there have been no changes, deviations failures and modifications to the production process.

VALIDATION PROTOCOL
A written plan of actions stating how process validation will be conducted; It must specify the minimum number of batches to be used for validation studies; it must specify the acceptance criteria and who will sign.

An ideal validation protocol contains the followings
1 Objective and General Information.
2 List of equipments and their qualification status.
3 Facilities qualification.
4 Manufacturing formula & manufacturing procedure.
5 Process flow diagram
6 Label claim
7 Process Flow Chart
8 List of critical processing parameters
9 Sampling test and specification
10 Acceptance criteria
11 Revalidation criteria

Validation Report
A written report should be available after completion of the validation. It should be approved and authorized (signed and dated). The report should include at least following:
- Title and objective of study
- Reference to protocol
- Details of material
- Equipment
- Details of procedures and test methods
- Result (compared with acceptance criteria)
- Recommendations on the limit and criteria to be applied on future basis.

CONCLUSION
From study, it can be stated that Process validation is an essential process in pharmaceutical organizations. It is the key element in assuring that quality goals are met. Pharmaceutical Process validation is most important parameter of cGMP. It is necessary, before approval of new drug that an accurate and reliable assessment for its effectiveness and safety for the intended indication. Finally, it can be concluded that Process validation is the key element in the quality assurance of pharmaceutical product.

REFERENCES


