Abstract
The process validation is establishing documented evidence which provides high degree of assurance that a specific process consistently produces a product meeting its predetermined specifications and quality characteristic. According to GMP validation studies are essential part of GMP these are required to be done as per predefined protocols. The validation study provides the accuracy, sensitivity, specificity and reproducibility of the test methods employed by the firms, shall be established and documented. Thus the validation is an essential part of the quality assurance.

Keywords: GMP, Quality Assurance, Pharmaceutical Validation

1. Introduction

Validation is a concept that has been evolving continuously since its first formal appearance in the United States in 1978. The concept of validation has expanded through the years to encompass a wide range of activities from analytical methods used for the quality control of the drug substances and drug products to computerized systems for clinical trials [1].

Validation is therefore one element of quality assurance associated with a particular process, as the process differs so widely, there is no universal approach to validation and regulatory bodies such as FDA and EC who have developed general non-mandatory guide lines. Then word validation simply means, ‘assessment of validity’ or action of proving effectiveness. According to European community for medicinal products, validation is ‘action of proving’, in accordance with the principles of GMP that any procedures, process, requirement, material, activity or system actually leads to expected results [2].

1.1 General Concept
Assurance of product quality is derived from careful attention to number of factors including selection of quality parts and materials, adequate product and process design, control of the process, and in-process and end product testing. Due to the complexity of today’s medical products, routine end product testing alone often is not sufficient to assure product quality for several reasons. Some end-products tests have limited sensitivity [3]. E.g.:– In some cases, where end product testing does not several all variations that may occur in the product, which may have an impact on safety and effectiveness, destructive testing is required to show that the manufacturing process is adequate.

1.2 US FDA Definition
Process validation is establishing documented evidence which provides a high degree of assurance that a specified process will consistently produce a product meeting its pre-determined
specifications and quality characteristics [4].

1.3 Benefits of Validation

- Processes consistently under control require less process support and will have less down time.
- Only fewer batch failures and may operate more efficiently with greater output.
- In addition, timely and appropriate validation studies will transmit a commitment to product quality, which may facilitate pre-approval inspection & expedite the granting of marketing authorization.
- Validation makes good business sense [5, 6].

1.4 Why Validation is Done?

- It would not be feasible to use the equipments without knowing whether it will produce the product we wanted or not.
- The pharmaceutical industry uses expensive materials, sophisticated facilities & equipments and highly qualified personnel.
- The efficient use of these resources is necessary for the continued success of the industry. The cost of product failures, rejects, reworks, recalls, complaints are the significant parts of the total production cost.
- Detailed study and control of the manufacturing process- validation is necessary if failure cost is to be reduced and productivity improved [6].

2. Types of Validation [7, 8]

2.1 Analytical Validation

Analytical validation is the evaluation of product quality attributes through testing, to demonstrate reliability is being maintained throughout the product life cycle and that the precision, accuracy, strength, purity and specification has not been compromised.

2.2 Equipment Validation

Validation of equipments is known as qualification. Equipment validation is divided into installation Qualification (IQ), Operational Qualification (OQ), and Performance Qualification (PQ).

An IQ documents specific static attributes of a facility or item to prove that the installation of the unit has been correctly performed and that the installation specifications of the manufacturer have been met. After installation it must be ensured that the equipment can deliver operating ranges as specified in the purchase order. This is called OQ. The PQ’s are concerned with proving that the process being investigated works as it is supposed to do.

2.3 Process Validation

Process validation is “A documented program which provides a high degree of assurance that a specific process will consistently produce a product meeting its predetermined specification and quality attributes”. Process validation is divided into different types as follows:-

(a) Prospective validation

It is defined as the establishment of documented evidence that a system does what it purports to do based on pre-planned protocol. This validation is
usually carried out prior to the introduction of new drugs and their manufacturing process. This approach to validation is normally undertaken whenever a new formula, process or facility must be validated before routine pharmaceutical formulation commences. **(b) Retrospective validation**

It is defined as the establishment of documented evidence that a system does what it purports to do based on review and analysis of historical data. This is achieved by the review of the historical manufacturing testing data to prove that the process has always remained in control. **(c) Concurrent validation**

It is similar to prospective, except the operating firm will sell the product during the qualification runs, to the public at its market price. This validation involves in process monitoring of critical processing steps and product testing. It is the repetition of a validation process or a specific part of it. This is carried out when there is any change or replacement in formulation, equipment, and plant or site location. **(d) Revalidation**

Batch size and in the case of sequential batches that do not meet product and process specifications. **2.4 Process/ Product Validation**

Process Validation is establishing documented evidence which provides a high degree of assurance that a specific system will consistently produce a product meeting its predetermined specifications and quality attributes.

**Phases in Process Validation**

The activities relating to validation studies may be classified into three phases:

**Phase 1:** This is the 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 scale batches, establishing stability conditions and storage, and handling of in-process and finished dosage forms, equipment qualification, installation qualification master production document, operational qualification and process capacity. **Phase 2:** This is the process validation phase. It is designed to verify that all established limits of the critical process parameter are valid and that satisfactory. Products can be produced even under the worst conditions. **Phase 3:** 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 and that all standard crepitating procedures (SOPs), including change control procedures, have been followed. At this stage, the validation team comprising of individuals representing all major departments also assures that there have been no changes/deviations that should have resulted in requalification and revalidation. A careful design and validation of systems and process controls can establish a high degree of confidence that all lots or batches produced will meet their intended specifications. It is assumed that throughout manufacturing and control, operations are conducted in accordance with the principle of good manufacturing practice (GMP) both in general and in specific reference to sterile product manufacture [9-12].

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3. Application of Validation
By definition, validation requires the accumulation of documentary evidence relating to a process, item or equipments or facility. This is achieved by means of a validation protocol, which details the test to be carried out, the frequency of testing and the result expected (the acceptance criteria). If the validation programmed is designed, and the protocol issued, before the equipment or facility comes on stream or before the product manufactured by the process being validated is distributed, then this constitutes prospective validation, sometimes, however, systems or processes are in place that have not previously been validated, but are functioning well and consistently producing good products, already in distribution. Validation of such facilities or process is called retrospective validation and is achieved by the review of historical manufacturing and testing data.
Prospective and retrospective validation may be combined advantageously in sequence to provide a higher level of assurance that is given by the pre marketing prospective validation alone. Concurrent validation is applied either to ongoing evaluation of historical data associated with retrospective validation. Revalidation is an act of repeating all or a portion of the validation as a result of any modification to the process or facilities that may be lead to changes in the quality or reproducibility of the product. Revalidation may be triggered by the operation of an established change control system it can also refer to the regular, planned repetition of validation steps for equipment or processes where performance may change with time [13].

4. Conclusion
Current review of literature states that pharmaceutical validation is the most important and recognized parameters of cGMP. Validation requires the accumulation of documentary evidence relating to a process, item or equipments or facility. Another important term related to validation process is revalidation. Revalidation may be triggered by the operation of an established change of control system it can also refer to the regular, planned repetition of validation steps. To comply with the requirements of current Good Manufacturing Practices (GMP). Pharmaceutical companies should have an overall validation policy which documents how validation will be performed. This will include the validation of: production process, cleaning procedures, analytical methods, in-process control test procedures and computerised systems. Overall we can conclude that the purpose of the validation is to show that processes involved in the development and manufacture of drugs, such as production, cleaning, and analytical testing.

Conflict of interest statement
We declare that we have no conflict of interest.

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