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A REVIEW ON PHARMACEUTICAL VALIDATION AND ITS IMPLICATIONS

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ABSTRACT

Process validation is the demonstrating documented proof which gives high intensity of affirmation that a specific process constantly produces a product meeting its proposed specifications and quality characteristic. According to GMP validation studies are important part of GMP these are needed to be done as per predefined protocols. The validation study gives the accuracy, sensitivity, specificity and reproducibility of the test methods hired by the firms, shall be established and documented. Thus the validation is an important part of the quality assurance.

KEYWORDS

GMP, Quality assurance and Pharmaceutical validation.

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INTRODUCTION

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

Validation is therefore one component of quality assurance associated with a specific process, as the process differs so extensively, there is no universal approach to validation and regulatory bodies such as FDA and EC who have developed general non-mandatory guidelines.Therefore the word validation commonly means, 'assessment of validity' or action

of proving effectiveness. According to the European community for medicinal products, validation is 'plan of proving', in conformity with the principles of GMP that any procedures, process, requirement, material, activity or system really leads to expected results[2].

General Concept

Assurance of product quality is acquire from careful attention to number of factors including selection of quality parts and materials, adequate product and process design, command of the process, and in-process and end product testing. Because of the intricacy of today's medical products, routine end product testing alone often is not satisfactory 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 effect on effectiveness and safety, destructive testing is required to show that the manufacturing process is sufficient.

US FDA Definition

Process validation is an establishing documented proof which gives a high degree of affirmation that a specified process will frequently produce a product meeting its proposed specifications and quality characteristics[4].

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 proper validation studies will broadcast a commitment to product quality, which may simple pre-approval inspection and hasten the granting of marketing authorization.
- Validation makes good businesssense[5,6].

Why validation is done?

- It would not be feasible to use the equipment's without knowing whether it will produce the product we wanted or not.
- The pharmaceutical production handling costly materials, sophisticated facilities & equipment's and highly qualified personnel.
- The efficient use of these resources is required for the continued success of the industry. The cost of product failures, rejects, reworks, recalls, complaints are the important 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].

TYPES OF VALIDATION[7,8]

Analytical Validation

The analytical validation is a assessment of product quality characteristics through testing, to determine reliability is being maintained overall the product life cycle and that the strength, purity, precision, specification and accuracy has not been negotiate.

Equipment Validation

Equipment validation is known as qualification. Equipment validation is classified 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 accurately performed and that the installation specifications of the manufacturer have been met. After installation it must be assured 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 method being investigated works because it is meant to try and do.

Process Validation

A documented program which gives a high degree of affirmation that a specific process will constantly achieve a product meeting its proposed specification and quality characteristics" is called as a process validation. Process validation is classified into different types as follows:

Prospective validation

It is defined as the establishment of documented evidence that a system does what it purports to do based on preplanned protocol. This validation is usually accomplish prior to the initiation of new drugs and their manufacturing process. This access to validation is normally undertaken whenever an advance formula, system and equipment should be

validated before routine pharmaceutical formulation initiate.

Retrospective validation

Retrospective process validation is validation of a process for a product already in distribution based upon accumulated production, testing and control data.

Concurrent validation

Concurrent validation is similar to prospective, except the operating firm will sell the product at the time of the qualification runs, to the public at its market price. This validation includes in process monitoring of critical processing steps and product testing. This is the repetition of a validation process or a specific part of it. This is carried out when there is any change or stand-in formulation, equipment, and plant or site location.

Revalidation

Batch size and in the case of sequential batches that do not meet product and process specifications.

Process/ Product Validation

A documented program which gives a high degree of affirmation that a specific process will constantly develop a product meeting its expected specification and quality characteristics" is called as a process validation.

Phases in Process Validation

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

Phase-1

Phase-1 is a pre-validation Qualification Phase. Phase-1 includes all activities which are relevant to product research and development, scale-up studies, formulation pilot batch studies, establishing stability conditions and storage, transfer of technology to commercial scale batches, and management of in-process and finished dosage forms, installation qualification, equipment qualification, master production document, operational qualification and process capacity.

Phase- 2

Phase-2 is a process validation phase. It is designed to verify that all established limits of the critical process parameter are accurate and that satisfactory. Products can be produced even under the bad conditions.

Phase-3

Phase-3 called as a validation maintenance phase. This phase-3 have demand constant review of all process relevant documents, along with validation of audit reports, to ensure that there have been no changes, aberration failures and modifications in the maufacturing process and that all standard operating procedures (SOPs), including the change control procedures, have been followed. At this time or stage the validation team constitute of individuals representing all large departments also assures that there have been no deviations/changes that should have resulted in re-validation and re-qualification. An accurate design and validation of systems and process controls can authorize a high degree of assurance that all lots or batches produced will meet their proposed specifications. It is assumed that throughout manufacturing and control, operations are organizes in consonance with the principle of good manufacturing practice (GMP) both in general and distinct allusion to sterile product manufacture[9-12].

CHANGE CONTROL[13]

Written procedures should be lay to clarify the actions to be taken if a change is proposed to a product component, process environment, process equipment, processing site, method of production or testing or any other change that may influence product quality or support system operations.

All changes should be formally requested, documented and accepted by the validation team. The likely outcome / risk of the change on the product must be assessed and the demand for the extent of re-validation should be determined.

Commitment of the corporate to mastery all changes to premises, helping utilities, systems, equipment, material and processes employed in the fabrication/packaging of pharmaceutical dosage forms is vital to make sure a continued validation status of the systems concerned.

The change system should ensure that each one notified or the requested changes are satisfactorily investigated, documented and authorized. Products made by processes subjected to changes mustn't be released purchasable without full awareness and consideration of the change by the validation team.

The team should decide if a re-validation must be conducted before execution the proposed change.

VALIDATION PROTOCOL[14]

A written plan stating how validation are organize, together with product characteristics, test parameter, production and packaging equipment, and decision points on what constitutes agreeable test results. This document should simplify of critical steps of the manufacturing process that have to be measured, the allowable range of variability and also the way within which the system are visiting be tested.

The validation protocol provides a synopsis of what's hoped to be accomplished. The protocol should list the elect process and control parameters, state the quantity of batches to be incorporated within the study, and specify how the knowledge, once gathered, are visiting be treated for relevance. The date of approval by the validation team should even be noted.

In the case where a protocol is revised or modified after its approval, appropriate reasoning for such a change must be documented.

The validation protocol should be numbered, signed and dated, and may contain as a minimum the subsequent information:

- The objectives, scope of coverage of the validation study.
- Validation team association, their qualifications and responsibilities.
- Type of validation: prospective, concurrent, retrospective, and re-validation.
- Number and selection of batches to induce on the validation study.
- A list of all equipment to be used; their normal and bad case operating parameters.
- Result of IQ, OQ for critical equipment.
- Need for calibration of all measuring devices.
- Critical process parameters and their corresponding tolerances.
- Description of the processing steps: copy of the master documents for the merchandise.
- Sampling points, stages of sampling, methods of sampling, sampling plans.
- Statistical tools to be employed in the analysis of knowledge.
- Validated test method's to be utilized in in-process testing and for the finished product.

VALIDATION MASTER PLAN

A validation master plan is a master document that compile the company's overall knowledge, purpose and path to be used for demonstrating performance ability. Validation master plan should be prescribed by management.

Validation normally requires cautious preparation and careful planning of the varied steps within the process. Additionally, all work should be allotted in an exceedingly structured path persistent with formally authorized standard operating procedures. All observations should be documented and where possible should be recorded as actual numerical results.

The validation master plan provide an outline of the complete validation process, its regulatory system, its content and planning. The most elements of it being the list inventory of the things to be validated and therefore the planning schedule. All validation activities referring to critical technical operations, relevant to product and process controls within a firm should be included within the validation plan. It should comprise all the prospective validation, concurrent validation and retrospective validations additionally as re-validation.

The validation master plan should be a summary document and will therefore be brief, concise and clear. It should not repeat information documented elsewhere but should ask existing documents like policy documents, SOP's and validation protocols and reports[15].

The format and content should include:

- Introduction: scope, validation policy, schedule and location.
- Regulatory structure: personnel accountability.
- Plant/ process /product description: rational for inclusions or exclusions and expansion of validation.
- Specific process considerations that are critical and people requiring extra attention.

- List of products/ processes/ systems to be validated, summarized during a matrix format, validation approach.
- Actual status, re-validation activities and future planning.
- Key acceptance criteria.

APPLICATION OF VALIDATION

By definition, validation requires the buildup of documentary evidence regarding a process, item or equipment's or facility. This can be achieved by means of a validation protocol, which details the test to be allotted, the frequency of testing and therefore the result expected (the acceptance criteria). If the validation programmed is intended, and also the protocol issued, before the equipment or facility comes on stream either or before the merchandise manufactured by the method is being validated and remain delivered, then this constitutes prospective validation, former, however, systems or processes are in situ that haven't 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.

CONCLUSION

Current study of literature states that pharmaceutical validation is that the most vital and accepted limit of cGMP. Validation requires the buildup of documentary evidence regarding a process, item or equipment's or facility. Another important term associated with validation process is revalidation. Re-validation is also triggered by the operation of a longtime change of system it may talk to the regular, planned repetition of validation steps. To adapt the necessities of current Good Manufacturing practice (GMP). Pharmaceutical companies should have an overall validation policy which documents how validation are going to be performed. This can include the validation of a manufacturing system, cleaning procedures, analytical methods, in-process control test procedures and computerized systems. Overall I will conclude that the aim of the validation is to indicate that processes involved within the development and manufacture of medicine, like production, cleaning, and analytical testing.

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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