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An Updated & Modern Concept of Validation

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ABSTRACT

Validation is a very important tool in GMP. Main aim & objective of GMP to all Pharmaceutical agencies are to provide a good & reasonable quality of Pharmaceutical products to people. To get that desired quality Validation is great support to all Pharmaceutical & other industry people. Validation is also a very important tool to save money, time, labourer, waste material etc. There are different types of Validation used all over the world by which we can achieve our goal very easily. In this review it is briefly described scope, importance, objectives & types of Validation as per international norms. Now days it became so important that without validation any process, method or instrument are not accepted globally.

Keywords: Validation, Quality, Pharmaceutical

INTRODUCTION [1]

Quality is designed and built into the process/method/premises functionality, consistency and repeatability is confirmed by Validation.

Validation is documented evidence that provides a high degree of assurance that a specific process will consistently produce a product that meets its predetermined specifications and quality attributes.

The documented act of proving that any procedure, process, equipment, material, activity or system actually leads to the expected results.

After the requirement for each aspect is determined, the responsible l engineers complete the design and it is again reviewed by the validation team. After the approved designs are constructed and/or installed, the validation cycle continues with the preparation and execution of the validation documents.

Scope of Validation[2] Pharmaceutical validation is a vast area of work & it practically covers every aspect of pharmaceutical processing activity.

However it will point out at least the following areas of for pharmaceutical validation.

Analytical, Instrument calibration, Process utility services, Raw material & packaging material, Equipments, Manufacturing operation, Facilities, Product design, Cleaning, Operator.

Objectives of validation[2]

- Is to form a basis for written procedures for production and process control.
- Which are designed to assure that the drug products have the identity, strength, quality and purity they are represented to possess.
- According to the FDA, the goal of validation is to: "establish documented evidence which provides a high degree of assurance that a specific process will consistently produce a product meeting its predetermined specifications and quality attributes."

Reasons / purpose of validation

- Enable scientist to communicate scientifically & effectively on technical matter.
- Cost saving, reducing testing, & elimination of product retesting.
- Useful for comparison of results compliance to cGMP/GLP.
- For addressing analytical problem to proper form.
- Assurance of Quality
- Safety

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CLASSIFICATION OF VALIDATION

Depending on time when it is performed relative to production it can be classified as:-

A. Process validation [2]

The goal of manufacturing organization is to make the same product reproducibly over the life cycle of the product. Process validation is the total activity which shows that the process will do what it is purported to do. Process validation is a QA tool because Quality standard of a process is established by validation of that particular process.

Objectives of process validation:

The 3 main objectives of process validation are:

- To demonstrate control over the process and finished product.
- To demonstrate that the process will consistently produce product which meets all specifications and quality attributes.
- To generate a knowledge base for the product as well as accommodate any further business needs**.**

Types of process validation:

1. Prospective validation: Also called as premarket validation. Carried out prior to distribution of new product or existing product made under a revised manufacturing processes where such revision may affect product specification or quality characteristic

This is employed when historical data of the product is not available or is not sufficient & in process & furnished product testing is not adequate to ensure reproducibility.

Such validation is conducted prior to release of either new product or product made under revised / new manufacturing process.

2. Retrospective validation: Conducted for a product already being marketed, and is based on extensive Historical data accumulated over several lots and over time.

Some essential elements of retrospective validation:-

- Batches manufactured for a defined period
- Batch size/ strength/ manufacturer/ year
- Master manufacturing/ packaging documents
- Current specifications for active materials/ finished products

3. Concurrent validation: Study is carried out during a course of normal production. It gives assurance of present batch being studied and offer limited assurance regarding consistency of quality from batch to batch.

4. Revalidation: Revalidation means repeating the original validation effort or any part of it, and includes investigative review of existing performance data. This approach is essential to maintain the validated status of the plant, equipment, manufacturing processes and computer systems. Possible reasons for starting the revalidation process include:

- The transfer of a product from one plant to another.
- Changes to the product, the plant, the manufacturing process, the cleaning process, or other changes that could affect product quality.
- The necessity of periodic checking of the validation results.
- Significant (usually order of magnitude) increase or decrease in batch size.
- Sequential batches that fail to meet product and process specifications.

B. Equipment validation [3]

Validation is one of the important steps in achieving and maintaining the quality of the final product batch after batch. Without equipment, we cannot manufacture a product. If equipment is validated, we can ensure that our product is of the best quality.

Qualification: Action of proving and documenting that equipment or ancillary systems are properly installed, work correctly, and actually lead to the expected results. Qualification is part of validation, but the individual qualification steps alone do not constitute process validation.

1. Design Qualification (D.Q) [3]**:** Once the decision to purchase the equipment has been narrowed to a few vendors, the project team is assembled to develop an overall implementation plan.

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- The vendor's previous experience in implementing similar projects
- The vendor's financial stability
- The vendor's guarantee of installation, training and start up support
- The client's degree of confidence in the vendor's ability
- The level of training offered by the vendor

2. Installation Qualification (I.Q): The equipment installation is the qualification of equipment as is to be installed. This qualification involves the coordinated efforts of vendor (equipment manufacturer), the operating department (owner or purchaser of equipment), and the project team that will provide input to the purchase, installation, operation, and maintenance of the equipment.

3. Operation Qualification (O.Q) [4]: The OQ process ensure that the specific modules of the system are operating according to the defined specification for accuracy, linearity & precision
It include:-
- Identification, objective & identification information.
- Visual inspection.
- Functioning of switches & indicator lights.
- Check & calibration of sensor, airflow rate & pressure etc.
- Cleaning procedure.
- To provide a high degree of assurance that the equipment functions as intended.

Component Operational Qualification of which calibration can be considered a large part.
System Operational Qualification to determine if the entire system operates as an integrated whole.

4. Process Qualification (P.Q) [5]: This stage could be considered the transitional stage for the roles of the individual team players. The project engineer or manager had a significant role prior to this phase to ensure proper delivery, installation, and operation as prescribed by the vendor's purchase order and equipment validation protocol.

C. Analytical method validation [6]:

Introduction: This document is complementary to the parent ICH guideline entitled "Text on Validation of Analytical Procedures," which presents a discussion of the characteristics that should be considered during the validation of analytical procedures.

1. Accuracy: The accuracy of an analytical procedure is the closeness of test results obtained by that procedure to the true value. The accuracy of an analytical procedure should be established across its range.

2. Precision: The precision of an analytical procedure expresses the closeness of agreement (degree of scatter) between a series of measurements obtained from multiple sampling of the same homogeneous sample under the prescribed conditions. Three types of Precision is there:

a. Repeatability: Repeatability expresses the precision under the same operating conditions over a short interval of time. Repeatability is also termed intra-assay precision.

b. Intermediate precision or ruggedness: Intermediate precision expresses within-laboratories variations: different days, different analysts, different equipment, etc.

c. Reproducibility: Reproducibility expresses the precision between laboratories

3. Linearity & Range: The linearity of an analytical procedure is its ability (within a given range) to obtain test results which are directly proportional to the concentration (amount) of analyte in the sample.

4. Robustness: The robustness of an analytical procedure is a measure of its capacity to remain unaffected by small changes, by deliberate variations in method parameters and provides an indication of its reliability during normal usage.

5. Specificity [7]: An investigation of specificity should be conducted during the validation of identification tests, the determination of impurities, and the assay.

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The procedures used to demonstrate specificity will depend on the intended objective of the analytical procedure.

6. System suitability parameters [8]: System suitability testing is an integral part of many analytical procedures. The tests are based upon the concept that the equipment, electronics, analytical operations, and samples to be analyzed constitute an integral system that can be evaluated as such.

D. Cleaning validation [9]:

In the manufacture of medicinal products and APIs, the cleaning of facilities and equipment is an important measure to avoid contamination and cross contamination. In compliance with the GMP regulations, cleaning is performed and documented according to the described procedures. In the past, cleaning effectiveness was often monitored only visually.

Importance of cleaning and its validation: Clean environment and clean operations is the heart of pharmaceutical activities. Cleaning is directly related to safety and purity of pharmaceutical products. The desired level of cleanliness is achieved by clean procedure which in turn depends on its validity. Cleaning method if performed confidently, method produces reproducible results.

Reproducibility of results is the heart of the validation procedure.

Needs of cleaning validation:

- Initial qualification of a process/equipment
- Critical change in a cleaning procedure
- Critical change in formulation
- Significant change in equipment
- Change in a cleaning process
- Change in a cleaning agent.

Cleaning validation process [10]**:**

Stage 1: Determine the most appropriate cleaning procedure for the equipment:

1. Generate acceptance criteria data for the contaminant.
2. The cleaning method will be determined by the process, the equipment, the cleaning agents, and the cleaning techniques available.
3. All aspects of the cleaning procedure should be clearly defined in the SOPs by the manual/ CIP/COP.

Stage 2: Develop and validate sampling and chosen analytical methods for the compound (s) being cleaned.

1. Swabbing: Swabs are solvent saturated, cotton, cloth or sponge.

Solvent may be either water or organic solvent like alcohol, etc.

2. Rinse sampling: A measured area of the cleaned surface is rinsed or solvent washed and the solvent is collected and tested for traces of contaminants.

3. Placebo method: This sampling can be used to detect residues on equipment through the processing of a placebo batch subsequent to the cleaning process.

Stage 3: Interim report

Generate interim cleaning validation reports on a clean by clean basis detailing the acceptability of the cleaning procedure for the equipment and the product. This is only required when there is a long time gap between manufacturing of the validation runs.

Stage 4: Generate a cleaning validation reports detailing the acceptability of the cleaning procedure for the equipment and the product.

This report should give a full detailed background and introduction to the cleaning validation study and should evaluate all data generated with respect to the acceptance criteria employed for the study.

E. Personnel validation: [11]

The body of persons employed by or active in an organization, business, or service administrative division of an organization concerned with the body of persons employed by active in it and often acting as a liaison between different departments. Personnel

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in the pharmaceutical industry may be from:
1. Quality assurance,
2. Quality control,
3. Manufacturing,
4. Technical,
5. H. R etc.

Personnel issues:
1. Hygiene and clothing,
2. Duties of key personnel,
3. Training,
4. Qualification & Responsibility.

Procedure for the personnel validation:
- Chemists should go through all the SOP'S and test procedures before the start of work.
- Trainee chemist should only be given analysed samples for one week.
- Results obtained by chemist should be compared with previous results obtained by trained personnel.
- Samples of unknown batch number should be given for complete analysis and the same should be carried out by trained personnel.
- The results of both should be comparable and is within the limit of two percent variation.

CONCLUSION

Four basic requirements of cGMP are safety, identity, strength and purity which can be achieved by proper validation. Pharmaceutical industry uses expensive materials, sophisticated facilities, equipment and highly qualified personnel. Efficient use of these resources is necessary for the continued success of the industry. The cost of product failures in the means of rejects, reworks, recalls complaints—is a significant part of the total production cost. To reduce the above problems, detailed study and control of the manufacturing process validation is necessary.

↓ REFERENCES

1. R. A. Nash, A. H. Watcher: A Pharmaceutical process Validation, Marcel Dekker Inc., New York, 2003.
2. M. Potdar Current Good Manufacturing Practices, Pharma book Syndicate, Hydrabad, 2006.
3. S. I. Haider , Pharmaceutical Master Validation Plan: the ultimate guide to FDA, GMP and GLP compliance: C R C press, Florida, 2001.
4. http://www.validation-online.net/process-qualification.html
5. Sravya K., Jena S. B., Goje A., Prasad D. N.; Equipment Qualification for RMG, FBD, Blender & Compression Machines-An Overview; Int. J. of Pharmacy & Biotechnology Technology; 2011; 1(3); 190-200.
6. Vogel's: The text book of quantitative chemical analysis, Pearson Education, 1145-52.
7. G. R. Chatwal: Pharmaceutical chemistry-inorganic, Himalaya Publishing House, New delhi 18-26.
8. http://www.chromatographyonline.com.
9. L. Nandhakumar, G. Dharmamoorthy, S. Rameshkumar and S. Chandrasekaran; An overview of pharmaceutical validation: quality assurance view point; Int. J. of research in pharmacy and chemistry; 2011; 1(4); 1004-1014.
10. http://www.apic.cefic.org/pub/4CleaningVal9909.pdf
11. http:// www.personnel validation\detailmini.jsp.htm