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Overall Compilation On Validation And Its Significant Approaches In Pharmaceuticals

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Abstract: The purpose of compilation of this review is to highlight the significant applications of validation and its regulatory aspects. The word validation means assessment of validity or an act of proving effectiveness of any system, object, process or proposed design. It is a team effort as it involves people from various disciplines. Validation is a process of establishing documentary evidence that a procedure, activity or test maintains the desired level of compliance at every step. It assures that a specific process consistently gives a product of high quality. Apart from compliance of product with standard, it is very necessary that the process used must produce the desired results reproducibly. The goal of the validation is to ensure that quality is maintained at every stage and not just at the end, so validation activities include training on production material and operating procedures, training of people involved and monitoring of the whole system as well as the process. It confirms that particular equipment has the capability of operating within required parameters. Validation does not improve only processes but also represents that the processes have been properly developed and are under control. Hence validation is considered to be an integral part of quality assurance.

Key words: Validation, cGMP, Regulatory issue, Qualification, Reproducibility.

INTRODUCTION

WHO defines validation as the documented act of proving any procedure, process, equipment, material, activity or system that actually leads to the expected results. As per cGMP guidelines, validation studies are an essential part of current good manufacturing practice (cGMP) and should be conducted in accordance with predefined protocols. USFDA defines validation as establishing documented evidence which provides high degree of assurance that a specific process will consistently produce a product meeting the quality characteristics. European Union (EU) definition tells that validation is documented evidence that the process, operated within established parameters, can perform effectively and reproducibly, to produce a medicinal product meeting its predetermined specifications [1, 2].

HISTORY

Since 1963, the process validation has been a legal requirement. 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. The concept of validation was first developed for equipment and processes and used in delivery of large pieces of equipment that would be manufactured, tested, delivered and accepted according to a contract. Bernard T. Loftus was director of drug manufacturing in the Food and drug administration (FDA) in the 1970s,

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when the concept of process validation was first applied to the pharmaceutical industry and became an important part of current good manufacturing practices (cGMP). The goal of the validation is to ensure that quality is built into the system at every step. Validation activities include training on production material and operating procedures, training of people involved and monitoring of the system during production [2, 3].

CONCEPT OF VALIDATION

Validation is an integral part of quality assurance that involves the systematic study of process, system and facilities aimed at determining whether they perform their intended function consistently as specified. A validated process is one which provides a high degree of assurance that uniform batches will be produced that meet the required specification. Validation is creating documented evidence that establishes a high degree of certainty that a particular process will consistently produce a product that provides quality attributes. Appropriate and complete documentation is recognized as crucial for the validation. Standard Operating Procedures (SOPs), production formulas, detailed documentation batch change control, experimental reporting systems, analytical documents, reports development and validation protocols are an integral part of validation. The validation of the documentation provides a source of information for the ongoing operation of the plant and is a resource that is used in the subsequent process of development or modification activities[3, 5].

REASONS FOR VALIDATION

The development of a drug product is a complex process involving drug discovery, laboratory testing, animal studies, clinical trials and regulatory registration. In order to further enhance the effectiveness and safety of the drug after its approval, many regulatory agencies specially FDA requires that drug must be tested for purity, identity, strength, quality and stability. Due to this reason pharmaceutical validation is required. FDA, or any other food and drugs regulatory agency around the globe not only ask for a product that meets its specification but also require that process, procedures, intermediate stages of inspections, and testing adopted during manufacturing are designed such that they produce consistently similar, reproducible results which meet the quality standard. This is to maintain and assure a higher degree of quality of food and drug products[4].

OBJECTIVES OF VALIDATION [5, 6]

• The manufacturing process, in addition to the individual equipment, must be validated.
• To design a robust manufacturing process that consistently produces a drug product with minimal variation.
• The product adheres to quality criteria of purity, identity, and potency.
• Major changes after the initial validation will result the necessity for subsequent revalidation.
• Process validation is must to ensure a robust product that is highly reproducible over time.

WHY IS VALIDATION REQUIRED? [5, 6]

- It would not be feasible to use the equipment without knowing whether it will produce the desired product.
- The pharmaceutical industry uses expensive materials, sophisticated facilities, costly equipment and highly qualified personnel. Hence validation is must to minimize wastes.
- The efficient use of resources is necessary for the continuous success of the industry.
- Validation is necessary if failure is to be reduced and productivity to be improved.
- Pharmaceutical industries are concerned about validation for assurance of quality, cost reduction and government regulation.

SIGNIFICANCE OF VALIDATION[5, 6]

• Gives full information about the processes involved in manufacture of drug.
• Decreases the risk of regulatory non-compliance.
• Ensures smooth running of a process.
• Avoids financial losses by means of controlling the production and quality of a drug product.
• Allows real time monitoring and adjustment of process.
• Decreases the risk of preventing problems and assures the smooth running of the process.
• Enhances ability to statistically evaluate process performance and product variables e.g.
individuals; mean; range; control limits.
• Enhances data and evaluation capabilities and increased confidence about process reproducibility and product quality.
• Improves ability to set target parameters and control limits for routine production, correlating with validation results.

MAJOR PHASES IN VALIDATION[1, 2]

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, handling of finished dosage forms, equipment qualification, installation qualification, master product 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: This is also called 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 to the production process and that all SOPs have been followed. At this stage, the validation team comprising of individuals representing all departments also assures that there have been no deviations that can result in revalidation. A careful design and validation of systems and process controls can establish a high degree of confidence that all batches produced will meet their intended specifications. It is assumed that throughout manufacturing process, operations are conducted in accordance with principle of cGMP.

STRATEGY FOR VALIDATION OF METHODS

The validity of a specific method should be demonstrated in laboratory experiments using standards that are similar to the unknown samples analyzed in the routine. The preparation and execution should follow a validation protocol format written as follows[7, 8]:

• Develop a validation protocol or operating procedure for the validation.
• Define the application purpose and scope of the method.
• Define the performance parameters and acceptance criteria.
• Define validation experiments.
• Verify relevant performance characteristics of the equipment.
• Select quality materials, e.g., standards and reagents.
• Perform pre-validation experiments.

• Adjust method parameters and/or acceptance criteria, if necessary.
• Perform full internal (and external) validation experiments.
• Develop SOPs for executing the method routinely.
• Define criteria for revalidation.
• Define type and frequency of system suitability tests and analytical quality control (AQC).
•Document validation experiments and results in the validation report.

VALIDATION MASTER PLAN

Validation master plan is an approved written plan of objectives and actions stating how and when a company will achieve compliance with the cGMP requirements regarding validation. It is a document that describes how and when the validation program will be executed in a system. It outlines the principles involved in the qualification of a facility, defines the areas and systems to be validated and provides a written program for achieving and maintaining a qualified facility with validated processes. It is the foundation for the validation program and should include process validation, facility and utility qualification and validation, equipment qualification, cleaning and computer validation. A validation master plan is a key document in the GMP regulated pharmaceutical industry. It helps to summarize the company's overall philosophy, intentions and approaches to be used for establishing performance adequacy. The validation master plan should provide an overview of the entire validation operation, its organizational structure, its content and planning. It should comprise all prospective, concurrent and retrospective validations as well as re-validation. The validation master plan is a summary document and should therefore be brief, concise and clear[9].

VALIDATION PROTOCOL

Validation Protocol is a written plan of actions stating how process validation will be conducted. It specifies who will conduct the various tasks and define testing parameters; sampling plans, testing methods and specifications; specifies product characteristics, and equipment to be used. It also specifies the minimum number of batches to be used for validation studies. This document gives details of critical steps of the manufacturing process that should be measured, the allowable range of variability and the manner in which the system will be tested. It must tell the acceptance criteria and who will sign/approve/ disapprove the conclusions derived from such a scientific study[3, 8].

VALIDATION TEAM[8, 10]

A multidisciplinary team is primarily responsible for conducting and supervising validation studies. Personnel qualified by training and experience in a relevant discipline may conduct such studies. The working party would usually include the following staff members such as;

• Head of quality assurance.
• Head of engineering.

- Validation manager.
- Production manager.
- Specialist validation discipline: all areas.
- The major functions of validation team are:
- The validation team must prepare the site validation master plan with the specific requirements as per the company policy.
- Meet regularly, to discuss the progress and compliance with the validation plan and schedule.
- Determine the equipments to be validated and the extent of validation to be carried out.
- Determine the frequency of validation.
- Prepare and evaluate the suitability of the protocols.
- Verify the adequacy of the tests used for proving that the objectives are achieved.
- Check and approve the compiled reports.
- Maintain records of validation studies and inform to the Corporate Quality Assurance of progress in terms of validation plan and schedule.

WHAT IS VALIDATED? [11, 12, 13]

General

All process steps, production equipment, systems and environment, directly relevant to the production of sterile and non-sterile products must be formally confirmed. All major packaging equipment and processes should be validated. All ancillary systems, which have no direct effect on product quality, have to be validated by a technical documentation.

Facility

It includes validation of the Manufacturing Area Design and Personnel & material flow, etc.

Process Equipment and Design

Process steps and equipment description, formulation, packaging, washing, equipment and cleaning, etc.

Utility Systems Design

Raw / steam cleaned, purified water, compressed air, air conditioning, vacuum, power, lighting, cooling water, wastewater, etc.

Computerized Systems Design

Information system, automated laboratory equipment, automated manufacturing equipment, electronic record set.

Following validations are required for any industry:

Cleaning validation (CV)

The term CV is used to describe the analytical investigation of cleaning. The means for evaluating the effectiveness of cleaning includes cleaning and disinfecting surfaces, sampling and inspection of product residues,

cleaning residues and bacteria contamination. The validation protocol should develop the criteria for acceptance, including chemical and microbiological specifications, limits of detection and the selection of sampling.

Method Validation (MV)

MV provides documented evidence that the internally-developed test methods are accurate, robust, efficient, reproducible and repeatable. The validation protocol should be based on background documentation on the reasons for determining the method detection limit and sensitivity.

Computer Validation

Computer validation is a proof to ensure systems are consistently documented in accordance with the predetermined specifications and quality function attributes throughout their lifecycle. Important aspects of this approach are the validation of formal management design (through a specification process), system quality (through systematic review and testing, risk (through the identification and evaluation of new and critical functions) and lifecycle (through sustainable change control).

TYPES OF VALIDATION[14, 15, 16]

1. Process Validation

Process validation is the means of ensuring and providing documentary evidences that process within their specified design parameters are capable of repeatedly and reliably producing a finished drug product of reliable quality.

Prerequisites for process validation

- Before process validation is started, the manufacturing equipments and formulation must be carefully observed.
- The pharmaceutical studies like stabilities, studies of drug, drug-drug interaction, and drug interaction with packaging materials must be checked.
- Facilities of the premises as per GMP guidelines are a major need of process validation.
- Water, air and power supply in the manufacturing section must be carefully checked.
- Proper training and motivation of personnel are prerequisites for successful process validation.

Procedure for process validation

i) Installation qualification (IQ)

This ensures that all major equipments have been installed in accordance with manufacturer recommendation in a proper manner and placed in an environment suitable for its intended purpose. It represents that the process or equipment meets all specifications, is installed correctly, and all required components and documentation needed for continued operation are installed properly. IQ is a proof that the equipment or system has been documented, developed, and installed in accordance with design drawings, vendor recommendations and in-house requirements.

ii) Operational qualification (OQ)

This is done to provide a high degree of assurance that the equipment works as intended. It is based on time to time accurate calibration of the equipments. It demonstrates that all facets of the process or equipment are operating correctly. All new devices should be fully taken into service before the start of OQ to ensure that the device is fully functional and that documentation is complete.

iii) Performance qualification (PQ)

It is performed to verify that the process is reproducible and is consistently producing a quality product. It demonstrates that the process or equipment performs as intended in a consistent manner over time. The goal of PQ is to produce a documented proof that particular equipment can perform satisfactorily while operating for a longer period at a defined operating point. PQ requires minimum three product batches for in-process and product testing. The PQ documentation should be on standard manufacturing procedures and describe the sampling and testing methodology.

iv) Design qualification (DQ)

It demonstrates that the proposed design will satisfy all the requirements that are defined and detailed in the user requirements specification (URS). Satisfactory execution of DQ is a mandatory requirement before procurement of the new design. The purpose of DQ is the planning of a manufacturing process including generation of user requirement specifications, verification of user requirement specification, supplier evaluation / audit, product quality impact assessment, factory acceptance test (FAT), site acceptance test (SAT) and commissioning procedures.

v) Component qualification (CQ)

It is a relatively new term developed in 2005. This term refers to the manufacturing of auxiliary components to ensure that they are manufactured to the correct design criteria. This can include packaging components such as folding cartons, shipping cases, labels or even phase change material.

2. Analytical method validation

Analytical method validation confirms that the analytical procedure employed for a specific test is suitable for its intended use. In order to validate an analytical procedure, certain characteristics are studied and if satisfactory results are obtained for these characteristics then method may be considered as validated.

According to WHO guidelines, there are several characteristics that must be validated for any analytical method:

Accuracy

It can be defined as the extent to which test results generated by the method agrees to the true (standard)

value. Accuracy of analytical method may be determined by the assay method used on a highly pure substance and compare it with the same material with a known established method.

Precision

Precision may be defined as the degree of agreement among a series of individual test results. The precision of analytical method is usually expressed as the standard deviation of a series of measurement. Precision is determined by taking sufficient number of readings of any experiment and then finding similarity among these observations. Suppose that one analyst shows observations in the form of 97.5%.97.6%, 97.9% and second analyst shows experimental results as 93.8%, 98.0%, 96%. It means first analyst gave precise result.

Limit of detection

Limit of detection may be defined as lowest amount of analyte in a sample that can be detected.

Linearity

The linearity of an analytical method may be defined as its ability to elicit tests that are directly proportional to the concentration of analyte in sample within a given range.

Range

The range of a method is defined as the interval between the upper and lower levels of analyte that can be determined using the method upto a suitable accuracy and precision.

Selectivity

The selectivity of a procedure is its ability to measure the analyte in a manner that it is free from other component (impurities or other degraded material present in trace amount) in the sample being analyzed.

Sensitivity

It is the capacity of test procedure to record small variations in concentrations.

Repeatability

It refers to the production of identical results, when a procedure is repeated under same set of conditions like same reagent, equipment, settings, laboratories etc.

Ruggedness

It is a measure of reproducibility of test results obtained by the analysis of same sample under a variety of operational conditions like different laboratories, different analysts, different instruments and different lots of reagent. The ruggedness of an analytical method is determined by analysis of aliquots of a sample in different laboratories by different analysts using different operational conditions. If difference of test results in such cases is under tolerable limits, the method is considered to be validated for ruggedness.

Robustness

The robustness of an analytical method may be defined as a measure of its capacity to remain unaffected by small but deliberate variations in operational parameters. Thus it provides an indication of the reliability of a method during its normal use. It can be simplified by the suitable example as: for determination of the robustness of a new chromatographic procedure, operational parameters like flow rate, column temperature, sample injection volume, mobile phase and composition are varied within specific range and their quantitative influence on the test results is determined. If the influence of the parameter is within a previously specified tolerance, the chromatographic procedure is considered to be validated for robustness.

3. Cleaning validation

Cleaning validation is a documented proof that, equipments and utensils are cleaned, maintained and sanitized at appropriate intervals to prevent contamination of products. Cleaning validation is required due to following reasons:

- It is a customer requirement.
- It is a regulatory requirement for manufacturing of active pharmaceutical ingredients.
- It assures quality of a process.
- It ensures safety and purity of a product.
- It confirms the accuracy and reproducibility of results.

Cleaning Reagents

Reagents used for cleaning are generally different types of chemical agents like surfactants, liquid soaps or liquid detergents. The cleaning agent must be compatible with the area/equipment to be cleaned. The concentration of cleaning agents must be decided on the nature of agents as well as type of equipment to be cleaned and the level of cleanliness required.

Validation method for cleaning

a) Sampling

For validation of cleaning sampling is required. This is done by taking samples for the surfaces that has been cleaned. Sampling is done by means of swab and rinses or solvent wash. Swabs are cotton plugs saturated with a suitable solvent (water, alcohol). The swab is used to collect sample from the cleaned surface. This swab is now tested for determination of contaminants present in it. For sampling by rinsing method, a measured area of the cleaned surface is rinsed or washed with solvent. This solvent is collected and tested for traces of contaminants.

b) Testing of the sample

There are different testing methods used for detection of residual contaminants after cleaning like visual inspection (Qualitative and rough estimation) and Analytical methods like spectroscopic techniques to qualitative and exactly determine the amount of residual contaminants and chromatographic techniques.

4. Computer system validation

In 1983, FDA published a guide to the inspection of computerized systems in pharmaceutical processing, also known as the 'bluebook'. Recently both the American

FDA and the UK Medicines and Healthcare products regulatory agency have added sections to the regulations specifically for the use of computer systems. In the UK, computer validation is covered in Annex. 11 of the EU GMP regulations (EMEA 2011). The FDA introduced 21 CFR Part 11 for rules on the use of electronic records, electronic signatures (FDA 1997). The FDA regulation is harmonized with ISO 8402: 1994, which treats "verification" and "validation" as separate and distinct terms. The computer systems require proper validation so as to assure that it provides satisfactory data having reproducibility. The computerized operations that should be validated before use include computer network, battery backup, input/output check, process documentation, shut down recovery, time to start and shut down, date reproducibility and sensitivity of results.

ELEMENTS OF VALIDATION[3, 8, 17]

Prospective validation

It refers to the validation process performed during the initial development stage of a product or a process. It is required during process development stage, product development stage, formulation development, defining experimental programme and establishing full experimental design. During initial developmental stage, prospective validation is performed until satisfactory performance and results are obtained. Most validation efforts require some degree of prospective experimentation in order to generate validation support data. This validation is usually carried out prior to distribution either of a new product or a product made under a revised manufacturing process performed on at least three consecutive batches.

Concurrent validation

After performing the prospective validation, the concurrent validation is carried out during the normal production stage of product. This is required for providing confirm documentary evidence that manufacturing process is in statistical control. In this approach only critical processing steps are evaluated by testing the finished product as well as important process. For example, in tablet manufacturing unit the concurrent validation is done by assessment of critical parameters like particle size/granule size distribution, moisture content, weight variation, tablet hardness, disintegration time, dissolution time and content uniformity. All data are collected simultaneously with the implementation of the process, to demonstrate sufficient information to process reproducibility. This is normally performed by conducting in-process testing and/or monitoring of critical operations during the manufacture of each production batch. This validation involves in monitoring of critical processing steps and product testing. This helps to generate documented evidence to show that the production process is in a state of control.

Retrospective Validation

This is based on analysis of accumulated data on the assumption that composition, procedures and equipment remain unchanged. If result of retrospective validation is satisfactory then process is not in need of immediate attention and it can be carried out as such. Retrospective validation is only acceptable for well established processes and will be inappropriate where there have been recent changes in the composition of the product, operating procedures or equipment.

Revalidation

Revalidation is the repetition of a validation process or a part of it. GMP guidelines state that revalidation is recommended whenever there are significant changes in equipment, process or starting materials of any process. Some conditions strictly require revalidation like change in location or site of manufacturing plant, change in equipments and facilities, change in raw material and primary packaging material, sequential failure of batches for a process or product specifications.

Revalidation may be divided into two broad categories:

i) Revalidation after changes:

Revalidation must be performed on introduction of any changes affecting a manufacturing and/or standard procedure. Such changes may include those in starting material, packaging material, manufacturing processes, equipment, in-process controls, manufacturing areas, or support systems (water, steam, etc.). Every such change requested should be reviewed by a qualified validation group, which will decide whether it is significant enough to justify revalidation and, if so, its extent.

ii) Periodic revalidation:

It is well known that process changes may occur gradually even if experienced operators work correctly according to established methods. Similarly, equipment wear may also cause gradual changes. Consequently, revalidation at scheduled times is advisable even if no changes have been deliberately made.

VALIDATION REPORT[2]

A written report should be available after completion of the validation. If found acceptable, it should be approved and authorized (signed and dated). The report should include the following:

- Title and objective of study;
- Reference to protocol;
- Details of material;
- Equipment;
- Programmes and cycles used;
- Details of procedures and test methods;
- Results (compared with acceptance criteria); and

- Recommendations on the limit and criteria to be applied on future basis

REGULATORY BASIS FOR VALIDATION[18, 19]

Since 1970s, the concept of validation is associated with current good manufacturing practice (cGMP) regulations. The Drug Product Quality Assurance Program of the 1960s and 1970s involved sampling and testing of finished batches of clinically significant drugs, then taking legal action against violative batches of drugs. This approach was not much satisfactory because samples are not representative of all batches. Finished product testing for sterility does not assure that the lot is sterile. Several incidents refocused FDA's attention to process inspections. FDA found serious content uniformity problems for several products (digoxin, digitoxin, prednisolone and prednisone) that were the result of poorly controlled manufacturing processes. FDA investigations did find deficiencies in the manufacturing process and there was no proof that the products were sterile. In the early 1990s, the concept of Pre-approval Inspection (PAI) came into existence and assured that approved validation protocols and schedules were designed for manufacturing. The comprehensive development, scale-up, bio-batch and commercial batch validation data were required in order to obtain a successful regulatory PAI audit. There are several benefits for validation of a product / process. First, manufacturers conform to cGMP regulations by proper validation. Second, good business indicates that a manufacturer avoids the possibility of rejected or recalled batches, Third, validation helps to ensure product uniformity, reproducibility and quality. The validation was initially directed towards prescription drugs, but the FDA Modernization Act of 1997 expanded the control of validation for manufacturing of over-the-counter (OTC) drugs to ensure compliance with cGMP.

Process validation for drugs is a legally enforceable requirement which states that, a drug product is deemed to be adulterated if its quality characteristics do not conform to current Good Manufacturing Practices requirements (cGMP). Part 21CFR 210 & 211 of cGMP specifies the validation of drug products. The validation of biologics has been represented in Part 21CFR 600 and validation of medical devices is in Part 21CFR 800 of cGMP.

VALIDATION EXAMPLES[19, 20, 21]

Validation of tablets

The tablet manufacturing process requires following validation parameters:

Particle size distribution of starting materials, blending time for the powder, granulation time and speed of granulation process, concentration of granulating fluid (binders), drying time of granules and final moisture content of granules, granule size distribution and its active content, tablet hardness, disintegration and dissolution time of tablets, tablet thickness, content uniformity of the tablets. For film coated tablets some additional parameters are required like concentration of coating solution, spray rate of coating solution, inlet and outlet air temperature, standard specification for coating polymer.

Validation of sterile products

The aseptically filled products must be validated for the parameters, namely sterility test for product and packaging material, sterility during filling sterilization and sealing procedure and leakage tests. All aseptic process must be carried out under grade A environment. The classification of air cleanliness is made on the basis of particles of size 0.5 μm and 5.0 μm present in a cubic meter (Table 1).

Table- 1: Classification of air cleanliness

Grade of Environment	At rest		In operation	
	Permitted particles per m^3		Permitted particles per m^3	
	0.5 μm	5.0 μm	0.5 μm	5.0 μm
Grade A	3500	0	3500	0
Grade B	3500	0	3500	0
Grade C	3,50,000	2000	3,50,000	2000
Grade D	35,00,000	20,000	Not defined	Not defined

Grade A= Class 100 (laminar air flow), Grade B=class 1000 (Turbulent), Grade C =Class 10000, Grade D= Class 10, 0000

Validation of lyophilized product

The validation parameters for lyophilized product include temperature of dryer shelf and pressure inside shelf, physical characteristics (color, texture, and structure) of freeze dried product, solubility characteristics of freeze dried product, residual moisture content of product, time required for reconstitution of dried product, characteristics of reconstituted solution (clarity, absence of particulate matter), stability of reconstituted solution, purity and potency of reconstituted product.

CONCLUSION

Finally it can be stated that validation is the most essential and recognized parameters of cGMP. It is a key element in the quality assurance of a product. Quality is always an important prerequisite while manufacturing any product, that's why drugs must be manufactured to the highest quality levels. Validation performs this task with proper control on quality of product as well as the process utilized for manufacturing the product. Pharmaceutical validation and process control is to show the accuracy, sensitivity, specificity and reproducibility of the methods used by the companies. Pharmaceutical validation also assures batch uniformity and integrity of the product manufactured. Proper validation helps to minimize the high degree of in- process and finished product testing.

The future scope of validation is expanding day by day with the worldwide scale up of pharmaceutical manufacturing. Several manufacturers are also developing strategies to decrease the validation cost and incorporate validation aspects during product design and development. At present validation is not just an FDA requirement; it has become an utmost parameter in World Health Organization (WHO), the Pharmaceutical Inspection Co-operation Scheme (PIC/S), and the European Union (EU) requirements, along with those of Australia, Canada, Japan, and other international authorities in order to have full control on quality attributes of products.

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