DOI: 10.21276/sajp

Scholars Academic Journal of Pharmacy (SAJP) **ISSN 2320-4206 (Online)**
Sch. Acad. J. Pharm., 2017; 6(6): 288-299 **ISSN 2347-9531 (Print)**

(An International Publisher for Academic and Scientific Resources)
www.saspublisher.com

Review Article

Validation: A Significant Tool for Enhancing Qualities of Pharmaceutical Products

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Abstract: Validation means confirmation of quality by with the documentation system. Quality is the main aspect of every pharmaceutical company and it is achieved with the help of validation process. Validation is the documented evidence that the process, procedure, activity or system operated within parameters, can perform effectively and reproducibly to produce a desire quality product. It is a fundamental part of quality assurance because it provides sensitivity, precision, efficiency, and reproducibility, at every stage of various processes which perform for different requirements. Through this overview the writers take the time to provide a summary of validation concept of carrying out validation trials and serve a perception to its significance in the pharmaceutical industry.
Keywords: Validation, Equipment validation, Validation master plan, Documentation.

INTRODUCTION [1, 2]

Validation is action of proving and documenting act, in accordance with the principal of WHO, that any process, equipment, material, procedure, system, activity actually operates effectively and leads to the expected result. Validation means confirmation of quality in equipment system, production processes, software and testing methods. The main aim of every pharmaceutical company is to manufacture products of essential property and quality consistently, at minimum prices. Quality is designed and built into the process, method, premises and functionality, consistency and repeatability is confirmed by validation. The Validation guidelines for finished pharmaceuticals products are describing by FDA regulations in current good manufacturing practice (cGMP) 21 CFR parts 210 and 211. The cGMP regulations charge that manufacturing processes be designed and controlled to assure that in-process materials and the finished product meet predetermined quality requirements and do so consistently and reliably. Process validation is established, in both general and specific terms, by the cGMP regulations in parts 210 and 211.

HISTORY OF VALIDATION [2, 3]

Ted Byers and Bud Loftus FDA officials, was first proposed concept of validation in the mid 1970's in order to improve the quality of pharmaceuticals products. It was proposed to solve the multiple problems of pharmaceutical companies. The first validation activities were focused on the processes involved in good manufacturing practices but quickly spread to associated processes including in all aspects of industries like environmental control, media fill, equipment sanitization and purified water production.

The aim of validation is to ensure that quality is built at every step into the system. it includes so many pharmaceuticals activities like training on production material and operating procedures, training of people involved and monitoring of the system during production.

Various organizations define the validation in various ways like:

- European commission: In 1991- Validation - "Act of proving, in accordance of GMPs that any process actually leads to expected results".
- European commission: In 2000 - Validation - "Documented evidence that the process, operated within parameters, can perform effectively and reproducibly to produce a medicinal product meeting its predetermined specifications and quality attributes."
- ICH: "Process Validation is the means of ensuring and providing documentary evidence that processes within their specified design parameters are capable of repeatedly and reliably producing a finished product of the required quality."
- US FDA: "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."

- WHO: "The documented act of proving that any procedure, process, equipment, material, activity or system actually leads to expected result."

BASIC CONCEPT OF VALIDATION [1, 3]

- Calibration, verification and maintenance of process equipment.
- Requalification or Revalidation.
- Establishing specifications and performance characteristics.
- Selection of methods, process and equipment to ensure the product meets specifications.
- Qualification or validation of process and equipment.
- Testing the final product, using validated analytical methods, in order to meet specifications.
- Challenging, auditing, monitoring or sampling the recognized critical key steps of the process.

VALIDATION OBJECTIVES [3-5]

- To minimize variation between other batches.
- To maintain the growth of all necessary quality assurance system within organization.
- To prove the robustness of the process.
- To allow a valuable degree of assurance of quality of the product.
- To decrease the risk of failing costs and regulatory noncompliance.
- A fully validated process may demand less in-process controls and end product testing.
- To maintain the consistency of the manufacturing operation and reproducibility of the process.

ADVANTAGES OF VALIDATION

- Decreases the risk of preventing problems and by means of this assure the smooth continually of the process.
- Expanded real time monitoring and arrangement of process.
- It is easily done process and moisture sensitive and heat sensitive products can also be processed.
- Improved ability to set target parameters and control limits for regular production, correlating with validation results.
- Enhanced ability to statistically manage process performance and product variables e.g. individuals, mean, range, control limits.
- Enhanced data and analysis capabilities and increased confidence about process reproducibility and product quality.

IMPORTANCE OF VALIDATION

- Assurance of quality.
- Process optimization.
- Time bound.
- Decreasing quality cost.
- Increasing output.
- Decreasing rejections.
- Avoiding of capital expenditures.
- Fewer complaints about process related failures.
- Reduced testing in process and in final products.
- Improved employee awareness of processes.
- Easier maintenance of equipment.

WHY PHARMACEUTICAL VALIDATION? [1, 5-8]

- The fundamental part of quality assurance is validation; it involves the systematic study of process, system and facilities aimed at determining whether they perform their intended function consistently as specified.
- Validation as such does not improve the process but it confirms and assures that the process has been well developed, maintained and it operates as it should.
- Highly efficient personals, detailed facilities and equipment and expensive material use by pharmaceutical industries.
- For reducing batch to batch variation.
- The factual use of basic resources is necessary for the continued growth of industries. The cost of product failure, rejects, reworks, recalls, complaints are the sufficient part of total production cost.
- Pharmaceutical industries are worried about validation due to assurance of quality, cost reduction and government regulation.
- It would not sensible to use the equipment without knowing whether it will produce the desired product.
- To ensure the product quality and uniformity.

WHEN PHARMACEUTICAL VALIDATION?

- For new equipment.
- For total new process.
- Process and equipment has been altered to suit changing priorities.
- Process where end product test is poor and unreliable indication of product quality.
- When major changes have been made.
- For new composition and components.
- For new manufacturing batch and site.
- Change in vendor of API or excipient.
- Change in quality parameters of product during Annual product review[APR]
- For new product and change in product as per SUPAC rules.

VALIDATION DONE BY WHOM?

- Head of quality assurance.
- Head of engineering.
- Validation manager.
- Production manager.
- Specialist validation discipline: all areas.

MAJOR PHASES IN VALIDATION

PHASE I PRE-VALIDATION OR QUALIFICATION PHASE: This phase covers all the 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 II PROCESS VALIDATION PHASE: It is built to check that all established limits of the critical process parameter are valid and that produced the satisfactory products even under the worst conditions.

PHASE III: VALIDATION MAINTENAN PHASE: It needs quick 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 operating 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 that should have resulted in requalification and revalidation.

APPROACH TO PROCESS VALIDATION

Process validation involves a series of activities taking place over the lifecycle of the product and process. This guidance describes process validation activities in three stages:

STAGE1 PROCESS DESIGN: The commercial manufacturing process is defined during this stage based on knowledge gained through development and scale-up activities.

STAGE2 PROCESS QUALIFICATION: During this stage, the process design is evaluated to determine if the process is capable of reproducible commercial manufacturing.

STAGE3 CONTINUED PROCESS VERIFICATION: Ongoing assurance is gained during routine production that the process remains in a state of control.

TYPES OF VALIDATION [1, 5, 6, 9]

ANALYTICAL VALIDATION: The quality of product is determine via testing to verify reliability is being maintain through the lifecycle of product and there is no compromised with accuracy, precision, purity, strength and specifications.

EQUIPMENT VALIDATIION:

The term "qualification" is used for validation of equipment. Qualification is mainly classify as:

- Design Qualification [DQ]: Action of proving that the recommend layout of equipment and system is acceptable for the intended aim.
- Installation Qualification [IQ]: Action of proving that equipment and system is installed or modified according to recommended layout by manufacture.
- Operational Qualification [OQ]: Action of proving that equipment and system can provide operating ranges that defines in purchasing order.
- Performance Qualification [PQ]: Action of proving that equipment and system can perform essentially and consistently, based on the permitted procedure technique and product specification.
- Verification Qualification [VQ]: Action of proving that the equipment and system can carry out successfully and reproducibly, based totally on the authorised technique method and genuinely leads to the expected results and utilizer requisites.
- Safety Qualification [SQ]: Action of proving that the equipment and system is installed and modified follows with the safety necessities of procedure, facility and employees.
- Maintenance Qualification [MQ]: Action of proving that the recommend maintenance schedule of the equipment and system is suitable for the meant reason.
- Re-Qualification [RQ]: It is needed as relocation of equipment, important change and due to growing old.

PROCESS VALIDATION:

According to USFDA "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." It is divided into four parts:

- Prospective validation:
  - It is performing for a new formula; process and facility require to be proven before pharmaceutical manufacturing starts.
  - The validation protocol is executed before the process is put into commercial use.
  - It is commonly taken into consideration proper that 3 consecutive batches/runs with inside the eventually agreed parameters giving product of the preferred fine would represent a proper validation of the process.
  - It is performed prior to the distribution of either a new product or a product made under a modified manufacturing method in which modifications are significant and

can have an effect on the goods characteristics.

- Concurrent validation: In this, monitor processing parameters is perform for current production batches. It help to create the documented evidence which signifies that manufacturing process is in state of control. It is suitable for:
  - When a previous validated process is transfer to contract manufacture or any other new site.
  - Process of manufacturing urgently needed drug due to shortage or absence of supply.
  - Large scale testing and monitoring ensures the desired quality of products with high degree of assurance .

- Retrospective validation:
  - It is perform for a product which already being marketed and validation process depend on collected historical production, testing control and other information.
  - This kind of validation make use of historical facts and information which can be observed in batch document, production log books, lot records, controls charts, take a look at and inspection results consumer complaints or loss of complaints subject, failure file, carrier file and audit report.
  - It is reasonable for properly set up specific methods and could be inappropriate in which there have current changes within the formula of the products, operating procedures, equipment and facilities.

- Revalidation: Revalidation is the repetition of the validation process or a specific part of it. It is performed when:
  - Changes in raw materials (Physical properties such as density, viscosity, particle size distribution and moisture etc. that may affect the process or product).
  - Changes in packaging material (Primary container/ closure system).
  - Changes in the plant/ facility, vendors of API and excipients.
  - Changes in the process (e.g. mixing time, drying temperature and batch size).

VARIETY OF DOCUMENTATION IN VALIDATION PROCESS [4,10-13]

VALIDATION MASTER PLAN:

It is written plan of objectives which is approved and activity define how at the same time organization will achieve compliance with the GMP specifications in regard to validation. The scope of validation is declaring by VMP report and marking the methods to be used for set up the overall performance capacity. The entire validation operation, its organizational layout, content and planning must be defined by VMP. It even holds the calibration and qualification of equipment, summary and conditions of Validation Protocol.

It should contain data on at least the following:

- Title page and authorization (approval signatures and dates)
- Table of contents;
- Abbreviations and glossary;
- Validation policy;
- Philosophy, intention and approach to validation;
- Roles and responsibilities of relevant personnel;
- Resources to ensure validation is done;
- Outsourced services (selection, qualification, management through life cycle);
- Deviation management in validation;
- Change control in validation;
- Risk management principles in validation;
- Training;
- Scope of validation;
- Documentation required in qualification and validation such as procedures, certificates, protocols
- Premises qualification;
- Utilities qualification;
- Equipment qualification;
- Process validation;
- Cleaning validation;
- Personnel qualification such as analyst qualification;
- Analytical method validation;
- Computerized system validation;
- Establishing acceptance criteria;
- Life-cycle management including retirement policy;
- Requalification and revalidation;
- Relationship with other quality management elements;
- Validation matrix;
- References

VALIDATION PROTOCOL:

It must be numbered, signed and dated, and contain as a minimum the following information:

- Protocol approval sheet
- Table of content
- Objective and Scope
- Validation team
- Steps for validation and acceptance criteria
- Process flow chart
- Manufacturing process
- Evaluation of formulation ingredients and packaging material.
- Evaluation of active raw material
- Evaluation of equipment
- Test instrument calibration.
- Product details
- Equipment detail
- Critical process parameters
- In-process specification
- Sampling procedure and testing plan

- Revalidation criteria
- Reference document.
- Change control
- Deviations
- Stability
- Documentation
- Summary
- Conclusion
- Report and approval

VALIDATION REPORT:

After finalization of validation, a written report must be available. It must be approved and authorized, if report is acceptable. The report data must contain as minimum following information:

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

DOCUMENTATION:

A written protocol must be installed that defines how qualification and validation will be carried out. The protocol must be reviewed and accepted. Essential steps and acceptance standards must specify in protocol. A report that include references, the qualification and/or validation protocol have to be prepared, summarizing the results received, commenting on any deviations observed, and drawing the essential conclusions, which includes recommending adjustments important to correct deficiencies. If any addition is plan into protocol must be documented with suitable reason. Documentation is important so that knowledge gained about a product and process is accessible and comprehensible to others involved in each stage of the lifecycle. Documents associated with qualification and validation includes:

- Validation master plan (VMP);
- Standard operating procedures (SOPs);
- Specifications;
- Protocols and reports;
- Risk assessment outcomes;
- Process flow charts;
- Operator manuals;
- Training records;
- Calibration procedures and records;
- Sampling plans;
- Testing plans and methods;
- Statistical methods and results;
- History of qualification or validation;
- Plan for ensuring review of validation status;
- Plan for ensuring maintaining a validated state.

QUALIFICATION OF PREMISES [14-17]

According to WHO in the GMP guidelines it is stated that "Premises must be located, designed, constructed, adapted and maintained to suit the operations to be carried out. Their layout and design must aim to minimize the risk of errors and permit effective cleaning and maintenance in order to avoid cross contamination, buildup of dust or dirt, and in general any adverse effect on the quality of products."

A new facility typically design by engineering process which include has the following phases:

- Conceptual study
- Design development
- Detailed engineering
- Procurement
- Construction
- Pre-commissioning
- Commissioning

It is carried out by a disciplinary team and design validation document should be signed by individual team members. There are many factors of development during this plan:

- Finalization of layout
- Defining all major items of equipment
- Designing pipe work and instrumentation
- Identification of the utility services[e.g. HVAC, steam, water, gas]
- Establishing policy for process control, containment and safety
- Identification of preliminary architectural details, building structure and foundation
- Ensuring the design meets GMPs requirements
- Defining cost estimates
- Detailed design and procurement is next step and it include salient objective:
- To provide detailed design to construction contractor
- To provide a detailed list of equipment and their specification
- To place orders for procurement of major items
- To develop construction strategy and program
- To ensure that all aspects of design qualification are met
- To develop strategy for start-up, commissioning and qualification

Qualification planning ought to be advanced along with the main project planning. The stage of information is needed to be considered for every area. There must be provision inside the settlement in order that contractor presents test strategies and certificates to qualify that the finishes of walls, floors and ceiling meet the standards laid down inside the specs and requisitions. It is really useful to develop a VMP on the begin of the specific design to cover all of the components of the design and set up segment. The

engineers ought to take a look at the system towards the design and creation drawings and make observations and document them.

After the development of building and set up of device is entire, the web page operation qualification [SOQ] commences. The SOQ has salient targets that is to ensure that the structures work and carry out as meant and second, to make sure that employees who will function the systems are trained.

If civil work is involved, these test functions are performed:

- Inspection of the facility vis-à-vis approved layout
- Inspection of floors in each room
- Inspection of painted surfaces in each room
- Determination of dimension of each room
- Inspection of windows, wherever provided
- Inspections of lights in each room
- Inspection of utilities penetration in each room
- Inspection of doors and interlocks
- Acceptance criteria include the following:
- Construction is in accordance with design specifications and GMP requirements
- Floor surfaces are smooth
- Painted surfaces have smooth coverage
- Dimensions of rooms conform to design specifications
- Doors open/close properly and interlock operate according to the design specifications
- Windows; if provided are correct type and are sealed with a material providing smooth surface
- Light is adequate at all work stations and light fixtures are flushed with ceiling/ wall surfaces
- Utilities penetration are correctly installed, labelled and sealed
- Communicators are correctly installed and sealed.

VALIDATION OF GASES [14-20]

In the manufacturing of drugs products, many gases are utilized like nitrogen gas, compressed air, carbon dioxide, etc. Gases directly or indirectly impact on quality. In case of directly impact, gas comes into contact with product or intermediate and in case of indirectly impact; it is released in the environment where manufacturing is being processed. So it is require that gas system must be validated to check that they operate under control. A typical nitrogen gas system include either of a nitrogen bottles, distribution pipes and filtration systems or liquid nitrogen storage tank and vaporizers. On the other hand, compressed air includes air compressors, driers [desiccant or refrigerated], distribution pipes and filtration system.

STEPS INVOLVED IN THE VALIDATION OF GASES ARE AS FOLLOWING:

- Supply of gas of desired purity in adequate quantity. Use of gas at maximum rate must be less than the systems can generate while meeting the pressure requirements.
- Storage facility for gas must be made of suitable material so that it is non-reactive with gas and should be adequate size.
- Like storage facility, distribution system should be made of appropriate material and of adequate size. It should not be interconnected to any other system that could contaminate the gas.

VALIDATION STEPS FOR NITROGEN SYSTEM:

- Storage tank: To perform the validation movement a check list need to be prepare which which include following points:
  - Check the garage tank for conformance to the acquisition specification. Make commentary on its potential in context with the call for.
  - Check whether the material of production comply with the acquisition specifications.
  - Conduct pressure maintain check [hydrostatic or pneumatic test] to determine whether the leak fee is within specifications.
  - Examine document laying down the technique for cleaning the tank after set up.
  - Check and file all stress fees for the tank in addition to additives against the acquisition specifications.
  - Calibrate all strain gauges and sensors, each tracking and controlling. If the power for calibration isn't to be had in-residence, out of doors corporation may be employed.
- Distribution system: the check list for IQ consist of following steps:
  - Confirm the fabric of construction and layout parameters specified via the agency.
  - Compare the design drawing of the structures and the “as-constructed” drawing and observe modifications made in the course of creation.
  - Pressure takes a look at the system and documents to affirm its integrity.
  - Examine the cleansing technique and documented observations following cleaning tactics.

- The check listing for OQ may want to encompass the following steps:
  - Check whether or not all use points have been used for:
  - Gas identification
  - Nonviable particles
  - Microbial matter
  - Check whether numerous worst case places have been examined for purity of nitrogen gasoline and dew point. Dew point checking out is beneficial to make sure that gadget is dry.

- Check whether or not filters had been examined for integrity periodically and documented.

- Performance Qualification [PQ]:

  It is consists of finishing the documentation from the various above noted steps and repeating the trying out precise within the validation protocol. As stated earlier, in case of equipment and systems, PQ may be bear in mind as validation.

VALIDATION OF COMPRESSED AIR STRUCTURES:

In Pharmaceutical corporations there are two kinds of compressed air systems. One, traditional oil lubricated compressors for working contraptions and machinery wherein no touch with product or the environment, wherein product is being manufactured is concerned. Two, an oil free compressed air systems utilized in easy room regions. As an instance handiest oil loose compressed air structures will be taken up for dialogue. Typically oil free compressed air structures includes an oil loose compressor, dryer, storage tank and distribution device. The validation manner of fuel system includes IQ, OQ and PQ.

VALIDATION OF WATER SYSTEM [21-24]

Water is one of the maximum usually used materials vehicle, raw materials, or an ingredient in the production, formulation, and processing of pharmaceuticals and also in the cleaning of manufacturing equipment's. Control of the inorganic, organic impurities and microbiological quality of water is important because propagation of micro-organism is ubiquitous in water and it may occur during the, distribution, refinement and storage of water. The USP identifies numerous grades of water that are desirable to be used in pharmaceuticals, and additionally defines the fine attributes for the producing of pharmaceuticals products according to its criticality as:

- Potable water
- Purified water
- Water for injection
- Sterile water for injection
- Sterile water for inhalation
- Sterile water for irrigation
- Sterile bacteriostatic water for injection

EQUIPMENTS AND SYSTEMS:

- Raw water: Well water supplied with the aid of municipalities with initial treatments like filtration and chlorination and many others.
- Water softening: Softening is a mechanism whereby the hardness ions of calcium and magnesium are exchanged for sodium ions in a column. Softening equipment considerations include:
  - Regeneration frequency
  - Requirements to sanitise the bed.
  - Replacement of resins
  - Monitoring pressure drop and hardness.

- Activated charcoal: These are used to remove chlorine and other organic materials from the water, sand and carbon filtration considerations:
  - Back wash frequency
  - Continuous re-circulation
  - Requirement to sanitize the beds
  - Replacement of carbon
  - Monitoring pressure drops
- Filtration: It is divided into 3 main class:
  - Pre-filtration to remove large particles
  - Micro-filters or "Bacteria retentive filters"[0.22µ size]
  - Ultra filters[Range 0.001-0.01 µm]

- Ion-Exchange: This is used to remove dissolved ionic impurities. De-ionization does nothing to improve the microbiological quality of water and usually contributes significantly to the bacteriological degradation of water. Fixed de-ionization equipment considerations include:
  - Measuring quality and condition at various stages e.g., influent, post anion, etc
  - Varying condition during the service cycle
  - Microbial condition of bed
  - Possible continue re-cycling of water through the resin bed
  - Quality of regeneration chemical e.g., H_2SO_4, HCL, NaOH
  - Condition and quality of air used for air blow on mixed bed units only
  - Dissolved and colloidal silica not detected by conductivity
  - Amines from resins- new and old.
  - Sanitization and re-generation
  - Frequency of regeneration and bed size
  - pH adjustments to meets USP requirements
  - pH measurements problem

- Reverse Osmosis [R.O.]: R.O. treatments will get rid of a huge part of dissolved salts and also particulates, microorganism and pyrogenic substances. It can also be sequenced with electro-de ionization system to get in addition purification of water. Reverse Osmosis considerations include:
  - Integrity test chemical and bacteriological rejection[Feed poor quality of water to unit and perform dye test]
  - Multiple modules- composite permeate
  - Temperature dependent flow rate
  - Sanitization and Flushing residuals time to flush
  - Replacement programs for modules
  - Monitoring flow, Pressure, temperature, pH reject rates and conductivity.
  - Ultra filtration: Some U.F. equipment is very similar to some R.O. equipments

except that the membrane porosity is greatly different.

- Distillation: In presently three methods of distillation are used:
- Single effect thermal distillation
- Multiple effect thermal distillation
- Vapor compression distillation

- Ultraviolet radiation: Validity of this method for pharmaceutical water usage is not validated and remains questionable.
- Heat: The heating and storing of water at 80º has been proven effective to govern the microbial best. This idea is expensive, energy consuming and requires that the storage tank and distribution system be insulated for heat conservations.

STEPS FOR VAIDATION OF WATER SYSTEM:

The critical process parameters and their operating ranges define by validation process. The following steps include in validation of water system:

- Establishing standards for quality attributes and operating parameters.
- Defining structures and subsystems appropriate to provide the desired quality attributes from the available source water.
- Selecting equipment, controls, and monitoring technologies.
- Establishing an IQ stage which include instrument calibration, inspection to confirm that the drawings accurately depict the as built configuration of the water system, and, wherein vital, special checks to affirm that the set up meets the layout requirements.
- Establishing an OQ degree consisting assessments and inspection to verify that the equipment, machine signals, and controls are running reliably and that appropriate alert and action degrees are established. This segment of qualification may overlap with elements of the next step.
- Developing a prospective PQ degree to verify the appropriateness of essential parameter working stages. A concurrent or retrospective PQ is carried out to illustrate device reproducibility over the suitable time period. Throughout this phase of validation, Alert and motion levels for key high-quality attributes and working parameters are confirmed.
- Supplementing a validation protection application (also called continuous validation lifestyles cycle) that includes a mechanism to govern changes to the water system and establishes and consists of out scheduled preventive preservation, which include recalibration of instruments? In addition, validation maintenance includes a monitoring program for critical process parameters and a corrective motion program.
- A graphical representation of validation for water system is given below in fig.1.

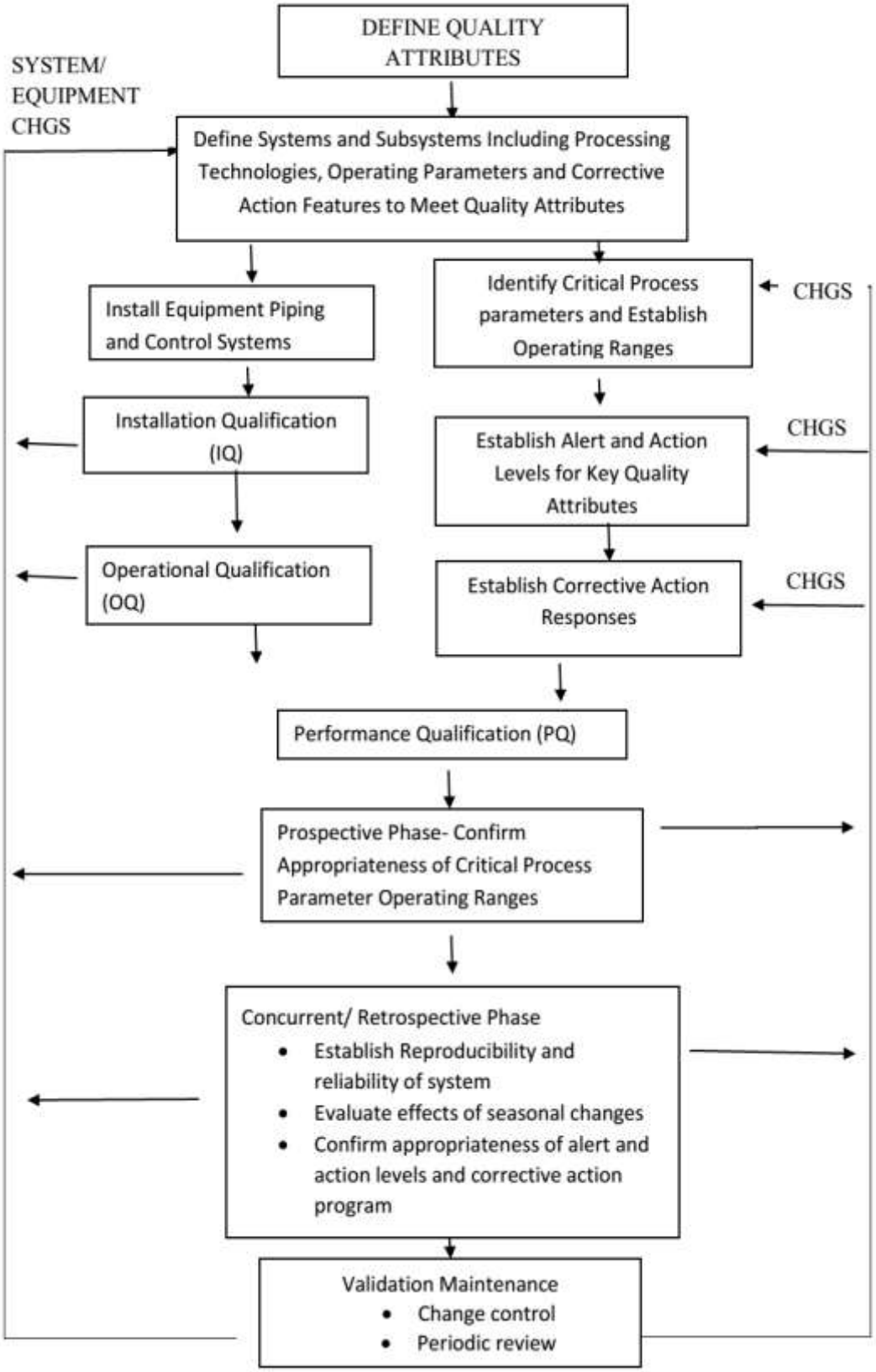
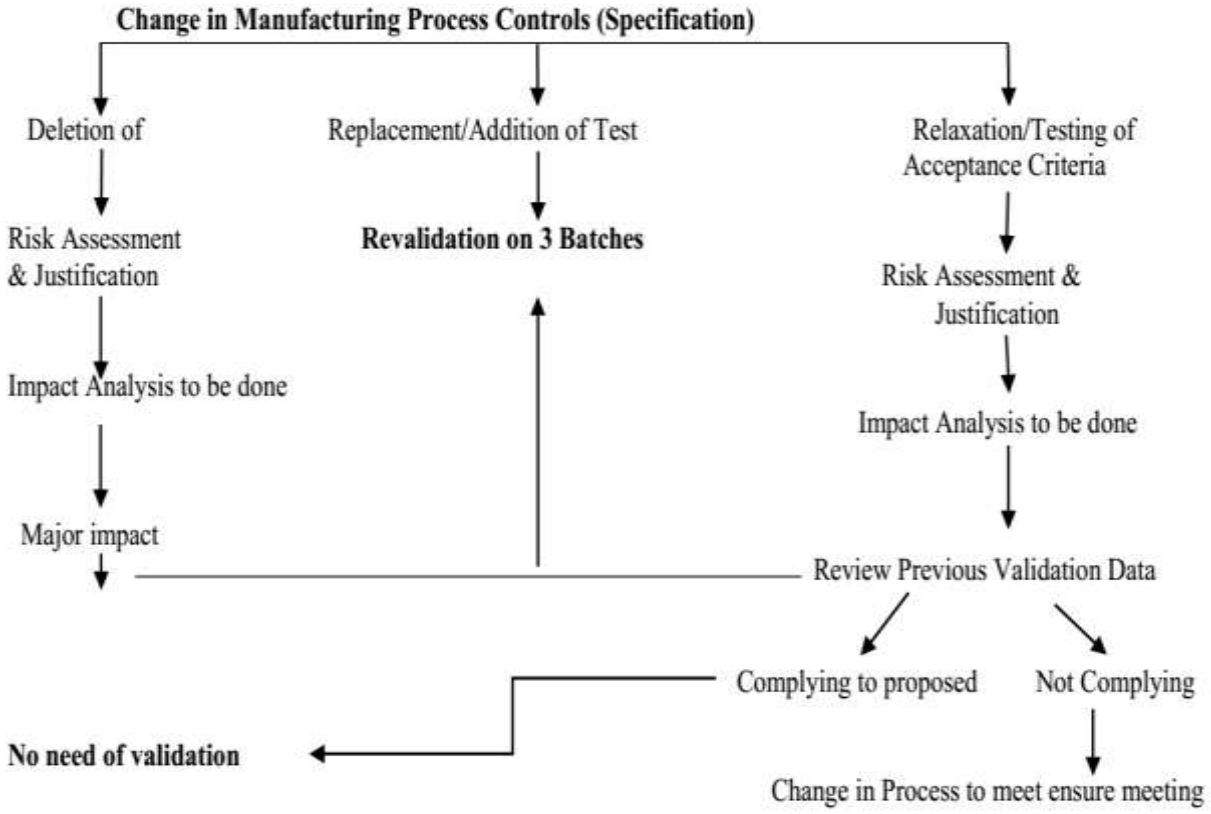
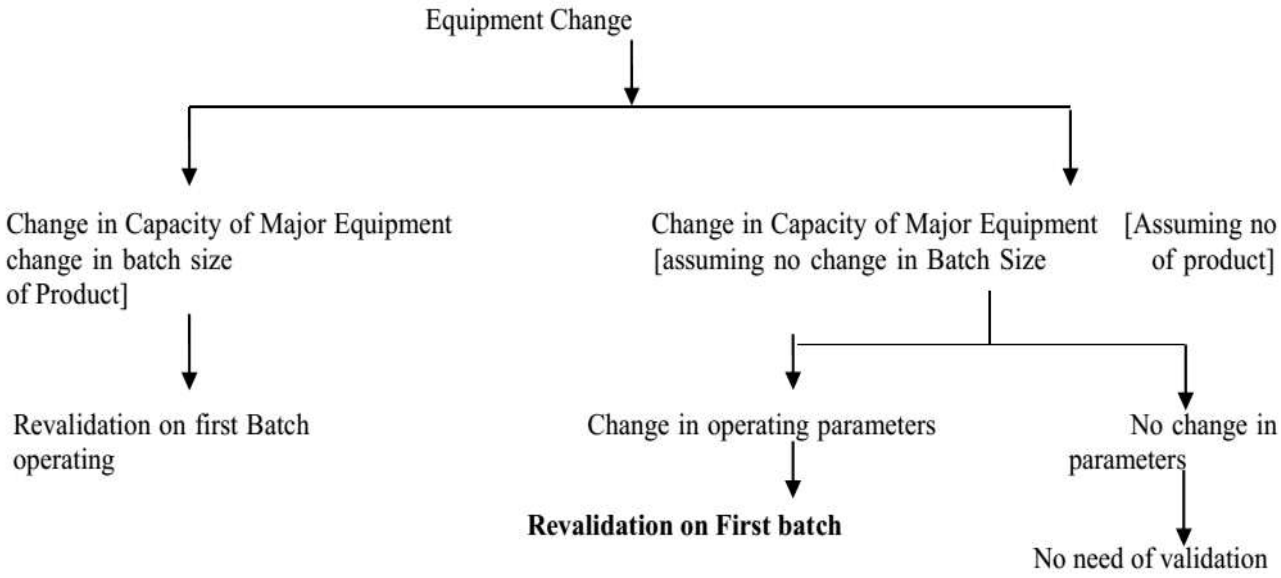


Fig-1: Water system validation life cycle

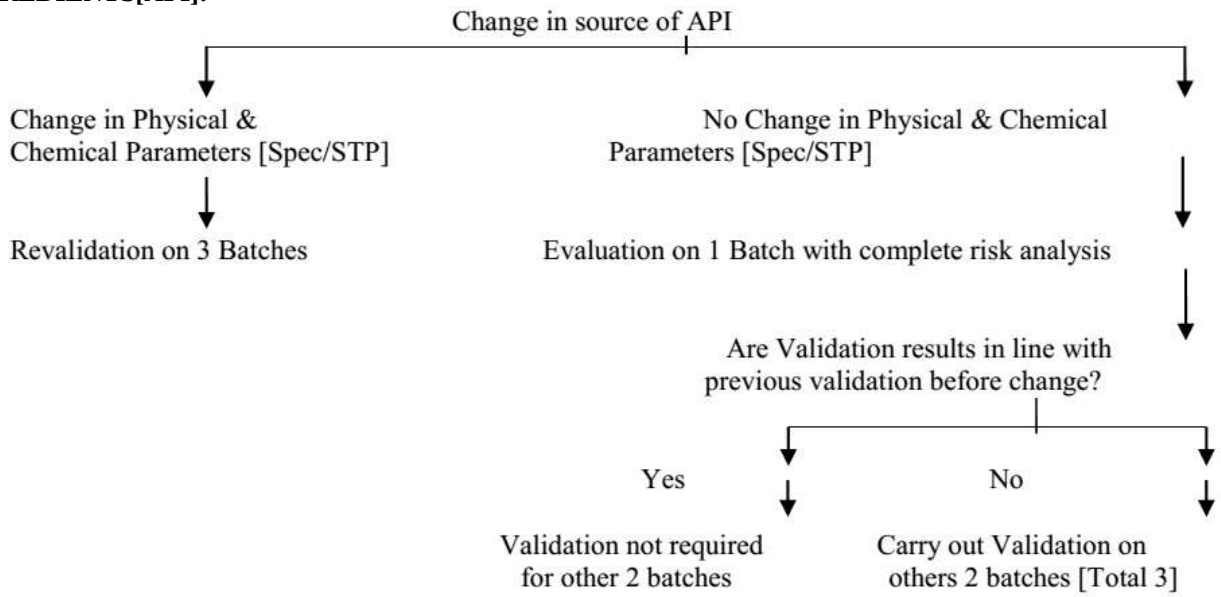
FOR CHANGE IN PROCESS CONTROLS OF MANUFACTURING PROCESS OF DRUG PRODUCTS:



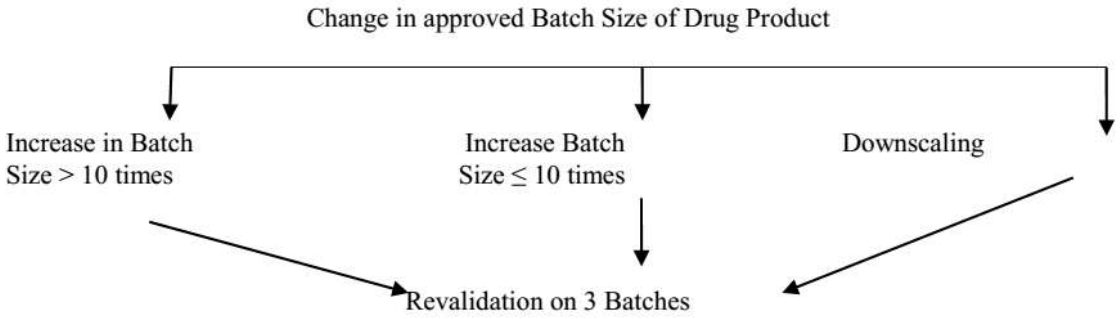
PROCESS VALIDATION DECISION TREE FOR CHANGE IN EQUIPMENT:



PROCESS VALIDATION TREE FOR CHANGE IN SOURCE OF ACTIVE PHARMACEUTICAL INGREDIENTS[API]:



PROCESS VALIDATION DECISION TREE FOR CHANGE IN BATCH SIZE OF DRUG PRODUCT:



CONCLUSION:

From the above study it is very clear that validation is a most important factor to achieve a desirable quality product because its provide high degree of assurance of purity at every stage of product manufacturing process and also in quality testing methods. It also deliver reduction within the cost related with method observation, sampling and testing pharmaceutical validation which cover assay validation, cleaning validation, instrumentation validation or stability analysis.

As well as Qualification of water system is also important because water is raw material for pharmaceutical formulation and also for several functions. Qualification of premises is also necessary to minimize the risk of errors and permits effective cleaning and prevent from cross contamination. Validation of various systems must be accomplished over a time frame with a view to show its reliability and robustness of the system for manufacturing desire quality of product with high degree of assurance and every data must be documented for higher work.

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