Review Article

Pharmaceutical Process Validation: An Overview

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ABSTRACT

The goal of the CGMPs for the 21st Century initiative such as advancing science and technological innovation. Update guidance based on regulatory experience since 1987. Process Validation emphasise on process design elements and maintaining process control during commercialization and communicate that process validation is an ongoing program and align process validation activities with product lifecycle. Process validation also emphasizes the role of objective measures and statistical tools & analyses and emphasizes knowledge, detection, and control of variability and gives assurance on consistent of quality/productivity throughout life cycle of product.

Key words: Process Validation, Process Validation Decision Tree, Process Validation Stages, Validation Acceptance Criteria, Deviation

INTRODUCTION

Pharmaceutical Process Validation is the most important and recognized parameters of CGMPs. The requirement of process validation appears of the quality system (QS) regulation. The goal of a quality system is to consistently produce products that are fit for their intended use. Process validation is a key element in assuring that these principles and goal are met. [1] The process validation is standardization of the validation documents that must be submitted with the submission file for marketing authorization.[2] The process validation is intended to assist manufacturers in understanding quality management system (QMS) requirements concerning process validation and has general applicability to manufacturing process.[3] According to FDA, assurance of product quality is derived from careful and systemic attention to a number of importance factors, including: selection of quality process through in-process and end-product testing. [4]

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REGULATORY REQUIREMENTS FOR PROCESS VALIDATION [1]

FDA regulation describing current good manufacturing practices (CGMPs) for finished pharmaceuticals are provided in 21 CFR parts 210 and 211. The CGMP regulations require 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 required, in both general and specific terms, by the CGMP regulations in parts 210 and 211. The foundation for process validation is provided in § 211.100 (a), which states that "here shall be written procedures for production and process control designed to assure that the drug products have the identity, strength, quality, and purity they purport or are represented to possess". The CGMP regulations regarding sampling set forth a

number of requirements for validation: samples must represent the batch under analysis (§ 211.160 (b)(3)); the sampling plan must result in statistical confidence (§ 211.165(c) and (d)); and the batch must meet its predetermined specifications (§ 211.165(a)). The CGPM regulations also provide norms for establishing in-process specifications as an aspect of process validation. Section 211.110(b) establishes two follow when establishing in-process specifications.

The first principle is that "in-process specifications for such characteristics [of in-process material and the drug product] shall be consistent with drug product final specifications". The second principle is this regulation further requires that in-process specifications "shall be derived determined by the application of suitable statistical procedures were appropriate". The CGMP regulations require that facilities in which drugs are manufactured be of suitable size, construction, and location to facilitate proper operations (§ 211.42). Equipment must be of appropriate design, adequate size, and suitable located to facilitate operations for its intended use (§ 211.63). Automated, mechanical and electronic equipment must be calibrated, inspected, or checked according to the written program designed to assure proper performance (§ 211.68).

In summary, the CGMP regulations require that manufacturing processes be designed and controlled to assure that in-process material and finished product meet predetermined quality requirements and do so consistently and reliability throughout product lifecycle.

PROCESS VALIDATION DEFINITION

According to US FDA

***In 1978,* [5]**

"A validation manufacturing process is one which has been proved to do what it purports or is represented to do. The proof of validation is obtained through the collection and evaluation of data, preferably, beginning from the process development phase and continuing the production phase. Validation necessarily includes process qualification (the qualification of materials, equipment, system, building, personnel), but it also includes the control on the entire process for repeated batches or runs".

***In 1987,* (6)**

"Process validation is establishing documented evidence which provides a high degree of assurance that a specific process (such as the manufacture of pharmaceutical dosage forms) will consistently produce a product meeting its predetermined specifications and quality characteristics".

***In 2008,* (6)**

"Process Validation is defined as the collection and evaluation of data, from the process design stage throughout production, which establishes scientific evidence that a process is capable of consistently delivering quality products".

In 2011,

"The revised guidance also provides recommendations that reflect some of the goals of FDA's initiative entities "Pharmaceuticals CGMPs for the 21st century – A Risk-Based Approach," particularly with regards to the use of technological advances in pharmaceutical manufacturing, as well as implementation of modern risk management and quality tools and concepts".

According to EMEA

In March 2012, (1)

"Process validation can be defined as documented evidence that the process, operated within established parameters, can perform effectively and reproducibly to produce a medical product meeting its predetermined specifications and quality attributes."

Continuous process verification (PCV) has been introduced to cover an alternative approach to process validation based on a continuous monitoring of manufacturing performance. This approach is based on the knowledge from product and process development studies and / or previous manufacturing experience. CPV may be applicable to both a traditional and enhanced approach to pharmaceutical development. It may use extensive in-line, on-line or at-line monitoring and / or controls to evaluate process performance. (7) Process validation should confirm that the control strategy is sufficient to support the process design and quality of the product. The validation should cover all manufactured strengths and all manufacturing sites used for production of the marketed product. (7)

BASIC PRNCIPLE FOR PROCESS VALIDATION (1, 3, 8, 12, 13)

The basic principle for validation may be stated as follows:

Installation Qualification (IQ): establishing by objective evidence that all key aspects of the process equipment and ancillary system installation adhere to the manufacturer's approved specification and that the recommendation of the supplier of the equipment are suitably considered.

IQ considerations are:

- Equipment design features (i.e. material of construction cleanability, etc.)
- Installation conditions (wiring, utility, functionality, etc.)
- Calibration, preventative maintenance, cleaning schedules.
- Safety features.
- Supplier documentation, prints, drawings and manuals.
- Software documented.
- Spare parts list.
- Environmental conditions (such as clean room requirements, temperature, and humidity).

Operational Qualification (OQ): Establishing by objective evidence process control limits and action levels which result in product that all predetermined requirements.

OQ considerations include:

- Process control limits (time, temperature, pressure, line speed, setup conditions, etc.)
- Software parameters.
- Raw material specifications
- Process operating procedures.
- Material handling requirements.
- Process change control.
- Training.
- Short term stability and capability of the process, (latitude studies or control charts).
- Potential failure modes, action levels and worst-case conditions.
- The use of statistically valid techniques such as screening experiments to optimize the process can be used during this phase.

Performance Qualification (PQ): establishing by objective evidence that the process, under anticipated conditions, consistently produces a

product which meets all predetermined requirements.

PQ considerations include:

- Actual product and process parameters and procedures established in OQ.
- Acceptability of the product.
- Assurance of process capability as established in OQ.
- Process repeatability, long term process stability.

Re – Qualification: Modification to, or relocation of equipment should follow satisfactory review and authorization of the documented change proposal through the change control procedure. This formal review should include consideration of re-qualification of the equipment. Minor changes or changes having no direct impact on final or in-process product quality should be handled through the documentation system of the preventive maintenance program.

PROCESS VALIDATION WITHIN THE QUALITY MANAGEMENT SYSTEM (3)

Process validation is part of the integrated requirements of a quality management system. It is conducted in the context of a system including design and development control, quality assurance, process control, and corrective and preventive action. The product should be design robustly enough to withstand variations in the manufacturing process and the manufacturing process should be capable and stable to assure continued safe products that perform adequately. Corrective actions often identify inadequate processes/process validations. Each corrective action applied to a manufacturing process should include the consideration for conducting process validation/ revalidation.

Process Validation Decision

The following model may be useful in determining whether or not a process should be validated:

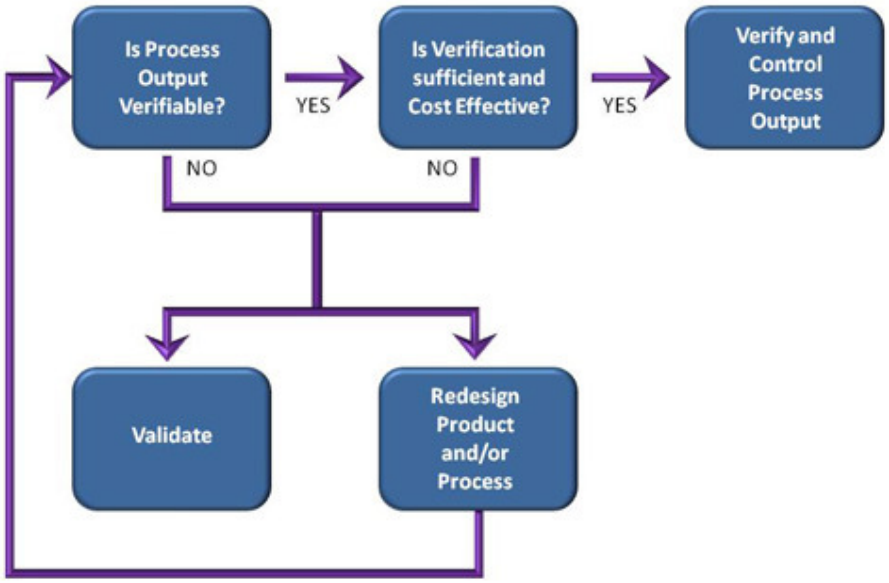


Figure 1: Process Validation Decision Tree

The manufacturer should consider whether the output can be verified by subsequent monitoring or measurement (A). If the answer is positive, then the consideration should be made as to whether or not verification alone is sufficient to eliminate unacceptable risk and is a cost effective

solution (B). If yes, the output should be verified and the process should be appropriately controlled (C). If the output of the process is not verifiable then the decision should be to validate the process (D): alternatively, it may be become apparent that the product or process should be redesigned to reduce variation and improve the product or process (E).

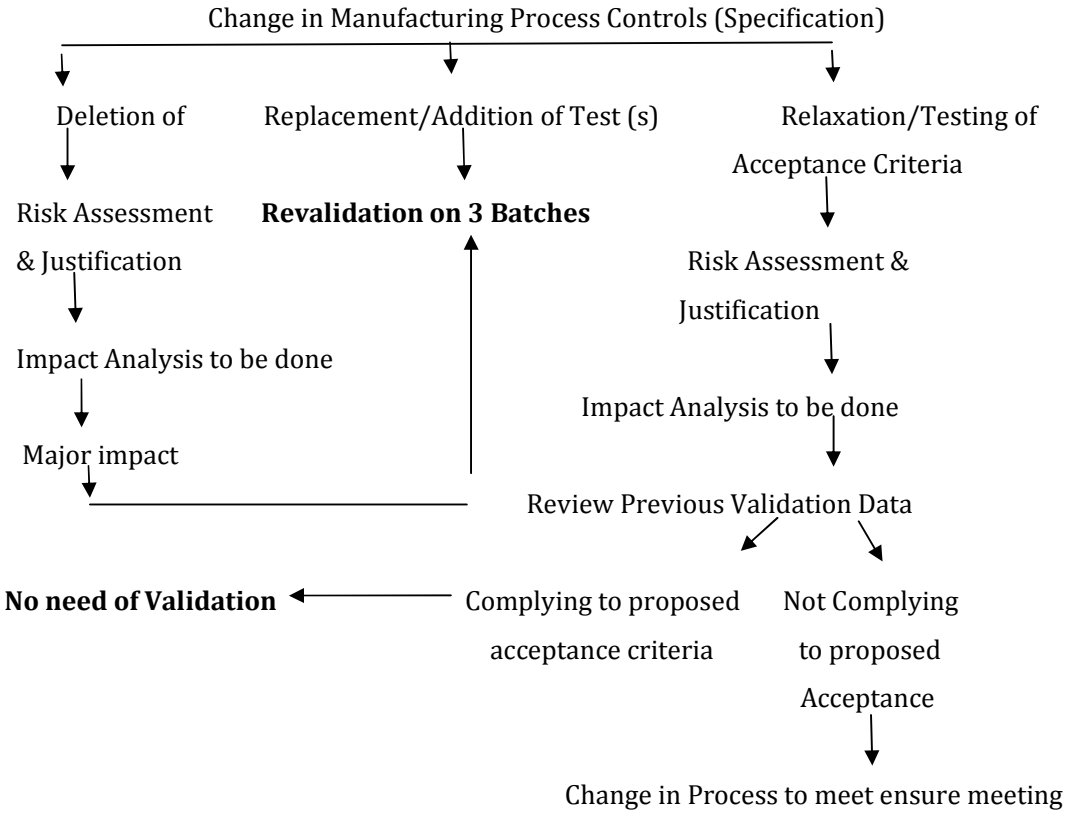
Reason for Process Validation

The possible reason of performing process validation may include:

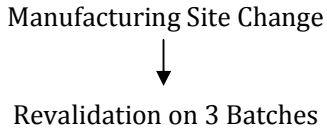
- New product or existing products as per SUPAC changes .
- Change in site of manufacturing.
- Change in batch size.
- Change in equipment.
- Change in process existing products.
- Change in composition or components.
- Change in the critical control parameters.
- Change in vendor of API or critical excipient.
- Change in specification on input material.
- Abnormal trends in quality parameters of product through review during Annual Product Review (APR).
- Trend of Out of Specification (OOS) or Out of Trend (OOT) in consecutive batches.

Process Validation Decision Tree

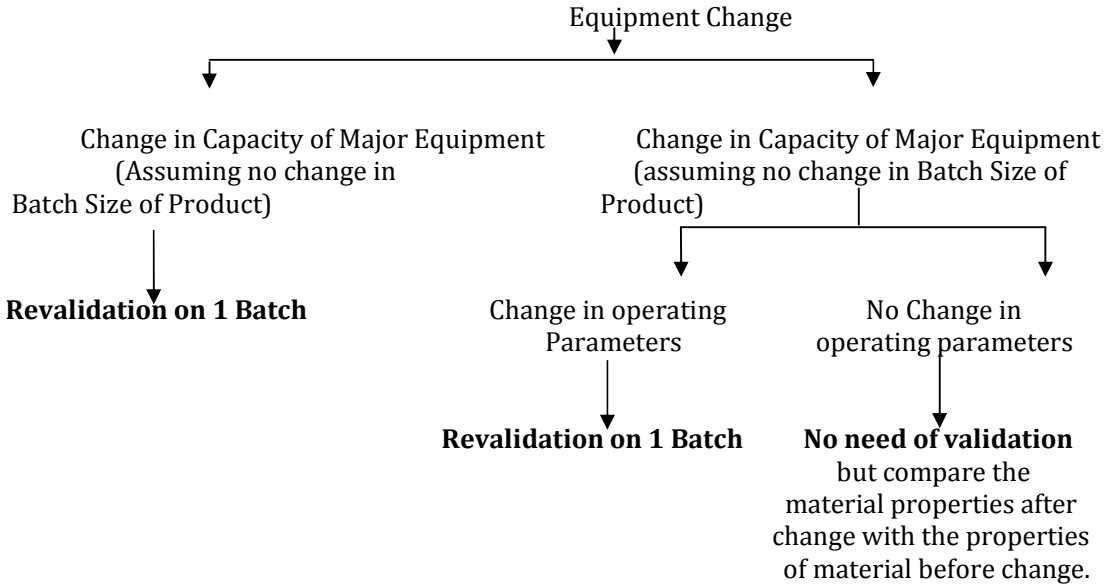
(i) Process Validation Decision Tree for change in process controls of manufacturing process of drug products:



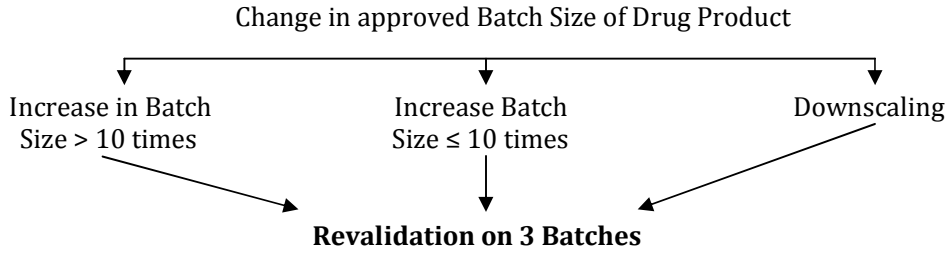
(ii) Process Validation Decision Tree for Change in Manufacturing Site of Drug Product:



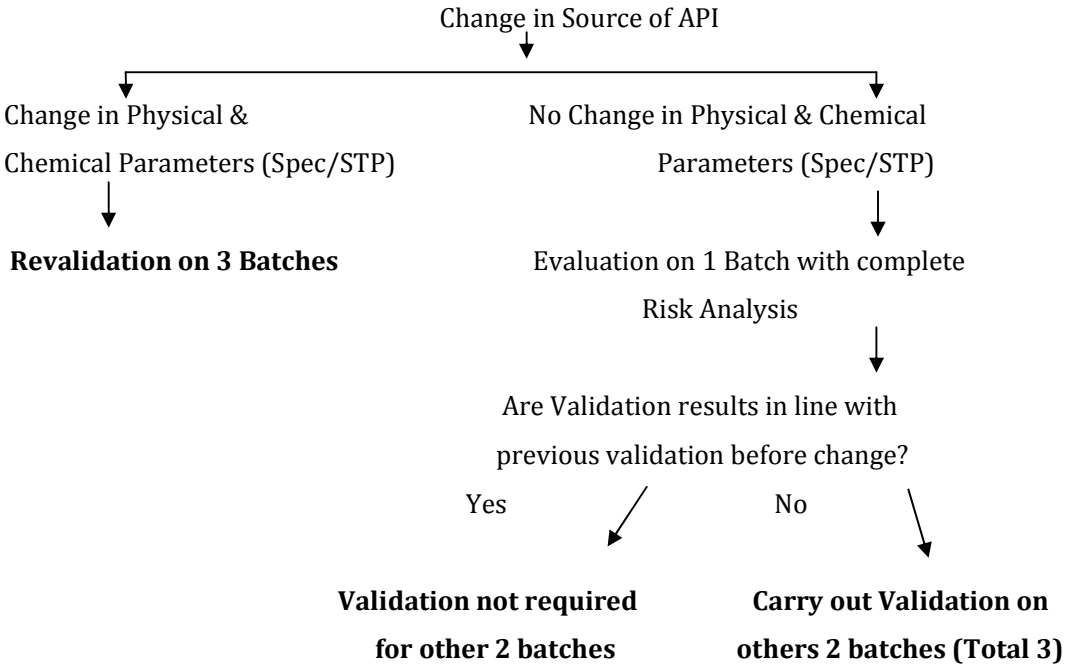
(iii) Process Validation Decision Tree for Change in Equipment:



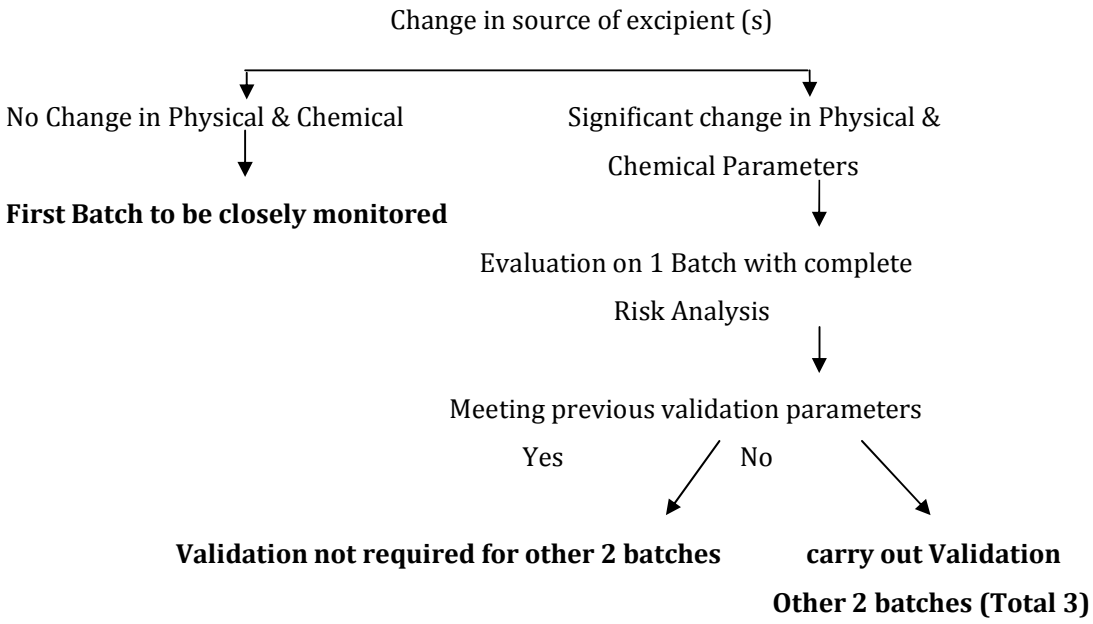
(iv) Process Validation Decision Tree for Change in Batch size of drug Product:



(v) Process Validation Decision Tree for Change in Source of Active Pharmaceutical Ingredients (API).



(vi) Process Validation Decision Tree for Change in Source of Excipient (s).



Responsibility department and their responsibility for Process Validation (12)

The validation working party is convened to define progress, coordinate and ultimately, approved the entire effort, including all of the documentation generated. The working party would usually include the following discipline members, preferably those with a good insight into the company's operation.

Department or Designee	Responsibility
3rd Level of Process Engineer	Prepare and review the validation protocol. Ensue regarding the Title, Market, Batch Size, Report no, Batch details, Product details, Reference documents.
2nd Level of Process Engineer	Responsible for execution of process validation batch. Ensure that the information regarding reason for validation, product specification & acceptance criteria, measuring device used, batch fabrication details, in-process characteristics, validation data, results & conclusion.
1st Level of Process Engineer	Review validation protocol and clarify validation report. Also ensure that batches are executed as per the plan and approved protocol. Prepare periodic revalidation calendar.
Validation	Review validation protocol and certify validation report. Review periodic revalidation calendar.
2nd level of Quality Assurance Manager	Responsible for withdrawing sample as defined in the validation protocol. Review the protocol with respect sampling plans and procedure, and validation sample analysis results. Responsible for analyzing the samples as per defined specification/procedure details in the protocol and responsible for review and approval of validation protocol and certify validation report.
Head (Engineering)	Review the equipment and area in perfect working condition as required shall certify the above in validation protocol and validation report.
Manager Operation	Review and ensure that the information regarding batch details, product details, pack details of input material, equipment used, batch fabrication details, in-process characteristics, yield monitoring, result & conclusion.
Authorised Regulatory Person	Review the batch details, product details, pack details of input material with respect to the regulatory requirements and approved dossier in case of commercialized products in the validation protocol and certify the validation report.
Head (Quality Assurance)	Approve the validation protocol for implementation and certify the validation report.

STAGES OF PROCESS VALIDATION (1, 2, 9, 13)

Process Validation is defined as the collection and evaluation of data**,** from the process design stage through commercial production, which establishes scientific evidence that a process is capable of consistently delivering quality product. Process Validation involves a series of activities taking place over the lifecycle of the product and process. The activities relating to validation studies may be classified into three stages:

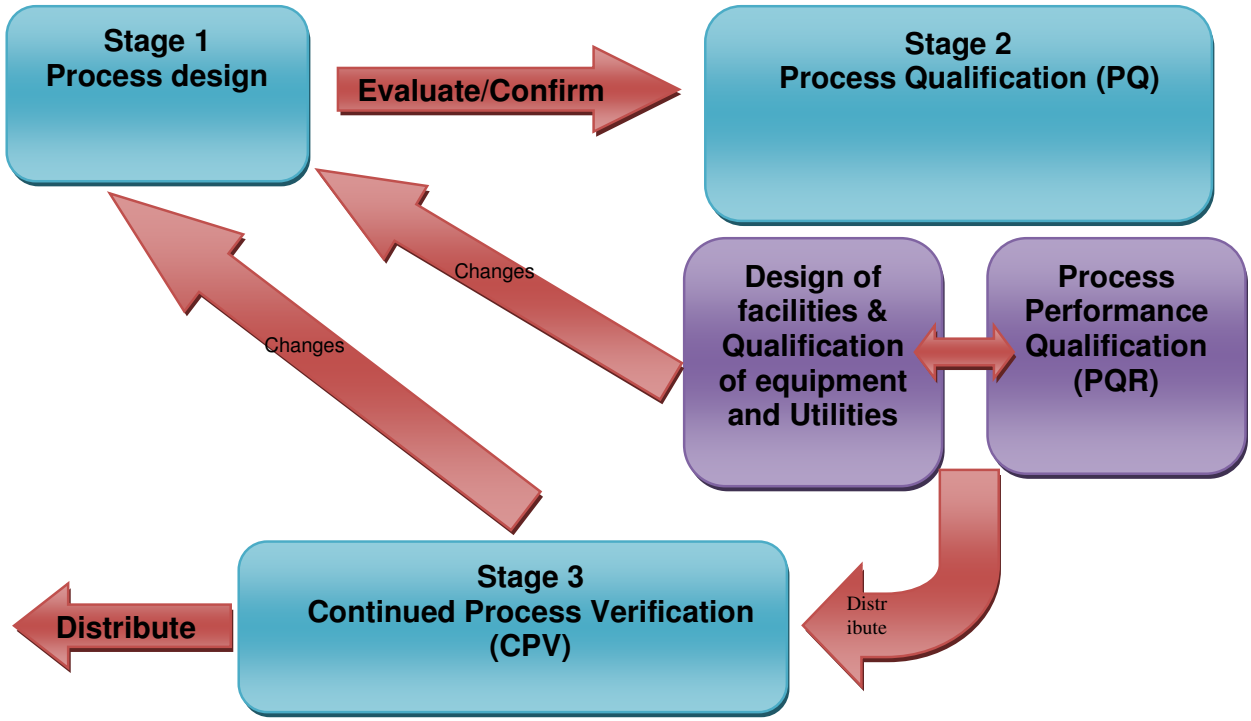


Figure 2: Three model of process validation according to FDA Guidance for Industry – Process Validation

Stage 1 – Process Design: "Focussing exclusively on qualification efforts without also understanding the manufacturing process is defined during this stage based on knowledge gained through development and scale-up activities. It 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, storage and handling of in-process and finished dosage forms, equipment qualification, installation qualification, master production documents ,operational qualification, process capability. Also this is the stage in which the establishment of a strategy for process control is taking place using accumulation knowledge and understanding of the process. "

Stage 2 – process Qualification: During this stage, the process design is evaluated to determine if the process is capable of reproducible commercial manufacturing. It confirm that all established limits of the Critical Process Parameters are valid and that satisfactory products can be produced even under "worst case" conditions. GMP compliant procedures must be followed in this stage and successful completion of this stage is necessary before commercial distribution of a product. There are two aspect of process qualification:

(a) Design of facilities and qualification of equipment and utilities

- Proper design of manufacturing facility is desired under 21 CFR part 211, subpart C, of the CGMP regulation on Buildings and Facilities.
- Activities performed to assure proper facility design and that the equipment and utilities are suitable for their intended use and perform properly.

(b) Process Performance qualification

"Criteria and process performance indicators that allow for a science and risk-based decision about the ability of the process to consistently produce quality products".

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- Part of the planning for stage 2 involves defining performance criteria and deciding what data to collect when, how much data, and appropriate analysis of the data.
- Likely consist of planned comparisons and evaluations of some combination of process measures as well as in-process and trial product attributes.
- Manufacturer must scientifically determine suitable criteria and justify it.
- Objective measures, where possible.
- May be possible to leverage earlier study data if relevant to the commercial scale.

Stage 3 – Continued Process Verification: ongoing assurance is gained during routine production that the process remains in a state of control. The validation maintenance stage requires frequent review of all process related documents, including validation audit reports to assure that there have been no changes, deviations, failures, modifications to the production process, and that all SOPs have been followed, including change control procedures. A successful validation program depends on the knowledge and understanding and the approach to control manufacturing processes. These include the source of variation, the limitation of the detection of the variation, and the attributes susceptible of the variation.

Stage	Intent	Typical Activities
Process Design	To define the commercial process on knowledge gained through development and scale up activities. The outcome is the design of a process suitable for routine manufacturing that will consistently deliver product the meets its critical quality attributes.	A combination of product and process design (Quality by Design-QBD). Experiments to determine process parameters, variability and necessary control. Risk assessments. Other activities required to define the commercial Process.
Process Qualification	To confirm the process design as capable of reproducible commercial manufacturing.	Design or experiment testing Facility design. Equipment & utilities qualification. Performance qualification (PQ). Strong emphasis on the use of statistical analysis of process data to understand process consistency and Performance.
Continued Process Verification	To provide ongoing assurance that the process remains in a state of control during routine production through quality procedures through quality procedures and continuous improvement initiatives.	Proceeduralised data collection from every batch. Data trending and statistical analysis product review. Equipment and facility maintenance calibration. Management review and production staff feedback. Improvement initiative through process experience.

TYPES OF PROCESS VALIDATION (1, 9)

Prospective Validation: Conducted prior to the distribution of either a new product or a product made under a modified production process, where the modifications are significant and may affect the products characteristics. It is a pre-planned scientific approach and includes the initial stages of formulation development, process development, setting of process

sampling plans, designing of batch records, defining raw material specifications, completion of pilot runs, transfer of technology from scale-up batches to commercial size batches, listing major process is executed and environmental controls. (8) In Prospective Validation, the validation protocol is executed before the process is put into commercial use. It is generally considered acceptable that three consecutive batches/runs within the finally agreed parameters, giving product of the desired quality would constitute a proper validation of the process. It is a confirmation on the commercial three batches before marketing. (9)

Concurrent Validation: A process where current production batches are used to monitor processing parameters. It gives of the present batch being studied, and offers limited assurance regarding consistency of quality from batch to batch. (8)

Concurrent Validation may be the practical approach under certain circumstances. Examples of these may be when: (9)

- A previous validated process is being transferred to a third party contract manufacturer or to another site.
- The product is a different strength of a previously validated product with the same ratio of active/inactive ingredients.
- The number of lots evaluated under the Retrospective Validation were not sufficient to obtain a high degree of assurance demonstrating that the process is fully under control.
- The number of batches produced are limited.
- Process with low production volume per batch and market demand.

drug due to shortage or absence of supply.

- In all above cases concurrent validation is valid, provided following conditions are appropriately.
- Pre-approved protocol for concurrent validation with rational
- A deviation shall be raised with justification and shall be approved by plant head /head process owner/Head-QMS.
- Product behaviour and history shall be reviewed based on developmental/scale up /test batches.
- A detailed procedure shall be planned for handling of the marketed product if any adverse reactions observed in concurrent validation process.
- Concurrent validation batches shall be compiled in interim report and shall be approved all key disciplines.

Retrospective Validation: Conducted fir a product already being marked, and is based on extensive data accumulated over several lots and over time. Retrospective Validation may be used for older products which were not validated by the fabricator at the time that they were first marketed, and which are now to be validated to confirm to the requirements of division 2, Part C of the Regulation to be Food and Drugs Act. Retrospective Validation is only acceptable for well established detailed processes and will be Inappropriate where there have recent changes in the formulation of the products, operating procedures, equipment and facility. (8)

Some of the essential elements for Retrospective Validation are: (9)

- Batches manufactured for a defined period (minimum of 10 last consecutive batches).

- Number of lots released per year.
- Batch size/strength/manufacturer/year/period.
- Master manufacturing/packaging documents.
- List of process deviations, corrective actions and changes to manufacturing documents.
- Data for stability testing for several batches.
- Trend analysis including those for quality related complaints.

Process Re-Validation: Required when there is a change in any of the critical process parameters, formulation, primary packaging components, raw material fabricator, major equipment or premises. Failure to meet product and process specifications in batches would also require process re-validation. (8)

- Re-Validation becomes necessary in certain situations. The following are examples of some of the planned or unplanned changes that may require re-validation:
- 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 the source of active raw material manufacturer.
- Changes in packaging material (primary container/closure system).
- Changes in the process (e.g., mixing time, drying temperatures and batch size).
- Changes in the equipment (e.g. addition of automatic detection system).
- Changes of equipment which involve the replacement of equipment on a "like for like" basis would not normally require a re-validation except that this new equipment
- Must be qualified.
- Changes in the plant/facility.
- Variations revealed by trend analysis (e.g. process drifts).

Primary packing validation approach: Primary packing will be done for individual packing ,the process validation protocol shall be clearly state the variable(s) which impact the integrity of the primary pack and set parameters range, primary packing is mostly change part specific and it is mandatory for all new products .

For exsiting products it shall be performed based on matrix approach w.r.t pocket size for blister /strip and different size of HDPE bottles/containers.

The activity starts with documenting the change part number and establishing the proven acceptance range- PAR for the machine set parameters

Eg: Sealing temp/speed in blister and strip packing machine, for dry syrups /sterile products speed and sealing torque, for tablets capsules bulk packed in HDPE bottles ,the speed and induction sealing ,power voltage and conveyer speed for topically filled in collapsible tubes ,speed and crimping quality PAR shall be established for each configuration.

PREREQUIST OF PROCESS VALIDATION:

- Process Development Designee shall review the product development report, data from pilot scale, scale up batch and proposed master formula document of product intended for manufacturing.
- Process Development Designee shall review/ensure the availability analytical method transfer report to the plant and plant preparedness for conducting validation testing and routine testing;

function shall co-ordinate with QC/QA in this regards.

- Process Development Designee shall prepare commercial/exibit batch production and control records which include the operational limits and overall strategy for process control based on development report.
- The Process Validation is performed after the facility, utility, and equipment, and laboratory test methods have been validated and released fir process validation activities. Where compendia method is used only limited analytical method validation shall be conducted.
- All raw material and packaging material specification shall be from approved vendors and shall be approved by quality control.
- All the equipment and instrument to be utilized are calibrated and preventive maintenance programs are in place.
- Relevant SOPs are in place and training is completed on equipment, operation, manufacturing instruction and sampling strategy.
- Key process steps and process variables are identified and their operating ranges have been established.
- All the master formula, manufacturing instruction, packaging instruction, testing procedure & specification shall be approved before execution of process validation batches.
- The cleaning of the area and equipment has been completed prior to the initiation of process validation.
- The validation team and operational team shall be trained from process engineer.

VALIDATION PROTOCOL (8, 10)

Detailed protocol for performing validations are essential to ensure that the process is adequately validated. Process validation protocols should include the following elements:

- Objectives, scope of coverage of the validation study.
- Validation team membership, their qualifications and responsibilities.
- Type of validation: prospective, concurrent, retrospective, re-validation.
- Number and selection of batches to be on the validation study.
- A list of all equipment to be used; their normal and worst case operating parameters.
- Outcome of IQ, OQ for critical equipment.
- Requirements for calibration of all measuring devices.
- Critical process parameters and their respective tolerances.
- Process variables and attributes with probable risk and prevention shall be captured.
- Description of the processing steps: copy of the master documents for the product.
- Sampling points, stages of sampling, methods of sampling, sampling plans.
- Statistical tools to be used in the analysis of data.
- Training requirements for the processing operators.
- Validated test methods to be used in in-process testing and for the finished product.
- Specifications for raw and packaging materials and test methods.
- Forms and charts to be used for documenting results.

- Format for presentation of results, documenting conclusions and for approval of study results.

VALIDATION MASTER PLAN (8, 11)

The validation master plan should provide an overview of the entire validation operation, its organizational structure, its content and planning. The main elements of it being the list/inventory of the items to be validated and the planning schedule. All validation activities relating to critical technical operations, relevant to product and process controls within a firm should be included in the validation master plan. It should comprise all prospective, concurrent and retrospective validations as well as re-validation.

The Validation Master Plan should be a summary document and should therefore be brief, concise and clear. It should not repeat information documented elsewhere but should refer to existing documents such as policy documents, SOP's and validation protocols and reports.

- The format and content should include:
- Introduction: validation policy, scope, location and schedule.
- Organizational structure: personnel responsibilities.
- Plant/process/product description: rational for inclusions or exclusions and extent of validation.
- Specific process considerations that are critical and those requiring extra attention.
- List of products/ processes/ systems to be validated, summarized in a matrix format, validation approach.
- Re-validation activities, actual status and future planning.
- Key acceptance criteria.
- Documentation format.
- Reference to the required SOP's.
- Time plans of each validation project and sub-project.

VALIDATION SAMPLING PROCEDURE AND ACCEPTANCE CRITERIA (1)

A validation plan shall be specific to be the requirement of validation run of a particular product. A detailed plan of sampling procedure of samples which shall be analyzed/ monitored during the validation run shall be outlined systematically.

The sampling plan including sampling points, number of samples and the frequency of sampling for each stage operation shall be decided based on characteristics of the product and deed or critical points of equipments. The number of samples should be adequate to provide sufficient statistical confidence of quality both within a batch and between batches. Quality of sample to be drawn from each sampling point shall be decided based on 1x – 3x formula in case of blend sample on case to case basis. As per USFDA sampling size can be increased from 1x – 10x provided on scientifically justified.

The acceptance criteria for each testing can be obtained from a particular pharmacopoeia reference/ laid specifications/ predetermined acceptance criteria and wherever sampling is done for the academic interest for future reference in product life cycle.

Sampling location are to be clearly indicated by diagram for any equipment from which the sample are withdrawn (where ever application). This shall be help process validation team.

Sampling in case of revalidation and process validation: following sampling plan is applicable for drug products which are already validated and or subjected to limited process validation or revalidation. The limited process validation/revalidation is generally carried out on one commercial batch which include following situations:

- When the source of excipient (s) is changed, with no change in physical and chemical parameters.
- When the source of excipient (s) is changed, with significant change in physical and chemical parameters.
- One process validation batch with the excipient from the new source shall be manufactured. Complete validation batch of one batch as per individual process protocol of that product shall be followed.

Acceptance Criteria and Inference

The validation test and the results obtained there by will be discussed against by the acceptance criteria of test or specification and the conformance to the same will be discussed to support the validation activity. Recommendations for limits, frequencies and action to be taken in the event of the limits being exceeded shall be specified in the report together with recommendations on the extent of monitoring and the in-process controls necessary for routine production.

Further the overall review of results should be checked for consistency and reproducibility. Results should demonstrate the control on the manufacturing process throughout all stages of manufacturing and the collected data to indicate the process consistency and reproducibility to yield a product which meets predetermined attributes.

Based on the results generated during the study performed as per approved validation protocol, a validation report shall be prepared.

Failure and Deviation

Any test during process validation shall investigate to determine the case of failure.

Where the case of failure is not obvious, it may useful to us an investigation procedure to ensure that all the possible areas of potential failure are covered.

Once the case of the process validation failure has been identified, the failure shall classified into the following categories.

Type I: where the failure can be attributed to an occurrence which is not intrinsic to the process for example, an equipment failure raw material that it can be agreed to complete the validation exercise substituting another batch for the one that failed. This investigation and the subsequent action shall be included in the validation report.

Type II: where the failure may be attribute failure or where the investigation is inconclusive than the validation exercise has failed.

In this case the validation terms decide and justify the course of action to be taken, recording its justification and recommendations.

This decision shall consider:

- Re-testing - if investigation of the analytical results supports the decision.
- Introduction a change in operation parameters, process steps.
- Changing the process equipment or the procedure for using the equipment.
- Suspension of the process validation exercise until further technical evaluation and/or development has been carried out.

- Changing the sampling regime.
- Review of historical data.
- Change of the process validation acceptance criteria.
- Change to an analytical procedure.

FINAL PROCESS VALIDATION REPORT (3)

At the conclusion of validation activities, a final report should be prepared. This report should summarize and reference all protocols and results. It should derive conclusions regarding the validation status of the process and necessary recommendation for routine process. The final report should be reviewed and approved by the validation team and appropriate management.

- A validation report shall be prepared to assess the adherence to the protocol after execution of batches.
- Data can be collected in pre design format during execution wherever application but not limited to.
- Name of ingredients, batch numbers of the ingredients used, quality of ingredients used and product batch number shall be checked against the formulation order of the validation batch processing records.
- Name of the equipments used at each processing stage, equipments numbers and make/model/capacity of the equipments shall be checked against the formulation order of the validation batch processing records.
- The environmental condition during batch execution at each processing stage shall be checked against the formulation order of the validation batch processing records.
- Stage of process, details of process variables the respective observations and recommendations shall be checked against the formulation order of the validation batch processing records.
- Any work done in addition to that specific in the protocol or any deviation from the protocol should be formally noted along with an explanation.
- List of all sampling location and identification any differences to the protocol.
- The actual yield obtained at different stages shall be checked against the formulation order of the validation batch processing records.

BENIITS OF PROCESS VALIDATION (4)

- Consistent through output.
- Reduction in rejections and reworks.
- Reduction in utility cost.
- Avoidance of capital expenditures.
- Fewer complaints about process related failure.
- Reduced testing I process and finished goods.
- More rapid and accurate investigations into process deviation.
- More rapid and reliable start-up of new equipment.
- Easier scale-up from development work.
- Easier maintenance of equipment.
- Improve employee awareness of processes.
- More rapid automation.

CONCLUSION

From the study it can be stated that pharmaceutical Process Validation is the most important and recognized parameters of cGMP.

The cGMP regulation require that manufacturing processes be designed and controlled to assure that in-process materials and finished product meet predetermined quality requirements and do so consistently and reliably. The product should be designed robustly enough to withstand variations in the manufacturing process and the manufacturing process should be capable and stable to assure continued safe products that perform adequately. Process validation involves a series of activities taking place over the lifecycle of the product and process.

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