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A REVIEW OF PHARMACEUTICAL PROCESS VALIDATION

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ABSTRACT

The most well-known and crucial GMP parameter is validation. According to the U.S. Food and Drug Administration, this article provides an overview of process validation of pharmaceutical manufacturing processes and discusses its significance (FDA). An introduction and general overview of the process validation of the pharmaceutical manufacturing process are included in this study. Quality must be built into the product at every stage and not merely tested for at the end using quality assurance tools. The production of a drug with reproducible quality will be ensured via process validation. Process Validation is used in the pharmaceutical industry to accomplish this task as, in accordance with ISO 9000:2000, it has demonstrated to be a key instrument for quality management of pharmaceuticals. Process validation is typically carried out prior to the release of a new product, if a change is made to an existing product, and on an ongoing basis to ensure the process is working as intended. A protocol should be established at the outset that details the parameters that will be tracked, the samples that will be collected, and the results that will be accepted.

Keywords: Process validation, Protocol, Quality, Quality Management

INTRODUCTION

A process, procedure, or approach is validated by demonstrating and documenting that it consistently produces the desired outcomes. An essential component of quality assurance is validation, which is a systemic analysis of systems, facilities, and processes to ascertain if they carry out their intended functions sufficiently and

consistently as defined. Although validation does not make a process better, it does assure that it has been designed correctly and is under control.

In order to enhance the quality of pharmaceuticals, two FDA officials, Ted Byers and Bud Loftus, originally suggested the idea of validation in the United States in 1979. Over time, it evolved into a crucial component of current good manufacturing practices. The idea of validation has grown over time to encompass a variety of activities, from computerized systems for clinical trials, labeling, or process control to analytical methods used for the monitoring of pharmaceutical drug substances and products for quality. Validation is founded on regulatory requirements but is not mandated by them, so it is usually regarded as a crucial and integral component of cGMP.

TYPES OF VALIDATION

- Analytical Method Validation
- Cleaning Validation
- Equipment Validation
- Process Validation

Analytical Method Validation

The method used to conduct the analysis is referred to as the analytical procedure. The procedures required to carry out each analytical test should be thoroughly explained. The sample, the reference standard, the reagent preparations, the usage of the equipment, the formation of the calibration curve, the use of the calculation formulae, etc. are only a few examples. The process of proving that an analytical technique is adequate for its intended use is known as analytical method validation. Before beginning validation investigations, the methodology and goal of the analytical techniques should be properly stated and understood. This knowledge is derived from method development and optimization research with a scientific foundation.

Cleaning Validation

Cleaning validation is the written assurance that cleaning practices are eradicating residues to acceptable levels, while taking into account variables like batch size, dosage, toxicity, and equipment size. To ensure that any

cleaning method is effective on all product contact equipment, cleaning validation should be carried out. With the right scientific reason, simulating agents may be used.

Equipment Validation

A systematic approach called equipment validation ensures that any component of equipment is sound functionally. The concept underlying equipment validation is that it must be created, maintained, and modified in order to perform the required activities. The fact that equipment is a procedure's key component gives equipment validation prior to performing it in the pharmaceutical sector its fundamental importance.

Process Validation

Process validation is the established assurance that a process can generate a drug product or intermediate that satisfies its predetermined specifications and quality attributes when it is operated within established parameters. (ICH Q7).

Process validation shouldn't be considered of as an isolated instance. Process validation includes a lifecycle strategy that connects the creation of the product and the process, the validation of the commercial manufacturing process, and the maintenance of the process in a controlled state throughout routine commercial production.

Effective process validation makes a substantial contribution to ensuring drug quality. A drug product should be created that is suitable for its intended purpose, according to the fundamental tenet of quality assurance. The following conditions must be met for this principle to apply:

- ✓ The product is created with quality, safety, and efficacy in mind.
- ✓ Merely inspecting or testing final products and in-process materials is insufficient to ensure quality.
- ✓ Every stage of the production process is monitored to ensure that the finished product satisfies all requirements for quality.

IMPORTANCE OF PROCESS VALIDATION

- ✓ Any process or system's parameters and controls are chosen during validation.
- ✓ It aids in identifying the worst-case scenario and the liabilities involved in producing a high-quality product.

- ✓ Investigating process irregularities is simplified with validation.
- ✓ Validation enables in-depth research and comprehension of the instrument and system.
- ✓ After validation, the risk of regulatory non-compliance is reduced.
- ✓ Less testing of finished samples and control is needed with a validated procedure.
- ✓ Due to process, system, and equipment validation, batch-to-batch variation is reduced.
- ✓ Lowers the cost of production.
- ✓ Increases manufacturing plant production by reducing rework and rejections.
- ✓ Reduces the likelihood of batch failure.

STAGES OF PROCESS VALIDATION

There are three stages of Process Validation.

1. Stage 1: Process Design

   During this phase, the commercial process is established using the expertise amassed during development and scale-up activities. Phase of qualification or prevalidation: It includes all activities related to product research and development, formulation, pilot batch studies, scale-up studies, technology transfer to commercial scale batches, setting up stabilization conditions, storing and handling in-process and finished dosage forms, equipment qualification installation qualification, master production documents, operational qualification, and process capability.

   This stage offers a crucial contribution to the product development studies that are conducted without the use of good manufacturing practices, which finally aids in the many design stages including predicted dosage form and manufacturing method.

2. Stage 2: Process Qualification

   At this stage, the process design is assessed in order to determine it can be used for repetitive commercial manufacturing. It is aimed at confirming that even in "worst case" scenarios, satisfactory goods can be produced and that the defined limitations of the important process parameters are true.

3. Stage 3: Continued process verification

Continual assurance that the process is under control is obtained during regular manufacturing. In the third stage, which is evaluation, all the ongoing data collected to maintain product quality is assessed. There are many different types of data contained, including critical quality attributes, critical process attributes, and critical quality attributes. From normal production, ongoing assurance that the process maintains a state of control is obtained.

TYPES OF PROCESS VALIDATION

The four types of process validation are

1. Prospective Validation
2. Concurrent Validation
3. Retrospective Validation
4. Revalidation

1. Prospective Validation

Based on a risk analysis of the manufacturing process that is broken down into individual phases, validation is carried out during the development stage. These processes are then assessed based on experience to see if they may result in catastrophic circumstances.

All API processes should typically undergo prospective validation. Before the final drug product made from an API is commercially distributed, prospective validation of the API process should be finished.

This kind of process validation frequently happens when a manufacturing process is transitioned from development to production.

2. Concurrent Validation:

To demonstrate that the manufacturing process is under control, this strategy comprises monitoring crucial processing steps and testing the final product of current production. Based on data produced during the true operation of the process, concurrent validation is used to establish recorded evidence that a facility and processes perform what they claim to do. To demonstrate that the manufacturing process is under control, this strategy comprises monitoring crucial processing steps and testing the final product of current production.

Validation is carried out throughout normal production of goods intended for sale when data from repeat production runs are unavailable due to the small number of batches produced, the frequency of batches produced, or batches produced using a validated method that has been modified.

3. Retrospective Validation

   Facilities, processes, and process controls that are currently in use but have not gone through a formally documented validation procedure are validated retrospectively. Using historical data, it can validate these facilities, processes, and process controls and give the requisite documentary proof that the process is performing as it should. Because of this, this kind of validation is only suited for established processes and is problematic in cases where there have been recent modifications to the equipment, operating procedures, or product composition.

4. Revalidation

   Re-validation of a previously-validated system (or portion thereof) to guarantee ongoing adherence to set standards.

   For a periodic review, re-validation is typically done to confirm initial validation. Revalidation provides proof that modifications made to a process or its surroundings do not adversely alter its characteristics or the quality of its output. The significant change in batch size, changes in the manufacturing process, change in the facility, and changes in equipment might be the possible reasons for initiating revalidation.

DOCUMENTATION

For efficient communication to take place in complex, extended, and multidisciplinary projects, documentation at every stage of the process validation lifecycle is crucial. Documentation is essential to ensure that information learned about a process or product is accessible to and understandable by those involved at every stage of its lifespan.

Documentation encompassing the whole validation lifecycle from product conception to full scale manufacturing is necessary for effective communication in challenging, protracted, and diverse projects. A process or product must be documented so that those involved in each stage

of its existence may access and comprehend the knowledge that has been generated about it.

Ideal documentation gives easy access to the manufacturing process from a scientific perspective and offers a full history of how the final product was created.

TYPES OF DOCUMENTATION

The various type of documents required for effective process validation are:

- ✓ Validation Master Plan
- ✓ Validation Protocol
- ✓ Validation Report
- ✓ Standard Operating Procedure
- ✓ Validation Master Plan

  A high-level document that outlines the manufacturer's concept and strategy in its entirety that will be used to determine whether a product's performance is acceptable. It gives information on the manufacturer's qualification and validation action plan, outlines the specifics and deadlines for the work to be done, and includes a list of who is responsible for what in the process of putting the plan into action.

  The Validation Master Plan is supposed to be a summary document, so it ought to be simple, clear, and short. It should refer to already-existing papers including policy documents, SOPs, validation methods, and reports rather than rehash data that has already been documented elsewhere.

- ✓ Validation Protocol

  Along with a documented action plan outlining how process validation will be carried out, the validation protocol will specify who will carry out the work activities, create testing criteria, sample plans, testing procedures, and requirements, and describe the equipment that will be used.

  The validation protocol should include

  Scope

  Objectives

  Responsibilities of Key personnel

  Sampling Plan

Critical Parameters

Acceptance Criteria

Deviation

Conclusion

- ✓ Validation Report

A document that lists and summarizes the records, outcomes, and validation evaluation. It should also include a summary of the validation's results. After the validation is complete, a written detailed report should be made available; if it is deemed appropriate, it should be accepted and authorized. A validation report should include:

Title of study

Objective

Details of Raw Materials

Equipment Details

Standard Operating Procedures

Specific Procedures (Sampling Plan)

Results with acceptance criteria

Deviations, If any

Conclusion

- ✓ Standard Operating Procedure

An approved written procedure that provides directions for carrying out procedures that are more broadly applicable and not necessarily specific to a particular product or material (e.g., equipment operation, preventive maintenance, and cleaning; validation; area cleaning and sanitization and environmental monitoring; sampling, and inspection). Supplementing product-specific master-batch manufacturing documents with relevant SOPs is possible.

CONCLUSION

From everything mentioned above, we can infer the significance of validation. PV is essential for sustaining high-quality processes and products. If everyone follows validated procedures, there won't be any compromises and high-quality products will be consistently and dependably produced. A thorough, disciplined validation ensures that the product and the process meet the established requirements.

To ensure that standards are being met, QA measures are helpful. When it comes to creating high-quality pharmaceutical products and patient-focused medical equipment, the pharmaceutical industry is more important than any other industry. First and foremost, validation is essential and is made up of cGMPs. Finally, it can be said that process validation is a crucial component of pharmaceutical product quality assurance because end-product testing is insufficient to guarantee the quality of the finished product.

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