SJIF Impact Factor (2024): 8.675| ISI I.F. Value: 1.241| Journal DOI: 10.36713/epra2016 ISSN: 2455-7838(Online)
EPRA International Journal of Research and Development (IJRD)
Volume: 9 | Issue: 11 | November 2024 - Peer Reviewed Journal

A REVIEW ON QUALIFICATION OF MANUFACTURING EQUIPMENT AUTOCLAVE, HOT AIR OVEN, TABLET COMPRESSION MACHINE

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ABSTRACT

Validation is one of the important steps in achieving and maintaining the quality of the final product batch after batch. Without equipment, we cannot manufacture a product. If equipment is validated, we can ensure that our product is of the best quality. Validation of the equipment is called the Qualification. This review focuses on the qualification of Autoclaves, Hot Air Ovens, and Tablet Compression Machines, essential equipment in pharmaceutical manufacturing. We discuss the systematic approach to qualification, including Installation Qualification (IQ), Operational Qualification (OQ), and Performance Qualification (PQ)

KEYWORDS: *Validation, Equipment Qualification, Autoclave, Hot air Oven & Tablet Compression Machine*

INTRODUCTION

In manufacturing facilities, validation test procedures are used to validate equipment and processes that may influence product quality. The tests for validation are used in accordance with approved written qualification procedures. All necessary activities and responsibilities for the qualification and validation are controlled and specified in this Validation Master Plan. Every step of the described validation program for facilities, equipment, processes, process controls, and cleaning is in accordance with the current European Community Guidelines for GMP and FDA, and the cGMP guideline for finished pharmaceutical manufacturers

DEFINITION

Validation may be defined as "Establishing documented evidence which provides a high degree of assurance that a specific process will consistently produce a product meeting its pre-determined specifications and quality attributes." It has been made mandatory by the regulatory bodies to prove the safety, efficacy, purity & effectiveness of the drug product, medical devices & biologics in the market place &health system.

IMPORTANCE OF VALIDATION

- Increased throughput
- Reduction in rejections and reworking
- Reduction in utility costs
- Avoidance of capital expenditures
- Fewer complaints about process-related failures
- Reduced testing in-process and in finished goods
- More rapid and reliable start-up of new equipment
- Easier scale-up from development work
- Easier maintenance of equipment
- Improved employee awareness of processes
- More rapid automation

EQUIPMENT QUALIFICATION

Qualification: Action of proving and documenting that equipment or ancillary systems are properly installed, work correctly, and actually lead to the expected results. Qualification is part of validation.

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The individual qualification steps alone do not constitute process validation.

1. Design Qualification(DQ)
2. Installation Qualification(IQ)
3. Operational Qualification(OQ)
4. Performance Qualification(PQ)
5. Maintenance Qualification(MQ)

Who should do Equipment Validation?

The vendor or the user has the ultimate responsibility for the accuracy of the analysis results and also for equipment qualification. DQ should always be done by the user. While IQ for a small and low cost instrument is usually done by the user, IQ for large, complex and high cost instruments should be done by the vendor. OQ can be done by either the user or the vendor. PQ should always be done by the user because it is very application specific, and the vendor may not be familiar with these. As PQ should be done on a daily basis, this practically limits this task to the user.

Design Qualification (DQ)

"Design qualification (DQ) defines the functional and operational specifications of the instrument and details for the conscious decisions in the selection of the supplier". The steps that should be considered for inclusion in a design qualification. Description of the analysis problem, Description of the intended use of the equipment, Description of the intended environment,Preliminary selection of the functional and performance specifications, Preliminary selection of the supplier, Final selection of the equipment, Final selection of the supplier, Development and documentation of final functional and operational specifications,

Installation Qualification (IQ)

“Installation qualification establishes that the instrument is received as designed and specified, that it is properly installed in the selected environment, and that this environment is suitable for the operation and use of the instrument.” The qualification involves the coordinated efforts of – The vendor. The operating department. The project team (which provide input into the purchase, installation, operation and maintenance of the equipment).

Operational Qualification (OQ)

"Operational qualification (OQ) is the process of demonstrating that an instrument will function according to its operational specification in the selected environment”. The proper operation of equipment is verified by performing the test functions specified in the protocol. A conclusion is drawn regarding the operation of equipment after the test functions are checked and all data has been analyzed. Following are the contents of equipment operation qualification:

1. Application S.O.P’s, 2.Utilization List, 3.Process Description,4. Test Instrument Utilized To Conduct Test, 5. Test Instrument Calibration, 6.Critical Parameters, 7. Test Function (List), 8. Test Function Summaries.

Performance Qualification (PQ)

"Performance Qualification (PQ) is the process of demonstrating that an instrument consistently performs according to a specification appropriate for its routine use ". PQ should always be performed under conditions that are similar to routine sample analysis. PQ should be performed on a daily basis or whenever the equipment is being used. In practice, PQ can mean system suitability testing, where critical key system performance characteristics are measured and compared with documented.

AUTOCLAVE

Autoclave is equipment that make use of pressurized steam in order to eliminate microorganisms. It is also used in sterilization of medical application .used in chemical industry for sterilization of vulcanizing rubber,curing composites and hydrothermal synthesis.

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STERILIZER	TEMPERATURE	PRESSURE	TIME
Steam Autoclave • Unwrapped Items • Lightly Wrapped Items • Totally Wrapped Items	121° C (250 ° F) 121° C (270 ° F) 132° C (270 ° F) 132° C (270 ° F)	15 psi 30 psi 30 psi 30 psi	15 min 3 min 8 min 10 min
Dry Heat Wrapped	170° C (340 ° F)		60 min
Chemical Vapor	132° C (270 ° F)	20-40 psi	20 min
Ethylene Oxide	Ambient		8-10 hr

Figure No. 1

Figure No. 2

- **Need and Importance**

1. Autoclave are known as steam sterilizers, it is used for healthcare and industrial applications.
2. It can also uses steam under pressure to kill harmful bacteria, virus, fungi and spores on items.
3. Autoclave used to sterilize surgical equipment, laboratory instruments, pharmaceutical item and other materials.
4. It also sterilize solid ,liquid ,hallows and instruments of various shape and sizes

- **Basic Qualification Approach**

User Requirement specification: The set of owner, user and engineering requirements necessary and sufficient to create a feasible design meeting the intended purpose of the system.

1 Design Qualification (DQ): The documented verification that the proposed design of facility, system and equipment is suitable for intended purpose.

2 Installation Qualification (IQ): The documented verification that the facility, system and equipment as installed or modified comply with approved design and the manufactures' recommendations.

3 Operational Qualification (OQ): The documented verification that the facility, system and equipment as installed or modified performance as intended throughout the anticipated operating ranges.

4 Performance Qualification (PQ): he documented verification that the facility, system and equipment as connected together, can perform effectively and reproducibly, based on approved process methods and products specifications.

Hot air Oven

Air oven are electrical devices used in sterilization. The oven uses dry heat to sterilize articles over several hours to destroy microorganisms and bacterial spores. Generally, they can be operated from 50°C to 200 °C. It is found in hospitals and laboratories where medical professionals and laboratory technicians use it. Examples of items that aren't sterilized in a hot air oven are surgical dressings, rubber items, or plastic material.

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Higher Temperatures and Longer exposure time required

Typical Cycles

- 160°C for 120minutes
- 170°C foe 60 minutes
- 180°C for 30 minutes

Figure No. 3

Used for

✓ Glassware and product container used in aseptic manufacture, non aqueous thermostable powders and liquids (oils)

✓ Also used for depyrogenation of glassware.

The hot air oven is the equipment which is utilized to provide the dry heat medium and it must be validated to ensure that the system is able to provides sterile and depyrogenated components, on a reproducible basis

Design Qualification

- The DQ outline the key features of the system designed to address the user requirement, regulatory compliance and selection rationale of a particular supplier.

- **The following are the key considerations for DQ**

➢ Physical dimensions of the equipment and accessories
➢ Suitable operating environment of the instrument
➢ Health and safety requirement

Installation Qualification

- It is carried out after or concurrently with the installation of the equipment at the user's premises.
- The purpose is to provide documentary evidence that the correct equipment has been received and installed as per plan and protocol.
- IQ documents should be reviewed and approved by designated responsible individuals.

It includes details of-

➢ **Structural-** Check dimensions, presence of seal
➢ **Filters-** Proper identification,type,size,air capacity, flow rate
➢ **Electrical -** Proper identification, safety cutoff
➢ **HVAC-** System provides the temperature and pressure differential required.
➢ **Air supply-** Identify source, duct size.
➢ **Air or natural gas-** Check that the source and type of supply are consistent with the manufacturer's recommendations.
➢ **Heaters-** Record the manufacturer's model no., the no. of heating elements.
➢ **Blowers-** Check for use of correct fan belt & that is in good condition.

Operational Qualification

- It is documented verification that the system or subsystem performs as intended throughout all specified operating range
- The OQ document should be reviewed and signed by the required department representatives.
- The components of system must satisfy the operating ranges as determined by the purchase order specifications.
- Each of the following process components must be identified & the operating performance & range determined.

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- **Temperature Monitors**
- **Cycle Timer**

The accuracy of timer must be determined, so that assurance is provided for cycle time.

- **Door Interlocks**

If a unit is equipped with double doors, the interlocks must operate such that the door leading to the aseptic area cannot be opened if the door to the non-aseptic area is opened.

- **Heaters**

All of the heating elements must be functional.

- **Blowers**

The air velocity consistent and motor speed of blowers should be noted in the OQ records.

- **Cooling Coils**

If coils are present, the type and size of the coils and temperature of the cooling medium at the inlet and outlet of the coils should be recorded.

- **Chamber Leaks**

The perimeter of the doors for batch sterilizers should be checked for air leakage while operating.

- **Particulates Counts**

Particulate count should be checked within the containers before and after sterilization to quantitate the particle load contributed to the product by sterilization process

Performance Qualification

Verifies that the equipment performs according to design specifications and user defined requirements in a reliable & reproducible manner under normal production conditions

Physical

- Heat penetration studies on empty chamber
- Heat distribution study on loaded chamber
- Heat penetration study on loaded chamber

Microbiological

- Bio-challenge/ Pyro-challenge studies

Tablet Compression Machine

The press is automatic, high speed rotary press. A motor drives the press at speeds that vary from 410 to 1630 tablets per minute (rpm). The material being tableted is fed from a hopper by gravity through the feed frame into dies. Regulating the weight adjusting cam controls the weight of material in each tablet can be adjusted.

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Figure No.4 Tablet Compression Machine

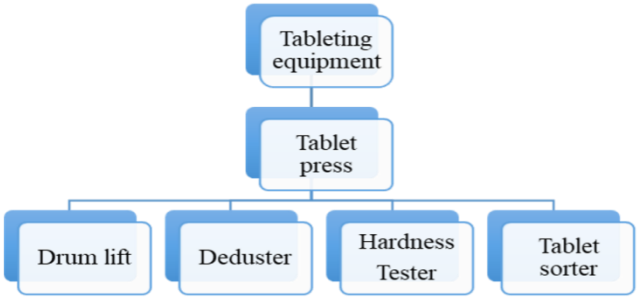

Figure No.5 Components of tableting Equipment

Installation Qualification

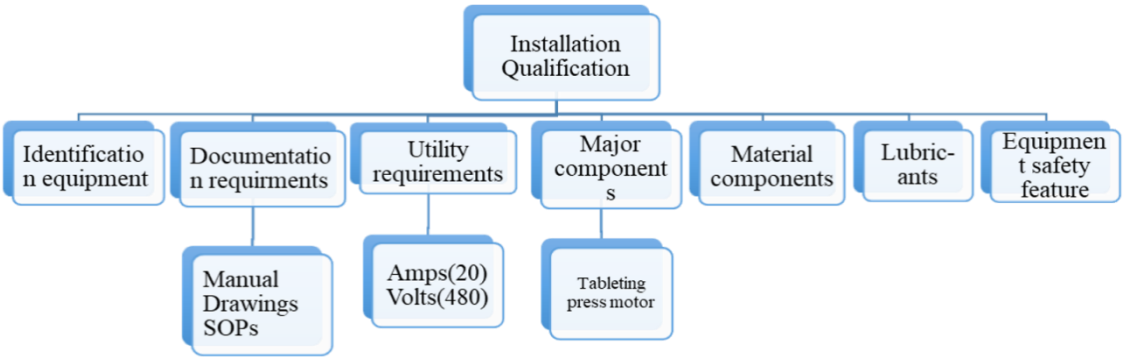

Figure No.6 IQ elements of a tablet press

The supporting electrical utilities must meet all electrical codes.
The information required for an IQ evaluation is equipment identification, required documentation, equipment utility requirements,majorcomponentspecifications, component material, lubricants and equipment safety features.

Equipment Identification
Record the equipment identification numbers,along with the following information:

- Model number

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- Serial number
- Company assigned equipment number and
- Location of the equipment

Required Documentation
Record the equipment manufacturer's operation and maintenance manual and drawings. Record the SOP that cover the setup, operation and cleaning of the tablet press.

Equipment Utility Requirements:
Compare the manufacturer's specified volts
(V) and amps (A) requirements to their as- found conditions at the time of qualification testing and record. Also record the location of the power supply source.

Major Component Specifications
The component specifications section ofthe protocol verifies that the tablet press components purchased were delivered and installed.

Component Material
Record the material of each component that contacts the product.

Lubricants
Record the lubricants used to operate the tablet press and indicate if they make contact with the product.

Equipment Safety Features
The objective of testing equipment safety features is to verify that the safety features on the tablet press functionaccording to the manufacturer'sspecifications. This test is performed with the tablet press empty. Verify that all of the guards are present and record the results.

Operational Qualification
An OQ evaluation should establish that the equipment can operate within specified tolerances and limits. The mechanical ranges of the tablet press are challenged, along with the basic tablet press operations. The tablet press will be validated for its operating ability, not how well it makes tablets. Information required for the OQ evaluation is: calibration of the instruments used to control the tablet press, equipment control functions (switches and push buttons) and equipment operation (cam tracks, upper punches, lower punches, feed frames, take off bars, rotor head direction, tablet press speed).

Calibration Requirements
Verify that all the critical instrumentson the equipment have been logged into the calibration system, have calibration procedures in place and are in calibrationat the time of qualification testing. Record all information for calibrated instruments used to control the tablet press.

Equipment Control Functions
The objective of testing equipment control functions is to verify that the switches and push buttons on the tablet press operate per the manufacturer's specifications. The tests will be performed with the tablet press empty. Operate each control and verify its proper position.

Equipment Operation

A) Cam Tracks Test
The objective of the cam track test is to verify that the upper and lower cam tracks make contact with the upper punches according to the manufacturer's specification. Use the following procedure and record the results.

- Install the punches and verify that the cams are contacting the punch head angles onthe both the sides of the double-sided cams.
- Verify that the punches are contacting one side of the single-sided came through a full cam track, upper and lower.

B) Upper Punch Test
The objective of the upper punch test is to verify that the upper punch penetration isaccording to the manufacturer's specification. A verniercaliper is required for this test, which is performed as follows:

- Attach a piece of tape to mark the depth of penetration of an upper punch when it isset to a standard depth.

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- Remove the upper punch and use a calibrated vernier caliper to measure the depth of penetration into the die. Record the results and instrument used to measure the depth.

C) Lower Punch Test

The objective of the lower punch test is to verify that the lower punch height is set according to the manufacturer's specification. A dial indicator test is required. Measure the height of the lower punch above the die with a dial indicator and record the results and the instrument used to measure the height.

D) Feed Frame Test

The objective of the feed frame test is to verify that the feed frame distance above the rotor head is according to the manufacturer's specification. Feeler gauge test: Measure the clearance between the feed frame and the motor head with a feeler gauge and record the results and the instrument used to measure the clearance.

E) Take Off Bar Test

The objective of the take-off bar test isto verify that the take-off bars do not makecontact with the lower punches. Turn the tablet press by hand and verify that the takeoff bars do not make contact with the lower punches. Record the results.

F)Tablet Press Rotation Direction

The objective of the rotation direction test is to verify that the rotor head rotates in the proper direction. The tests will be performed with the tablet press empty. Press the start switch and observe the direction of the rotation of the rotor head as viewed from front of the press and record the results.

G) Tablet Press Speed

The objective of the speed test is to verify that the measured speeds are within ± 10% of the manufacturer's specification of a minimum of 9 rpm and a maximum of 36 rpm. This test will be performed with the press empty. A stop watch is required for this test. Measure the speed of the rotor head with a calibrated stopwatch. Verify that the measured speeds are within ± 10 % of the manufacturer's specification and record the results and the instrument used to measure the speed

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Performance Qualification

Once the equipment is properly installed and functioning within is properly installed and functioning within specified operating parameters, it must be shown that the tablet press can operate reliably under routine, minimum and maximum operating conditions.

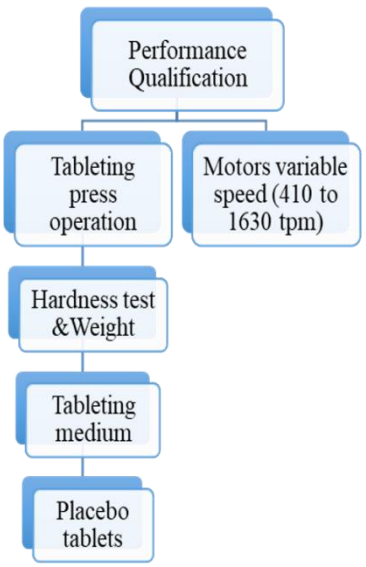

Figure No.7 PQ elements of a tablet press.

The objective of the weight and hardness test is to verify that tablet weight and hardness can be maintained consistently throughout the entire weight and hardness setting range.

The materials and instruments required for this test are a placebo and a weight, hardness, and thickness gauge.

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Compress tablets using placebogranulation. Record the placebo used. Obtainthe average weight and hardness of 5 tablets at start up, 10, 20 and 30 min and record the results and the instrument used to measure the weight and hardness.

Test Functions

1. Perform Installation Qualification.
2. Perform general operational controls verification testing.
3. Operate system throughout the range of operating design specifications or range of intended use.
4. Verify that all safety devices of the tablet press are operating as specified in the manual.
5. Verify that recommended lubricants are used during machine operation.
6. Perform controller security challenges to verify that specified parameters cannot be altered without appropriate supervisory control.
7. Perform capability and consistency studies to check the weight variation of each product as per SOP.

Acceptance Criteria

1. The system is installed in accordance with design specifications, manufacturer recommendations, and GMPs. Instruments are calibrated, identified, and entered into the calibration program.
2. General controls and alarms operate in accordance with design specifications.
3. The system operates in accordance with design specifications throughout theoperating range or range of intended use.
4. The safety devices must operate as specified in the manual
5. The recommended lubricants must be used as specified in the manual.
6. The storage location of the lubricants must be according to manufacturer recommendations.
7. Unauthorized changes to cycle parameters must not be allowed without supervisorycontrol or password.

The machine must be in statistical controlas per capability and consistency studies.

CONCLUSION

Allot extra time for validation. It always takes longer than we think, particularly with a new installation. All phases of validation successfully completed and final report signed off. Review overall validation process and deviations to determine how process could be handled better in the future. The important points are: Carefully write protocols and acceptance criteria, try to anticipate problems or issues in advance. Coordination with other ongoing activities to ensure required resources will be available when needed. Coordination with vendors. Unless equipment qualification has not already been legally mandated today, in the near future it will have overriding importance, primarily in the pharmaceutical industry and in the food and cosmetics sectors. The main goal in qualifying laboratory equipment is to ensure the validity of data. The current equipment qualification programs and procedures used within the pharmaceutical industry are based on regulatory requirements, voluntary standards,vendor practices, and industry practices. The result is considerable variation in the way pharmaceutical companies approach the qualification of laboratory equipment and the way they interpret the often vague requirements.

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