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Review Article

QUALIFICATION OF EQUIPMENTS: A SYSTEMATIC APPROACH

Kiranbala jain*, Meenakshi Bharkatiya

B. N. Institute of Pharmaceutical Sciences, BN University, Udaipur-313001 Rajasthan, India.

Qualification as a part of validation is the task performed to identify or check that utilities, equipment and ancillary systems are capable of operating within limits for their intended use. Equipment qualification is a key element in the pharmaceutical quality system. In recent times regulatory agencies are more focusing on qualification of equipment. Qualification of the equipment starts from design of the equipment based on the user requirement specification and functional requirement specification. The review article provides information on Design Qualification which is done to identify whether the proposed design of facilities, system and equipment is suitable for intended purpose, Installation Qualification which is done to check whether the equipment is built and installed in compliance with design specification, Operational Qualification in which the process parameters shall be challenged to assure that product meets all requirements and finally Performance Qualification to demonstrate that the process will produce acceptable product consistently under normal operating conditions.

Key words: Qualification, equipments, Regulatory requirements

INTRODUCTION

Calibration of equipment needs to be carried out on a regular basis. This is because instruments tend to deviate owing to hard operating conditions, mechanical shocks or exposure to extreme temperature or pressure. Frequency of calibration would depend on the tolerance level. When the objective of the measurement is critical calibration would need to be carried out more frequently and with great accuracy. [1]

Whilst such informal checks are advantageous to ensure that performance requirements are met, it is of much greater benefit to conduct this process on a formal, documented basis, known as Equipment Qualification. In addition to checks performed during the commissioning of a measuring system, Equipment Qualification also documents regular performance checks conducted throughout the equipment's operational life. As well as being a regulatory requirement for some industries, Equipment Qualification gives the following benefits to all analylsts:

• Proof that new equipment is fit for its intended purpose. This is achieved by fully defining all of the required characteristics of the measuring system and then proving that the selected equipment meets these requirements before using it for analysis.

• Reduced likelihood of incorrect test results as the equipment's performance has been proved to be suitable for its intended purpose both before it is used for test sample analysis and during its working life.

• A template for troubleshooting any problem that may occur whilst the conductivity measuring system is in service. The Equipment Qualification

documentation can act as a checklist for determining and rectifying the source of any measuring problems.

Equipment Qualification plays a fundamental role in a laboratory's quality system as it assists the development and validation of suitable test methods and helps identify the Quality Control and Quality Assurance measures that will be required to ensure that test measurements are fit for purpose. Equipment Qualification ensures that measuring equipment is capable of generating test measurements that are fit for purpose.[2]

Regulatory requirements:[3]

The ICH Q7a guideline demonstrates that facilities, systems, equipment and utilities are properly qualified and maintained to assure data and product integrity. Additional guidance is provided by PIC/S: "While it is not possible to undertake the details of neither an Installation Qualification for established equipment nor the detailed approach for an Operational Qualification, nevertheless there should be data available to support and verify the operating parameters and limits for the critical variables of the operating equipment. Additionally, the procedures such as calibration, cleaning, preventative maintenance, operating procedures and operator training for the use of the equipment should be documented and in use kept as standard operating procedures (SOPs)."

Qualification of utilities and equipment generally include the following activities:[4]

- Based on their specific uses, the selection of utilities, equipment construction materials, operating principles and performance characteristics is done.
- In compliance with the design specifications, verification of utility systems and equipment are built and installed (e.g., built as designed with proper materials, capacity, and functions, and properly connected and calibrated).
- Verifying that utility systems and equipment operate in accordance with the process requirements in all anticipated operating ranges. This should include challenging the equipment or system functions while under load comparable to that expected during routine production. It should also include the performance of interventions, stoppage, and start-up as is expected during routine production. During routine production, operating ranges should be shown capable of being held as long as would be necessary.

Elements of Qualification[5-8]

Action of proving any equipment works correctly and leads to the expected results.

Design qualification (DQ)

The documented verification that the proposed design of the equipment and system is suitable for the intended purpose.

Installation Qualification (IQ)

The documented verification that the equipment and system as installed or modified, comply with the approved design and the manufacturer's recommendations.

Operational Qualification (OQ)

The documented verification that the equipment

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and system, as installed or modified, perform as intended throughout the anticipated operating ranges.

Performance Qualification (PQ)

The documented verification that the equipment and system, as connected together, can perform effectively and reproducibly, based on the approved process method and product specification.

Verification Qualification (VQ)

The documented verification that the equipment and system, as connected together, still in the state of art and actually leads to the expected results and user requirements.

Safety Qualification (SQ)

The documented verification that the equipment and system as installed or modified, comply with the safety requirements of process, facility and personnel.

Maintenance Qualification (MQ)

The documented verification that the proposed maintenance program of the equipment and system is suitable for the intended purpose.

Re-Qualification (RQ)

The documented verification that the systems, as connected together, are still performing satisfactorily. Re-qualification is required as an outcome of relocation, major modification and due to ageing.

Need for calibration:

Calibration can be called for

- With a new instruments
- When a specified time period is elapsed
- When a specified usage (operating hours) has elapsed
- When an instrument has had a shock or vibration which potentially may have put it out of calibration
- Sudden change in weather
- Whenever observation appears questionable

The status of the instruments is identified by checking the calibration tag of the instruments. Tag consists of information regarding instruments like name of instrument, date of procurement, date of calibration, next calibration date and signature of calibrated person with date. Calibration of instruments is done in two ways internal calibration and external calibration. Internal calibration is done the in-house officials whom have sound knowledge on it. External calibration is done according to the instructions of the manufacturer and should be done in the government approved individual or institution.

Qualification of Laboratory Equipments

1. Friability Test Apparatus[9]

- Switch on the power supply.
- Set the RPM to 25 and start the machine simultaneously with the stop watch. Count the actual rotations and not the time required for the same.
- Similarly set the RPM to 100 and note the time required and actual rotations.
- Apparatus is in proper working condition if,

✓ Time required for 25 rotations is 1 min ± 05 sec.

✓ Time required for 100 rotations is 4 min ±

20 sec.

- Record the observation in the calibration record.
- Affix a "Calibration Status" label on the instrument.
- In case of any discrepancy, report the observations to QC manager / QA Manager and notify the defect to Engg. Department. Affix an 'UNDER MAINTENANCE" label on the instrument.

Frequency: Once in a month and after each maintenance job.

2. Hardness Tester[10]

Take out the force gauge to be calibrated and hold vertically up.

- Adjust the zero on the force gauge.
- Standard Weights are then applied to the hook of force gauge and measure the tension of the spring on the force gauge.
- When 1 kg of standard weight is applied, scale on the force gauge should also show 1 kg tension produced from the initial point where pointer is adjusted.
- Adjust the zero on the force gauge again.
- Follow the same procedure for other weights.
- The test to be carried out for 1.0 kg, 2.0 kg, 5.0 kg, 10.0 kg, 20.0 kg & 30.0 kg standard weights.

Tolerance: ± 0.25 kg / ± 0.1 kg

Frequency: Once in 6 months.

Maintenance / Repair When the instrument does not comply with the requirement specified above; the instrument should be labelled as "Out of Calibration" and should get repaired / serviced. After repairing / servicing the instrument before taking for use, the instrument must be calibrated as per the above-mentioned procedure.

3. Disintegration Test Apparatus [11]

A. Calibration for Number of Oscillations per minute

- Take a pre-calibrated stopwatch. Operate the apparatus as per SOP. Start the apparatus and stopwatch simultaneously and count the number of oscillations per minute.
- Repeat the same for five times and note down the number of oscillations per minute for each time.
- The oscillations per minute shall be within the limit of 29 to 32 through a distance of 53 to 57 mm throughout the period of operation. Record the observation.

B. Calibration for Temperature:

- Switch on apparatus and press key.
- Turn on the heater by pressing 'ON' key.
- Set the bath temperature by pressing scroll keys.
- Wait till the temperature of beaker A and beaker B attain the set value.
- Screen shall show the set temperature of bath and the temperature of beaker A and beaker B.
- Take a pre-calibrated thermometer and check the temperature of beaker A and beaker B.
- Record the observation.

C. Timer Calibration

- Set the timer for '30 minutes' and start the equipment and stop watch simultaneously. Note down the stop watch reading immediately when

the equipment stops and note down the observation.

- Observed time should not deviate by '± 1 min' of set time.

D. Sieve Integrity Test

Check the 'integrity' of woven stainless steel cloth (sieve) attached to the base plate of each basket with a pre-calibrated vernier calliper. The sieve has weaven squares of aperture of 1.8 – 2.2 mm and wire diameter of 0.57 to 0.66 mm. Note the observations.

- Affix the 'CALIBRATION STATUS' tag duly filled and signed on the equipment after completion of calibration.
- If the instrument is out of calibration then affix 'UNDER MAINTENANCE' tag and inform to maintenance department.
- The frequency for calibration of Disintegration Test apparatus shall be after every one month or after every maintenance work.

4. Dissolution Test Apparatus[12]

Part 'A'

The instrument shall be calibrated for RPM and Temperature.

For Temperature Calibration

Measure the temperature of the water bath and of each jar with a calibrated thermometer and compare the result against the digital display on the apparatus.

Acceptance Criteria: 37°C ± 0.5°C

For RPM Calibration

Calibrate the apparatus at 50 and 100 RPM.

Compare the RPM shown on the digital display of the apparatus with the RPM measured with a stopwatch or Taco meter.

Acceptable criteria: ± 1 RPM – for 50 RPM

± 2 RPM – for 100 RPM

Part 'B' Apparatus Suitability Test

Disintegrating Type

1. Use USP dissolution calibrator disintegrating type 50 mg prednisone tablets.
2. This USP Dissolution Calibrator is provided for the Apparatus Suitability Test in the general chapter of USP 24 or as per the method specified in the documents received along with the respective lot of the tablet.
3. Do not expose the tablets to excessive humidity. Store in dry, cool place.
4. Dissolution Media: Distilled water 500 ml.
5. Using a membrane filter, with stirring for about 5 minutes.
6. Weigh accurately about 10 mg of prednisone reference standard (already dried on 105°C for 3 hour into a 100 ml volumetric flask and dissolve in 5 ml of ethanol. Make up to volume with distilled water.
7. Dilute 10 ml of the solution to 50 ml with distilled water.
8. Conduct the suitability test at conditions mentioned in the certificate of tablets using apparatus I and II.
9. After completion of the dissolution time withdraw filter and aliquot of the solution.
10. Heat the medium with gentle stirring, to about 45° C, immediately filter under vacuum
11. Discard the first 2 ml of solution and

measure the concentration of prednisone at 242 nm against the absorbance of prednisone USP reference standard solution.

12. The apparatus is suitable if each of the individual calculated values for each apparatus at all indicated speeds are within the specified ranges.

Apparatus Suitability Test Non-disintegration Type

a. Apparatus suitability test for non-disintegrating type Salicylic Acid 30 mg tablets.

b. This USP Dissolution Calibrator is provided for the Apparatus Suitability Test in the general chapter of USP 24 or as per the method specified in the documents received along with the respective lot of the tablet.

c. These tablets are pure salicylic acid with no binders or fillers, because of the physical properties of such tablets, some sticking may occur during storage. Gentle tapping of the bottle may be used to separate the tablets.

d. Do not expose the tablets to excessive humidity. Store in a dry, cool place.

e. Dissolution Medium – 0.05 M phosphate buffer pH 7.4 ± 0.05, 900 ml.

f. Weigh accurately about 27.22 g of monobasic potassium phosphate and dilute to 1000 ml with water. (Solution A)

g. Weigh accurately about 8 g sodium hydroxide and dilute to 1000 ml with water 0.2M Solution (Solution B).

h. Place 500 ml of solution A and 391 ml of solution B and dilute to 2000 ml with water and adjust the pH to 7.4 ± 0.05 with either of the solution A/B.

i. Dry a portion of salicylic acid working standard over silica gel for 3 hours before use.

j. Weigh accurately about 33 mg of salicylic acid working standard into a 100 ml volumetric flask, add 1 ml methanol and dissolve the powder, Dilute to volume with phosphate buffer. Dilute 5 ml to 50 ml with buffer.

k. Place one Salicylic acid Non-disintegrating type tablet in each of the 6 containers and operate the apparatus at each of the speeds indicated in the certificates. Withdraw and filter an aliquot of the solution

l. Discard the first 2 ml of solution. Dilute 5ml of the filtrate to 50 ml with dissolution medium (phosphate buffer) and measure the concentration of Salicylic acid at 296 nm against the absorbance of Salicylic acid reference standard solution.

m. The apparatus is suitable if each of the individual calculated values for each apparatus at all indicated speed is within the specified ranges.

The frequency for calibration of Dissolution Test apparatus shall be after every three month or after every maintenance work.

5. Tap Density Tester [13]

- Measure the tapping height(3mm or 14mm) with a ruler
- Obtain calibrated cylinder(250mL or other volume) from qualified supplier
- Measure the length of the cylinder

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Table 1. Basket and Basket Shaft Measurement

S.No.	Name Of Element	Usp Limit (Mm)
1.	Diameter of shaft	9.4-10.1
2.	Vent hole	2.0
3.	Clear operating	20.2 ± 0.1
4.	Shaft base	5.1 ± 0.5
5.	Outer diameter of basket base	26.4 ± 3
6.	Inner diameter of basket base	20.2 ± 1
7.	Outer length of basket	36.8 ± 3
8.	Inner length of basket	27.0 ± 3
9.	Outer diameter of screen	22.2 ± 1

Table 2. Paddle and Paddle Shaft Measurement

S.No.	Name of Element	Usp Limit (Mm)
1.	Longer width of paddle	74.0 – 75.0
2.	Weight of the paddle	19.0 ± 0.5
3.	Lower width of paddle	42.0
4.	Width of paddle	04.0 ± 1
5.	Diameter of shaft	9.4 – 10.1

- Set the count number and start tapping
- Count the tapping number using a stopwatch setting to 1 minute, check the allowed tap number error range as per specific international standard.
- Weigh the tapping device including the cylinder

CONCLUSION

The purpose of the use of analytical instruments is to generate reliable data. Manufacturing is mainly depends on the performance of the equipment. Consistent performance of the equipment is only possible when the equipment is properly qualified, verified and maintained. Equipment Qualification's components of fully defining the equipment's required performance, ensuring that suitable equipment is selected and ensuring that the equipment's performance is consistently of the required standard have many benefits for the analyst:

• Attaining the correct result and proof of the correct result (in conjunction with other QA and QC measures)

• Reduced incidence of test measurements that are not of the required quality.

• Rapid identification and rectification of any problems that may occur with the measuring equipment during its entire working life.

• Subsequent long term savings of both time and money.

Validation is the recognized means of demonstrating that the functioning of each constituent element of equipment complies with specification. This confers absolute confidence in the analytical measurements. It ensures that the accuracy, reliability and perfection of the

equipment are not compromised in any manner. However, to maintain the accuracy of an instrument in use, instrument calibration is needed.

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