

PHARMACEUTICAL VALIDATION



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Definition:

□ **Validation:** A “*documented programme*”, which provides a ***high degree of assurance*** that a specific process will consistently produce, a product ***meeting its pre-determined specification and a quality attributes***.

➤ Types of validation:

1. Process validation: 
- a) Prospective validation
 - b) Concurrent validation
 - c) re-validation
 - d) Retrospective validation
2. Cleaning validation
3. Validation of analytical methods

Calibration:

□ **Definition:** Calibration is a process where a comparison is made between two entities, **one whose value has to be measured and the other entity, known as the standard**, which is used as the reference in the comparison.

➤ Methods for calibration:

1. Standard Calibration
2. Calibration with Data
3. ISO 17025 Accredited
ation



Methods used for calibration:

- 1. Standard Calibration:** This method is mostly preferred for calibrating instrument that are non-critical to quality or not required for accreditation and license purposes
- 2. Calibration With Data:** Procedure for calibration with data are similar to that of accredited calibration. Only exception being that these procedure are not accredited to the ISO standard. Moreover, they not accompanied by data on measurement uncertainties.
- 3. ISO 17025 Accredited Calibration:** This has to be a strictest method of calibration. Generally it requires a measurement reports which has the details of the measurement that are maid against the standard of "as found" (before calibration is started) & "as left" (once the calibration is completed). If the calibration is done bye service provider they must issue a certificate of the same.

Qualification

- ❑ **Definition:** Qualification is a process of assurance that the *specific system, premises or equipment are able to achieve the predetermined acceptance criteria* to confirm the attributes wh at it purports to do.
- Qualification can be considered to be a part of the validation process. It can be further divided into:
 - 1) Design qualification
 - 2) Installation qualification
 - 3) Operation qualification
 - 4) Performance qualification
- 1. **Design qualification(DQ):** It is documented evidence that proposed design of the facilities, system and equipment is suitable for intended use.
- **Purpose:** To ensure that all the requirements for the final system have been clearly defined at the start.

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2. Installation Qualification (IQ): It is documented evidence that the premises, supporting utilities, the equipment have been built and installed in compliance with design specifications.

➤ **Purpose**: To check the installation site/ environment & verifies the condition of installed equipment. Also to ensure that all aspect of equipment installed correctly and complies with the original design.

3. Operation Qualification (OQ): It is the process of demonstrating that an instrument will function according to the its operational specification in the selected environment.

➤ **Purpose**: To ensure that all the dynamic attributes comply with original design.

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4. **Performance Qualification (PQ)**: It is the process that ensure the process under anticipated conditions, consistently produces a product which meets all pre-determined requirements.
- **Purpose**: It is ensure that the instrument is performing within specified limits.

Scope/ Purpose of calibration:

- Calibration can be perform for the following purpose:
- To make sure that the readings of equipment or instruments are consistent with other measurements and display the correct readings every single time.

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- To determine the accuracy, precision, reliability and deviation of the measurements produced by all the instruments.
- Accuracy: Closeness to the test results obtained by that method to the true value.
 - Precision: Degree of agreement among individual results when the method is applied repeatedly to multiple sampling of a homogeneous sample.
 - Reliability: Degree to which an assessment tool produce stable & consistent result under the same condition.

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- Deviation: Is a measured difference between observed value & expected or std. value for a process or product.
 - To establish the reliability of the instrument being used and whether it can be trusted to deliver repeatable results each time.
 - To map the 'drift' as documented. Instruments have a tendency to produce inaccurate measurements over a period of time, following repeated use.

Frequency of calibration:

- Calibration interval may be based on calendar.
- The frequency of calibration depends on following factors:
 - a) What is level of accuracy desired?
 - b) What is the recommendation of manufacturer?

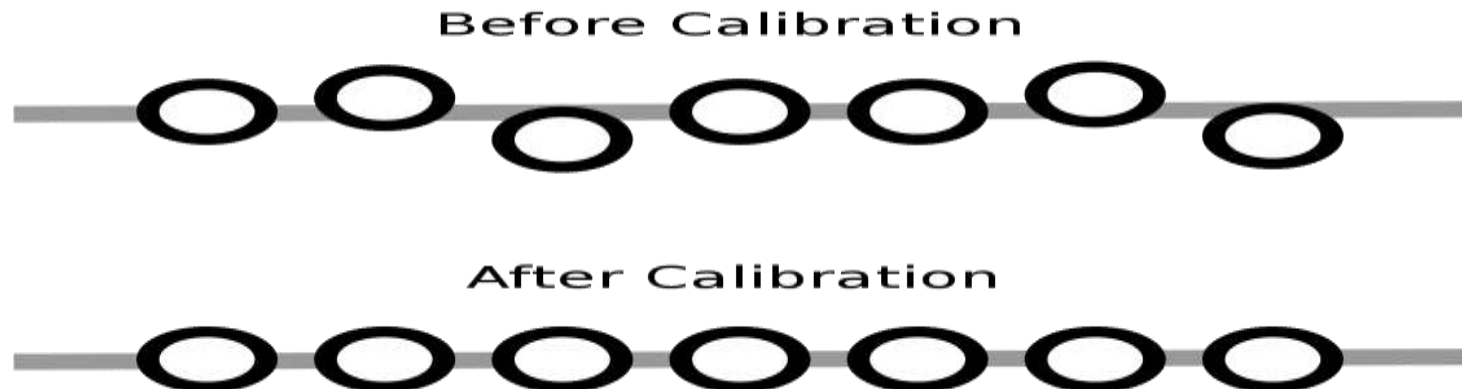
- The interval between calibration varies as:
 - a) Weekly
 - b) Monthly or bi-monthly
 - c) Annually or semi-annually
 - d) After every heavy usage of equipment or instrument.

Importance of calibration:

- Calibration is responsible for defining the accuracy of any measurement and its quality that is recorded by any instrument.
- Regularly calibration of any equipment can eliminate the draft at its building stage instead of allowing it to grow till it affects the measurement in significant ways.
- Calibration helps in quantifying and controlling errors and uncertainties within various measurement process to an acceptable level.
- Further, it helps in improving the accuracy of the measuring device, which in turn improves the quality of the FPP.

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- In short regular calibration allows pharmaceutical companies to have confidence in their result which they can record monitor and control.
- Calibration are not optional but needed for regulatory compliance



Scope of validation:

- Analytical test methods: (eg. Accuracy, precision, specificity, limit of detection, linearity etc...)
- Instruments calibration: (eg. Temp., Weight, pH, humidity etc)
- Process utility services: (eg. Water, steam, HVAC system etc)
- Raw materials & Packaging materials: (eg. Specification, vendor certificate)
- Equipment: Equipment qualification programme start with Users Requirement Specifications & Functional Requirement Specifications these two requirements will result in to the Design Qualification.

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- Facilities: (eg. Construction, building maintenance, certificate of constricted facilities etc)
- Manufacturing operations: (eg. Tablet mfg.)
- Product design: (F&D, package compatibility, define specification for RM/PM, Define process & test method etc)
- Cleaning: (equipment & process containers, product containers & closures, facility etc)
- Operators: (knowledge, skills & attitude)

Importance/ advantages of validation:

- The four major advantages of validation includes:
 - 1) Reduction of quality cost
 - 2) Process optimization
 - 3) Assurance of quality &
 - 4) safety

Difference in Calibration & Validation

	Calibration	Validation
1	Calibration assures accuracy of measurements.	Validation provides proof of consistency across all the processes, batches of products or methods being used.
2	Calibration is a process that ensures that accuracy is maintained in the measurements produced by your equipment.	Validation is a documented process that provides assurance that a product, service or system consistently provides results within the acceptable criteria.
3	Calibration performance of any equipment is compared against a reference standard.	There are no reference standards used in validation.
4	It should be performed as per calibration SOP.	It should be performed as per the validation protocol.
5	You must periodically calibrate your instruments. Identify if there is a 'drift' in the measurements and eliminate it through calibration.	There are no such requirements for validation. It should be performed when you make any change in the existing system or when the revalidation period has reached.

Thanks...