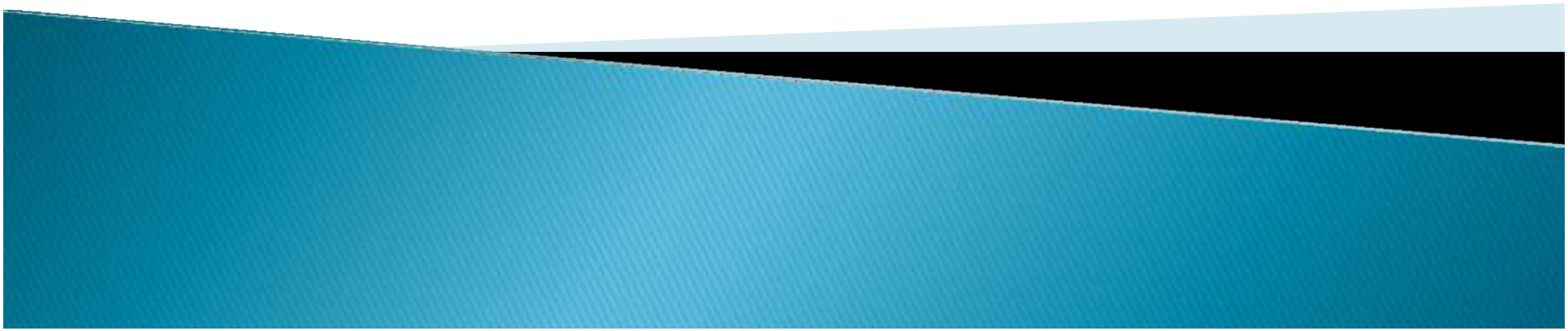
Equipment Qualification



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What is Validation?

- According to the Food and Drug Administration (FDA), the goal of validation is to:

  "Establish documented evidence which provides a high degree of assurance that a specific process will consistently produce a product meeting its predetermined specifications and quality attributes."

- It is a requirement for Good Manufacturing Practices and other regulatory requirements.

- What does this mean?
  - An quantitative approach is needed to prove quality, functionality, and performance of a pharmaceutical/biotechnological manufacturing process.
  - This approach will be applied to individual pieces of equipment as well as the manufacturing process as a whole.
  - Guidelines for validation are set by the FDA, but the specifications of validation are determined by the pharmaceutical/biotech company.

USER REQUIREMENTS SPECIFICATION.

- **User Requirements Specification** (URS), is the most critical of documents and yet, the most often bungled. Whether the system is purely mechanical, or a mix of electro-mechanical, or solely a software program, the successful compilation and execution of the Installation Qualification (IQ) (for installation), Operational Qualification (OQ) (for functionality) and the Performance / Product Qualification (PQ) (for operability), is dependent on an User Requirements Specification (URS) containing clear, concise and testable requirements.

Once the end user requirements specification is documented, agreed and approved they form the basic URS Level-1 document. The engineers (or vendor) can then commence the preliminary design to establish exactly what functions are required for each of the items specified in the user requirements specification, the end user has listed. Once this functionality is documented and approved it forms URS Level-2 document. This is the final level of the URS unless software is used.

If software is to be used, the URS Level-2 document, is passed to the code writers. As the code is written, lines, or groups of lines, of code must be attributed to the individual functions that necessitate their presence. The completion of this task results in the completion of the URS Level-3 document

Developing the URS to this level is unique in most industries, but is, standard practice in strictly regulated industries, as it is a major building block in the creation of quality software. The URS Level-3 document, contains all the traceability which is deemed mandatory for software assessed to be critical to product quality, in the pharmaceutical regulated industries.

Structure and Content of the URS

- The URS can contain a large number of requirements and should therefore be structured in a way that will permit easy access to information.
- The requirement specification must be formally reviewed and approved by the pharmaceutical manufacturer.

- **The following guidelines should be followed during the production of the URS :**

1. Each requirement statement to be uniquely referenced,and no longer than 250 words.
2. Requirement statements should not be duplicated nor contradicted.

3. The URS should express requirements and not design solutions.

4. Each requirement should be testable.

5.The URS must be understood by both user and supplier; ambiguity and jargon should be avoided.

6. The use of diagrams is often useful.

7.The scope for readers to make assumptions or misinterpret should be minimized.

8.Wherever possible, the URS should distinguish between mandatory/regulatory requirements and desirable features.

FORMAT

The URS for a GMP computer control system application will typically address the following:

Scope of system supply

- Project objectives
- Regulatory requirements
- Process overview
- System boundaries
- Operational considerations
- Manufacturing design data
- Instrument application data
- Data records
- System functions
- System software
- System hardware and peripherals

System interfaces
Environmental conditions
Access security
Diagnostics
System availability
Safety
Test and calibration
Quality procedures
Software development life cycle
Documentation requirements
Training
Engineering/installation standards
Ongoing support
Warranty
Delivery/commercial requirements

Newly sanctioned systems will require compliance with regulations for GMP electronic records and electronic signatures, and definition of the functionality required will need to be included.

The structure of the URS be used as the basis for the presentation format of the **FDS and hardware and software design specifications**; this helps ensure design decisions are auditable back to the source requirement.

Once reviewed and approved internally, **the URS is issued to prospective suppliers** as part of the tender document set so that detailed quotations for the system application can be obtained.

URS provides the following key benefits for the validation program:

1. Clarifies technical, quality, and documentation requirements to the vendor(s).
2. Enables the pharmaceutical manufacturer to assess the technical, regulatory, and commercial compliance (or otherwise) of submitted bids against a formal specification.
3. Ensures the basis of a structured approach to the presentation of information.

4. Provides a basis for testing and test acceptance criteria.

5. Provide a baseline for validation and verification..

User Requirements Specification Justification (URS)

- They must be comprehensive. Each and every requirement relating to product safety, identity, strength, purity, and quality must be identified. Hence, Quality Assurance (QA) must have a significant role in reviewing and approving the final set of requirements, and must be an approver of changes to any requirement that can affect the above product or process attributes (e.g., cGMP's).

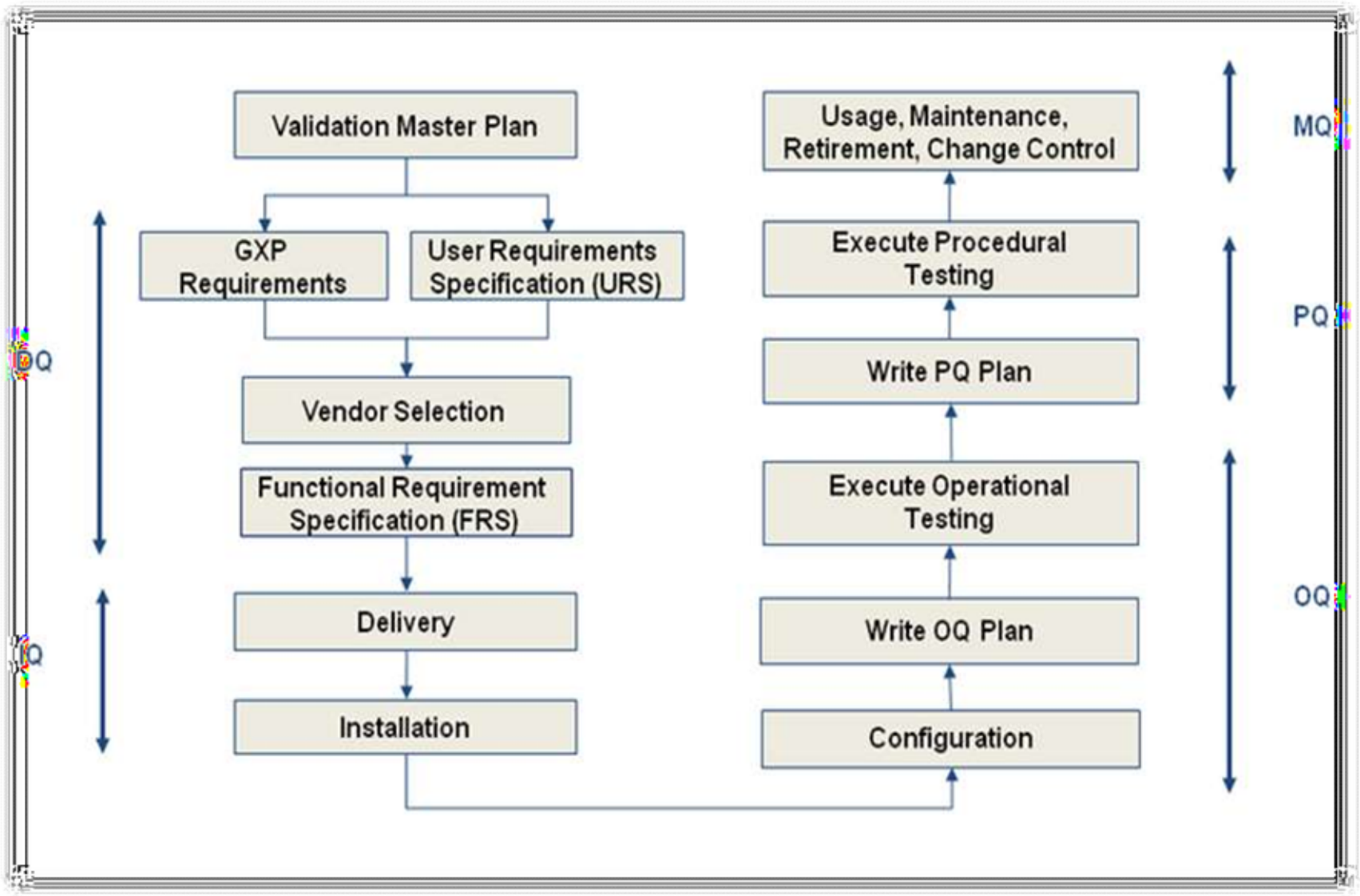
- Given a comprehensive **User Requirements Specification** that has been approved by QA and is under project change management, the Design Qualification(DQ) process then can be reduced to two key objectives:

- Documented verification that the overall design appears to address, by some means, each and every **requirement** affecting the product and performance of the manufacturing process (or, in the case of unknown product or multi-product manufacturing facility, the required equipment/ system performance capabilities).

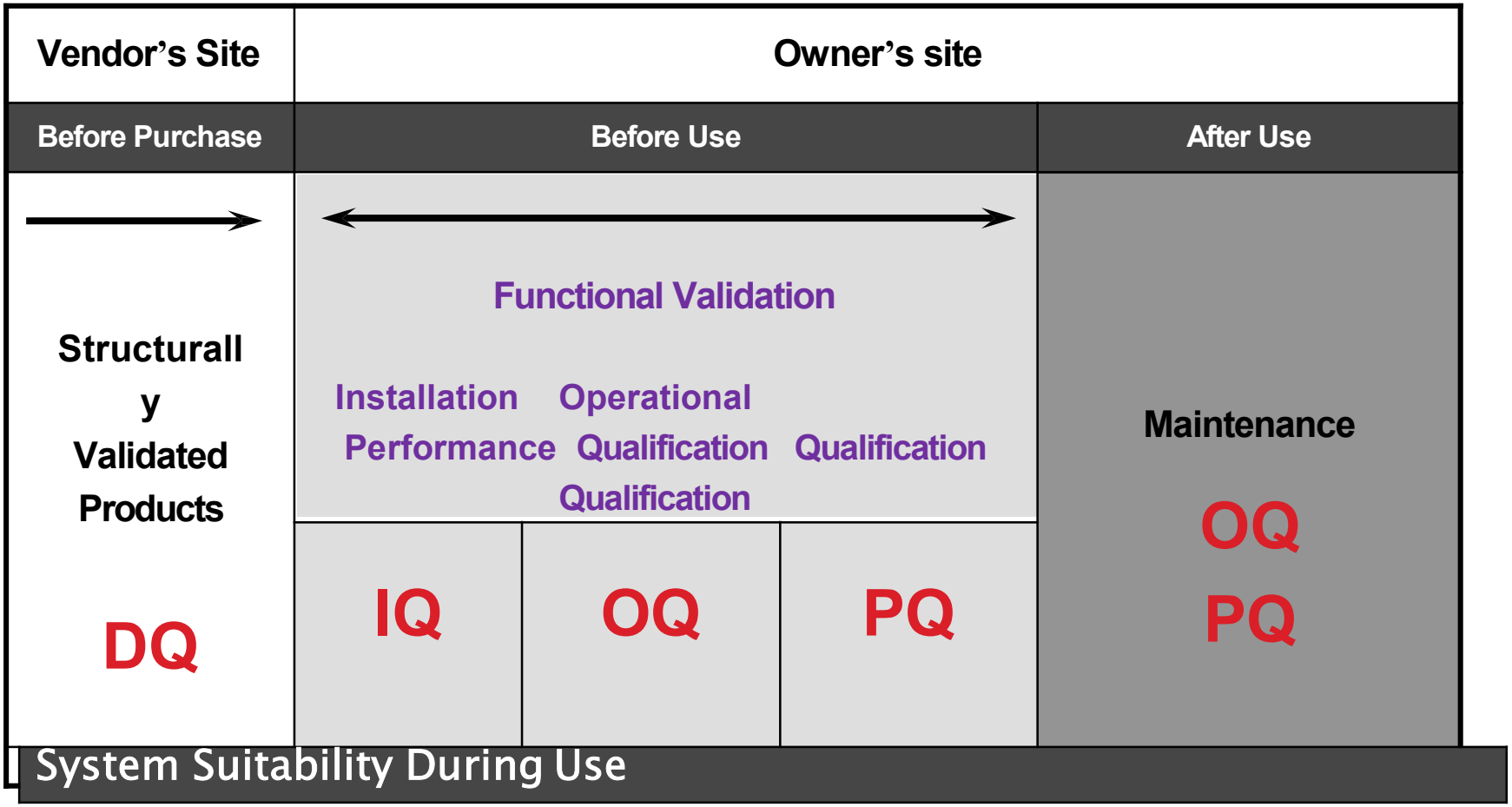
- Identification (and documentation) of the critical individual physical components, attributes, and operational features that directly support meeting each **requirement**.

Phases of Validation.

- Validation is broken down into 5 main phases,
- Design qualification (DQ).
- Installation qualification (IQ).
- Operational qualification (OQ).
- Performance qualification (PQ).
- Maintenance Qualification (MQ)
- Component qualification (CQ).


Validation Master Plan
GXP Requirements
User Requirements Specification (URS)
Vendor Selection
Functional Requirement Specification (FRS)
Delivery
Installation
Usage, Maintenance, Retirement, Change Control
Execute Procedural Testing
Write PQ Plan
Execute Operational Testing
Write OQ Plan
Configuration
MQ
PQ
OQ
Q
IQ

Validation Time Line.



Validation vs. Qualification.

- **Validation:**

  - Refers to the total life cycle of a product from development through use and maintenance.
  - **Owners** are responsible for **Validating Their Processes** (personnel, equipment, methods, SOPs) to ensure compliance to cGMP/GLP regulations.

- **Qualification:** (Inspection, functional testing and documentationreview)

  - Is a part of the validation process which verifies module and system functional performance prior to being placed on-line and thereafter according to a standard operating procedure.

Quality Management Equipment Qualification

Equipment Qualification

- It is a basic requirement of good analytical chemistry that balances and other analytical instruments must be suitable for the purpose for which they are used and that they must be appropriately calibrated. As a consequence, Equipment Qualification is gaining more and more importance in ensuring the validity of results. Regulatory bodies also seem to be turning their attention increasingly to this area, and manufacturers of analytical equipment are forced to play a significant role in the various steps of Equipment Qualification.

The 5 steps of Equipment Qualification

Step 1: Design Qualification (DQ) defines the functional and operational specifications of a balance or instrument.

Step 2 :Installation Qualification (IQ) ensures that a balance or instrument is received as designed and specified. It documents the installation in the selected user environment.

Step 3: Operational Qualification (OQ) demonstrates that a balance or instrument will function according to its operational specification in the selected environment.

Step 4: Performance Qualification (PQ) demonstrates that a balance or instrument consistently performs according to a specification appropriate to its routine use.

Step 5: Maintenance Qualification (MQ) describes and documents any maintenance required on the equipment.

Design qualification (DQ)

Design qualification (DQ) is the process of completing and documenting design reviews to illustrate that all quality aspects have been fully considered at the design stage. The purpose is to ensure that all the requirements for the final systems have been clearly defined at the start.

Design Qualification (DQ) defines the functional and operational specifications of the instrument and details the conscious decisions made in the selection of the supplier. DQ should ensure that instruments have all the necessary functions and performance criteria that will enable them to be successfully implemented for the intended application and to meet user requirements.

The list below shows the recommended steps that should be considered for inclusion in a Design Qualification.

- Description of the analysis problem
- Description of the intended use for the equipment
- Description of the intended environment
-Preliminary selection of the functional and performance specifications (technical, environmental, safety)
- Preliminary selection of the supplier
- Final selection of the supplier and equipment
-Development and documentation of final functional and operational specifications

Vendor Qualification as part of DQ

- As part of the design qualification process, the vendor should be qualified; the question is how should this be done? Is an established and documented quality system enough (e.g. ISO 9001), or should there be a direct audit?

  The answer is that there may be situations where a vendor audit is recommended: for example, when complex computer systems are being developed for a specific user. However, this is rarely the case for balances and analytical instruments.

  If equipment does not include a computer system, a good reputation, one's own experience or good references from other users - together with ISO 9001 certification - can be sufficient.

Installation Qualification (IQ)

Installation qualification (IQ) is the process of checking the installation, to ensure that the components meet the approved specification and are installed correctly, and to see how that information is recorded. The purpose is to ensure that all aspects (static attributes) of the facility or equipment are installed correctly and comply with the original design.
all of the instrumentation components are identified and checked against the manufacturer's component listing.
The working environment conditions are documented and checked to ensure that they are suitable for the operation of the instrument.

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.

Before installation:
-Obtain manufacturer's recommendations for installation site requirements.
-Check the site for the fulfillment of the manufacturer's recommendations (utilities such as electricity, water and gases plus environmental conditions such as humidity, temperature, vibration level and dust).
-Allow sufficient shelf space for the equipment itself, related SOPs, operating manuals, logbooks and software.

Operation Qualification (OQ)

Operational qualification (OQ) is the process of testing to ensure that the individual and combined systems function to meet agreed performance criteria and to check how the result of testing is recorded. The purpose is to ensure that all the dynamic attributes comply with the original design. Each of the instrument's function are checked to ensure that they conform to the manufacturer's specifications.

This includes the use of certified, traceable electrical simulators and standards to verify that the equipment is processing input signals correctly.

Performance Qualification (PQ)

Performance qualification (PQ), also called process qualification, is the process of testing to ensure that the individual and combined systems function to meet agreed performance criteria on a consistent basis and to check how the result of testing is recorded. The purpose is to ensure that the criteria specified can be achieved on a reliable basis over a period of time.

The performance of the equipment for its routine analytical use is checked to ensure that this complies with its specification.

The temperature sensor readings are compared with a certified reference thermometer. After calibration, the conductivity sensor readings are compared using certified, traceable control standards.

Control Standards of similar values to the intended test samples must be used for PQ.

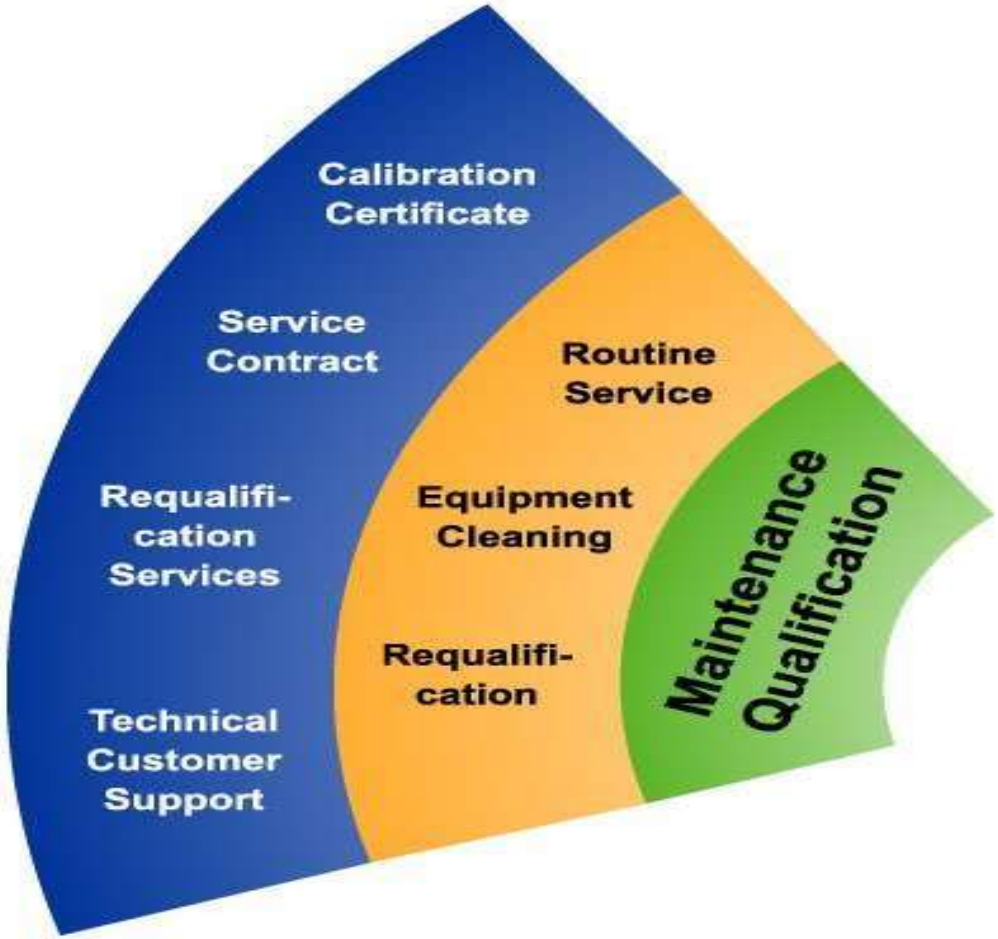
Performance Qualification (PQ) is the process of demonstrating that an instrument consistently performs according to a specification appropriate to its routine use.

Important here is the word consistently. The test frequency is much higher than for OQ. Another difference is that PQ should always be performed under conditions that are similar to routine sample analysis.

PQ should be performed on a daily (or at least a weekly) basis, or whenever the instrument is used. The test frequency depends not only on the stability of the equipment but also on everything in the system that may contribute to the analysis results.

1. Define the performance criteria and test procedures.
2. Select critical parameters.
3. Define the test intervals.

Maintenance Qualification (MQ)



The MQ describes and documents any maintenance required on the equipment. This includes routine servicing and any repairs necessary. Details of any maintenance contracts are also documented in this section, together with a list of authorized service engineers. In addition, the MQ includes the routine cleaning of the equipment and also its ultimate disposal.

Component qualification (CQ)

- Component qualification (CQ) – is a relatively new term developed in 2005. This term refers to the manufacturing of auxiliary components to ensure that they are manufactured to the correct design criteria. This could include packaging components such as folding cartons, shipping cases, labels or even phase change material. All of these components must have some type of random inspection to ensure that the third party manufacturer's process is consistently producing components that are used in the world of GMP at drug or biologic manufacturer.

Instrument Re-Qualification

- Instrument Validation should not be viewed as a one-off event – confidence in analytical results is required for the whole of the instrument's working life.
- To ensure that this confidence is retained, the instrument validation process should be repeated at regular intervals during the instruments operational life.
- The difference between Installation Validation and Re-Qualification is that IQ is omitted for the Re-Qualification
- Re-Qualification should be performed at least annually and should be performed more frequently for applications whose test results have critical implications

REFERENCES

- **Nash. A.Robert and Wachter H. Alfred "Pharmaceutical Process Validation" an international 3rd edition volume 129 revised and expended**
- **WORLD HEALTH ORGANIZATION ORGANISATION MONDIALE DE LA SANTE SUPPLEMENTARY GUIDELINES ON GOOD MANUFACTURING PRACTICES (GMP):VALIDATION**
- **ICH Topic Q 7 Good Manufacturing Practice for Active Pharmaceutical Ingredients.**
- **Validation in pharmaceutical industries by P.P. Sharma**
- http://www.validationworld.com/kb/eq_generic_pq.aspx
- http://www.urswriter.com/index.html?UserRequirements
- http://www.validation-online.net/design-qualification.html
- http://www.coleyconsulting.co.uk/require.htm
- http://www4.informatik.tumuenchen.de/proj/va/SRS.pdf
- http://www.chem.agilent.com/Library/primers/Public/5990-3288EN.pdf
- http://www.gmp-publishing.com/media/files/logbuch/Logfile-8-2011-design-qualification_AC.pdf