Qualification of Equipment as Part of Process Validation for Medical Devices

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An essential part of quality management according to the General Medicine Act (MPG) and the US FDA's Code of Federal Regulations (CFR), is the validation of all processes, and equipment/computer-controlled systems which have direct impact on the quality of product manufacturing.

Process validation is defined as the collection and evaluation of data, from the process design stage throughout production, which establishes scientific evidence that a process is capable of consistently delivering quality products [1].
Regulations and ISO standards applicable for medical devices require that validation of a manufacturing process shall be performed. The Global Harmonization Task Force (GHTF) guidance document (GHTF/SG3/N99-10:2004 (Edition 2)), which is an internationally harmonized document recognized by both the US FDA and ISO, provides guidance on how to qualify your machinery and equipment in manufacturing.

To qualify your machinery and equipment Design Qualification (DQ), Installation Qualification (IQ), Operational Qualification (OQ) and Performance Qualification (PQ) are required to perform.

This white paper will provide you an overview of the individual qualification steps for equipment in manufacturing.

DESIGN QUALIFICATION (DQ)

DQ stands for Design Qualification and is the process of completing and documenting design reviews to demonstrate that all aspects of quality have been fully considered at the design stage. The purpose is to ensure that all requirements for the final systems are clearly defined at the beginning of the project/process.
DQ should ensure that the instruments have all the necessary functions and performance criteria to enable them to be used successfully for the intended application and user requirements [2, 3].

Following is a list of potential steps which should be considered:

- Description of the intended use for the equipment
- Description of the environment
- List of required functional and performance specifications
- Preliminary selection of supplier
- Vendor Qualification
- Final selection of supplier and equipment

INSTALLATION QUALIFICATION (IQ)

IQ stands for Installation Qualification and is intended to verify that the final system/equipment installed for the manufacturing, measuring and/or testing of the product is properly installed, maintained and calibrated. All instrumentation components are identified and checked against the supplier's component list.

This step in the validation process ensures that the manufacturing process meets his expectations. Often the basis for IQ is the design specification with installation requirements. It is therefore important to ensure that all necessary documents, drawings and manuals are available [2, 3, 4].

The contents of Installation Qualification include:

- Installation conditions, such as: wiring, utilities, water supply, power supply, air supply, auxiliary equipment etc.
- Installation environment, such as: clean room requirements, temperature, humidity etc.
- Checking supplier documents, prints, drawings, manuals and so on. Software-controlled device needs to consider software backup and inspect installation environment.
- Checking equipment / component operation and safety devices.
- Ensure that the main technical parameters of the device, including software functionality, are met.

Apart from qualification after the initial installation, requalification also needs to be carried out after any major maintenance work or changes have been made to equipment, or as part of a regular quality assurance schedule.

OPERATIONAL QUALIFICATION (OQ)

OQ stands for Operational Qualification. This phase checks whether the performance of the equipment matches the specification of user requirements.
During the OQ phase, test runs determine the highest, lowest and medium operating parameters. You use the process parameters to define control limits and action limits. They help you to make the process reproducible. You "challenge" the process by using the “worst case” conditions.
If the operational qualification is successful, it is validation that the process control limits and action levels lead to a product that meets all requirements [2, 3, 4].

The main purpose of OQ is to identify and inspect features of the equipment that can influence final product quality, like:

- Display units and signaling LEDs
- Temperature controls and fluctuations
- Overheating and low-temperature protection systems and alarms
- Pressure/Vacuum controlling systems
- CO2 controlling systems
- Humidity measuring and controlling systems
- Fan and fan-speed controllers
- Servo motors and air flap controllers
- Card readers and access controllers

PERFORMANCE QUALIFICATION (PQ)

PQ stands for Performance Qualification and is the last step in the qualification of equipment. In this step it is checked and documented that the equipment works reproducible within a certain working range. Here the system runs several times under normal and challenging operating conditions.

The PQ is intended to demonstrate that the process consistently (long-term runs) produces a product that meets all the specified requirements in terms of functionality and safety.

Before the qualification begins, a detailed test plan is created, based on the process description [2, 3, 4].

Following is a list of potential steps which should be considered in the protocols:

- Manufacturing conditions like equipment limits, operating parameters and component inputs
- A list of the data that should be recorded or analyzed during tests, calibration and validation
- Tests that need to be performed to ensure consistent quality at various steps of production
- A sampling plan which outlines the sampling methods used during and in between production batches
- Defining variability limits and contingency plans for handling non-conformance
- Approval of the PQ protocol by relevant departments

CONCLUSION

Writing effective IQ/OQ/PQ protocols is a must in order to comply with FDA and/or EU requirements for equipment, systems and utilities, to demonstrate suitability for the intended use and to work according to their design and functional specifications. To prove that the requirements are met, qualification protocols must be written and followed. These protocols are documented evidence that manufacturing companies comply with the guidelines. Following these guidelines, your facility's IQ/OQ/PQ protocols will be effective and provide adequate proof of compliance.

We are offering our customers to support them with all validation steps which are required by quality management system requirements in the EU and in the US.
Therefore, If you need any advice or assistance e.g. for manufacturing of your pre-filled syringe, autoinjector, or on-body device project please do not hesitate to reach us at info@anteris-medical.com.
We are very happy to provide a first opinion quickly and free of charge and to help you with your specific project challenge.

LIST OF REFERENCES

[1] U. D. o. H. a. H. Services, *Guidance for Industry - Process Validation: General Principles and Practices Revision 1,* January 2011.

[2] "www.validation-online.net," [Online]. Available: https://www.validation-online.net/process-qualification.html. [Accessed 25 January 2019].

[3] E. C. D.-G. F. H. A. F. SAFETY, *EudraLex: EU Guidelines for Good Manufacturing Practice for Medicinal Products for Human and Veterinary Use Annex 15: Qualification and Validation,* 30. March 2015.

[4] SG3, *Quality Management Systems - Process,* Global Harmonization Task Force, November 2014.