Important Things To Know When Performing Operational Qualification (OQ) For Medical Devices

By Alec Alpert

As part of process validation, Operational Qualification (OQ) establishes process capability and proves that the output of the process is both predictable and understood and that the process is capable at its extremes. The purpose of OQ is to establish that:

- The process works
- The process inputs are known and characterized
- The process capability is acceptable
- The process outputs meet specifications and requirements
- The process outputs are predictable and well understood

OQs will differ depending on the product and the manufacturing process. The OQs for injection molding, pharmaceuticals, and the manual assembly of electronic systems will differ greatly in their methodologies, equipment, sophistication, and scope. Accordingly, manufacturers establish their own process validation policies and procedures that reflect the type of products and processes at hand. However, OQs typically must comply with these key regulations and standards for medical devices:

- 21 CFR 820, Quality System Regulation
- ISO 13485, Medical Devices – Quality Management Systems Requirements
- ISO 14971, Application of Risk Management to Medical Devices
- ISO 9001, Quality Management Systems Requirements
- EU MDR 2017/745, Regulation of the European Parliament and of the Council

This article addresses OQs for the manual assembly of electronic medical devices.

OQ can be perceived as the discovery phase in process validation, which, among other things, addresses the reduction of product and business risk, including the risk of rejection, recall, and scrap.

Measuring, evaluating, and documenting process parameters and routine production and process controls during OQ enables the making of adjustments at various levels in the manufacturing process, thus allowing manufacturers to maintain process robustness and a state of control while avoiding coming near to "worst-case conditions."

Do we always need an OQ? No, not always. If the process has no worst-case conditions, OQ may not be needed. If no worst-case exists for a particular process or for an output within that process, then one should document in the OQ protocol the rationale for omitting the OQ.

OQ Prerequisites

Before OQ activities can begin, certain OQ prerequisites must be completed:

- Process definition documented and approved
- Process map developed
- Test methods and inspections qualified and released
- OQ protocol approved and released
- All personnel participating in the OQ trained
- Installation Qualification (IQ) completed and the IQ report released
- OQ acceptance criteria defined

Process Optimization

Process optimization is typically part of the OQ activities and may include:

- Conducting Design of Experiments (DOEs) for process optimization to establish key process parameters
- Using DOEs to find the optimized processing window and to identify the key effects of the inputs to the process, such as:
  - Identifying main inputs
  - Defining process windows
  - Defining preferable operating settings
  - Defining the preferred nominal settings for the subsequent Performance Qualification (PQ)

- Reduction of variation
- Mistake-proofing

Furthermore, define the following process parameters/settings in the OQ protocol:

- Edge of failure
- Worst-case operating range
- Acceptable operating range
- Normal operating range

Edge of Failure

Edge of Failure signifies the extreme values of the process parameter that could result in an undesirable impact to the process or product; basically, it represents points of process failure. These points can be determined during validation studies by varying the process settings until failure occurs.

Worst-Case Operating Range

The worst-case operating range comprises the highest and lowest values of a control parameter. It does not necessarily represent the edge of failure and may, in fact, be far from the point at which the product or process is unacceptable. Worst-case testing combinations should be performed during OQ and defined in the OQ protocol.

Acceptable Operating Range

Acceptable operating range is defined as the values of the control parameters that fall between the upper and lower worst-case values. They are typically determined through limit testing that demonstrates that the process produces acceptable output at the limits of the specification or setting that is qualified during OQ. The goal of determining the acceptable range is to establish the operational ranges that consistently produce acceptable product in a production environment.

When testing for acceptable operating range determination, multiple series of runs should be performed with key control parameters adjusted to span a range outside the estimated normal operation but within the defined acceptable range.

Normal Operating Range

The normal (nominal) operating range is the range of values permitted for use in normal day-to-day operations. This range should be based on process capability at the proven normal operating range and should be documented in the manufacturing procedures.

The important point to keep in mind is that this range should be encompassed within the proven acceptable range, thus ensuring the increased reliability of the production settings. It is possible to have the normal operating range the same as the acceptable range, but it cannot be greater than the acceptable range.

OQ Outcome

The key achievements of the successful OQ include documented evidence that the acceptance criteria have been met along with a well-established correlation between the process inputs and the process outputs.

OQ Protocol

OQ activities begin with preparation of the OQ protocol. Although companies have their own guidelines for OQ protocols, resulting in OQ protocol structures unique to specific companies, the sections in the OQ protocol typically include:

Purpose

The purpose of the OQ protocol should comprise a summary of the intended purpose of the document.

Scope

Describe in this section the products and processes being qualified. If applicable, include site identification and equipment identification information. If the protocol is intended for repeated use without modification and without updates for duplicate pieces of equipment, you must ensure that the scope states that the protocol applies to any identical model of equipment, irrespective of the usage site.

Background

In this section, describe the need for the OQ, including a brief summary of the events and decisions leading to the need for the OQ.

Should there be any items or activities that need to be excluded from the scope of the OQ, describe those exclusions and their rationale.

Reference Documents

List in this section the procedures and other documents that define the requirements or provide guidance for the content and the approach described in the protocol, such as:

- Manufacturing procedures
- Work instructions
- Process FMEA
- Test methods
- Inspection methods
- Process optimization study
- IQ report
- Equipment specifications

- Product specifications
- Validation master plan

Process Description

In this section, describe the processes that constitute the scope of the OQ, including:

- Materials involved
- Key requirements and controls
- Relevant process parameters
- Process execution logistics
- Process map
- Equipment, procedures, and part numbers

Responsibilities

Identify in this section the functional groups needed to conduct the OQ and spell out their responsibilities.

Qualification Strategy and Methodology

This section documents the individual steps of the OQ protocol that will be completed during the protocol execution and which should be listed in logical, chronological order. Structuring the protocol in this manner will help the personnel executing the protocol to understand the following:

- The steps for executing the qualification
- When the steps should be completed
- How the steps should be completed
- How the material is to be obtained
- The rationale for product sample size and selected material
- How the material should be disposed of
- Equipment used as part of the manufacturing process

Depending on your product and process, the details of the OQ protocol will be different, of course, but typical items may include:

- Temperature
- Humidity
- Environmental contaminants
- Lighting conditions
- Parameter fixed set point
- Minimum setting
- Nominal setting
- Maximum setting
- Control monitoring method

- Flow chart
- Evaluation method
- Data to be collected
- Software validation
- Number of qualification runs
- Build quantity per run
- Material handling requirements
- Production shifts to be used
- Operators to be used
- Required operator qualifications
- Personnel gowning
- Personal protective equipment

Sample Test Requirements

In this section, identify the specific characteristics to be evaluated that will demonstrate the item's ability to meet the specifications and quality attributes.

The required elements may include the following:

- Challenge parameters
- Parameter settings
- Applicable specifications and requirements
- Associated risk classification
- Test methods
- Sample-size requirements
- Criteria categorization (attribute or variable)
- Statistical analysis to be employed to evaluate the data
- Sample storage and handling requirements

Additionally, this section should document how the test samples will be packaged, whether they must be sterilized and conditioned, and the assembly-level traceability and in-process data requirements.

Qualification Acceptance Criteria

In general, the acceptance criteria should be based on whether the process produces acceptable output at the upper and lower worst-case operating ranges established during OQ.

OQ Protocol Execution

Once the OQ protocol is approved and formally released, the next step is its execution by trained and qualified personnel. The OQ protocol execution boils down to:

- Implementing all the steps of the OQ protocol
- Gathering and documenting the data

- Assessing whether the acceptance criteria have been met
- Concluding whether the process is considered acceptable for use and/or further qualification

OQ Report

For the OQ report, document the results of the OQ, including any data analysis that is required. Also, a narrative description of the activities may be provided, with reference to attached records.

OQ Report's Conclusion

In the Conclusion section, provide a brief summary of the conclusion drawn from the observed results. A statement of whether the acceptance criteria have been met must be provided, and any deviations and issues encountered during the OQ protocol execution should be addressed. The Conclusion should state whether the process is considered acceptable for use and/or further qualification.

Appendix

Include in the appendix all the information that was referenced in the protocol, such as raw data recording sheets, and ensure that the appendix is paginated.

About the Author

Alec Alpert is a Quality Engineer and Consultant with an extensive background in quality and compliance for medical devices from new product development, to operations, to post-market activities. He has helped to improve product quality and compliance at the leading medical device companies in applications ranging from linear accelerators, anesthesia systems, and implantable orthopedic devices to electronic imaging systems, infectious disease diagnostic systems, and electrosurgical generators. Alec is the owner of Alpert Engineering, LLC, an engineering consulting company that provides services to medical device companies. Alec is also the owner of www.alecalpert.com, where he publishes articles and white papers with practical advice on medical device technology, quality assurance, and compliance.