1. **Purpose**

This document defines the policies and procedures for executing and maintaining process validation activities. This contains the procedures and requirements for conducting a process validation and maintaining a state of control.

1. **Scope**

This procedure applies to all manufacturing and quality system processes that are utilized in the production of medical devices.

1. **General** 
   1. **Definitions** 
      * **Installation Qualification (IQ)** – Establishing by objective evidence that all key aspects of the process equipment and ancillary system installation adhere to the manufacturer’s approved specification and that the recommendations of the supplier of the equipment are suitably considered.
      * **Operational Qualification (OQ)** – Establishing by objective evidence process control limits and actions levels which result in product that meets all predetermined requirements.
      * **Performance Qualification (PQ)** – Establishing by objective evidence that the process, under anticipated conditions, consistently produces a product which meets all predetermined requirements.
      * **Process Validation** – Establishing by objective evidence that a process consistently produces a result or product meeting its predetermined requirements.
      * **Verification** – Confirmation by examination and provision of objective evidence that the specified requirements have been fulfilled.
   2. **Responsibilities**

**Engineering** – Engineering is responsible for participating in validation activities including planning, approval of protocols and final reports, and execution of validations.

**Quality** – Quality is responsible for participating in validation activities including planning, approval of protocols and final reports, and execution of validations. Quality is also responsible for maintaining validation records.

* 1. **Equipment and Materials** – N/A
  2. **Safety Precautions** – N/A
  3. **Training Requirement** – Engineering and Quality personnel shall be trained to this document based upon their responsibilities.
  4. **Record Management** – Process validation records are managed and maintained by the Quality Department for a minimum of five (5) years following the last manufacturer of the associated medical device.
  5. **Reference Documents and Materials**

**FDA CFR 21 Part 820** – Quality System Regulations

**MDR 2017/745** – EU Medical Device Regulation

**MDD 93/42/EEC** – EUMedical Device Directive

**SOR/98-282** – Canadian Medical Device Regulations

**ISO 13485 –** Medical Device Quality Management Systems

**QP-0002** – Design Control Process

**QP-0009** – Change Control Process

**QP-0012** – Corrective and Preventive Action Process

1. **Process Validation Procedure**
   1. **Process Validation Decision**

A process is required to be validated if the output of the process is not fully verified by subsequent inspection and testing or verification is not sufficient or cost effective. A process may be large and/or complex and composed of many sub-processes. Each sub-process shall be considered individually as well as part of the full process.

* 1. **Validation Planning**

Validation planning is necessary for a successful validation. Following is a list of activities which may be considered during the validation planning stage.

* Form multi-functional team for validation
* Plan the approach and define the requirements
* Identify and describe the processes
* Specify process parameters and desired output
* Decide on verification and/or validation
* Create a master validation plan
* Select methods and tools for validation
* Create validation protocols
* Perform IQ, OQ, PQ and document results
* Determine continuous process controls
  1. **Protocol Development**

Detailed protocols for performing validations are essential to ensure that the process is adequately validated. Process validation protocols may consider the following elements:

* Identification of the process to be validated
* Identification of device(s) to be manufactured using this process
* Objective and measurable criteria for a successful validation
* Length and duration of the validation
* Shifts, operators, equipment to be used in the process
* Identification of utilities for the process equipment and quality of the utilities
* Identification of operators and required operator qualification
* Relevant specifications that relate to the product, components, manufacturing materials, etc.
* Process parameters to be monitored, and methods for controlling and monitoring
* Product characteristics to be monitored and method for monitoring
* Criteria for revalidation
* Deviation resolution

For all three phases, IQ, OQ, and PQ, based on product/process requirements:

* Determine what to verify/measure
* Determine how to verify/measure
* Determine how many to verify/measure, i.e. statistical significance
* Determine when to verify/measure
* Define acceptance/rejection criteria
* Define required documentation
  1. **Installation Qualification**

The IQ validates that the process and/or equipment is installed correctly. IQ considerations include:

* Equipment design features (i.e. materials of construction cleanability, etc.)
* Installation conditions (wiring, utilities, functionality, etc.)
* Calibration, preventative maintenance, cleaning schedules
* Safety features
* Supplier documentation, prints, drawings and manuals
* Software documentation
* Environmental conditions (such as clean room requirements, temperature, humidity)
  1. **Operational Qualification**

During the OQ phase the process parameters should be challenged to assure that they will result in a product that meets all defined requirements under all anticipated conditions of manufacturing, i.e., worst case testing. During routine production and process control, it is desirable to measure process parameters and/or product characteristics to allow for the adjustment of the manufacturing process at various action level(s) and maintain a state of control. These action levels should be evaluated, established and documented during process validation to determine the robustness of the process and ability to avoid approaching “worst case conditions.”

OQ considerations include:

* Process control limits (time, temperature, pressure, linespeed, setup conditions, etc.)
* Software parameters
* Raw material specifications
* Process operating procedures
* Material handling requirements
* Process change control and training
* Potential failure modes, action levels and worst-case conditions (Failure Mode and Effects Analysis, Fault Tree Analysis)
* The use of statistically valid techniques such as screening experiments to establish key process parameters and statistically designed experiments to optimize the process can be used during this phase.
  1. **Performance Qualification**

In this phase the key objective is to demonstrate the process will consistently produce acceptable product under normal operating conditions. PQ considerations include:

* Actual product and process parameters and procedures established in OQ
* Acceptability of the product
* Assurance of process capability as established in OQ
* Process repeatability, long term process stability

Challenges to the process should simulate conditions that will be encountered during actual manufacturing. Challenges should include the range of conditions as defined by the various action levels allowed in written standard operating procedures as established in the OQ phase. The challenges should be repeated enough times to assure that the results are meaningful and consistent. A minimum of 3 productions runs is required unless otherwise justified. These production runs may be shortened as necessary to complete the PQ in a reasonable timeframe.

* 1. **Final Report**

At the conclusion of validation activities, a final report should be prepared. This report should summarize and reference all protocols and results. It should derive conclusions regarding the validation status of the process. The final report should be reviewed and approved by the validation team and appropriate management.

1. **Maintaining a State of Validation**
   1. **Monitor and Control**

Trends in the process should be monitored to ensure the process remains within the established parameters. When monitoring data on quality characteristics demonstrates a negative trend, the cause should be investigated, corrective action may be taken and revalidation considered.

* 1. **Changes in Process and/or Product**

Any changes in the process and/or product including changes in procedure, equipment, personnel, etc. should be evaluated in accordance with QP-0009 to determine the effects of those changes and the extent of revalidation considered.

* 1. **Continued State of Control**

Various changes may occur in raw materials and/or processes, which are undetected, or considered at the time to be inconsequential. These changes may cumulatively affect the validation status of the process. Periodic revalidation should be considered for these types of processes.

1. **Revision History**

| **Rev #** | **Doc #** | **Effective Date** | **CHO** | **Description of Change** |
| --- | --- | --- | --- | --- |
| 00 | QP-0026 |  |  | Initial release of the procedure for process validations. |