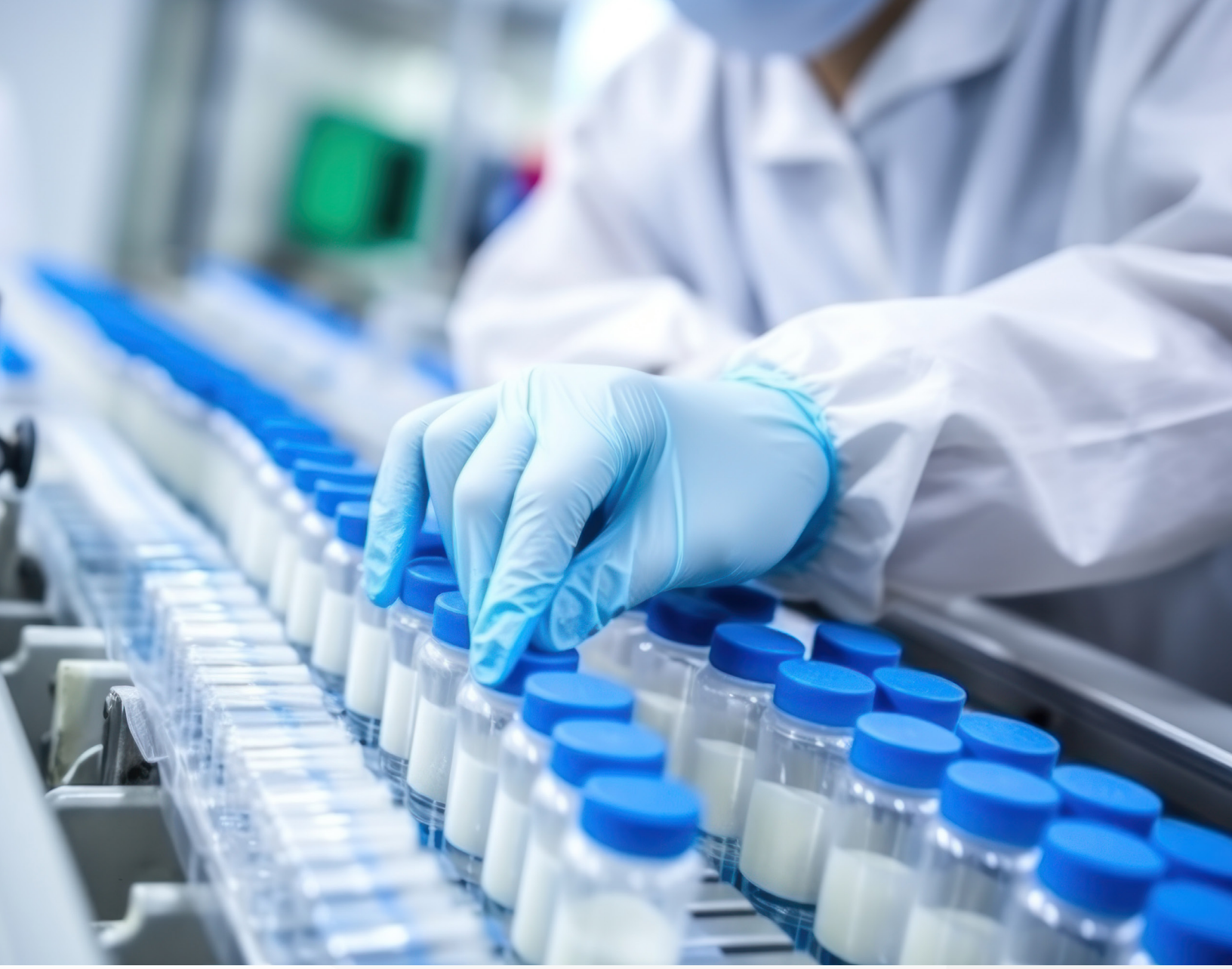

Medical Device Packaging Verification and Validation

ISO 11607 PART 2

AdeptGroup

ENGINEERING EXCELLENCE

Verification and Validation

Thoroughly testing packaging equipment and processes is a crucial part of ensuring the quality and efficacy of medical devices and meeting the requirements of ISO 11607 Part 2.

Adherence to the ISO 11607 standard helps regulatory bodies such as the U.S. Food and Drug Administration (FDA) understand that packaging for medical devices has been appropriately validated and tested to ensure the safety and efficacy of the product.

ISO 11607 Part 2 specifies requirements for the development and validation processes related to terminally sterilized medical devices. A thorough validation process ensures equipment performs properly and development of related processes, such as forming and sealing, accounts for critical parameters to ensure quality and consistency.

This white paper covers key considerations for each step of the validation process with details about relevant sections of the ISO 11607 Part 2 standard where applicable. Our primer on ISO 11607 Part 1 is available in a separate document here.

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Key Considerations

Validation Process Overview

A thorough validation includes several important steps:

- Process Development – A study used to determine the optimal process windows and limits for production based on the package's design requirements
- Installation Qualification (IQ) – This step culminates in a report that captures equipment and facility readiness to produce the packaging
- Operational Qualification (OQ) – This step culminates in a report that captures the performance of the packaging equipment at the limits of the process window
- Performance Qualification (PQ) – This step culminates in a report that captures variability in the manufacturing environment by conducting tests on multiple batches/lots of product
- Process Control – This final evaluation ensures that the output of the process does not deviate from the established limits

Process Development

Process Development focuses on design specification limits.

This includes evaluating package dimensions to ensure the product fits properly within the package, retaining features function properly and the package maintains its shape and overall function. An evaluation of seal strength establishes the minimum and maximum strength and the temperature at which the material will burn or lead to delamination and/or curling. Reviewing materials and material thickness helps determine the point at which barrier performance begins to decline. A review of cosmetic defects checks for any cinders, clearing, burning, smearing, spreading or fading of inks.

When developing process parameters, it is important to evaluate variables in multiple outputs from the packaging process, including optimal time, temperature and pressure for forming, sealing and cooling packaging components. Other key points to evaluate include equipment speeds, vacuum strengths, energy levels for ultrasonic welding and torque limits for lid/cap closure systems.

The process development stage is also the time to create inspection procedures for process variables and product attributes that must be monitored to ensure the packaging process remains in a state of control. These inspection procedures will be used throughout equipment setup.

Common testing standards used to measure process outputs include:

- For packaging system integrity testing:
  - ASTM F2096 Bubble Test
  - ASTM F1929 Dye Penetration Test
- For seal integrity:
  - ASTM F1886 Visual Inspection
- For seal strength:
  - ASTM F88 Peel Test
  - ASTM F1140 Burst Test
- For packaging dimensions
  - ASTM F2203 Linear Measurement
  - ASTM F2251 Thickness Measurement

Specific packaging applications may call for other tests, many of which are listed in Annex B of ISO 11607-1.

Installation Qualification (IQ)

The purpose of IQ is to confirm and document that the machine and manufacturing facility are equipped to produce packages in line with the packaging design requirements.

ISO 11607 Part 2 Section 5.2 states "The following shall be considered: equipment design features; installation conditions, such as wiring, utilities, functionality, etc.; safety features; equipment operating within the stated design parameters; supplier documentation, prints, drawing and manuals; spare-parts lists; software and/or firmware validation; environmental conditions such as cleanliness, temperature, humidity, lighting; documented operator training; operating manual or procedure."

IQ should also include equipment checks such as verifying process variable controls, alarm systems and machine stops where process windows are validated, and calibration of equipment. Maintenance and cleaning procedures and schedules are also an important part of IQ.

There are a handful of potential pitfalls packaging teams can avoid through a thorough IQ:

- **Utilities:** Utility service both within the building and with regional utility suppliers should be reviewed to ensure it's compatible with packaging equipment's needs. Regional electric supply and the electrical service within the facility need to match the power requirements of the machines. Water quality is an important factor for cooling systems, as rusty pipes and other sources of contamination may create a need for frequent filter changes to ensure the machinery remains free of contamination.
- **Equipment Quality:** Packaging teams should establish confidence in the quality of the equipment prior to purchase. Teams must research the supplier to ensure they're a well-established business with a high level of commitment to customer service.
- **Equipment Functionality:** In addition to quality, packaging teams should do due diligence to ensure the equipment can perform in its intended role. Trade shows, supplier visits and factory acceptance tests (FATs) provide opportunities to review equipment functionality and confirm it meets performance requirements.
- **Maintenance Procedures:** Input from the supplier can help shape a maintenance plan that keeps packaging equipment running properly. The supplier can be especially helpful in building out a schedule for servicing or replacing components that wear out with use. Items such as sealing bands, gaskets, bladders, blades and chains should be serviced or replaced at regular intervals. Using equipment at higher speeds, temperatures and pressures will accelerate wear and tear. Suppliers can be helpful in determining how often this maintenance should take place under the conditions the equipment is used.

Operational Qualification (OQ)

The purpose of OQ is to challenge the production process to confirm and document that the machine can produce packages in line with the packaging design requirements.

This qualification should account for variability in the manufacturing environment by producing and testing multiple lots/batches of product with nominal equipment settings, the operators who will run the packaging line day-to-day and normal manufacturing procedures in place.

OQ should include testing at least three runs of product or justification for why fewer runs were used. As the standard instructs, "The OQ of the process shall include at least three production runs with adequate sampling to demonstrate variability within a run and reproducibility to assess variability within a run and reproducibility between different runs."

A thorough OQ will reveal if there's any variability in packaging produced from one lot to another, including soon after equipment startup, before shutdown or returning from a break.

ISO 11607 Part 2 Section 5.4 calls for several things to document during OQ:

- Whether process validation activities used actual product or simulated content
- Confirmation that validation activities used nominal process parameters established during OQ
- Verification of product/packaging requirements
- Assurance of process control and capability
- Proof of process repeatability and reproducibility
- How the process is challenged such as: machine set-up and change-over procedures; process start-up and restart procedures; power failure and variations; and multiple shifts
- Documented procedures and/or process specifications for the forming, assembly, sealing or closing operations shall be established and incorporated into the OQ

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Extension of the Process

Process Control

It is common to consider PQ the final stage of the verification process, but it is helpful to think of Process Control activities as an extension of the process.

Process Control is conducted on the manufacturing process after the qualification/validation activities are complete with the intent of ensuring process drift doesn't lead to the packaging design falling out of specification. These activities are a safeguard against issues that may have avoided detection during previous validations. It's an opportunity to review previous actions, determine when a potential failure started and take corrective action before product reaches the market.

Issues that may have avoided detection during validation can cause packages to fail, and strong Process Control can catch those issues before they cause problems. Small details such as interactions between packaging adhesives and release agents on gloves used by operators or unforeseen errors such as incorrect tooling change-overs can lead to major problems if they go undetected.

Ongoing Process Control activities work in tandem with maintenance procedures to provide a failsafe against anything missed during initial validation activities.

Lean on the Experts

When to Retest

Per ISO 11607 Part 2 Section 5.7, “Processes shall be revalidated if changes are made to the equipment, contents, packaging materials or packaging process which compromise the original validation.”

Specific items that may lead to necessary retesting include:

- Raw material changes that can impact the process parameters variables
- Changes or exchanges to a main part of the equipment which can affect one or more of the established parameters
- Modification or refurbishment of equipment
- Transfer of processes and/or equipment from one facility or location to another or relocation within the same facility
- Sterilization-process changes
- Negative trends in quality or process control indicators

In some cases, very small changes to these factors may not require a retest, but it is important to evaluate the potential impact of any changes before determining whether or not to retest.

CONTACT US

Thorough validation of equipment and processes is important for compliance with the ISO 11607 standard. Meeting this standard ensures regulatory compliance in the largest and most important global territories, and perhaps more importantly, ensures terminally sterilized medical devices are packaged safely and effectively for the end user.

If your organization could use help conducting a thorough validation to confirm equipment and processes align with the ISO 11607 standard, Adept Group can help. Get in touch to learn more about how our team of experts in packaging, testing and regulatory compliance can guide you through these processes and optimize your speed to market.