

Demystifying Medical Device Package Validation for Manufacturers

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Many medical device manufacturers struggle on a daily basis with what they need to do to set up a shelf-life package validation and what it takes to satisfy regulatory requirements regarding sterile medical packaging. This article will demystify the validation process for manufacturers by answering 10 frequently asked questions, using the ISO 11607 standard as a reference guide.

1) What is validation?

According to the FDA, validation is documented evidence providing assurance that a specific process will produce a product that meets predetermined requirements and quality attributes.

2) Why should I validate my package?

Medical device manufacturers are required to obtain 510(K) approval on each medical device package. According to the ISO 11607 standard, the manufacturer "must ensure the product and package system combine to create a total product which performs efficiently, safely, and effectively in the hands of the user."

3) What is the ISO 11607 standard?

According to section 1.1.3, "The intent of this international standard is to provide designers and manufacturers of medical devices with a framework of laboratory tests and evaluations that can be used to qualify the overall performance of the package used to protect the device components during handling, distribution, and storage."

ISO 11607 considers the following attributes:

- Selection of material
- Design of the package
- Process validation
- Final package validation

4) What must I do prior to the validation process?

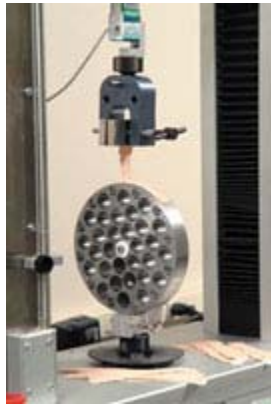
Before a final shelf-life package validation can be put together, specific questions need to be answered to proceed.

- What type of packages are we validating?
- What type of expiration date do we want?
- What is the overall package configuration?
- Which strength and integrity methods do I utilize?
- What are the glass transition, melt, and heat distortion temperatures of the package and product?

5) Which kind of testing methodologies are implemented?

Package Strength

In order to produce acceptable packages on a daily basis and throughout a determined shelf-life validation, it is important to evaluate the strength characteristic. Not only does the strength characteristic play a key role in a shelf-life validation, it lets the medical device manufacturer determine on a daily basis that their process for sealing packages is staying consistent to their predetermined specification set in the process validation.



There seems to be some confusion within the medical device industry regarding the strength of a package versus the integrity of a package. Package strength concerns the force required to separate two components of the package. It could be the force to separate two flexible components of a pouch, or a flexible lid and a thermoform tray. These forces may be measured in pounds per inch width, as in the seal/peel test; or in pounds per square inch, as in the burst test method. Alone, these tests of package strength values do not necessarily prove the integrity of the entire package. In fact, the seal width that was actually measured may be within the strength specification but may have a channel leak that could breach the package and negate integrity.

The main culprit for poor package strength is the seal-sealing parameters. If a proper process validation of the sealer is not performed, the medical device manufacturer can expect failure. Some very typical package strength tests include:

- Package Strength Testing by Seal Peel Testing: ASTM F88-00
- Package Strength Testing by Burst Testing: ASTM F-1140-00

Package Integrity

In order to maintain the sterility of an enclosed product until it reaches its point of end use, the packaging must provide a microbial barrier in the post-sterilization environment. The manufacturer must demonstrate that, under the rigors of distribution, storage, handling, and aging, the sterile package integrity is maintained at least for the claimed shelf-life of the medical device. The microbial barrier properties of the package materials and design must be evaluated after exposure to the environmental and dynamic stresses expected for the finished package. Several methods may be used to satisfy these requirements. They involve evaluating the material performance itself and the whole, finished package as produced on the packaging line.

Packages may lose their integrity as a result of the dynamic related events that occur during processing and/or distribution. Physical test methods may be used to validate that the package integrity has been maintained throughout the package's processing, expected shelf life, and handling. Testing includes:

- Package Leak Testing by Dye Penetration: ASTM F1929-98
- Package Leak Testing by Bubble Emission: ASTM F2096-02
- Package Leak Testing by Vacuum: ASTM D3079-02, ASTM D4991-94

6) What is the "accelerated aging rationale?"

Accelerated aging is performed on packaged medical devices to document shelf life and expiration times for products. Real time aging can be performed; however, products are often obsolete by the time a three-year expiration date is validated.



Accelerated aging is based on a thermodynamic temperature coefficient formulated by Von't Hof that states "for every 10 degree C rise in temperature the rate of chemical reaction will double." However, this formula was based on rate kinetics of a single chemical reaction, not to packages with various kinds of materials. So, the direct extrapolation of this theory to the aging of packaging materials must be used with caution. But the industry, and FDA, believes the theory is useful in defining and justifying accelerated aging test programs.

7) How is accelerated aging performed?

Temperature selection for the accelerated aging study should be determined by the temperature that avoids unrealistic failure conditions such as deformation due to melting. Real time aging must be performed in conjunction with any accelerated aging study to correlate the results found during accelerated aging.

In order to perform accelerated aging, the following information is required:

- Volume of material (this is the size of the individual packages that will be placed inside the environment chamber)
- Test temperature (this is the temperature the chamber will be set at)
- Expiration date (this is the desired shelf life of the product/package system)
- Ambient temperature (this is the temperature at which the product will most likely be stored)
- Aging factor (the most common aging factor is 2.0)
- The main test methodology utilized for accelerated aging: ASTM F1980-02

8) How are packages tested for shipping and distribution endurance?

Manufacturers must evaluate the packages ability to adequately protect the medical device through the handling and distribution environment. Damage such as material puncture, abrasion, and seal failure may result from the dynamic events to which packages are subjected.

Tests performed include:

- ASTM D4169 Test Sequence
- ISTA Various Procedures

All of these test procedures address three common variable for ship testing.

- Shock/drop testing
- Vibration test
- Compression test

9) Why should I develop a test protocol?

Since documentation is key to the sterile medical packaging validation process, developing a protocol, therefore, is essential for satisfying the ISO 11607 requirement.

10) What happens after testing is complete?

A final test report must be generated to document the test results, corrective actions, or other issues found during the validation process.

Closing Advice

Make sure you allow adequate time to perform a thorough package evaluation validation. The time taken to complete the validation can vary from 1 to 9 months. You should expect to spend \$5 to \$15,000 on a shelf-life package system validation depending on the experience and expertise of the instructed packaging engineers.

Remember: the ISO 11607 test standard is only a framework. The final objective of developing a safe and effective package system can be achieved through many different paths.

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