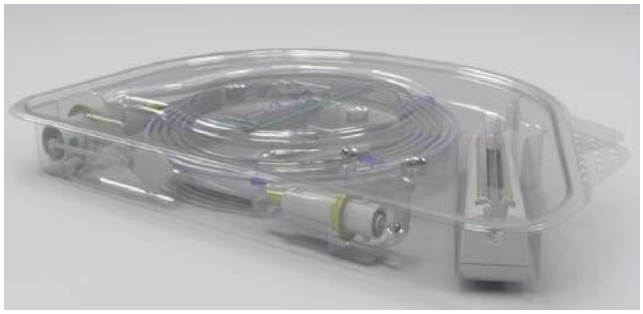
Using Pre-Validated Medical Device Packaging to Speed Time to Market

Introduction



There is a lot of excitement in the medical device packaging industry about pre-validated packaging. Using pre-validated packaging may reduce time to market and minimize package development and validation expenses. However, international standards defining medical device validation requirements are complex, involving materials selection, design qualification, process validation, and design controls. Pre-validated packaging may not comply with all the requirements depending on the specific device involved. Nevertheless, pre-validated packaging can be a helpful strategy if adequately implemented by the device packager within the framework of these standards. This paper aims to clarify when pre-validated packaging makes sense and how its cost and lead time compare to a custom-designed package.

Packaging standards for terminally sterilized devices

Sterile packaging systems need to ensure the sterility of their contents from shipping through the point of use. The sterile barrier system (SBS) must allow aseptic presentation into the sterile field. ISO 11607 (part 1 and part 2) is the global standard governing packaging for terminally sterilized medical devices. Part 1 of the standard defines requirements for SBS materials selection and their design and testing. Part 2 defines manufacturing critical process validation requirements for forming, sealing, and assembly processes.

Key definitions

ISO 11607 provides precise terminology used for medical device and healthcare packaging.

Sterile Barrier System (SBS): *The minimum package that minimizes the risk of ingress of microorganisms and allows aseptic presentation of the*

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sterile contents to the point of use. For example, a thermoformed tray with a Tyvek lid can be an SBS. Header bags and Chevron pouches are standard sterile barrier systems.

Protective Packaging: *The configuration of materials designed to prevent damage to the sterile barrier system and its contents from the time of their assembly until the point of use.* These include shelf cartons and shipping boxes.

Pre-formed Sterile Barrier System**:** *A sterile barrier system supplied partially assembled for filling and final closure or sealing*. Examples include porous and nonporous chevron pouches, header bags, and patch bags. These are typically purchased from packaging suppliers partially assembled and used during final packaging by making a final closure seal. A thermoformed tray also falls within this definition.

Packaging System: *The combination of the sterile barrier system and protective packaging.* Both work in tandem to protect the product and the sterile barrier.

How is sterile packaging validated?

ISO 11607 and ISO 11135 define the requirements for validating terminally sterilized medical device packaging.

1. **Design Qualification**. Packaging materials must be selected and documented within a quality system based on the requirements of the device and sterilization method used. These include the adequacy of the microbial barrier, biocompatibility and toxicity attributes, sterilization effects, sealing effectiveness, compatibility of the device and SBS materials that contact each other, and compatibility with labeling.

2. **Stability Tests.** The sterile barrier seals must be proven to maintain sterility over time. Validation involves a post-sterilization stability study. The sealing and sterilization parameters for this test must be under worst-case conditions. The FDA allows accelerated stability testing if real-time testing occurs in parallel.

3. **Sealing Validation.** The sterile barrier system's sealing process must be validated.

This requires a critical manufacturing process validation, which includes an IQ, OQ, and PQ on the sealing equipment performed at the manufacturing location.

4. **Transit Simulation.** Transit testing must reflect how the product will be shipped

5. **Sterilization Validation.** Sterilization results in a 10^{-6} probability of any infecting microbes surviving the sterilization process.

What is pre-validated packaging?

A pre-validated package eliminates the need for design qualification (1), stability testing (2), and sealing validation (3). It does not negate the need for transit testing because each packaged product may impact the seal differently. Likewise, sterilization validation is still required because it is unique to the product – not the package.

When is pre-validated packaging preferred?

Pre-Validated Packaging

- √ High probability package will change
- √ A clinical trial is the next step

Custom Packaging

- √ Low probability package will change
- √ Commercial launch is the next step

What sterilization validation methods are typical?

The available sterilization validation methods are "full validation" and "single batch release." A full validation validates the cycle parameters and the specific equipment. The single batch release verifies each lot separately. Three single batch releases performed in twelve months may equate to a full validation after a retrospective analysis.

Batch Release Sterilization

- √ High probability package will change
- √ Commercial launch in <16 weeks
- √ Higher Cost

Sterilization Validation

- √ Low probability package will change
- √ Commercial launch >16 weeks

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Time and cost savings

	FDA REQUIRED	Pre-Validated	Custom
Package Design	ISO 11607-1		
Requirements and Concepts			**X**
CAD Model			**X**
Prototype/Rendering			**X**
Carton Design			**X**
Label Design		**X**	**X**
Package Validation	ISO 11607-2		
Tooling			**X**
Raw Materials			**X**
Sealing Process OQ			**X**
Engineering Build		**X**	**X**
2X Sterilization		**X**	**X**
Transit Test		**X**	**X**
Accelerated Aging (1 Yr)			**X**
Sterilization	ISO 11135		
Seterilization (J-Pac EO)		**X**	**X**
Single Batch Release		**X**	**X**
Time & Cost	ISO 11135		
Time (Weeks)		**13 Weeks**	**25 Weeks**
Cost		**$60K**	**$110K**

Typical project plan for pre-validated packaging

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PRE-VALIDATED PACKAGE WITH SINGLE BATCH RELEASE	FDA REQUIRED X	WEEKS															
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
Package Design	ISO 11607-1		1K														
Requirements and Concepts																	
CAD Model																	
Prototype/Rendering																	
Carton Design																	
Label Design	X																
Package Validation	ISO 11607-2																
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Single Batch Release	X																

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Conclusion

Pre-validated sterile packaging is a novel concept that, if properly executed, can help MDMs reduce expenses and improve time to market. However, the ISO 11607 standard (Parts 1 and 2) is complex and cites three critical components of a "validated" packaging system. (A) The design and development of the packaging system include material selection, design, and packaging qualification testing, (B) qualifying or validating or providing proof of the stability of the SBS materials and seals, and (C) sealing process validation.

The MDM's unique devices, sterilization cycle, distribution environment, and manufacturing processes often require pre-validated packaging solutions to undergo additional qualification and validation testing to satisfy regulatory requirements. MDMs should ask specific questions to understand how pre-validated packaging meets these requirements and identify any further testing that may be required. Finally, MDMs must ensure that all validation data is maintained in their design history files, as they are ultimately responsible.

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Additional Resources

ISO 11607-1:2006/(R) 2010 *Packaging for terminally sterilized medical devices— Part 1: Requirements for materials, sterile barrier systems, and packaging systems* and **ISO 11607-1: 2006/A1: 2014** *Packaging for terminally sterilized medical devices – Part 1: Requirements for materials, sterile barrier systems, and packaging, Amendment 1*

ISO 11607-2:2006/(R) 2010 *Packaging for terminally sterilized medical devices— Part 2: Validation requirements for forming, sealing and assembly processes* and **ISO 11607-2: 2006/A1: 2014** *Packaging for terminally sterilized medical devices – Part 2: Validation requirements for forming, sealing, and assembly processes, Amendment 1*

ANSI/AAMI/ISO TIR16775: 2014*, Technical Information Report, Packaging for terminally sterilized medical devices-Guidance on the application of ISO 11607-1 and ISO 11607-2.*