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# 10 Things You Should Do Before You Validate Your Next Package

Package integrity testing is important in determining the sterility and the shelf life of a medical device or product. Package integrity testing includes dye leak, vacuum leak, and bubble leak testing.

**Before you set out to validate a medical device package design or process, you've got to do your homework. "You need to understand what is critical so you build the proper foundation," explains Scott Levy, senior packaging engineer for DDL, a testing laboratory that serves the medical device packaging community. If your company is marketing a sterile medical device, "your goal is to develop a sterile barrier system and avoid a breach of that system," he says. With DDL for nearly 20 years, Levy helps medical device packaging professionals with package testing programs to support package design and process validation. He offers the following 10 points to consider before beginning any validation effort.**

## 1 Understand the regulatory requirements (FDA, EU, etc.)

In general, regulators expect you to prove that your packaging system ensures sterility maintenance of that device and to confirm the consistency of your processes, explains Levy.

Quality System Regulation in the United States defines validation (under 21 CFR Part 820.3) as "confirmation by examination and provision of objective evidence that the particular requirements for a specific intended use can be consistently fulfilled." It defines process validation as "establishing by objective evidence that a process consistently produces a result or product meeting its predetermined specifications."

Expectations for device packaging are described under 21 CFR Part 820.130: "Each manufacturer shall ensure that device packaging and shipping containers are designed and constructed to protect the device from

alteration or damage during the customary conditions of processing, storage, handling, and distribution." It also outlines expectations for medical device design controls (21 CFR Part 820.30), including design validation. If your medical device is intended to be labeled as sterile, you are expected to establish and maintain procedures for validating the sterile barrier system for that device.

Process validation is outlined under 21 CFR Part 820.75, which explains "where the results of a process cannot be fully verified by subsequent inspection and test, the process shall be validated with a high degree of assurance and approved according to established procedures." The European Union's Medical Device Directives state (in Annex I 8.3) that "devices delivered in a sterile state must be designed, manufactured, and packed in a non-reusable pack and/or according to appropriate procedures to ensure that they are sterile when placed on the market and remain sterile, under the storage and transport conditions laid down, until the protective packaging is damaged or opened." The directives also state (in Annex I 8.4) that "devices delivered in a sterile state must have been manufactured and sterilized by an appropriate, validated method."

## 2 Read and familiarize yourself with ISO 11607 so you understand your validation responsibilities

To obtain a CE mark for marketing your medical device in the EU, you must be in compliance with ISO 11607. The good news is that ISO 11607 is also recognized by the U.S. FDA as a consensus standard, so if you are in conformance with it, you will have a much easier time complying with the FDA. "It's fantastic—it spells out exactly what you need to do for sterility maintenance," explains Scott Levy. "Part 1 covers materials, and Part 2 covers processes." Part 1 3.28 defines validation in general, and 3.29 defines process validation. And the document goes into greater depth throughout both parts, particularly on installation qualification, operational qualification, and performance qualification (IQ/OQ/PQ).

## 3 Get your package professionals involved upfront in the product design process

"Packaging professionals should be working with colleagues in regulatory, product development, and quality as early as possible during medical device development," says Levy. For instance, "get the geometry of the product and work toward the shipping configuration. A lot of times this happens at the end, and then you run into problems. Get involved early and work closely with your entire team—these professionals can help you further understand the risk assessment of the device so you can plan sample sizes accordingly."

Also, during product design verification, "conduct feasibility testing to understand the product and package interactions," he says. "You can then avoid later problems during testing."

## 4 Perform a risk assessment of the medical device you are packaging

Determine the specified attribute data for your package, identify all potential failure modes that could cause (or result from) an out-of-specification package, and then determine the sample size needed to catch those failures. "The chosen sample size and resulting confidence level will depend upon the overall risk assessment (Failure Mode Effects Analysis; FMEA) that the MDM puts in place for any given device," says Levy.


Accelerated aging is performed on materials, products, and packaging systems including packaged medical devices to provide a theoretical equivalent to real time shelf life.

## 5 Talk to your suppliers and service providers

"Your vendors have a lot of knowledge about materials and processes, especially when it comes to materials for packages such as pouches and trays, for instance," he says. Get as much data as possible from material providers, thermoformers, and package converters, and don't forget to work closely with machinery providers, who in addition to providing process validation support might also consult on material performance. "The last step would be to work with

a qualified and knowledgeable test laboratory that not only understands the regulatory requirements, but can further guide and partner with you to make sure that specific regulatory requirements are being met," he says.

## 6 Write your packaging protocol and establish clear acceptance criteria

"Your protocol should have the following: a purpose, a scope, a reference section listing all standards and test procedures, descriptions of all materials and equipment, all attribute data, a sequence of events or a flow chart of what will transpire, and a summary of the chosen sample size and acceptance criteria," says Levy. "It is important to document everything. And the protocol can help you manage your processes with outside vendors. We can help customers put it all together."

Levy adds that some companies have long-established protocols that may appear to be "set in stone." Such an approach may help packaging professionals meet minimum quality system thresholds, but "it is important to stay on top of all new standards and allow the potential use of them," he says. In addition, it could be missing "new key attributes."

## 7 Know your worst cases

"Review your product families to define all worst-case scenarios," says Levy. "For instance, for a family of catheter products, decide which catheter you feel is the worst case. You then may not need to test the other family members that are similar. When identifying a worst case, look for the heaviest, the lightest, the largest, and the smallest. It is a hard question to answer, but you are looking for what potentially can cause the most adverse effects to the package." You'll also want to ensure that the product materials are the same, he adds.

You should also consider how the particular package would be packed out in your shipping configuration. "Will I need a shelf box? Or are there other elements within that box to help mitigate the potential for abrasion issues, etc.?" He also cautions against folding pouches to make them fit properly into a pre-existing configuration. "If a package is folded, consider what may happen with that particular product at that folded intersection," he says.

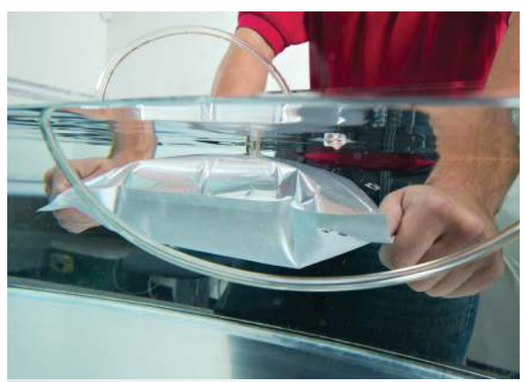

Photo of bubble immersion.

## 8 Understand the differences between package seal strength and whole package integrity as well as stability testing and package performance

"People start using test methods before they understand the standards," says Levy. "For instance, they start using ASTM F88 [Standard Test Method for Seal Strength of Flexible Barrier Materials] before they realize that there are three different methods within this procedure. Or they test for a 1-lb minimum seal strength without even knowing where that specification came from."

In addition, engineers cannot solely test packages for seal strength. Packaging engineers also need to test for whole package integrity, using a method such as ASTM F2096 (Standard Test Method for Detecting Gross Leaks in Packaging by Internal Pressurization [Bubble Test]), says Levy. Engineers should also consider the microbial barrier properties of the materials selected for their sterile barrier system. It is important to note that validated physical package integrity test methods can sufficiently demonstrate sterility maintenance (instead of using whole package microbial challenge testing).

Medical device manufacturers obtaining 510(k) approval on medical devices use a variety of testing to ensure the integrity of the medical device packaging and compliance with ISO standards, such as ISO 11607.

Another major issue, says Levy, is "you cannot just use the tests without going through test method validation. The difference between 'guides and standards' is the guides provide a roadmap, and the standards tell you how to drive. Following the standard allows you to compare your own results to those in the precision and bias statements."

Testing will also likely be performed in stages. ISO 11607 separates stability testing from performance testing, unless you don't have enough samples for testing, advises Levy. Stability testing looks at the effects of aging on seal strength and package integrity and helps you determine a shelf life, whereas performance testing looks at the effects of handling and distribution on seal strength and package integrity. Separating these evaluations allows you to identify the causes of seal failure or compromised integrity.

Bottom line: understand what you are testing, look for test methods that have been validated, and then validate that you can perform them according to the standardized methods. "We challenge our customers a lot to justify why they are performing a given test," he says.

## 9 Do a gap analysis of the test standards that you have previously utilized to what is current

You'll want to do a gap analysis when any new standards are released, he adds. "Ask yourself these questions: How does the new standard impact an older validation? Am I still in compliance? And a gap analysis is also necessary if there is a change in packaging materials or processes."

## 10 Make sound technical science-based justifications if needed

If making a justification, you need to take a look at all factors for a particular justification and make it science based and defendable, Levy advises. "When making any justification, you need to look further at all risks involved, whether it is product based or packaging based. Too many times, organizations are trying to meet a timeline and utilize loose justifications in order to meet that timeline."

In addition, "Use your suppliers and leverage their knowledge and use them as a sounding board," Levy advises. "As I tell my customer, we are all in this together to help bring safe and effective devices to market. We need to get this right."

In the end, medical device packaging professionals simply need to understand what they are putting into packages, says Levy. "If they do their homework with materials and processes and understand what they need to do before validation, they'll build a successful validation program."

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