Laying the Foundation for a Sound Package Testing Program

Ensuring the medical device packaging is sufficient to meet the needs of all challenges during a device's journey is as important as the integrity of the device itself. This article outlines four key considerations OEMs need to address in order to ensure they are establishing a solid foundation upon which to build their package testing program.

By Britt Jones

Manufacturers of terminally sterilized medical devices and combination products are required to test and validate product packaging in accordance with the ISO 11607 guidelines. Compliance with these guidelines will help ensure that products remain sterile while being exposed to hazards that may arise from manufacturing, sterilization, distribution, and storage environments.

The ISO documents do not specify which package integrity tests to use but merely offer guidance for the manufacturer trying to determine the ideal testing panel. Blindly following ISO 11607 presents two risk scenarios: a manufacturer might be led to waste time and money by over-testing; or, by under-testing, fail to provide appropriately comprehensive results to verify the performance and integrity of the product packaging.

The establishment of an optimal testing program, then, requires a decision framework that aims to minimize expense without compromising results. Whether beginning the process of developing an appropriate testing panel or evaluating a package testing partner to perform the testing, many device manufacturers will find that a strong foundation for a successful package testing strategy starts with four key considerations:

Approach:
Should the testing program be one of physical integrity or microbiological assessment? What about different packaging sizes?

Defects:
What integrity tests are best suited to a product's possible defects in packaging?

Shelf-Life:
What are the shelf-life expectations? (This is a major factor in determining how long the testing will take.)

Distribution Effects:
What distribution conditions will the packaging likely endure?

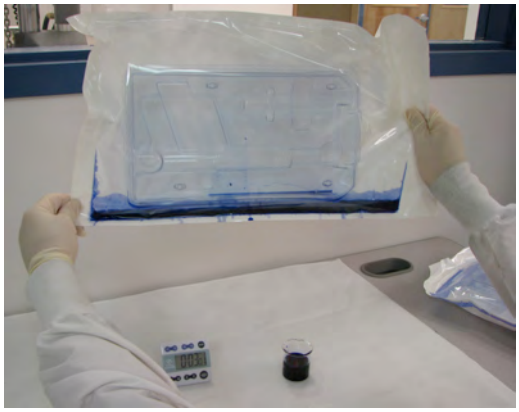
Environmental chambers at WuXi AppTec used for accelerated aging offer a range of temperature and relative humidity settings for conducting package stability performance testing.

Combination products – consisting of two or more regulated components, such as a drug- or biologic-coated device – pose their own additional challenges, including special stability issues and whether the packaging ensures the drug or biologic component remains active. Package testing requirements for combination products can be found in CBER Guidance for Container Closure Systems for Packaging Human Drugs and Biologics and CDER Guidance for Stability Testing of Drug Substances and Drug Products.

Consideration I: Approach
In recent years, the medical device industry has moved toward physical integrity testing of packages rather than taking a microbiological assessment approach. The physical integrity concept maintains that if the package and seals remain intact after sterilization and all performance testing, then the sterile barrier has not been compromised.

It is not unusual for device manufacturers to package similar products in various sized packages. Many novice manufacturers make the mistake of revalidating their packaging for each individual case, which is unnecessary and not required by ISO 11607. It is perfectly acceptable to conduct performance testing on what is considered the worst-case challenge to the sterile barrier system being produced.

The advent of combination products requires additional package testing considerations since combination packaging must be capable of not only maintaining sterility but also of preserving drug or biologic components while providing adequate protection from light, water vapor absorption and loss of solvent.



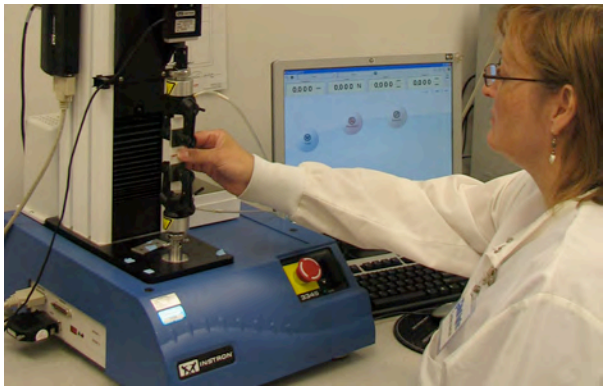
Dye penetration testing is used to determine the integrity of heat-sealed flexible packages by detecting gross leaks, openings, or channels in package seals.

Consideration II: Defects
Defects commonly seen in medical device packaging – due to manufacturing, the sterilization process, handling, and/or storage – include cuts, tears, pinholes, and cracked thermoform trays. To detect these types of defects, the package integrity tests typically

used are the bubble emission (ASTM F-2096) and dye penetration (ASTM F-1929) tests. The bubble emission test works by internally pressurizing the package and examining the exterior for leaks while it is submerged. This test will detect leaks in the seals as well as the face and back of the package.

For the dye penetration test, a liquid dye solution is injected into the package and rotated so that it comes in contact with each seal for a specified time. The seal areas are then visually examined for leaks. Seal strength integrity tests, such as ASTM F-88, should be performed during the initial package validation step prior to the package performance testing. This will provide the device manufacturer with baseline data, which will help establish a target value for quality control purposes. It is also a good idea to perform this test at various time points during a stability study to measure the effects time/aging has on seal strength.

Packaging for combination products requires additional, further testing, such as moisture gain or loss, evaluation of leachables (USP 661), and stability testing.



Adhesion Strength Method is used to determine the adhesion strength of a bond between similar or dissimilar materials.

Consideration III: Shelf-Life

With package testing being one of the last steps before regulatory submission or product release, a crucial question is: "How long will it take to perform the necessary package testing?" The answer is that manufacturers need to allow for a testing period that could take from weeks to months, depending on the type of testing required.

A major factor dictating the time needed for a full package performance qualification is the desired storage shelf-life. Once the shelf-life is selected, stability testing is performed on packages using real-time aging. For expiration date claims, ISO 11607 allows accelerated aging to be considered sufficient evidence. The most common accelerated aging temperature is 55°C, but other parameters may be used. It is important that the device manufacturer select a temperature that is compatible with the particular package type to reduce the risk of unrealistic failures, such as warping and curling. Manufacturers should allow two to six months of testing time for a one-year expiration date, depending on the accelerated aging temperature chosen. Real-time and accelerated aging studies typically begin simultaneously.

Consideration IV: Distribution Effects

To verify that packaging will maintain the sterility and quality of a device during shipping and handling, manufacturers are required to perform simulated distribution testing on their package system.

Drop testing of loaded boxes by the free-fall method.

This testing is designed to simulate events and conditions seen in the distribution environment, such as stacking, shipping vibration, changes in atmospheric pressure, and extreme high and low temperatures. Common laboratory test methods that are used to measure the effects of these anticipated hazards are ASTM D-4169 and ISTA (International Safe Transit Association) preshipment tests.

Because packaging defects are more likely to be due to hazards encountered in the distribution and handling environment than from sitting on a shelf, it is important to adequately test package integrity after these performance tests.

Conclusion

Whether a manufacturer performs packaging validation internally or by working with an independent testing facility, the critical first step should be development of a testing framework specific to the device. Building on ISO 11607, CBER, and CDER guidelines and applying the key considerations outlined in this article, a testing program foundation can be established that will help prevent both over- and under-testing – minimizing expenses and providing a path to appropriate, comprehensive results to verify the performance and integrity of the packaging system in maintaining product sterility.

References

• ISO 11607, "Packaging for Terminally Sterilized Medical Devices" Geneva; International Organization for Standardization, 2006.
• ASTM F1929-04, "Standard Test Method for Detecting Leaks in Porous Medical Packaging by Dye Penetration" West Conshohocken, PA: ASTM International, 2008.
• ASTM F2096-04, "Standard Test Method for Detecting Gross Leaks in Medical Packaging by Internal Pressurization (Bubble test)."
• ASTM F88-07, "Standard Test Method for Seal Strength of Flexible Barrier Materials."
• ASTM D4169-08, "Standard Practice for Performance Testing of Shipping Containers and Systems."
• CBER Guidance for Container Closure Systems for Packaging Human Drugs and Biologics.
• CDER Guidance for Stability Testing of Drug Substances and Drug Products.

Online

For additional information on the technologies and products discussed in this article, see MDT online at www.mdtmag.com or WuXi AppTec at www.wuxiapptec.com.

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