



PACKAGE TESTING AND VALIDATION SERVICES

A sterile medical device, which includes the packaging, must function as labeled for the shelf-life claimed for the device. The primary package must maintain its sterile barrier properties for this period of time, and must be able to maintain its seal strength and package integrity under the stress of production, sterilization, distribution and handling, and after aging for the shelf-life claimed.

WuXi AppTec's experts can help you plan a package testing program that will meet your needs and the applicable regulatory requirements. A package validation program (per ANSI / AAMI / ISO 11607) would include such services as: Protocol, Sealer Performance Verification, Product Qualification (3 lots), Simulated Shipping Qualification, Shelf Life Studies (Aging) and Summary Report(s).

IN THIS SECTION

The test methods described in this section provide a comprehensive means of establishing that package integrity is compliant with International Standard ISO 11607, "Packaging for Terminally Sterilized Medical Devices."

- **Seal Integrity Testing**
 - Seal Peel Strength – ASTM F 88
 - Burst/Creep Strength – ASTM F 1140
- **Package Integrity Testing**
 - Bubble Emission Test – FPA/SPMC 005-98 and ASTM F 2096
 - Dye Penetration Test – ASTM F 1929
 - Microbial Challenge – Aerosol, Talc, or Immersion
- **Transportation/Distribution Simulation Testing**
 - Distribution Simulation Shipper Test – ASTM D 4169
 - Transportation Simulation Test – ISTA Project 1A , 2A and 3A
 - Environmental Conditioning – ISTA Project 2A
 - Environmental Conditioning – ASTM 810 E
- **Accelerated Aging / Shelf-Life Studies**
 - Accelerated Aging – ASTM F 1980

SEAL INTEGRITY TESTING

Regulations dictate that the seal strength and specification limits be determined for pre-sterilization sealer performance verification (high, low & standard parameter settings) and seal strength consistency qualified for post-sterilization production, shipping and shelf-life qualifications.

38030

Seal Tensile Strength
[ASTM F 88]

This method will determine the strength of a specific area of the seal for a medical device package. It may be used for pouch or tray/lid type packages having two components joined by an adhesive or heat seal process. The method does not measure seal continuity. Its most common application is for establishing process control parameters and package performance specifications, and to support package validation.

SAMPLE REQUIREMENTS 10 (minimum) primary packages per process variable

38039

Burst Strength
[ASTM F 1140]

This method is used to determine a package's ability to resist internal pressure and is a measure of the strength of the package seals. Its most common application is for establishing process control parameters and package performance specifications, and to support package validation.

SAMPLE REQUIREMENTS 10 (minimum) primary packages per process variable

38040

Creep Strength
[ASTM F 1140]

PACKAGE INTEGRITY TESTING

Regulations dictate that the integrity of sterile packages be maintained during the production, shipping and shelf-life of the product. Physical testing for package leaks has been shown to be more sensitive than the microbial challenge test, and is the generally preferred method.

This method, which covers the determination of gross leaks in flexible packaging, is applicable to nonporous packaging and to porous packaging that has its porous component sealed using a blocking agent. It is used to detect leakage of air through a channel in the seal or pin-hole in the package. The test is performed by submerging the package underwater and observing for leaks. This provides attribute data on the integrity of the primary package directly after production or after experiencing a dynamic or environmental related event.

SAMPLE REQUIREMENTS 30 primary packages recommended
Note: For test code 38152 at least one (1) additional sample is needed for test setup.

38033
Bubble Emission Test
[FPA/SPMC 005-98]

38152
Bubble Emission Test
[ASTM F 2096]

This method, which covers the determination of gross leaks in flexible packaging, is applicable to porous and nonporous medical device packages. It is used to detect small leaks in materials or seals of packages where harmful biological or particulate contamination may enter. The method may be used to detect holes in package materials or channels in seals as small as 0.0025 inches. This provides attribute data on the integrity of the primary package directly after production or after experiencing a dynamic or environmental related event.

SAMPLE REQUIREMENTS 30 primary packages recommended

38038
Dye Penetration
[ASTM F 1929]

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PACKAGE INTEGRITY TESTING

MICROBIAL BARRIER PERFORMANCE TESTS

38051

**Whole Package Microbial
Aerosol Challenge with
Sterility Test**

This method is used to evaluate the ability of an intact, production package to maintain its sterile environment until it reaches its point of end use. The procedure includes preliminary test validation with the subject package, followed by an aerosol or talc challenge in the test chamber, package exterior decontamination, and subsequent sterility testing to determine the presence of the indicator organism inside the package or on the product. The aerosol may be performed under static or dynamic conditions. Dual-barrier packages may have one or both barriers validated for sterility.

38059

**Whole Package Microbial Talc
Challenge with Sterility Test**

SAMPLE REQUIREMENTS 12 primary packages recommended
(10 test, 1 positive control, 1 negative control)

38060

**Microbial Ingress / Immersion
Challenge**

This method is used to assess the ability of a non-porous package to provide a microbial barrier. Packages containing sterile growth medium are immersed in a buffer solution containing a known concentration of an indicator organism. After the challenge, the packages are dried under laminar flow, then incubated and inspected for growth of the indicator organism. The method may be used for foil-lidded trays, foil pouches, and rigid containers with closures.

SAMPLE REQUIREMENTS 30 packages recommended

Manufacturers must evaluate the package's and shipper's ability to adequately protect the product through the handling, shipping and distribution environment. Damage such as puncture, abrasion and seal failure may result.

NOTE: The ASTM procedure is the method of choice as it provides a more realistic simulation of the distribution environment and uses test levels which are more indicative of actual occurrences.

This test method is performed by subjecting shipping units to a test plan consisting of a sequence of hazard elements (e.g., shock, drop, vibration, compression) which are encountered in various distribution environments. The test plan provides a uniform basis of evaluating, in a controlled and repeatable laboratory environment, the ability of the shipping units and contents to withstand the distribution environment. The test plan uses established test methods at levels representative of those encountered in actual distribution. The Distribution Cycle (DC) most commonly used for medical device packages is DC 13, Assurance Level I, which is designed for the small parcel and overnight shipping mode. Customized distribution cycles can be designed when the anticipated distribution of the product is well understood and defined.

SAMPLE REQUIREMENTS One or more shippers
(to provide 40 units for seal and package integrity tests)

38052

**Distribution Simulation
Shipper Test**

[ASTM D 4169 – DC 13]

These tests provide a means for a manufacturer to predetermine the probability of the safe arrival of their packaged-products at their destination through the utilization of tests developed to simulate the shocks and stresses normally encountered during handling and transportation.

SAMPLE REQUIREMENTS One or more shippers
(to provide 40 units for seal and package integrity tests)

38057

**Transportation Simulation
Test**

**[ISTA Project 1A, 2A
and 3A]**

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TRANSPORTATION / DISTRIBUTION SIMULATION TESTING

30659

ISTA Environmental
Conditioning
[ISTA Project 2A]

Temperature Cycling Sequence

1. Frozen or winter ambient
-29°C for 72 hours, no RH control
2. Tropical wet then dry
38°C @ 85%RH for 72 hours,
then 60°C @ 30% RH for 6 hours

SAMPLE REQUIREMENTS Varies

30660

ASTM Environmental
Conditioning
[ASTM 810 E]

Temperature Cycling Sequence

1. 50°C/20% RH, 30 minute transfer, 30 minute dwell
2. -40°C, 30 minute transfer, 30 minute dwell
3. Repeat 1.0 and 2.0 five times
4. 50°C/20% RH, 30 minute transfer, 24 hour dwell
5. 40°C/80% RH, 30 minute transfer, 24 hour dwell
6. -40°C, 30 minute transfer, 24 hour dwell

SAMPLE REQUIREMENTS Varies

Some domestic regulations and all international directives require expiration dating on sterile medical device packages. The package integrity and maintenance of a sterile barrier must be supported by documented test data after accelerated and/or real-time aging for the shelf-life claimed. Environmental factors such as exposure to low and high humidity as well as freezing conditions are also considerations.

ACCELERATED AGING TESTING (ASTM F 1980)

INFORMATION REQUIRED:

- Volume of Material
- Expiration Date
- Test Temperature
- Ambient (Storage) Temperature
- Aging Factor (Q_{10}) [*The most common Q_{10} is 2.0*]

Condition primary packages at a test temperature of 55°C for a period of 1 year of equivalent real time aging. This test may include exposure to high humidity and low humidity plus 2 days of freezing conditions to provide maximum stress to packages. Ambient storage temperature = 22°C.

TEST DURATION 40 days = 1 year RTE (Real Time Equivalent)

38034

**Accelerated Aging
@ 55°C/1 year**

Condition primary packages at a test temperature of 60°C for a period of 1 year of equivalent real time aging. This test may include exposure to high humidity and low humidity plus 2 days of freezing conditions to provide maximum stress to packages. Ambient storage temperature = 22°C.

TEST DURATION 29 days = RTE (Real Time Equivalent)

38036

**Accelerated Aging
@ 60°C/1 year**

Condition primary packages at a custom test temperature for an equivalent real time aging period to be determined. Environmental factors may be considered.

TEST DURATION Equation is used to determine RTE (Real Time Equivalent).

38037

Accelerated Aging – Custom