TECHTIP

A GUIDE TO DETERMINING THE MOST APPROPRIATE DISTRIBUTION SIMULATION FOR A MEDICAL OR PHARMACEUTICAL DEVICE

Introduction

The packaging of sterile medical and pharmaceutical devices needs to ensure that the product shall function as intended and remain sterile to the point of use, from both a patient safety and regulatory requirement perspective. As part of product development, the manufacturer needs to consider the risks associated with the complete range of distribution possibilities, storage conditions and shelf-life claims to plan and test accordingly.

Many medical device manufacturers have straightforward package testing needs. Often, they have a single product that they wish to bring to market, and the associated packaging systems need to be validated. In this case, the packaged product must be able to withstand the typical hazards associated with distribution when being put through a course of testing to recognized standards without defect or loss of sterility. The challenging part is deciding which standard to use, and which tests are required, all of which will have to have documented justifications outlining the reasons for selecting each test or set of tests.

What are the most common standards used for distribution testing?

ASTM and ISTA are two international standard bodies that provide test methods for distribution simulation. Both are readily accepted by regulatory authorities and contain enough different tests to cover virtually all scenarios. These standards meet and exceed test methods for challenging the resilience of packaging systems.

The primary test standards are used for distribution simulation testing are:

- ASTM D4169 (Standard Practice for Performance Testing of Shipping Containers and Systems)
- ISTA 2 Series (Partial Simulation Performance Tests)
- ISTA 3 Series (General Simulation Performance Tests)

Other standards, such as ASTM D7386 (Standard Practice for Performance Testing of Packages for Single Parcel Delivery Systems), provide guidelines to evaluate the ability to withstand hazards for single shipping units that do not exceed 150 lb (68kg).

For the purposes of this TechTip, we will concentrate on ASTM D4169 as it is the most utilized standard by our Customers internationally. This is due to several factors, including the variety of tests available and regulatory considerations such as FDA consensus listings and its inclusion in ISO 11607-1 Annex B.

What are the typical risks evaluated by distribution testing and how are they identified?

Transport of any package, including medical devices and pharmaceuticals, carries inherent risk. These risks should be assessed with respect to maintenance of both sterile barrier and device functionality. The performance of the packaging system and contents must be challenged to prove or validate that the design is fit-for-purpose. This is relevant to both non-sterile and sterile devices alike as a non-sterile device must also be protected to its point of use. An accepted method of assessing these risks in a controlled laboratory setting is to conduct simulated distribution test.

These risks include, but are not limited to, distribution environment hazards. For example:

- Temperature and relative humidity
- Shock (from either manual or mechanical handling)
- Vibration (as seen in truck and air transport)
- Compression
- Low pressure (high altitude)
- Concentrated impact

Each of these environmental or mechanical stresses carry the potential to negatively impact both the sterile barrier system and device functionality.

The ASTM D4169 umbrella standard covers a broad range and level of tests and provides a wide spectrum of challenge conditions and hazards. They are used to assess the predetermined risks to ultimately answer the primary question:

“Does the packaging system protect the product and sterile barrier during distribution?”

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How do you define the "shipping unit"?

The first requirement for conducting a packaging validation is to formally define the shipping unit. A shipping unit is the smallest complete unit that will be subject to the distribution environment, and is typically a shipping container and the internal product. It is important to document the system weight, dimensions, construction method, and materials used.

The test acceptance criteria must be established prior to test commencement. These are defined as the desired or expected condition of both the product and package after a distribution cycle. ASTM advises to compare the historical damage from actual distribution and handling where possible. ASTM also notes that it is often the case that acceptance criteria are detailed as:

- Criterion 1—Product is damage-free
- Criterion 2—Package is intact
- Criterion 3—Both criteria 1 and 2

And of course, when testing a sterile device, the sterile barrier must be maintained.

How do you select the appropriate test parameters?

Choosing the right combination of distribution cycle and assurance level is crucial to ensure your product and packaging system will withstand the distribution process and arrive intact to the end user.

As above, when assessing distribution cycles, risks need to be considered based on modes of transportation rather than the package type.

The worst-case packaging configuration should be considered for testing as per ISO 11607 (Packaging for terminally sterilized medical devices — Part 1: Requirements for materials, sterile barrier systems and packaging systems). This is typically understood to be the lowest level of package that will be shipped. In most cases this will be a small package or single shippers, either completely full or partially full of the primary product and associated packaging materials.

The next step is to decide which combination of distribution methods apply to your actual distribution network, including:

- Truck
- Air
- Rail
- Sea
- All

Once these questions are answered, the following table from ASTM D4169 will help determine the appropriate distribution cycle (DC) number and, ultimately, the test schedule. The most common distribution cycles used in the medical device industry are:

- DC13 small package / single shippers
- DC 6 for unitized loads / palletized product
- DC12 for larger packages / unitized loads / palletize products
- DC2 can also be used to investigate a particular issue with the packaging or packaged product. Individual tests can be chosen from test schedule "A" through "J" as shown on the next page:

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DC	Distribution Cycle
1	General cycle – undefined distribution system
2	Specially defined distribution system, user specified
3	Single package without pallet or skid, Less Than Load (LTL) motor freight
4	Single package with pallet or skid, Less Than Load (LTL) motor freight
5	Motor freight, Total Load (TL), not unitized
6	Motor freight, Total Load (TL), or Less Than Load (LTL) - unitized
7	Rail only, bulk loaded
8	Rail only, unitized
9	Rail and motor freight, not unitized
10	Rail and motor freight, unitized
11	Rail, Trailer On Flat Car (TOFC) or Container On Flat Car (COFC)
12	Air (intercity) and motor freight (local), over 150lb (61.8 kg), or unitized
13	Air (intercity) and motor freight (local), single package up to 150 lb. (61.8 kg).
14	Warehousing (partial cycle to be added to other cycles as needed)
15	Export/import shipment for intermodal container or roll on/roll off trailer (partial cycle to be added to other cycles as needed)
16	Export/import shipment for palletized cargo ship (partial cycle to be added to other cycles as needed)
17	Export/import shipment for break bulk cargo ship (partial cycle to be added to other cycles as needed)
18	Non-commercial government shipments per MIL-STD-2073

How is the appropriate assurance level of test selected?

Once the appropriate distribution cycle has been chosen, the next step is to select the assurance level (AL). The assurance level is defined as the level of test intensity based on its probability of occurrence in a typical distribution cycle. There are three pre-established levels:

- Level I is a high level of test intensity and has a low probability of occurrence.
- Level II is between the extremes of Level I and Level III.
- Level III is a low level of test intensity but has a correspondingly high probability of occurrence.

When selecting the AL, there should also be consideration for product value, acceptable level of anticipated damage, number of units being shipped, and knowledge of shipping environment along with the fragility of the product.

Assurance level II is the most commonly chosen level and is recommended by ASTM D4196 unless conditions dictate otherwise.

How long should the conditioning be carried out for?

Conditioning the product is essential to gaining knowledge on how the packaging and packaged product will work together throughout the distribution cycle. The temperatures or climatic regions are defined in ASTM D4332 as:

- Ambient,
- Frozen or winter ambient
- Tropical (wet)
- Desert dry

The conditioning should be carried out for a defined period as determined by the manufacturer. If no time period is specified, a period of at least 72 hours, or that time required to reach equilibrium (which may be shorter or longer in duration than 72 hours), is recommended. An equilibrium study can be carried out to determine how long it takes the product at the center of the packaging to reach the exposure temperature within the environmental chamber.

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What are the different tests that included in a distribution simulation test?

There are 10 potential tests or test schedules detailed in ASTM D4169. The sequence of tests isdetermined by the distribution cycle selected.

Schedule	Hazard Element	Test Type
A	Handling – manual and mechanica	Drop, impact, stability
B	Warehouse stacking	Compression
C	Vehicle stacking	Compression
D	Stacked vibration	Vibration
E	Vehicle vibration	Vibration
F	Loose load vibration	Repetitive shock
G	Rail switching	Longitudinal shock
H	Environmental hazard	Temperature/humidity
I	Low pressure hazard (High altitude)	Vacuum
J	Concentrated impact	Impact

The tests should be performed sequentially on all shipping units in the sequence defined in ASTM D4169. When carrying out performance testing, the shipping unit should remain unopened until all tests are completed.

The table below shows an example of a typical testing sequence for distribution cycle 13 air and motor freight, single package up to 150lb (61.8 kg).

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Sequence	Test Schedule	Test Type	Standards	Test Description
1	Conditioning	Temperature and Relative Humidity	ASTM D4332	Simulates worldwide environmental conditions including ambient, frozen, or winter ambient, tropical (wet), and desert (dry).
2	A – Handling (Manual)	Drop	ASTM D5276	Simulates manual handling including loading, unloading, stacking, sorting, or palletizing. The main hazards from these activities are the impacts caused by dropping or throwing.
3	C – Vehicle Stacking	Compression	ASTM D642	Simulates vehicle stacking considerations including container stacking pattern, container strength variability, method of load transport, and vibration.
4	F – Loose Load Vibration	Vibration	ASTM D999	Simulates the repetitive shocks that occur during the transportation of bulk or loose loads.
5	I – Low Pressure (High Altitude)	Vacuum	ASTM D6653	Simulates the reduction in pressure when transported via certain methods including feeder aircraft or by ground over mountain passes.
6	E – Vehicle Vibratio	Vibration	ASTM D4728	Simulates truck and air vibration testing.
7	J – Concentrated Impact	Impact	ASTM D6344	Simulates packaging impacts from corners or edges during sorting operations and in transit.
8	A - Handling (Manual)	Drop	ASTM D5276	Simulates manual handling including loading, unloading, stacking, sorting, or palletizing. The main hazards from these activities are the impacts caused by dropping or throwing.

Customized distribution cycles can also be designed when the anticipated distribution of the product is well understood and defined.

What are the considerations for testing of palletized products?

Shipping by pallet is essential to many industries and most products will be shipped on a pallet at some point, especially as the demand for the product increases. If a pallet fails to provide a safe and stable mechanism to protect the packaged products, they may be damaged. This could be the result of excessivetop loading from other palletized products, or by poor handling.

The overall loading of the pallets can be assessed to determine if they can retain and support full unit loads of the packaged products throughout the distribution process.

Often palletized products are tested using distribution cycle 6 (motor freight, total load (TL), or less than load (LTL) - unitized).

See the following table on the next page as an example of a typical distribution cycle 6 testing sequence:

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Sequence	Test Schedule	Test Type	Standards	Test Description
1	Conditioning	Temperature and Relative Humidity	ASTM D4332	Tests the stability of packaged products when subjected to worldwide environmental conditions including ambient, frozen, or winter ambient, tropical (wet), and desert (dry).
2	A: Handling (Manual)	Forklift Pickup Obstacle Course	ASTM D6055	Tests the mechanical stability of the palletized load during handling.
3	A: Handling (Manual)	Incline Impact	ASTM D880	
4	A: Handling (Manual)	Forklift Truck Handling	ASTM D6179	
5	C: Vehicle Compression	Compression	ASTM D642	Tests the load bearing capability of the palettized load for vehicle transportation.
6	E: Vehicle / Random Vibration	Vibration – Truck sequence	ASTM D4728	Tests the stability of the palletized load during handling.
7	J: Concentrated Impact	Vibration	ASTM D6344	Tests the capability of the palletized load to withstand impacts from external sources.
8	A: Mechanical Handling	Forklift Pickup Obstacle Course	ASTM D6055	Tests the mechanical stability of the palletized load during handling.
9	A: Mechanical Handling	Incline Impact	ASTM D4728	
10	A: Mechanical Handling	Forklift Truck Handling	ASTM D6179	
11	B: Warehouse Compression	Compression	ASTM D642	Tests the load bearing capability of the palettized load for warehouse stacking / storage.

Is pallet level testing always necessary?

Testing at pallet level may not always be necessary as testing should be conducted on a worst-case shipping configuration, which is typically considered the lowest product/package level that can be shipped. In many cases, this is a single shipping unit. The reason for this is that palletized packaging, by its very nature, provides additional protection to the packaged product when compared to a single shipping unit. However, palletized loads also need to be considered and it may be sensible to include such testing, particularly if this is a new product configuration.

Conclusion

It is key to remember that the goal of a packaging validation is to prove that a packaging system can adequately deliver a functioning device at the point of use, while facilitating aseptic presentation.

With the right planning, this does not need to be an onerous task. However, avoidable challenges are occasionally encountered due to its lower priority when developing a device and bringing it to market.

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In summary, the following points must be considered and documented prior to execution of any testing:

- Analysis of historical distribution issues
- Standards selection
- Development of testing plan
- Distribution cycle selection
- Assurance level selection
- Defining acceptance criteria

For additional queries in relation to packaging and product testing projects, failure analysis and remediation strategy, please contact the STERIS team of packaging professionals.

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