ISO 11607 - 1 & 2 Packaging for Terminally Sterilized Medical Devices

Jan Gates: Adept Packaging LLC

10X Conference, May 2019
Over 35+ years in medical devices, foods, pharmaceutical and detergent industries

Packaging engineering experience in design, material and distribution testing, material and equipment validations, PMA submissions, REACH/RoHS, EU Packaging Waste Directives, and sustainability

SoCal Institute of Packaging Professionals Chapter, Co-President

IoPP Medical Device Packaging Technical Committee, member

ASTM F02, Flexible Barrier Packaging member

ASTM D10, Rigid/Environmental Packaging and Testing committee member

D10.96 ISO TC122 SC3 TAG Liaison Chair

ISO TC122 WG5 Covenor – Vocabulary

ISO TC122 WG13 (Labels) & WG16 (Controlled Temperature Packaging) SME
Some of My Old Work
Some of My Current Work
Package Engineering Summary

- Minimize sizing to optimize shipping costs
- Reduce product breakage
- Develop packaging human factors for users (end and production)
- Good packaging is sustainable
- Minimize sizing to optimize warehousing
- Optimize packaging materials for product shelf life and costs
- Assure label legibility with use and time
- Enhanced Functionality/Utility

Package Engineering saves money
Standard Titles

ISO 11607-1: Packaging for terminally sterilized medical devices – part one
✓ Design and development

ISO 11607-2: Packaging for terminally sterilized medical devices – part two
✓ Equipment and process validations

Current revisions: 2019 February
Background

**EN ISO 11607-1 & -2**
- Replaced EN 868-1
- FDA harmonized with standard in 2006

**AAMI TIR 22**
- Issued April 2007
- US Guidance Document to EN ISO 11607-1 & -2
- More DDD guidance included for FDA

**ISO/TS 16775**
- Issued, May 2014, replaced TIR 22
- ISO Guidance on the application of ISO 11607-1 and ISO 11607-2
- Minor revisions to the ISO 11607-1/-2 standard

**Revised ISO**
- 11607-1/-2 published, February 2019
- Revisions with human factors/use added and critical process parameter definition changes
ISO 11607-1/-2 Standards

Standardized packaging for terminally sterilized medical devices

(placed packaging on the same importance level as the product; a medical device does not remain sterile without acceptable packaging; qualify/validate the packaging system)
New Terminology was Introduced

- Terminal Sterilization
- Sterile Barrier System (SBS)
- Preformed Sterile Barrier System
- Protective Packaging
- Packaging System
- Seal Integrity
- Aseptic Presentation
- Stability Testing
- Performance Testing
Sterilization validation
✓ Follow sterilization standards with worst-case situations for packaging
✓ Understand Biological Indicators (BI) and placements

Short hand → Sterilization kills the microbes inside the packaging; packaging must not have holes until opened for use
<keep holes out of the SBS during packaging, storage, shipment, and handling>

Common Types of Sterilization

- Gamma
- Ethylene oxide
- E-beam
- Hydrogen Peroxide
Shall Statements : Statements required for compliance
Sampling of Shall Statements

Over 115 “SHALL” statements in the ISO 11607 documents, this includes:

✓ Shall use sampling plans based on statistically valid rationale (-1, Clause 4.3)
✓ Shall establish and record a rationale for appropriate tests and acceptance criteria (-1/-2, Clause 4.4)
✓ Shall allow aseptic product presentation from the sterile barrier system. Note: Completing a usability evaluation can demonstration this. (-1, Clause 6.1.2)
✓ Shall have procedures for packaging system design and development (-1, Clause 6.2.1)
✓ Shall have test methods validated and documented by the laboratory performing the test (-1, Clause 4.4.3)
✓ Shall have EQ: IQ/OQ equipment (-2, Clauses 5.2 and 5.3)
✓ Shall have written preventative maintenance and cleaning schedules (-2, Clause 5.2.6)
✓ Shall have a minimum of three production runs for a PQ (-2, 5.4.4)
✓ Shall test product for acceptability after transit testing with or without the sterile barrier integrity testing (-1, Clause 8.2.1 Note 2)
✓ Shall start real time stability testing within three months of accelerated testing before commercialization (-1, Clause 8.3.4)
✓ Stability and performance testing are separate entities (-1, Clause 8.1 Note 2)
Statistical Justification

A sampling strategy is needed for a statistical justification

- Risk Assessment
- Risk Based Confidence and Reliability
- Statistically Based Sample Size

ISO standards available
Individualized by company – include a defect catalogue
ISO/ASTM standards and many books available

Statistical justification/rationale: -1, Clause 4.3
Test Method Validation

ASTM test methods must be validated in the laboratory conducting the test; publication of a method by a standards body does not make it validated in any laboratory (1, Clause 4.4.3 Note).
Shall have procedures for packaging system design and development (-1, Clause 6.2.1)

✓ Most companies have gate checks for devices included in the DDD

✓ Need to include the packaging work or have a separate DDD for packaging
Equipment EQ: IQ and OQ (-2; Clause 5.2) or EIOQ
Production Qualification (PQ)

Must be a minimum of three lots (-2; Clause 5.4.4)

Best practices include:

✓ Analyze the test lots separately to assure they are statistically equivalent*
✓ Consecutive lots used
✓ Production stoppages, material lot changes, and similar that may occur should occur during the qualification to simulate ‘normal’ production

* Remember there can be ‘no practical difference’ when something is ‘not statistically equivalent’, this must be explained in the protocol before testing or a deviation or a protocol failure is required.
Packaging Stability Testing

Aging the packaging system is independent of the physical configuration or contents, as long as:

✓ The processing is the same, and
✓ The contents do not affect the materials
✓ -1, Clause 8.1 Note 2


✓ Uses a modified Arrhenius equation:
  • Assumes the chemical reaction rate in a material is a logarithmic change for each 10 degree increase
    - $Q_{10} = 2$ is the usual assumption
    - $Q_{10} \neq 2$ for most PETG (many thermal formed trays)
  • Humidity is not part of the Arrhenius aging considerations
**Relative Humidity Note**

- **Relative Humidity** is the number of water molecules in the air.
- The number of molecules in the air is affected by **Temperature**.
- **Temperature and humidity** are inversely proportional (with a given quantity of moisture).

Relative Humidity = \( \frac{\text{actual vapor density}}{\text{saturation vapor density}} \) \times 100\%
Aging verses Performance Testing

Two separate entities per the FDA, ISO, and chemistry books

**Aging tests** a material’s stability over time

**Performance testing** evaluates the interaction between the packaging system and the products in response to the stresses imposed by the manufacturing (and sterilization) processes and the handling, storage, and shipping environment
# Performance Testing – ASTM D4169

<table>
<thead>
<tr>
<th>Test Plan</th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td>Handling</td>
<td>6 impacts, 24 inch</td>
</tr>
<tr>
<td>Vehicle Stacking</td>
<td>Apply &amp; release calculated top load</td>
</tr>
<tr>
<td>(Compression)</td>
<td></td>
</tr>
<tr>
<td>Loose Load Vibration</td>
<td>Repetitive shock 1 hour</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>High Altitude</td>
<td>14,000 ft 1 hour</td>
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<tr>
<td>Random Vibration</td>
<td>Three levels for trucks 3 hours</td>
</tr>
<tr>
<td>Concentrated Impact</td>
<td>1 impact 36 inches</td>
</tr>
<tr>
<td>Handling</td>
<td>5 impacts, 24 inch 6th at 48&quot;</td>
</tr>
</tbody>
</table>

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**Notes:**
- The test plan includes various environmental conditions and handling scenarios.
- The descriptions cover impacts, vehicle stacking, loose load vibration, high altitude, random vibration, and concentrated impact.
- Each test scenario has specific parameters, such as the number of impacts, inches, and duration.

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**Image:**
- Images of packaging materials and tests set up, likely demonstrating the actual test setup and conditions.
Performance Test Standards

- **ASTM D4169**: Standard Practice for Performance Testing of Shipping Containers and Systems
- **ASTM D7386**: Standard Practice Performance Testing of Packages for Single Parcel Delivery Systems
- **ISTA 3A or Higher**
- **ISTA 2A** Package Conditioning for Testing
- **ASTM D4332**: Standard Practice for Conditioning Containers, Packages, or Packaging Components for Testing
- **ASTM F2825**: Standard Practice for Climatic Stressing of Packaging Systems for Single Parcel Delivery

Develop performance standards based on company distribution system → the best option but hard for many companies
Performance Defect Example

✓ Performance defect (package design issue), not an aging defect

✓ Do not confuse the two types of defects
Product Acceptability after Performance/ Distribution/Transit/Ship Testing

“Shall” statement to test product (-1, Clause 8.2.1 Note 2)

Package Engineering or Product Development must test the product after transit tests

Logistically, usually easiest to keep product testing and package testing separate

✓ However, must assure both departments use the same transit tests
✓ Many companies test packaging and product separately
Understand the Distribution System Using...
Distribution Mapping -- General

Pack for sterilization → Load truck → Ship to hub

Note: 1 to 200 Hz vibration

Unload truck → Transfer/sorting hub

Note: Over 150 g drops measured

Load truck → Ship to airport → Unload truck

Ship to customer

Note: Some 82°C measured

Load truck → Stack in tarmac

Unload plane → Fly

Note: -15°C measured, 10 to 300 Hz

Load plane → Stack in tarmac

Unload plane

Note: Over 150 g drops measured

用户

Customer unloads shipper → Prep product for use → User

Note: 82°C have been measured

Summary: Many drops, temperature extremes and vibration points seen with distribution mapping.
### Domestic System and Domestic Repetition

<table>
<thead>
<tr>
<th>Round trip</th>
<th>Handling</th>
<th>Truck Transit</th>
<th>Plane Transit</th>
<th>Compression</th>
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<td>6</td>
<td>1</td>
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### International with Subassembly and International Repetition

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<td>47</td>
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</tbody>
</table>
2019 ISO 11607-1/-2 Standards:
New Changes in the revised documents
Opinions on the ISO 11607-1/-2 Revisions

Most revisions for clarifications

*My opinion:*
The revisions have some good changes by removing a few unnecessary complications. The wording more clearly defines some previously implied intents and adds human factors (called “usability requirements”).

Removing “critical” process parameters in -2 gives more focus on the whole production process.
Major Changes Summary from ISO 11607-1 (2014)

- Eliminates the sample testing requirements of 23°C ± 1°C and 50% RH ± 2%
- The sterile barrier system shall allow the product to be presented in an aseptic manner (with notation to see the “usability” clause).
- New clause on Usability Evaluation added (human factors)
- Clause added for Reusable Sterile Barrier Systems and potential degradation limiting shelf life labeling requirements
- More explanation on “hazards” and “performance testing” with worst-case packaging system/SBS, and validated packaging system changes
- Real-time testing and accelerated testing shall start within three months of each other
- Sustainability Annex D added
- Labeling requirements for sterile barrier system to be inspected for integrity before use (Annex E)
Major Changes Summary from ISO 11607-2 (2014)

- New definitions for process - variables, parameter, and specification
- Added Risk Management section
- Harmonize definitions with ISO 11139
- “Critical” process parameters is discontinued - to include all elements required to manufacture a product that consistently meets specifications
- Note added to “revalidation” allowing targeted process validations based on design validation work
- Periodic review removed with minor process changes to be documented for potential to require the process validation status to be reviewed
Information to Understand

Human factors

✓ FDA and AAMI have guidance documents
  • Both are very device oriented so hard to determine what is best
  • Pharmaceuticals are conducting human factor testing on child resistant closures and blister tablets
  • Michigan State University, Dr. Bix and her graduate students, are doing studies
  • Document the company studies
Human Factors and Design
ISO 11607-1: 2019

Complying with the new ISO 11607-1 requires:
✓ Sterile barrier inspection before use required and a symbol to show what is the sterile barrier layer
✓ Proposed symbols are not finalized and require validation

Note: UDI for Europe and the USA to comply with trace-ability requirements but is not discussed in ISO 11607-1/-2 standards or in this presentation
New Challenges: New Concerns in Discussion
Third Party Distributors

✓ Product often packed into plastic boxes, placed on wire racks, and shipped by truck to a hospital

✓ Some are repacking, relabeling, and bundling products without performing validations

✓ Handling unclear
Hospital Handling
ANY QUESTIONS?
Jan Gates
Adept Packaging
VP, Client Solutions - West Coast
E-mail: jan.gates@adeptpackaging.com
Based in Temecula, CA