Writing Package Validation Protocol per ISO 11607 to Minimize Time to Market

Herb Schueneman
President & CEO
Presenter

Nora Crivello
Vice President
Presenter

Kevin Fernandez
Quality Manager
Presenter
Agenda

- Description of a packaging system
- FDA requirements for package validation
- ISO 11607
- Common sections in a package validation protocol
- Common issues when developing the your protocol
- Choosing a package test lab
- Partnering with your lab to minimize time to market
Packaging System

• Sterile Barrier System
  – Primary package that allows for sterilization and provides an acceptable microbial barrier

• Protective Packaging
  – Secondary and tertiary packaging
  – Contains and protects the SBS
FDA Requirements

- The packaging system must provide adequate protection against damage during shipping and maintain sterility of the device for the duration of the intended shelf-life.
- Prove that your packaging can do this with:
  - Recommends being compliant with ISO 11607 *Packaging for Terminally Sterilized Medical Devices*
ISO 11607

- The guidance document for validating sterilized medical device packaging
- Compliance shows that your packaging system allows sterilization, provides physical protection, and maintains sterility up to the point of use.
- FDA Recognized Consensus Standard and required for European Regulation for a CE mark
ISO 11607

• Just a guidance document
• Requirements that must be satisfied for compliance
• Does not identify which specific testing must be conducted
Common Sections in a Protocol

- Purpose
- Scope
- Referenced Documents
- Sample Size
- Equipment
- Responsibilities
- Sample Preparation
- Sterilization
- Package Integrity Testing
- Shelf-life Aging
- Sterile Barrier System Integrity Testing
- Acceptance Criteria
Common Sections in a Protocol

• Purpose - reason for the protocol
• Scope – the extent of what the protocol applies to or deals with
• Responsibilities – what parties are responsible for what sections of a protocol
• Sample Prep – details on pkg configuration, numbering, live or dummy units, testing designation, etc.
• Sterilization – details of sterilization following packaging prior to testing
Referenced Documents

Industry standards or SOP’s referenced for executing the protocol

– Issues often seen
  • Referencing old versions of documents
    – Consult your package test lab for information on revisions and changes.
  • Referencing internal SOP’s and not providing them to the lab.
Sample Size

– Use company SOP’s for sample size and rationale

– In the absence of an SOP or supporting data
  • Based on Attribute Sampling, use 59 samples for 95% confidence/95% reliability
  • A total of 59 sterilized units or primary packages
  • If you want more detailed information on this and the rationale behind it, we can assist you offline if you contact us.
Equipment

– Equipment used will be in current calibration
– Packaging test lab will provide equipment identification and calibration dates in their final report
Package Integrity Testing

- Distribution simulation to challenge your package system to the shipping and distribution environment

- ASTM D4169, ASTM D7386, ISTA sequences, or custom sequence
  - Climatic conditioning
  - Drop testing
  - Compression testing
  - Vibration testing
  - Concentrated impacts
  - Low pressure
Package Integrity Testing

• Test Procedure Recommendation?
  • FDA Recognized: ASTM D4169 and ASTM 7386
    » Consensus standards, sequences and inputs are designed from empirical data, and are recognized by the FDA

• Consult your package test lab for guidance
Shelf-Life Aging

- Real time aging
- Accelerated aging to accelerate the adverse of aging with increased temperature
Shelf-Life Aging

• What accelerated aging temperature to use?
  – Based on different variables (Q, RT temperature, shelf life, etc.) in ASTM F1980
  – Higher the temperature = faster aging
  – Typically 50°C, 55°C, 60°C

• Know your packaging material and product characteristics
  – Avoid temperatures that would damage your product or packaging
Sterile Barrier System Integrity Testing

To identify any breaches in the SBS following package performance testing and aging

- Gross Leak Detection (bubble) testing,
- Dye Penetration
- Visual Inspections

To demonstrate adequate seal strength

- Peel Testing
- Burst Testing
Visual Inspections, Gross Leak Detection (bubble) testing, or Dye Penetration Testing?

- Visual Inspections detection rate as low as 60%
- Dye Penetration evaluates only the seals of the SBS
- Gross Leak Detection evaluates the entire SBS
  - Our internal validation demonstrated >90% detection rate with this method
Sterile Barrier System Integrity Testing

• Seal strength testing (peel) testing or Burst Testing?
  • Peel testing measures the strength of your seals
  • Burst testing identifies weak spots or evaluates how the seals hold up to pressure differentials
Pitfalls in the validation process can stall the launch of a product.

Avoiding these pitfalls can help speed your product to market.
Allow Ability to Decrease Top Load

Box: 24” x 12” x 12”
Top load: 1,600 lb

Box: 24” x 12” x 11.5”
Top load: 709 lb.

H = 108”
F = 10
Load = 1,600 lb

H = 54”
F = 10
Load = 709 lb
Allow Ability to Decrease Top Load

Box: 24” x 12” x 12”
Top load: 1,600 lb

H = 108”
F = 10
Load = 1,600 lb

Box: 24” x 12” x 12”
Top load: 800 lb.

H = 108”
F = 5
Load = 800 lb
• Attribute data acceptance criteria typically 1.0 lbf/in seal.

• Fails validation if 0.98 lbf/in?
  – Suggest that mean should be ≥1.0 lbf/in, absolute min could dip to 0.8, 0.6, etc.
  – EN 868- states “minimum value for seal strength shall be 1,5N per 15mm for steam sterilization processes and 1,2N per 15mm for other sterilization processes”
  – Equates to 0.57 lbf/in for 1.0” seal
Flexibility in Aging

\[
(AAT) = \frac{(RT)}{Q_{10}^{(T_{AA} - T_{RT})}}
\]

• Manipulation of variables can decrease test duration.
• Beware of glass transition point!

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<tr>
<th>Variable</th>
<th>Definition</th>
<th>Purpose</th>
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<tr>
<td>AAT</td>
<td>Accelerated Aging Time</td>
<td>How long the packages will be in the chamber</td>
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<tr>
<td>RT</td>
<td>Real Time</td>
<td>What is the actual duration you are trying to simulate</td>
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<tr>
<td>T_{AA}</td>
<td>Accelerated Aging Temperature (°C)</td>
<td>What temperature will the test be conducted at</td>
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<tr>
<td>T_{RT}</td>
<td>Ambient Temperature</td>
<td>Representation of actual product storage (generally between 20-25°C)</td>
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<tr>
<td>Q_{10}</td>
<td>Rate of Coefficient</td>
<td>Reaction rate; generally Q_{10}=2</td>
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</table>
Accelerated Aging Calculator

In order to sell a medical device or pharmaceutical product in the United States, the FDA requires that the manufacturer prove the sterility and viability of the product on the expiration date prior to selling the product. That means if you market a product "use before June 17, 2019", you must prove that the product is viable on that date before you begin selling it today. To accomplish this, manufacturers employ a derivation of the Arrhenius equation which states (in essence) that molecular activity doubles in organic molecules for every 10°C rise in temperature above ambient. Since ambient temperature is (conservatively) considered to be 25°C, storing a product for six months at 35°C will result in a one-year accelerated aging. Similarly, storing a product at 45°C for three months will result in an accelerated aging period of one year, and so on. Obviously there is a limit to the upper temperature at which this process is valid and, as a practical matter, most accelerated aging occurs at temperatures at or below 55°C.

To validate this information, most practitioners use a process of real-time aging wherein samples subjected to accelerated aging are compared to those from an equivalent "real-time". For example, at the beginning of the sales cycle, product can be real-time aged for 3 to 6 months and compared to samples subjected to accelerated aging for the same accelerated period, say 6 months. If the samples of both groups showed similar characteristics, accelerated aging is considered to be validated with real-time aging results. In this manner, a manufacturer can post a lengthy expiration date, begin distributing the product with real-time validation of accelerated aging data, and continue this process through the expiration date of the medical device. It is crucial to maintain careful records throughout this process to avoid recalls and other disastrous potential results.

www.medicalpackagetesting.com
Stay Inside Your Wheelhouse

• **In house** attribute testing may save money, but it rarely saves time or more work in the long run.

  – Outsourcing full validation protocol to a test lab collates all calibration, engineer and data into one report.
Know your Product and Protocol

- Is the shipper over-packed?
- What is the strength of the corrugated?
- Which surface do you consider the base?
- What is the purpose of testing?
- What is the strength of the corrugated?
Planning for The Unforeseen

• While every effort is made to avoid a non-conformance, errors occur.

Memo: to file
Date: 2014/10/09
Justification: re: Validation anomaly
  • An error occurred during the testing of <Product’s package> which should not effect the results of testing based on x – y – z.
Summary of Discussion

- Decrease compression load
- Understand Peel test criteria
- Enable to speed to market by incorporating into protocol
- Utilize accelerated aging factors
- Stay inside your wheelhouse
- Planning for unforeseen
- Know your product and protocol
Testing Laboratory Certifications

ISTA Certification

Demonstrates compliance to conduct ISTA testing

9001 Certification

Focus on quality management, consistency, documentation

17025 Accreditation

9001+ accredited cal, UoM budgets, etc. Highest standard
Partnering With Your Lab

• Create an atmosphere of partnership with your testing lab. Learn each other’s purpose for testing and processes for efficiency.
Partnering With Your Lab

• Discuss early and often any urgencies you are up against.

WARNING

DEADLINES ARE MUCH CLOSER THAN THEY APPEAR
Partnering With Your Lab

• Relay all critical information.
• Communicate visual inspection criteria.
Partnering With Your Lab

- Contact the lab early to set timing expectations.

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Legend:
- MagView task
- Customer task
- Joint task
Conclusions

• FDA Requirements for Package Validation
• ISO 11607 requirements
• Common Sections in a Validation Protocol
• Common issues and things to avoid when developing the your protocol
• What to look for when choosing a third party test lab to execute your protocol
• How you should work closely with your lab
Two Locations:

San Jose Laboratory
83 Great Oaks Boulevard
San Jose, CA 95119
408-224-1300

www.westpak.com
projects@westpak.com

San Diego Laboratory
10326 Roselle Street
San Diego, CA 92121
858-623-8100
Please feel free to Contact Us with any questions or assistance with your testing needs.

Herb Schueneman  
President and CEO  
Herb@westpak.com

Nora Crivello  
VP, San Jose  
nora@westpak.com

Kevin Fernandez  
Quality Manager  
Kevin@westpak.com

projects@westpak.com