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

Jan Gates: Adept Packaging LLC

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Jan Gates

Principal Packaging Engineer, Adept Packaging

VP Client Solutions, West Coast

- 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

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Some of My Current Work

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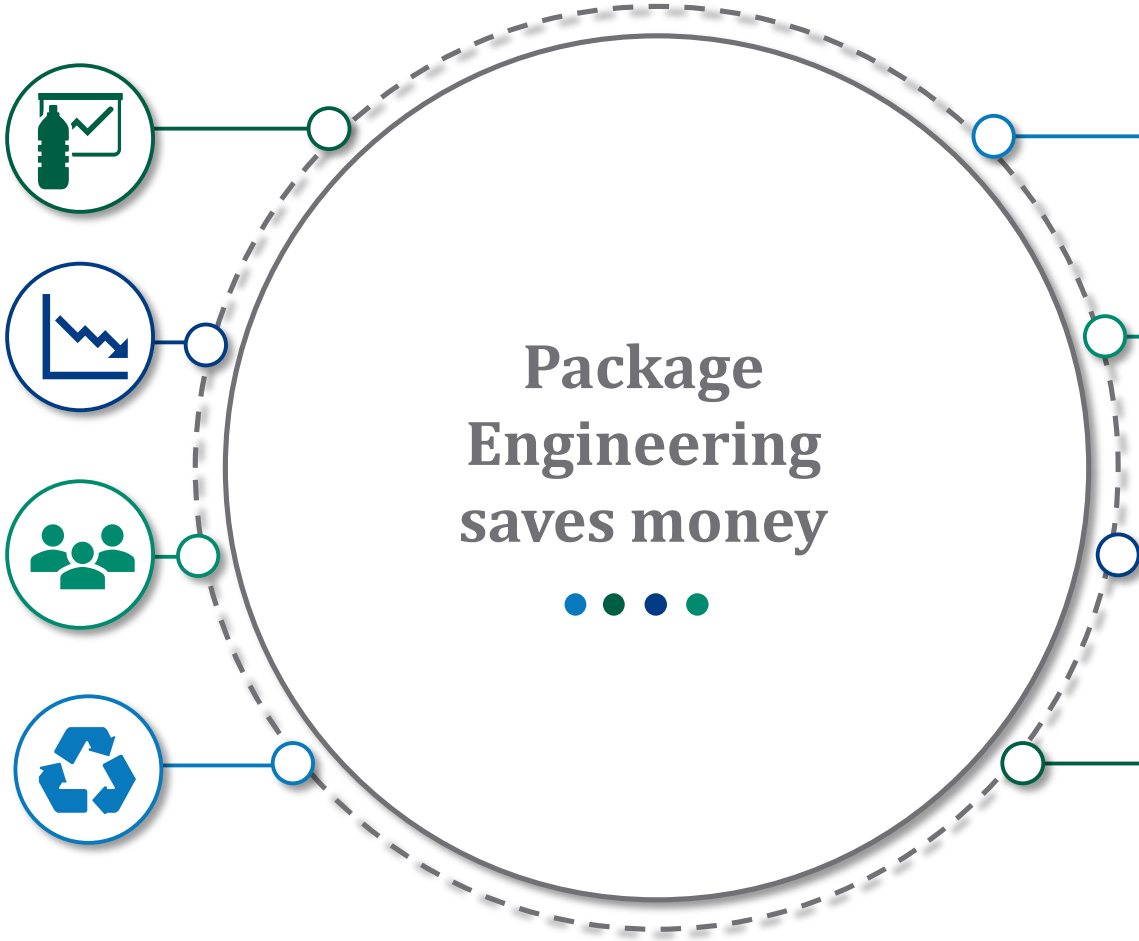
Package Engineering Summary



- 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

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Standard Titles

ISO 11607-1: *Packaging for terminally sterilized medical devices – part one*

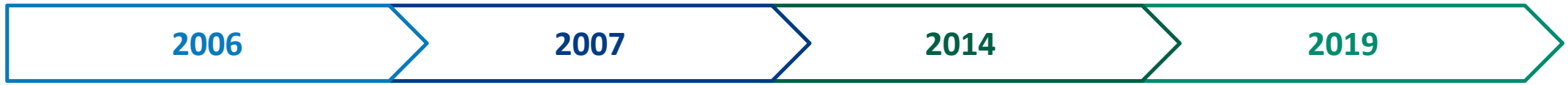
✓ Design and development

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

Terminal Sterilization & Packaging

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

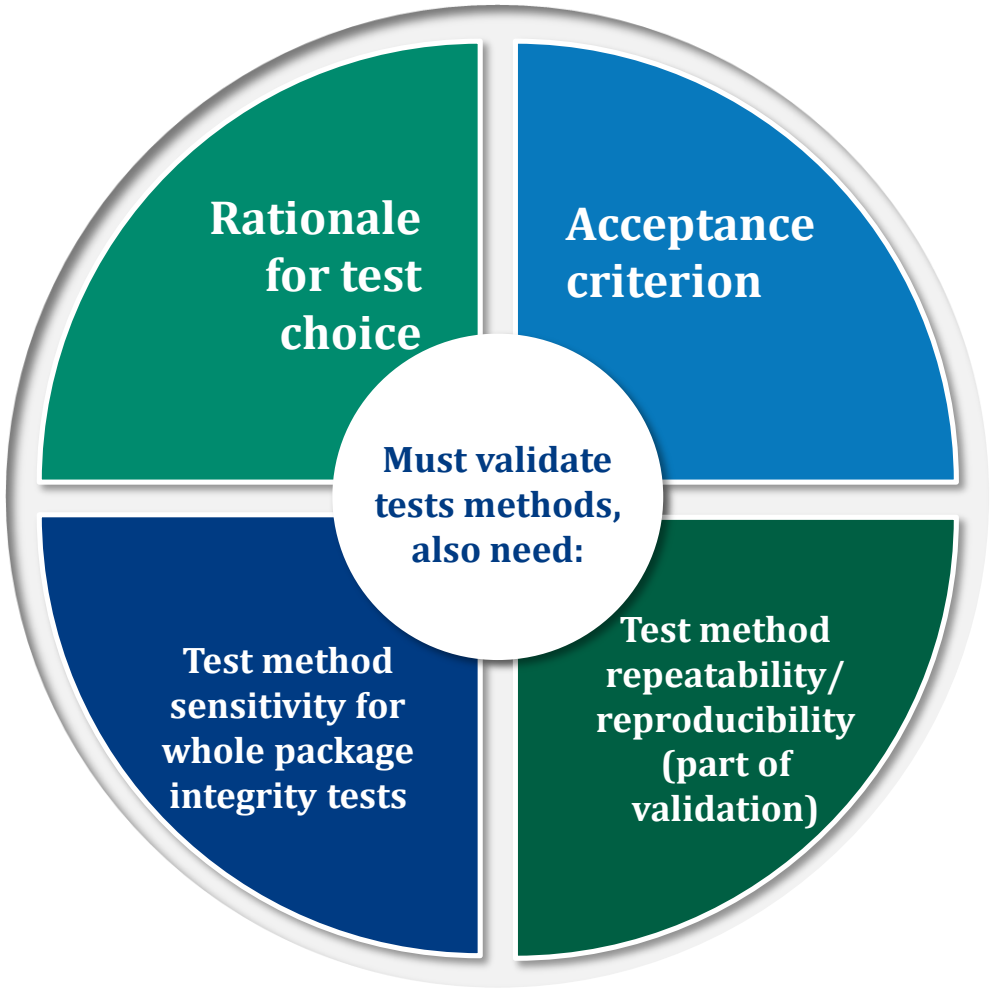
ISO standards available

Individualized by company – include a defect catalogue

ISO/ASTM standards and many books available

Statistical justification/rationale: -1, Clause 4.3

Test Method Validation



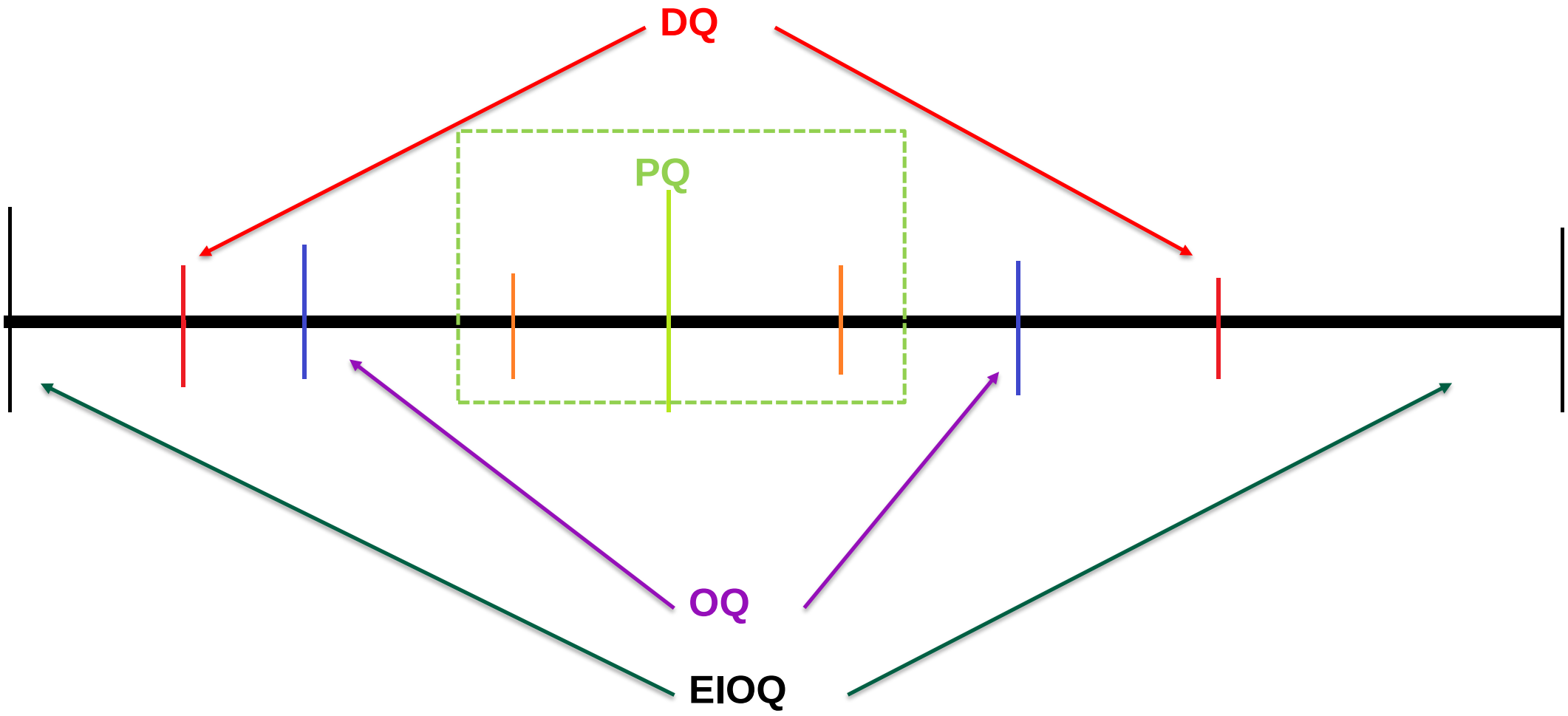
ASTM test methods must be validated in the laboratory conducting the test; publication of a method by a standards body does not make it validated in any laboratory (-1, Clause 4.4.3 Note).

Design and Development Documentation (DDD)

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

ASTM F1980 *Standard Guide for Accelerated Aging of Sterile Barrier Systems for Medical Devices*

- ✓ 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

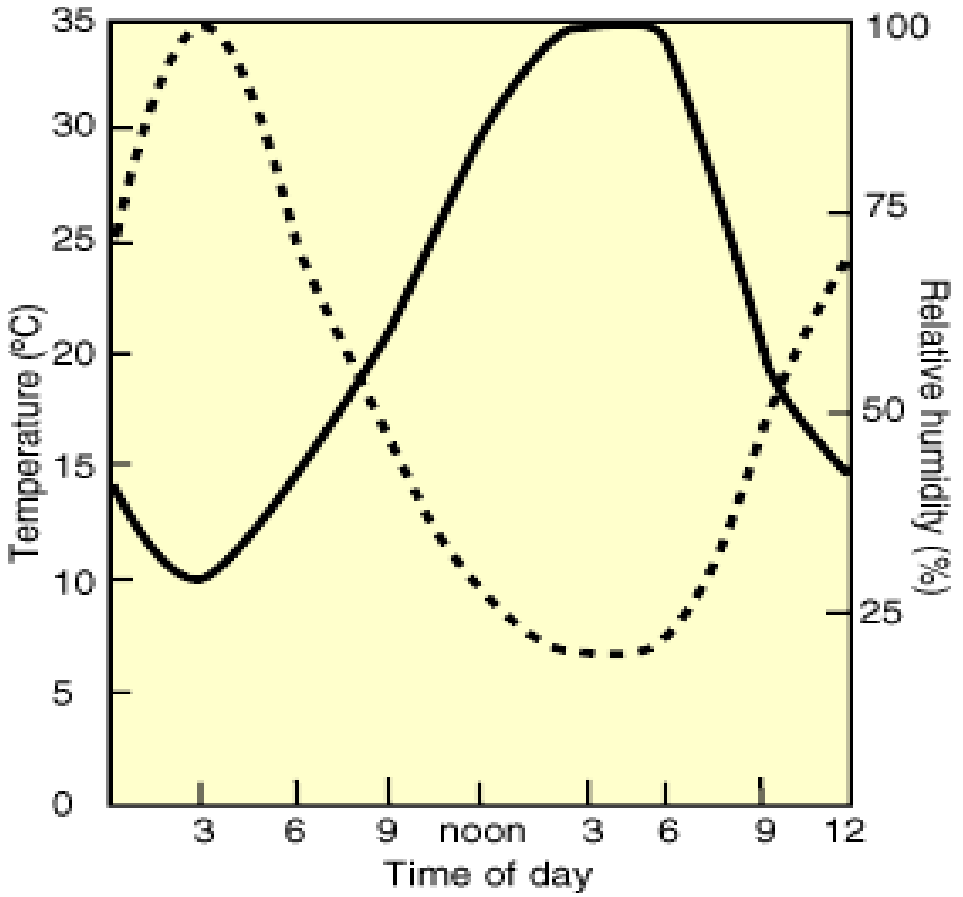
Relative Humidity Note

Relative Humidity is the number of water molecules in the air

The number of molecules in the air is effected by **Temperature**

Temperature and humidity are inversely proportional (with a given quantity of moisture)

$$Relative\ Humidity = \frac{actual\ vapor\ density}{saturation\ vapor\ density} x100\%$$



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

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

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

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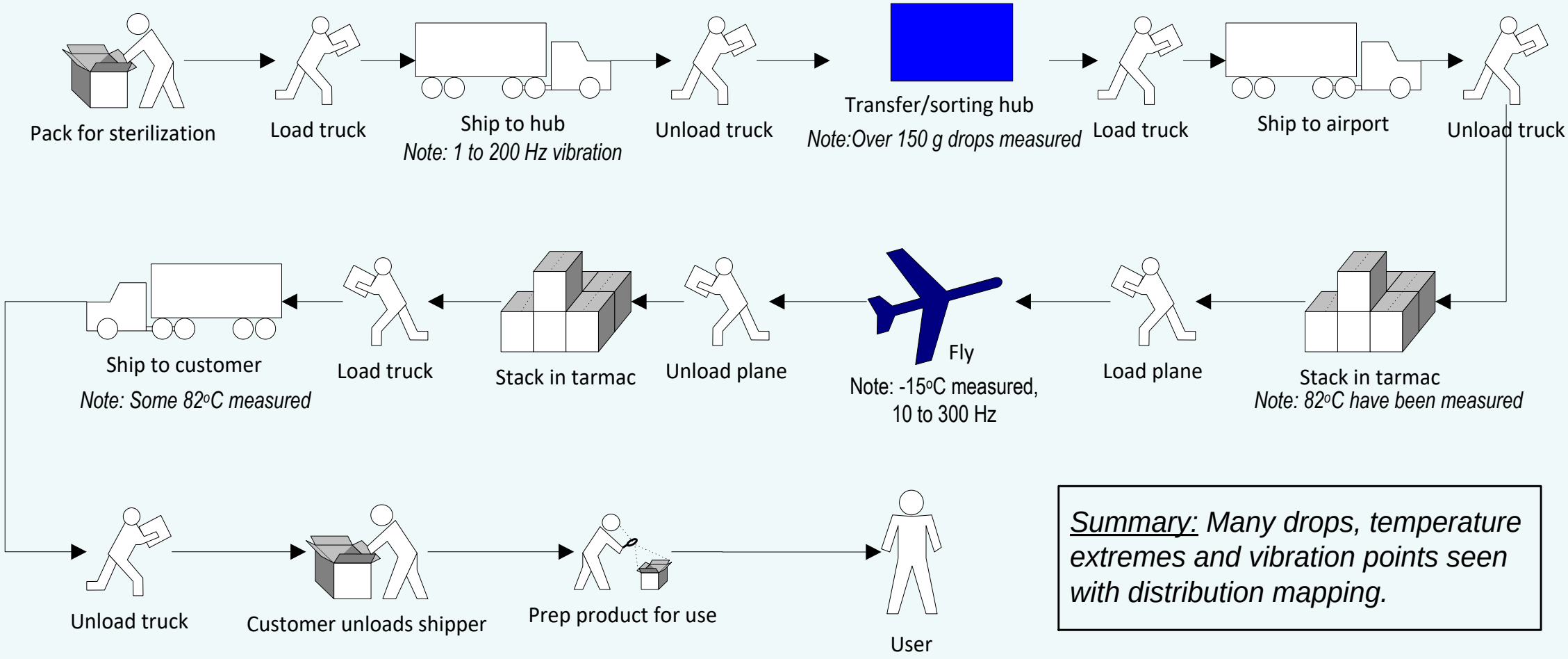
Distribution Mapping -- General



Summary: *Many drops, temperature extremes and vibration points seen with distribution mapping.*

Distribution Mapping: Detailed Multiple Shipping Count Example

Domestic System and Domestic Repetition

Round trip	Handling	Truck Transit	Plane Transit	Compression
1	23	6	1	3
2	47	13	3	7
3	71	20	5	11
4	95	27	7	15
5	119	34	9	19
6	143	41	11	23

International with Subassembly and International Repetition

Round trip	Handling	Truck Transit	Plane Transit	Compression
1	37	10	3	7
2	77	21	7	15
3	124	32	11	23
4	171	43	15	31
5	218	54	19	39
6	265	65	23	47

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

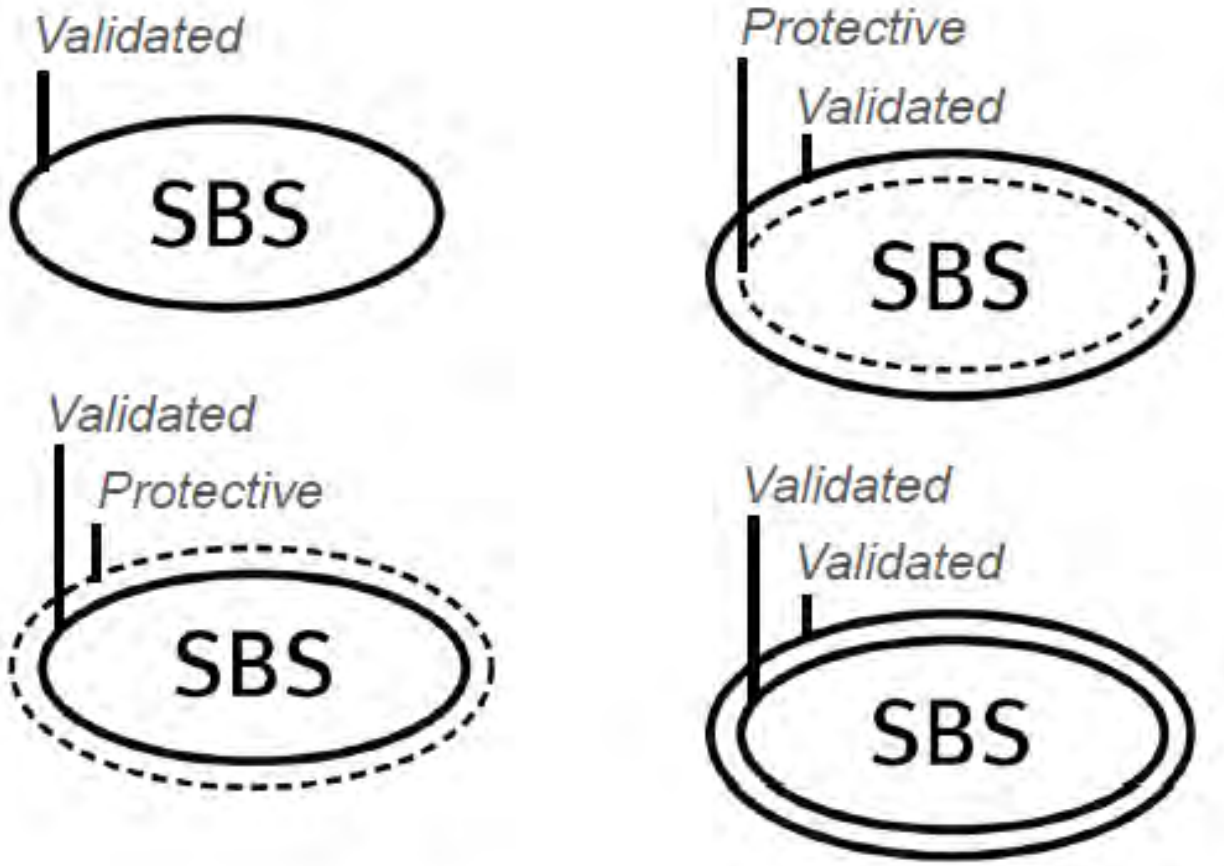
ISO 11607-1: 2019

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

Proposed New Symbol Examples



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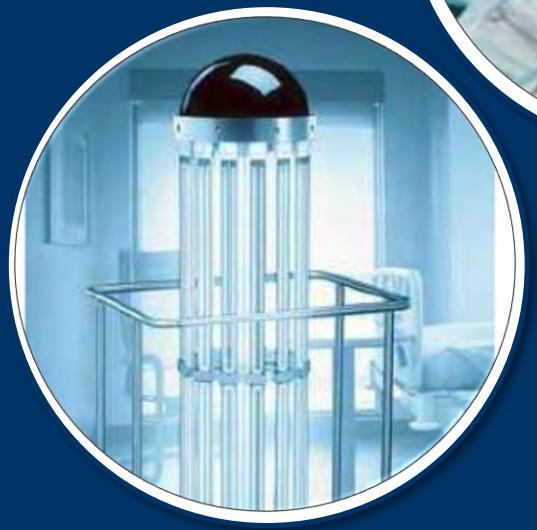
New Challenges: New Concerns in Discussion

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?

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Engineering Packaging Excellence

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