Case Studies and Practical Interpretations of ISO11607

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QTS is a Medical Device Outsourcing company that provides the expertise, responsiveness and exceptional quality required to rapidly bring devices to a highly regulated market.
• We are located in Minneapolis, MN.

• We service a variety of Medical Device clients, in all Classes and major market segments.

• We operate Class 7 Cleanrooms, and are ISO 13485 certified, FDA registered and JPAL compliant.
• What follows are examples of real-world applications of the 11607 Standard, for discussion (and perhaps debate).

• Beyond the gawker appeal, QTS makes no claim to the validity or logic of these examples.

• ... our Customers make interesting decisions.

• Results not typical. Individual results may vary.
ISO11607 Overview

• Packaging for terminally sterilized medical devices

• [a] means to show compliance to the relevant Essential Requirements of the European MDD.

• FDA-recognized consensus standard.
ISO11607 Overview

- Note the emphasis on "systems"
- Sterile barrier systems
- Packaging systems
- Forming, sealing and assembly systems
ISO11607 Overview

• Written in two (2) parts
• 11607-1: Requirements for
  • Materials
  • Sterile barrier systems and
  • Packaging systems
ISO11607 Overview

- Written in two (2) parts
- 11607-2: Validation requirements for
  - Forming
  - Sealing and
  - Assembly processes
ISO11607 – What it is not

• Describes tensile testing, does not specify 1.0 PLI

• Requires statistical validity, does not define sample sizes

• Requires the labeling system to remain "intact and legible"; does not describe how to evaluate those properties
The CASE OF THE DESTRUCTIVE DISTRIBUTION

SHE DID A SHELF-LIFE AND A DISTRIBUTION, on the SAME SAMPLES!
Background

• Client acquired a product line with:
  • No package performance testing
  • No shelf life justification

• A limited number of expired, market-return units were available

• Client wanted to backfill and prove performance & barrier in one shot
Study Overview

- Customer preferred to use their corporate packaging protocol
- No [zero] units were reserved for baseline evaluation
- Test population consisted of market returns, expired product
Package System Overview
Package System Overview
• Samples n=22

Distribution Sequence using AL1
[most severe, least likely to occur]

Visual Evaluation

Peel Strength
n=8 (x4 = 32)

Dye Test
n=14
Let's Set Up the Loss

- Visual: F1886 [ Seal Integrity ]
- Peel Test: F88 [ Seal Strength ]
- Dye Test: F1929 [ Seal Leaks ]

- Whole-package integrity test - missing.
- Worst-case [AL1] Distribution, but *no* controls or history on sealing, sterilization, etc.
Let's Set Up the Loss

- "Corporate" standard not in sync with 11607
- No Control Population
- Using AL1 Sequence a.k.a. BTLSOOTs
- Is n=22 "Statistically Valid"
- Convolution of Performance and Stability Testing
Visual Results - PASS; *Seals* appeared hermetic
  - Whole package suspect

Tensile Test - PASS; Above acceptance criteria

Dye Test - PASS; effective width > min.
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Dye Test - Real World Failures
Dye Test - Real World Failures
Dye Test - Real World Failures
Visual Results
Whole-Package
Integrity

- Whole package suspect
- Not formally conducted
Visual Results - Whole package suspect
Whole-Package - Not formally conducted
Integrity
Visual Results - Whole package suspect
Whole-Package - Not formally conducted
Integrity
Visual Results  -  Whole package suspect
Whole-Package -  Not formally conducted
Integrity
Visual Results - Whole package suspect
Whole-Package - Not formally conducted
Integrity
Whole-Package Integrity: Fail (?)
Whole-Package Integrity: Fail (?)
Whole-Package Integrity: Fail (?)
Whole-Package Integrity: Fail (?)
Visual Results - PASS; Seals appeared hermetic

Tensile Test - PASS; Above acceptance criteria

Dye Test - PASS; effective width > min.

Whole-Package Integrity - Apparently a FAIL
What did QTS learn?

• Recall we discovered whole-package failures using a seal integrity test. Was that a "validated" test?

• Internal Pressurization [ "bubble leak" ] and other methods are better techniques to evaluate whole package integrity
What did QTS learn?

• Whole package integrity evaluation was NOT part of the pre-determined acceptance criteria

• There were obvious failures ...

• Observations beyond the pre-determined acceptance criteria are just that: they start as observations
What did QTS learn?

• The lack of (any) baseline sample made final interpretation problematic

• Use of "real-time" units, should be carefully considered

• Realistic dunnage might have been more appropriate
So, was this study 11607 "compliant"?

• In a way, the customer simply used Annex B to select test methods

• No attempt to justify the (limited) sample size; no claim of validity

• Convoluting of shelf life and distribution testing
  [stability testing & packaging-system performance testing]
Convolution of stability testing & packaging-system performance testing

• Do you perform distribution simulation, as a pre-conditioning step, in your shelf-life study?

• Do you combine distribution and shelf-life in a single "packaging" study?
Convolution of stability testing & packaging-system performance testing

• 11607-1: Stability testing and packaging system performance testing are separate entities

• 16775 [draft], Annex M: There are several reasons why stability testing and packaging system performance testing should NOT be combined
Study Design
Study Design

• Previous example was undershooting the intent of 11607.

• It is just as easy to design a study that goes beyond the intent of the Standard.

• Requirements and test methods for materials and package systems that are: “intended maintain the sterility of the terminally sterilized medical devices until the point of use.”
Study Design

Gerry's Case Study

ISO11607-Part 1

Current Example

Annex B
Study Design

• Recent project required a new validation: Seal Strength, Seal Integrity

• They chose to include extensive visual requirements unrelated to sterile barrier:
  • Any Label creasing, wrinkles, smudging
  • Any holes, wrinkles in Shrink Wrap
  • Any crease, bulge of Shelf Box
Study Design

• These visual requirements were driven by marketing reasons, *not* 11607 requirements.

Results:

• First 2 sets of samples never made it to strength or integrity testing.

• Made several changes to packaging configuration between runs.

• Study was repeated *3 times* with the full sample size.
Study Design

• What could have been done differently?
• Small study with limited sample size to define the packaging configuration
• Second study to meet the requirements of 11607

• Keep marketing out of it?
TENSILE TEST:
KING OF THE VARIABLE DATA

EVERYONE ELSE TENSILE TESTS THEIR PACKAGE,
but what if YOU CAN’T?
Test Methods

- The medical world loves Tensile Testing
Test Methods

• Tray isn’t big enough to tensile test all sides.

• Now what? We need a new plan!
Test Methods

Plan B – Burst Test it

• Time for a comparison study
Test Methods

- Build Samples at Low Parameters

Visual Evaluation

Tensile Test

Burst Test

Develop a Baseline
ATTACK OF
THE
STANDARD
DEVIATION

WAS THE SAMPLE SIZE BIG ENOUGH, CAN IT BE
JUSTIFIED, \textit{will the} STATISTICS PASS?
• What does the (standard) say about sample sizes?

• Section 4.3: Sampling

• “Sampling plans shall be based upon a statistically valid rationale.”
Statistical Validity

• What does “statistically valid” really mean and how do you achieve it?

• Common Approach to determining sample sizes Risk Based Confidence and Reliability

• What about: Business Reasons

• Reality
  Typically it ends up being a combination of factors
Statistical Validity

• Confidence and Reliability Approach
  Corporate standards for testing require confidence and reliability numbers of 95/99 or n=298 for Bubble Leak testing.

• Business Reason Approach
  Only 5 devices are available for Bubble Leak testing. Working backwards, this equates to a 80/70 confidence and reliability.

• So who’s right?

• Both. Each company believes they have a statistically valid sample size, both based off widely accepted sample plans.
So, what does a "proper" ISO11607 packaging study look like?

- Under the guise of a Quality System
- Statistically valid sample plans
- Validated test methods
- Established acceptance criteria
- Suitable material selection
So, what does a "proper" ISO11607 packaging study look like?

- Mat'l's: Microbial barrier properties
- Formal design and development process
- "Real" packages, including devices & dunnage
- Evaluate: Sterile barrier system (stability)
- Evaluate: Packaging performance
Resources

• Packaging (Material) Suppliers – Partner for Packaging studies

• TIR-22

• ISO 16775 (presently in ballot)
Questions?

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