EN 868-5 and ASTM F88

Jordan Montgomery
Senior Principal Packaging Engineer/Technical Fellow
Medtronic CRDM
Dave Olson – 3-time presenter
Highlights

• Acknowledgments
• Requirements
• Test Methods
• Divergent Paths
• Initial Comparison Study
  – Study Design
  – Results
  – Analysis
• Summary / Conclusion / Next Steps
Acknowledgements

- Sameer Upadhyaya
- Salin Yousefnia
- Mark Ralph
- Dee Hemgren
- Jim Domke
Sterile Barrier System Requirements

• ISO 11607-1
  – Clause 5.1.8 c) Materials shall demonstrate minimum specified seal strength when a seal is formed with another specified material under specified conditions.
  
  – Clause 5.1.9 b) If formed by sealing, the specified requirements for seal width and seal strength (tensile and/or burst) shall be met.
Seal Strength Test Methods

- ISO 11607-1, Annex B
  - Seal Strength
    - ASTM F88 – Standard test method for seal strength of flexible barrier materials
    - ASTM F1140 – Standard test method for failure resistance of unrestrained and non rigid packages for medical applications
    - ASTM F2054 – Standard test method for burst testing of flexible package seals using internal air pressurization within restraining plates
    - EN 868-5:1999, Annex D – Packaging materials and systems for medical devices which are to be sterilized – Part 5 Heat and self sealable pouches and reels of paper and plastic film construction – Requirements and test methods

As listed in 11607-1
Seal Strength Test Methods

- ISO 11607-1, Annex B
  - Seal Strength
    - ASTM F88 – Standard test method for seal strength of flexible barrier materials
    - ASTM F1140 – Standard test method for failure resistance of unrestrained and non rigid packages for medical applications
    - ASTM 2054 – Standard test method for burst testing of flexible package seals using internal air pressurization within restraining plates
  - EN 868-5:1999, Annex D – Packaging materials and systems for medical devices which are to be sterilized – Part 5 Heat and self sealable pouches and reels of paper and plastic film construction – Requirements and test methods

As listed in 11607-1
Divergent Paths

United States
- FDA
  - Consensus Standards
    - ISO 11607-1
      - ASTM F88

Europe
- Notified Body
  - Harmonized Standards
    - EN ISO 11607-1
      - EN 868-5: Annex D

State of the Art
Divergent Paths

United States
- FDA
- Consensus Standards
  - ISO 11607-1
  - ASTM F88

Europe
- Notified Body
- Harmonized Standards
  - EN ISO 11607-1
  - EN 868-5: Annex D

Requirement and Value
Test Method
EN 868-5 A closer look

- Particular requirements of clause 4.2 and 4.5 can be used to demonstrate compliance with one or more but not all requirements of EN ISO 11607-1.
- 4.2 – Materials
  - 4.2.1 Porous material
  - 4.2.2 Plastic film
- 4.5 - Performance requirements and test methods

  Scope: Appears limited to pouches and reels.
4.5 - Performance requirements and test methods

- 4.5.1 When tested in accordance with the method described in Annex D the strength of the seal joint shall not be less than required for the intended purpose, both before and after being subjected to the sterilization process.
  
  • Requirement (Healthcare facility for steam) = 1.5N / 15mm
  • Requirement (all other sterilization) = 1.2N / 15 mm

• NOTE 2: For applications outside of healthcare facilities, requirements are given in EN ISO 11607-1.
EN 868-5 - Annex D (normative)
Method for the determination of the strength of the seal joint for pouches and reel material

• Units: N / 15mm
• Principal: strips cut at 90° through seals (right angles)
• Preparation: 15 ± 0.1 mm
• Procedure: rate of separation 200 ± 10 mm / minute
• Report:
  – Record max strength in N / 15mm width
  – Supported/unsupported, specs, data sheets
  – Electronic device frequency rate
  – Identification of the product under test, test house, date
  – Number of the standard used for the test.

15mm – 8”/minute
ASTM F88 – A closer look

• Current designation: F88/F88M-09
  – Title: Standard Test Method for Seal Strength of Flexible Barrier Materials

• Scope:
  – Measurement of seal strength between flexible materials
  – May be used on seals between a flexible material and a rigid material
  – Measure the force required to separate the test strip of material containing the seal as well as the mode of specimen failure.
ASTM F88 – A closer look

• Significance and Use
  – Discusses minimum and maximum seal strength, but does not have a required value.
  – Discusses maximum force and average force
  – Discusses / provides basic guidance on techniques and consistent use of a technique

![Diagram of Tail Holding Methods](image)
ASTM F88 – A closer look

• Procedure:
  – Calibrated tensile tester
  – Sample prep, perpendicular to the seal, width = 1 inch (also calls out 0.984, and 0.591)
  – Sealed area approximately equidistant between the grips
  – Center the test strip laterally in the grips
  – Detail any technique used to control tail orientation
  – Rate of separation 8 to 12 inches /minute
  – Record maximum force and mode of failure
  – If the strip peels apart in the seal area, average force may be important
  – Plot of force vs. grip travel is useful
  – Caution on the effect of other failure modes (elongation, break, delamination)
Comparison Study

• A small study was conducted to form a baseline for comparison between the methods.
• Key variables for comparison chosen:
  – Test strip width (1 inch vs. 15mm)
  – Rate of Separation (8 inches / minute vs. 12 inches / minute)
Comparison Study Design

- One material used throughout:
  - Porous web: Tyvek 1073B coated with CR-27
  - Film: 36603-S, 5 mil nylon laminated

- All test strips came from one lot of pouches

- All test strips cut from approximately the same location.

- All samples prepped in 1 lab, by 1 person
Comparison Study Design

- Samples were not subjected to sterilization
- Sample size of 15 used for each group
- 3 labs
- 4 groups per lab
- Unsupported tail
- Maximum force recorded in lbs / width
## Comparison Study Design

<table>
<thead>
<tr>
<th>Test Group</th>
<th>Lab</th>
<th>Sample Width</th>
<th>Rate of Separation</th>
<th>Sample Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>CRDM</td>
<td>1 inch</td>
<td>8 inch / min</td>
<td>15</td>
</tr>
<tr>
<td>B</td>
<td>CV</td>
<td>1 inch</td>
<td>8 inch / min</td>
<td>15</td>
</tr>
<tr>
<td>C</td>
<td>Neuromodulation</td>
<td>1 inch</td>
<td>8 inch / min</td>
<td>15</td>
</tr>
<tr>
<td>D</td>
<td>CRDM</td>
<td>1 inch</td>
<td>12 inch / min</td>
<td>15</td>
</tr>
<tr>
<td>E</td>
<td>CV</td>
<td>1 inch</td>
<td>12 inch / min</td>
<td>15</td>
</tr>
<tr>
<td>F</td>
<td>Neuromodulation</td>
<td>1 inch</td>
<td>12 inch / min</td>
<td>15</td>
</tr>
<tr>
<td>G</td>
<td>CRDM</td>
<td>15mm</td>
<td>8 inch / min</td>
<td>15</td>
</tr>
<tr>
<td>H</td>
<td>CV</td>
<td>15mm</td>
<td>8 inch / min</td>
<td>15</td>
</tr>
<tr>
<td>I</td>
<td>Neuromodulation</td>
<td>15mm</td>
<td>8 inch / min</td>
<td>15</td>
</tr>
<tr>
<td>J</td>
<td>CRDM</td>
<td>15mm</td>
<td>12 inch / min</td>
<td>15</td>
</tr>
<tr>
<td>K</td>
<td>CV</td>
<td>15mm</td>
<td>12 inch / min</td>
<td>15</td>
</tr>
<tr>
<td>L</td>
<td>Neuromodulation</td>
<td>15mm</td>
<td>12 inch / min</td>
<td>15</td>
</tr>
</tbody>
</table>
Results – Pooled Data (n = 45)

<table>
<thead>
<tr>
<th>Test (width – speed)</th>
<th>Average* (lbs / width)</th>
<th>Standard Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1” – 8”/minute</td>
<td>1.16</td>
<td>0.13</td>
</tr>
<tr>
<td>1” – 12”/minute</td>
<td>1.14</td>
<td>0.10</td>
</tr>
<tr>
<td>15mm – 8”/minute</td>
<td>0.69</td>
<td>0.06</td>
</tr>
<tr>
<td>15mm – 12”/minute</td>
<td>0.68</td>
<td>0.07</td>
</tr>
</tbody>
</table>

* Average of the peak values
Conversion of units...

Conversion of lbs/inch width to N / 15mm:

\[
\frac{1.16 \text{ lb}}{25.4\text{ mm}} \times \frac{4.45\text{ N}}{1 \text{ lb}} \times \left( \frac{15}{25.4} \right) = 3.05 \text{ N/15mm}
\]

Conversion of lbs/15mm width to N / 15mm:

\[
\frac{0.69 \text{ lb}}{15\text{ mm}} \times \frac{4.45\text{ N}}{1 \text{ lb}} = 3.07 \text{ N/15mm}
\]

1 inch = 25.4 mm
## Results – Pooled Data (n = 45)

<table>
<thead>
<tr>
<th>Test (width – speed)</th>
<th>Average* (N / 15mm)</th>
<th>Standard Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1” – 8”/minute</td>
<td>3.05</td>
<td>0.35</td>
</tr>
<tr>
<td>1” – 12”/minute</td>
<td>3.00</td>
<td>0.27</td>
</tr>
<tr>
<td>15mm – 8”/minute</td>
<td>3.07</td>
<td>0.28</td>
</tr>
<tr>
<td>15mm – 12”/minute</td>
<td>3.03</td>
<td>0.32</td>
</tr>
</tbody>
</table>

* Average of the peak values
Boxplot of the results
Boxplot of the results – with spec limits used for y-axis

- Spec limits:
  - 0.5 lbs/in – 6.0 lbs/in
  - 1.3 N/15mm – 15.8 N/15mm
**ANOVA – Pooled Data (n = 45)**

One-way ANOVA: 1" - 8"/min, 1" - 12"/min, 15mm - 8"/min, 15mm - 12"/min

<table>
<thead>
<tr>
<th>Source</th>
<th>DF</th>
<th>SS</th>
<th>MS</th>
<th>F</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Factor</td>
<td>3</td>
<td>0.1190</td>
<td>0.0397</td>
<td>0.42</td>
<td>0.740</td>
</tr>
<tr>
<td>Error</td>
<td>176</td>
<td>16.7012</td>
<td>0.0949</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>179</td>
<td>16.8202</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

S = 0.3080  R-Sq = 0.71%  R-Sq(adj) = 0.00%

---

Individual 95% CIs For Mean Based on Pooled StDev

<table>
<thead>
<tr>
<th>Level</th>
<th>N</th>
<th>Mean</th>
<th>StDev</th>
</tr>
</thead>
<tbody>
<tr>
<td>1&quot; - 8&quot;/min</td>
<td>45</td>
<td>3.0541</td>
<td>0.3523</td>
</tr>
<tr>
<td>1&quot; - 12&quot;/min</td>
<td>45</td>
<td>3.0018</td>
<td>0.2745</td>
</tr>
<tr>
<td>15mm - 8&quot;/min</td>
<td>45</td>
<td>3.0682</td>
<td>0.2782</td>
</tr>
<tr>
<td>15mm - 12&quot;/min</td>
<td>45</td>
<td>3.0251</td>
<td>0.3204</td>
</tr>
</tbody>
</table>

Pooled StDev = 0.3080

Result – no difference signaled.
Comparison of test strip width
1 inch and 15 mm test strips @ 8” / minute

Two-Sample T-Test and CI: 1” - 8”/min, 15mm - 8”/min

Two-sample T for 1” - 8”/min vs 15mm - 8”/min

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>Mean</th>
<th>StDev</th>
<th>SE Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>1” - 8”/min</td>
<td>45</td>
<td>3.054</td>
<td>0.352</td>
<td>0.053</td>
</tr>
<tr>
<td>15mm - 8”/min</td>
<td>45</td>
<td>3.068</td>
<td>0.278</td>
<td>0.041</td>
</tr>
</tbody>
</table>

Difference = mu (1” - 8”/min) - mu (15mm - 8”/min)
Estimate for difference: -0.0141
95% CI for difference: (-0.1472, 0.1190)
T-Test of difference = 0 (vs not =): T-Value = -0.21 P-Value = 0.833 DF = 83

Result – no difference signaled.
Comparison of test strip width
1 inch and 15 mm test strips @ 12" / minute

Two-Sample T-Test and CI: 1" - 12"/min, 15mm - 12"/min

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>Mean</th>
<th>StDev</th>
<th>SE Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>1&quot; - 12&quot;/min</td>
<td>45</td>
<td>3.002</td>
<td>0.275</td>
<td>0.041</td>
</tr>
<tr>
<td>15mm - 12&quot;/min</td>
<td>45</td>
<td>3.025</td>
<td>0.320</td>
<td>0.048</td>
</tr>
</tbody>
</table>

Difference = mu (1" - 12"/min) - mu (15mm - 12"/min)
Estimate for difference:  -0.0233
95% CI for difference:  (-0.1483, 0.1018)
T-Test of difference = 0 (vs not =):  T-Value = -0.37  P-Value = 0.712  DF = 85

Result – no difference signaled.
Comparison of test speed, 8”/minute vs. 12”/minute with 1” width test strips

Two-Sample T-Test and CI: 1" - 8"/min, 1" - 12"/min

Two-sample T for 1" - 8"/min vs 1" - 12"/min

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>Mean</th>
<th>StDev</th>
<th>SE Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>1&quot; - 8&quot;/min</td>
<td>45</td>
<td>3.054</td>
<td>0.352</td>
<td>0.053</td>
</tr>
<tr>
<td>1&quot; - 12&quot;/min</td>
<td>45</td>
<td>3.002</td>
<td>0.275</td>
<td>0.041</td>
</tr>
</tbody>
</table>

Difference = mu (1" - 8"/min) - mu (1" - 12"/min)
Estimate for difference: 0.0523
95% CI for difference: (-0.0802, 0.1847)
T-Test of difference = 0 (vs not =): T-Value = 0.78 P-Value = 0.435 DF = 83

Result – no difference signaled.
Comparison of test speed, 8”/minute vs. 12”/minute with 15mm width test strips

Two-Sample T-Test and CI: 15mm - 8”/min, 15mm - 12”/min

Two-sample T for 15mm - 8”/min vs 15mm - 12”/min

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>Mean</th>
<th>StDev</th>
<th>SE Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>15mm - 8”/min</td>
<td>45</td>
<td>3.068</td>
<td>0.278</td>
<td>0.041</td>
</tr>
<tr>
<td>15mm - 12”/min</td>
<td>45</td>
<td>3.025</td>
<td>0.320</td>
<td>0.048</td>
</tr>
</tbody>
</table>

Difference = mu (15mm - 8”/min) - mu (15mm - 12”/min)

Estimate for difference: 0.0431

95% CI for difference: (-0.0826, 0.1689)

T-Test of difference = 0 (vs not =): T-Value = 0.68  P-Value = 0.497  DF = 86

Result – no difference signaled.
Comparison Between Labs: Data adjusted to N/15mm

This analysis method has been developed in order to compare measurement variability between operators while avoiding an increased chance of failing the requirement if sample sizes larger than the minimum are used. In contrast, the usual hypothesis test comparing standard deviations or variances has an increased chance of detecting small differences when larger sample sizes are used.
Comparison Between Labs: Data adjusted to N/15mm

One-way ANOVA: Measurement versus Lab

<table>
<thead>
<tr>
<th>Source</th>
<th>DF</th>
<th>SS</th>
<th>MS</th>
<th>F</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lab</td>
<td>2</td>
<td>2.7636</td>
<td>1.3818</td>
<td>17.40</td>
<td>0.000</td>
</tr>
<tr>
<td>Error</td>
<td>177</td>
<td>14.0567</td>
<td>0.0794</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>179</td>
<td>16.8202</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

S = 0.2818  R-Sq = 16.43%  R-Sq(adj) = 15.49%

Individual 95% CIs For Mean Based on Pooled StDev

Level N Mean StDev
CRDM 60 2.9655 0.2646
CV 60 3.2116 0.3008
Neuro 60 2.9348 0.2789

Pooled StDev = 0.2818

\[
\sigma_{\text{Reproducibility}} = \sqrt{\frac{(MSSLab - MSerror)}{r}} \\
\sigma_{\text{Reproducibility}} = \sqrt{\frac{(1.3818 - 0.0794)}{60}} \\
\sigma_{\text{Reproducibility}} = 0.14
\]

% Tolerance for Reproducibility:

\[
= 100 \times \frac{6 \times \text{Gage Reproducibility Standard Deviation}}{USL - LSL} \\
= 100 \times \frac{6 \times 0.14}{15.8 - 1.3} \\
= 5.8\%
\]
Comparison Between Labs: Data adjusted to N/15mm

<table>
<thead>
<tr>
<th>Variable</th>
<th>Lab</th>
<th>StDev</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measurement</td>
<td>CRDM</td>
<td>0.2646</td>
</tr>
<tr>
<td></td>
<td>CV</td>
<td>0.3008</td>
</tr>
<tr>
<td></td>
<td>Neuro</td>
<td>0.2789</td>
</tr>
</tbody>
</table>

\[
StDevRatio = \frac{\sigma_{\text{max}}}{\sigma_{\text{min}}}
\]

\[
StDevRatio = \frac{0.3008}{0.2646}
\]

\[
StDevRatio = 1.14
\]

Standard Deviation Ratio is less than the critical value of 2.92. Therefore, no significant difference between labs.
Preliminary Findings

- No significant difference between test speeds.
- No significant difference between test strip widths when the data is converted to equivalent units.
- No significant difference in results between the labs participating.
Observation: Relationship between test strip width ratio and ratio of the results

\[
\text{Test strip width ratio} = \frac{15 \text{ mm}}{25.4 \text{ mm}} = 0.591
\]

\[
\frac{15\text{mm - 8''/minute}}{25.4\text{mm - 8''/minute}} \rightarrow \frac{0.69}{1.16} = 0.595
\]

\[
\frac{15\text{mm - 12''/minute}}{25.4\text{mm - 12''/minute}} \rightarrow \frac{0.68}{1.14} = 0.596
\]

ASTM F88: 1 inch = 25.4mm
EN 868-5: 15mm
Preliminary Findings

• No significant difference between test speeds.
• No significant difference between test strip widths when the data is converted to equivalent units.
• No significant difference in results between the labs participating.

• *Ratio of test strip width provides a means of correlating the result to the alternate method.*
Conclusion

- Initial data suggests a relationship between the result of seal strength measurement using ASTM F88 and EN 868-5.

Next Steps

- Create an ASTM Work Item do conduct a formal ILS utilizing ASTM statisticians.
- Use data from the ILS and create an informative annex in F88 with guidance on use of the 2 methods and subsequent comparisons.
Thank You!
Sterile Barrier System Requirements

• ISO 11607-1
  – Clause 5.1.9 c) Peel Open characteristics shall be continuous and homogenous, without delamination or tearing of the material that can affect aseptic opening and presentation.
Peel Open Characteristics Test Methods

• ISO 11607-1, Annex B
  – EN 868-5:1999 - Packaging materials and systems for medical devices which are to be sterilized – Part 5 Heat and self sealable pouches and reels of paper and plastic film construction – Requirements and test methods (Annex C: Determination of peel open characteristics of paper/plastic laminate products)