The Path to Package Integrity
Outline

- Package integrity logic and thought process.
- Establishing quality standards.
- Evaluation of common methodologies.
- Alternative methodologies.
- Driving forward with package integrity solutions.
Package Integrity

- Package Integrity – maintaining a sterile barrier.
- Package integrity is a sub-category of quality and is exclusive of:
  - Peel Strength
  - Burst Testing
  - Visual Inspection
Implications of Integrity Deviations

- Transfer of environmental contaminants.
- Release of critical ingredients/flavors.
- Synergistic effects of contaminants ($O_2$, $H_2O$, Bacteria).
- Defects that will progress to leakage.
How to discuss integrity?

- What is important to your customer?
- What is important to the product?
- What is Important to the package?

Integrity can be defined.  
Level of assurance is open to discussion.
Six Sigma Framework - DMAIC

- Define
- Measure
- Analyze
- Improve
- Control
Foundation of Quality Control

Define
Quality cannot be controlled without discrete and measurable characterizations of quality.

Measure
Quality cannot be controlled without accurate and definitive measures of quality.
Determining Critical to Quality Baseline

- Package validation via ISO 11607.
- Package validation should include CTQ defect studies respective of the product.
  - Desiccant weight gain
  - Flavor evaluation
  - Product performance

What level of defect will deteriorate my product?
Microbes & Target Leak Sizes


Characterizing Defects

- Pinholes
- Flex Cracks
- Channel Defects <3mm
- Incomplete Seal >3mm
- Torturous path of channel defects.
- Pinhole is not equal to a channel defect

Flow Rate is the Critical Parameter

Pinhole vs. Channel Defect

75µ Pinhole – ~44 sccm

75µ 20mm Channel – ~6.4 sccm

75µ 40mm Channel – ~3.2 sccm
Common Approaches to Defining Package Integrity

- “Looks good”
- Capability (Best Available Technology)
- Equal to/Better than
- Third Party White Papers
- Grandfathered Industry Standards
- “Critical, Major, Minor”
The Ideal Test Method

Informative
Accurate
Simple
Cost Effective
Reduces Waste
Increases Productivity
Navigating Regulation

• FDA recognizes methodology.
• Manufacturers must prove validated methodology consistent with product requirements for label claims.
• Methods listed by organizations (ASTM, ISO, USP) are only guidance's.
• Listened methodologies:
  – Capabilities are irrespective of package/product requirements.
  – Capabilities vary based on package a product characteristics.
Direct Measures of Quality
ISO 11607 – Annex B

- Vacuum Decay (ASTM F2338)
- Seal Strength (ASTM F88)
- Airborne Ultrasound Seal Inspection*
- Visual Inspection (ASTM F1886)
- Dye Migration (F1929)
- High Voltage Leak Detection*
- Burst Strength (ASTM F2054)
- Bubble Immersion (ASTM F2096, D3078)

* Not listed in ISO 11607 or ASTM
Test Method Cost

- Water Bath – Flexible Barrier Systems
- Moisture/Flavor critical defect size – 15 microns
- Water bath sensitive to 25-50 microns
- Typically test 20 pouches/line/hour
- Current market price of coffee > $2.00/lb

**Green Coffee Wholesale Prices**

![Graph showing green coffee wholesale prices from Jan 09 to Jul 11.

\[
\text{Bags Tested} \times 1 \text{lb Bags} \times \$2/lb \times 24 \times 7 \times 52 \times 0.5 = \$174,720
\]
# Cost of Deploying Destructive Methods

<table>
<thead>
<tr>
<th>Product</th>
<th>Cost of Raw Materials</th>
<th>Quantity Tested</th>
<th>Frequency</th>
<th>Cost/8 Hour Shift</th>
<th>Cost/Year (2 Shifts, 250 Days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dry Fill Soup Mix</td>
<td>$0.23</td>
<td>8</td>
<td>Every 30 min.</td>
<td>$29.44</td>
<td>$14,720</td>
</tr>
<tr>
<td>Effervescent Tablets</td>
<td>$0.04</td>
<td>80</td>
<td>Every 30 min.</td>
<td>$51.20</td>
<td>$25,600</td>
</tr>
<tr>
<td>Coffee Singles Pod</td>
<td>$0.06</td>
<td>200</td>
<td>Every Hour</td>
<td>$96</td>
<td>$48,000</td>
</tr>
<tr>
<td>Luer-Lok Syringe</td>
<td>$0.20</td>
<td>50</td>
<td>Every 30 min.</td>
<td>$160</td>
<td>$80,000</td>
</tr>
<tr>
<td>Pharma Blister Pack</td>
<td>$1.12</td>
<td>10</td>
<td>Every 30 min.</td>
<td>$179.20</td>
<td>$89,600</td>
</tr>
</tbody>
</table>
Test Method Effectivity

➢ Channel leaks down to “75 μm [0.003 in.] with a 60–100 % probability”\(^1\).

Assumptions

1,000 Packs/Day  1% Defect Rate
10 Defects/Day    ~2,500 Defects Per Year
80% POD (Above Average)

100% Inspection = 500 Defects/Year
200% Inspection = 100 Defects/Year

400% Inspection (4 Operators)
4 Undetected Defects/Year
0.16% probability that a defect will go undetected.

\(^1\)http://www.astm.org/Standards/F1886.htm
Cost of Slow Information

- $O_2$ Head Space Analysis.
- 6 day dwell.
- 3% pass/fail limit.
- 50 micron defect 700 gr. dry fill pouch.
- $O_2$ shifted from ~1% to ~2.5%.

\[
\frac{ppm}{60 \times 0.5 \times 60 \times 24 \times 6} = \text{Units} = 259,200
\]

\[
\frac{kg/unit}{259,200 \times 0.7 \times \$4.41} = \$800,150
\]
Consider Alternative Methods

• Non-Destructive vs. Destructive
• Quantitative vs. Attribute
• Non-Subjective vs. Operator Dependent
• Calibration Capability
• Validation Effectiveness
• Simple Methodology (no sample prep)
Direct Measures of Quality
ISO 11607 – Annex B

- Vacuum Decay (ASTM F2338)
- Seal Strength (ASTM F88)
- Airborne Ultrasound Seal Inspection*
- Visual Inspection (ASTM F1886)
- Dye Migration (F1929)
- High Voltage Leak Detection*
- Burst Strength (ASTM F2054)
- Bubble Immersion (ASTM F2096, D3078)

* Not listed in ISO 11607 or ASTM
Non-Subjective, Quantitative

- Vacuum Decay (ASTM F2338)
- Seal Strength (ASTM F88)
- Airborne Ultrasound Seal Inspection

- High Voltage Leak Detection
- Burst Strength (ASTM F2054)
Non-Destructive

• Vacuum Decay (ASTM F2338)

• Airborne Ultrasound Seal Inspection

• High Voltage Leak Detection
Vacuum Decay Leak Testing
Vacuum Decay Test Method

![Graph showing vacuum levels and test cycle progression.](image)
## Vacuum Decay for Flexible Packaging

**TEST PARAMETERS**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TStroke</td>
<td>1.50</td>
</tr>
<tr>
<td>TEqual</td>
<td>20.00</td>
</tr>
<tr>
<td>TTest</td>
<td>5.00</td>
</tr>
<tr>
<td>dP/dt, Pa/s</td>
<td>35.2</td>
</tr>
<tr>
<td>TFill, s</td>
<td>15.00</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Test #</th>
<th>Vacuum, mb</th>
<th>dP/dt, Pa/s</th>
<th>Pass/Fail</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>644.8</td>
<td>27.3</td>
<td>P</td>
<td>Good Product</td>
</tr>
<tr>
<td>2</td>
<td>639.3</td>
<td>27.5</td>
<td>P</td>
<td>Good Product</td>
</tr>
<tr>
<td>3</td>
<td>635.7</td>
<td>26.7</td>
<td>P</td>
<td>Good Product</td>
</tr>
<tr>
<td>4</td>
<td>638.0</td>
<td>25.7</td>
<td>P</td>
<td>Good Product</td>
</tr>
<tr>
<td>5</td>
<td>633.7</td>
<td>26.7</td>
<td>P</td>
<td>Good Product</td>
</tr>
<tr>
<td>6</td>
<td>586.6</td>
<td>95.4</td>
<td>F</td>
<td>25 micron</td>
</tr>
<tr>
<td>7</td>
<td>576.8</td>
<td>90.5</td>
<td>F</td>
<td>25 micron</td>
</tr>
<tr>
<td>8</td>
<td>638.0</td>
<td>56.6</td>
<td>F</td>
<td>15 micron</td>
</tr>
<tr>
<td>9</td>
<td>634.7</td>
<td>52.4</td>
<td>F</td>
<td>15 micron</td>
</tr>
<tr>
<td>10</td>
<td>636.0</td>
<td>40.4</td>
<td>F</td>
<td>10 micron</td>
</tr>
<tr>
<td>11</td>
<td>641.6</td>
<td>39.4</td>
<td>F</td>
<td>10 micron</td>
</tr>
</tbody>
</table>

**Differential Pressure, Pa/sec (Secondary Transducer)**

**Vacuum Level Below Atmospheric Pressure, mb**

**Test Cycle**

- **Test Cycle Pass**
- **dP Pass**
- **dP Fail**

**Comments**

**Ref** 450.2
Micro Leak Detection

![Graph showing leakage rate vs. differential pressure. The graph includes a line for average dp, an upper 99% limit, and a lower 99% limit. The x-axis represents leakage rate in cc/min, and the y-axis represents differential pressure in Pa. Sample points are marked at 0, 0.1, and 0.5 leakage rates, corresponding to 3.4 μm and 7.5 μm respectively.]

- **Avg dp**
- **Upper 99% Limit**
- **Lower 99% Limit**
Vacuum Decay Application

- Flexible/Rigid Barrier
- Air/Liquid Contents
- No Sample Preparation
- Quantitative and Repeatable Test Data
- Non-Subjective
- Zero Waste
Airborne Ultrasound Through Transmission
Ultrasonic Signal

Propagate through single or multiple layers of well bonded materials.

Reflection/absorption of sound waves by multiple layers.
## Analysis of Ultrasonic Sealing

<table>
<thead>
<tr>
<th>Power Setting (Joules)</th>
<th>C-scan Image</th>
<th>Average Signal</th>
</tr>
</thead>
<tbody>
<tr>
<td>105</td>
<td>105</td>
<td>-0.7</td>
</tr>
<tr>
<td>90</td>
<td>90</td>
<td>-2.2</td>
</tr>
<tr>
<td>75</td>
<td>75</td>
<td>-5.6</td>
</tr>
<tr>
<td>60</td>
<td>60</td>
<td>-10.1</td>
</tr>
<tr>
<td>45</td>
<td>45</td>
<td>-20.6</td>
</tr>
<tr>
<td>Side Seal (Heat Seal)</td>
<td>105</td>
<td>-17.6</td>
</tr>
<tr>
<td>Side Seal (Heat Seal)</td>
<td>90</td>
<td>-16.9</td>
</tr>
</tbody>
</table>
Seal-Scan® Online Pouch Seal Inspection
Integrated Solution
Airborne Ultrasound Application

- Non-Destructive Seal Inspection
- Quantitative Materials Analysis
- Flexible and Semi-Rigid Packaging
- Seal Process Optimization
- On-line Defect Detection
High Voltage Leak Detection (HVLD)
HVLD Defect Detection for Pouches

- Micro leaks down to 5 microns
- Pinholes
- Cracks
- Crystallized leaks
- Channel defects
HVLD Technology

- High voltage applied to container
- Ideally non-conductive materials
- Liquid triggers conductivity spike
HVLD Detection
HVLD Application

• Quantitative High Speed Inspection
• Non-porous, Non-conductive Materials
• Package Contents:
  - liquid products
  - protein based liquids
  - suspensions or emulsions
• Flexible or Rigid Barrier
When to Develop Methodology

• Should begin at the point of package development.
• Phase III Pharma Development.
• New production line engineering.
• When the method in place has failed.
• Packaging that is immune to test methodology plagues the industry.
Pitfalls

• Mixing methods and test requirements.
• Taking test method standards as law and not guidance.
• Taking white papers as applied fact to specific applications.
• Process improvements are vulnerable to validation hurdles.
• Patching the problem, not developing a solution.
What’s ahead?

• PDA’s TR27 – Moving to quantitative test methodology.
• Track & Trace – Connecting non-destructive test results with specific units.
• Green Initiatives – Eliminating line waste with non-destructive methods.
• CTQ defect stability package validation.
• Automated SPC testing.
Package Integrity

- Package Integrity – maintaining a sterile barrier.
- Package integrity is a sub-category of quality and is exclusive of:
  - Peel Strength
  - Burst Testing
  - Visual Inspection
Foundation of Quality Control

Define

Quality cannot be controlled without discrete and measurable characterizations of quality.

Measure

Quality cannot be controlled without accurate and definitive measures of quality.
Thank You!

Oliver Stauffer
o.stauffer@ptiusa.com
914.337.2005
www.ptiusa.com
Simple Cases in Testing

• Some products are moisture sensitive, but contents are marginally affected by leaks. Detection to the moisture level may be over kill.

• Some product have desiccants to keep them dry, but real concern may be mold or bacteria. Common methods may not cut it.

• Some production processes have high incidence of random catastrophic defects. Statistical Process Control (SPC) will not meet quality needs.
Quantitative Measures Provide Greater Access to Statistical Tools

- Ultrasonic Attenuation
- Thickness
- Peel Strength
- Permeation
- Leak Rate

Attribute data fails to produce predictive measures of quality.