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PROTECTIVE BLISTER PACKAGING MATERIALS: ACLAR®

THOMAS DRIES

Amsterdam October 15, 2019
ROADMAP

What is Aclar?
Honeywell
How & where it is made
Key features

Moisture Barrier Concept
Aclar film range
Flat-film MVTR & barrier

Impact of Forming
Weight gain testing of blisters
Estimating formed cavity MVTR

Benefits & Value Prop.
Aluminum / Aluminum
High Barrier PVdC

Measurements vs MVTR Estimates
Weight gain testing results versus per cavity MVTR estimates

Q&A

## HONEYWELL | GREAT BUSINESSES IN GROWING INDUSTRIES

<table>
<thead>
<tr>
<th>Segment</th>
<th>Sales</th>
<th>Our Business</th>
<th>Why We Win</th>
</tr>
</thead>
</table>
| Aerospace                    | ~$15.5B | Our products are used on virtually every commercial and defense aircraft platform and in 100M+ vehicles worldwide and include aircraft propulsion, cockpit systems, satellite communications, and vehicle turbochargers. | • Big wins on the right aircraft  
• Largest installed base in the industry…and growing |
| Home and Building Technologies | ~$9.3B | Our products, software and technologies are in more than 150 million homes and 10 million buildings worldwide, helping customers control their comfort, security, and energy use. | • Comprehensive Connected Building offering improving performance and efficiency  
• Broadening software and services opportunities |
| Performance Materials and Technologies | ~$10.7B | We develop advanced materials, process technologies, automation solutions, and industrial software that are revolutionizing industries around the world. | • Connected Plant enhancing customer operations  
• Solstice® low-global-warming products reduce carbon emissions across many industries  
• Aclar® moisture barrier films |
| Safety and Productivity Solutions | ~$6.3B | We improve enterprise performance and worker productivity and safety with our scanning and mobile computers, software, warehouse automation solutions, and personal protective equipment. | • New, innovative product launches in Productivity business  
• Piloting Connected Worker with numerous customers |

Positive Macro Trends Underpin Our Businesses
Aclar® Film

**Aclar** (PCTFE) is a crystal clear, bio-chemically inert, chemical resistant, plasticizer and stabilizer free film. It provides the highest moisture barrier per thickness of any thermoformable films.

**Poly-Chloro-Tri-Fluoro-Ethylene**
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ACLAR® RANGE OF FILMS

• For moisture-sensitive drug products in all climatic zones
ACLAR® RANGE OF FILMS

- **Rx160 / .60 mil / 15 µ**
- **Rx 20e / .80 mil / 20 µ**
- **SupRx 900 / .90 mil / 23 µ**
- **Accel 1700 / 1.7 mil / 43 µ**
- **UltRx 2000 / 2 mil / 51 µ**
- **UltRx 3000 / 3 mil / 76 µ**
- **UltRx 4000 / 4 mil / 102 µ**
- **UltRx 6000 / 6 mil / 152 µ**

- **NEW!**

Portfolio designed to meeting wide range of moisture-barrier needs
MVTR (FLAT-FILM) @ ICH TESTING CONDITIONS

Source: Honeywell Aclar Datasheets

MVTR pattern at different ICH testing conditions

Source: Honeywell Aclar Datasheets
MOISTURE VAPOR TRANSMISSION RATE

Get started with flat Aclar film MVTR

Moisture Vapor Transmission Rate \(=\) \(\frac{\text{Permeability}}{\text{Gauge}}\)

Increasing gauge (barrier) by a factor of \(N\) reduces MVTR by a factor of \(\frac{1}{N}\)

At constant T & RH “Moisture Barrier” should be proportional to film gauge.
Flat-Film Moisture Vapor Barrier is predictable & proportional to film gauge
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COMMON ACLAR®- LAMINATES

Duplex
• Asymmetrical structure
  – Aclar moisture barrier
  – Web carrier such PVC, PP, PETG

Triplex (and Quadruplex)
• Symmetrical structure
  – Aclar moisture barrier
  – Two outer layers such PVC, PP, COC, PETG

• Asymmetrical structure
  – Aclar moisture barrier
  – Web carrier such PVC, PP, COC, PETG
  – Oxygen barrier layer such EVOH
  – Other functional layers such as PE
IMPACT OF FORMING

- Creation of greater surface \( S(\text{cavity}) \)
- Reduction of film thickness \( d(\text{cavity}) \)
- Reduction in barrier
- Thickness distribution of the barrier layer over entire surface area*

Options to assess MVTR (cavity)
1. Measurements (i.e. weight-gain)
2. Estimates via “Barrier Calculator”
3. (Finite-Element-Analysis FEA)*

* Refer presentation Daniel Stagnaro KP

Blister produced with Klöckner Pentaplast’s Pentapharm® Aclar PA200 /02 laminate

Formed cavity MVTR critical for drug product stability
WEIGHT-GAIN TESTING – SIZE #1 CAPSULE

Example of weight gain testing according to USP 671

40°C / 75%RH

Draw Ratio = 2.344
S(base) = 193.2 mm²
S (cavity) = 452.8 mm²
## TYPICAL WEIGHT-GAIN TESTING PROTOCOL*

Size#1 capsule packed in Pentapharm® Aclar PA200 run with plug-assist

<table>
<thead>
<tr>
<th>Pack#</th>
<th>Weight Gain (g/package)</th>
<th>Day 6</th>
<th>Day 7</th>
<th>Day 13</th>
<th>Day 20</th>
<th>Day 27</th>
<th>Day 34</th>
<th>Day 37</th>
<th>Day 58</th>
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<tbody>
<tr>
<td>1</td>
<td>0.00580</td>
<td>0.00650</td>
<td>0.01092</td>
<td>0.01574</td>
<td>0.02028</td>
<td>0.02518</td>
<td>0.02726</td>
<td>0.04195</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>0.00576</td>
<td>0.00643</td>
<td>0.01088</td>
<td>0.01564</td>
<td>0.02028</td>
<td>0.02507</td>
<td>0.02702</td>
<td>0.04169</td>
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</tr>
<tr>
<td>3</td>
<td>0.00595</td>
<td>0.00674</td>
<td>0.01141</td>
<td>0.01645</td>
<td>0.02134</td>
<td>0.02640</td>
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<tr>
<td>4</td>
<td>0.00574</td>
<td>0.00656</td>
<td>0.01095</td>
<td>0.01603</td>
<td>0.02113</td>
<td>0.02605</td>
<td>0.02803</td>
<td>0.04317</td>
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<tr>
<td>5</td>
<td>0.00570</td>
<td>0.00631</td>
<td>0.01073</td>
<td>0.01568</td>
<td>0.02039</td>
<td>0.02522</td>
<td>0.02720</td>
<td>0.04196</td>
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</tr>
<tr>
<td>6</td>
<td>0.00559</td>
<td>0.00638</td>
<td>0.01085</td>
<td>0.01567</td>
<td>0.02052</td>
<td>0.02548</td>
<td>0.02746</td>
<td>0.04231</td>
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<tr>
<td></td>
<td>Average</td>
<td>0.00576</td>
<td>0.00649</td>
<td>0.01096</td>
<td>0.01587</td>
<td>0.02066</td>
<td>0.02557</td>
<td>0.02759</td>
<td>0.04251</td>
</tr>
<tr>
<td></td>
<td>Std. Dev.</td>
<td>0.00012</td>
<td>0.00015</td>
<td>0.00023</td>
<td>0.00032</td>
<td>0.00046</td>
<td>0.00054</td>
<td>0.00058</td>
<td>0.00089</td>
</tr>
<tr>
<td></td>
<td>Variation</td>
<td>2.1%</td>
<td>2.3%</td>
<td>2.1%</td>
<td>2.0%</td>
<td>2.2%</td>
<td>2.1%</td>
<td>2.1%</td>
<td>2.1%</td>
</tr>
</tbody>
</table>

Need to pay attention to:
- Variation between samples
- Aberrant data points
  - Saturated desiccant
  - Faulty samples

* In accordance with USP 671

A minimum of 6 blister cards recommended for weight-gain testing.
BARRIER CALCULATOR - EXAMPLE

Assumption: Aclar-thickness in cavity is constant and scales with draw ratio

\[
d(cavity) = \frac{S(base)}{S(cavity)} \times d(flatfilm)
\]

\[
MVTR(cavity) = S(base) \times MVTR(flatfilm) \times \text{Draw Ratio}^2
\]

- **Draw Ratio** = 2.344
- **S(base)** = 193.2 mm²
- **S (cavity)** = 452.8 mm²
- UltRx4000

**MVTR of formed blister increases quadratically with surface area formed**

**Graph:**
- **MVTR (cavity) @ 40°C / 75% RH**
- **Ultx4000 / PVC**
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Good correlation of weight gain testing results with estimates.

**PER CAVITY MVTR - MEASURED VS CALCULATED**

Size#1 capsule run with plug-assist and weight-gain-tested by Honeywell @ 40°C/75%RH

- **MVTR (mg/cavity*day) @ 40°C/75% RH**

<table>
<thead>
<tr>
<th></th>
<th>UltRx2000</th>
<th>UltRx4000</th>
<th>Accel5400</th>
<th>UltRx6000</th>
</tr>
</thead>
<tbody>
<tr>
<td>wt.-gain Calc.</td>
<td>0.103</td>
<td>0.108</td>
<td>0.058</td>
<td>0.051</td>
</tr>
<tr>
<td>wt.-gain Calc.</td>
<td>0.108</td>
<td>0.108</td>
<td>0.051</td>
<td>0.051</td>
</tr>
<tr>
<td>wt.-gain Calc.</td>
<td>0.04</td>
<td>0.04</td>
<td>0.036</td>
<td>0.037</td>
</tr>
<tr>
<td>wt.-gain Calc.</td>
<td>0.032</td>
<td>0.032</td>
<td>0.032</td>
<td>0.032</td>
</tr>
</tbody>
</table>

Deviations measured vs estimated are in the range of -5% - +13.5%
Decent correlation of weight gain testing results with estimates
MOISTURE BARRIER OPTIMIZATION CASE-STUDY

Optimized Design

LOWER RISK for STABILITY-FAILURE

S (base) = 304.0 mm²
S (cavity) = 643.7 mm²
Draw ratio: 2.117

Customer standard tool

HIGH RISK for STABILITY-FAILURE

S (base) = 304.0 mm²
S (cavity) = 746.7 mm²
Draw ratio: 2.457

Optimized tool design resulted in 34.6% higher barrier (25.7% lower MVTR)

Need to be very mindful about cavity design - in particular for low dosage strengths & small tablet sizes which tend to be more vulnerable against moisture ingress
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Example: Size 0 capsule

PACK-SIZE COMPARISON ACLAR/PVC VS ALU-ALU

Blister Footprint: 55% less

Cavity Surface Area: 62% less

Up to 55% reduction in area & 62% in volume, respectively
BENEFITS THERMOFORMING VS ALU-ALU

- Patient discretion
- Ease of extraction
- Portability
- Longevity (Robustness)
- Less Medication Errors

➤ Higher Patient Adherence

Reduction of
- Pack Weight
- Pack Volume
- Shipping cost

Gains in
- Productivity
- Capacity
- Space

Reductions of
- Total Cost

ASAP-study to compare shelf-life Aclar/PVC vs Alu/Alu advised
PENTAPHARM ACLAR/PVC VS HB PVDC

HB PVdC Range *

351 µm
+13.6%

358 µm
+6.6%

394 µm
+7.9%

Pentapharm®/Aclar®**

Aclar UltRx4000

PA300 SO3

PA400 SO3

PA200 /02

Aclar UltR2000

PENTAPHARM ACLAR/PVC VS HB PVDC

HB PVdC up to 13.6% thicker than Pentapharm Aclar at comparable flat-film MVTR

** Pentapharm® is a registered trademark of Klöckner Pentaplast

* Marketed HB PVdC-Films
Significantly lower haze & no yellowing HB Aclar/PVC vs HB PVdC
BENEFITS ACLAR VS HB PVDC

Reduction
- Line stoppages
- Change-overs time
- Corrosion of parts

Gains
- User experience
- User confidence
- Marketability
- Packaging yield
- Process reliability
- Productivity (OEE)

Demonstrable and significant benefits Aclar vs HB PVdC
Physically stable and biochemically inert, non-ageing, non-yellowing

Fully backward integrated supply chain

Highest moisture barrier per unit thickness

Predictible barrier performance

Enabler for improved user experience

Aclar – a most-trusted brand
ACKNOWLEDGEMENTS

RON SEIBERT
WALTER GRUPP
GARY SKWAREK

Feel free to contact me using my e-mail: thomas.dries@honeywell.com
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