Avanços e inovação em aplicações Single Use

Pablo Fernandez
Field Applications Specialist
BioProduction
What’s new?

- Quick review
- In the last 6 months…
  - 5:1 SUB
  - DHX
  - SUF
  - Micro-carrier separation
  - Freezing
  - Perfusion

- Questions
11 Years ago we launched the SUB...
Quick Review

We have launched a SU Heat Exchanger
What’s new?

Keep pushing boundaries

- Find new opportunities
- Listen to the customers
- Customize
- Open architecture
What’s new?

Microcarrier Separation
Single-Use Bioprocess containers allow for quick customization

A bag within a bag
What’s new

Single-Use Fermentor

- Exhaust port
- Filter cartridge
- Film chamber
- BPC or condenser chamber
S.U.F. drilled Hole Sparge designed for high \( \text{O}_2 \) transfer with strong mixing

- 30L 1xDHS 25 holes at 0.062” dia (1.58mm)
- 300L 2xDHS 25 holes at 0.062” dia (1.58mm)
What’s new

5:1 SUB

best performance, reliable scale-up

consistent O2 transfer & CO2 removal
What’s new

250 L 5:1, CO₂ stripping, 40 W/m³

Large increase in CO₂ stripping utilizing Cross-Flow Sparger, Overlay/CFS = 14 L/min air

- 250 L, CFS
- 250 L, Standard Overlay
- 250 L, No Overlay
Freezing Applications: Current Situation

• **Situation**
  - Many BioProduction processes require freezing for stability in the manufacturing process.
  - Industry reports indicate as high as 50% of biologics are frozen in some step within the manufacturing process.

• **Problem**
  - Single-use systems currently available in the market are not reliable and have high failure rates.
  - Feedback from the market is a failure rate is as high as 20%.

• **Implications**
  - Customers are limiting their use of SUT in freezing application.
  - High cost and value product is being destroyed.

• **Payoff**
  - Provided a integrated cost competitive solution that can provide higher reliability with validated shipping and handling solutions will address many of the unmet needs of the freezing market today.
Acclimate: Frozen Handling System

Active Ingredients

• Highly valuable
• Frozen
• Reduce degradation
• Transportation
  • Kept frozen
  • Kept safe
• Time to Freeze
• Time to Thaw
The glass transition temperature ($T_g$) is the temperature at which a polymeric material changes from a viscous or rubbery state to a brittle or glassy state.
Bag inside a hard protective shell
Acclimate features

• Hard shell
• Grooves
  – to lock in place
  – to promote heath transfer
• Stackable
Knuckle design

Access window

Separator enclosed protective compartments

Dimpled shell

Knuckle shell design
Does it Freeze/Thaw quickly?

- Freeze and thaw test was performed on 5 of the single trays from each size and film type. No damage was observed on any of the bags due to Freeze and thaw test.
Freeze/Thaw

16-0119 THERMOFISHER SCIENTIFIC
FREEZE AND THAW TEST
2L CX5-14 TRAYS
RUN # 161207102

REVIEWED BY: AP 19 DEC 2016
Frozen Shipping

Qualify a Shipper

- CX5-14 or Aegis5-14 films in Acclimate Systems (2, 6, 12, and 16 L sizes) by:

<table>
<thead>
<tr>
<th>Specimen Number(s)</th>
<th>Test Specs</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 Trays (all sizes)</td>
<td>Freeze and Thaw Test (-70°C to Room Temp)</td>
</tr>
<tr>
<td>3 Pallets (2X4, 2X3 &amp; 1X1 Configurations)</td>
<td>ISTA 3B</td>
</tr>
<tr>
<td>3 Pallets (2X4, 2X3 &amp; 1X1 Configurations)</td>
<td>Modified ISTA 7D – 120 Hours</td>
</tr>
</tbody>
</table>

- ISTA International Safe Transit Association
The Acclimate shipping container is an optional solution for users who need to safely transport the frozen applications between separate locations.

The Acclimate shipping container has been tested by a third party test house to:

- ISTA 3B
- ISTA 7D

<table>
<thead>
<tr>
<th>Tray size</th>
<th>Units per SKU</th>
<th>Cat. No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 L</td>
<td>1</td>
<td>B113154-N</td>
</tr>
<tr>
<td>6 L</td>
<td>1</td>
<td>B113155-N</td>
</tr>
<tr>
<td>12 L</td>
<td>1</td>
<td>B113156-N</td>
</tr>
<tr>
<td>16 L</td>
<td>1</td>
<td>B113157-N</td>
</tr>
</tbody>
</table>
Does it stay Frozen?

96 hour test

- Maintains below -70°C ± 10°C for 96+ hours.
- 30 of each size per frozen shipper system at 100% fill (10 Aegis, 10 CX5-14, 10 EVA 1028).
Does it stay Frozen?

120 hour test

- Maintains below -40°C ± 5°C for 120+ hours.
- 30 of each size per frozen shipper system at 100% fill (10 Aegis, 10 CX5-14, 10 EVA 1028).
**Impact Testing-ISTA 3B**

**Tip/tip over test:**

<table>
<thead>
<tr>
<th>Orientation</th>
<th>Pass / Fail</th>
</tr>
</thead>
<tbody>
<tr>
<td>22° on Edge 3 - 5</td>
<td>Pass</td>
</tr>
<tr>
<td>22° on Edge 3 - 5</td>
<td>Pass</td>
</tr>
</tbody>
</table>

**Rotational edge and corner drop:**

<table>
<thead>
<tr>
<th>Drop Height</th>
<th>Impact Orientation</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 or 9 Inches with the opposite end supported by 3.5”</td>
<td>Edge (3 – 6)</td>
</tr>
<tr>
<td></td>
<td>Opposite Corner (3 – 4 – 5)</td>
</tr>
</tbody>
</table>

**Vehicle vibration:**

<table>
<thead>
<tr>
<th>Frequency (Hz)</th>
<th>PSD (g²/Hz)</th>
<th>Frequency (Hz)</th>
<th>PSD (g²/Hz)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.0</td>
<td>0.00072</td>
<td>25.0</td>
<td>0.0036</td>
</tr>
<tr>
<td>3.0</td>
<td>0.018</td>
<td>30.0</td>
<td>0.00072</td>
</tr>
<tr>
<td>4.0</td>
<td>0.018</td>
<td>40.0</td>
<td>0.0036</td>
</tr>
<tr>
<td>6.0</td>
<td>0.00072</td>
<td>80.0</td>
<td>0.0036</td>
</tr>
<tr>
<td>12.0</td>
<td>0.00072</td>
<td>100.0</td>
<td>0.00036</td>
</tr>
<tr>
<td>16.0</td>
<td>0.0036</td>
<td>200.0</td>
<td>0.000018</td>
</tr>
</tbody>
</table>

Over-all gms: 0.54  
Duration: 120 Minutes

- Shock – rotational edge and corner drop.
- Shock – concentrated impact.
- Shock – forklift truck handling.
- Shock – mechanical handling.
- Shock – impact test.
Qualified through extensive testing.

Acclimate: Frozen Handling System
Questions?

- Thank you!
## Acclimate specifications

<table>
<thead>
<tr>
<th></th>
<th>2 L</th>
<th>6 L</th>
<th>12 L</th>
<th>16 L</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nominal volume</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shell dimensions (L x W x D)</td>
<td>58.4 x 38.1 x 10.9 cm</td>
<td>78.7 x 43.2 x 10.7 cm</td>
<td>74.9 x 52.3 x 10.9 cm</td>
<td>78.7 x 58.4 x 10.7 cm</td>
</tr>
<tr>
<td>BPC dimensions (L x W)</td>
<td>32 x 32 cm</td>
<td>57.2 x 38.1 cm</td>
<td>54.6 x 50.8 cm</td>
<td>62.9 x 55.9 cm</td>
</tr>
<tr>
<td>Shell and BPC weight (empty BPC)</td>
<td>2.9 kg</td>
<td>4.1 kg</td>
<td>5.32 kg</td>
<td>5.6 kg</td>
</tr>
<tr>
<td>Knuckle design quantity</td>
<td>2 (one on each shell)</td>
<td>4 (two on each shell)</td>
<td>2 (one on each shell)</td>
<td>2 (one on each shell)</td>
</tr>
<tr>
<td>Shell and clip material</td>
<td>High density polyethylene (HDPE)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BPC material</td>
<td>Aegis™5-14 film: five-layer, 14 mil cast film produced in a cGMP facility. The outer layer is a polyester elastomer coextruded with an ethyl vinyl alcohol (EVOH) barrier layer and an ultra-low density polyethylene product contact layer.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Port specifications</td>
<td>MPC quick-coupling (polycarbonate with silicone o-ring) inlet and outlet ports, C-Flex™ 374 tubing</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cleaning agent compatibility</td>
<td>The container and side clip material of construction are compatible with clean room–grade cleaners including: isopropyl alcohol and Spor-Klenz sterilant (acetic acid and hydrogen peroxide)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
The Acclimate shipping container has been designed with durability and environmental control in mind. The Acclimate shipping container is made of mostly recyclable materials. It is constructed with a heavy duty double-walled outer packaging box to provide strength for stacking and built to withstand shipping conditions.

**Specifications**

<table>
<thead>
<tr>
<th>Nominal volume</th>
<th>2 L</th>
<th>6 L</th>
<th>12 L</th>
<th>16 L</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dimensions</td>
<td>76.84 x 56.52 x 39.94 cm</td>
<td>97.16 x 61.59 x 39.94 cm</td>
<td>89.54 x 70.74 x 39.94 cm</td>
<td>97.16 x 76.52 x 39.94 cm</td>
</tr>
<tr>
<td>Dry ice requirement</td>
<td>27—29 kg</td>
<td>32—34 kg</td>
<td>39—41 kg</td>
<td>43—45 kg</td>
</tr>
<tr>
<td>Insulation materials</td>
<td>• Double-walled cardboard box</td>
<td>• EPS panels: Thickness: 8.89 cm (3.5 in.)</td>
<td>• Foil liner</td>
<td>• Cardboard box divider</td>
</tr>
</tbody>
</table>