Establishing Single-Use Systems as Robust Technology Platforms in Biopharmaceutical Manufacturing

ISPE DACH and France Affiliate Joint Workshop
Scott Probst
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Chromatography Skid Design Cycle

- User Requirements
- PFD
- Process Description
- Risk Assessment
- Functional Spec.
- Component Specs
- P&ID
- 3D Model Review
- Weekly Telcos
- Mid-point Inspection
- Software Reviews
- Software Testing
- FAT
- Commissioning Tests
- IQ, OQ, PQ
- As-Built Docs
A total of 10 assemblies or items are needed
Design Cycle for Single-Use Elements

“I need a 200-L bag with weldable tubing and some sample bags.”

“Owner’s Engineering”

- User Requirements
- Sketch
- Calculations
- Specifications
- Design review
- Competitive bidding
- Prototype testing
Conceptual Design Considerations

- Who develops the concept for how single-use systems will be used?
- Are costs, trade-offs, and risks well known before committing to a design concept?
- Does each single-use element have a business case? How is convenience and ergonomics balanced by cost?
- Are logistics and sustainability included in the concept (e.g. waste disposal and carbon footprint)?
Project Planning Considerations

- Who is responsible for designing the single use systems? What tasks are performed by “owner’s engineering” and what tasks are performed by the vendor?
- Who establishes new raw materials and manages change control?
- How does a capital project pay for this design work?
- Has time and money been allocated for prototype testing?
The Case for Design, Part 1: Flow and Pressure Drop

All single-use hoses require cleaning.

Solution by Gravity

15 psig

Average Flow Rate = 21 LPM

1/2" ID Tubing

Filtration Time = 71 minutes

1500-L

Solution by Gravity

15 psig

Average Flow Rate = 37.5 LPM

1" ID Reusable Hose

Filtration Time = 40 minutes

1500-L

Hoses require cleaning

All single-use
Is the tubing rated for the pressure?

Will the pinch valve still close?

Are the fittings / engagements rated for the pressure?
How can you be sure the right bag is connected to the right port?

Both pinch valves must be open to permit flow.
The Case for Design, Part 4: Bagging Manifold

- Is the tubing appropriate for pumping?
- Does the tubing size support desired fill rate?
- Are the size and number of sample bags appropriate?
# Robustness Issues for Single-Use Platforms

<table>
<thead>
<tr>
<th>Category</th>
<th>Issue</th>
<th>Solution or Mitigation</th>
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</thead>
</table>
| High Pressure / High Flow | • What is the MAWP?  
  • What is the burst pressure?  
  • Will my engagement hold? | • More transparency into vendor testing and data  
  • Standardized protocols for common parameters  
  • Access to engagement libraries |
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<thead>
<tr>
<th>Category</th>
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<tbody>
<tr>
<td>Leaks</td>
<td>• Damaged bag</td>
<td>• Hoists for better deployment</td>
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<tr>
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<td>• Damaged tubing</td>
<td>• Smooth interior surfaces for bins</td>
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<td></td>
<td>• Leak at engagement</td>
<td>• Tough and flexible films</td>
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<td>• Bag drop testing</td>
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<td>• Organized routes for tubing</td>
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<td>• In-line pressure measurement</td>
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<td>• Fastening procedures</td>
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<td>• Molding tolerances</td>
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<td>• Operator training and awareness</td>
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## Robustness Issues for Single-Use Platforms (Page 3 of 3)

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<td>Quality Assurance</td>
<td>• Presence of endotoxins</td>
<td>• Endotoxin testing</td>
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<td>• My “vessels” and “piping” are outsourced</td>
<td>• When are components rinsed in the vendor’s process?</td>
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<td>• Rigorous vendor auditing program</td>
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Single-Use Design in the Project Lifecycle

- Concept Review
  - Single-Use Concept
  - Planning Sheet
  - Business Cases
  - Logistics & Sustainability

- Detailed Design
  - User Requirements
  - Sketches & Calcs
  - Data Sheets & Specs
  - Design Review

- Procurement
  - Vendor Audits
  - Competitive Bidding
  - Establish New Materials

- Commissioning & Qualification
  - Testing and Modification

- Manufacturing
  - Change Control
  - Regular Audits
Conclusions

Design processes evolved for stainless steel technology platforms

Design processes for single-use systems are still evolving

Owner's engineering is needed to support design activities

Resources allocated for design and testing of single-use systems should be commensurate with …

- The degree to which they are used in the process
- Their contribution to costs of goods
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