Advances in single-use manufacturing that enable more cost effective, environmentally friendly processing of biopharmaceuticals

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Abstract

• The uptake of single-use technologies within the biopharmaceutical industry is continuing to grow at over 20% a year. There are a number of process steps, such as cell culture and normal flow filtration, where this technology is well established.

• This poster focuses on recent developments around other upstream and downstream process steps where single-use/disposable technologies can be a cost effective alternative to the more traditional stainless steel equipment that is currently in use.

• A case study will be presented which focuses on facility design and resource optimization for multi-product vaccine manufacturing and also addresses the concern of implementing single-use technologies from an environmental perspective.
Introduction

The single-use market is growing rapidly at over 20% a year for many reasons, including:

- Growing biopharmaceutical markets with a demand of higher capacity bandwidth.

- New technologies (higher yields, drug delivery) and smaller markets (personalized medicine) allow smaller batch sizes.

- Cost pressure by healthcare reform and biosimilars.

When users are asked, the most important advantages of single-use technologies are related to process intensification (Figure 1).

Figure 1. Results of a survey: Relative importance of benefits of single-use technologies [1].
Environmental Impact

- In collaboration with Biopharm Services and GE Research Center a peer-reviewed cradle-to-grave Life Cycle Assessment study comparing single-use and traditional technology was performed.

- The third party critical review panel consisted of experts from CIRAIG, Merck Serono and Genentech.

- The results show that the main energy demand and carbon dioxide emission is related to the use phase caused by WFI, process water and steam supply (Figure 2).
Remarkably, single-use technology exhibits lower environmental impact in all 18 categories studied in the environmental impact assessment (Figure 3).

Figure 3. Environmental impact of single-use and traditional systems in 18 different categories. Impact of traditional systems was normalized to 100% [2].
Single use technology applications

An entire monoclonal antibody process from vial thaw to final formulation using single-use ReadyToProcess™ and traditional systems was performed.

Table 1. Process yield and quality with ReadyToProcess

<table>
<thead>
<tr>
<th>Quality measurement</th>
<th>Traditional process</th>
<th>ReadyToProcess platform</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bioreactor titer</td>
<td>1.06 g/L</td>
<td>0.91 g/L</td>
</tr>
<tr>
<td>Overall yield</td>
<td>81%</td>
<td>81%</td>
</tr>
<tr>
<td>Aggregate level</td>
<td>0.6%</td>
<td>0.6%</td>
</tr>
<tr>
<td>Host cell protein</td>
<td>1.0 ppm</td>
<td>1.0 ppm</td>
</tr>
<tr>
<td>Leached protein A</td>
<td>&lt; LOQ</td>
<td>0.1 ppm</td>
</tr>
</tbody>
</table>
Single use technology applications

- The results have shown that product yield and quality were comparable (Figure 4).
- Process time could be reduced by 50% when using single use systems.

**Figure 4.** Comparable up-and down stream results. 50% time savings. (Note: cell culture includes set up time only)
Single use technology applications

Example applications

Internal perfusion with a WAVE Bioreactor™ to produce a HA mAB with S2 cells (Figure 5) showed 20x higher productivity and 85% reduced upstream consumable costs compared to batch process [3].

Figure 5. Viablity (square) and cell conc. (circles) in a S2 batch (red) and perfusion process (blue) [3].
Single use technology applications

• External perfusion with a WAVE Bioreactor™ (25 L working volume) and hollow fiber cartridges to produce a IgG allows process times of more than 6 weeks [4].

• Single-use assemblies (Figure 6) preserved cell density and viability during media exchange and increased yield in a 2-phase fed batch CHO culture [5].

Figure 6. Single-use assembly for media exchange and product separation in 2-phase fed batch CHO culture [5].
Conclusions

• Single-use has perhaps been the most important development for biomanufacturing in the past decade.

• Adoption of single-use technology has been proven to deliver measurable time savings, environmental benefits and improved facility flexibility and throughput.
References

1. 8th Annual Report and Survey of Biopharmaceutical Manufacturing Capacity and Production. (*BioPlan, 2011*)


4. Using Pre-Sterilized External Filters in Long-Term Perfusion Cell Culture Applications. (*Bioprocess J. 10(2), 2011*)

Acknowledgments

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