**Single-use solutions for cell culture scale-up and technology transfer**

A question and answer session with Barbara Paldus, Ph.D.
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What types of single-use equipment are most accepted by industry and what is still lacking in these technologies?

Single-use media and storage bags are the most routinely used in bioprocessing. Single-use bioreactors up to 1,000L volumes have also gained significant ground. However, robust single-use sensors are now available but not integrated into these bioreactor platforms; the mainstream adoption of pH and dissolved oxygen optical sensors is hopefully imminent.

What trends do you see in single-use technologies?

We see the increasing adoption of single-use sensors for upstream bioprocessing for pH, dissolved oxygen, and pressure. We see increasing interest in 2,000L bioreactors for large-scale production. Finally, we see increasing efforts being placed in developing small-scale single-use bioreactors with integrated optical sensors for research and process development.

What are the main requests by single-use technology end-users?

On the upstream side of single-use, integrated single-use sensors and intelligent automation are the two most significant requests. Price has also become a touch point with customers. On the downstream side, there is increasing demand for single-use solutions and sensors as well.

What processes are easiest to transition to disposable technologies and why?

Media mixing and buffer preparation unit operations are the easiest to transition to disposable technologies because the processes are very robust and do not involve significant real-time measurement or control. The single-use vessels employed most mimic their stainless steel counterparts in geometry and functionality so that process transfer to single-use can occur rapidly. Because change-over of the solution composition is frequent in mixing applications, the single-use liners and bags present an immediate advantage as they are sterile and prevent any form of cross-contamination from batch to batch.

The next easiest process to transition is cell culture as again the bioreactor vessels and sensors have been modeled on their stainless steel predecessors. While process automation is more complex in cell growth than in mixing applications, control solutions exist today that put single-use skids on equal footing with their sterilizable counterparts. In fact, overall titers in single-use bioreactors are increasing to levels that allow for higher yields in smaller vessel volumes today. Moreover, the flexible configuration of single-use bioreactor bags provides an advantage in the development of continuous processes in single-use over stainless steel.

Do you see the future for disposable technologies as quite bright. The shorter lead times, easier operation, and consistent yields that result from a transition to single-use will continue to drive the conversion to disposable technologies.

What do you see as the future for disposable technologies specifically regarding their adoption, materials of construction, and processing capabilities?

At Finesse, we see the future for disposable technologies as quite bright. The shorter lead times, easier operation, and consistent yields that result from a transition to single-use will continue to drive the conversion to disposable technologies. Having witnessed the early adoption cycle (2006 to 2011), we believe that single-use applications in mixing and cell culture are now firmly entrenched, and will continue to expand for orphan drugs to biosimilars. As downstream technologies evolve, filtration and chromatography steps will follow in adopting of single-use platforms.

In the last three years, most of the large consumable vendors have updated their films to minimize not only leachables and extractables profiles, but also by-products from the multi-layer film tie layers. Many suppliers have introduced at least one new film indicating progress in producing higher purity materials for both bags and tubing sets. We see ongoing development and evolution of these materials as the community understands the requirements on these plastics better and optimizes them for bioprocessing.

Do you see any existing or emerging companies currently gaining competitive advantages through single-use processes?

Emerging and existing CMOs are focusing on single-use technologies. In most cases, single-use enables emerging companies to create capabilities at greatly reduced capital expenditures and gain a foothold in the market. For established companies, single-use allows them to increase capacity quickly, diversify their offering and more fully utilize their capacity.

How accepted are single-use processes with regulators?

Single-use technologies appear to be gaining not only widespread acceptance but support with regulators. While existing cGMP processes are likely to continue using stainless steel infrastructure, many new products are going directly into single-use production equipment.

If a pharma company were looking to adopt single-use technologies for the first time, what advice would you give them?

There are three key considerations:

1. **Costs**: Single-use operating costs will far exceed the initial capital investment, so do not lock yourself into a single-source situation, especially on the bag films and tubing sets. Quality at least two vendors for each unit operation of your processes to ensure security of supply chain and price. Consider using universal controllers for each unit operation to facilitate the interchange of bioreactors, filters, and chromatography columns.

2. **Scale-up**: Transition as many process steps to single-use as possible in the development phase, to not duplicate process optimization and validation efforts. Growth or separation yields can be quite different in single-use equipment, so the earlier you know what works and what doesn’t for your cell line and your product, the more informed decision you will make when planning a single-use pilot or production facility.

3. **Training**: Don’t shy away from hybrid solutions, because certain downstream unit operations do not yet exist in single-use, especially for large-scale production processes. Select the production volumes that make sense at each process step, and create a best-of-breed solution. Many stainless skids work well with CIP sterilization and do not require significant plant infrastructure such as high pressure steam.

What are the hurdles to broader adoption of single-use technologies?

End-users urge CMOs to continue investing in the technologies and assume that they require no attention to detail. This can often lead to misuse of the equipment compared to its intended use. Also, a lack of due diligence on vendors can lead to wrong decisions and failed expectations.

What do you see as the future for disposable technologies specifically regarding their adoption, materials of construction, and processing capabilities?

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Finally, with a strong incipient movement to continuous processing underway, we see processing capabilities increasing with perfusion in smaller volumes. This should ultimately lead to solutions for personalized medicine.*