Single-Use Products in BioManufacturing: Innovations Driving the Industry
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Biopharmaceutical manufacturers and CMOs are continuing to integrate single use products into their production and research facilities. Broad adoption of single-use devices, however, is becoming increasingly dependent on vendors' innovation and R&D, as the industry continues to need and demand new and better devices.

The need for more effective, standardized single use equipment is generally felt by both vendors and end-users. To identify specifically where those needs exist, we quantified the demand for innovation in our 2011 *8th Annual Report and Survey of Biomanufacturing Capacity and Production*[1]. In the study, we asked over 325 global biomanufacturers to identify where they want vendors to put their new product development efforts into researching new and better products. We found that the interest in innovation in disposable/single-use systems in biomanufacturing tops the list of nearly 25 key products and devices (Table 1).

Table 1: Top Areas Where Vendors & Suppliers Should Focus New Product Development Efforts *(selected results)*

Product/service Area	Response Percent
Disposable products, bags connectors, etc	38.9%
Disposable product: purification	38.7%
Disposable product: probes, sensors, etc	36.9%
Chromatography products	34.5%
Analytical assays	32.1%
Process development (downstream) services	29.8%
Cell culture media	29.0%
Disposable product: bioreactors	28.6%

Source: 8th Annual Report and Survey of Biopharmaceutical Manufacturing; Preliminary data, pub April 2011; BioPlan Associates, Inc. www.bioplanassociates.com

These responses reflect both the growing acceptance of disposable/single-use devices, and the growing needs for better systems. Nearly 39% of the industry is looking to their vendors for greater production innovation in certain single-use devices. In fact, the data suggest that significant opportunities exist for companies with creative R&D and product development capabilities. Companies able to deliver the economic benefits of lean manufacturing, and those able to reduce problems associated with current disposables integration will stand to benefit.

Respondents to the study are looking to their vendors, and associations for support in standardization of designs for greater interchangeability among suppliers, simplification of operations, and general

cost reduction. Specific factors that respondents indicated as needing improvements are included in Table 2:

Table 2: Reasons for Restricting Use of Single-Use Devices, 2011 vs. 2010 ***(Percent indicating 'strongly agree' or 'agree')***

Reason for Restricting Use	2011 Results	2010 Results
Leachables and extractables are a concern	74%	68%
Breakage of bags and loss of production material concerns	68%	63%
High cost of disposables (consumables)	66%	68%
Material incompatibility with process fluids	52%	52%

Source: 8th Annual Report and Survey of Biopharmaceutical Manufacturing; Preliminary data, pub April 2011; BioPlan Associates, Inc. www.bioplanassociates.com

The study indicates that the biggest factor restricting the use of single-use devices remains "leachables and extractables" (cited by 74% of respondents answering "Strongly Agree" or "Agree", and up from 68% in 2010). These data suggest an opportunity for vendors with R&D into better materials. Other areas where problems exist include:

- Simplifying change-over and cleaning operations
- Reducing overall capital investments
- Reducing risks of product cross-contamination
- Speeding up time to get facility up and running
- Improving campaign turnaround times
- Standardizing devices to avoid costs of system modifications
- More 'modular' approaches
- Reducing space requirements
- Improving assurance of sterility
- Decreasing documentation requirements; simplify QA/QC
- Improving sterile-sampling
- Simplifying overall operations to reduce learning curve for new operators
- Improving control of bioreactors
- Reducing the need for operations staff
- Improving strength and reliability—to reduce bag breakage

Some of these innovations are substantial, but many are small, incremental developments; these may provide the improvements that actually facilitate how devices are used by operators. Solving these issues will require more innovative leadership, process documentation, and training to demonstrate how devices can be effectively integrated into operations.

In fact, many in the industry believe that the real growth in the single-use segment will occur through process simplification. Rather than just focusing on replacing stainless steel with plastics, companies that focus on simplifying overall manufacturing will stand to benefit. And as single use systems permit more efficient, more 'idiot-proof' processes, we are likely to see faster adoption. Thus, to get beyond the current steady rate of adoption, innovation may focus on making production easier for people with fewer skills, on a global perspective.

Creating simpler devices also requires standardization. As the industry has grown, so has the proliferation of unique designs and devices. Now, the next level of growth will likely require more 'plug-and-play' devices to guide product design and innovation. This kind of standardization will also permit greater efficiency and lower costs.

Industry Innovations Today

Virtually all single-use device suppliers have R&D and innovation programs. As this segment continues to mature, the successful vendors appear to be combining an education-based approach with their research.

Examples of where vendors are currently working to support industry growth:

- Help end-users of disposable multicomponent systems build qualitative and quantitative profiles for their total systems, (e.g., extractables studies on single-use sterile connectors and filter capsules using model solvents under worst-case conditions, flexible tubing and polymeric film biocontainers, and other innovations).
- Provide project management support with end-users for implementing biodisposables in new and retrofit facility environment, which may include technology risk analysis, design and facility layout, process simulation, economic analysis, and validation support
- Create simpler devices and processes that are enabled through standardization. As the industry has grown, so has the proliferation of unique designs and devices. Biodisposables do well where 'plug-and-play' is a natural fit.
- In novel technologies, such as membrane-chromatography, develop systems that behave like existing devices, such as filters. This reduces the need for additional expertise. Plug-and-play devices that fit the process will enable greater growth.
- Adoption of common frameworks for development and integration, especially where product and company partnerships can be developed to create new, more integrated disposable systems.
- Simpler, more rapid deployment is a big factor in adoption. This can permit additional manufacturing capacity to be created fast, and flexibly. Some vendors are working on such portable biomanufacturing platforms to reduce costs compared with conventional technology. This can take advantage of single-use flexibility to eliminate clean- and steam-in-place requirements and clean room infrastructure.

Many believe that there will not be an 'all-or-nothing' approach to installing single use equipment. End users are increasingly looking to their vendors to support the dove-tailing of disposable systems into existing facilities and processes. Innovation in this area is likely to increase biodisposable technology adoption. Genentech [2] says it has accomplished this at its Oceanside Clinical Plant, the location of implementation of freeze-bulk disposable containers, "a relatively novel application in the disposables industry." Genentech reports that current advances "in this technology have brought biodisposable systems to geometrically, mechanically and operationally match all characteristics of the traditional stainless steel bioreactor platform…allowing industry to shift their processing platform to this technology seamlessly."

Motivations Behind Single-Use Innovations: Faster Drug Development, Lower Costs

Drug companies continually seek ways to reduce costs, and speed drug development times. Single-use systems are recognized as playing an important role. For example, in this year's Annual BioPlan study, 37% of biomanufacturers noted that over the past year, they used more single-use devices in manufacturing *specifically* to speed drug development timelines (e.g., to shorten time from research to commercialization). This is a strong motivator for single-use systems suppliers, because the opportunity to reduce drug development times can create a strong incentive to implement disposable systems.

"Single-use adoption provides a cost-effective strategy for increasing the speed to market for many biologics," observes Gustavo Mahler, President and CEO, CMC Biologics, a contract biologics manufacturer. "As process yields continue to increase…the need for costly high-volume stainless steel tank facilities will decline for some products. We believe this trend will continue to push bioprocessing toward single-use technology."

Jerrold Martin, Senior Vice President of Global Scientific Affairs, Pall Life Sciences, points out the number of industry submarkets, many of which have very different needs, and different growth levels. "Overall, the industry may still be considered quite young, but in the smaller companies and among startups, single-use is gaining full acceptance because it enables these companies to produce their own clinical batches onsite and without much capital risk."

Similarly, we found that cost-cutting had a role in decisions for adopting disposables. In 2011, the study showed that, over the past 12 months, biomanufacturers addressed cost reduction in a wide variety of ways, but nearly 33% indicated they "Accepted Single-Use (disposable) systems into *clinical manufacturing* operations" specifically to reduce costs (a lower percentage indicated adoption at commercial scale operations). Decision-makers are now focusing on *how* these devices can fit their needs. As such, product innovation, and utility will play a much larger role in adoption decisions.

Summary

As the industry advances, successful single-use systems vendors will be paying close attention to customer needs, and will need to have in place the new-product development processes required to bring to market more innovative systems. As with many newly introduced technologies, where end-user have not fully defined their own needs, strong relationships between vendors and end-users become critical for successful new product development. Successful vendors will continue to support their clients by providing improved:

- Plug-and-play standardization to ease implementation
- New materials that improve performance
- Device designs that can be more easily used by operators
- Vendor validation data, and
- Service support for how devices are actually to be used by operators, and how to control materials behavior in actual use.

Growth and acceptance of disposables is clearly tied to the ability to meet end-users' needs. There is now plenty of data available on these systems, and decision-makers have had enough time to start evaluating single-use applications and models for their specific operation. So the engine for growth in this industry segment is more likely to be new product innovations that meet end-user needs. This will require stamina and resources on the part of industry vendors to invest in new product development, additional services, and consensus best practices that support end users.

References

[1] 8th Annual Report and Survey of Biopharmaceutical Manufacturing Capacity and Production; Preliminary data, pub April 2011; BioPlan Associates, Inc. www.bioplanassociates.com
[2] Allotta, T., et. al. Process Research and Development, Oceanside Process Research & Development, Genentech, Inc., Oceanside, CA 92056

