

Pharm. Bioprocess.
(2013) 1(5), 415–418

Future proofing biopharmaceutical manufacturing: the industry seeks a leaner version of itself

/// Future-proofing in bioprocessing today involves adding flexibility into manufacturing strategy. ///

Keywords: biopharmaceutical process improvements, bioprocess monitoring, bioprocessing, flexible facility, modular biomanufacturing, process control, single-use bioprocessing

How detrimental is it for a biopharmaceutical company to be stuck with legacy technologies, watching competitors transition to new, more efficient, and more cost-effective platforms? That question is facing many biopharmaceutical manufacturers as the industry gradually shifts away from the use of traditional stainless steel equipment and moves into greater adoption of newer technologies, such as single-use devices, modular, and continuous processing systems.

Future-proofing in bioprocessing today involves adding flexibility into manufacturing strategy. Modular bioprocessing facilities is an example that involves the integration of pre-fabricated bioprocessing modules or suites in a ‘plug and play’ manner that allow companies to assemble bioprocessing systems using off-the-shelf modules that easily hook up with other modules. The spread of such modular bioprocessing facilities, along with wider penetration of single-use systems for commercial manufacturing, could revolutionize bioprocessing, particularly in emerging markets (where local populations increasingly demand products) and facilitate more global standardization of manufacturing.

Although single-use equipment and module bioprocessing involve unique systems, they are being increasingly adopted because they offer advantages over legacy technologies: more adaptability; more efficient capacity utilization; and more portability. In fact, one of the main reasons the industry is looking to increase its use of disposables is for the flexibility of the ‘modular’ approach. This is the direction the industry is moving in – and it’s a far cry from the large, fixed, multi-million-dollar stainless steel systems that have dominated manufacturing. Indeed, late last year when we surveyed the more than 450 global subject matter experts and senior participants who make up our Biotechnology Industry Council™ [1], single-use applications and adoption emerged as one of the key ‘future vision’ bioprocessing trends. Other key trends involving design strategies pointed to topics such as:

- » Flexibility: modular single-use system, computer numerical control, clean room space;
- » Adaptability to new enabling technologies;
- » Clone-ability: move, duplicate, repurpose spaces;
- » Equipment separation (physical, procedural, documentation);
- » Centralized material support (non-product-contact).



Eric S Langer

Author for correspondence:
BioPlan Associates, Inc., 2275
Research Blvd, Suite 500, Rockville,
MD 20850, USA
Tel.: +1 301 921 9074
E-mail: elanger@
bioplanassociates.com



Ron Rader

BioPlan Associates, Inc., 2275
Research Blvd, Suite 500, Rockville,
MD 20850, USA

**FUTURE
SCIENCE**

Fully single-use facilities on the horizon

Virtually all marketed biopharmaceutical products today are manufactured commercially using fixed bioreactors and other stainless steel equipment. There are far fewer instances of approvals for commercial-scale cGMP manufacture involving mostly single-use equipment.

However, from our *10th Annual Report and Survey of Biopharmaceutical Manufacturers* [101], we have found that over the past few years, demand for single-use products has grown rapidly, and some disposable devices have almost fully penetrated the market in pre-commercial manufacture. It seems to be only a matter of time before they will be widely adopted in commercial manufacture, as well.

In our study, we surveyed 235 biopharmaceutical industry bioprocessing decision-makers. Almost half (46%) of respondents strongly agreed (18.4%) or agreed (27.6%) that they expect to see a 100% disposable facility in operation within 5 years. US respondents were particularly bullish about the prospects of a fully disposable facility, with 57.1% agreeing that they expect to see one in 5 years by comparison, 43.5% of Western European respondents concurred.

And yet, respondents to our study feel that it is more likely that the industry will retrofit existing facilities with disposables, rather than designing entirely new facilities, with a slight majority (53.6%) agreeing with that outlook. That appears to be an acknowledgment that for many, single-use devices will have to be integrated into current systems, an understandable business rationale given the tens or hundreds of millions of US dollars already invested into validated stainless steel facilities that can support multiproduct manufacture. This suggests that future proofing is likely to involve retrofitting and careful integration of legacy systems.

While single-use equipment has the advantage of being able to be retrofitted into existing operations (something not really possible with fixed stainless steel systems), these swap-ins will not realize the full extent of the advantages presented by a fully disposable – and increasingly modular – facility.

/// Future proofing is likely to involve retrofitting and careful integration of legacy systems. ///

Demand for innovation favors single-use devices

This is by no means an argument that investments in stainless steel systems are a mistake – or even short-sighted. But the rapid changes on the horizon beg careful examination of manufacturing strategies so as to avoid being stuck with legacy technologies. Part of the process of future proofing biopharmaceutical manufacturing involves an evaluation of which systems and facility types will become industry standards and which will be far surpassed by others in the years to come.

Facilities can view emerging trends by analyzing the innovation taking place in the industry. On this front, data tend to point toward the continuing emergence of single-use products as the dominant basis for future manufacturing. That is, the most popular new product development areas of interest relate to disposable devices, with innovation in stainless steel equipment almost an afterthought. That suggests that rather than try to improve on existing models, the industry envisions a future where such equipment is replaced by new, single-use, modular systems.

Losing the flexibility to take advantage of new platforms

An analysis of the major reasons for increasing – and decreasing – use of disposables yields some important factors related to future proofing. In our latest study, we asked not only the reasons why the industry is increasing its use of these devices, but also what the single most critical reason is for greater adoption. The clear winner? Reducing capital investment in facility and equipment, cited by 26.1% as the most critical reason (up from 17.1% in last year's study, 21% in 2011 and 14.4% in 2009). Part of the attraction of single-use systems is that they do not require huge up-front investments in facilities that can be expensive to modify at later dates, or that lock facilities in for the foreseeable future. With single-use equipment disposed of after each process run, updating equipment and keeping up with technological advances is relatively easy. That advantage stands in stark contrast with the inflexibility and the costs of a stainless steel facility.

Indeed, when we asked respondents their single most important reason for not increasing use of disposable technologies, the second-most common answer given was that they had already invested in equipment for their current systems. Many respondents would presumably like to increase their use of single-use equipment, but are stuck with legacy, mostly stainless steel equipment, that is very hard to replace or modify.

What the industry is doing to future proof

In the biopharmaceutical industry, regulators, especially in the USA and EU, can inhibit process changes in manufacturing. Once a manufacturing process has been approved, the industry avoids making changes. Thus, specifying processes that could become obsolete in the near term creates a significant risk to long-term competitiveness. To understand how companies are addressing this risk, we asked BioPlan's (MD, USA) Biotechnology Industry Council™ panel of over 450 bioprocessing industry decision-makers what they are doing to avoid being stuck with inefficient, legacy manufacturing systems during their drug product's life cycle. Many of the responses were consistent. Here are a few representative comments:

- » To future proof our biomanufacturing strategies, we try to evaluate as many applicable new technologies as possible. This includes screening and implementing upstream, single use technologies, and downstream novel resins, new media and feeds. We also evaluate process improvement technologies;
- » As part of our approach to increasing flexibility, we are switching our manufacturing to more disposable, flexible systems. We are having our chromatography columns custom packed in disposable column bodies and have eliminated our production column hardware;
- » We make sure we have a good understanding of our own current capability and capacity, so that we can determine how best to introduce new processes. As a prelude to the future, we have fully automated our facility, and we got rid of paper batch records. We have also given ourselves room to expand;
- » We constantly seek new manufacturing tools and technologies that will make us more competitive. If we need to change our equipment configuration, we do. We do not allow ourselves to become locked into a legacy technology.

Looking forward and making plans

Future proofing is an important activity for any industry. Results from our study indicate that the biopharmaceutical manufacturing community does remain concerned about becoming too invested in legacy or inflexible platforms. This concern has led to an interest in systems and processes that are more flexible than the rigid stainless steel equipment they have long been used to.

Making the right decisions requires keeping a pulse on the industry's movements and transitions and determining how manufacturing decisions taken now can help fight off possible future issues. There are signs that the industry is already turning to single-use and modular production systems to head off future capacity constraints. With many expecting capacity bottlenecks in the future, a greater number of facilities are looking to the development of more 'modularized' production systems as an important area to avoid constraints and capture the cost, efficiency, product quality and other benefits of newer technologies. This reflects a desire for facilities to be leaner – with cost reductions, increased productivity and improved quality – and more flexible than their current platforms allow.

As is common in this industry, transitioning to new platforms and processes will take time – and there may be little willingness on the part of the industry's suppliers to go beyond their existing product lines. By the time some companies are ready to adopt new manufacturing processes, even newer and improved ones start to enter the market.

The industry's focus on bioprocessing flexibility, including single-use and modular systems, may well be a response to this quandary – the industry's own version of future proofing, providing ready options for updating bioprocessing capacity.

Financial & competing interests disclosure

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

No writing assistance was utilized in the production of this manuscript.

References

- 1 BioPlan Associates' 2013 Biotechnology Industry Council™ Trends Analysis Study. Rockville, MD, USA (2013).

Website

- 101 10th Annual Report and Survey of Biopharmaceutical Manufacturing Capacity and Production, April 2013, Rockville, MD.
www.bioplanassociates.com/10th