



Choosing the right single-use bioreactor platform

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Choosing the right single-use bioreactor platform

When selecting a bioreactor, you can choose stainless steel or single-use technologies, depending on your biomanufacturing requirements. The bioreactor is a key component of your bioprocessing workflow and should be regarded as a strategic asset. It is important that this core technology is carefully chosen, specified, designed, and supported, both now and in the future.

Stainless steel bioreactors, at capacities of 10 000 to 20 000 liters or greater, are still the preferred option when producing large-scale products. But single-use bioreactors, typically 1000 or 2000 liters, are quickly becoming the preferred option for small-scale production.

When producing biologics, single-use can provide benefits such as lower capital investment, lower operating expenses, and lower environmental footprint. It also offers the flexibility to produce larger numbers of smaller batches, with faster turnaround times compared to traditional stainless steel.

Cell densities are predicted to continue to rise, as is the need to produce greater quantities of proteins, all in an environment of increasing regulatory requirements. If you decide to opt for single-use, it's important to select the bioreactor that meets not just your current needs but also is able to support the demands of future processes.



“Adoption of single-use technology has allowed us to continue to be flexible enough to meet all of our customers’ varied needs”

Sharyn Farnsworth,
Associate Principal Scientist –
Group Leader,
Fujifilm Diosynth Biotechnologies,
North Carolina, USA

“The right pairing of automation and control systems leads to an overall improved level of quality assurance and compliance”

Parrish Galliher,
Chief Technology Officer –
Upstream BioProcess,
GE Healthcare Life Sciences

5 key considerations when choosing a single-use bioreactor platform

1) Process performance

When making your assessment, one of the key considerations should be process performance. You should look for single-use technology that is equal to or better than traditional stainless steel; in terms of consistency, reliability, reproducibility, robustness, and, most importantly, flexibility.

Contract development and manufacturing organization (CDMO) Fujifilm Diosynth needed a single-use platform that outperformed stainless steel across all these parameters. In addition, the single-use bioreactor itself needed to have optimal mixing capabilities, optimal mass transfer, and flexible sparging options.

Fujifilm Diosynth needed to accommodate the demands of its proprietary Apollo™ expression platform and Saturn™ mAb platform, as well as a significant number of differing client platforms. Adoption of GE Healthcare’s BioProcess™ Xcellerex™ bioreactor platform allowed them the flexibility to meet all of the needs of such varied processes. Of particular note was the novel design that allows a 5:1 turndown for a wide range of output volumes.

2) Control system and automation

The choice of the automation and control systems are critical to the success of your project. Pairing the right control systems with sophisticated automation can deliver clear benefits. These range from remote control and remote monitoring, frequent sampling at predefined time intervals, and enhanced traceability of the manufacturing process, through to advantages of standardization across a facility. Automation also reduces the amount of human interaction with the process and can limit the chance for human error.

Implementation of the right control systems leads to an overall improved level of quality assurance and compliance of the operating process, as well as increasing efficiency and reproducibility, which is especially important for cGMP manufacturing.

3) Ease of implementation and qualification

One of the key advantages of single-use is that the bag is the reactor, and therefore you can take the “family” approach. That means if you already have single-use technologies in place, previous qualification data can be leveraged for new bioreactors when the same type of bag is used, in terms of materials and design. This can dramatically simplify and speed up the qualification process.

Fujifilm Diosynth already had a fully qualified and operational Xcellerex XDR-2000 at their Research Triangle Park site in North Carolina, USA, that they were happy with, so it made sense to duplicate this capacity at their Billingham manufacturing site in the UK. Installing the same equipment enabled three months to be taken off the installation time.

In addition, the experience Fujifilm Diosynth had in North Carolina helped in the technology transfer and qualification stages of the single-use facilities at the Billingham site. This family approach also means that the amount of work to validate additional capacity in the future will also be reduced.

4) Flexible design – Choose a design that allows you to scale down

When manufacturing biologics, it is important to have a bioreactor, or bioreactors, in place that allow volume flexibility. Biologics are high value products so you want to be able to manufacture only what is needed and minimize waste. You need to understand not only the maximum capacity of a run, but also the minimum operating volume before deciding on your bioreactor.

The turndown ratio of a bioreactor is the difference between maximum operating volume and the minimum operating volume. Having a larger turndown factor has a number of benefits, for example, the size of the inoculum train can be reduced, because the inoculum is much smaller for the starting volume and the production reactor. That reduces the number of vessels that you need to buy, the size of facility you need to build, and the number of bags consumed per batch. It also reduces the overall operating and capital cost expenditures for the facility.

The innovative design of the GE Healthcare Xcellerex-XDR bioreactor allows for up to a 5:1 volume turndown. This gives biomanufacturers like Fujifilm Diosynth a large dynamic range of volumes, allowing their processes to be run in a vessel that is specific for output needs and beneficial in minimizing waste.

“We can exploit the family approach in single-use manufacturing to reduce the amount of work to validate additional capacity as we expand our facility”

Parrish Galliher



“A large turndown ratio is important because it not only allows us to have a lot of varied options for scale-down, but it also allows us to have options for scaling up”

Sharyn Farnsworth

5) Flexible design – Choose a design that is future-proof

Bioreactors can be specifically designed to readily support production scale changes. For single-use, if the whole range has a common overlapping design space, then the output from a 50 L, 100 L, 500 L, 1000 L, or 2000 L bioreactor will be the same, as long as the control parameters are kept within the recommended ranges.

This not only provides a whole range to pick and choose from, but means bioreactors can be “bolted on” anywhere along the workflow to suit needs. And, it simplifies the validation process.

At their North Carolina site, Fujifilm Diosynth had a range of bioreactors up to 1000 L from GE Healthcare’s BioProcess Xcellerex platform and added an additional 2000 L bioreactor in 2014. They decided to mirror this approach at their Billingham site, where Xcellerex bioreactors up to 1000 L were initially installed and then later, in 2015, a 2000 L bioreactor was added.

This future-proofing concept was factored into the additional facility design. By taking a phased approach, Fujifilm Diosynth were able to start meeting customers’ needs and then add additional capacity as demand increased.

By adding duplicate single-use capacity, Fujifilm Diosynth had the ability to build on the experience they had from North Carolina and also had the flexibility to move customers’ “projects” from one site to another as capacity became available. This gives them the ability to efficiently serve customers through the drug development lifecycle.

Closing remark

Whatever technology platform you choose, it should have the performance, reliability, flexibility, and robustness to meet the demands of your processes. Beyond process performance, it is important to consider how control systems and automation come into play, how easy it is to implement the platform, and if the design is flexible enough to support varying production volumes today and in the future.

“Having a bioreactor range from small scale through to large and then duplicating this capacity gave us the ability to serve customers through the drug development lifecycle”

Mark Douglas,
Head of Strategic Business Development,
Fujifilm Diosynth Biotechnologies,
Billingham, UK



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