A Perspective on Process Equipment Customization for Biopharmaceutical Manufacturing

OTHER INDUSTRIES STANDARDIZE, WHY NOT BIOPHARM?

BRADY COLE, VP OF MARKET DEVELOPMENT

JANUARY 2024

A little over 20 years ago, I shifted my career from managing capital equipment products for semiconductor manufacturing to capital equipment for biopharmaceutical manufacturing. At the time, I recall seeing my first bioreactors and fermenters and thinking, "Well those sure look simpler than plasma etchers." (In retrospect, that judgement was a bit hasty!)

Although semiconductor manufacturing equipment is complex, we would generally engineer the products to meet the requirements of particular steps in the chip manufacturing process, lock down that design, then provide it to the entire market. The trick was to prove your technology was best for the latest device technologies, then, once you did, chip manufacturers would buy that design with very little customization. So why couldn't this be done with bioreactors and fermenters that, at least on first glance, were simpler?

Additionally, when I joined ABEC, our primary bioreactor/fermenter competitor was focused on a standard product approach. They would offer the same design over and over, win on price, and for some applications that was that. However, in many cases, some amount of customization was critical, and those clients either had to sacrifice productivity, incur other costs, or pay expensive change orders to meet their needs. In fact, a few of those customers actually cancelled the order with the competitor and came back to us...it was much more cost-effective overall to get exactly what they needed without the angst of change orders.

I recall in those all-stainless days many spirited debates across the industry on the question of standardization. Moving into the single use era, it hasn't even been a debate until recently. The industry is dominated by large legacy consumables suppliers who were first to market with standardized, catalogue systems. And surely by eliminating the complexity of clean-in-place and steam-in-place, we could now finally have the ultimate standard bioreactors and fermenters and realize the cost, efficiency, and time to market benefits that standardization has brought to other industries. So for single use processing, is the custom versus standard case now closed?

Biopharm Industry Challenges

It actually took me a while to fully appreciate the value that customization brings to bioprocessing. Regardless of whether we're talking about stainless steel or single use, the value of customization lies in the fact that biopharmaceutical manufacturing is inherently more complex than other industries. Consider:

- There are thousands of different biopharm drug substances with unique process requirements, and each molecule has its own process development history.
- Required production quantities can range from a few grams for pre-clinical requirements, to a few kilograms for clinical trials, to metric tons for commercial manufacturing.
- Equipment is being integrated into greenfield, brownfield, and existing facilities.
- Technology is evolving with new product modalities such as genetic medicine, and improvements of existing modalities such as high-density cell culture for intensified mAb production.
- Regulatory compliance is absolute and impacts operational elements such as process automation and turnover documentation.
- Related to all of the above, a wide array of business factors are at play, such as time to market, clinical risk, pricing/profit margins, contract vs. in-house manufacturing, and so on.

Other industries may have a couple of the above considerations at best, but not all of them as is the case in biopharm.

Customization Benefits

Given the above complexities, we find that flexibility can buy a lot. Any added capital or consumable cost to customize is often easily overcome by savings realized with:

- Yield/productivity enhancement
- Facilities cost reduction
- Faster and simpler technology transfer
- Operational/Uptime savings from instrument/component flexibility, ergonomic improvement, automation flexibility and enhanced serviceability
- Reduced compliance risk

See below some specific examples.

No Absolutes

Certainly catalogue single use systems have been successfully deployed across the production spectrum, from pre-clinical work to commercial manufacturing, and customization is not needed for all cases. Catalogue systems fulfill various needs, particularly in pre- or early-clinical applications where scalability, productivity, and compliance are not as critical. The drivers for customization become more significant in the clinical and commercial manufacturing spaces, although we are seeing customization for next-generation processes in some process development labs. It should also be noted that even for manufacturing it does not need to be a complete re-design every time. For many customers, we create a custom design that becomes their standard which is repeated over time, thereby realizing cost and schedule savings over the long term.

Summary

Because single use manufacturing has its roots with legacy consumables suppliers, it is understandable that the catalogue product paradigm is so strong. However, ABEC is showing that the fundamental needs of the biopharm industry haven't really changed much since the all-stainless days. Single use or stainless steel, customization can bring real value.

Brady Cole has over 30 years of technical and commercial experience in high technology industries. He began his career developing plasma deposition and etch processes for advanced microelectronics. He later moved on to product development and product management roles in the semiconductor capital equipment industry.

Since joining ABEC in 2002, Brady has held leadership positions in product management, applications, and sales. During his tenure, ABEC significantly expanded its products, services, and global reach, and Brady currently oversees ABEC's new product development and marketing functions.

10 X 6,000L SINGLE-USE BIOREACTOR SUITE

EXAMPLE OF HOW CUSTOMIZATION GREATLY IMPROVES YOUR DAY-TO-DAY OPERATIONS:

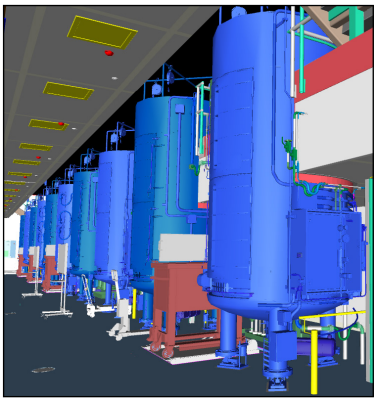
Customized Solution Examples

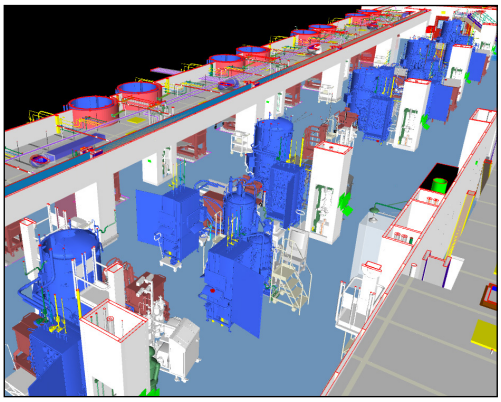
- Scaled and transferred an existing process to 6,000L single-use CSR Production Bioreactors
- Customized design and engineering of upstream layout with platforms and strategic transfer

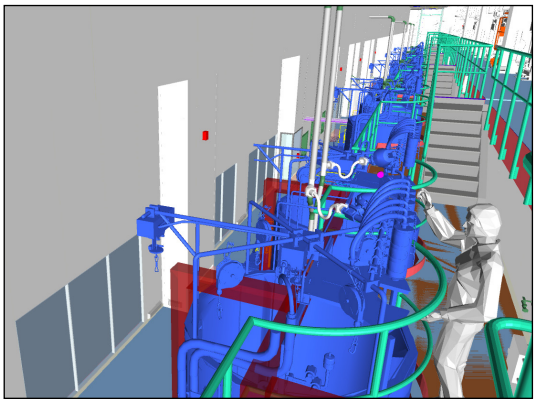
Value from Customization

- Seamless technology transfer
- Reduced facility footprint
- Maximized operational efficiency and productivity

A customized equipment layout promotes productivity through more efficient operations.







HIGH CELL DENSITY PERFUSION PROCESS

EXAMPLE OF HOW CUSTOMIZATION SIGNIFICANTLY BENEFITS YOUR PRODUCT YIELD:

Customized Solution Examples

- Integrated single-use equipment with the customer's unique perfusion technology
- Designed a sparger to meet the mass transfer needs of the process

Value from Customization

- Enabled 5x productivity compared to the legacy fed batch process

500L CSR holder designed with ports to support customer's unique perfusion process at multiple working volumes

NEUROTOXIN BIOREACTOR TECHNOLOGY TRANSFER

EXAMPLE OF HOW CUSTOMIZATION HELPS YOU WITH COMPLIANCE AND REDUCES RISK:

Customized Solution Examples

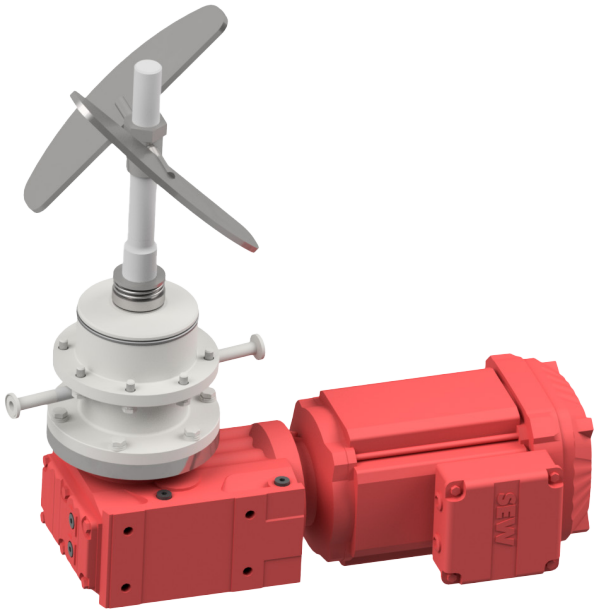
- A configured single-use fermenter mimics the performance of the legacy stainless systems the process is traditionally manufactured in

Value from Customization

- Faster and lower cost of technology transfer
- Reduced regulatory risk

Stainless Features Designed into Single Use Equipment:

- Elephant ear impeller design
- SEW gearmotor
- Stainless shaft



Left: Motor assembly for stainless steel reactor

Right: Motor assembly for single use reactor

DEMANDING FERMENTATION PROCESS IN A CONSTRICTED PROCESS AREA

EXAMPLE OF HOW CUSTOMIZATION ENABLES SEAMLESS EQUIPMENT INTEGRATION INTO AN EXISTING FACILITY:

Customized Solution Examples

- A ceiling height restriction resulted in a single use fermenter designed with a lower aspect ratio, and consequently, a unique two impeller agitator.

Value from Customization

- Reduced time to market
- Reduced facility costs
- Avoided costs for building modifications
- Increased yield and productivity in a smaller footprint

A 300L single use CSR Fermenter customized for a facility's existing space