Xcellerex®

THE FLEXIBLE FACTORY CONCEPT:

A flexible bioprocessing platform to meet
the changing needs of biomanufacturing

Introduction

For the past several years, the biopharma industry has been buffeted by dynamic market conditions that are rapidly reshaping manufacturing requirements. These factors include:

- The rise of small-market pharmaceuticals that do not require the production scale of the previous “blockbuster” drug model
- Increased titers and process productivity that generate more bulk-product within a much smaller manufacturing footprint
- The emergence of biosimilars and continued evolution of healthcare reform, which will increasingly pressure drug pricing and require greater cost discipline
- Greater competition and shorter patent protection timelines, which will further ratchet up time-to-market pressures
- Tighter capital markets that will create heightened scrutiny for all new investment projects

As manufacturing and facilities managers confront this changing world, they are still tasked with meeting today’s capacity needs. Many are turning to a new flexible factory platform that will accelerate their implementation of biomanufacturing capacity while lowering risk, increasing speed, and reducing capital costs. This approach enables the deployment of new production capabilities in 9 to 18 months (versus 3 to 5 years for today’s technology) at a total cost of less than 50% to 80% of conventional plants.

The Flexible Biomanufacturing Factory

The flexible factory is a modular, portable biomanufacturing platform that leverages single-use technology, advanced process automation, and compact clean room architecture. Its major components include:

1.Single-Use Technologies

Flexible factory systems feature single-use technologies for nearly every process operation. This eliminates the expense and time required to design, construct, and validate conventional stainless steel clean-in-place/steam-in-place infrastructure. Single-use technology also provides operational savings and quality improvements by reducing cross-contamination and slashing batch-to-batch and product-to-product turnover times.

2. Environmental Control Strategies

Flexible factories utilize controlled environmental modules (CEMs) to enclose each unit operation. This eliminates the need for multiple clean suites and asso¬ciated HVAC, gowning, hallways, and other expensive infrastructure. In fact, because each unit operation is self-contained in its own miniature clean environment, the entire suite does not need to be engineered to traditional clean room standards. Together, these factors further reduce the cost and complexity of constructing and validating a new plant. Because of the self-contained nature of the CEM, purified downstream product is less likely to be exposed to contaminants, such as viruses, than in a conventional shared clean suite. This means that an entire flexible biomanufacturing line can be co-located in a single inexpensive Class 300,000 clean room, and that a single team of operators can move freely from one unit operation to the next without the burden of multi-level gowning and degowning.

The combination of CEM architecture and single-use technology means that different products can be safely produced in the same plant — even simultaneously. This represents a great leap forward in flexibility and asset utilization in the capital market. It also makes obsolete the traditional, high-risk approach of building a capital-intensive plant for a drug that may not progress into a commercial product.

3. Integrated Automation & Electronic Batch Records

Flexible factory production lines are controlled by robust automation that readily inte¬grates with a client's existing systems. By utilizing proven control technology, manufacturers save the time and expense required to develop and integrate an automation package.

"....the [Pfizer] PGM biomanufacturing network will lead to multiproduct and multipur¬pose facilities.... After we implement our new network strategy, none of our facilities will be dedicated. This is truly a transformational strategy."

Lou Schmuckler SVP — Pfizer BGM Operating Unit

GEN Magazine — March 1, 2011

The backbone of the flexible platform is "open" and ties in to the client's existing plant automation architecture, regardless of brand. The user-friendly human interface portion is designed to the latest CFR Part 11 standards, and provides fail-safe controls to enforce operating and quality protocols. An electronic watchdog feature protects against unauthorized actions and provides instant alerts when a protocol is breached. This enables the operator to take remedial action immediately, often in time to save a batch. The control system also provides menu-based data trending that enables plant engineers and operators to monitor performance in real time. At the end of a batch, review-and-release can be accomplished by reviewing just the exceptions and deviations, without having to laboriously review the entire record.

4. Services

In addition to the equipment and automation platform, a flexible factory installation can benefit from a services operation dedicated to accelerating deployment and lowering its risk. Key elements of the services package include:

- **Transition sourcing:** The capability to have product manufactured for pre-clinical or clinical requirements during flexible factory installation can be very attractive. This enables the client to (a) clear clinical risk milestones before committing extensive capital in a new facility, and/or (b) begin drug production in parallel with construction of their own facility, thus considerably shortening start-up time. When the client's new production line is ready, the flexible factory supplier can transplant the pre-validated operation into their new facility, and the client's operators (already trained at the supplier's facility) can commence production almost immediately. With transition sourcing, biopharma producers gain rapid access to production capacity while maintaining long-term control of their manufacturing economics and process.

- **Facility design:** The flexible factory supplier's experience in designing, building, and operating biomanufacturing facilities helps clients plan their new production lines with efficient workflows.

- **Tech transfer and scale-up:** Facility design aside, tech transfer and scale-up can repre¬sent a time-consuming and risky detour on the way to the deployment of new capacity. The flexible factory supplier's services team can offer deep expertise in tech transfer and scale-up in single-use technology, and have experience with nearly all leading technology brands. By avoiding common mistakes and known blind-alleys, clients get their processes proven and up-and-running faster.

- **SOP development & operator training:** Developing robust SOPs and training the op¬erating team are essential steps in the start-up of any new plant, and are critical in ensuring product quality and regulatory compliance. Meanwhile, as one executive recently described the endeavor, "It would take us more than 100 FTE weeks to accomplish this, and then we would spend the next 4 years debugging the work we've done." The flexible factory provider can work with the client's production team to adapt SOPs, codify them in automation systems, and train operators in its facility.
  This enables timely, confident start-up of the client's new production system.

"In addition, small volumes, and flexible factories are increasingly common, as a result of changes to a bioreactor and associated equipment design. Now, small manufacturing suites can often match the capacity of massive, earlier-generation facilities."

Eric Langer President
BioPlan Associates, Inc.

Using the flexible factory approach, clients can deploy new biomanufacturing capacity — for biotherapeutics, vaccines or biosimilars — within timelines that were never before thought possible, and at investment levels that dwarfed historical norms. Now biopharma facility executives are equipped with new tools to meet the aggressive timelines dictated by the development and clinical process, while gaining the luxury of postponing investment until a product's clinical risks and commercial prospects are much better understood.

Strategic Advantages and Benefits

The selection of a flexible biomanufacturing platform delivers unequaled gains in speed, economics, risk mitigation, and flexibility.

Speed: Flexible factory technology allows production line startup within 6 to 18 months, much shorter than the 3 to 5 years required for conventional systems. This rapid installation enables more informed investment decisions, faster product changeovers, and rapid expansion of manufacturing capacity.

"....the supply chain needs to invest in improving its manufacturing base with better, more flexible facilities, higher levels of automation and Quality by Design engineering."

Pharma 2020: Supplying the Future
PricewaterhouseCoopers

Greater Flexibility: Flexible factories have compact clean room architecture that is modular and portable. Operators can easily access their entire line. In addition, multiple products can be manufactured on one production system and long-term relationships with contract manufacturers can be avoided.

Lower Risk: The flexible factory approach significantly reduces operating risk for biopharma providers. Pre-trained production teams avoid start-up mistakes. Quality assurance is automated. Operators are removed from the clean rooms, eliminating gowning and human contamination. And disposables minimize cross contamination. The technology's rapid start-up time also permits biomanufacturers to make more informed capital decisions further into the drug development cycle, when processes are known and there is higher confidence in the ultimate success of the drug candidate.

Attractive Economics: Substantial financial benefits can be realized with a flexible factory system. These include reductions of 50% in capital, 30% in labor and growing costs, 30% in plant space, 75% in water utilization, and 55% in overall carbon footprint. Biopharma providers experience higher asset utilization, shorter time to product revenue and much less environmental impact.

About Xcellerex

Xcellerex is commercializing turnkey biomanufacturing solutions that transform the speed and economics of producing therapeutic proteins, including biosimilars and vaccines. The company's FlexFactory® is a complete modular and portable production train based on single-use technologies, advanced process automation, and compact clean room architecture. FlexFactory allows deployment of GMP manufacturing capacity more rapidly and at greatly reduced costs compared with traditional facilities. Through its BridgeSourcing™ services, Xcellerex manufactures a partner's biomolecules while the partner prepares for commissioning of its own new FlexFactory. When the partner's facility is ready, Xcellerex deploys its TransPlant™ process to install, validate, and train partner personnel in their own FlexFactory. This parallel-path model both accelerates time to clinical and commercial manufacturing and allows partners to manage the development and market risks associated with adding manufacturing capacity. Xcellerex also leverages its proprietary single-use technologies through the sale of XDR™ bioreactors, XDM™ Quad Mixers, and related single-use assemblies. To date, more than 20 therapeutic proteins and vaccines have been manufactured for clinical trials using Xcellerex technology.

To learn more about how a flexible factory approach might work for your organization, please contact: By email: flexfactory@xcellerex.com • Phone: 1.866.Xcellerex or +1 508.480.9235

Our team will schedule a review with you to understand your process and business needs, describe our recommended approach, and answer any questions.

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