MADE SCIENTIFIC

The Payoff is in the Details: The Importance of Process Optimization

Process changes are costly. The earlier you evaluate and optimize your cell therapy manufacturing approach, the better positioned you are to mitigate errors, reduce contamination risks, and accelerate processing times.

A rushed transition from process development to clinical and commercial manufacturing can carry with it unnecessary, non-value-added expenses in the future. While the pressure to move out of process development and into clinical manufacturing can be high, taking a methodical approach to refine processes can yield significant long-term benefits.

Identifying opportunities for optimization, whether by limiting product contamination risks, improving scalability, or increasing overall efficiency, can directly impact manufacturing success. The key is to strategically evaluate where further process improvements provide the greatest return on investment.

Utilizing a Process Economic Model for Decision-Making

With the continuous emergence of new technologies, analyzing their integration in relation to your project is paramount. Start by considering how that new technology will fit into your current workflow.

For example, if you are going to introduce a new tool or technique into the workflow at the unit operation level, you must assess:

- Comparability of outputs
- Upstream and downstream process impact
- Integration into existing systems

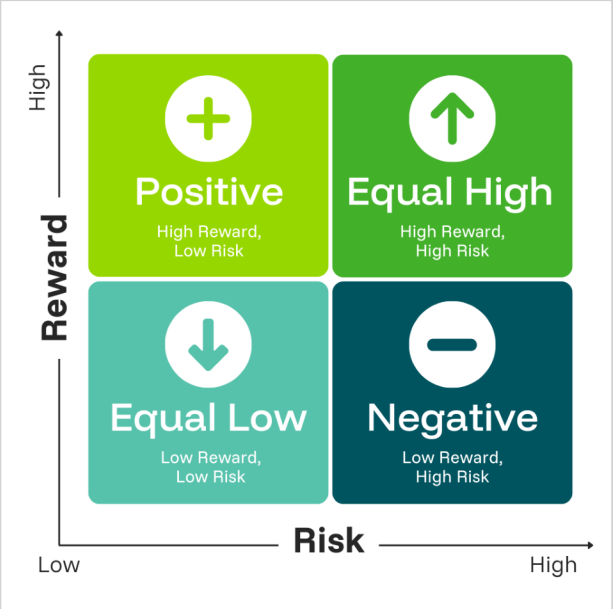
For workflows designed around all-in-one, fully closed systems, adoption may be straightforward. However, many workflows require a more bespoke approach to ensure successful integration and efficacy. A holistic workflow assessment helps pinpoint existing gaps, while a market model analysis will help you determine how, where, and with whom you will manufacture. Once you have that big picture in mind, you can consider the cost of comparability and understand the impact of the transfer from one piece of technology to another.

Equally important is reviewing the full range of relative benefits from any change vis-à-vis the amount of costs introduced in terms of regulatory risks, labor, personnel, etc. Engaging with subject matter experts on both

the therapeutic and manufacturing domains allows for a comprehensive assessment of whether any given obstacle is large enough to justify the cost and effort of that process improvement.

Refining processes early isn't just about efficiency—it's about ensuring long-term success. The decisions we make today impact scalability, quality, and GMP readiness down the line.

- David Smith, VP and Head of Development



Striking a Balance

While there is a push to be commercial process ready from day one, that can lead to unwanted results down the line. The process development phase must follow its own lifecycle. For instance, open processes and manual operations are common early on as they provide flexibility and the chance to do more with the system you have in place. At the same time, they carry risks (such as contamination) and typically require process changes down the line, which can result in expensive comparability studies.

As you can see, there is no universal answer regarding when to incorporate new technologies. Ultimately, it remains a business decision. The goal is to find a balance between entering the clinic quickly and having a manufacturing process that is reliable and repeatable. Only you and your stakeholders understand your current abilities to deliver a safe and effective product and the overarching clinical and funding milestones of your program — which is why only you can determine when you should invest in process improvements.

Identifying Non-Negotiable Process Improvements

Determining GMP-readiness is case-specific, but one guiding rule applies to all processes. If your ability to deliver to patients is put at risk, then further process work is an absolute must. The barriers to deliver to patients may stem from cost, reproducibility, safety, potency, or other critical factors.

Given that the patients in need of novel therapies have limited to no other options, the goal is to treat as many of those patients

as we can, as quickly as possible. To do so, it is crucial to consider all the requirements you will have to meet. Requirements vary based on:

- Sourcing starting materials that are patient-derived vs. a cell bank
- Manufacture at the point of care vs. centralized facility
- Addressing the needs of all the parties across the supply chain from the manufacturing team, logistics partners, receiving departments at the clinical sites, clinicians who will administer your product, and the patients themselves

Analyzing the requirements along the full journey of your product and being honest with yourself about the current status of your project will help you understand if further process development is unavoidable.

The Changing Role of Early-Stage Biotech Companies

Over the past decade, the role cell therapy developers play in getting their novel therapies to patients worldwide has changed dramatically. The previous role of developers was to collect early data, achieve proof-of-concept in humans, and then effectively transition the assets to pharmaceutical partners who would progress the product and bring it to market.

Today, it is incumbent upon the developer to grow the business, enter clinical trials, demonstrate effectiveness of the product in a Phase 2 clinical trial, and then partner.

The key takeaway here is that you, as the early-stage biotech, must be equipped to critically assess your own GMP-readiness, thereby setting the stage for long-term successful clinical and commercial manufacturing.

Managing Investor Expectations While Prioritizing Process Integrity

Investors want to see returns as quickly as possible, often applying pressure they think will help speed things along. Managing these expectations requires transparent communication and data-driven decision-making. Here are key recommendations to align stakeholder interests:

- **Organize a comprehensive product lifecycle plan:** If you are working with a CDMO, leverage their expertise to outline a realistic timeline and major milestones. This will help in confidently leading fact-based discussions with your investors.

- **Portray risk-benefit tradeoffs effectively:** Investors need to understand not just the timeline, but also the impact of process decisions on cost, quality, and regulatory compliance.
- **Align on success indicators:** From the perspective of the investors, they need to weigh trade-offs based on their exit strategy. By understanding their priorities, you can better come to an agreement on expectations from return on investments.

At Made Scientific, we see day-after-day how a well-structured plan can minimize rework and eliminate non-value-added expenses related to process optimization. To meet this critical need, we have established systems and workflows that can accelerate our clients' processes and products.

Our process development and analytical method development groups work closely every step of the way to ensure early and proper identification of your cell therapy product's quality attributes and critical process parameters. Our team possesses the expertise to optimize for product quality and yield based on the unique characteristics of the target product.

About Made Scientific

Made Scientific is a leading cell therapy contract development and manufacturing organization (CDMO) dedicated to advancing the field of cell therapy. Since 2019, the company has specialized in developing, manufacturing, and releasing autologous and allogeneic cell therapy products for early- to mid-stage clinical trials, and has evolved into an end-to-end clinical-to-commercial service provider. Operating from two U.S.-based manufacturing facilities, Made Scientific combines the flexibility and entrepreneurial spirit of a specialist CDMO with the global expertise and resources of GC Corporation of South Korea, a global leader in the pharmaceutical and biotechnology sectors.

> madescientific.com

MADE SCIENTIFIC | Defy Limits. Deliver Results.