

Ushering in Industry 4.0 with the IDMO Model to Solve the CGT Manufacturing Bottleneck

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Global scale-up requires developing replicable processes that work the same no matter where they are performed. This can be accomplished with smart factories that utilize fully automated manufacturing platforms.

Despite the tremendous therapeutic promise of cell and gene therapies (CGTs) for patients globally, the space is at a crossroads. Long-standing issues around patient accessibility have contributed to investor pullback, biotech companies shuttering, and even a few life-saving therapies being pulled from markets.

The industry needs to do better to support all patients in need. The biggest obstacle to accessibility has been pharma's need to effectively reinvent manufacturing for living drugs made from human cells. It has not been possible to develop large-batch manufacturing as is done for most other therapeutic modalities, meaning commercial-scale manufacturing has until now been unrealistic. Finally, the industry is beginning to incorporate Industry 4.0 concepts that have worked well for other types of manufacturing, including automation.

Industry 4.0 is more than just the types of technology that are deployed. Rather, these approaches underscore integration across the end-to-end patient journey. Many biopharmaceutical companies are still thinking about a black box (or several) to swap in for specific manufacturing processes, but that won't enable the kind of scale most therapies will need to meet total patient demand. Still others are relying on contract development and manufacturing organizations (CDMOs) to enable scale through next-genera-

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tion end-to-end platforms, which can still be capacity constrained by upstream and downstream processes.

A new model is the integrated development and manufacturing organization (IDMO). As the name implies, this includes fully integrated smart manufacturing facilities for true end-to-end scale. It relies on flexible manufacturing capabilities without requiring changes to hardware, meaning process modifications are entirely managed through software. As a result, technology transfer between smart facilities in any geography is streamlined through the leverage of platform standards. Combined, these aspects will make it easier to scale cell therapies globally and meet total patient demand.

Developing the IDMO

The tenets of the IDMO concept can be viewed from the top down: manufacturing facilities must be standardized and interconnected, technology within each smart factory must ensure end-to-end integration, and the platform technologies themselves must be robust enough to serve multiple functions.

Execution starts from the bottom up. From its beginnings, the biggest choke point in the cell therapy space has been manufacturing, which makes that the first place to start.

Today, commercial cell therapies have progressed toward becoming front-line treatments for certain hematological malignancies, meaning tens of thousands of additional patients may soon be eligible for these therapies. However, that number of batches haven't even been manufactured yet in aggregate. It likely will not be long before cell therapies are also approved in other indications, including autoimmune diseases. Even with heavy investment from pharma companies and the CDMO sector in new facilities and streamlined processes, traditional manufacturing is years away from meeting total patient demand.

Manufacturing at scale requires reducing the footprint, eliminating manual processes, increasing throughput, and lowering cost of goods. The most robust approach to address these issues is the deployment of fully closed and automated end-to-end manufacturing platforms. These platforms do not require traditional cleanroom spaces because manual process steps are eliminated through robotic orchestration of streamlined and fully integrated manufacturing processes.

"End-to-end" can be misleading. If a therapeutic developer or CDMO has just purchased multiple units with the intent to scale, they will need to develop all new upstream and downstream systems to match the system's throughput. Even the best manufacturing system, in isolation, might just mask a bottleneck, rather than fix it.

The IDMO smart factory approach incorporates multiple ancillary technologies to enable the full value proposition of end-to-end automated manufacturing. That includes designed-for-purpose infrastructure and facilities, requiring a high degree of engineering expertise.

Integral pieces

A smart cell therapy factory must implement Industry 4.0 concepts across the end-to-end supply chain. Much of the field has yet to grapple with complicating factors outside of manufacturing itself because few have attempted deploying manufacturing platforms at scale, but a holistic approach is required for the IDMO model.

The biggest ancillary consideration is a quality control (QC) system that incorporates in-process and release assays, and keeping up with the pace of a fully integrated manufacturing platform will require the system to be automated as well. In fact, for this reason, much of the facility will need to be streamlined and integrated.

Upstream, streamlining includes processes such as kitting and media manufacturing. Downstream, integration includes processes such as drug product storage and waste management. Even the cleaning process in material accession rooms can be automated through the adoption of vaporized hydrogen peroxide. Everything must be balanced and streamlined within an IDMO smart factory to match the production throughput across the end-to-end manufacturing journey, from the moment apheresis material arrives at the facility to the moment the final drug product is shipped back out for infusion.

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One key enabler for the IDMO approach is the integration of these automated platforms across unit operations within the pharma software ecosystem. Specifically, the interface and integration of these systems with enterprise resource planning systems for supply chain management, manufacturing execution systems for electronic batch records, and lab-

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oratory information management systems for QC data collection can streamline data connection and analysis for drug product release. The deployment of process analytical technology and artificial intelligence could further optimize the end-to-end supply chain for cell therapies within the IDMO model.

This full-stack, in-house integration is a key advantage of the IDMO approach, because it lends itself well to the kind of standardization the industry desperately needs for long-term success. It is more seamless than assembling systems that may not have been fit for purpose or designed to interface and work together smoothly. It also is a way of ensuring the accessibility of reliable data on where a specific batch is in the manufacturing process at all times—allowing cell therapy companies to focus on what is most meaningful for their patients while still offering the "white glove" service physicians and hospitals require for these complex products.

True decentralization

When people in this space discuss decentralized manufacturing, they typically mean something close to point-of-care, with miniaturized technology to fit in a hospital or a mobile unit nearby. The IDMO approach adopts some of the key advantages associated with decentralization, while decreasing the relevance of others.

Integrating all data systems requires cloud-based management, which is useful for securing data and means that servers do not need to be onsite. It also enables remote monitoring. There is less need to have someone on the shop floor in a manufacturing cleanroom when systems are fully closed and integrated.

By comparison, decentralized manufacturing will have to balance some degree of remote oversight with extensive training protocols that empower hospital staff to perform manufacturing themselves. Today, hospitals do not have the capabilities, experience, or desire to be in the drug manufacturing business.

Because so much of the manufacturing flexibility operates at the software level, with standardized hardware pieces at each location instead of different staff requiring new training, remote monitoring can also make technology transfer more fluid. That is highly relevant for an IDMO because it means smart factories can be built in multiple geographies and quickly scale to meet total patient demand once a therapeutic developer secures a new market approval.

At the same time, much of the allure of decentralization has been the promise of reducing the complexity of logistics. Hospitals wouldn't have to manage and track therapies using a different system for each manufacturer. The biggest advantage would be reducing vein-to-vein time, getting autologous therapies back to patients faster. But the IDMO can simplify this in different ways.

For one, the scalability of smart factories means they will not be capacity constrained the same way the modern CGT manufacturing facility tends to be—or how a hospital could be if local demand outstrips the number of units they have on site. That lack of constraint helps with the predictability of the process, which has positive downstream benefits, as a hospital can more reliably allocate beds and resources when they know an infusion is going to happen for a patient on a specific date.

That is going to be a big differentiator with the next wave of cell therapies, which are expected to branch out into autoimmune indications with much larger patient populations. The modular, local approach will mean an inconsistent but persistent need to add more manufacturing capacity, and many hospitals are already space constrained. No manufacturing approach beyond the IDMO is positioned to meet the need for tens or hundreds of thousands of doses per year, decentralized or centralized.

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The need for scale

The entire CGT field needs to be able to scale capacity, and nowhere is that more important than for early-stage developers and young companies. The nature of the CGT space is that many of these companies are born from exciting ideas in academia. One downside is that few academic institutions have access to scalable manufacturing platforms and developing commercial-scale processes.

As a result, therapeutic developers that partner with academic institutions often get locked into processes and workflows that are not scalable. While the impact may not truly be felt until a therapy moves into later stages of development, changes at those stages require multiple comparability studies that can stymie or even end a clinical program. In parallel, facilities need to be built or bought, staff needs to be trained, and bottlenecks have to be addressed anew.



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Small to mid-sized companies increasingly are recognizing the benefit of the IDMO approach. Technology transfer is relatively quick, and once processes are locked in, scaling to meet the new demand of each clinical or commercial product is straightforward. At the same time, they can leverage the benefits of automation, including significantly lower batch costs and a reduction in the cost of goods.

That scale-up can be over multiple geographies, which simplifies global clinical trials as well as manufacturing for disparate markets. It further reduces the need to move biological materials through customs or plan for special regulatory inspections.

FDA has been a welcoming partner for the smart factory approach through its Advanced Manufacturing Technology Designation Program (1). An automated and fully closed CGT manufacturing platform was the first to receive the designation, which allows for establishment of a standardized reference base process that can streamline the drug development process (2).

The AMT program lead to faster development timelines, with particular relevance for therapies being developed for rare or orphan diseases. Commercialized CGTs for rare diseases have been at highest risk of being removed from markets globally. By reducing the need for developers to repeatedly demonstrate the robustness of identical processes over multiple therapies, IDMOs can cut both development costs and regulatory red tape.

Ultimately, the promise of the IDMO is to accelerate access to life-saving cell therapies for all patients in need. Patients are not concerned about how their drug is manufactured, so long as it is safe, efficacious, affordable, and available when they need it. As such, the IDMO model is well positioned to solve the CGT bottlenecks. This will allow therapeutic developers to focus on what truly matters to their patients and not the manufacturing process, which will further drive drug development innovations across therapeutic indications.

> **“Small to mid-sized companies increasingly are recognizing the benefit of the IDMO approach.”**

References

1. FDA. *Advanced Manufacturing Technologies Designation Program, Guidance for Industry* (CDER, CBER, December 2024).
2. Cellares. Cellares’ Cell Shuttle Receives FDA Advanced Manufacturing Technology (AMT) Designation for Automated Cell Therapy Manufacturing. Press Release. April 1, 2025. ■

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Drug Digest: Keeping Pace with Progressive Technologies in Biopharma Development

The biopharma industry is at a time where progressive technologies such as artificial intelligence, machine learning, and digitalization technologies are making a significant impact on how drug discovery, development, and manufacturing are being driven. Yet the question remains as to how the industry itself is keeping up with the fast-paced innovation churning out from these advanced technologies. This episode of Drug Digest will examine where the significant bottlenecks are in the development and manufacturing of new molecules resulting from these progressive technologies, and how best to approach these challenges. Panelists include Kevin Dondarski, principal, Life Sciences R&D, Deloitte Consulting; Maryland Franklin, PhD, vice-president and Enterprise Head, Cell and Gene Therapy, Labcorp; Lidia Serina, PhD, head of Development Services at Simtra BioPharma Solutions; and Sean Tucker, PhD, founder and chief scientific officer, Vaxart.



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