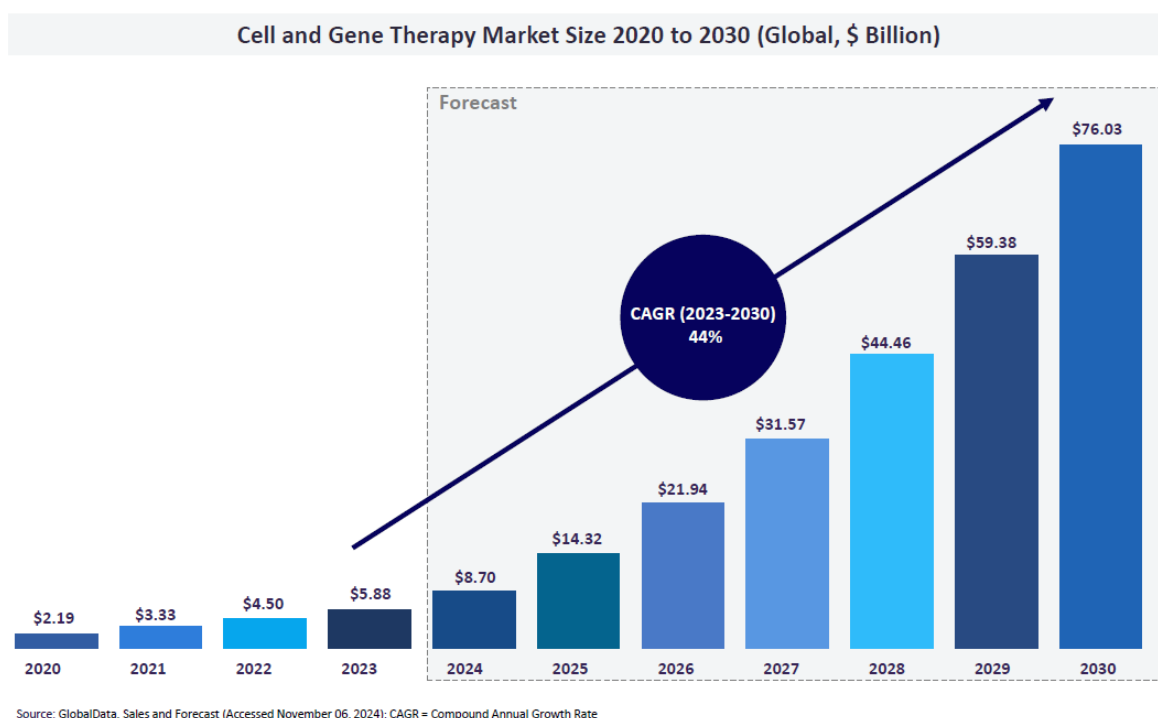


## Challenges in Technology Transfer of Cell Therapies

### 1. Executive Summary

Advanced Therapy Medicinal Products (ATMPs) represent a transformative approach in modern medicine, encompassing gene therapies, cell therapies, and tissue-engineered products. These therapies offer potential cures for previously untreatable conditions, such as certain cancers, genetic disorders, and autoimmune diseases.

The driving force within the ATMP market comprises Cell and Gene Therapies (CGT). According to an analysis by Global Data, the market was valued at USD 8.7 billion in 2024 and is projected to reach over USD 76 billion by 2030, growing at a compound annual growth rate (CAGR) of 44% during the forecast period:



This expansion underscores the increasing demand for efficient and reliable manufacturing processes. Establishing manufacturing capabilities across at least two regions—especially spanning Europe and the U.S. offers sponsors significant strategic advantages, including faster market access, regulatory agility, and risk mitigation through supply chain diversification.

However, transferring ATMP production between/to Contract Development and Manufacturing Organizations (CDMOs), presents unique challenges. These include aligning regulatory requirements, maintaining process consistency, and ensuring the integrity of complex biologic products.

This white paper explores the critical challenges associated with ATMP technology transfers and outlines strategic approaches to navigate these complexities. By leveraging expertise and fostering collaborative partnerships, stakeholders can enhance the success and efficiency of these vital processes.

## 2. Why ATMP tech transfer is unique

Technology transfer is always a critical phase in pharmaceutical development—but when it comes to ATMPs, the stakes are exponentially higher.

Transferring an ATMP is far more than handing over a manufacturing protocol. It is a hands-on, collaborative reconstruction of the process in a new environment—requiring time, coordination, and a truly multidisciplinary approach. Quality, production, and regulatory experts must work side by side to expedite an effective transfer of process knowledge across sites.

What makes ATMP tech transfer fundamentally different is the nature of the products themselves. These therapies are living, dynamic, and highly sensitive to changes in environment, handling, and execution. Unlike traditional pharmaceuticals, their successful transfer cannot rely principally on documentation or standardized procedures.

Instead, the process demands deep cross-functional alignment, shared responsibility, and a readiness to adapt. Even subtle differences in raw materials, equipment, or personnel can significantly affect product performance and compliance. In this context, ATMP tech transfer is not just a technical operation—it is a strategic, trust-based collaboration where every detail matters.

## 3. Key challenges in CDMO transfers of ATMPs

ATMPs introduce a distinct set of challenges when undergoing technology transfer. This multitude of challenges stems from their biological nature, manual processes, and the fact that small deviations may trigger significant consequences. As a result, every transfer must be tailored, often requiring site-specific adaptations rather than plug-and-play solutions.

Process replication is also constrained by variability in local infrastructure. Even with a well-documented process, factors such as different cleanroom areas, equipment models, consumables, and utility systems can alter critical process parameters. Achieving equivalence requires careful qualification of alternative materials and revalidation of manufacturing steps, often under time pressure and regulatory scrutiny. Operational factors compound this issue. ATMPs are highly

sensitive to environmental and procedural nuances. Changes in raw materials, cell culture conditions, or even operator technique can drastically impact product quality. The transfer process must therefore extend far beyond documentation: it includes hands-on support, operator training, and often collaborative runs to align techniques and expectations.

Unlike traditional pharmaceuticals, ATMPs—such as cell, gene, or tissue-based therapies—are biologically active products characterized by inherent variability and sensitivity. Their starting materials, often derived from living cells or tissues, are characterized as thoroughly as possible using available analytical techniques. However, due to the complexity of biological systems, full characterization is never entirely achievable. At the same time the quality of the starting material is critical, as it directly influences the outcome of the manufacturing process. In this context, the well-known maxim “the process is the product” holds especially true: each manufacturing step must be reproduced with exceptional precision to maintain consistent safety, potency, and quality. The following subsections break some of these key considerations out further.

### 3.1. Early Vision for Manufacturing Scale and Material Requirements

One unique challenge with ATMPs lies in the limited availability of standardized manufacturing platforms. While some solutions—particularly those supporting autologous therapies—have emerged, they are not widely applicable across the diverse spectrum of ATMPs. Many products remain highly customized or small-scale, which constrains scalability and complicates replication across facilities. Consequently, each technology transfer requires careful adaptation to the unique characteristics of the process and production environment. Early engagement with a CDMO partner will help develop a scaling strategy for the process before it becomes an impediment to later stage clinical progression.

Building on these operational complexities, technology transfers introduce additional unique challenges. Variability in supply chains, legal requirements, and temperature-controlled logistics can disrupt process continuity. A particularly sensitive aspect is the handling of living biological starting materials—such as donor-derived cells or tissues—which may require tightly coordinated logistics, time-sensitive collection, and sometimes initial processing steps before manufacturing. Maintaining material integrity, identity, and compliance throughout these steps demands careful planning and close collaboration across all parties involved.

### 3.2. Early Incorporation of an Analytical Strategy

Analytical strategy and method transfer is another major consideration for ATMPs that needs to be assessed early in development. Because ATMPs often rely on complex, non-compendial assays, method standardization across sites is

rarely straightforward. Transferring these assays demands not only technical documentation but also side-by-side validation, often requiring analyst training and inter-laboratory comparisons. Variability in instrumentation, materials, and even local interpretation of results can introduce critical inconsistencies unless carefully managed. Selection of a vendor with internal expertise and where required, an established 3<sup>rd</sup>-party network to meet these requirements, is crucial.

### 3.3. Evolving Regulatory Landscape for ATMPs and International Differences

From a regulatory standpoint, ATMPs are subject to highly complex and evolving frameworks. Regulatory authorities such as the EMA and FDA have detailed and often equivalent requirements. However, there are important differences between them that must be understood and considered during technology transfer, such as a Qualified Person's involvement in Europe and even the facility-specific design in relation to the FDA or EMA's requirements.

### 3.4. Selecting an Appropriate CDMO Partner

A key program strategic decision every company faces is where a program is to be launched and where it will be manufactured. For example – if a US company wishes to launch or expand to the EU, early consideration should be given to establishing an EU CDMO partnership. The global environment and advances with technology communication combined with built-in EMA alignment and supply chain considerations noted above are worth considering to avoid potential issues down the road with a challenging tech transfer and unexpected regulatory hurdles.

As transfers involve human-derived starting materials, differences in donor qualification requirements between jurisdictions present further obstacles. Regulatory expectations around donor eligibility, consents, traceability, serological screening, and documentation vary significantly between regions such as the EU, US, and other territories. These discrepancies can complicate import/export, impact timelines, and require bespoke risk assessments or additional testing to bridge the regulatory gap. Early understanding of these differences is particularly important to prevent downstream issues and ensure a smooth transfer process.

ATMP tech transfer demands more than documentation. It requires intensive practical support—joint manufacturing runs, hands-on operator training, and thorough process validation. A crucial element of this transfer is the execution of shared or comparative manufacturing runs between the sending and receiving sites. These collaborative runs enable alignment of expectations, thorough assessment of reproducibility, and early identification of subtle process variations. Comparative production is particularly valuable for cell-based products, where even minor deviations in technique or material handling can

significantly impact product attributes. Last but certainly not least, tacit knowledge—the practical, non-written expertise held by operators—is critical. Many ATMP processes are manual or semi-manual, and successful reproduction hinges on transferring this know-how effectively. This point is especially important given the inherent variability of ATMPs. The contribution and experience not only in manufacturing but also in understanding the significance of operators' hands-on knowledge is absolutely crucial. Without structured training and shared production runs, quality deviations are not just likely—they're expected.

Together, these challenges underscore the need for careful, collaborative, and expertly managed ATMP tech transfers within CDMO partnerships. Success depends on early alignment, mutual transparency, and a shared commitment to scientific and operational excellence.

#### 4. Facilitating a smooth ATMP technology transfer

- Successful ATMP technology transfer requires close collaboration and careful coordination between the sending and receiving sites to address the unique complexities of these products, ensuring quality and timeline alignment throughout the process.
- Strategic transfer planning - including setting realistic timelines and engaging the right teams at the appropriate stages—is crucial for success.
- Clear and open communication - regular, transparent communication between all stakeholders guarantee alignment, timely issue resolution, and smooth coordination throughout the transfer process.
- Partnering on the creation of critical documents — ensures consistency and clarity across sites, reducing ambiguities and supporting regulatory compliance.
- Bridging technology gaps - when documentation is incomplete or certain process steps lack definition, a transferring CDMO with integrated development support becomes invaluable.
- Pilot Batches and Bridging Studies- are a smart investment—they verify process consistency early and reveal potential issues before validation. Identifying gaps at this stage saves valuable time and prevents costly delays later in the project.
- Training and Shadowing- are essential to successful ATMP transfers. Practical experience builds confidence, ensures consistency, and helps teams replicate complex manual steps with precision.
- Navigating regulatory landscapes - quickly identifying critical differences between EMA, FDA and other requirements is key to avoiding delays. It will support efficient planning, timely updates, and sustained compliance during the transfer.

## 5. Closing thoughts: choose a Partner who knows the map

ATMP technology transfer is never just a copy-paste exercise — it is a complex operation that demands strategic thinking, regulatory insight, and true collaboration. In such a landscape, the right partner is not just a contractor, but a navigator — one who understands the stakes, asks the right questions early, and adapts with you as the journey unfolds. If you want to safeguard your product's potential, choose a partner who not only knows the map — but knows how to read the terrain.

---

[Bramble Bio](#) can help you overcome many of the issues highlighted above, including manufacturing, logistics and regulatory guidance. If you'd like to discuss any of our services, please don't hesitate to [get in touch](#).