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Streamlining Advanced Therapy Tech Transfer: Balancing Early-Stage Needs with Future Success

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The complexity surrounding advanced therapy manufacturing necessitates striving to achieve success through highly skilled precise handling, thorough analysis, and extensive standardization. Regulatory agencies have strict guidelines for cell therapy manufacturing to ensure patient safety and product efficacy; meeting these standards requires meticulous documentation, robust quality control measures, and adherence to cGMP.

Streamlining the tech transfer process should be a critical consideration for shortening overall development timelines. Ultimately, nearly every part of cell therapy development should focus on identifying critical process parameters (CPPs) and critical quality attributes (CQAs). CPPs must be monitored throughout early clinical trial phases ensuring CQAs are not impacted or compromised, thus generating product desired quality and efficacy. Product quality should be the salient point, and the focus of the tech transfer must be on the CPPs as part of manufacturing process risk mitigation. Other factors, such as experience and overall capabilities, can likewise create challenges for companies attempting to perform technology transfer.

Improved tech transfer will also serve to control costs, another critical variable for many small and emergent cell therapy developers today. By finding a CDMO partner that can foster a tech transfer approach centered on a well-defined and comprehensive road map, tailored to a company's capital and resources, and flexible enough to accommodate bespoke processes, cell therapy developers can reduce risk, curb costs, and maximize their molecule's chances of late-stage success.

Beyond Standard Biologics: Tailoring Tech Transfer for Bespoke Therapies

When it comes to tech transfer of an early phase process, time is one of the primary challenges nascent biotherapeutics companies face. Typically, it can take anywhere from one year to 16 months to perform tech transfer for a cell therapy product, and in that time, a company may be inundated with wide-ranging asks from a CDMO partner. This is often because, for biologics with more longstanding history in the space, the drive to optimize as much of a process as possible as early as possible is the standard for their development and scale-up, owing to the level of standardization that has been achieved when compared to more nascent advanced therapies.

For many of the highly bespoke cell therapies in the pipeline today, however, this type of early optimization and standardization is not only infeasible but also potentially detrimental to a program's long-term prospects. The needs and technical considerations that typify a cell therapy manufacturing paradigm are likely to change as a program scales; this, combined with the needs of the patient populations most often targeted by these bespoke drugs and the costs and time constraints associated with rework, make getting tech transfer right an important bellwether for these companies and drugs.

Likewise, expediting tech transfer for these therapies comes down to experienced personnel. While more longstanding modalities have more standardized or platformed processes, replete with automation and capable of being scaled into larger and larger equipment, many of the cell therapies in development today are produced using highly manual and open processes. This in itself requires well-trained and skilled personnel, but other key considerations, such as the volume of documentation necessary to a process and how to template it for use by a CDMO's personnel, can serve to slow tech transfer. Therefore, it is important to determine whether the CDMO has the experience, knowledge, and overall capabilities to perform the tech transfer in a timely manner and without any disruptions or delay in timelines, regardless of the state of the manufacturing process.

Tech transfer for cell therapy products today must focus on an asset's unique needs in order to prepare it for Phase 1 clinical trials. For open processes, a phase-appropriate approach can be established around controls for manual manipulations that meet GMP standards without revising a process significantly, but for other considerations, such as deep characterization, balancing late-stage wants with early-stage resource management can be challenging. This is important, as overextending resources to

try to establish commercial endpoints may be feasible for some applications but, for many, it creates undue risk in earlier development. Often, developers are urged to gather as much clinical data as possible as quickly as possible to attract additional investment. The right risk management, change controls, and validation and qualification work can create the sort of consistency an early-stage clinical process needs to progress, and the right CDMO can perform subsequent optimization to further streamline a process, even those that will require scale-out rather than scale-up.

Partnering For Expertise – Analytics Edition

The complexity of cell therapies often necessitates leveraging equally complex analytics to demonstrate their safety and quality. Depending on the application, an analytical approach may include multiple highly specialized assays and technologies, and transferring those analytics can prove challenging, depending on a CDMO's experience and bandwidth. These applications use a diverse range of analytical methods to assess a product's critical and key quality attributes, and often, developers leverage assays for deeper characterization early on, rather than just release testing. This can create a wide range of possibilities when it comes to an analytical paradigm, and a CDMO positioned to work with cell therapy modalities must be prepared to handle each in turn. Many of the methods employed by a company may not be fully validated, which is crucial to regulatory acceptance; moreover, a company may need to rely on a CDMO's expertise to develop additional assays.

Companies may or may not have well-established manufacturing and analytical processes in place prior to engaging a CDMO to perform tech transfer and scale. Finding a CDMO with the necessary capabilities to perform additional process or analytical development is therefore important; an end-to-end CDMO partner can help a company arrive at processes ready to be transferred smoothly and better iterate on processes downstream as needed for these modalities.

The Importance of Project Management – A Recipe For Success

Cellular therapy is complex, presenting its own set of development and manufacturing challenges even before moving processes between facilities, across working groups, and into different clinical phases. An adept and involved project management team plays an integral role in both the success of the technology transfer and in the strength of the overall product's program lifecycle. A robust project management team will establish clear, regular communication and project management structure as an essential component in a successful collaboration.

As with a technology team, the project manager leading a project should possess an in-depth understanding of the product and its requirements, but their involvement doesn't end there. Working independently of technical operations, a skilled project manager will utilize their knowledge of the organization's processes, capabilities and personnel, as well as their experience in moving therapies through development, to ensure things go smoothly, staying on time and in budget. This often begins before tech transfer takes place, with assembly and evaluation of available documentation on the product and overall project during knowledge transfer. Armed with this information, the project manager will conduct a gap analysis, timeline, and budget. This helps to allocate resources, identify and mitigate risk and ensure quality throughout the project.

Whether a customer is an early-stage company transferring a product from preclinical to Phase 1 trials or one closer to commercialization, a skilled project manager will understand a project's goals and develop a plan to get an application to its next milestone.

Conclusion

Comprehensive Cell Solutions (CCS), a CDMO focused on cell and gene therapy production, has positioned itself as a specialized provider of critical capacity for early-stage developers. Its platform-agnostic approach to cGMP manufacturing has been leveraged across the space on a range of different programs based in lentiviral vectors, plasmids, linearized DNA and mRNA, among others. Its team of expert personnel and more than 50 years' experience in blood operations, coupled with an extensive network of collection facilities in 17 states and partnerships with major hospitals, have made CCS a pioneering partner in the advancement of cell therapies.

From gap assessment to validation and GMP manufacturing and scale-up, Comprehensive Cell Solutions can offer cell therapy companies a right-sized approach to tech transfer that balances their application's near-term needs with their long-term goals. With additional expertise in process and analytical development and a proven track record of excellence, CCS can offer clients an expansive network of services, apheresis procurement, regulatory consulting, and ready capacity.

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