DARK HORSE CONSULTING

Our PROJECT & PROGRAM MANAGEMENT white paper mini-series continues with:

former Dark Horse, **Ryan Duffy**

ON THE TOPIC OF:

Key Considerations for Successful Technology Transfer

The end goal of Knowledge and Technology Transfer activities associated with a manufacturing process and analytical assays is moving the production, testing, and release of a Drug Product from one manufacturing location to another, while preserving the integrity of all components upon which the quality of the generated material relies. For a Cell or Gene Therapy, these processes and methods are often highly complex and reliant on multiple unit operations and process intermediates. To be successful they require the planning, execution, and oversight of individuals with deep domain expertise in the nuanced project management of such activities.

For early-stage development candidates, critical elements of the manufacturing process are often based on a limited framework of information. Further, the often still-to-be-determined analytical panel requires additional considerations that need to be well understood in order to be carefully managed, irrespective of the sending and receiving entities involved. For more established processes and methods associated with a candidate asset already in clinical development, the criticality of successful execution of Technology and Knowledge Transfers can be even more complex, while often more characterized.

While critical success factors associated with efficient Technology Transfer are numerous, this article focuses on five topics identified as arguably of highest significance, namely (i) effective, early decision-making, (ii) acknowledgment and assessment of risk, (iii) preparation of pragmatic, informed timelines, (iv) importance of developing and nurturing positive working relationships, and (v) building in appropriate quality systems to both enable visible control and alleviate negative impacts on cost, quality, and timelines.

Making an informed choice

Successful Technology and Knowledge Transfer is predicated on early and effective decision-making. The development of a robust and purpose-driven [Request for Proposal] enables informed navigation and decision-making regarding the numerous manufacturing options available, based on responses to a bespoke set of User Requirements and Specifications (URS). Some of the factors that must be thoughtfully scrutinized and evaluated include not only the manufacturing capabilities of prospective partners and their experience with similar drug products, but also quality systems and analytical capabilities, in addition to tenure, experience, and attrition rate of employees. DHC's industry-leading, unbiased quantitative [RFP Response] assessment is built by authors with a strong technical understanding of Cell and Gene Therapy aseptic manufacturing, testing, and release, to inform effective comparison and decision-making.

During discussions preceding partner selection, corporate milestones may be discussed to orient potential service providers. While it may be enticing to hear a rapid "yes" to proposed timelines, a service provider that demonstrates the ability to thoughtfully scrutinize, and even sometimes challenge, timeline assumptions should be appreciated. Far too often, service providers agree to timelines without discussion or pushback at the RFP stage, only to later fail to meet those timelines. A robust discussion of timeline assumptions during contracting generates confidence that both parties are aligned on expectations and have confidence in their respective abilities to meet their obligations to make those timelines a reality.

Another critical component that should precede the initiation of Technology Transfer is the development and agreement of a Quality Technical Agreement (QTA). This quality "road map" is fundamental to the success of your program within a C(D)MO and needs to be negotiated and agreed upon as soon as possible. During the execution of a program, the sending and receiving entities' quality organizations should work in concert during all quality-driven activities (e.g., deviations, change controls, audits, etc.), which require the determination and agreement of clearly defined roles and responsibilities, as well as communication and reconciliation

pathways to mitigate any potential challenges or delays encountered. In the latter stages of Technology Transfer, the QTA will be leveraged to ensure product disposition is executed to both the agreed-upon timeframe and established specification. Achieving alignment on this crucial activity early within the initial review of the document will enable effective scheduling of downstream activities, such as patient infusion, with informed confidence.

Comprehensive risk assessment and management

Once roles and responsibilities have been established and the relationship is set to commence, one of the first aspects to be considered is a comprehensive assessment of risk and its management. At the outset of strategic planning for this process, adequate time and resources must be applied to define success factors and develop plans to address identified risks.

Raw materials are a common source of potential risk and are regularly associated with delays and challenges to successful Technology Transfer. The establishment of a robust supply chain related to single-source components remains a significant challenge for the manufacturing of Cell and Gene Therapies. Even before the rise of COVID-19, it was best practice to identify secondary and tertiary vendors for components identified through risk assessment as critical. The importance of this practice has only been further emphasized by the supply chain challenges brought about by and prevailing well beyond the global pandemic. It is highly recommended that Sponsors work with the receiving entity during the earliest stages of Technology Transfer to develop a risk-based approach to materials sourcing and procurement, including the identification of the high-risk items within the Bill of Materials (BOM) and the development of mitigation strategies to ensure uninterrupted supply.

Establishing and nurturing an environment for success

Clients frequently enter into a C(D)MO relationship with pre-existing project timelines that have already been communicated to senior management, the board, and investors/shareholders. It is essential that these timelines, which the project Sponsor will be beholden to, are realistically constructed and as comprehensively informed as possible. If sufficient time has not been built into project timelines for the time-consuming and often critical path activities of process development, Technology Transfer, and cGMP manufacturing, the company is unlikely to be successful in achieving a significant value inflection in time to enable a subsequent round of financing.

Similarly, in the initial planning stages of a Technology Transfer, it is essential to create timelines that provide sufficient buffers for unforeseen delays. While you do not know exactly what will go wrong, for a highly novel product with a complex manufacturing process (as is true of most Cell and Gene Therapy products), not everything will go perfectly to plan the first time. Give your project team a chance to come together, triage, and overcome unforeseen impediments as they arise. For example, it might be a good idea to build in one extra Technology Transfer run than the anticipated required minimum, to allow for either a failed run or a supply chain-related cancellation/challenge.

When impediments do emerge, clear and succinct communication channels and decisive decision-making are central to expedient resolution. A communication and governance plan is an essential

tool that should be in place at the onset of a Technology Transfer and updated as the project progresses. This tool will outline the key stakeholders with whom accountability, responsibility, and decision-making authority lie, to take on specific challenges and drive remediation.

The pivotal relationship that defines success

Establishing and maintaining all aspects of a development organization's relationship with manufacturing partner(s) will directly and positively impact the successful execution of critical objectives.

Your chosen C(D)MO partner should be expected to acknowledge the inherent responsibility of providing top-tier service and support to each of its clients, ensuring that each feels valued and respected. Failure to agree on key responsibilities and communication plans at the outset of the project can result in a tumultuous relationship with negative consequences on overall progress and the potential to limit project momentum. If both parties continually invest in and develop this relationship, the resulting positive and collaborative environment will smooth the process of navigating the inevitable challenges. This includes committing to regular in-person interactions, especially during times of challenge. Consistent transparency regarding expectations and clear, timely communication are critical components of continued alignment.

At the project team level, ongoing responsibility for creating and sustaining momentum, setting the overall tone of the project, and nurturing a positive atmosphere throughout the duration of the program resides to a great extent with the respective project managers.

Quality early and throughout

A robust Quality Management System (QMS) is fundamental to controlling all activities related to manufacturing, testing, and release of a Drug Product, together with control for inventory management. Operating within an appropriate QMS is critical at all stages of the product lifecycle to ensure product quality, consistency, and (most importantly) patient safety. During the nonclinical stages of development and into Phase 1, adherence to relevant quality standards should be continually assessed and maintained relative to the development phase. For early-stage programs, the environment needs to enable nimbleness while defining and setting appropriate product specifications, establishing critical quality attributes, and developing a Quality Target Product Profile (QTPP). To capitalize on this period most effectively, we encourage Sponsors to adopt a phase-appropriate quality mindset.

Both the quality mindset and systems, together with specifications and the QTPP, need to mature as progress is made through the development life cycle. Throughout this maturation, Quality should be continually built into the manufacturing process and analytical testing by adhering to a QbD (Quality by Design) concept. During later stages of the product lifecycle, it is fundamental to have a manufacturing partner that can adequately assist with QbD studies, define risk, and remediate ahead of PPQ (Process Performance Qualification). These activities, all in preparation of a PAI (pre-approval inspection) and filing of a license application, require a robust, fully matured Quality system to be in place, in use, and in control. A thoughtful balance must be maintained between agility and control at each stage of development. Identification of a manufacturing partner offering a phase-appropriate QMS to support

this natural and necessary progression is essential to supporting success throughout the development and commercialization process.

Final thoughts

Technology Transfers represent both a critical endeavor in the lifecycle of any product and one of the most challenging activities—for development-stage organizations and larger organizations alike—to execute without failure or delay. Dark Horse Consulting can provide key support to ensure that the right partners are selected, informed plans (along with cohesive and pragmatic timelines) are developed, and execution against those timelines is driven with maximum efficiency. With the early identification of risk and continued development of mitigation strategies, we can alleviate strain on cost, scope, and time. By deploying our unmatched Manufacturing, Quality, and Regulatory expertise, we establish an environment for success on the path to approval for your Drug Product. Noting and acting upon the key success factors identified in this article will positively impact the likelihood of regulatory, clinical, and, ultimately, commercial success.

Dark Horse Consulting Group's

PROJECT & PROGRAM MANAGEMENT

white paper mini-series will also include papers on the topics of:

Effective P&PM for C&GT

by **Kevin Whittlesey, Ph.D.**
PUBLISHED!
Available here.

Facility Design and Build-Out

by **Phil Bowles, MSc**
PUBLISHED!
Available here.

Navigating Relationships in P&PM

by **Sara Masterson, MBA**

Device Engineering

by **Michael Kinzie**

P&PM Throughout the C&GT Product Lifecycle

by **Heather Todd, M.S.**

Visit our mini-series online

DARK HORSE CONSULTING

www.darkhorseconsultinggroup.com