Technical Transfer to CDMO – Case Study Best Practices for Success

Posted: May 20, 2018

By: *Sandra Wassink*

- Pharmatech Associates

Introduction

Technical transfer to a contract development and manufacturing organization (CDMO) mobilizes the efforts of a technical team, from start through commercialization activities and throughout the life cycle of a product. In the case we will describe, the selection process identified key areas that will need CDMO collaboration. Since this is a Phase II/Phase III product, several agreements to organize the efforts will be put in place. These agreements are development and quality agreements. The end goal is to provide all the details, the "good, bad, and the ugly" of the drug product to have a thorough transfer to the CDMO and be capable of building the design space and manufacturing the drug product. This article details the steps and considerations throughout the tech transfer, including risk assessment, and capturing information in development reports that prepare for regulatory submission.

First: There is Starting, and Running…

Technical transfer of a Phase II development project to a CDMO for Phase III clinical development and ultimately for commercial manufacturing is a daunting activity, only because there are so many steps along the way. Prior to beginning the process, the drug sponsor has gone through the CDMO due diligence selection process. A letter of intent (LOI) has been agreed upon and executed. So what comes next? The key departments (development, manufacturing operations, analytical, quality control, quality assurance) need to align from the start of the transfer, as they are implicated in the planning and execution of the drug product manufacturing all the way through to commercialization.

So, the sponsor should prepare a technical transfer package to share and review with the CDMO. While this complete download of the development history may not have been done during the due diligence process, it now needs to be performed to guarantee successful work, communication alignment, and continuity at the CDMO. The effort will start with the complete technical transfer of the development scale information to begin making the Phase III clinical supplies that will be used.

The key activities to cover at this phase in the technical transfer are the following: target product

CONNECT WITH US

RELATED CATEGORIES

Pharmaceutical Formulation Development »

Clinical Trial Development Services / Clinical Outsourcing »

FOLLOW PO

Keep up with our latest articles, news and events. Plus, get special offers and more delivered to your inbox.

Your Email Address

profile, drug substance, excipients, packaging components, critical quality attributes of the drug product and excipients, and the manufacturing process. Each one of these elements should have preliminary specifications and test methods identified.

Next, drug substance critical attributes need to be identified and controlled through the technical transfer process and subsequent manufacturing of Phase III and commercial product. The excipients will have specifications to ensure the drug product meets its specifications. If during development the excipient is identified as being critical to drug product performance, then controls need to be in place. If there is a critical attribute for an excipient - such as particle size - then it too has to be controlled and monitored and compared throughout the transfer and manufacturing of Phase III and commercial product.

After identifying the critical attributes for the drug substance and excipients and implementing a control strategy, then a manufacturing assessment should be conducted. Will the existing equipment be acceptable for manufacturing the drug product, or will it be necessary to purchase new equipment? Either way, a plan should be developed to confirm the existing or elaborate new manufacturing parameters on the equipment selected. Throughout the manufacturing development process, a series of various activities - risk assessments,[1] design of experiments[2] and identification of critical attributes - will support the technical transfer to the CDMO and aid in implementation of the drug product.

Based on this information package, the companies need to outline the elements of work for the transition from sponsor to CDMO. Executing a development agreement is an important document to lay out the transfer activities and responsibilities. The development agreement should be flexible as the transfer proceeds, but ultimately the outcome of the development efforts will be the bridge to the commercial activities and the final supply and quality agreements.

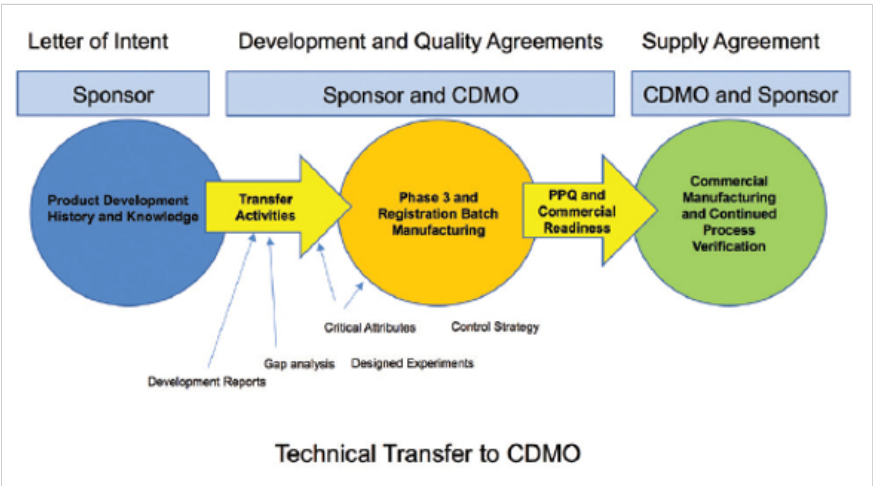

Figure 1. Risk Assessment

Ready to Manufacture Phase III Clinical Materials?

Once the information has been transferred, it is time to conduct a gap analysis to identify key items that can impact the successful manufacture of Phase III supplies. This could entail equipment comparisons, batch size scale-up, analytical capabilities, etc. Here, a strategy needs to be developed to handle any gaps. For example, if this transfer effort entails a scale-up from development to Phase III then a design of experiments should be developed. Prior knowledge from small-scale work can help simplify the design of experiments focusing on the critical parameters.

After the design of experiments (DOE) are completed, the new information can be utilized to continue to build the design space. At the point of manufacturing the Phase III/registration batches, the controls should be in place for drug substance, excipients and manufacturing process. Information on these materials and processes will continue to be gathered during Phase III manufacturing to facilitate defining the final proposed specifications and manufacturing processes.

The sponsor will prepare the regulatory application with the information from development through

The sponsor will prepare the regulatory application with the information from development through the manufacturing of the registration and clinical batches. The CDMO and sponsor will need to collaborate closely through this preparation process. What the CDMO "actually does" needs to be reflected in the filling. It can be an intense period preparing the filing and waiting for regulatory information requests. This will test both companies' professionalism and experience. A successful regulatory filing is the ultimate goal for both parties.

Ready for Commercialization?

Most sponsors elect to begin the Process Qualification (PQ)3 during the regulatory review period. The strategy for the PQ was included in the regulatory filing, and the approach was justified based on the product and process development history. Is the batch size for the commercialization to be the same as the registration batches? If not, then engineering batches should be manufactured to ensure the drug product meets the acceptance criteria. There may be a set of experiments at commercial scale to confirm reproducibility. Once the number of process performance qualification (PPQ) batches is determined, the Master Validation Plan and the PPQ protocols can be prepared.

The successful completion of the PPQ batches is not the end of the road for commercialization. Once commercialization begins, continued process verification practice must be in place. This is to ensure that the process remains the same during and throughout commercialization. It is important that this continual process verification be included in the quality agreement.

Alpha and Omega

In the very beginning, the sponsor had a small-scale development product. They transferred the product to a CDMO for Phase III and commercialization. It seems so simple, yet there are a great many steps along the way. The success in manufacturing at the CDMO is reliant on full disclosure of early development history, collaborative fine-tuning of the critical attributes through Phase III and continued teamwork into commercial manufacturing. These key factors for success are laid out in agreements but ultimately the flexibility, experience and professionalism of both companies is required to achieve safe, consistent and quality product commercialization.

References

1. Reference Q9 Quality Risk Management, June 2006 http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/09/WC500002873.pdf
2. Reference Q8 (R2) Pharmaceutical Development, November 2009 https://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Quality/Q8_R1/Step4/Q8_R2_Guideline.pdf
3. Reference Guidance for Industry Process Validation: General Principles and Practices, January 2011. https://www.fda.gov/downloads/drugs/guidances/ucm070336.pdf

COMMENTS

ALSO ON PHARMACEUTICAL OUTSOURCING

Managing Cold Chain Distribution Across the Global Supply Chain: …

1 comment • 2 years ago

Jayshree Makadia — While cold chain 3PLs may be incentivized to deliver more reliably while staying cost-efficient for …

The Rise of Patient Engagement in Clinical Trials | Pharmaceutical …

2 comments • 2 years ago

Shahz from Mosio — Thank you for this, Chris! Yes, adherence programs are part of patient engagement. Any patient touch …

When Things Go Wrong: Planning for the Unexpected | Pharmaceutical …

1 comment • 3 years ago

Dr. Ningaraddi Belavagi — The article is very informative and is very real.....All chemists who reads it likes a lot.

The United States Pharmacopeia (USP) New Chapter on the Storage and …

2 comments • 2 years ago

SONJA HELENA BORGES — Thank you for clarification. It helps me to speak on my courses in Brazil. This discussion is very …