After the Scope of Work is Complete

After the work has begun and after the quality and regulatory management phase has been addressed, there are still many activities that must continue. *This is the final installment of a four-part series of articles addressing best practices for a successful relationship with your service partners.*

LISA COZZA - PRINCIPAL CONSULTANT, TUNNELL CONSULTING

In our fourth and final installment, we continue our discussion of how contract service providers are an integral part of your process from beginning to end. We will discuss the situations that many don't think about when the partnership is just starting out because they happen after your first scope(s) of work are completed.

In our last three installments, we discussed how to select partners and negotiate contracts as you enter the relationship, how to negotiate the delivery phase and build a productive collaboration, and how to understand quality and regulatory management issues and challenges. As most firms today rely on external contract service support, overpromising and organizational misalignment may be an issue and must be planned for, along with how success is measured to create a successful path forward and a win-win solution.

In this fourth part, we will discuss what happens after the work has begun and after the quality and regulatory management phase has been addressed. This includes ongoing stability testing and investigations, change controls and updates to the BLA or NDA, critical material and equipment management, resins/filter storage, data management and keeping staff on top of any process or documentation revisions that will occur during the perceived "quiet" time between operational execution and sunsetting the relationship.

Once you have released and received your product, whether it is bulk API or BDS, or final filled product, the job is far from over with your partner. Here are some of the most common challenges that partners face long after the product was released.

STABILITY

Most CDMO partners are executing your stability pulls and testing protocols. As the sponsor, you must keep your own calendar of the pull dates and testing requirements. This is important because your CDMO could miss a pull in the time

window specified in your stability protocol. In our experience, stability programs tend to surprise sponsors when deviations occur. Since all this data is eventually presented to the agency via updates to your IND, BLA or NDA, it is very important to be vigilant with stability. It is also possible to get OOS (out of specification) during stability. An OOS event can become a major or critical deviation if no root cause or unresolvable cause is determined. This is why keeping project management on the project even after the production part is completed is very important.

UPDATE TO FILINGS

Each year at a minimum, you must update your filings with the agency. During the year, you would update the stability results, any major process changes, and any major investigation results as well as any ongoing Post Marketing Requirements and/or Post Marketing Commitments that the agency requires after approval. Although most firms have a regulatory team, in some small virtual companies, these updates can come as a surprise.

DATA MANAGEMENT

Many small virtual companies tend to rely heavily on their partners for data management, data storage, and quality management systems. This is a mistake. The sooner you build your own data and document repository, the better off you will be. This information is the historical record of your product and process. It must be readily available and owned by the sponsor. A simple SharePoint and Excel system will suffice. You can purchase an off-the-shelf QMS system that will ensure you meet agency standards. The quality systems analysts will focus on assessing the maturity level and culture of your QMS. This should address the design and development of an effective QMS, global QMS management, SOP authoring support, QMS optimization, root cause analysis and continuous improvement including CAPA management, quality risk management and QMS maturity level assessment.

MANAGING CRITICAL MATERIALS AND EQUIPMENT

If the plan is to perform additional production with your partner, you must ensure that you have a robust cGMP process for storage and ongoing maintenance of process specific materials and equipment. This includes appropriate storage, equipment maintenance records and long-term storage protocols for product contact materials, such as columns, resins, UF membranes, etc. This may even require changing out storage solutions and documenting the process with cGMP protocols. You also must keep an eye on expiry dates of materials and ensure that any replacement materials will be ordered and received in time for the next campaign.

PRODUCT AND SAMPLE MANAGEMENT

After production, some of your materials will not be needed right away. Your partner will have storage fees outlined for long-term storage—typically one to three months after full release—but some may not have the capacity to store your product long term. Make sure you understand that situation and if necessary, prepare to move your materials to a cGMP storage facility that has the proper storage conditions. The same is true for retains and in-process samples that are not required as part of the batch documentation. If you want to keep these samples, you may have to find alternative storage locations. If the CDMO does keep your samples and materials, make sure they have a robust management system. You should perform routine inventory verifications and perform them in-person if the product is high value and very likely to be used in the future.

STAFF

It is common that staff in CDMOs move rapidly up or out of the firm. If you wait a full year, you may be shocked by the turnover of the team that worked on your program. If you are the sponsor, you will need to make time to work with the staff at the CDMO and perform training and/or some lectures on the nuances of your program. Providing information to the folks who do the work as opposed to just the leadership will go a long way in developing relationships. Get to know the supervisors and shift leaders. Let them ask you questions or provide observations about what they remember as challenging aspects of executing your process. Buy pizza and/or great Italian subs to show your appreciation as your campaign start date approaches. If a year goes by since your last production slot, you will have to do a mini-knowledge transfer all over again.

CDMO AND CRITICAL MATERIAL CHANGE CONTROLS

It is important that you take CDMO change notifications seriously and you must review each one. They could impact your process and if they do, you must perform an impact assessment and possibly update the filings. This is true for facility or equipment changes or upgrades. Direct product contact material changes may come from 3rd party vendors but still must be evaluated for impact.

SUNSETTING

When the clinical results do not support moving a program forward, you must consider how to sunset the relationship with your partner. In most cases, there will be very little new work to be done and decisions must be made on what to do with cancellation provisions, equipment, excess dedicated materials, staff reductions (if necessary) and all the historical data that is maintained within the CDMO. Hopefully the contract has cancellation provisions detailed in the MSA, however most of the time there will be nuances that are not in writing. If you had a good partnership and supported each other through the process, the exit will be less painful. There is no winner when projects fail, but when each party does what it can to minimize

the financial stress, it leaves the door open for the next project.

As we wrap up this series, remember that your partner is part of your process. Keeping that in mind and having a dedicated and educated project manager to oversee all the key parts of a successful project and using expert talent to navigate all the CMC challenges that face both partners will help ensure you have the best possible experience. Mitigate all these risks by:

- Employing an experienced Project Manager
- Engaging expert talent full time (or temporarily) to help manage analytical and process challenges
- Auditing and mapping the whole process, from cell bank storage through data and retain storage
- Understanding QMS requirements and ensuring both the sponsor and CDMO have reliable systems
- Staying current with stability pulls and results, and updating the filings each time point, to avoid falling behind
- Working as partners to ensure knowledge transfer is adequate and continuous as staffing changes are inevitable

Too often companies on both sides of the partnership will take a penny-wise, pound-foolish approach by trying to navigate complex situations without expert talent. What may have cost $20,000 may end up over many millions in lost product, lost revenue or excess costs, and worse, significant program delays.

There are several stages to a successful relationship, before, during and after the contract has been signed and success is dependent on a solid contract provider strategy, your company's operational strategy, core capabilities, corporate culture, and the ability to support a supplier ecosystem that may span multiple locations. Be a good partner. Seek expert advice and make sure you have the talent to make the right decisions. **CP**

LISA COZZA is a seasoned executive with over 35 years' experience in biomanufacturing and cGMP operations, quality, and supply chain for bulk drug and final drug product in all stages of clinical and commercial production. She also has extensive knowledge of operations leadership, lean process improvements, external supplier management, CDMO contract negotiations, business development, sales and marketing and alliance leadership. Before rejoining Tunnell, Lisa was COO at Ridgeback Biotherapeutics, VP at Catalent, Executive Principal at BDO, Executive Director at AZ and spent 9 years with Human Genome Sciences and 9 years with Lonza Portsmouth, all in roles that directly worked with CDMOs.