Avoiding Sponsor-Supplier Relationship Pitfalls

The right CMO-sponsor relationship can result in mutually beneficial outcomes

Relationships between contractors and sponsors have traditionally been fraught with issues and tensions. A good relationship can lead to success for both parties, while a bad relationship might spell disaster for one or both parties. Recently, the FDA issued a Warning Letter to a contract manufacturer that manufactured toxic materials on the same line as a drug product. The FDA also issued a Warning Letter to the sponsor of the drug product, citing, among other things, that the sponsor needed to ensure that their drugs were manufactured so as to assure safety, identity, strength, quality, and purity of the drug product. This is an example of the contractor/sponsor relationship gone bad.

Not all issues are as significant as the one indicated above, but still deserve to be addressed. What can contractors and sponsors do to minimize the potential hazards? What are the complex problems that require increased communication and attention?

Sponsors can minimize potential issues by first choosing a quality supplier. There's an old saying that "cheap and good don't always go together." Never is that more apparent than in the choice for a contract manufacturing organization (CMO). Don't get me wrong, price is important. A sponsor who can't make any money selling a product isn't going to succeed, but cost needs to be a factor, not the sole decision maker. A robust supplier selection process includes quality factors in addition to business factors. Many times, the supplier selection is complete before an audit is completed, and then everyone tries to "fix" the supplier. In situations where there is a specific technology or patent or some other specific factor that prevents selection of another supplier, then remediating the supplier is understandable. However, in the aggregate, involving quality early on is worth the effort. A supplier questionnaire, a supplier audit, and a robust quality agreement are key elements to start the process.

After making the commitment to one supplier, a sponsor can take additional steps to help make the relationship a success, such as having measurable metrics for the supplier, developing a communications plan, and implementing a balanced scorecard. Robust metrics and the balanced scorecard can help the sponsor anticipate potential issues, as well as determine the amount of effort and oversight needed. Developing a communications plan goes both ways. A frequent complaint we hear from CMOs is that sponsors don't communicate with them—that all the communication goes one way, and that the only time a CMO hears from the sponsor is when there is something negative to convey, or they want to schedule an audit. Consistent and effective communication with CMOs is key, not only to forging a good relationship, but also to heading off potential quality issues.

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The sponsor also needs to make sure that it doesn't try to impose its own quality system on the CMO. This will often lead to failure as the CMO tries mold to multiple quality systems. There are many ways to meet GMP requirements, and as long as the CMO complies with the requirements, the "how" shouldn't matter.

Increasingly, there are many sponsor companies that are "virtual companies", with no in-house manufacturing experience. Often, these companies are focused on sales and marketing, have minimal quality units, and even more minimal manufacturing personnel. This is a potential pitfall, and even the leanest virtual company could benefit by having strong, experienced quality and manufacturing personnel. This is important for many reasons, not the least is evaluating technical documents such as investigations reports. A virtual company with little or no quality or manufacturing expertise is left at the mercy of the CMO. This is not to say that the CMO is trying to do something wrong, but healthy discussion and debate among all stakeholders is one key to a robust and high-quality product. The need to have experienced quality and manufacturing personnel also applies to pharma companies that have a manufacturing presence in addition to outsourcing some products. Often, the responsibility for oversight falls to procurement or supply chain personnel who may not have the deep experience to provide input.

For the CMO, early partnering with the sponsor in terms of setting expectations and norms early on is key. Allowing the sponsor to visit the site frequently for meetings, project reviews, batch witnessing, and batch record review, among other activities, can foster a good working relationship.

The CMO needs to be honest in its capabilities and capacity. It shouldn't overpromise. And, as difficult as it is, it shouldn't let the sponsor push it into things it can't accomplish. If the production and release time is a certain time, then the CMO should not agree to a much shorter timeframe. The same goes for the capabilities.

Developing and, as much as possible, enforcing a sound, robust technical transfer process can help early on with process, product, and method understanding. Depending on the stage of the product, different types of information may be available. A product that has been made for 10 years has 10 years of annual product reviews, investigations, complaints, and institutional knowledge for the CMO to build on. Why should a CMO accept just a batch record for the transfer. On the other hand, a product in development may only have pilot scale batches manufactured to date, so development data is very important.

Changes happen. The CMO needs to communicate potential changes with a real quality impact to the sponsor and to provide enough information to satisfy the review—hopefully by someone with a technical background. The types of changes to be communicated before the change and after the change need to be outlined in the quality agreement, and the quality agreement needs to be a living document for both the CMO and the sponsor. Hand-in-hand with changes is continuous process improvement. Some CMOs are change adverse, so suggesting changes to improve a process may be an issue, however, that shouldn't stop a CMO from striving to improve process.

The CMO also needs to develop a communications plan. When does the sponsor need to know certain things, and when don't they need to know? This isn't to say that the CMO should "hide" things from the sponsor, but timely communication is key. Early partnering with the sponsor should alleviate some of these concerns.

Even the best CMO/sponsor relationship could hit a bump in the road. Deviations and batch failures are two of the most complex issues. These situations generally involve a lot of finger pointing and blame. However, if some of the topics discussed above have been implemented, then communication should be smoother and more effective. The CMO needs to be allowed to fully investigate and receive input from the sponsor as needed. Ultimately, significant deviations often come down to a decision about releasing or rejecting a batch. Care needs to be taken to assure that one voice doesn't drown out the other. In particular, the FDA has made it clear that the CMO is responsible for GMPs at its site, and the sponsor can't delegate its quality responsibilities (see for example FDA's "Contract Manufacturing Arrangements for Drugs: Quality Agreements – Guidance for Industry" (Nov. 2016)). Sometimes the CMO will take a position that the batch is releasable, and the sponsor doesn't agree, or vice versa. These situations can be like a landmine, and care must be taken.

Occasionally, sponsors make commitments to a regulatory agency that either the CMO is not aware of, or hasn't agreed to. This is particularly troublesome when the FDA visits the CMO for a PAI or general inspection. This could include method or specification changes, process changes, or other filed information. Due to the occasional lack of communication between regulatory and third party oversight in sponsor organizations and the CMO, this could have disastrous consequences ranging from regulatory citations, to withholding approval recommendations, to the inability to reliably manufacture a product. These situations can be avoided with frequent communication, and viewing the CMO as a partner, and not just a supplier.

Done right, the CMO-sponsor relationship can result in mutually beneficial outcomes, with profitability for both parties and a quality product benefitting the patient. Done wrong, the results could be disastrous. Many of the suggestions set forth above are little more than common sense, but implemented together, may help ease the tensions and pitfalls many companies experience. **CP**