

Getting the Most from Your CMO Relationships:

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Effectively managing multiple CMO relationships is critical to successful commercialization, product launch, and profitability.



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A Life Cycle Approach

For biopharmaceutical manufacturers, the relationship with a contract manufacturing organization (CMO) is much more than a typical customer-vendor relationship. CMOs provide products or services that have a direct impact on product quality and integrity, supply continuity, and cost. CMOs also play important roles in ensuring Good Manufacturing Practice (GMP) and other compliance requirements, and are typically subject to supply and quality agreements. Relationships with these partners usually span many years, and have the potential either to constrain a company's growth or add significant value to their business.

Because many biopharmaceutical companies outsource large portions, or even their entire supply chains, relationships with one or more manufacturers, fill-finish providers, and packagers, create a truly distributed supply network. For these "virtual" companies, effec-

tively managing multiple CMO relationships is critical to successful product launch, commercialization, and profitability. Because they lose direct control, these organizations must build a core competency in managing these multiple strategic relationships. While important areas of expertise may be outsourced, managing the overall supply chain is still the critical responsibility of the drug license holder.

CMO RELATIONSHIP CHALLENGES

In far too many cases, CMO relationships are established and managed without considering the strategic nature of these partnerships. Long-term business requirements are often neglected in the rush to establish short-term capabilities. Day-to-day operating principles are assumed to be known and understood without setting expectations and establishing specific processes. Future demand and technical and business

uncertainties are assumed, rather than explicitly addressed.

At one emerging biotechnology company, for example, an Active Pharmaceutical Ingredient (API) provider relationship was established early in the product's development phase by a team with no commercial experience, which had assumed that the supplier would be capable of commercial production of their product. It was not until the beginning of Phase 3 production that questions were raised about the CMO's ability to provide GMP product at commercial volumes, and the relationship had to be revisited to ensure a proper fit.

During the evaluation and selection process, much attention is paid to a contract manufacturer's technical capabilities, while establishing an effective working relationship and management structures are often overlooked or ignored. Common mistakes fall into several categories, including:

- **Lack of clear long-term partnering objectives.** Sourcing and partnering efforts, particularly at emerging companies, overemphasize tactical goals related to finding the required material or capabilities and negotiating a favorable price. Overall, longer-term objectives are rarely considered.
- **Incomplete or casual evaluation and selection process.** The selection process typically focuses on finding a supplier that meets technical specifications at the lowest unit price. A rigorous selection process is seldom followed and the selection decision does not thoroughly consider all factors.
- **Poorly defined working relationship.** There is often a lack of clarity

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about responsibilities, roles, processes, and metrics that will guide interaction between the two organizations on a daily basis. Additionally, there is usually not a plan for resolving issues.

- **Lack of business and partnership metrics.** Usually, there are no defined service or performance expectations or specific remedies for non-performance.
- **Lack of future flexibility.** Often, CMO relationships are defined too rigidly and can limit the ability of companies to adapt effectively as their business environment changes.

The causes of these problems are no secret. Many CMO relationships are established while a product is early in clinical or even preclinical development. At this stage, decisions tend to be made by product or process development personnel, with the goal of simply finding the required material or capabilities to facilitate further study of the product.

Even later in a company's development, employees who lead commercial sourcing efforts are not sourcing professionals, but are the same people charged with different roles in the ongoing clinical trial process. Stretched across multiple priorities and ill-trained for sourcing, they tend to focus the selection process on finding a supplier that meets technical and volume

specifications at the lowest unit price. In other cases, constrained resources may find the selection made for them by default. With time running short to build commercial supply relationships, one client found their options limited to their current supplier materials—not only because of sound technical business qualifications, but because they were the only source not requiring a technology transfer and could be viable with the required timeframe.

CMO LIFECYCLE MODEL

Emerging, established, and mature life sciences companies can foster both highly effective, as well as ineffective, CMO relationships and business practices. In the dynamic environment of most companies, decisions made about establishing and maintaining CMO partnerships can easily revert into a reactive, crisis-management perspective. To help companies establish and manage critical relationships, it is useful to consider the CMO relationship as a lifecycle. This perspective helps companies establish and manage these critical relationships. The model (Figure 1) consists of a business process view of each stage in the CMO lifecycle.

By viewing the relationship as a series of discrete business processes, consideration can be given to the downstream activities required at each stage. For example, language should be included in the contract that recognizes and allows a process to address issues in ongoing operations, as well as mechanisms for changing the scope and scale of the relationship in response to changes in the company's business environment.

In executing the model, it is also

Figure 1. CMO Lifecycle Model



recommended that companies plan for and engage the services of a trained sourcing professional to establish critical CMO and vendor relationships. Sourcing professionals bring a level of structure and rigor typically not found in emerging companies, in areas such as market analysis, financial analysis, supplier performance, and development.

CMO RELATIONSHIP BEST PRACTICES

Aligned with each stage of the life-cycle model are seven best practices for establishing effective and long-lasting CMO relationships:

1. Develop partnering strategies aligned with your long-term business needs.

An important initial step in establishing a CMO relationship is to develop a clear set of objectives for the relationship and the material or capability to be outsourced. For example ask these questions:

- Is this material or capability a core competency for our company?
- Do we ultimately intend to bring it in-house or keep it outsourced?
- Do we intend to develop alternate sources?
- Is this relationship intended to be long-term or short-term in duration?

Answers to these questions will require an understanding of the company's long-term business objectives and strategies, and knowledge of the technical and competitive environment of the material or capability to be outsourced.

A well-developed strategy will guide subsequent stages of the CMO lifecycle. For example, attributes of the partnership strategy can be included in the evaluation requirements. Negotiation priorities should be linked closely to the partnering strategies, and thereby aligned with the business needs.

2. Employ a structured evaluation and selection process.

For biopharmaceutical companies, the importance of a sound contracting process is made clear by the reg-

CMO evaluation and selection should be based on a formal, structured process that examines a comprehensive set of criteria. . . .

ulatory requirements for qualifying key vendors. And more recently, achieving Sarbanes-Oxley compliance provides additional incentive for rigor and due diligence in CMO selection and contracting. Base evaluation and selection on a formal, structured process that examines a comprehensive set of criteria beyond just technical capabilities and cost, including:

- Business requirements fit/gap
- Product and process technical capabilities
- Partnership attributes
- Total cost of partnership
- Risks

The selection process should include:

- Identification of qualified candidates
- A formal Request for Proposal (RFP) process and detailed examination of proposals
- Supporting capabilities and technology transfer plans

3. Clearly define the operating processes.

Often overlooked is a brief but critical set of activities designed to properly establish an effective working relationship with a partner. Reliable performance against mutually agreed upon goals depends on clearly articulated expectations.

"Without a doubt, the most difficult issues we have experienced revolve around the difference in quality or compliance standards between the CMO and the client company," remarked Mickey Koplove, vice president of the

Operations Network at Wyeth BioPharma (Andover, MA). "The implications are substantial, and affect both supply and financial payments. Significant effort must be given to working out these issues in great detail before anything gets signed."

The success of the relationship ultimately hinges on open communication and clearly outlined processes at the onset of the relationship. It is imperative to define expectations and responsibilities on both ends, implement a frequent review process, and work contingencies into the plan so that if something goes wrong, all parties know what to do.

Work together with the CMO to develop a Partnership Operating Framework, or a set of Joint Operating Procedures (JOPs) to avoid confusion and inefficiencies. A well-structured operating framework will clarify:

- Scope and goals of the partnership
- Individual roles and responsibilities
- Lines of communication and decision-making
- Issue resolution and escalation
- Performance expectations and metrics
- Annual budgeting and planning processes

While not typically included in the formal supply agreement, the framework may be referenced within the agreement as the mechanism, which will guide the day-to-day operating relationship. Development of JOPs should begin during contract negotiation.

4. Identify performance-based metrics.

An issue that consistently arises is the limited use of metrics and data for ongoing performance management of CMOs. Typically, there is a lack of formal processes established for periodic performance reviews, mechanisms for joint performance improvement initiatives, and joint ownership of improvements and benefits.

"One thing we would like to do

differently,” says Vin Kosewski, executive director of Supply Chain Operations for Sepracor, Inc. (Marlborough, MA), is “to build in stricter remedies and recourse for non-performance.”

Because of the complex and uncertain processing environment of many biologics and other pharmaceutical products, performance-based metrics are used, not to be punitive, but to limit liability, specify compensation, and provide alternatives in the event of real non-performance.

5. Leverage information technology.

A major challenge in managing CMO relationships is the lack of visibility of the CMO’s internal operations. Biopharmaceutical companies rely on contract manufacturers to act as an extension of the supply chain; the need for integration among systems, visibility into the supply chain, and reporting capabilities such as dashboards and scorecards, has never been greater. Inventory levels, lot tracking, and release status are the most commonly mentioned data elements requested by supply chain managers. By increasing proactive visibility into the manufacturing process, providing overall supply chain monitoring, and ensuring quick access to data, biopharmaceutical companies can accelerate supply cycle times, speed decision making, and improve overall compliance.

Information technology can be deployed in several ways, including portal visibility, data exchange, and true integration. Establishing the proper technology framework allows the outsourcing life sciences company to monitor production processes and status as closely as if they were internal, without the additional overhead costs.

6. Build in flexibility for changing needs.

Companies face enormous uncer-

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tainties in bringing products to market. Clinical and regulatory uncertainties, manufacturing scale-up risks, along with technical and demand uncertainties make planning for future requirements a daunting task. Unfortunately, managers at many emerging life sciences companies tend to believe they lack the leverage required to build flexibility into their agreements. When dealing with established CMOs, this leads to acceptance of terms mandating strict volume commitments and minimum orders, thereby limiting future flexibility.

While there are situations where leverage is minimal—specifically with low-volume products with complex requirements that only a few (or just one) contractors can satisfy—building flexibility into an agreement is not necessarily a win-lose proposition. Biopharmaceutical manufacturers should work with their partners in advance to develop creative strategies that provide some ability to accommodate changing business conditions. Flexibility to adjust to changing conditions can allow both parties to limit their exposure to downside risks, and enable them to quickly seize opportunities on the upside.

7. Re-evaluate the relationship on a regular basis.

Successful CMO relationships are long-term, mutually beneficial arrangements. While managers with foresight and insight will build flexibility into negotiated agreements, a key to ensuring success over time is

the understanding of what and when to change and restructure the relationship over time. We recommend a periodic re-evaluation of the partnership at regular intervals. Such an evaluation should include asking and answering the following questions:

- Are the objectives and strategy for this partnership still valid? Do they need to be revised?
- Is this CMO partner still the best fit for realizing these objectives?
- Does the current negotiated agreement encourage the partners to achieve beneficial results?

Performing such a re-evaluation regularly will enable emerging and established life sciences companies to adjust, expand, or phase out their relationships as conditions warrant, thereby keeping their CMO relationships relevant.

CONCLUSION

For life sciences companies that do not have the time or resources to build their own facilities, contract manufacturing provides a competitive advantage. Companies that integrate management of CMOs into their business model can quickly reach commercial scale, reduce capital expenditures, and attain greater overall flexibility. By applying a life-cycle framework and best practices, CMO relationships can be leveraged to manage overall business risks, accelerate innovation, and speed products to market. ♦

Quick Recap

- Success of relationships hinges on open communication and clearly outlined processes
- A well-defined strategy will guide subsequent stages of the CMO lifecycle
- CMO relationships should periodically be re-evaluated to determine their effectiveness

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