GLOBAL SELECTION CONSIDERATIONS FOR CMOS WHEN CONDUCTING DUE DILIGENCE

by Maxine K. Fritz

Due to the increase in outsourcing manufacturing materials and product to other countries, contract manufacturing organizations (CMOs) are often engaged for pharmaceutical product manufacturing. CMOs can offer a relatively low-cost, highly skilled and educated workforce, and with the convergence of global supply chains, it is not surprising that they continue to experience rapid growth.

This growth is sometimes aided by government incentives and the infusion of foreign and domestic capital. The industry is experiencing a period of expansion and consolidation among domestic players, while leading multinational companies also continue to expand their operations to outside the U.S.

However, deciding to use a CMO requires a thorough due diligence exercise conducted both as desktop and on-site reviews. This white paper provides the fundamental factors to consider when engaging a CMO.

CMO DUE DILIGENCE

Due diligence is the single most important activity when considering contract manufacturing. The use of third parties can help companies evaluate a prospective CMO's regulatory and quality capability, which includes the regulatory applications, facilities, utilities, equipment, manufacturing and supply capability, laboratory testing, warehousing and distribution.

The due diligence assessment should include a comprehensive legal, regulatory and quality systems review that includes an on-site inspection of the contract manufacturing site.

The review of any prospective CMO should consider, at a minimum, the following key questions:

- Are the CMO's financials sound?
- Is the management team experienced and competent?
- Does the manufacturer have experience providing contract manufacturing services to foreign customers and is it able to provide references?
- How easy is it to communicate (e.g. language, responsiveness to email or phone requests) with CMO management and project managers? Any potential contractual or quality issues will only be exacerbated by an inability to communicate clearly and engage readily.
- Has the site been inspected by a regulatory agency? Does it have a report from the regulatory agency indicating a successful inspection and current registration status?
- Does the CMO staff understand quality system/GMP requirements? Can they demonstrate that the quality system is in use?

- Does the CMO currently have the capacity, facilities, utilities and equipment needed to manufacture your product?
- Does the CMO manufacture antibiotics (cephalosporin, penicillin) or hormones in the same building as your products? Does it manufacture these products anywhere on the site? If so, is there complete separation and segregation of personnel, materials and equipment?
- Does the CMO have laboratories that can support in-process, finished product and stability testing of your product?
- Does it have a GMP training program? Is competency training part of its curricula?
- Does the staff understand deviations, including how to report and investigate them thoroughly?
- Has the CMO been the subject of any enforcement actions by SFDA, FDA or other relevant regulators? If so, have the underlying issues been satisfactorily resolved?
- Who will perform the batch record review and approval?
- Will the CMO sign a quality agreement?

The above questions are not all inclusive but should be considered as part of your due diligence.

In addition, your company's audit of the actual manufacturing site for your product should be performed by a qualified auditor(s) who is accompanied by qualified translator(s) (i.e. do not rely on the CMO for translation).

In order to protect customers, limit liability and maintain brand value, your company should take steps to ensure that the CMO meets quality requirements as clearly stipulated in the contract manufacturing agreements. In addition to the quality systems and regulatory compliance assessments/audits conducted as part of the due diligence process, there are factors to consider once you hire and start working with a CMO. Consider proactive approaches such as providing oversight during the initial manufacturing of your products, frequent visits and review of the quality test data and quality records to assure that your products are manufactured to meet your expectations.

In addition, provisions of the CMO agreement should include a Technical Agreement that contains your specifications and a Quality Agreement that includes the following:

- Provisions for frequent visits
- Oversight during the manufacturing of your products
- Requirements for approval of any changes to the facility, equipment, materials, components, etc. prior to implementation
- Notification of any initial out-of-specification (OOS) test results or stability failures
- The ability to evaluate any deviations and/or investigations
- The ability to review the manufacturing batch record

NSF's executive management team and expert consultants can help you with due diligence if you are considering contract manufacturing. We can help you evaluate and assess a prospective CMO's regulatory and quality capability, we have experienced and qualified auditors on-hand to audit manufacturing sites and we can also assist you when you start working with a CMO.

ABOUT THE AUTHOR

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