REGULATORY FOCUS

Legal Considerations When Outsourcing: Hold on Loosely, but Don't Let Go

By Alan Minsk, JD

In 1981, the US rock band .38 Special sang "Hold on Loosely, But Don't Let Go." This song lyric about love also holds true when considering whether to outsource regulatory responsibilities. Companies can attempt to contractually delegate to third parties, and it might make sense in many cases. However, it is important to recognize that a company regulated by the US Food and Drug Administration (FDA) remains on the hook to comply with the *Federal Food, Drug, and Cosmetic Act* (*FD&C Act*) and FDA's implementing regulations. That company also has liability exposure if a problem arises. This article, written from a regulatory lawyer's perspective, identifies some issues and lists some precautions that companies should consider when evaluating outsourcing opportunities.

Regulatory Outsourcing: Rationales and Risks

Several scenarios can lead to regulatory outsourcing. Virtual companies may lack the financial or personnel resources to take on complex regulatory responsibilities. Large companies might decide it is more efficient to outsource certain obligations due to concerns that bureaucracy might lead to micromanagement or over-analysis or, at the other extreme, things may fall through the cracks. FDA acknowledges that delegation of regulatory responsibilities, such as to a contract research organization, can occur. The agency recognizes the importance of quality agreements. For example, companies involved in contract manufacturing of drugs allow sponsors to use quality agreements to describe and delineate responsibilities and assure drug quality, safety and efficacy.[1] Nevertheless, FDA will not absolve a company that is registered with the agency, has its name on the product label or both, from regulatory compliance. Whether it involves lack of auditing or monitoring, failure to properly document compliance or a poorly drafted quality or distribution agreement, an FDA-regulated company cannot shift blame to another entity.

As noted, a sponsor simply cannot escape regulatory responsibility by merely shifting its obligations to another. However, the use of quality agreements and outsourcing obligations overseas may help the sponsor alleviate its burden by delegating some activities to another, so long as there is oversight and accountability.

Quality Agreements

Many companies enter into quality agreements with contract manufacturers or other third parties to delineate roles and responsibilities—such as maximizing acceptable product quality and quality management, to name only two—to ensure the safe manufacture of drug products. The agreement also describes communication between the parties and the documentation required. In fact, FDA encourages such agreements, as demonstrated by the issuance of a draft guidance document in 2013.[2] However, such agreements do not allow companies to abdicate their regulatory responsibilities. The quality agreement is not a substitute for compliance.

Furthermore, problems have arisen when the agreement was unclear as to which entity should be contacted regarding certain issues or there was a lack of specificity with timing or notice obligations (e.g., adverse event reporting or changes to product that could affect regulatory status). For example, quality agreement terminology such as "promptly" or "as soon as possible" fails to recognize FDA's requirements may impose specific deadlines. Such quality agreements can be a useful outsourcing tool, but clarity and specificity are needed to maximize regulatory compliance. This agreement attempts to outline those activities the third party must take (or not take) to produce quality products in accordance with the law, product specifications and best industry practices.

A quality agreement addendum that includes a matrix or chart defining primary and secondary performance roles can be helpful. However, problems have arisen when the chart identifies both parties as primarily responsible, which is either impractical or inconsistent with the terms of the quality agreement itself, or indicates the responsibility is shared. Thus, while the outsourcing effort is intended to be collaborative, the agreement can, at times, cause confusion.

An important provision in an outsourcing quality agreement is the company's ability to audit and monitor the provider for compliance. Too often, companies merely rely, to their detriment, on the other party's contractual obligation to perform. A handshake on a golf course or "we've been doing this for years" is not enough. Verifiable trust and oversight are musts.

Anyone can enter into a quality agreement, but it is the oversight, control and execution that maximize regulatory compliance.

Outsourcing Overseas

Production of an FDA-compliant product is usually an international effort. Active pharmaceutical ingredients, device parts or components and services frequently are outsourced overseas for commercial reasons. Commercial reasons, however, do not excuse or override regulatory compliance. There is nothing inherently wrong with this approach, but it is important to remember, at the end of the day, the sponsor/applicant must abide by FDA regulations.

Many companies fall into a false sense of security believing—or hoping—that because a foreign site has passed a local regulatory inspection, it will also pass FDA inspection. This is not necessarily true. FDA is increasing the number of foreign inspections, and failure to pass an agency audit can have devastating effects: product approval delays, Warning Letters or import alerts, as examples.

Outsourcing to foreign sites, whether for clinical or commercial operations, can have merit but, as previously noted, it is imperative to audit and monitor these sites to ensure compliance. Benign neglect and good faith trust are not enough.

Recommendations

Steps companies can take to minimize the potential regulatory risks of outsourcing include:

- Oversight, monitoring and involvement—Risk management should be used to determine the level of oversight and involvement for each step.

- Due diligence—With any outsourcing opportunity, the company should know its partner's ability to support FDA compliance and perform the job. While much of the company's compliance information is publicly available, the potential partner should be asked directly for any FDA-related enforcement correspondence (e.g., FDA-483 inspectional reports, adverse event reports, Warning Letters).
- Obligations should be described in writing, with specificity and detail, and considering the "What if?" scenarios. In addition, the company should ensure that communication between parties is frequent and clear.
- Adherence to the law—The company should be familiar with regulatory obligations and FDA's interpretations of such obligations (looking at others' enforcement examples is useful).
- Proactive planning—As noted above for oversight, knowledge of law and due diligence.
- Verifiable trust—Presumably, outsourcing should lead to cooperation and collaboration, so companies should negotiate in good faith, be flexible but detailed, listen to one another and share information in an open and timely manner. At the same time, the company should verify, challenge and stand its ground, as appropriate, to ensure regulatory compliance.

The Bottom Line

This article has identified only a few areas where companies outsource. Any decision to outsource should be based on the situation, and this article is not intended to encourage or discourage the practice. Rather, the author has attempted to identify potential considerations and emphasize that outsourcing without verification, auditing and oversight can present regulatory and liability challenges. Failure to consider the worst-case scenarios and to be specific in communications contributes to noncompliance. Remember—companies should hold on loosely, but don't let it go. They don't want to lose control.

References

1. See, e.g., 21.CFR § 312.52.
2. *Guidance for Industry, Contract Manufacturing Arrangements for Drugs: Quality Agreements*. FDA website. http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM353925.pdf. Published May 2013. Accessed 25 April 2014.

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