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OUTSOURCING IN THE PHARMACEUTICAL INDUSTRY

Most if not all major pharmaceutical companies have outsourced, or are evaluating the benefits of outsourcing, one or more of their non-core business functions to a third-party service provider. Over the last five years, pharmaceutical companies have primarily been outsourcing all or part of their back-office information technology (IT) infrastructure, such as the mainframe, midrange, desktop or application maintenance functions. Recently, however, pharmaceutical companies have become more and more innovative in the types of business functions that they consider ripe for outsourcing. Functions that are being considered include human resources (operations or payroll), financial transaction processing (particularly accounts payable), procurement, distribution and logistics, and clinical data management.

Why Outsource?

Like with most other companies, the leading factors motivating pharmaceutical companies to outsource include:

- Overall cost savings
- Flexible/variable pricing (not fixed/dedicated resources)
- Access to a broad pool of competent, trained resources
- Continued and early access to state-of-the-art technologies and processes
- Rapid standardization or globalization

Outsourcing Options and the "Offshoring" Issue

There are several different types of outsourcing options to be evaluated. The most common options at this time are: "onshoring" (where the provider of services is in the same country as the recipient of services is located); "offshoring" (where the provider of services is in a low-cost country far from the country where the recipient of services is located, such as for U.S. companies India, the Philippines, China or some of the Eastern Bloc countries); "nearshoring" (where the provider of services is from a lower-cost country close to the recipient

country's borders, such as for U.S. companies Canada, Mexico or the Caribbean); and, finally, and likely the most common, a hybrid of all or some of these types (where a portion of the services will be provided onshore and a portion will be provided offshore).

As one may have gleaned from the recent electoral campaigns, offshoring is the most controversial of the various types of outsourcing, largely due to the perception that offshoring means the loss of U.S. jobs. Despite the negative press surrounding offshoring, leading analysts continue to state that most if not all major companies have considered it as a strategic sourcing option. With heightened focus on offshore outsourcing by internal management at all levels, it is important to understand the key due diligence and legal considerations unique to an offshore outsourcing transaction, as well as the current state of anti-offshoring legislation.

Due Diligence

One of the concerns that companies have about outsourcing is the implicit loss of control over a business function's day-to-day operations. This concern is heightened in an offshore transaction because the personnel responsible for the daily operations are not only not down the hall, they are not even in the same country. Because of the perception that the loss of control is greater when offshoring, the due diligence process around offshoring is often more comprehensive (and more lengthy) than that around an onshore transaction.

Key action items that should be reviewed as part of the due diligence of an offshore outsourcing company or a U.S.-based company with offshore operations include:

1. What is the financial viability of the offshore enterprise? What is the relationship with the onshore enterprise (if any)? How will disputes be handled? How will notices be served? Will there be an onshore presence for service of process purposes?
2. What are the business continuity options offered by the outsourcing service provider?

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Where is the secondary site? Can documents be moved between sites or back onshore?

3. What experience does the offshore service provider have in the U.S. market? Who are its U.S. references?

4. Does the offshore service provider have procurement and financial responsibility for obtaining certain software and hardware required for service delivery? Are there any specific requirements necessary to enable compatibility between customer and service provider systems? Does the service provider have expertise in all of the customer's technologies and processes?

5. What type of data, network and physical security infrastructure does the service provider have in place?

6. Does the offshore service provider have the ability to recruit a broad employee base to allow for growth?

7. Will there be a good cultural fit? Are there any language or cultural issues?

8. Can the service provider provide onsite resources if requested? What are the relevant visa/immigration issues? Which company is

responsible for the cost of travel when meetings or knowledge transfer is necessary?

9. What communication lines will the service provider put in place?

10. Does the service provider have the necessary language capabilities?

Anti-Offshoring Legislation

Slow economic recovery, coupled with increasing offshore transaction volume and election-year promises, has led to a flurry of legislative proposals intended to reduce or prohibit offshore outsourcing. At this time, at least 36 states have pending anti-offshoring legislation (with a total of more than 150 pending laws). The major categories of anti-offshoring legislation are set forth below, along with examples of each:

- **“Buy American” Initiatives:** No performance of state/federal contract work by offshore workers or non-U.S. citizens (e.g., Dodd Amendment; many pending state laws)
- **Offshore Call Center Law:** Any call must be rerouted to the company's U.S. call center if the caller requests (e.g., proposed N.J. law)
- **Privacy Initiatives:** No transmission of personal medical, financial or other data offshore without individual's prior consent unless offshore privacy protections are certified as adequate by FTC (e.g., H. Clinton-sponsored S. 2312)
- **Immigration Law Initiatives:** Proposed limitations on H-1B and L-1 Visa Legislation

The actual impact of any of this legislation is not known at this time. In the near term, it appears to largely impact outsourcing by government entities, but this may extend to government contractors and companies with government funding as well.

Unique Legal Issues

In addition to the myriad legal issues that arise in connection with outsourcing, there are several issues that are specific to or have increased significance in an offshore deal. Examples include:

- Data privacy
- Import/export laws
- Immigration issues
- Proprietary rights
- Local law concerns
- Enforcement issues
- Ability to relocate/terminate

Regulatory Compliance — A Key Differentiating Factor

The regulatory regime of the pharmaceutical industry mandates that both the customer and the service provider understand the specific compliance requirements applicable to the specific outsourcing transaction at hand. A key part of negotiations will involve determining which laws the customer and the service provider will be responsible for monitoring and complying with and how the costs will be allocated for changes required by new laws (including different interpretations of existing ones). Some questions to consider include:

- *Which company will be responsible for interpreting regulations specifically promulgated for implementation by the pharmaceutical industry?*
- *If the customer retains responsibility for interpreting such pharma-specific laws, how will the service provider implement them? Will the customer provide guidelines or protocols?*
- *Will the service provider have validation responsibilities? Will the service provider have to validate its own software and hardware? Will it have to validate customer software and hardware, or maintain already validated software and hardware? Will the service provider follow the customer's validation procedures? Who will determine when software or hardware has actually been “validated”?*
- *How will Sarbanes-Oxley compliance be handled? What are the service provider's responsibilities? A key issue that the customer's auditors will want reassurance on is the ability of the service provider to provide SAS 70 reports if and when required.*
- *For business processes, is the customer or service provider best suited for monitoring and complying with laws specific to the service (e.g., in HR deals, will the customer retain the legal compliance function or will the relevant employees be terminated or transferred to the service provider)?*

A Quick Checklist of Other Major Legal Issues

In addition to the industry-specific and offshore-specific issues discussed above, there are many other issues for legal, business and technical teams to consider in connection with an outsourcing transaction. A checklist of some of the key legal issues is set forth below:

- Scope of services
- Terms applicable to the transfer of employees and assets

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LEGAL AND REGULATORY IMPLICATIONS OF FDA'S MODERNIZATION OF PHARMACEUTICAL cGMPs

On September 29, 2004, the Food and Drug Administration (FDA) issued its final report on the Agency's two-year initiative to enhance and modernize pharmaceutical current Good Manufacturing Practice (cGMP) requirements. This initiative, termed "Pharmaceutical cGMPs for the 21st Century," was launched in 2002 to modernize the regulatory scheme for pharmaceutical cGMPs, which has not been significantly revised since its inception in 1978.

Because of the complexity of drug manufacturing, FDA has exercised extensive control over virtually every aspect of the product manufacturing process, which is part of and extends beyond the approval process. Consequently, pharmaceutical manufacturers have often been reluctant to change their manufacturing processes, equipment, and technology because of perceived, and sometimes actual, regulatory hurdles and delays in amending new drug applications, and demonstrating to FDA the validity of the new procedures. Notwithstanding this reluctance, significant advances have been made in manufacturing science, quality management systems, and risk management to improve manufacturing quality and efficiency. FDA's cGMP initiative was intended to remove the regulatory barriers to the adoption of these new manufacturing technologies.

The result of the Agency's cGMP initiative is the articulation of a new regulatory framework, set forth in a series of guidance documents, white papers, and policy positions, premised on quality systems and risk management concepts. More specifically, the guiding principles of the new regulatory framework are as follows:

- Risk-based orientation;
- Science-based policies and standards;
- Integrated quality systems orientation;
- International cooperation and harmonization; and
- Strong public health protection.

The most significant guidance and other documents promulgated to date address quality systems approaches, process analytical technology, and a risk-based model for inspectional oversight. Additional documents have been developed concerning a preapproval risk-based pharmaceutical assessment system, cGMP Warning Letters, aseptic processing, continuous

improvement in pharmaceutical manufacturing, process validation for active pharmaceutical ingredients, dispute resolution related to cGMPs, electronic records and signatures, and international cooperation efforts. Taken together, the new policies will have significant legal and regulatory implications for pharmaceutical manufacturers. Importantly, however, the Agency has not yet proposed any revisions to the cGMP regulations.

Modernization Approach

In the final report, FDA stated that it intends to take an incremental approach to modernizing the cGMP regulations, and that its new non-binding guidance is intended to "bridge" the cGMP regulations to a quality systems model, used initially in the medical device industry and other international standards such as the European Union GMPs. The guidance stresses that manufacturers are not obligated to adopt the recommendations, and that FDA is not raising the regulatory standards for cGMP compliance. That is, manufacturers that want to adopt suggested new approaches and systems will not be penalized or obstructed by FDA, and manufacturers that wish to maintain the status quo will not be required to upgrade their systems or make other improvements in order to be in compliance.

Enforcement Implications

Under FDA's risk-based approach, the degree of regulatory oversight of a given drug manufacturing operation will be based on a number of risk factors, including the extent of product and process understanding, the robustness of quality systems, the complexity of the process, the compliance status of the

manufacturer, and whether the product has a significant public health impact.

Manufacturing operations determined to be higher risk will be inspected more frequently, and such inspections will be broader in scope. For example, more regulatory attention will be paid to sterile drug manufacturing operations and drug manufacturers with negative compliance histories. On the other hand, manufacturers that can demonstrate that they have sufficient process understanding and effective quality systems may be subject to reduced inspectional frequency and scope.

Regardless of the inspectional priority for a given drug, FDA has instituted new processes to ensure a relatively deliberate approach to enforcement. FDA is continuing the current process for the review of Warning Letters by the relevant Center(s) and the Office of the Chief Counsel before issuance, and has clarified that Form 483 observations should not be used as cGMP guidance. FDA is instituting a new cGMP question-and-answer website, similar to the previous publication of *cGMP Notes*, to promote adherence to these principles. The Agency has also developed proposed procedures for resolving scientific and technical disputes related to cGMP inspectional findings, which involve a two-tiered system where resolution is first attempted at the Office of Regulatory Affairs or at Center level, with further review by a dispute resolution panel if necessary.

Manufacturing Improvement Implications

Through its guidance on process analytical technology (PAT) and quality systems, FDA is seeking to provide incentives for increased process and product understanding, to encourage industry to consider manufacturing issues during the early stages of research and development, and to continue process

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- Structure of and approval rights over project staff
- Responsibility for third-party consents (e.g., software access/use rights)
- Performance standards and benchmarking
- Regulatory compliance issues
- Approval rights over service locations (and right to force relocation)
- Ownership and use rights in existing and newly developed intellectual property
- Audit rights
- Rights to terminate

- Exit rights and termination assistance
- Applicable fee structure, including adjustment mechanism, inflation risk, tax responsibility and invoicing

Conclusion

The complex nature of outsourcing transactions requires that the customer's negotiating team be knowledgeable not only about the company's business and current and future service environments, but also terms applicable to such issues as asset transfer, employee transfer, data privacy, audit, insurance, regulatory compliance,

tax, business continuity and risk management. In order to achieve a good business and legal deal and construct a contract that has the flexibility to survive for the duration of the deal (which can be for as long as 10 years), the team must fully understand all of the many issues that can arise in an outsourcing transaction and be able to formulate reasonable positions and alternative approaches.

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optimization throughout the product life cycle. There are important risks and rewards for manufacturers in connection with the adoption of these recommendations.

The potential rewards include reduced regulatory impediments to changes in manufacturing and the implementation of new technologies, which FDA hopes will promote continuous process optimization and industry hopes will result in manufacturing efficiencies. This new technology will enhance manufacturers' understanding of their processes, thereby improving their ability to manage and/or reduce product deviations.

The risks of adopting PAT and quality systems approaches are generally short term and include increased investment in the technologies, systems, and human resources to

develop and implement these systems, more in-depth FDA inspections of the new systems, and an absence of predictability concerning Agency expectations of acceptable implementation of the new technologies. More generally, the risk of adopting PAT, and, to a lesser extent, quality systems approaches, is that these technologies/systems will generate significant additional amounts of data about the manufacturing process — if manufacturers do not have a comprehensive understanding of their process and/or do not have clear procedures for how to address out-of-specification results, there could be considerable negative regulatory and other implications, as described above.

Depending on the size and resources of a drug manufacturer, the risks and rewards of adopting PAT and quality systems will differ

somewhat. Larger enterprises, which can more easily absorb the necessary investments in technologies, systems, and human resources, are more likely to perceive the risks of adopting PAT and quality systems to be manageable, while smaller companies may view such investments and the related risks as more significant barriers to adopting these approaches.

Product Liability Implications

While FDA is seeking to encourage voluntary industry adoption of innovative manufacturing technologies and quality systems, the existence of related guidance recommendations may have the consequential effects of raising industry standards and subjecting manufacturers that do not adopt them to increased legal exposure, including product liability claims. Generally speaking, guidance recommendations, particularly those that have received careful attention such as those associated with FDA's cGMP initiative, often serve as the impetus for changes in industry practice and behavior that at some point become state of the art and represent the industry standard.

If a manufacturer chooses not to adopt these additional recommendations and a product it manufactures subsequently injures a consumer, the manufacturer may have difficulty demonstrating that its manufacturing operations are state of the art in the industry.

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