DPT Thought Leadership
Issue 2

ENSURING QUALITY & REGULATORY COMPLIANCE WHEN COLLABORATING WITH A SERVICE PROVIDER

INTRODUCTION

In recent years, the pharmaceutical industry has given greater priority and attention to quality assurance and regulatory compliance than ever before. With the FDA's heightened focus on safety, regulatory agencies are increasing their presence in the manufacturing arena to ensure Current Good Manufacturing Practices (cGMP) are top of mind, and sponsors are placing greater responsibility for meeting cGMP requirements onto their outsourcing partners. While both sponsor companies and service providers must adhere to robust quality standards and undergo regular regulatory inspections, manufacturers are ultimately held responsible by regulatory agencies when it comes to adhering to cGMPs.

RATIONALE

It is critical for pharmaceutical companies today to feel confident in the quality of services provided by their service providers and develop an effective, collaborative working relationship that ensures compliance. As early as the due diligence audit for choosing a service provider, sponsors not only look at the service provider's capabilities, financial stability, and experience, but are just as concerned about the service provider's quality systems and regulatory performance.

A recent survey of pharmaceutical and biotech leaders[1] found that strong regulatory compliance and reliability ranked the highest in their criteria for choosing an outsourcing partner. Unlike in the past, price was not the main driver of outsourcing decisions. Participants reported that success on these two criteria is predictive of quality, and gives them a strong understanding of the service provider's business stability, dependability, and ability to fulfill projects.

This paper reviews the importance of ensuring compliance in outsource partnerships, strategies for choosing the right partner and implementing an effective Quality Assurance (QA) program, and working together to continuously make improvements.

Ensuring Compliance in a Changing Environment

Three industry trends have focused greater attention to quality and regulatory compliance in outsourcing partnerships — increased outsourcing by pharmaceutical companies, industry globalization, and a heightened, more complex regulatory environment.

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Historically, pharmaceutical companies have kept a majority of their functions in-house, preferring to maintain control and privacy in a highly regulated, competitive industry. Outsourcing was an option for companies looking for efficiencies, expertise and cost savings.

In the 21st century, the industry landscape has dramatically changed, with increased pressure to ramp up shrinking pipelines and margins, reduce costs and time to market, and produce innovative new drugs in a challenging economic environment. These shifts have created new comprehensive approaches to R&D and manufacturing that have enabled companies of all sizes to recognize the benefits in partnering with a single-source provider, and expand their outsourcing in order to remain efficient, competitive and viable.

According to the 2011 *Contract Pharma* Outsourcing Survey, nearly half (49%) of all industry companies reported that their outsourcing spending grew in the previous year. And 54% of companies expect their outsourcing spending will grow in the coming year, particularly big pharma (57%), emerging biopharma (69%), top ten biopharma (61%) and generic companies (78%).[2]

Other trends driving heightened attention to quality are industry globalization and greater government oversight and regulatory requirements. Sponsors are responsible for ensuring that their outsource companies are fully compliant with regulatory requirements in all U.S. and global sites related to their contracted services.

With an increased focus on drug safety, agencies such as the U.S. Food and Drug Administration (FDA), with new management, budgets and resources, have increased their scrutiny. When Margaret A. Hamburg, M.D. was appointed new Commissioner of the U.S. Food and Drug Administration (FDA) in 2009, she announced plans for a stronger FDA, with a greater focus on ensuring regulatory compliance and safety, and increased FDA oversight. She stated that the FDA would take a more aggressive approach in dealing with drug companies, including greater scrutiny and faster action to speed up enforcement in order to ensure access to safe and effective drugs.[2]

Since then, companies have been devoting greater attention to ensuring that both their company and outsource partners are fully compliant. FDA has expanded its inspection teams and is conducting more risk-based inspections. Sponsors and their contract service providers alike are experiencing an increased frequency of inspections. Service providers — who are involved with the development, site transfers, and launching of many new products — are considered in a higher-risk category, and therefore likely to be inspected more often. Both partners must be inspection-ready at all times, and able to demonstrate compliance and adherence to quality standards.

There are three elements to consider to ensure optimal compliance and product safety, purity and potency: careful choice of a service provider, effective management of the partnership, and a mutual commitment to constant improvement.

Choosing a Service Provider

Careful choice of a service provider is the essential first step to ensure high quality services. Today sponsors review a service provider's quality programs as early as the due diligence audit in the selection process. They seek partners who adhere to cGMP regulations and other regulatory requirements and have strong quality management systems. They also look for service providers who have robust operating procedures, thoroughly research suppliers and inspect raw materials, investigate product quality deviations, and maintain reliable testing laboratories. The provider should have and follow current rigorous standard operating procedures (SOPs) and best practices.

In addition to looking at basic qualifications, capabilities and costs, pharmaceutical companies should assess the following in their audit:

- Is the provider's regulatory compliance record stellar, demonstrating its knowledge and understanding of the approval process?
- Are the service provider's quality management systems (QMS), operating practices and resources current, robust, and up to the sponsor's standards at all provider sites?

- Does the provider have a competent, highly qualified staff, from machine operator to senior management?
- What global regulatory organizations regulate the service provider, and what is the service provider's record of performance? Is the provider knowledgeable about regulatory requirements in the countries where the product will be sold?
- Is the provider a secure business that invests sufficiently in maintaining up-to-date technologies? Is it capable of providing accurate, comprehensive, timely information?
- Can the service provider demonstrate work excellence, a commitment to quality, continuous improvement, and satisfied customers? Does it have an excellent reputation in the industry and a history of successful projects?
- Are you satisfied with your review of the provider's SOPs for the services you intend to outsource, the results of previous audits and regulatory inspections, and your inspection of the QMS, operations, plant, and production records?
- Will the provider be a good fit with your corporate culture? Are you comfortable with the provider and is there good chemistry with the team assigned to you?

Effective Partnership Management

An effective partnership involves establishing a clear, comprehensive quality agreement; transparent communications, and a system of measuring results.

Establish a Quality Agreement. The first step in effective partnering to ensure compliance is for the sponsor and service provider to establish a quality agreement that describes the scope of required services, quality specification responsibilities, quality management strategy, and communication mechanisms. The agreement should clearly define roles, responsibilities, and approvals, and state specific expectations.

The agreement should also define the level of sponsor involvement. Larger pharmaceutical companies, for example, typically share their own set of global quality standards with their service providers and expect them to adhere to their clearly specified critical compliance requirements. Mid-tier and smaller companies typically rely on the quality standards of the service provider.

Other important contents of the agreement are clearly defined ways of handling and communicating deviations and errors, cGMP compliance requirements and methods of QA oversight by sponsor and service provider.

Transparency Is Critical. Another essential requirement for partnership success is clear, frequent, open communication and collaboration. Transparency is critical to ensure compliance and maintenance of quality standards. Regular planning and review sessions should be held and IT systems kept current to ensure that each party is fully informed of the project status and potential roadblocks.

Any current or potential quality issues should be shared between partners immediately, so that they can quickly react before a bigger problem arises. Both parties should have robust procedures in place for quickly informing the other partner about all deviations, complaints, adverse events, test and investigation results and corrective actions. Rapid identification and immediate mutual resolution of issues in a positive manner will help prevent quality and compliance problems, and keep the partnership running smoothly.

Both partners should establish an information infrastructure that includes data-sharing systems, dedicated management contact people at both parties, and periodic meetings and reviews. The sponsor must have access to the status of their project at all times. Companies with advanced quality data management systems can quickly track information, such as deviations, corrective and preventive actions (CAPA), investigations and change control procedures.

Partners should arrange for periodic visits to inspect the development or manufacturing of the contracted product, monitor and audit the service provider's operation, and should perform an annual product quality review. The sponsor must ensure that QC testing is done with qualified methods and production/testing records are complete.

Evaluate Results. The best way to keep track of a project's progress is to mutually establish performance measures that can be easily quantified. Success can be measured by setting key performance indicators (KPIs) at different levels of production. The KPIs should be specified in the service agreement. Also your service provider should be proactively alerting you about the latest industry news and forecasts that can affect your product, and providing suggestions for improvements.

Example of Effective Partnering for Compliance

As an example of how a service provider works to ensure compliance and quality excellence, DPT Laboratories, a contract development and manufacturing organization, shares its quality and compliance management practices. DPT has a rigorous, transparent QMS program with advanced technologies to support its internal quality practices and communications with partners.

DPT communicates regularly with each client to review the status of services. Each client has a designated point of contact on both the business side and in QA. Updates of service status include weekly calls that address all quality-related matters and monthly or quarterly quality management review meetings. During these meetings, DPT's quality and regulatory representatives and the client's management representatives review KPIs relating to quality, and discuss any issues or suggestions. All clients are entitled to a two-day audit of DPT operations once a year. During the audit, the sponsor reviews manufacturing performance, deviations, facilities, and consumer complaints, as well as SOPs, training, and batch records, and inspects the facility. The sponsor then gives DPT a report of its findings and DPT addresses any concerns.

As a convenient means of communication, DPT establishes an interactive e-Room® for each client, a private secure Web space where both DPT and the client post documents and communicate about a client's products. The documents may include test data, executed batch records, pertinent industry or product updates or other applicable information. Both parties can then access and respond to the information at any time. The e-Room® also facilitates reviews by enabling clients to edit and return a posted record review, and reduces email traffic.

Internally, DPT conducts monthly qualitative metric reviews at the highest level of management, and performs systems reviews quarterly and annually. DPT's quality organization has more than 150 personnel, who cover every aspect of quality control in all service areas. QC representatives thoroughly inspect every incoming component and ingredient, and are integral to the manufacturing process, providing verification and serving as the first line of defense on quality issues. In addition, several laboratories test the product at various points. The release group looks at all records and batch quality before the product is released to the client. QA, the umbrella department, oversees the entire process.

DPT utilizes a number of integrated electronic systems to enhance communication and visibility throughout the organization. One of the electronic systems is a Quality Information System (QIS) which was developed in-house to compile data from the entire quality organization and generate a single document for the client. This system generates laboratory worksheets which include customer and product specific information. This eliminates the use of hand-written notebooks, reduces compliance exposure and streamlines the QC process. TrackWise® Quality Management System (QMS) is also used at DPT to track deviations, complaints, investigations and Corrective and Preventative Actions (CAPAs). In addition, TrackWise® manages change control, audit tracking, and training management. Documentum®, DPT's document content management system, is also integrated with TrackWise®

and QIS. Combined, these systems provide a strong foundation for an unparalleled compliance record.

CONCLUSION

In today's more complex, global industry environment, with greater outsourcing by pharmaceutical companies of all sizes, it is more important than ever to be extremely vigilant about compliance and QA to ensure product safety. Successful partnering for quality and compliance excellence involves careful choice of a service provider, an effective partnering strategy, a clear quality agreement, complete transparency, and a collaborative commitment to success. The service provider, along with the sponsor, should be forward-thinking — always looking to the future for continuous improvement, greater time and cost efficiencies, and opportunities to enhance their quality systems. Having these elements in place helps ensure a successful partnership, an excellent compliance record, and the production of safe, effective products.

REFERENCES:

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ABOUT DPT LABORATORIES:

DPT is a contract development and manufacturing organization (CDMO) providing companies the best solutions to their sterile and non-sterile pharmaceutical development and manufacturing needs through innovation, technology, and service. Specializing in semi-solid and liquid dosage forms, DPT has a reputation for quality, unmatched technical expertise, extensive manufacturing capabilities, and an exemplary regulatory compliance record. With five cGMP facilities in San Antonio, Texas, and Lakewood, New Jersey, DPT offers full-service outsourcing solutions, including stand-alone development, site transfers, state-of-the-art manufacturing, packaging, and worldwide distribution.

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