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## OUTSOURCING

### Global Contract Manufacturing Avoid Pitfalls of Picking a Contract Manufacturer

By Michael Kosko and Macdara Lynch



Contract manufacturers can accommodate many sterile project types, from lyophilized and aseptic filling to a wide variety of vials, and pre-filled syringes to blow/fill/seal services.

#### Outsourcing allows a company to be flexible and competitive

Historically, the pharmaceutical industry has abided by the philosophy of sell what you make and make what you sell. Over the last five to 10 years, however, the concept of outsourcing has made considerable inroads into manufacturing, largely because manufacturing now accounts for nearly 25% of company costs. Recent data indicate that the global contract manufacturing organization (CMO) market has grown into a \$20 billion industry and is expected to show an annual growth of approximately 10% for years to come.<sup>1</sup>

According to a survey published earlier this year in *Pharmaceutical Formulation & Quality*, many pharmaceutical companies are stepping up their outsourcing activities due to increased cost containment pressures in the current global economic crisis.<sup>2</sup> Respondents also cited the growing number and complexity of projects; need for specialization; ability to free up in-house resources for other projects;

and improved flexibility in terms of supply chain, timelines, and regulatory management as other key factors in the decision to move outside the parent organization.

Companies with capacity constraints or in need of a unique technology that does not already exist within their current infrastructure are prime candidates for contract manufacturing. But a number of other industry-wide developments are propelling the move as well. For one, pharmaceutical technologies are constantly changing — the number of biotechnology-based drugs in development now far exceeds the number of conventional drugs — and the capital investment required to produce niche products is becoming increasingly cost-prohibitive and risky.

In addition, demand projections are inaccurate by nature, and new products need time to prove their viability. Outsourcing provides a means of balancing supply chain fluctuations with unknown demand in an uncertain environment filled with aggressive competition, increasing regulatory pressures, and eroding margins.

The need to reduce the cost of goods on major products that have lost their exclusivity and now face competition from generics, as well as the focus on growing emerging markets where prescription drugs are a luxury many can't afford, are additional factors driving more efficient and cost-effective manufacturing. Some companies prefer to launch a new product in house, at least initially, to maintain the highest levels of control over the process and associated intellectual property, opting to outsource at a later date once they are comfortable with managing the product's potential risk.

## Suppliers Capabilities, Competencies Vary

CMO structures vary from specialized single-focus providers to outsourcing subsidiaries of major international pharmaceutical companies, both of which have experienced steady growth in recent years. Because entry barriers into manufacturing are so substantial, even lesser known suppliers have track records with local pharmaceutical clients before venturing into the global scene. There may have been changes in ownership, such as the entry of a venture capital partner, but the underlying business generally remains largely the same, and its performance history is easy to investigate.

While niche manufacturers may be more one-on-one customer focused, with dedicated capacity that allows them to bring a particular product to market quickly, there is a corresponding risk for companies that outsource in putting all their eggs in one basket. Large organizations, on the other hand, can often bring to the table state-of-the-art facilities, substantial technical and manufacturing resources, and expertise that can be tapped for troubleshooting, greater financial stability, and site production in regions convenient to customer markets.

Even the largest CMOs cannot provide every conceivable service at the risk of diluting their core competencies, however—nor should they. Companies that concentrate on the production of specific products or processes are more adept at navigating the complex regulatory environment and distribution channels for these product types. Ironically, these realities have also created a reverse flow of outsourcing business as pharmaceutical companies in developing markets seek strong outsourcing partners with manufacturing and related extended capabilities in their own target markets, such as North America and Europe.

The bulk of the global trend is still represented by companies shifting manufacturing operations to low-cost countries such as India and China. Between 2006 and 2007, contract service revenues of Asia-based CMOs increased by 44%; these are expected to increase for the foreseeable future, although perhaps not at the same staggering rate.

While off-shoring to Asia may offer considerable savings and growth possibilities, depending on the production requirements, CMOs in the region may not have the levels of technical infrastructure or regulatory capabilities some customers require, which can be unnerving to the company ultimately responsible for the manufacturing process and adherence to good manufacturing practices (GMPs).

Large pharmaceutical companies with a global footprint may have support teams on the ground worldwide, teams with intimate knowledge of and personal experience with local suppliers and requirements. When services are needed, these teams are in the best position to create a short list of qualified candidates and conduct an investigation into their overall performance record, quality history, health and environmental safety practices, finances, supply chain and logistical systems, and organizational structure to get a broad sense of the operation and its strategic vision.

The movement to second-tier countries, though, will develop more slowly until regulatory structures are strengthened to acceptable levels. There are enough outsourcing opportunities left within India and China for a company prepared to make the investment of developing a strong supplier base.



**State-of-the art capabilities, full technology transfer, process optimization and validation, and dedicated technical and customer service teams allow qualified contract manufacturers to handle complex pharmaceutical and biopharmaceutical formulations.**

## The Right Long-Term Partner

Success — or failure — of a contract manufacturing project ultimately lies in effective technology transfer. And while cost is certainly a key criterion, quality, GMPs, confidentiality, and timeliness are equally important factors in the selection of a CMO.<sup>3</sup> Part of this evaluation includes the investigation of lead times, shipping costs, inventory levels, and the CMO's ability to respond in a timely manner to changes in demand, new business opportunities, and global economic influences. Over the next few years, it is also likely that there will be some consolidation in the CMO market; the survivors will have the strongest technical knowledge base, well-developed quality systems, top-notch facilities, and customer focus.

Rigorous vendor selection and ongoing monitoring, including scheduled and unscheduled site visits, can prevent any number of time-consuming snafus. This approach can help keep a project on track by emphasizing the importance of the work, building trust between the customer and the CMO, and creating a culture of transparency conducive to a long-term relationship.

Because the client company assumes the risk of drug failure, it is critical to adopt a wide array of risk mitigation measures covering timelines and technical data, including the use of a scale that will trigger visits and independent quality testing, if needed. These protections actually work both ways; client information also needs to be accurate and in sufficient detail to ensure the proper transfer of technology to the CMO.

In addition to technology issues, GMP standards and government regulations are becoming more stringent and are changing constantly in both emerging and mature markets (i.e., the FDA Globalization Act of 2009 and the call for the FDA to inspect overseas facilities). Pharmaceutical companies and their CMOs must ensure that they are meeting appropriate compliance and quality standards across the supply chain to avoid any unexpected production challenges. And, in some countries, regulatory changes are not always broadly communicated, requiring someone at the local level to proactively monitor agencies and their internal workings.

Along the same lines, potential customers should also examine a vendor's culture of continuous improvement, adoption of Lean and Six Sigma methodologies, and sensitivity to green and ethical manufacturing practices. Many suppliers are already quite competent, and even those needing improvement are often receptive to working with the client on key changes. A good understanding between the two companies and their respective supply chain dynamics helps quicken responses to changing market trends and alleviate slowdowns caused by internal business processes and poor supplier/customer relationships and bottlenecks.

CMOs evaluate potential customers as well. Specifically, CMOs want to know where the client stands in the product's development process, how well the technical package transfers to their manufacturing plants, the ability of the customer to adhere to timelines, and whether the potential client has the wherewithal to bring its product to market completely. If the goal of the potential customer is to sell the product to a third party, the CMO runs the risk of investing years into a start-up without securing the long-term commercial production contract.



Aseptic/sterile production and injectable manufacturing processes require a significant investment in terms of expertise, equipment, process, technology, and quality control.

## A Practice Destined to Grow

Globalization of the pharmaceutical industry has spawned an intricate web of collaborative relationships. Companies from large multinationals to small start-ups are leveraging their supply-chain partners' expertise and capabilities in order to shift prized resources to their areas of strength. In fact, it is estimated that by 2010, nearly 30% of all pharmaceutical manufacturing will be produced via third parties as companies scale back on production and focus on core competencies.

Outsourcing manufacturing allows a company to be agile, flexible, and competitive in a fluid business environment, which is essential for companies hoping to align their supply chains with constant shifts in global product demand. Even if the company has the internal capabilities, going outside allows an organization to spread the risk rather than to be too heavily invested in one product or technology. Given the level of co-dependency among operators in the industry,

pharmaceutical firms must have a firm understanding of the intricacies of the CMO relationship in order to facilitate the manufacturing process.

CMOs can provide innovative, state-of-the-art processes and production technologies to support the rapid technical transfer of products from research and development to commercial manufacturing. The effective management of the CMO relationship is critical, however, not only in satisfying regulatory requirements amid growing concerns over quality control, but also in meeting the overall commercial aim of the project.

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3. Outsourcing Survey. Contract Pharma. May 2008.

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