The Rise of Biopharmaceutical Outsourcing to Indian CDMOs

by Siddharth J Advant and Jaby Jacob

India is becoming an increasingly attractive destination for outsourcing biotechnology services by global biopharmaceutical companies. As "Big Pharma" continues on its path of finding ways to lower costs for development and manufacturing of biopharmaceuticals, Indian contract development and manufacturing organizations (CDMOs) are being viewed as capable and beneficial service providers that possess the necessary technical expertise and regulatory-compliant facilities.


Kemwell Biopharma's manufacturing and R&D site in Bangalore, India

According to its 11th annual report on biopharmaceutical manufacturing capacity and production, BioPlan Associates ranked India fourth in the world as a potential outsourcing destination (**1**). Survey respondents gave it a "likelihood" or a "strong likelihood" as an option. According to the same report, companies may be seeking CDMOs that are suitable for long-term support of biopharmaceutical development projects: from clinical supplies manufacturing and associated regulatory filings through to eventual commercial supply.

In addition to lowering cost of goods, many companies are likely to outsource the manufacture of their biopharmaceutical products to Asia for clinical trials or sales in a specific market within that region. Furthermore, those same companies may look specifically to India to manufacture biosimilars first for the local market, with the United States and Europe being the ultimate destination once appropriate regulatory pathways have been established.

Here, we explore a number of factors that have influenced the rise of companies outsourcing biopharmaceutical development and manufacturing to India.

Cost Benefit

The biggest advantage of outsourcing to India is the cost benefit it can provide with comparable quality standards to those found in the United States and Europe. Our company estimates that the cost of manufacturing in India is ~35–40% lower than in the United States or Europe. This is primarily attributable to two factors:

- Lower capital and equipment expenses lead to lower depreciation and interest costs.
- Talent-pool costs are lower by about 50–60% compared with Western counterparts, including both skilled professionals and senior management.

With the 2009–2013 economic downturn, both large- and mid-sized biotechnology companies are recognizing the impact of such cost savings to their bottom line. Moreover, outsourcing in general can lower the total cost of product ownership by helping sponsor companies achieve process efficiencies and streamline their supply chains. When companies use a combination of captive and outsourced facilities, such capacity optimization provides overall savings to the organization. The increased margins that competitive pricing delivers is a big influencing factor in most companies' decisions about outsourcing to India.

Facility and Infrastructure Indian CDMOs have built world-class facilities to cater to global business requirements, often using design consultants with global expertise for plant construction. Installed equipment comes from leading global manufacturers such as Sartorius Stedim Biotech, GE Healthcare, EMD/Merck Millipore, Asahi Kasei, GEA Westfalia, Thermo Fisher, and Groupe Novasep. Many of those vendors have established development and manufacturing centers across India, enabling quick and easy access to their products and services for installation and maintenance of equipment at a competitive cost.

Among many other Indian companies, Kemwell Biopharma showcases facilities that are compliant with expectations from global regulatory agencies: the European Medicines Agency (EMA), US Food and Drug Administration (FDA), Japan's Pharmaceuticals and Medical Devices Agency (PMDA), and


Bioreactor room


Analytical laboratory

Australia's Therapeutic Goods Administration (TGA). Based on two 2,000-L current good manufacturing practice (CGMP) bioreactors, the company's mammalian cell culture manufacturing facility in Bangalore (including technology transfer and process development up to 80 L) was designed and built under technical guidance from Boehringer Ingelheim. Most critical equipment was supplied by globally reputed manufacturers, including Sartorius Stedim Biotech (for upstream processes), GEA Westfalia (for harvesting), and EMD/Merck Millipore and GE Healthcare (for downstream processing). As described elsewhere, "Kemwell's facilities use an intelligent hybrid system approach in which both technologies — stainless steel systems and single-use systems — have been combined in the best possible manner" (**2**).

Technical Expertise

India has witnessed a rise in the number of educational institutions that cater to pharmaceutical and biopharmaceutical sciences and industries. They are contributing to a rapid increase in the availability of local scientific talent ranging from bachelor to doctoral-level degrees. Apart from the several hundred state universities, a network of research institutions provides opportunities for advanced learning and research leading up to a PhD in branches of science, technology, and agriculture. With recent capacity additions, India now has the capability to graduate more than 500,000 engineers (with four-year undergraduate degrees) annually and more than 1.2 million scientists. Furthermore, each year the nation is enrolling at least 350,000 students in its engineering diploma programs (with plans to incrase this to ~400,000). Thus, India's annual enrollment of scientists, engineers, and technicians now exceeds 2 million (**3**).

It should also be noted that because English is the preferred language for writing in India, standard operating procedures (SOPs), batch records, change controls, and all reports are originated in English with no need for translation. This greatly facilitates communications and intercompany project management for CDMO projects.

Historically, local talent from India has travelled west to find the best job opportunities. But the Indian government, multinational companies, and local major pharmaceutical companies are working hard to attract and retain home-grown talent. India's new "economic powerhouse" status has been a major factor in attracting talent from overseas, as well. The vast majority of those have returned from the United States, Germany, and Great Britain, but other scientists have come from South Korea and Japan. Programs designed to entice nonresident Indians (NRIs) to return to India include schemes set up by the Indian government such as the Ramanujam Fellowship, the Innovation in Science Pursuit for Inspired Research (INSPIRE) Program, and the Ramalingaswamy Fellowship (**4**).

Meanwhile, CDMOs have increased their focus on building senior management teams that have international experience and can operate on a global level. Western-trained and -experienced senior management and global-spanning partnerships have greatly improved the overall scientific acumen of such companies.

Outsourcing to India

Some prominent Indian contract manufacturing organizations (CMOs) and contract research organizations (CROs) serving the global biopharmaceutical industry include

- Emcure Pharmaceuticals (www.emcure.co.in)
- Intas Pharmaceuticals (www.intaspharma.com)
- Kemwell Biopharma (www.kemwellbiopharma.com)
- Shasun Pharma Solutions (www.shasun.com)
- Syngene International (www.syngeneintl.com)

Many of them have offices in Western countries, as well.

Quality Systems

The FDA's growing scrutiny on compliance is causing ripples throughout the world beyond the United States to affect biopharmaceutical facilities (operated by both big and small companies) in the European Union and Asia. Although most companies that have received warning letters and consent decrees are product companies, CDMOs are not immune to such scrutiny or issuance of warning letters.

A big difference for CDMOs, however, is that their regulatory compliance is under constant review by regulators and customers. Such routine scrutiny helps keep a CDMO's GMPs to the highest standards and drive it toward ever more rigorous continuous improvement.

Traditionally, Indian CDMOs have had a strong track record in regulatory and quality compliance. The country is

Aseptic processing area for fill and finish

Analytical testing in a biosafety cabinet

home to a large number of FDA- and EMA-compliant facilities, housing the highest number of US FDA facilities outside the United States. Recently, however, several Indian pharmaceutical companies have been plagued by FDA concerns regarding quality systems and data integrity. To address some of those issues, agency commissioner Margaret Hamburg mentioned during a recent visit to India that the FDA has decided to expand its offices there, add inspectors, and train local regulatory officials while stepping up inspections of such overseas plants (**6**).

In light of the concerns raised by some regulatory agencies, many Indian CDMOs are proactively taking steps to ensure that their quality systems meet the highest standards. They are taking a multipronged approach to reinforcing those systems:

- Implement cross-learning across sites to share best quality practices.
- Train to help create awareness and build a quality culture from the shop floor to the boardroom.
- Create quality metrics that are reported and visible to senior management and customers.
- Build compliance teams and quality review teams to maintain high compliance levels.
- Investment in software such as laboratory information management systems (LIMS), quality management systems (QMS), and document management systems (DMS) to help automate quality systems and reduce data-integrity concerns.
- Make employees aware of findings from other FDA audits that are available to the public.
- Create a culture of "all-time readiness" for audits.
- Set environmental health and safety (EHS) policy and guidelines according to global standards, and train employees accordingly.

Track Record in Outsourcing Even though biopharmaceutical outsourcing to India is relatively new, the country has shown its prowess in the outsourcing of various knowledge-driven or "high-end" processes that require specialized domain expertise. These include such varied areas as R&D, insurance underwriting and risk assessment, financial analysis, data mining, investment research, statistical analysis, tax preparation, engineering and design, animation, graphics simulation, medical services, clinical trials, legal services, and more (**7**).

In the pharmaceutical industry, India is one of the largest exporters of over-the-counter and prescription drugs to the United States. Its pharmaceutical industry supplies 40% of the over-the-counter and generic prescription drugs consumed in the United States (**8**).

Thus, Indian CDMOs have decades of experience in pharmaceutical development and manufacturing. That has enabled them to build business practices and quality systems compliant to global standards. For example, Kemwell has been a 100% CDMO for over 30 years, serving global pharmaceutical companies such as Bayer, Boehringer Ingelheim, GlaxoSmithKline, Merck KGaA, Novartis, and Pfizer, and supplying products to more than 80 countries worldwide. The company has built upon that foundation to put the necessary systems and processes in place to serve the biopharmaceutical industry.

Confidentiality and Intellectual Property Rights Upon signing onto the World Trade Organization's Agreement on Trade-Related Aspects of Intellectual Property Rights ("TRIPs Agreement") and amendments in the Indian Patent Act, India became part of a global treaty in which technological innovations are encouraged and protected (**9, 10**). Pressure from the global community for India to respect the intellectual property rights (IPR) of others has made "IPR compliance" a priority for all Indian CDMOs.

Most such companies are creating internal processes to ensure compliance and adherence to global IP rights and implementing effective information governance measures. Some steps taken to encourage IPR compliance include

- Strict confidential disclosure agreements (CDAs) with employees, vendors, and service providers
- Internal training programs on the importance of IP
- Information technology (IT) measures including restricted access to data based on roles and responsibilities, monitoring of network and emails, fingerprint access to critical laboratories and storage rooms given to employees according to their roles, and using secured applications to share information with customers.

It is also important to note that India is a major hub for the knowledge process outsourcing (KPO) industry, which involves valuable data, trade secrets, and so on. Many Western companies have successfully managed to outsource such processes to India while ensuring adequate protection of information and data (see the "Valuable Knowledge" box).

Valuable Knowledge

Other IP-critical work ongoing in India includes

- drug discovery and development (new targets, compound screening, toxicology screening)
- clinical trials (phase 2, 3, and 4 studies performed by many drug and biologic companies)
- clinical data management (companies such as Novartis and Pfizer with thousands of employees managing clinical data in India).

Project Management

Setting up and implementing efficient project management systems are critical tasks for managing all outsourced activities. Biopharmaceutical contract manufacturing depends highly on smooth and efficient knowledge transfer and regular interactions between product sponsors and CDMOs. Two practical challenges need to be addressed when outsourcing to India: time-zone differences and effective means of communication.

Flexible approaches to work schedules are necessary to manage the time-zone challenge. Based on customer project requirements, many Indian CDMOs provide the necessary work-schedule flexibility to make available the required overlap in working hours between customers and CDMO project teams for meetings and discussions. Flexible approaches to work scheduling have been remarkably successful in the IT and business process outsourcing (BPO) industries in India for managing challenges arising from time-zone differences. Several companies are also tackling the communication gap by implementing rigorous training for their employees to ensure that nothing will be lost in translation.

Technological advancements have helped bridge the gap in these capabilities between Indian CDMOs and their western counterparts. Frequent use of video chats, email, and intranet network capabilities ensure effective communication.

A Value Proposition

Indian CDMOs are poised to provide a winning combination of quality and value for companies that consider outsourcing biopharmaceutical development and manufacturing. World- class facilities, infrastructure, and technical expertise can be obtained in India at significantly lower costs than similar work in the United States or Europe. With such undeniable benefits, it seems that biopharmaceutical outsourcing to India will continue to grow as global biopharmaceutical companies use this opportunity to fuel efficient growth.

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