

NERMEEN VARAWALLA

Outsourcing pharmaceutical services to India

The value of the outsourced pharmaceutical services industry is expected to double to approximately 55 billion USD by 2010. Contract manufacturing and the outsourcing of clinical trials account for the majority of activity in this sector. The compelling need for capturing efficiencies and cost savings has persuaded the pharmaceutical industry to follow the example of other industries that have elected to focus on core competencies and develop outsourcing relationships for non-core activities. Further there has been a sharp increase in the number of "virtual" pharmaceutical and biotechnology companies who seek to outsource all their manufacturing and clinical trial activities.

GROWTH OPPORTUNITY FOR INDIA

Although at the present time India's share of the outsourced pharmaceutical services industry is relatively modest there is every indication that the sector is poised for tremendous growth. This is being driven by domestic industry changes and local availability of the essential competencies. India's impressive track record in the world class delivery of IT and business process outsourcing services has firmly placed Indian companies on the global service provider map. In addition India's generic pharmaceutical companies rank amongst the world leading players in this sector. Equally importantly India has begun to demonstrate her intention to uphold Intellectual Property Protection in accordance with international WTO standards. Since January 2005 India appears to be intent on enforcing legislation to protect Intellectual Property patents for both products and processes across a number of knowledge based industries. The changes in Indian Patent legislation have prompted India's more ambitious domestic pharmaceutical companies to develop strategies to reduce their dependence on the domestic generics market. Two main business models are emerging: (i) entry to regulated international markets with generics, formulations and specialty pharmaceuticals with a longer term aspiration to develop their own NCEs and (ii) provide contract services to the international pharmaceutical industry in the fields of contract manufacturing for marketed drugs as well as clinical trial supplies, clinical trial services and synthetic chemistry for drug discovery. India's English speaking, IT literate and cost effective graduate work force with degrees in sciences, IT and medicine is central to its attractiveness as a destination for outsourced services. The scientific and technical workforce in India has 3 million individuals, in addition there are 1 million graduate engineers and 0.8 million post graduate scientists. India has over 500,000 medical doctors, 171 medical colleges and 17,000 medical doctors graduating each year. Medical education in India is delivered in

English and is based on a system inherited from the British. Most of India's leading specialists have received their post graduate medical training in the USA or UK. It is India's cost effective labour force that enables the cost of pre-clinical discovery to be approximately one-fifth of that in the US and that of clinical development one-third. Furthermore there are numerous government incentives to encourage the development of this pharmaceutical contract services sector. As a result a growing list of international pharmaceutical companies that includes the majority of the world's top ten companies is accessing pharmaceutical services from India. The services include contract manufacturing, clinical trials and contract research to support drug discovery. This is being conducted either via their own Indian local operating companies or via outsourcing alliances with local providers or global vendors with Indian capabilities.

CONTRACT MANUFACTURING



As a consequence of a thriving generics, formulation and bulk drug industry India has developed world class synthetic chemistry skills and invested in state of the art manufacturing facilities. Today apart from the USA, India has the largest number of FDA approved pharmaceutical manufacturing plants. Indian companies account for about 25-30 percent of the total DMFs (Drug Master Files) filed with the US-FDA. There are available well developed chemistry and process innovation skills instilled by years of fierce competition in the generics domestic sector. Thus India is able to offer services across the contract manufacturing value chain – from custom chemical synthesis to APIs to formulations with a potential for significant cost savings. The labor costs for a skilled chemist in India is 7 percent of that in the US, 10 percent of that in Italy, 50 percent of Hungary and 120 percent of China. In addition capital costs of building manufacturing facilities are up to 40 percent lower than in Western Europe or North America. Thus manufacturing costs in FDA approved and non-approved plants in India are 35-40 percent and 25 – 30 percent of that in the US, respectively. In 2005 India's share of the 15 billion USD global contract manufacturing market was 100 million USD almost entirely comprised of API and intermediates manufacturing. By 2010 India's share is expected to increase to 1 billion USD of a 30 billion USD global market with one fifth of revenues being accrued from the manufacture of formulations.

CLINICAL TRIALS

India offers a compelling opportunity for swift, meticulous and cost effective global clinical trial conduct because of

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patient access, motivated English speaking investigators and a stable regulatory environment.

Although India has a population of about 1 billion, it are the 350 million individuals residing in metropolitan India that form the population base for clinical trial recruitment. In addition to widely prevalent infectious and tropical diseases, rapid and extensive urbanization has resulted in a disease prevalence similar to that found in developed countries as exemplified below.

- 0.7 to 0.9 million new cases of cancer are detected every year
- India has the largest number of individuals with a diagnosis of the metabolic syndrome (a combination of insulin resistance, hyperlipidaemia and obesity)
- 80 million individuals suffer from cardiovascular disease & 15 percent of the population is hypertensive

There are relatively few competitor trials; this contributes to rapid patient recruitment rates - up to seven times faster than in the USA, particularly for oncology studies. India has a mixed healthcare system comprising of both state subsidised and private healthcare. Both the state and private hospitals in India's cities and large towns are well suited to be clinical trials sites as they have the required patient attendance, motivated staff and equipment. Patient concentration at urban specialist sites improves the efficiencies of clinical trial execution as site management and monitoring is streamlined. Clinical trial conduct in India offers the opportunity for up to 40 percent cost savings as compared to North America and Western Europe. Considering the labour intensity of clinical trial execution the lower labour costs for clinical operations personnel i.e. project managers, monitors, medical writers, data processors, programmers etc account for a substantial amount of these cost savings. In addition there are lower costs for domestic travel and support services. Investigator fees in India are about 30 - 40 percent of those in the US and Western Europe.

Clinical data from India contributing towards pivotal global clinical trials has now been accepted by the FDA and EMEA on numerous occasions. The first FDA audit in India took place in 2005; two clinical sites participating in a global study for an anti-infective product were audited with no relevant findings.

Availability of an IT skilled workforce makes India an ideal location for off shoring clinical data management for global clinical trials. Numerous global pharmaceutical companies are enjoying this advantage either by establishing their own capabilities or via outsourcing arrangements that vary from a few selected trials to large, long term off shoring contracts.

Over the past few years India has also gained recognition as a key provider of high quality and cost effective bioavailability and bioequivalence studies. Although conduct of first in man studies for international sponsors continues to be restricted, local CROs offering bioequivalence studies have been successful in attracting business from international generic companies. Indeed some of the world's leading generic companies such as Actavis and Pliva have established their own product development capabilities in India.

India's nascent CRO industry composed of local CROs, Indian subsidiaries of global CROs and niche data management providers is experiencing annual growth rates of 40 percent. Revenues in 2005 were 100 million USD. However in spite of India's compelling attractions for the global clinical development the proportion of the world's clinical trials conducted in India continues to be minimal. The reason for this is sponsors concerns related

to regulatory approval timelines, data quality and compliance with international ethical standards. Although India's regulatory authority - the Drugs Controller General of India has been able to reduce the regulatory approval timeline to 12 weeks, the approvals process needs to be further streamlined. There are numerous initiatives both industry and government led to address issues of GCP training and quality assurance. These measures are intended to ensure a robust clinical development environment across industry players, government institutions and clinical sites so that India will be able to effectively compete in the global clinical development market place.

CONTRACT RESEARCH

India's chemistry capabilities that form the basis for contract manufacturing services are also being utilised to provide high end chemistry research services to support drug discovery. Medicinal chemistry services provided by Indian companies include the synthesis of building blocks, scaffolds and intermediates for generating analogues; compounds for assays and animal models; custom designed small molecules for Lead Generation and Lead Optimization; compound libraries as well as lead compounds in grams or kilos. Service offerings that combine chemistry with informatics include molecular modelling, virtual screening, ADME and toxicology prediction and crystallography. The contract research sector is also enjoying growth with many successful companies that vary in size from a dozen chemists to those with several hundred. Revenues for India's contract chemistry research sector for 2005 are estimated to be 50 million USD.

CONCLUSIONS

India is poised to offer the global pharmaceutical industry high quality and cost effective contract services to support drug discovery, clinical trial conduct, data management and manufacturing. As the sector matures the primary driver for outsourcing will change from cost saving to the quest for high quality and speed. Skills developed by the Indian workforce through a thriving contract pharmaceutical services industry will help India's more ambitious pharmaceutical companies to fulfil their aspirations of becoming players in the global ethical pharmaceutical industry.

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