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India leads in clinical trials

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Globally, clinical research - the business of testing new medications for safety and efficacy in human patients to gain required government approvals - was estimated to be a US$5-6 billion market in 2002, and is expected to reach $10 billion by the end of this year. According to a 2003 study by Connecticut-based Business Communications Co (BCC), US-based spending on clinical trials is growing at 12% per year - and should generate $26.5 billion by 2007. The reason the business is growing so rapidly is that the pharmaceutical industry is required by government regulations to conduct human trials before marketing new drugs.

Bearing in mind a looming March 1, 2005, deadline, when all countries had to adopt patent rules in line with WTO rules, pharma companies worldwide have been concentrating on new drug development. It is estimated that the number of drugs developed has gone up from 4,194 in 1997 to 7,067 in 2002, which underlines the necessity for increased demand for Clinical Research Organization (CRO) services.

An independent CRO provides committed resources for clinical studies. This helps to maintain the high standards set by the industry, such as strict adherence to protocols, excellent clinical practices and complete and accurate documentation. The personal attention to detail given by CROs and their ability to provide timely and proficient trials speed up the process of clinical studies.

India is increasingly emerging as a preferred destination for the outsourcing of clinical trials. Currently, about 80 government and privately owned Indian hospitals are engaged in global and local clinical trials.

Advantages of conducting trials in India

- A large pool of patients, from multiethnic and multiracial backgrounds
- Rapid patient recruitment, which significantly reduces the clinical development process
- Wide spectrum of diseases. Multidrug-resistant pneumonia, Hepatitis B, diabetes, and some cancers are far more prevalent in India than in the West
- Drug companies can save 30%-50% by conducting trials in India as compared to the West
- Data generated in India is accepted by all major conferences and journals
- Investigators are mostly trained in the West
- All hospitals and private institutions store comprehensive source data, mostly in English
- Subject recruitment is the most common rate-limiting step in the drug development process. Sponsors normally cannot reduce study timelines without sacrificing quality and incurring increased costs. India offers sponsors the opportunity to recruit subjects quickly while maintaining a high level of quality. The relative cost savings result not only from shorter timelines but also from the low cost of performing studies in India

Due to the high population density of urban areas and the relatively small number of hospitals, recruiting a large number of subjects within a short time frame is not difficult. Also, the accessibility of these hospitals allows for cost-effective monitoring of studies. Subject compliance is an important aspect of clinical trials. Subjects recruited in the studies performed in India are not only treatment-naive but also recognize that study participation can offer access to quality health care and medicines that may not be otherwise affordable. As result, subjects are compliant and keenly attend all study visits. An independent study by a global CRO concluded that India has one of the best subject return rates in the world.

India is today identified as a major resource center for conducting clinical trials and data management services. With its large patient population, well-trained and enthusiastic investigators and trial costs considerably lower than those in developed nations, India has gained wide recognition as a nation capable of offering unique opportunities for conducting clinical trials. Its increased regulatory control and acceptance of the International Conference on Harmonization (ICH) guideline for good clinical practice further enhances India's reputation as an ideal location to conduct clinical trials.

Regulations pertaining to clinical trials in India are governed by Schedule "Y" of the Drug and Cosmetic Act. It deals with regulations relating to clinical trial requirements for the import, manufacture and obtaining marketing approval for a new drug in India. The procedure for applying for marketing approval depends on the status of the new drug, which can be broadly classified into three categories: new drug substances discovered that are already approved/marketed in other countries; new drug substances discovered that are not approved/marketed in other countries; and new drug substances discovered in India.

In case of the first category, it is sufficient if confirmatory trials (phase III) are conducted to obtain data about the efficacy and safety of the drug in a large number of patients (minimum 100, in 3-4 centers), generally in comparison with a standard drug or a placebo, to confirm efficacy and safety claims made in the product monograph.

For the second category, permission for clinical trials is given with a "phase lag". Phase I of a new drug substance, for example, is allowed only if the drug has completed phase I and moved to phase II in other countries; similarly phase II is allowed in India only after completion of phase II in other countries and phase III has commenced. Phase I trials cannot be initiated in India for new drug substances discovered in other countries unless phase I data from other countries is available. In the case of new drug substances discovered in India, clinical trials have to be carried out as human/clinical pharmacology trials (phase I). The phase I trials are carried out on healthy human volunteers (minimum two at each dose level) to determine the maximum tolerated dose in humans, adverse reactions, etc.

Exploratory trials, or phase II trials, are carried out on limited number of patients (normally 10-12 at each dose level) to determine therapeutic uses, effective dose range and further evaluation. Confirmatory trials, or phase III trials, are conducted to obtain sufficient data about the efficacy and safety of the drug in a larger number of patients (minimum 100 in 3-4 centers), again in comparison with a standard drug or a placebo, to confirm efficacy and safety claims made in the product monograph. If the new drug substance is not marketed in any other country, phase III trials should be conducted on a minimum of 500 patients spread across 10-15 centers.

In the case of new drug substances discovered that are not approved or marketed in other countries, Schedule Y would previously put India back by a step as compared to other countries due to the phase lag that needed to be adhered to. This has been recently revised, and now allows clinical trials to be carried out in India concurrently with trials abroad.

Some, however, have raised fears that India still lacks appropriate provisions to ensure that human subjects used for the trials are volunteers and not people compelled by poverty to offer themselves as "guinea pigs". Since India does not have high literacy levels, it might also be possible that volunteers would not be adequately informed about the risks they are undertaking. However, the ills associated with clinical trials in India are now said to be a thing of the past. Compliance to International Conference on Harmonization-Good Clinical Practice (ICH-GCP) norms, trained investigators, a growing population of experienced monitors and exposure to international protocols have enabled the industry in India to offer a viable alternative to the hugely expensive sites in the West.

As things stand today, CROs are still in their infancy in India. Even though a handful of international CROs have a presence in India, either on their own or via local partners, the industry remains on the threshold of a major expansion. The total market value of clinical research performed in India in 2001-02 was about $70-80 million. The firm increase in CRO activities can be attributed to large subject pools in

most major therapeutic areas, improved medical infrastructure, and increased awareness of the ICH Guideline for Good Clinical Practice and formation of specialized researchers.

Backed by the recent government notification amending Schedule Y, multinationals like Pfizer, Eli Lilly, GlaxoSmithKline and Aventis have kickstarted simultaneous and stand-alone clinical trials in various therapeutic segments. Many new CROs have also outlined plans to tap India's large pool of patients suffering from cancer, diabetes and other maladies. Pfizer, which has invested $13 million on clinical research in India, has already earmarked a city in North-east India to conduct clinical trials on 300 patients. The trial will test a new malaria cocktail drug that combines chloroquine (to which Indian malarial strains have developed resistance) and azithromycin - an antibiotic.

Other MNCs are close to setting up shop in India. A case in point is that of Belgium-based CRO Trainor and Partners (T&P). Bullish on India, it is now scouting for partners to start a franchise. The optimism stems from the fact that a huge drug trials market is emerging in India. Global consultancy major McKinsey estimates that by 2010, global pharma majors would invest $1-1.5 billion in the Indian market.

The pace of drug trials in the country has forced US-based Clinical Data Interchange Standards Consortium (CDISC), a non-profit organization, to look at setting up a chapter here. Eli Lilly has over 17 large and small clinical research projects running in 40 hospitals across India, while GSK Plc has started seven simultaneous clinical trials of its vaccines and drugs. The Schedule Y booster shot is clearly working.

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