CLINICAL TRIAL IN INDIA-AN OVERVIEW

Debjit Bhowmik*,Chiranjib.B
Rajiv Gandhi college of Pharmacy
Nautanwa, Maharajganj,Uttar Pradesh
Email-debjit_cr@yahoo.com

ABSTRACT

Global Pharmaceutical companies based in developed countries are increasingly turning to developing countries and emerging economies around the world for conducting clinical trials. Reduced costs combined with easy availability of patients with varied diseases makes developing countries favourite destinations for clinical research outsourcing. Drug trials, commonly known as clinical trials, are scientific tests made on human volunteers. Such trials are carried out in 3phases. In the first phase, studies are carried out on volunteers to determine the safety of the drug. In the second phase, on persons having the disease or medical condition to determine whether the drug has some level of therapeutic effect. In the last phase, trials are long-term studies on patients to determine whether the drug will be truly effective in normal medical settings. India, a country with the largest pool of patients suffering from cancer, diabetes and other maladies, has become the global hub for carrying out clinical trials at random. Almost all the top pharmaceutical companies of the world have set up clinical trial facilities in major cities, like Ahmedabad, Hyderabad, etc.A large native patient population pool, various disease profiles and robust infrastructure position India high on the outsourcing list. Today, 122 clinical trials are being conducted in India. GlaxoSmithKline, among the world's top ten global pharma majors, is currently carrying out the largest number of clinical trials in India. Apart from the development of vaccines, the UK-based pharma major is conducting 13 drug trials in India for the treatment of diseases such as cancer, arthritis, epilepsy, heart disease and constipation. These trials include phase II, III as well as phase IV clinical drug trials. AstraZeneca is another global pharma company outsourcing a significant number of its trials to India. Out of the 186 clinical trials the company is at the moment conducting worldwide, about nine have investigation centres in India. These studies include drug trials for schizophrenia, bipolar disorder, cancer, diabetes and testotoxicosis and are conducted on adults and, in certain cases, children.
Likewise, Johnson & Johnson and Eli Lilly are conducting respectively eight studies in India, while seven drugs trials are lead by Pfizer. Sanofi-Aventis, Merck, Wyeth, Bristol-Myers Squibb and Roche also count among the list of companies conducting clinical research here. To understand why developing countries have become a hot spot for clinical research, one needs to look at the drug development process in totality. This process, which starts in the research labs and ends with a drug being launched in the market, is not only time consuming; it is also extremely expensive. The cost of drug development is estimated at $1bn, and clinical trials on humans -- a critical phase in new drug development -- account for 40% of the total cost. Outsourcing clinical research to developing countries can allow global pharma companies to considerably trim costs. Clinical trials in India, for instance, cost 50% to 60% less than the average cost in the US.

INTRODUCTION

India is emerging as a major centre for clinical trials in new products by multinational pharmaceutical companies. The country with a diverse patient pool holds good business potential in this field. Clinical research is emerging as a big business opportunity in India and hospitals in the country can take advantage of it .Recognizing this potential, several clinical research organisations (CROs) and multinational companies have already set up facilities for research in India. There is a fear in India that in the absence of an adequate regulatory system for clinical trials, pharma companies may take advantage of the situation, treating innocent patients as guinea pigs. It is alleged that as most of the patients undergoing trials are illiterate, no adequate compensation or insurance cover is being given to them by CROs or the companies. But, according to pharma company officials, this fear is unwarranted as the Indian Government is soon expected to come out with laws governing clinical trials. Some guidelines are already in place. However, a practical problem in India is that several hospitals are not equipped with adequate and proper equipments to undertake clinical research in certain products. But more than cost, time is a crucial factor for pharma companies. Considering the fact that a patent lasts 20 years, starting from the moment the drug is discovered and approved for clinical trials, more than half of the time is already gone by the time the trials are over and the drug is finally marketed. Indeed, clinical trials alone can last up to 10 years. And the best way to reduce time is to recruit patients quickly, which is increasingly difficult to achieve in Western countries. Patients enrolling in clinical trials are not financially compensated for their participation but simply benefit from free treatment, including doctors' consultations, transportation, etc. Considering that health expenses are almost entirely covered by the government in European countries, patients have little incentive to enroll in clinical trials. Similarly, in the United States, patients are more often than not covered by health insurance policies. As a result it is those most vulnerable, with few resources of their own and living in countries with poor social security systems, who are likely to enroll more easily in drug trials. Clinical trials bring in new technology and new treatments and they also sensitise the bio-medical community towards the country's need to advance medical and clinical research. However, when clinical trials are conducted in areas where patients are mostly uneducated and destitute, ensuring adherence to ethical clinical practices can prove difficult. In fact, if most countries, including India, have issued national guidelines, instances of unethical and illegal trials have often been brought to the limelight.

CLINICAL TRIALS IN INDIA: COST EFFECTIVENESS

Cost of conducting clinical trials in US is as follows:

Phase-1-$5404
Phase-2-$6538
Phase-3-$7635

Clinical trial for one drug in US costs approximately $1 billion. US infrastructure for conducting clinical trials is for sure unbeatable till now. While US continue to conduct clinical trials in flow, India and China are now seen as potential targets to conduct clinical trials.Potential contract research targets have been kept away from China owing to its week regulatory practices in the past, while with its recent entry into WTO; China is also considered as a platform for clinical research. China is a low cost hub for drug manufacturers. Indian infrastructure cuts down the cost of conducting clinical trials of new drugs to almost 60% of the cost in first and second world countries.The CRO business in India ranges between $100-$120m per year.. This is a huge factor which is making the pharmaceutical countries flock towards Indian CROs manage many functions of a sponsor, monitoring the work in phase II-IV. Currently, there are almost 30 CRO in India. India gives a low cost advantage with high quality fast output.There has been a meteoric rise in the clinical research infrastructure in India as compared to early nineties, when there was negligible clinical research experience, improper documentation, poor infrastructure, and weak regulatory environment with non functional ethics committee.
The potential for good practices is being realized now and clinical research facilities are being centralized in hospitals. Sites with well equipped laboratories and good research facilities allow the implementation of new and standardized policies. Simultaneously, with these new approaches, the interest of sponsors for clinical research in India is also developing at an accelerating pace.Above all, the investigators from different parts of the country are well trained in GCP compliant clinical research. Additionally, the availability of patients from different therapeutic areas and less time consumption add to the advantage of low cost clinical trials in India.There is a symbiotic relationship between the Indian infrastructure and clinical research. As, the Indian services are beneficial for clinical trials in terms of quality , training and costs, it adds more incentives to Indian platform when the sponsors provide highly sophisticated instruments to ensure good trial standards. The funds from sponsors are utilized to raise the standard trial sites.

CLINICAL TRIALS IN INDIA: THE CHALLENGE AND OPPOURTUNITIES

India comes at the first place in terms of education and trained doctors when compared with US and China.The doctors of India are always in demand all over the world because of high standard of medical education in the country. Also, these doctors are trained to cure a wide range of diseases. Trained manpower is the key to success for Indian clinical research organizations. India has become a part of IPR regime and has passed the patent act. The academy of clinical excellence has added to the points of India's capability to conduct clinical trials. Moreover, doctors are well trained as per CDSO/GCP guidelines too.The 2005 amendment to the schedule Y of drug and cosmetic act is taking India towards acceptance of ICH guidelines for clinical research. China in this context is still in the developing stage for the regulatory issues and the trained manpower lags behind India. Moreover, the common language spoken is Chinese and not English. This is a major drawback for China. US equals India in terms of education and qualified doctors, but the points for skilled labor still go in the lap of India.India has emerged as one of the preferred destinations for the clinical trials of drugs by multinational pharmaceutical companies in recent years. The reasons for this include reasonably high standards of quality healthcare and healthcare professionals, use of the English language and the sheer size of target populations available in our country. Clinical trials are usually multi-centric but trials in North America and Europe turn out to be time consuming and expensive. While clinical trials in the west are not totally free from compromised interest, mishaps and litigation, the medical research organisations (MRO) are licensed and highly regulated and people are sufficiently aware of the possible risks of such trials and also aware of their rights to healthcare. In India, the scenario is very different. A non-uniform healthcare system, with varying standards in the government and private sectors, desperate poverty and lack of access to healthcare, illiteracy, lack of information and poor enforcement constitute a chaotic milieu which is a major challenge for a programme as critical as a clinical trial. It is unfortunate that the international media has often reacted with unfair outbursts, criticising the regulators, the government or the pharmaceutical companies without a contextual understanding of the realities that exist here. Since India stands to benefit from these trials by much-needed investment into healthcare and access to beneficial drugs, there is an urgent need to create a conducive environment by raising awareness in the general public and ensuring ethical clinical practice. It would also be necessary to strengthen relevant laws and build systems of accountability in this area. In planning a trial in India one would also have to take into account the vast cultural, economic, social and educational differences that exist. It is just unrealistic for the pharmaceutical company to parachute the western model of a trial into the complex situation that exists here. The absence of specific laws and poor enforcement of guidelines can result in exploitation of our vulnerable populations by anyone with a vested interest. Compassion, ethics and honesty get compromised in the race to complete mandated trials and collect the compensation handed out by the pharmaceutical company.

Conducting clinical trials in India is an average of 44% less expensive than conducting US-based trials, according survey data. A new study by pharmaceutical business intelligence leader Cutting Edge Information, "Streamlining Clinical Trials," finds that the average clinical trial costs pharmaceutical companies $125 million in the US compared to $70 million in India, on average.The report explores other reasons that companies outsource clinical trials as well -- cost savings is only one of many factors that help determine trial

location. Other challenges in the US, such as patient recruitment and retention, have spurred companies to look for solutions outside of the US. In addition to India, other countries including Russia, China, and Brazil are all prime locations for clinical trials, in part due to improved trial conditions in those countries.

PHASES OF CLINICAL TRIAL

A clinical trial is a research study to answer specific questions about vaccines or new therapies or new ways of using known treatments. Clinical trials (also called medical research and research studies) are used to determine whether new drugs or treatments are both safe and effective. Carefully conducted clinical trials are the fastest and safest way to find treatments that work.Once researchers test new therapies or procedures in the laboratory and get promising results, they begin planning Phase 1 clinical trials. New therapies are tested on people only after laboratory and animal studies show promising results.

Each clinical trial is conducted in four phases. The Food and Drug Administration (FDA) must approve each phase before the study can continue.

Phase I: In this phase, a new drug or treatment is tested on a small group of healthy people to determine safe dosage, study how the drug works in the body, and see if it has any side effects. The overall safety of the drug is not known during this phase.

Phase II: The drug or treatment can now be tested on a larger group of people to see if it is effective and to further test its overall safety. Rating scales are developed and used to record data during this phase.

Phase III: Now the drug or treatment is ready to be tested on even larger numbers of people. The study will look even more closely at the drug's effectiveness, if it has any side effects, overall safety, and how it can improve a person's quality of life. Most drugs that reach this phase are considered for FDA approval.

Phase IV: Once given FDA approval, the trial can enter into the final phase, which involves monitoring the drug after it has been released to the public. In this phase, researchers look for additional information such as risks, benefits, and optimal or additional uses of the drug. In some cases this phase is used to test the drug on a sub-group of people (such as patients over a certain age).

BENEFITS AND RISKS WITH CLINICAL TRIALS

There are both benefits and risks associated with clinical trials. By participating in a clinical trial, you can:

- Take an active role in your own health care
- Gain access to new treatments that are not available to the public
- Obtain expert medical care at leading health care facilities during the trial
- Help others by contributing to medical research

Clinical trials have risks:

- There may be side effects or adverse reactions to medications or treatments
- The treatment may not be effective for you
- The protocol may require a lot of your time for trips to the study site, treatments, hospital stays or complex dosage requirements

HUB OF CLINICAL TRIALS IN INDIA

India is fast-emerging as an attractive destination for clinical trials. Today, the market value of clinical research outsourced to India is estimated at US$100 million. A clinical trial is a costly as well as time-consuming process. The cost of conducting clinical trials for a specific drug ranges between US$350 and US$500 million. Now about 20 organizations in India specialize in clinical trails. These companies have the skills to comply with standards such as ICH-GCP guidelines. Currently, 20 to 30 per cent of the clinical development activity is outsourced to Clinical Research Organizations (CROs) in developing countries such as India due to lower costs. The cost of conducting clinical trials in India ranges between 20 and 60 per cent of the cost in western countries. According to industry sources, a volunteer in a developing country is paid between US$70 and US$350, based on the nature of the study, for participating in three studies a year. By contrast, volunteers in western countries are paid relatively higher amounts. Not surprisingly, research-based global drug companies are keen to outsource clinical trails to developing countries such as India. Today, about 80 government and private hospitals in India are engaged in global and local clinical trials. Multinationals drug companies are also entering India, drawn by the vast pool of scientific talent. The multinationals in the CRO segment include ICON Clinical Research, Omnicare Clinical Research, Pharmanet global, Pharm-Olam, ClinTec International and Quintiles Spectral. The Indian clinical market is likely to be worth US$1.5-2 billion by 2010, provided the number of patients in Indian trial sites constitutes 20 per cent of patients in global clinical trials. This report provides an in-depth understanding of clinical trials in India. While front-end sections such as Executive Summary and Highlights provide the essence of the report in a few pages, the remaining part of the report provides an exhaustive analysis of clinical trails in India. The middle of the report focuses on market scenario and major players. It also comprises an in-depth analysis of the growth prospects of the industry. But one of the most important legislative changes has been the amendment of schedule Y of the Indian Drugs and Cosmetics Act to comply with the regulations of the International Conference on Harmonization. Prior to the amendment, there was a phase-lag rule in effect that barred earlier-phase trials from being conducted in India before being conducted elsewhere in the world. “What that did is, it said, if you're doing a trial in India, you need to be one trial further advanced in the rest of the world. So if you were doing a phase III trial in Europe, you could do phase III trials in India, but you could not do phase II trials, and that was really to protect the country.” The amendment means companies can include India in global, multi-center trials in all phases. That allows companies to conduct their clinical trials more quickly and efficiently. Many pharmaceutical and biotechnology companies are turning to CROs like Quintiles and

Accenture to take their trials outside the US and Western Europe. Similarly many of the CROs are specialized now operating in Indian subcontinent because of local geographical knowledge. Certainly India becomes the more obvious choice because it is home to over 16,000 hospitals and 500,000 doctors, making it an ideal country in which to conduct clinical trials. Whereas one of the challenges of conducting clinical trials in China is that simply getting a clinical trial application approval can take from seven to 10 months.

BOOMING CLINICAL TRIALS MARKET IN INDIA

 CLINICAL TRIALS market in India is estimated at $200 million and is expected to grow to $1 billion by 2010.The market has grown at almost 400 per cent in the past two years and is pegged to grow even more by 2010. Currently, India has a global market share of almost 50 per cent in the clinical trials business. India is fast becoming one of the biggest hubs for conducting global clinical trials. In 2007, the country conducted around 220 clinical trials, making up for less than 2% of the global clinical trials But according to "Booming Clinical Trials Market in India", a new research report by RNCOS, a number of factors such as low cost, large patient pool, easy recruitment, strong government support and strengthening of its intellectual property environment will enable India to conduct nearly 5% of the global clinical trials by 2012.As per the report, India scores well above many other destinations in almost every factor analyzed. For instance, India provides one of the largest patient pools for both infectious and chronic diseases. Moreover, the country has 40 million diabetics, representing the largest in any country. Similarly, India also has one of the highest numbers of patients for other chronic diseases such as cardiovascular, neurological disorders, respiratory disorders and obesity. Apart from chronic disorders, the country also provides one of the largest numbers of patients for such infectious diseases as HIV, malaria and tuberculosis.The findings of the report suggest that not only does India provide a large patient pool, the recruitment of these patients is also among the fastest in the world. As most of the healthcare costs in India are paid "out of pocket", a large patient population continues to have unmet medical needs. As a result, they readily volunteer to participate in clinical trials to get free treatment.
Booming Clinical Trials Market in Indiagives an extensive and objective analysis on the Indian clinical trials market. It investigates the advantages and disadvantages India has over other countries to become a global clinical trials hub. The report exhaustively evaluates and compares the key factors that drug companies and CROs look before outsourcing clinical trials to a country. These include factors such as patient pool, regulatory environment, cost, infrastructure, human resources and past performance in conducting clinical trials.Thus, the report serves as a useful guide for drug manufacturers, CROs, consultants and investors who are planning to enter the Indian clinical trials market.

CONCLUSION

It might take somewhere between 10 and 15 years for the drug development process from pre-clinical to complete phase III clinical trials. Out of which, the phase II and III clinical trials consume almost half of the time. Given this situation, it looks imperative that pharmaceutical and biotechnology companies ought to look for ways to conduct trials faster and with less spending. However, they have often failed to meet the challenge and hit the market with the drug as planned.The reasons have been the *d*ropping enrollment for clinical trials in the US and Western Europe and that has led companies to think of alternative places where they can have trial sites and which can help them enroll more volunteer to conduct trials faster. The recent attentions of the companies have been to look forward to the countries like India and China as a solution.It is believed that one of the advantages of conducting clinical trials in areas such as Eastern Europe and Asia is the speed at which patients can be recruited; as it is very difficult to get patients to enroll now in the U.S. Enrollment rates in the Far East and China and Eastern Europe and India are much faster. So, if you needed 200 patients for an oncology trial, your chance of getting them in India within a three-month enrollment period is much higher, whereas it might take you a year or more in the US. While there have been a number of challenges to conducting these clinical trials, several countries, most notably India, have taken a number of steps to make the process more user-friendly. In 2005, the Indian government increased intellectual property protection on patents, a key change in a country's enforcement of laws protecting patents and clinical trial data. That made companies a little more comfortable coming to India. Another legislative change was for sweeping, mandatory global clinical practices for conducting trials.

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