India's Clinical Trials Market Accelerates

There has been a perceptible change from skepticism to acceptance in how India is viewed for clinical trials

There has been a lot of speculation recently in the Indian and international media regarding the possibility of the US Food and Drug Administration (FDA) establishing a formal presence in India. Much of this media coverage arose as a result of the January visit of US Health and Human Service (HHS) Secretary Michael Leavitt and FDA Commissioner Andrew Von Eschenbach to India.[1,2] In his own blog, Leavitt stated that much of his discussion with the Indian Minister of Health and Family Welfare, Anbumani Ramadoss, centered on regulatory issues.[3] Specifically, the talks included assistance to create an equivalent of the FDA in India. In line with the approach used for China, both HHS and FDA will put teams together to examine the issues.

Faiz Kermani, PhD, NEED JOB TITLE and AFFILIATIONS.

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REGULATORY RUMORS

In contrast to this description, the media believe that FDA officials will eventually be stationed in India. Although some may see negative connotations as FDA officials presumably evaluate food safety for US bound products, there is a more positive angle from an Indian perspective. These developments clearly show that India is maturing as an important pharmaceutical location. The interest of foreign regulatory agencies may initially be linked to assistance in order to help grow domestic regulatory expertise and for monitoring purposes, but it must also be in response to India's transformation into a recognized hub for drug development.

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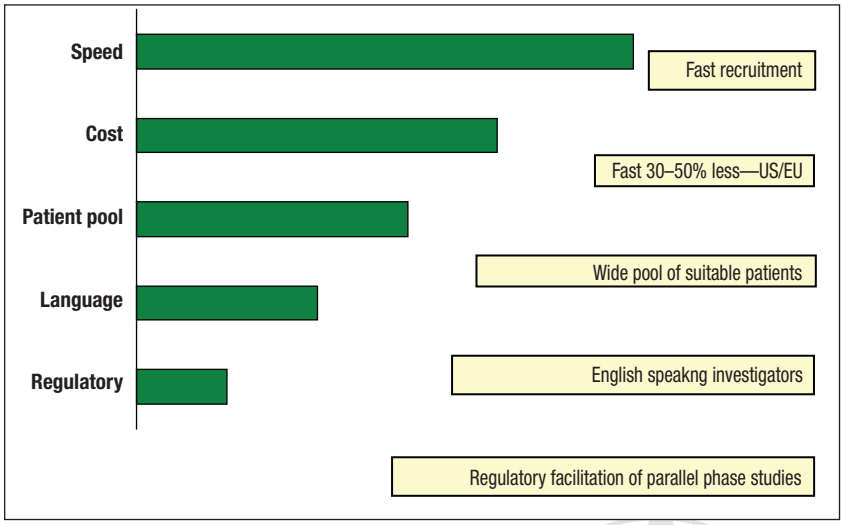
In particular, the surge in multinational pharmaceutical company-sponsored clinical trials in India must be of interest to foreign regulatory agencies and such wider issues must have at least been touched upon in top level discussions. Certainly over the past decade, there has been a perceptible change from skepticism to acceptance in how India is viewed for clinical trials; many consider it a core region for global plans (Figures 1 and 2). As a result, many global pharmaceutical players including Pfizer, Novartis, AstraZeneca, Eli Lilly, GlaxoSmithKline, Aventis, Novo Nordisk, Bristol-Myers Squibb, Roche, and Amgen have expanded their existing clinical research investment and infrastructure in India.[4] According to the *Asia Times*, in 2002, outsourced clinical trials generated an estimated $70 million in revenues for Indian companies in this sector, and the number was predicted to grow to $200 million by 2007. There are predictions that the Indian clinical trials market will be valued between $500 million and $1 billion by 2010.[5]

THE EMERGENCE OF THE INDIAN CRO SECTOR

In the early 1990s, the contract research organization (CRO) sector was considered virtually nonexistent in India. Because CROs were not operating in the country, there was a lack of

PHARMA INFORMATICS

Figure 1. Major advantages of conducting clinical trials in India



commercial awareness concerning clinical trials, and to a degree, this created considerable apprehension in the minds of the prospective clinical trial professionals.[4] Pharmaceutical companies who were identified to perform clinical trials were mostly aiding their parent company in regulatory support and medical marketing functions. In fact, professionally qualified pharmacists and medical doctors interested in pursuing a career in the industry were not considering clinical research as an attractive career option, preferring a career in pharmaceutical sales and medical marketing. Only a handful of senior reputed doctors were serving as investigators for global multicenter studies under the direct monitoring of international sponsors.

Attitudes have changed in the last decade, however, as foreign companies that had invested in Indian clinical trials found themselves pleasantly surprised with the results. In many cases, it was only severe competition elsewhere in the global market that forced companies to expand their outlook to India. Currently, most local and global CROs consider an operational presence in India as key to their overall business plans.

Most Big Pharma companies have overcome the psychological hurdle concerning data quality in India.

To achieve greater economies of scale and increase profitability, there have even been instances where global CROs have reduced their existing operations in more established markets and expanded similar operations in India. In particular, there has been a trend to conduct the data management side of clinical trials in India. Hence, to a degree, there has been a steady business expansion from the US and Europe to India and other emerging market countries. The key enablers for the Indian CRO business have been the availability of high-quality talented staff, a lower cost of operations, improving infrastructure, growing regulatory support from the government, and better investor involvement. The existence of well-qualified investigators and other clinical research professionals means that such business expansion is predicted to continue well into the foreseeable future.

FROM ACCEPTANCE TO ATTRACTION

Early pharmaceutical pioneers in India faced a daunting task in operating in a regulatory and ethics environment that was overtly unfriendly for quality clinical trials. To make matters worse there was a dearth of experienced investigators and clinical research professionals. However, with patience and persistence, these organizations and their supporters brought about a change in the quality of research professionals, increased awareness of good clinical practice (GCP) compliance, and made efforts to improve ethical aspects of clinical trial operations.

A decade ago, India had little in the way of clearcut regulatory guidelines for clinical trials, but it slowly progressed towards GCP clinical trial standards.[4] Because of pressure from the industry and proactive initiatives of the regulators, the Central Ethics Committee on Human Research (CECHR) of the Indian Council of Medical Research (ICMR), New Delhi, issued Ethical Guidelines for Biomedical Research on Human Subjects in 2000. Subsequently in 2001, a central expert committee was set up by the Central Drugs Standard Control Organization (CDSCO) to develop Indian GCP guidelines in line with the latest WHO, ICH, FDA, and MHRA guidelines. A continuation of this regulatory revolution has been revision of Schedule Y. Schedule Y deals with regulations relating to clinical trial requirements for the import, manufacture, and of obtaining marketing approval for a new drug in India. The procedure for applying for marketing approval

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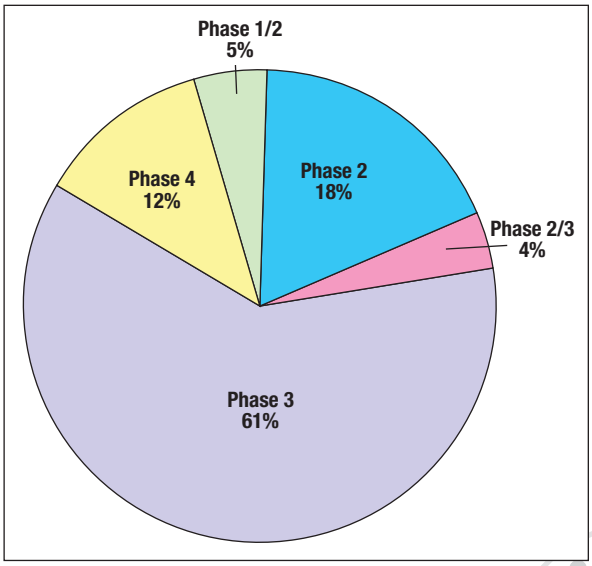
Figure 2. Clinical trials in India are on the rise



depends on the status of the new drug. When the revised Schedule Y fully comes into force, it will confirm India's image as a reliable clinical research destination.

In the early 1990s, sponsors often posed the question "Are Indian clinical trials acceptable globally?" and this remained difficult to answer. Yet, it has become much easier to convince sponsors to consider India for their major clinical research plans. In a similar way to how other emerging markets developed, India has now shown that quality data can be generated to satisfy major regulatory agencies. Most major pharmaceutical companies have overcome the psychological hurdle concerning data quality and routinely include India in their plans. This is why FDA's recent visit to the country generated such media interest.

ENSURING AN ETHICAL EVOLUTION

With so much attention focused on the financial aspects of the clinical trials market in India, it is important that issues such as ethics do not take second place. There have been occasional allegations that poor and illiterate patients in India are being used, often unknowingly, by some CROs in India as "human guinea pigs" to test new drugs.[6] This, of course, is unacceptable and the industry must send a clear message to its staff about the high standards it expects for the conduct of clinical trials. All those involved in drug development must ensure that they adhere to international and local regulations in order to protect patients.

Sponsors must verify, and not just assume, that investigators completely understand and respect ICH–GCP, the consent process and the need for documentation of the consent process, and the ethics process. There should also be a formal training of clinical trials staff so that the required standards can be upheld. For example, according to Umakanta Sahoo, managing director of Chiltern International, Mumbai, in 2006, his organization set up a dedicated network of investigators in India (CINISTA), to serve as the preferred primary contact for the company and function as principal or coordinating investigators.[6] In addition, the CINISTA participants provide trial sponsors with their views and advice for areas such as trial design, study conduct, and interim analysis. Through this system the sponsors also learn about domestic clinical trial requirements from Indian clinical trials professionals.

FUTURE OUTLOOK

India is clearly on course to become a major center for clinical trials, and is routinely considered by international sponsors for their global trials. The involvement of regulatory agencies, such as the FDA, should be seen as a beneficial step to ensure that the clinical trials environment evolves in an appropriate fashion and that standards used to protect patients in other markets are also applied in India. Although companies face continuing pressure to reduce clinical development timelines and costs, it is important that these factors do not encourage staff to let standards slip in particular markets. It is in the pharmaceutical industry's interest to fully engage with Indian patients in their work. Patient participation is essential if future drugs are to be developed successfully in India. If the public have confidence in the industry, then rapid patient recruitment will be enhanced. ◆

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