



**COVER STORY**

# INDIA ON TRIAL

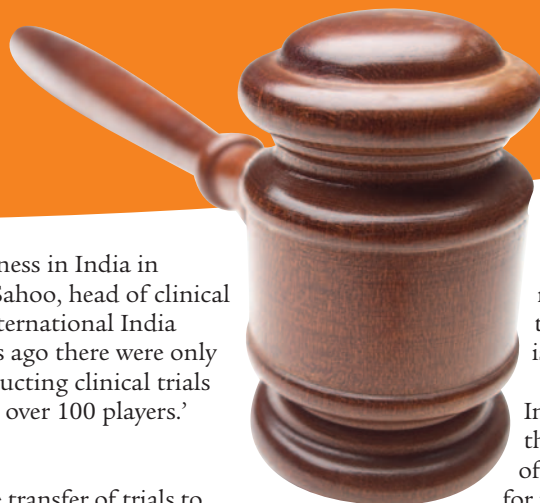
India, with its cost advantages and bank of educated professionals, has much to offer the clinical trials industry. However, some pharmaceutical companies are not yet convinced that clinical data in India and the available pool of trial subjects match their exacting standards. *World Pharmaceutical Frontiers* talks to four leading clinical trials specialists about what attracts pharmaceutical companies to India, and what problems the country must still overcome if it is to fulfil its huge potential.

**O**ver the last three to four years, major pharmaceutical companies have started to outsource or relocate clinical trials to India. The clinical trials business in India is now worth \$170 million, and this figure is expected to rise over the next three years to between \$500 million and \$1 billion.

So how much clinical trial work has gone to India? This is difficult to quantify, but global registry figures say that currently 357 trials have recruited subjects. Most of the trials appear to be small, although several Phase III vaccine trials have recruited large numbers of subjects in India.

Indian contract research organisations (CROs) offer all the facilities needed to successfully conduct Phase II-IV clinical trials. In terms of Phase 0 and Phase I trials, the capability is currently being developed and it won't be long before these trials are conducted in India on a significant scale.

It is important to remember that Phase I investigational drug trials are not permitted in India where there is no intention of registering or making the drug available in India from the outset. Similarly, Indian CROs and regulatory authorities are still not open to the idea of conducting a first-in-man trials in India for a drug that is developed outside India.



Putting the drug trials business in India in perspective, Dr Umakanta Sahoo, head of clinical research for the Chiltern International India office, says: 'About ten years ago there were only one or two companies conducting clinical trials here, but now there are well over 100 players.'

### Clean data

One big issue relevant to the transfer of trials to India is the quality of data and the ability of Indian CROs to relay it back for analysis. However, according to Sahoo, there is a wide acceptance of clinical data from India. 'Both the EMEA and FDA accept that clinical data from India is clean and of high quality,' he says, 'but the FDA has issued specific guidelines for international clinical trials.'

Dr Mahadev Murthy, founder of the Institute of Strategic Biotechnology, Health and Training (ISBHT), in Bangalore, believes that India and other developing countries 'need to focus on developing the right clinical infrastructure, which is close to US and EU standards'. India, he says, needs to follow ICH (International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use) guidelines.

#### THE ISSUES

- Is clinical trial data gathered and processed to international standards?
- Are the subjects of trials sufficiently informed to give consent?
- Is the largely Indian population suitably diverse for wide-ranging studies?
- Are the IRBs sufficiently competent to review clinical processes?

Vinod Matoo, medical director for Eli Lilly (India) says there is no problem with Indian trial data, 'provided privacy/safe harbour principles are in place and as long as the data generated are to the same ICH-GCP standards applicable in other developed economies'. He adds: 'There has been concern in the past about "poor quality" data and the exploitation of research subjects in developing countries, but done properly, data from India has the same validity as data from any other country.'

### Demographic issues

A pressing consideration for companies considering relocating clinical trials to India is the diversity of the population and treatment naivety. Some question whether a trial is still valid if the subjects are only drawn from one ethnic group. On

the other hand, it can also be argued that a trial might be more valid if subjects have had no prior treatment at all for their condition, something that is rare in the West, but far less uncommon in India.

India is different from the West in other ways. 'Under the current regulations, no company can have 100% of patients on candidate drugs that are being tested for the US and EU markets,' says Murthy. 'And there are other restrictions that a company must recognise in global clinical trials. One cannot do a Phase III trial with subjects solely from India and get approval for either the US or EU markets, unless it is in the area of communicable diseases.'

Sahoo says: 'Poverty has an impact on trial subjects in India. We get many patients with advanced conditions, and these may not be considered suitable, as the protocols for the majority of trials are designed around moderate conditions.'

Most trials in India are part of multi-country protocols, and Matoo is only aware of a few instances where trials wholly based in India have been submitted to the US FDA and been approved for the US. 'India has the diseases of the developing world plus the diseases of the developed world,' he says. 'The disease pattern has changed significantly in the last 15 years or so. Heart disease is now the commonest cause of death in India, the prevalence of hypertension is about 20%, and India currently has a huge number of patients with diabetes.'

Recruitment for studies is easier and faster in India than in the West. India has a large and diverse patient population (of over 1.1 billion) from which to draw, with a diversity of maladies, including Western diseases and those, such as malaria and tuberculosis, which are rarely seen in the West.

India has excellent hospital infrastructure with English-speaking staff and international standards. Murthy says: 'There is an excellent infrastructure base, such as computing for clinical data management, and the quality of trained staff is also excellent.'

### Patient consent

Recruiting subjects in India is certainly easier and quicker than in the West, but there are complex issues involved, relating to informed consent, the language barrier and financial incentives. Murthy says: 'The process in India is still evolving, and many issues still need to be resolved. For example, how do we administer informed consent to people with language and educational problems? Can they understand informed consent? How much control would a physician have on patients when it comes to recruitment to a particular trial?'

'Both the EMEA and FDA accept that clinical data from India is clean and of high quality.'

Dr Umakanta Sahoo

What about financial compensation? Are the institutional review boards competent to review clinical protocols?

Sahoo says: 'There are many other considerations. Protocols can be really difficult to satisfy, but it is usually as simple as being in touch with the larger hospitals and medical colleges where research into the relevant areas is going on.' The ability to enrol patients quickly and get quality clinical data on time allows the drug development process to be more rapid.

Matoo says: 'Difficulties in recruitment arise from the educational status of patients (the difficulty in delivering adequate informed consent), language issues, the widespread use of traditional herbal medication that could potentially confound trial results, and the limited number of hospitals with properly constituted ethics committees.'

#### ADVANTAGE INDIA

A number of factors make India a favourable destination for clinical trials:

- Approximately 20,000 doctors graduate every year, while India has 70,000 hospitals and 221 medical colleges.
- The salaries of professionals are 30% of those in the West.
- Infrastructure and IT are well developed.
- There is a 30–40% overall cost advantage in undertaking drug trials in India.
- Faster patient recruitment is possible, due to India's large population.
- India's population in urban areas is keen to volunteer for trials.
- A wide range of diseases are prevalent in India
- The time taken for trials is 30–40% less in India.
- Quality is assured, with Indian investigators following ICH-GCP guidelines.

India now seems an even better option following February 2007's announcement of a tax exemption on all services carried out by the contract research and clinical trials industry in India from 1 April 2007. This will mean a saving of 12% on service tax, removing a previous stumbling block for international pharmaceutical sponsors considering using contract research organisations in India.



India has a large population of willing drug trial subjects.

The number of clinical trials being conducted in India is growing. The major driver is costs savings in bringing a drug to market. Matoo says: 'Grant costs are about 30% to 40% lower compared to the major economies.'

According to Mahesh Sawant, programme manager in the healthcare practice of Frost & Sullivan for the South Asia and Middle East region, the major advantages of conducting trials in India are the time and the cost savings. 'Major activities such as patient recruitment and regulatory approvals can be done 30–35% quicker in India than in highly regulated countries,' he explains. 'This has a cost advantage. Add to that lower wages and the easy availability of trained personnel, and the cost saving comes close to 40%.'

#### Bright prospects

Although there are still difficulties to overcome, India has excellent infrastructure in terms of clinical centres and hospitals and also from an IT and data handling perspective. In fact, there are opportunities for India to capitalise on the clinical data management segment much more quickly than on clinical trials, where quality, compliance, drug safety, risk management and regulatory considerations dominate the new drug development arena.

According to Sawant, the clinical trial (Phase I–IV) market in India is currently valued at approximately \$38 million, with growth of close to 37% per year. The clinical services market is valued at \$140 million, growing at 20% per year. This includes allied services such as data management, central lab services and bioavailability-bioequivalence services. The total clinical services market is expected to grow to \$830 million by 2013 at a CAGR of 29%.

This phenomenal growth is expected to come from trials being outsourced to India by the big pharma companies. However, India's promise in terms of clinical trials outsourcing does not negate the many challenges that the country needs to address to achieve global standards. **END**