



Clinically Speaking

India has suddenly become the hotbed of clinical research with foreign pharma companies tying up with Indian majors.

Vikas Dandekar takes a detailed look at the sector that seems set for an explosive growth.

We have serious problems in drug development in the U.S. and Western Europe," William Haseltine, the founder of Human Genome Sciences, said after a meeting during early May 2004, of the American Association of Pharmaceutical Scientists in Boston, where he made it plain to members why drug makers have no option but to go East. Haseltine truly was prescient.

Scientists at Vimta Labs — a small contract research firm in the southern city of Hyderabad in India are a busy lot. In the last two years, Vimta has seen orders flowing from multinationals and mid-sized European companies to take forward their experimental drugs through Phase two and three clinical studies.

Scientists there are also busy doing bio-availability/bioequivalence studies and analytical tests for dozens of smaller Indian drug firms. Bioequivalence and bioavailability are mandatory tests to check if the strength of the drug matches with the reference standard. The toil seems to be paying off. Investment firm Merrill Lynch initiated coverage on the company in June 2004 and stated in its report that Vimta expects to grow its revenues by a spectacular 80 per cent every year.

It is, therefore, investing heavily in increasing its bed capacity. There is data to



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Pfizer's clinical research group has grown to over 46 employees from a mere four and is by far the largest group within the medical and research division who work across various Pfizer's global projects.

Says Dr Shoibal Mukherjee, senior director and head of Pfizer's clinical development, "While for companies like ours it is important to speed up our Phase two and three studies to cut down drug development time, for several patients faced with life threatening diseases like cancer, it could be an opportunity to save their lives."

And, thus far, Pfizer is only doing a fraction of its global clinical development work considering that it has one of the richest product pipelines. "India, though high on the agenda, is still to match up with more ideal conditions to get more attention for all global trials," he says.

The \$ 24 billion Novartis too is following the same line. Two years ago, the Swiss major expressed its desire to set up one of its global clinical management and biometrics divisions in India — an envied position in the company's scheme of things. Experts agree that the centre in Mumbai houses some of the best statisticians and is contributing immensely to Novartis' global drug development programme.

The same bullishness has been displayed by US drug maker Wyeth, but taken forward through the time tested outsourcing route. Wyeth has farmed out a large part of its biometrics operations — a study of clinical test results done in various multicentric trials and tabulated in a scientific form for submission to the regulators to global consulting firm Accenture in Bangalore. The work has kept growing as Accenture, over the last two years, had to employ almost 400 data management professionals to cater to the pressure.

Among the latest to ramp up clinical research in India are European drug makers GlaxoSmithKline and F Hoffman La Roche. Tachi Yamada, chairman & head of research committee, GlaxoSmithKline on

CLINICAL RESEARCH WILL SLASH DEVELOPMENT TIME: Dr. Shoibal Mukherjee

back up. For financial year 04 (which ended in March 2004), Vimta's revenues grew by above 80 per cent to touch \$ 7.3 million and net profit grew by more than 300 per cent at \$ 1.7 million.

Vimta — being the only clinical research and analytical testing company listed at the Indian bourses — is in the spotlight now but is not the only one to achieve this scorching pace of growth. There are a few others, like Siro Clinpharm, I-Gate, ClinInvent (a Soros Chatterjee company, the Soros being derived from its link with US investor George Soros) and Lambda, which are generating strong revenues.

But these are only a handful clinical research and bio-equivalence services firms. The sector seems set for an explosive growth. According to a ML industry report of 2004, there are some 270 contract or clinical research companies in North America while Europe houses 466 clinical research organisations. As compared, India

has just around ten full-service CROs — pathetically low for a sunrise sector and least ready to accommodate the demand. This small number of CROs also underscores the enormous potential for growth of the business in India.

Sensing the overflow of opportunity and a plethora of advantages of clinical research in India — way ahead than others could — multinationals queued their direct clinical research operations in India. Leading the way was Pfizer, the top drug behemoth that set up its own Indian clinical research group a decade ago in 1995.

The Terminology of Clinical Trials

Phase	Requirements	Purpose
One	Testing on healthy humans — 25 to 50 (may vary)	To test the safety profile of the drug candidate
Two	Testing on patients (150 to 200 patients)	To test the efficacy of the drug
Three	Testing on a larger mass of patients in multicentric trials	To see if the drug is tolerated well in mass patients (upto 1000 patients)

his recent visit to India said GSK will be investing heavily in taking up clinical projects in India.

There are obvious issues like costs and time for drug development forcing these transnational companies take a relook at India. Nonetheless, the current investments — there is no audited data available — estimated at \$ 50 to 100 million annually is just a scratch on the surface.

Consider this. The global pharmaceutical industry is pegged at around \$ 400 billion currently. Of this, the entire drug industry, innovators and generics taken together, have an average research spend of 10 per cent of sales that is \$ 40 billion roughly. While clinical research between Phase one, two and three is known to take almost 50 to 60 per cent of the drug development costs, global drug majors are targeting this particular segment for cost controls. And so India is an important destination.

Experts say cost controls on clinical trials will be more relevant for a mid-sized company or entities such as universities since there budgets are more strained on research as compared to a bigger MNC drug firm. Sources say prestigious universities like Johns Hopkins University may look at India for clinical trials on their drug candidates.

It could not be better timed from the Indian regulator's angle. While there is an air of scepticism on allowing concurrent trials for Phase two and three studies, the Indian government, in tandem with the recommendations of the Raghunath Mashelkar



CONCENTRATE ON BASIC CHALLENGES: Dr. Arun Bhatt

Multinationals are looking for a whole bouquet rather than a piece-meal approach to farming out their clinical research

Committee, is keen on a single window clearance for human trials. This will mean that Schedule Y of the Drugs and Cosmetics Act will see sweeping changes in the way drug trials are cleared.

R S Nadig, medical director Eli Lilly says there are no objections raised on effective regulations; what is undesirable is the delay in drug trial approvals due to multiplicity of approvals needed.

These fears were, however, allayed by Dr Raghunath Mashelkar, director general, Council of Scientific and Industrial Research at a recent Science conference held in New Delhi. He said, "The evolution of India as a research destination should come more naturally. The government needs to be more cautious in allowing the right moves so that the future flow of investments in research and development could be more pronounced and permanent in nature." Dr Mashelkar, however, remains guarded on allowing Phase one trials in India. Safety trials are not allowed in India if those trials are not done in any other country.

There are concerns at the policy levels and matter immensely to a typical multinational while considering long-term investments. Ranjit Shahani, MD at Novartis India voiced his dissatisfaction over progress made on the issue of data exclusivity. The Indian government has not expressly guaranteed data exclusivity for drugs undergoing trials and invented by multinationals. On the face of it, it appears to be a legitimate



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ANALYTICAL TESTS: Enormous potential for growth in the business



DANANJAY LOKHANDI

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demand from the multinationals' angle.

There is an obvious reluctance to test drugs discovered painstakingly by multinationals in the haven of generic manufacturers. Though patent protection is guaranteed by India after 2005, PhRMA — a US based pressure group of top drug majors — says the exclusive trials data submitted to Indian regulators may be pilfered by Indian companies to sell products in least developed countries that will allow copies of invented drugs beyond 2005.

Dr Arun Bhatt, who worked as medical director with Swiss drug major Novartis India and currently heads ClinInvent, feels India needs to concentrate on more basic challenges. "Everyone talks about the patient population in India but with the current healthcare infrastructure, we do not have a structured database of patients available for trials." Experts view this in the same light.

China, Russia and some countries in Central Europe are catching up to prove that they are ahead on clinical development business and are working on databases that can enable companies pick and choose clin-

ical trial candidates.

Dr Mukherjee says with minimal infrastructure changes in our rural hospitals, we can outnumber other countries in facilities and eligible patient population. The numbers speak for themselves. Last year, an international journal on Good Clinical Practices put the average cost per patient for clinical development in Phase three at \$ 7000 in the US, the figure was \$ 5000 per patient in Europe and in India it could be done in around \$ 700, the publication said.

Dr Bhatt agrees. CT scans in the US are more than 10 times costly than in India. Then there are other cost additions like travel to patient sites, organising investigators meetings and other medical examination costs like X-ray, pathology etc. But are these positives really attracting global trials? No, not to a great extent says an analyst with an Indian brokerage house. He cites a Centrewatch study done in 2002.

The study showed that out of several hundreds of trials done by global drug majors, only about 40 to 50 studies were routed to India. The reason is quite a sur-

prising one. Beyond getting drugs tested in a short time and with minimum costs, drug majors want to build up a longer relationship with the medical fraternity so that marketing of those drugs become easier when they are ready to be sold.

As such, countries that have a patent protection in place (India will respect product patent from Jan 1, 2005) like China have a headstart over India since the same experimental drugs may reach the market and get a quicker endorsement from the local doctors. This will help them achieve revenue projections head on. In this matter, the Indian market size, with copies of invented drugs instantly available, is too small to bring in the experimental drugs.

At the operational level, there are more serious questions that global MNCs are asking. Dr Bhatt, being in-charge of an independent clinical research company says that pharmaceutical company backed clinical development centres are not looking very attractive from the global pharma major's perspective as it raises doubts on intellectual property protection.

Neither are there too many examples of such entities in India. One of them is the Wellquest Research Centre belonging to the Nicholas Piramal group, a heavy-weight in the domestic formulations business with sales exceeding \$ 250 million. Nicholas Piramal sources, however, say the company has received accreditation from European agencies and have been getting a good flow of actual clinical development work as against merely bio-equivalence studies. Nicholas officials say being a full service CRO always helps.

Multinationals are looking for a whole bouquet rather than a piecemeal approach to farming out their clinical development and research work. These may be contradictions but betters prospects for the clinical trials business to thrive.

Dr Braj Bhushan Lohray, a hardcore discovery scientist and heading the discovery efforts with Indian drug company Zydus Cadila says, medically speaking, conditions are just right for an independent CRO to prosper. With more than 40 million asthmatics, 36 million diabetics, 10 million HIV cases, 8 million epilepsy cases, 3 million cancer patients and 15 per cent of the population having hypertension problems, world clinical research will be incomplete without including such a mass disease pattern. 🌈

The Majors in Clinical Trials in India

Pfizer	Biometrics centre, Phase two and Phase three clinical trials
Novartis	Biometrics centre, Phase two and Phase three clinical trials
Altana	Completed five Phase two and three trials for global submissions
Bausch & Lomb	Largest clinical trial done outside US for a drug delivery device
Quintiles	Clinical research services for many multinational companies