What Ails Clinical Trials Industry?

Controversies and litigations threaten to derail a sector that once saw immense potential in India

Joe C Mathew

TEXT SIZE : A | A | A

TOOLS

- e-mail this story
- print view
- view only pictures
- story in single page
- <="" script=""> share

RELATED STORIES

The Future Of Indian IT

The Price Of Globalisation

Mirror,Mirror On The Wall

Maximising Losses

In comparison, total trials registered in India is just 2,059, far less than those in China (3,254), Korea (3,717) and Taiwan (2,729). According to BCG, India has been losing share to China and Korea in the past seven years. While India had a 36 per cent share of the market among the three countries in 2005, the share slipped to 35 in 2007, 27 in 2009 and stood at a mere 20 per cent in 2011.

According to industry estimates, about 150 companies are engaged in clinical trials in India. These include pharmaceutical companies conducting trials on their own and about 80 contract research organisations (CRO) — multinational and domestic — that take up trials for drug

discovery companies. While all prominent players continue to remain in the market — Quintiles being the market leader with about 50 per cent of the CRO business — their share of revenues from clinical trials (as compared with revenues from related services) is falling.

"Our revenues (from India) are mostly non-clinical. About 70 per cent comes from data management, pharmacovigilance (the science of detecting drug-related problems), bio-statistics management and so on. Clinical sector is not doing well," says Shoibal Mukherjee, vice-president, medical, Quintiles India.

The Firefight

At the receiving end is the Indian Society for Clinical Research (ISCR), a body of professionals engaged in clinical trials. It has not done its credibility any favour by housing itself in the premises of the Indian arm of the world's largest pharma company, Pfizer India, in Mumbai. It's in a firefighting mode. ISCR is busy issuing clarifications on media reports, parliamentarians' views and the government's interventions. The lobby group has a media council to "accurately portray" the image of the clinical research sector at a time when its image has, perhaps, hit a nadir in the eyes of the public.

KIRAN MAZUMDAR-SHAW CMD, Biocon "THESE ALLEGATIONS ARE BLOWN OUT OF PROPORTION. WE HAVE A REGULATORY SYSTEM IN PLACE" (BW pic by Jagadeesh NV)

The US government's clinical trial registry indicates that India is carrying out 2,059 trials at the moment, including the 538 cases where companies are seeking new patient recruitments. Obviously, ISCR has a lot of tackling to do. It went into war mode after a parliamentary panel pulled up the health ministry for not maintaining any records of clinical trial deaths or compensation payments in 2010. Following the report, 22 payments were made by MNCs as compensation towards clinical trial-related deaths in 2010. In 2011 , this stood at 15.

The payments, however, raised more questions than answers. First, the instances of clinical trial-related injuries and deaths before 2010. The quantum of compensation paid and the methodology used to calculate the amount of compensation was another. A fresh parliamentary panel probe is now figuring out issues related to clinical trials.

"The compensation issue has had a snowballing effect. We are going out (to the industry and media) to explain our position as our business has suffered. It has been flat growth this year (for CROs). If the situation continues, we will have to consider setting up facilities outside the country," said Arun Bhatt, an executive committee member of ISCR. Bhatt heads an Indian CRO, ClinInvent Research.

With over 150,000 volunteers being tested for new drugs in India (as estimated by the Monthly Index of Medical Specialities (MIMS), a journal that lists formulations of major drugs), every single death of a clinical trial subject or every alleged instance of unethical conduct of trial — irrespective of whether clinical trial was the cause of the death or injury — is having a major

impact on the sector, necessitating continuous "awareness campaigns" by the ISCR, though the merit of these allegations remains a subject of intense scientific debate and medical scrutiny.

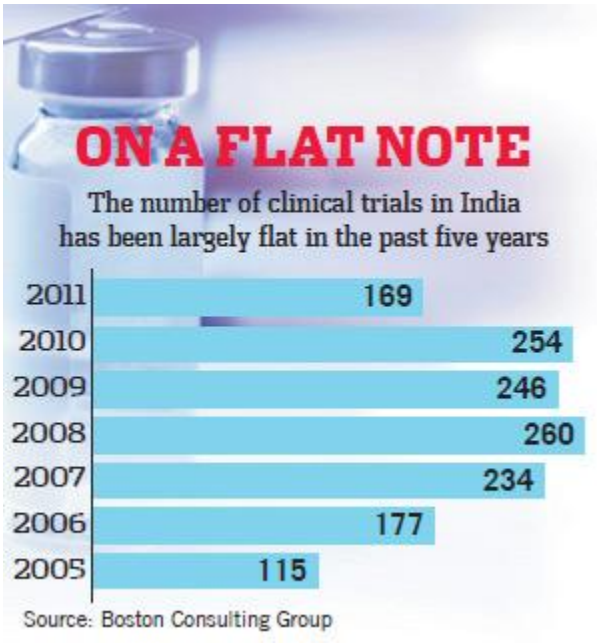
"Due to continued delays and challenges in getting approvals, global sponsors and CROs are carefully assessing the situation," says Ranjit Shahani, president, Organisation of Pharmaceutical Producers of India (OPPI) and vice-chairman, Novartis India.

But the opponents are unrelenting in their attack. "About 99 per cent of the patients who are asked to take such medicines are poor and are unaware of their enrolment in clinical trials. We have documented instances where doctors are even charging such patients consultation fee," says Nidhi of Swasthya Adhikar Manch. "Rules insist that medicines and consultations should be free for patients undergoing trials."

"Signing a legal consent form has no meaning for the vast majority of India's poor. Most of them just draw their signatures without understanding the details," says Chinmay Mishra of Swasthya Adhikar Manch. "A better way to track down unethical clinical trials is to tell people to let us know if they get free medicines."

"These allegations are blown out of proportion," says Kiran Mazumdar-Shaw, CMD of pharma major Biocon, adding, "we have a regulatory system that mandates global standards of ethics and good clinical practice. Like all sectors, if a few companies are non-compliant, regulators need to act swiftly and sternly, but not discredit all the others who are compliant. This should not be a trial by fire, which is what the media and NGOs resort to."

"The recent controversy over clinical trials is worrisome. These individuals and entities are whipping up emotions by portraying only the darker side — showing how some terminally ill patients didn't survive a clinical trial ," Mazumdar-Shaw says and argues that those participating in trials are already afflicted. Their death, therefore, was not due to the drug. If, at all, it proves that the drug was not as effective as anticipated, she says.



Monitoring Handicap

Here is the catch. No one, including the DCGI under the Ministry of Health and Family Welfare, has the ability to verify the actual number of clinical trial-induced deaths or injuries as stated by the industry.

According to available data, the number of deaths in all clinical trials reported during the last three years (2009, 2010 and 2011) were 637, 668 and 438, respectively. With regulatory monitoring virtually non-existent, official data relies heavily on industry-fed information, the credibility of which is questioned by activists. “We are not against trials. We want regulation; ethics need to be followed during trials,” says George Pulikuthiyil, executive director, Jananeethi.

“Streamlining our regulatory procedures and reducing ambiguity would put India on the map of global drug development programmes,” adds Gopakumar Menon, CEO of Siro Clinpharm.

break-page-page

Unethical Practices

With the demand for control and monitoring of clinical trials gathering pace, the government has evolved an interim solution: making ethics committees (which are supposed to track the clinical trials they approve) responsible for their ethical conduct. The Medical Council of India will be responsible for punishing erring doctors.

Experts such as C.M. Gulhati, a medical expert who edits MIMS, are quick to point out the lacunae in the ethics committees, which are of three types. The first, institutional ethics committees (IEC) of government colleges, are, according to Gulhati, the best of the lot. The reason being, government doctors are at least free to oppose unethical practices. Next come IECs of private hospitals and colleges. The doctors here, Gulhati points out, are consultants and hence dependent on hospitals for whom clinical trials are a revenue model. “Consultants, mostly working on a revenue-sharing basis in these hospitals, cannot be expected to raise their voice against unethical practices,” explains Gulhati. The third, he says, are independent ethics committees. “They are the worst of all as they neither have the competence, nor integrity. They are not worth the paper on which they are constituted,” he says. To correct this anomaly, the government is looking at do away with independent ethics committees altogether.

According to Gulhati, ethics committees do not have any legal liability. “An independent ethics committee in Pune can approve a trial in Kolkata. These are commercial committees. You pay them, they sign,” he says. “India is the only country other than the US that has such ethics committees. But in the US, they are responsible. Individuals can end up in jail for a lifetime if they indulge in unethical practices.”

“How do you explain instances of a single ethics panel clearing 300 trials?” asks Sarojini N. of Delhi-based Sama: Resource Group for Women and Health. Sama is at the forefront of groups protesting against the cervical cancer vaccine trials on children conducted in Andhra Pradesh

COST OF ERROR

In 2011, compensation for clinical trial-related deaths was paid in 16 cases

Entity	Drug	Compensation*
Apothecaries	Moxifloxacin / placebo	2,16,000
Fresenius	Paclitaxel nanoparticle	50,000
ICON	Erlotinib	2,70,000
Lambda	Amphotericin	2,00,000
Pfizer	Axitinib	1,50,000
Sanofi	Cabazitaxel	1,00,000
Sun Pharma	Paclitaxel for nano dispersion	3,00,000

*in Rs

Source: RTI response to Anand Rai, Indore

and Gujarat. “Issues of conflict of interest (of doctors), unequal social context, etc., of participants should be looked into when talking about clinical trials,” says Sarojini.

The industry disagrees. It says clinical trial protocols and the conduct of trials are all being audited regularly by the world’s best regulators, such as the USFDA. “We work in a highly professional manner. Documents are preserved for at least five years,” says T.S. Jaishankar, managing director of Chennai based Quest Life Sciences. “We recruit healthy volunteers from a database shared among all CROs in South India. None of them will be allowed to take part in more than one trial at a time; we do fingerprint identification before enrolling them.”

Managing Director, Quest Life Sciences “WE WORK IN A HIGHLY PROFESSIONAL MANNER” (BW pic by G.Keshav Raj)

Echoing him, Mukherjee of Quintiles says his team has “nearly 400 (clinical trial) sites across the country”. “We do make sure that all of them function in the same manner. I would still want regulatory inspections, surprise checks. It will make the industry more careful,” he says.

CROs and pharma companies point out that no amount of monitoring can prevent illegal and unethical trials from happening as despite all mandatory safeguards put in by them, there still exists a Chinese wall between the doctors and the rest of the stakeholders. “The patients are recruited by doctors and consent forms are collected by them. No one can intervene in that process,” says a senior CRO executive. “The fact remains that the action is happening in hospitals,” says Arun Bhatt, president, Clininvent.

CROs prefer to approach doctors who can enrol the maximum number of patients.This, in turn, will ensure speedy completion of the trials. The doctors, in order to meet targets, at times recruit patients who do not qualify. “If the investigator (the doctor) fudges data, how can an ethics committee — forget about the pharmaceutical company — find out what happened?” says the director of a research-based drug MNC in India. “The country does not have a law to handle such fraud. If you inform DCGI, he will ask us to go to the police station as he has no powers over doctors.”

The problem is restricted to “chronic clinical investigators” who consider trials as a means to make money, says Gulhati. Last year, the Economic Offences Wing of the Madhya Pradesh government found that a few government doctors attached to M.Y. Hospital in Indore had made several crores of rupees through clinical trials. While one such doctor earned Rs 1.53 crore from 15 trials by enrolling 400 patients, another made Rs 1.7 crore from 25 trials with 2,500 patients.

The modus operandi in the Indore case was simple. The doctors entered into contracts with clinical trial companies in their individual capacity, but recruited patients from the government hospital. The payments — a good amount of which is meant to conduct expensive tests, maintain records and provide travel fare to patients — were pocketed by them since the tests were done in the government hospital. Several of the accused refused to comment when contacted by BW.

SHOIBAL MUKHERJEE Vice-President-Medical, Quintiles India "REGULATORY CHECKS WILL MAKE THE INDUSTRY MORE CAREFUL" (BW pic by Bivash Banerjee)

Curbing Malpractices

Once the government approves a trial, companies are free to conduct it wherever they like. Often, local authorities remain in the dark.

Experts says this needs to be regulated through a trials registry in the public domain. "Local people and doctors should be aware of ongoing trials. Information on clinical trials and compensations should be disseminated through public announcements. Let not Indian public be made guinea pigs," says R. Desikan, founder trustee of Chennai-based Consumer Association of India.

The industry believes denying approvals for trials — the practice resorted to by the government — is not going to help. "The problem can only be tackled through awareness campaigns. Let the process of obtaining informed consent be videographed and regulators given access to it," says Mukherjee of Quintiles. "After this stage, you can go back to them with a questionnaire to re-confirm whether they have understood the conditions or not." He is candid. "Do whatever you can, but do not create a stumbling block for clinical research in India."

In its response, the health ministry recently came out with draft rules containing guidelines for registration of CROs, provisions for payment of compensation for injury or death of the trial subjects and expanding responsibilities of ethics committees, investigators and sponsors. It has notified a draft format for informed consent, and another to authorise the drug regulator to allow state authorities to take administrative actions — such as restriction of investigator, sponsor/CRO from conducting future clinical trials in case of non-compliance. Provisions specifying needs and guidelines for registering ethics committees is another suggestion.

C.M. GULHATI
Editor, Monthly Index Of Medical Specialities
“ETHICS PANELS DO NOT HAVE ANY LEGAL LIABILITY. YOU PAY, THEY SIGN” (BW pic by Sanjay Sakaria)

The industry has mooted its own suggestions. According to Shahani, they include: the regulator should start inspections; film informed consent; better oversight from ethics bodies; clear rules on patient compensation; and making registration of sponsors or CROs, ethics committees and investigator sites mandatory. Over time, the government should also accredit ethics committees and investigator sites to bring in greater transparency.

Interestingly, these are the very same measures that are being sought by the civil society groups. But, where shall the twain meet?

joe(dot)mathew(at)abp(dot)in

(This story was published in Businessworld Issue Dated 08-10-2012)

Source: http://www.businessworld.in/en/storypage/-/bw/what-ails-clinical-trials-industry/555784.37489/page/1