

Clinical trials: Regulating chaos-Vidya Krishnan and Malia Politzer

-Live Mint

*The first in a two-part series examining the opaque world of clinical trials in India*

A hospital in Indore has been able to get away with unethical medical trials in which 32 people have died over five years, according to the state government. This despite several investigations, a state government ban and Supreme Court strictures—a classic example of the lawless nature of the clinical trial business in India.

Lata Mehra, who works in a government-run healthcare centre, was desperate when doctors told her in 2009 that she would be on medication for the rest of her life after a heart attack. The monthly medical bill, a little less than half her salary of Rs.1,000 per month, would leave her with enough to just cover food and rent.

Then, Anil Bharani, a professor of medicine at the state-run Maharaja Yashwantrao Hospital in Indore, offered the 47-year-old a dream deal that he called a “company plan”. The Rs.1,300 a month plan would pay for the drugs and also reimburse Mehra for transportation.

What Mehra did not know was that the “company plan” was part of an unauthorized drug trial of anticoagulants. Nor was she aware that Bharani and some of his colleagues were already being investigated by the state government over allegations of misconduct in clinical trials, an investigation that eventually led to the banning of the trial by the Madhya Pradesh government in October 2010.

Regardless, Bharani continued the trials despite the ban, and Mehra unknowingly became a test case for the drugs.

The ban was imposed after it was uncovered that informed consent was not taken, and the patients subjected to clinical trials included newborns, children, pregnant women and mentally challenged persons.

The state followed up with more action, and in January barred Bharani and another doctor from conducting trials, and pulled up 12 other doctors at Maharaja Yashwantrao Hospital and 78 other private doctors for refusing to cooperate in the investigation.

That too hasn't stopped the trials.

Bharani and officials at the hospital declined comment.

The Indore case highlights glaring gaps in regulation and enforcement in India's rapidly growing clinical trial industry. A 2011 Associated Chambers of Commerce and Industry of India report put the value of the business at Rs.8,000 crore, or \$1.8 billion.

On Monday, the Supreme Court turned the spotlight on the business of clinical trials, when it threatened to impose a blanket ban on clinical trials across the country if the Union government didn't act. The court has given the Union health ministry a month to provide the apex court with information on deaths, compensation and general practices when new drugs are tested on Indians.

“We can even issue a one-line direction that all these clinical trials which affect many people must stop forthwith,” justices R.M. Lodha and A.R. Dave said, hearing public interest cases dealing with the incidents at the Indore hospital.

The court's order has once again drawn attention to India's inadequate regime to regulate such trials. Not all clinical trials run in India violate norms, yet, Mehra's experience exposes the gaps in both regulation and enforcement in clinical trials, which, in some instances, have caused deaths, in addition to violating fundamental human rights.

### *Government apathy*

Mehra was more than happy with the “company plan” until her neighbour Mangilal Shreevas died suddenly, in early 2012.

“He was also a heart patient covered under the same ‘company plan’ at the same hospital and under the same doctor,” said the healthcare worker. “We took the same pills and we went to the hospital together for check-ups. After Mangilal's death, his wife wanted his medical case sheets to lodge a complaint, but the hospital refused. I was disturbed by this and wanted a different doctor to have a look at my case sheet.”

The rest of her story is similar to that of several such participants in unauthorized clinical trials who express reservations. The doctors refused to hand over the medical file, saying it was “hospital property” and took Mehra off the “plan”. The reimbursements were discontinued.

Meanwhile, in January this year, the state government gave two doctors, Bharani and Ashish Patel, a rap on the knuckles, telling them to refrain from conducting clinical trials for six months; it also fined 12 doctors Rs.5,000 each for not cooperating with investigators.

The fines have not yet been paid, and despite the ban, the trials continue, according to petitioners Swasthya Adhikar Manch, an activist group and Dr Anand Rai, a whistle-blower who filed two separate public interest litigations (PILs) in February 2012 bringing the subject to the court's attention.

So far, 32 people enrolled in various trials at Maharaja Yashwantrao Hospital have died between 2005 and 2010; the state government has attributed the deaths directly to the testing.

Bharani and Maharaja Yashwantrao Hospital are the targets of both a central probe by a parliamentary committee looking into irregularities in clinical trials across the country, as well as a state level investigation of ethical violations in 94 clinical trials conducted at the hospital.

### *Judicial activism*

Mounting evidence prompted the Supreme Court to step in. Hearing the PILs on the Indore trials, the same two-judge bench of the Supreme Court came down hard on the government and said on 17 July: “There has to be some sense of responsibility (on the part of the government). Human beings are being treated as guinea pigs. This is unfortunate.”

Meanwhile, the ethical committees that were supposed to have overseen the trials continue to function, said Amulya Nidhi, an Indore-based public health activist belonging to the Swasthya Adhikar Manch.

Complaints made to the Human Rights Commission—both state and national—are yet to yield results. In 2011, the joint director of health, Indore division, constituted a four-member committee that recommended the state impose a lifetime medical practice ban on each guilty doctor at Maharaja Yashwantrao Hospital and cancel registrations. That has had no impact.

### *Powerless government*

As disturbing as the trials is the government’s apparent inability to do anything to regulate them.

In 2011, the Madhya Pradesh economic offences wing (EOW) submitted a report on clinical trials at Maharaja Yashwantrao Hospital that established a conflict of interest, pointing out that pharmaceutical companies had sent principal investigators in several trials on “foreign trips and money was received (by doctors)”. Mint has reviewed a copy of the report.

The same month, a joint director in the state government submitted a second report advising the state government to initiate criminal proceedings against doctors for ignoring protocol.

The EOW report stated that 81 “serious adverse events” were reported in various clinical trials at Maharaja Yashwantrao Hospital.

Besides these cases, 1,833 children from the Chacha Nehru Bal Chikitsalaya (the paediatric hospital affiliated with MGM Medical College) and 233 mentally ill patients had been enrolled in clinical trials without any consent, according to documents submitted to the Supreme Court.

“As per government rules, guardians of mentally ill patients and children have to give an informed consent before they can enrol in trials,” said Nidhi of Swasthya Adhikar Manch, referring to the report.

In total, 12 doctors were named in the two reports. The EOW investigation listed Bharani (medicine), Salil Bhargava (superintendent), Ashoka Vajpayee (former superintendent), Pushpa Verma (dean), Hemant Jain (paediatrician) and Apoorv Puranik (neurologist), recommending that the Medical Council of India (MCI) initiate disciplinary action against them under Indian Council of Medical Research rules. Except for Verma, who maintained she was not involved in the drug trial controversy, none of the doctors were available for comment.

The “disciplinary measures”, including the Rs.5,000 fine, have to be compared with the Rs.5 crore that doctors earned for the trials, according to Swasthya Adhikar Manch’s PIL. Mint couldn’t independently verify this figure.

All but one of the doctors continue to practice medicine. Verma was promoted to the office of dean in January.

Over the past two years, victims and activists claim to have registered complaints at various forums, including the Central Vigilance Commission, EOW, the state police, the National Human Rights Commission, the medical education department, MCI, the Enforcement Directorate and the Central Drug Standard Control Organization. None of them seem to have had much effect.

Sarat Pandit, the joint director who submitted the 2011 report that recommends criminal proceedings against the doctors involved, blamed the delays on red tape and the involvement of too many government departments.

### *Victims languish*

“Our mandate was to investigate the goings-on in Maharaja Yashwantrao Hospital and we did just that. Several irregularities in protocol and ethics were clearly established and we recommended action,” said Pandit. “The report is now lying with the government and it is up to them to act on it. The matter has now become sub judice. While several agencies are investigating the case, nothing is being done for the safety of people exposed to these doctors.”

There have been attempts to rally support for the victims. In January, Communist Party of India (Marxist) leader Brinda Karat sent a memorandum to then drug controller general of India, V.G. Somani, seeking action against the doctors.

“Families are upset and angry, and there is a clear groundswell. It is outrageous that Indians are being used as guinea pigs,” Karat said.

Mint has seen a copy of the letter.

The Madhya Pradesh state assembly has seen about 40 questions being asked in the past two years about trials, according to whistle-blower Rai.

“When RTI (Right to Information) replies were vague, we approached local politicians to raise the issue in the state assembly,” added Rai, who worked at Maharaja Yashwantrao Hospital and first exposed the trials. “Most of the information I have was collected by this route.”

The Union government has been trying to pursue the issue without much success.

“What happened in Indore was truly horrendous,” said Keshav Desiraju, additional secretary in the health ministry, who has been trying to get more information from the state government. “They have not responded to my queries.”

The parliamentary committee, which recently exposed the alleged nexus involving the drug regulator's office, pharmaceutical companies and doctors, is to visit Indore to investigate the matter. Its report is expected to be tabled in the winter session of Parliament.

According to the health ministry, more than 1,500 people have died in clinical trials since 2008, a figure that's contested by public health activists. According to documents presented in the Rajya Sabha, 2,163 people have died in India due to clinical trials since 2007.

"In Indore alone, trial subjects have died as recently as February, and this does not reflect in the government investigations. The whole subject is technical, and even when deaths occur during the trial, it is very difficult to attribute it directly to the drug tested. Several committees have pointed out that doctors do not maintain proper records of severe drug events," added Nidhi of Swasthya Adhikar Manch.

No one has been compensated yet.

And what about those like Mehra, who participated in the clinical trial to obtain critical medication and then chose to be the whistle-blower?

"This is the cost of speaking up against doctors," she said. "They have taken me off the company plan."

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