News

Clinical trials in India: ethical concerns

Transnational drug companies are moving their clinical trials business to India, giving a new urgency to clinical trials registry reform there. Patralekha Chatterjee reports.

According to the Associated Chambers of Commerce and Industry, an influential national industry association, India is set to grab clinical trials business valued at approximately US$ 1 billion by 2010, up from US$ 200 million last year, making the subcontinent one of the world's preferred destinations for clinical trials.

Drug companies are drawn to India for several reasons, including a technically competent workforce, patient availability, low costs and a friendly drug-control system. While good news for India's economy, the booming clinical trial industry is raising concerns because of a lack of regulation of private trials and the uneven application of requirements for informed consent and proper ethics review.

Dr Ambujam Nair Kapoor, a senior scientist of the Indian Council of Medical Research (ICMR), states the problem bluntly: "Unless we put in place systems that ensure safety of patients and good quality of trials, people will get away with whatever they can get away with." ICMR, a national body responsible for the formulation, coordination and promotion of biomedical research, is striving to do just that with the Clinical Trials Registry of India, which it launched in July 2007.

The Clinical Trials Registry encourages the registration of all clinical trials conducted in India before the enrolment of the first participant. "The registry is meant to bring transparency to clinical trials conducted in India," explains Kapoor, who is all too aware of the shortcomings of current trial publication practices, including a tendency to publish trial results only when they are positive. "Trials done earlier where the drug has not been found to be effective are sometimes not publicized," she says, adding that information about failures should also be put in a publicly searchable database.

Working together with the Indian Journal of Medical Research, the Clinical Trial Registry also brought together the editors of 12 Indian biomedical journals at the beginning of the year to develop policy covering the publication of clinical trials. The editors issued a statement in April urging all those conducting and/or planning to conduct clinical trials involving human subjects to register their trials in the Clinical Trials Registry or any other primary clinical trial register. From January 2010 these journals will consider publication of a trial started in or after June 2008 only if it has been previously registered.

"We are wearing down the resistance [to registration]," says Dr Prathap Tharyan, professor of psychiatry at the Christian Medical College, Vellore, India. Tharyan is the coordinator of the South Asian Cochrane Network, and a member of the Scientific Advisory Group of the WHO International Clinical Trials Registry Platform (ICTRP) and of the steering group of the Clinical Trials Registry. "Investigators who want to publish in good journals have to register. In other words, if I want my research to be internationally known, I have to go to good journals who will increasingly insist on registration of the trials."

The latest developments in India reflect a concerted effort on the part of the global public health community to push clinical trials issues to the fore in the wake of several high-profile cases in which pharmaceutical companies were shown to be withholding information from regulators. In September 2004, for example, the members of the influential International Committee of Medical Journal Editors (ICMJE) published a joint editorial promoting registration of all clinical trials. The ICMJE stated that, beginning 1 July 2005, only registered trials would be eligible for journal publication. In 2007 the ICMJE stated that it would consider a trial for publication if it had been registered in any WHO Primary Registry.

The World Health Organization (WHO) has played a catalytic role in pushing this process forward. WHO's involvement in clinical trial registration began in October 2003 with consultations with different stakeholders to identify a potential basis for collaboration to address complex issues related to trial registration and reporting. This culminated in the establishment of the ICTRP Secretariat.

KEYSTONE /AP Photo/Gurinder Osa

Men pray before dinner at Sahara Centre for Residential Care and Rehabilitation for drug users in New Delhi, India, in 2004, before participating in a clinical trial of a vaccine to prevent HIV/AIDS.

Hosted by WHO, the ICTRP started operations on 1 August 2005. It is committed to harmonizing standards within which trial registers and databases worldwide can operate in a coordinated fashion, providing a global trial identification and search capability, and promoting compliance. WHO has also established a network of clinical trials registries, participation in which is voluntary.

According to Dr Davina Ghersi, coordinator of WHO's Registry Platform, the Indian registry is active in this network, but she points out that there is no legal requirement to register a trial there. Ghersi goes on to say that there is such a requirement if researchers want to publish the trial in journals affiliated with either the ICMJE or the Indian journal editors initiative.

Ghersi believes that one of the things that can be achieved through registration is stronger regulation, but also thinks there will be other benefits, notably greater transparency about what sort of research is being done, "For example," Ghersi says, "if every piece of research conducted in India were available on a publicly searchable database somewhere, one would know what issues are being addressed, and if they are relevant to the population in which the research is being conducted."

India's Clinical Trials Registry has all the 20 items of the WHO Clinical Trials Registry Platform. In addition, there are items such as: declaration of principal investigator's name and address; name of the ethics committee and approval status; regulatory clearance obtained from the Drugs Controller General of India; estimated duration of trial; site(s) of study; phase of trial; brief summary; method of generating randomization sequence; method of allocation concealment; and finally method of blinding and masking.

WHO/ K Selleck

Dr Davina Ghersi

WHO/ P Virot

Street scene in India, one of the world's preferred destinations for clinical trials.

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> *Dr Chandra Gulhati*

Though the launch of the Clinical Trials Registry marks a new chapter in the clinical trial registration process in India, there are daunting challenges ahead. Since its launch in 2007, 64 clinical trials have been registered, but there is still no legal obligation to register. Steps are being taken to encourage voluntary registration, including the Clinical Trials Registry workshops to which people likely to be conducting clinical trials – medical colleges, research institutions, state drug controllers, and nongovernmental organizations – are invited, but for some, such steps are inadequate.

Dr Chandra Gulhati, editor of the Monthly Index of Medical Specialities, for example, would like to see more teeth in the clinical registration process in the country. "The first step should be the Drugs Controller General of India making it obligatory for all trials to be registered on the Clinical Trials Registry site before permission is granted to conduct them," Gulhati says. "The failure to do so should carry a penalty. In addition, while registering trials, the composition of hospital ethics committees, which approved the trial, should be disclosed."

Gulhati is particularly concerned about ethics committees lacking independence. "Fewer than 40 Ethics Committees in India are properly constituted and functioning, which means that the safety of the subjects of clinical trials is on the back burner," he says, adding that it is also worrying that there is no legal requirement for investigators or members of the Ethics Committees to declare a conflict of interest. He considers this a particularly serious problem given the increasing number of hospitals now owned by drug companies. "Clinical trials at such hospitals should carry a statement of disclosure about the relationship," Gulhati says. ■