Poor definitions threaten drug trial safety in India

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India has become a hotbed of clinical trials, but recent reports of safety lapses have prompted calls for better regulation in this area. Currently, trial requirements can be relaxed if doing so is in the 'public interest', but a clearer definition of what this means is needed before this provision should be used.

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The outsourcing of clinical trials to India has mushroomed in recent years, growing around 30% since 2006 to reach an estimated $400 million in 2012 (ref. 1). This steady increase was spurred by an amendment to the Drugs and Cosmetic Rules (DCR) act, passed by the Indian Ministry of Health and Family Welfare in 2005, which allowed drug manufacturers to initiate and conduct phase 2 and 3 trials in the country involving drugs that had not previously completed testing elsewhere.

In 2009, a total of 546 clinical trials were registered in the database of the Indian Council of Medical Research (ICMR), and this number jumped up to 806 in 2010, according to numbers presented to the country's Parliament on 11 December. But alongside that increase there have been recurrent news reports of faulty drug trials resulting in medical emergencies and even deaths of participants. Last January, the media reported that more than 200 mentally ill patients had been put into drug trials in Indore without proper consent. This prompted the National Human Rights Commission (NHRC) of India to issue a notice to the State Government of Madhya Pradesh demanding information on the regulatory approvals. Subsequently, in August the commission issued notices to India's Health Secretary, the secretary of the ICMR and the Drug Controller General of India (DCGI) asking their response on media reports on the deaths of 1,725 people over the last four years in clinical trials. The NHRC concluded that this indicated "complete ineffectiveness of regulatory controls" (ref. 2). Most recently, the Supreme Court of India has asked the central government for details of ongoing clinical trials throughout the country, including the number and nature of side effects and deaths and details of any compensation paid to subjects.

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The DCR empowers the DCGI, the chief regulator of clinical trials taking place in the country, to waive clinical trial requirements—specifically, the submission of results of local clinical trials—in applications for grant of approval for importation or manufacture of a new drug in the 'public interest'. Perhaps legislators meant to tie the definition of public interest to a related clause in the DCR that says clinical trial requirements may also be waived in cases of life-threatening diseases or diseases special relevance to the India. But no explicit definition of the term public interest exists within the DCR. Further, the DCR fails to say how many members institutional ethics committees (IECs) should have and what qualifications each member should hold.

Given that an IEC's approval is a vital step in getting a trial off the ground, all of its deliberations should be recorded, and its decisions should be in writing and based on detailed reasoning, thereby allowing public scrutiny. Central registration of all ethics committees is necessary for the ICMR to ensure better supervision and transparency, both of which are missing in the current system. The IEC functions as a delegated regulatory authority, and hence its decisions should be open to legal challenge. It is also unfortunate that the DCGI has prioritized the expansion of a for-profit clinical trials market in India. This is a fundamental conflict of interest and reflects confusion over the primary policy goal that should drive the functioning of an agency tasked with ensuring public health and patient safety.

Volunteers entering into contracts with sponsors to participate in clinical trials in India are mostly drawn from disadvantaged backgrounds[3], making them more vulnerable to exploitation than better-off participants. Here, the NHRC should become more active in helping draft protocols for obtaining informed consent and assisting in an improved framework for processing claims related to compensation in case of injury to subjects. The state should either regulate by recognizing and protecting the legal rights of volunteers or ensure that standard clauses having the same effect are made mandatory for inclusion in such contracts.

The government has taken incremental steps toward improving oversight of clinical trials—among other things, since 2009 making trial registration mandatory in the ICMR's Clinical Trials Registry and establishing 12 New Drug Advisory Committees consisting of experts and specialists drawn from the public sector and private institutions to evaluate all requests for clinical trials. However, a bill to clarify who should serve on IECs and ensure they do not have conflicts of interest, as well as to ensure that sponsors provide adequate compensation in the case of trial-related injuries or death, has languished in India's parliament for the last eight years. Moving ahead with this legislation, as well as improving the definition of what is in the public interest, will ensure the safety of clinical trials in India and ultimately make them more successful enterprises for all.

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