

Compensation for Victims of Clinical Trials: A Discussion on How Current Indian Rules and Guidelines are Hurting India

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According to the amended Drugs and Cosmetics Rules of the Government of India, participants in clinical trial are entitled to medical treatment and financial compensation in the event of permanent injury or death, but the quantum of compensation is to be decided by same Ethics Committee that sanctioned the trial in the first place. If there is a dispute regarding the amount of compensation the injured party may appeal again to the Ethics Committee for a review and reconsideration. The decision of the Ethics Committee after the review is final [1].

This editorial discusses the merits of the scheme from the point of view of making India a hub for international clinical research.

GROWTH OF CLINICAL TRIALS INDUSTRY AND GOVERNMENT INCENTIVES

In 2002-3 the clinical trials industry in India was worth only US\$ 35 million. However its potential for growth was recognized [2]. To enable it to reach that potential, the Government of India enacted suitable laws. The previous rules permitted phase 2 trials in India only if phase 3 trials were in progress elsewhere. In January 2005, it allowed foreign pharmaceutical companies to conduct trials in India in the same phase that they were being conducted abroad. Further, to give a fillip to the clinical trial industry, the service tax on clinical trials was withdrawn in 2007-08 [3].

The clinical trial industry responded favorably. It was both easier and cheaper to do a clinical trial in India than in the West. A drug trial in the United States could cost \$150 million where as it could be done in India for \$ 90 million – at 60 per cent of the cost [4]. Recruitment of patients is also much easier in India. Germany's Mucos Pharma GmbH did a clinical trial for a drug to treat head and neck cancer. The local contract research organisation had to go to only five hospitals in India to recruit 650 out of the 750 volunteers needed for the trial and the recruitment from India was complete within 18 months. To recruit the remaining 100 volunteers in Europe, Mucos Pharma spent twice as much time and had to go to 22 hospitals [2]. The clinical trials enterprise grew into a US\$ 160 industry by 2006-7. According to a report in 2008 to the Planning Commission New Delhi, the market value of clinical trials outsourced to India was expected to touch \$1.5-2 billion by 2010 [5].

MULTIPLE WINNERS

This appeared to be a win-win proposition. Private institutions obtained equipment through joining trials. Pfizer for example donated \$100,000 bone density measuring instruments to six hospitals testing its new osteoporosis drug [4]. Investigators in private hospitals were paid recruitment fees of between Rs 60,000 and Rs 120,000 per patient [6]. The principle investigators in government hospitals, who could not accept a recruitment incentive, were given all-expense-paid trips to conferences abroad

[6]. Impoverished patients begged to be included in trials because that was their only affordable means of getting any medical care. The hospitals, the doctors and the patients, all seemed to benefit.

THE DOWNSIDE

In a study 76% of patients in clinical trials said that the principal investigator was their primary physician. Another 21% said they were referred to the research unit by their primary physician. Thus 97% of those who entered clinical trials did so because of their primary physician [6]. Patients are easily influenced by their doctors. When physicians are paid a recruitment fees to induct patients into clinical trials, there is a direct conflict of interest [7].

Independent ethics committees and institutional ethics committees were set up to evaluate clinical trials. Ethics committees often charge a review fee of Rs 10,000 to Rs 50,000 for considering trials. 97% ethic committees' members get paid an honorarium [8]. In an interview Dr C M Gulhati the editor of the Monthly Index of Medical Specialties noted that as a 'commercial concern' and 'service provider' for their clients (the researchers), such ethics committees have no obligation towards the subjects of the trial [9].

LAX REGULATION BEGINS TO BITE

In this exploitative situation, with lax governmental regulation, serious problems have arisen. The Health Minister Ghulam Nabi Azad reported to Parliament that there had been 1,725 deaths among subjects participating in clinical trials over a four-year period (2007-10). The yearly figure for deaths went up sharply from 132 in 2007 to 668 in 2010. There was a fall in deaths in 2011 to 438 which has been attributed to a decrease in the total number of trials conducted which fell from 254 in 2010 to 169 in 2011. Of the clinical trial deaths after 2007, only 22 have received any compensation. Compensation was only paid to trial victims who were injured or died in 2010-11, and that after a committee chaired by Maneka Gandhi, Member of Parliament, probed the matter last year. No action has been taken against any pharma company, ethics committee that oversees clinical trials or contract research organisation that conducted the trials [10].

Criticism was expressed from diverse quarters. Justice R M Lodha commented on the situation. "Human beings are being treated as animals. This is unfortunate", he said. Dr Lalit Kumar an oncologist from All India Institute of Medical Science pointed out that the lack of supervision by Indian health officials has created a culture of impunity among drug research companies and the doctors who work for them [11].

ETHIC COMMITTEES AND COMPENSATION

The Government has now decided that Ethics Committees must decide compensation. This is indeed unfortunate. The whole matter

of causality assessment is complicated and requires great medical expertise. Many of the persons undergoing trials have an underlying disease which could well be the cause of death. This allows the committee to blame 'other causes' for any adverse event even if it may have been caused by the trial drug. The ethics committees are not equipped to make these evaluations. Even the 'Association of Clinical Research Organizations' (ACRO) which represents the world's leading global clinical research organizations has objected to this, saying that the decision was a backward step that would make high quality research impossible in India [12,13]. They have pointed out that ethics committees lack the scientific and medical know-how necessary to accurately identify *Serious Adverse Event* (SAE) causation and hence the level of compensation. In addition to medical knowledge anyone making decisions on compensation would need to be experts in law and proficient in actuarial science. Ethics committees are often associated with the institution where the research is taking place and this leads to a conflicts of interest. ACRO have suggested that an independent body must make the decisions about compensation.

One method of calculating compensation is the multiplier method used by the claims tribunal under the Motor Vehicle Act 1988 which is administered by a legal tribunal [13]. This seems a practical way forward. However there is another suggestion that the Government adopt the United States National Vaccine Injury Compensation model. This is a "no fault" system which provides compensation to all legitimate claimants of vaccine injury from tax money. This may sound attractive because victims now have to go from pillar to post to prove casualty [14]. Paradoxically the scheme may in fact harm more patients by making clinical trial organizations more reckless, assured that they may never have to take blame for any adverse event. Without heeding the critics the Central Drug Standard Organisation (CDSCO) has gone ahead and developed new guidelines for ethics committees to calculate compensation [15].

However there is still hope. Trials done in this environment are losing credibility and beginning to tarnish the image of the pharmaceutical companies doing trials in India. Pharmaceutical companies doing trials have begun to quit India. Last year out of 118,804 human trials in 178 countries, less than 2,000, or 2%, were done in India compared to 9,352, or 8%, in neighboring China, according to the US government's www.clinicaltrials.gov web site. India's current share of 2% is a fraction of the 15% predicted by lobby group Associated Chambers of Commerce and Industry of India (Assocham) [16].

This exodus of clinical trials away from India may make the government realize the folly of its short sighted strategies. The Government may yet come to realize that it makes long term economic sense to jealously guard its poor from exploitation by the

pharmaceutical industry. Ultimately it is the duty of the Government to protect its poor and vulnerable citizens.

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