CORRESPONDENCE

Clinical trials: a matter of principle

While I wholeheartedly support the sentiments expressed by Dr Gulhati in his editorial (1), I have reservations about the data cited and the manner in which they are presented.

Dr Gulhati cites several examples of unethical human research. There is not a single reference given in support of these 'facts'. It is possible that these data are factual; yet, without appropriate reference to the source, these examples become mere opinions.

Moreover, in an academic journal, the facts should speak for themselves, there should be no hyperbole. There are many differences between the USA and India. Stating that '...women have been treated worse than animals in America' serves no purpose.

The examples of poor protocols for drug trials that were approved by the DCGI also do not cite references. One must assume that these are based on personal communication to the author and the reader has to accept these assessments at face value. In the last paragraph, he writes: 'No wonder American companies have found doctors in Vietnam as competent as those in India in this field'. The implication here is that Vietnamese doctors are inferior to Indian ones. This smacks of cultural chauvinism.

I wish the author had given concrete suggestions for improving oversight in research trials and ways to decentralise the process so that it becomes more transparent and accountable.

I have come to expect higher academic and literary standards from the *Indian Journal of Medical Ethics* and hope the editors will sustain these principles.

Reference

1. Gulhati CM. Needed: closer scrutiny of clinical trials. *Indian Journal of Medical Ethics*. 2004;**1**:4–5.

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The author clarifies

All the cases of illegal (not merely unethical) drug trials cited in the article have been widely reported in the highly circulated print and electronic media. References are required for scientific articles where data are being quoted or interpreted and not to support the occurrence of events or while reporting plain news. Besides, none of the sponsors or investigators have raised any objection to the factual part of these press reports.

Webster's unabridged dictionary defines 'hyperbolic' as 'exaggerating or diminishing beyond the facts or exceeding the truth.' Not one word in the article meets this definition. I may add here that several newspapers such as the *Hindustan Times*, *The Indian Express* and *Business Standard* have picked up large portions from this article to focus the nation's attention on the malady of illegal and unethical drug trials. They have used exactly the same language as I did.

How can there be 'references' for poor protocols? The quoted protocols have been examined and reported in the article.

Foreign sponsors have been publicly arguing that drug trials require 'competent investigators, efficient infra-structure (research hospitals with world-class laboratories) and multi-ethnic patients' in support of their reasons for selecting India as the base for clinical trials. The real reasons are of course different: lower costs, lax implementation of laws and abundant availability of poor, illiterate patients. My reference to Vietnam is to show the hollowness of the sponsors' claims. Vietnamese doctors may be good clinicians but they do not have the infrastructure for drug trials comparable to those in India. Besides, there is only one ethnic population. Why, then, are American companies conducting drug trials there?

In an editorial, it is not possible to cover all aspects of drug trials such as improving the oversight functions. In any case, the Central Government is moving in the reverse direction: the new Schedule Y that governs trials is being 'liberalised', so that it would be easier to conduct trials in future.

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Bashir Mamdani's rejoinder

In his response, Dr Gulhati's states that his article did not deal with scientific content and therefore did not need to give scientific references; that newspaper accounts of deaths in the trials were adequate proof of something wrong happening in the trial; that newspapers have their own rules and regulations for responsible reporting.

I fully sympathise with Dr Gulhati's aims to bring greater scrutiny to research trials but I differ with him on how one should go about it.

I hesitate to rely on newspaper accounts for proof of wrongdoing as they are often incomplete and inaccurate.

Therefore, as a sole source of information, they are not and should not be equated to proof of medical malpractice. While a newspaper may publish Dr Gulhati's article without references, that would be inappropriate in an academic journal such as the *Indian Journal of Medical Ethics*, which must insist on appropriate scientific references in all articles accepted for publication. If the *Indian Journal of Medical Ethics* publishes an article alleging serious malpractice based exclusively on newspaper reports, then it would be guilty of editorial malpractice.

What we lack in India is a credible mechanism for airing complaints or serious misgivings by well-intentioned outsiders about a particular research trial. In the USA, at the public hospital where I practised for 30 years, if any member of the public had serious doubts about a trial conducted in the hospital, he/she could approach a lay member of the hospital's Institutional Review Board (IRB). The details of the complaint were discussed by the IRB and, when indicated, an independent reviewer was appointed to investigate such charges. The findings were made public in a timely manner. I do not know if such mechanisms exist in India. If not, these are critically needed and would protect researchers from baseless charges.

Research is a vital necessity for India. While we must protect people from unscrupulous or fraudulent research trials, we must not discourage research by painting most researchers with a tarred brush.

Bashir Mamdani

Clinical trials: in the crossfire

Dr Gulhati has lamented about the unscrupulous methods adopted while conducting clinical trials and has called for strengthening regulatory authorities. While we appreciate the spirit of the article, we are sorry to note that Shantha Biotechnics has unnecessarily been mentioned in the opening paragraph. Now it is public knowledge that a tussle between two government agencies has dragged us into the controversy. Several articles are still appearing in *Bio Spectrum*, *Business World,* etc. questioning the GEAC's stand in this case. How can a committee, formed to monitor environmental issues supervise and evaluate clinical trials ?

We have not passed on the buck as alleged in the article. As per the new guidelines, the DCGI alone is competent to clear clinical trials and we have approached them. If GEAC has not updated its records, we cannot help the situation. Further, the GEAC has relied too much upon a Bangalore-based NGO's false allegations such as trials being shifted to Bangalore in view of deaths, the volunteers not being insured, etc. Since the NGO inflated the number of deaths from two to eight and tried to blackmail us, we have filed a suit against them. It is unfortunate that Dr Gulhati did not crosscheck with us before writing the article.

Does Dr Gulhati sincerely believe that there would not have been any deaths during clinical trials had we obtained clearance from the GEAC? In any trial, volunteers are chosen at different stages of the disease to test the efficacy and safety of the drug. It is but natural for some of them to succumb during the trial. In the case of r-streptokinase comparative double-blind trials, out of 96 patients administered Shankinase (our r-streptokinase) three died (mortality rate 3.1%) and out of the 54 administered Streptase (comparative drug) another three died (mortality rate 5.5%). The *Indian Heart Journal*, in its latest issue states that the normal range is 8%–12.5%. The DCGI informed GEAC that the accepted range is 6% (*Economic Times;* March 12, 2003).

Shantha Biotechnics values life highly and carries the logo 'Inspired by life'. Our motto is to make world-class health care products at an affordable cost to improve the quality of life. Shankinase is our third product. Both our earlier products won prestigious DSIR and National Technology Awards individually. Anyone can look at our track record to see how we suffered while conducting interferon alpha trials on monkeys. We agree with Dr Gulhati that clinical trials have to be monitored closely to see that unethical practices are not allowed. But tagging our name along with violators is most painful and regrettable. We are ready to share further information with the author.

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The author defends

With regard to reference to Shantha Biotechnics, I wrote the following:

'How many people know that eight patients in Hyderabad who were administered recombinant streptokinase to test its efficacy and safety have died? According to the Genetic Engineering Approval Committee (GEAC), the trial was being conducted by the drug's manufacturer Shantha Biotechnics without taking clearance. Not surprisingly, the Company denies the allegation claiming that it had taken permission from the DCGI. In this game of passing the buck, no one is shedding any tears on the lives lost or compensating the families of those whose loved ones have died. Without any independent enquiry, the death of 'trial subjects', as they are impersonally called, has been attributed to 'causes other than the use' of the drug!'

In his rejoinder, Mr Prasad has not disputed any point except the number of reported deaths. I made the following