

## **Call for regulation of drug trials in India**

Participants at the National Consultation on Regulation of Drug Trials, organized by Sama, Locost, CSER, AIPSN and Daf-K, in New Delhi on 26-27 September, 2011, expressed their deep concern about the unregulated proliferation of ill-regulated clinical trials in India following the liberalisation of norms for conduct of such trials in 2005.

The government has aggressively encouraged foreign drug trials in India without even putting in place structures protecting participants. Regulatory mechanisms have proved to be grossly inadequate and ineffective. The Central Drugs Standard Control Organisation (CDSCO), the principal regulatory agency, lacks both capacity and will to carry out its functions that include the scientific review of trial protocols and monitoring the conduct of trials. Ethics committees are ill-equipped, untrained, and not accountable for their decisions.

There is no evidence that the liberalization of norms is contributing to an improvement in access to essential medicines in India or to the enhancement of the country's scientific and research capacity.

On the other hand there is mounting evidence of human rights violations and other harms to participants in these trials. Physicians receive incentives to recruit patients into trials, and do this without obtaining informed consent. Participants are subjected to unethical practices such as deprivation of effective medicines. Medical treatment and compensation are denied for the growing number of trial-related injuries and deaths. Bioequivalence trials offer participants large payments in blatant violation of existing ethical guidelines, inducing poor people to risk their lives in these trials.

Such practices are situated in the overall context of unethical medical practice in a system where health care is either inaccessible or unaffordable.

Clearly, liberalization of norms for the conduct of clinical trials in India has belied its promise and introduced fresh challenges for the health care needs of the country.

The Consultation also made the following specific recommendations:

### **Update laws and guidelines on clinical trials**

1. The 2005 amendments to Schedule Y of the Drugs and Cosmetics Act liberalizing the conduct of clinical trials in India need to be reversed <sup>[ss1]</sup>and various gaps, leading to deficiencies in regulation, need to be addressed. Noncompliance with provisions in the DCA needs to be made justiciable and punishable. Various pending draft guidelines related to trial monitoring must be finalized urgently.
2. The Bill on Biomedical Research on Human Participants, incorporating the ICMR's ethical guidelines for research on human participants, has been pending since 2006. The Bill must be circulated for public consultation, finalized, and codified in law, with rules for its enforcement.
3. The ICMR's ethical guidelines must be revised to remove many inconsistencies and loopholes, and updated to take into account developments since 2006.

### **Regulate sponsors, trial organizations and investigators**

1. Pharmaceutical companies, who are the major sponsors of clinical trials, work through Contract Research Organizations (CROs) and a network of individual researchers in government and private medical colleges as well as in large and small hospitals.
2. Regulation is necessary at all levels of this network – the drug company, the CRO, the institution conducting the trial and the individual researchers involved – to ensure that drug trials are conducted in compliance with the ICMR's ethical guidelines in addition to guidelines of Good Clinical Practice.
3. CROs must be regulated through registration, accreditation of those who meet standards, and a code of ethical conduct. Violations of this code should be actionable. Trial sponsors as well as CROs will be held accountable for any violations.
4. Recruitment incentives to investigators should be banned. Compensation to participants cannot be so large that it serves as an incentive.
5. Complaints of unethical research must be investigated immediately and punitive action taken when necessary. The reports of unethical and illegal drug trials in Bhopal, Indore, Ahmedabad and Bhadrachalam as well as elsewhere must be investigated, the findings made public and the perpetrators punished.
6. Whistleblowers must be provided protection.

### **Ensure reporting, treatment and compensation in injury or deaths in trials**

1. Companies should be required to provide comprehensive health insurance for all trial participants to take care of all health needs (including ancillary care).
2. The CDSCO must ensure that CROs send prompt notification of all injuries or deaths in a trial, followed by the investigation findings and the action taken on these findings. It must follow up on all reports to ensure that participants are provided immediate and long-term medical treatment and compensation is given for injury or death. Compensation details must be finalised before the start of any trial.
3. In case of study related injury, disability and death in human participants, the law should hold the sponsor accountable and liable.

### **Strengthen regulating institutions**

1. The CDSCO must be assured sufficient resources and trained humanpower to conduct technical review of applications and monitor the conduct of trials including surveillance and safety studies.
2. Ethics committees (ECs) must be registered, accredited, and made accountable and liable for their decisions. EC members must trained, and it needs to be ensured that ECs have the capacity, resources and independence to review and monitor drug trials.

3. The current system of ethics review needs revision. The current law in no way addresses the important issue of conflict of interest amongst EC members and other aspects of clinical trials. At the same time, ethics review and monitoring cannot be run on a voluntary basis. Alternate structures need to be considered, such as public funding of central, state, regional and local ethics committees.

#### **Protect participants' rights**

1. A charter of participant rights must be developed and made justiciable. The details must be proactively disclosed [ss2]by all parties responsible for the conduct of clinical trials.
2. A database of participants must be developed to monitor for any long-term effects of trial participation. A study of trial subjects, including their backgrounds, reasons for entering trials and treatment received, is also necessary.

#### **Restrict research on vulnerable populations**

1. Poor and marginalized sections of society and in areas without health services are particularly vulnerable to the medical establishment which has a dubious track record in matters of patient safety.
2. Research on vulnerable populations must have explicit justification -- such as a condition found primarily among them -- and assurance that these participants will have health benefits from participation. This assurance should not be viewed as an incentive to enter the trial.

#### **Ensure post-trial access**

1. All drugs developed through trials in India must be made available to the trial population free of cost until they are available in the country, after which time they must be available to everyone at an affordable price. Drug sponsors must be required to sign an agreement to this effect.

#### **Ensure transparency**

1. Trial-related information of public relevance – including applications made, sites, ethics review decisions, adverse events and follow-up, and positive and negative results – should be available in the public domain. Modifications are necessary in the Clinical Trials Registry-India to enable tracking of changes in trial data.
2. It is falsely claimed that information about trials is covered by Intellectual Property provisions. The Indian IP Act does not provide for such protection; neither is such protection a requirement of the TRIPS agreement. Confidentiality clauses, in agreements between trial sponsors and regulators, and sponsors and investigators, need to be modified so that they do not prevent bona fide access to information on clinical trials which has a bearing on the health of trial participants.

#### **Support public research**

1. Industry-funded drug trials do not constitute research. We need to develop a strong research base starting from basic research to development and testing of drugs and other technologies relevant for public health and healthcare in India.

Public funding is necessary for research to be driven by our health needs rather than potential profitability.

2. An independent body must develop the scientific basis for government decisions in health. This includes undertaking studies on specific health conditions, public health issues, and the impact health policy measures; making recommendations on new and existing therapeutic and preventive medical technologies, and formulating quality indicators for various levels of and aspects of health care.
3. All medical research in India must incorporate the principles of transparency, accountability, respect for trial participants' rights, and benefit to the community