

ARTICLES

Justice in jeopardy: a qualitative study of institutional ethics committees in New Delhi

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Abstract

Protecting the safety and welfare of clinical trial subjects is the primary responsibility of the multidisciplinary ethics committee. In India, ethics committees have come under increasing criticism for functioning as "secret societies unaccountable to the public" (1). Yet, little effort has been made to undertake qualitative research on the ethics review bodies. This article describes the essential findings of a study that aimed at providing an insight into the structure and functioning of institutional ethics committees (IECs) in selected hospitals in Delhi. Importantly, the study also attempted to investigate the challenges faced by IEC members that pose barriers to IEC performance and thus jeopardise a just and effective system of protection for the human trial subject.

Introduction

While risks are inherent in a clinical trial, the human research subject can be exposed to various types of harm that lie beyond ethically and morally acceptable parameters. The protection of trial subjects in the clinical trial process is the task of an institutional ethics committee (IEC). In India, any agency conducting biomedical research using human subjects is required by law to seek approval of its research protocol from an ethics committee before a clinical trial begins, under Schedule Y of the Drugs and Cosmetics Rules 1945, amended 2005 (2).

The need for establishing protective measures for human subjects in medical research was first codified in 1947 in the Nuremberg Code – a 10-point code of ethics in medical research that stressed the autonomy of the trial subject, the imperative of voluntary informed consent and the responsibility of physician-investigators towards the rights of the subject (3, 4). In the 1960s and 1970s, the idea of an ethics review of clinical research – over and above the responsibility of individual investigators towards trial subjects – gathered momentum in the West, particularly in the United States (US) (5). Investigations into state funded trials in the US that revealed the unethical use of prisoners, racial minorities, children and the mentally challenged as trial subjects led to the establishment of the National Research Act in 1974. The Act stated the need for review boards to assess the ethical conduct of medical research (6–8). International awareness of unethical human experimentation also led to the establishment of other ethical guidelines such as the 1964 Declaration of Helsinki that

introduced – in its 1975 revision – the need for an independent ethics review of clinical research (5, 9). Ethical guidelines of the Council for International Organizations of Medical Sciences (CIOMS), concerned primarily with the ethical conduct of clinical trials in the developing world, also stated guidelines for ethics committees (10).

An IEC comprises individuals with both medical/scientific and non-medical/non-scientific backgrounds. Schedule Y of India's Drugs and Cosmetics Rules, 1945, as amended – the main statute for clinical trial operations and ethical oversight – requires IECs to have "at least one member whose primary area of interest/specialization is non-scientific and at least one member who is independent of the institution/trial site" (2). This multidisciplinary foundation of the IEC rests on the understanding that an ethics review must be guided by diverse viewpoints so that there is an all-encompassing assessment of moral dilemmas that may arise before, during, and after a clinical trial. All members must endeavour to share the researcher's burden in seeking a balance between the pursuit of scientific interests on the one hand and the needs of society and the rights of research subjects on the other (5). The ethical review process must be free from institutional bias. IECs are, therefore, required to select a chairperson who is unaffiliated to the institution so that decisions made are objective and independent of the interests of investigators and institutions. In addition to the chairperson, the IEC is required to have a member secretary who is an employee of the institution and who is responsible for the administrative tasks of the committee (11).

An ethics committee must follow prescribed procedures – enumerated in the ethical guidelines for biomedical research on human subjects of the ICMR and the Drugs and Cosmetics Rules – to ensure and sustain both the scientific and ethical integrity of a research protocol. According to ICMR, "It is advisable to have separate committees for each [kind of protocol review], taking care that the scientific review precedes the scrutiny for ethical issues" (11: p 8). A scientific review involves an assessment of the technical value of the proposed clinical trial, its scientific design and the research methodology. An ethical review is concerned with the equitable selection of research subjects, of ensuring a fair distribution of risks and benefits across populations, examining informed consent documents and verifying the process by which informed consent is obtained. An ethics

review must also evaluate the appropriateness of monetary compensation offered to trial subjects for their participation, assess the relevance of the intervention to trial subjects and the community at large, review the provision of standard of care, ensure compensation by sponsors for trial-related injuries and examine the mechanisms by which post-trial access to beneficial treatment can be a possibility. In addition to initial ethical review, ethics committees are also responsible for the continued review of approved research that could involve assessing progress reports provided by investigators as well as visiting trial sites (2).

Implicit in the responsibilities of an ethics committee is the commitment to three fundamental ethical principles: respect for persons, beneficence and justice. The task of informed consent, for instance, conforms to the principle of respecting an individual's autonomy in deciding – without coercion or undue influence – whether or not to participate in a clinical trial. When applying the principle of beneficence, the IEC must review if the protocol has made all attempts to maximise the benefits and minimise the risks for trial subjects and establish that the risks they face are reasonable in relation to the benefits. To ensure justice in research, also defined as distributive justice particularly in the context of the developing world, an IEC would have to safeguard against certain kinds of individuals or groups being consistently selected for medical experiments because of their easy accessibility and social, economic or other vulnerabilities. In other words, trial subjects should not be disproportionately limited to those who are unlikely to have the means to enjoy the beneficial outcomes of research (5, 11).

Across the world, research conducted on the performance of ethics committees has revealed inadequacies in the structural and functional aspects of these ethical review bodies (12, 13). For example, in 1981, a survey was undertaken in Wessex, in the UK, of individual ethics committee members and other members of the medical profession, to understand their perceptions about the role of ethics committees. The survey's findings included polarized views among medical members regarding the role of non-medical members. On the one hand the role of lay ethics committee members were perceived by medical members as "purely window-dressing exercises serving little or no useful function" (12: p 64), and on the other, non-medical members were perceived as having an important role to play as they provide a balanced view of the research (12). In 1995, in the US, Raymond G De Vries from the Centre of Bioethics, University of Minnesota and Carl P Forsberg from Boston College in Massachusetts, surveyed a random sample of 89, of the 892 IECs registered with the Office of Human Research Protection. The survey attempted to look into the "black box" (13: p 200) of IECs so that reform in the systems of human subject protection could be initiated. The study found that membership of the IECs leaned towards whites, medical researchers and those connected with the institution. The study also raised the issue of the lack of administrative support for IECs that resulted in insufficient review and monitoring of trials. Among the key conclusions of this study was that "public failures of science are not the simple result of evil scientists

driven by greed or blind ambition. Rather they are a product of structural problems in the system of review created to protect human subjects" (13:p 213).

In India too, ethics committees have come under increasing criticism for functioning as "secret societies unaccountable to the public" (1:p 63). Yet, little effort has been made to undertake qualitative research on the ethical review bodies. Members of the committees are not willing to talk about the challenges they face, leaving little room for any discussion to facilitate a more streamlined and effective ethical review process (1). Research conducted on IECs in the country is limited to a handful of surveys. For instance, in the year 2002, ICMR conducted a World Health Organization (WHO)-sponsored survey of IECs associated with clinical trials or research projects funded by the ICMR. One of the survey's objectives was to understand lapses in ethical review mechanisms in organisations conducting biomedical research. The ICMR intended to conduct its survey on 149 ICMR-supported clinical trials or research projects across 71 institutions. However, only 36 institutions responded to ICMR. While all 36 institutions claimed to have IECs, only 23 had a standard operating procedure (SOP) in place; only 14 had trained their members in bioethics, and there was no response from more than half the committees about their status on training. The survey also found that of the 149 projects, IEC clearance certificates were available for only 107 projects (1, 15,16). In 2005, a survey was conducted by the Clinical Trials Unit of the National AIDS Research Institute, in the city of Pune, in Maharashtra, on the profile and role of members of ethics committees in hospitals and research organisations in Pune. 52 out of 87 ethics committee members participated in the study. The survey found that 44% of the participants had accurate knowledge of ethical principles and 79% expressed the need for organised training in ethics (17).

In the context of limited information on ethics committees in the country, disclosures by the media of unethical trials and an increasingly global environment of clinical trial operations in India, the study: 'The role of institutional ethics committees in clinical trials: a study of selected hospitals in New Delhi', was conducted in 2010–2011 for a degree at the Centre of Social Medicine and Community Health at the Jawaharlal Nehru University, in New Delhi. This paper describes the essential findings of the research that attempted to provide an insight into the structure and function of IECs. Moreover, the study also examined the kinds of challenges faced by IECs that pose barriers to IEC performance and thus jeopardise a just and effective system of protection for the human trial subject. Generalisations of the entire population of IECs in the city of Delhi, however, cannot be made on the basis of this research that represents only the views and experiences of specific IEC members and the workings of their ethics committees.

The context

Today, over 60% of the global pharmaceutical market share belongs to the drug industry operating in the US that includes both European and American drug companies (7). By the

early 1990s, clinical trial operations of these pharmaceutical firms had expanded to non-traditional research locations such as Eastern Europe, Africa and Latin America (7). High infrastructure costs in the developed world and a shortage of willing research subjects were among the main reasons cited for the globalisation of clinical trials (18, 19). Moreover, the “treatment saturated” US population, consuming many more drugs than it used to, was rendered unsuitable for participating in clinical trials. The industry therefore needed “treatment naïve” populations or those who were not taking drugs at the time of a clinical trial, as interactions of different types of drugs can interfere with research outcomes (18, 20). India and China have emerged as attractive options for clinical trial operations in recent years. The US Food and Drug Administration (FDA) figures from 2006 on the number of clinical trial investigators enrolled with the agency show that Russia had 623, the largest number of investigators, followed by India with 464 investigators (7).

The expansion of clinical trial operations in India was largely facilitated by an amendment to the Drugs and Cosmetics Rules in 2005. The amendment allowed foreign drug companies to conduct clinical trials in the country concurrently with other trials being run outside India. Before the liberalisation of the country’s drug development laws, clinical trials for new drugs of foreign origin were permitted only if a later phase of the trial had already been conducted in a foreign country. For example, Phase II trials – conducted primarily to establish efficacy of an intervention in patients – could be conducted in the country only on the condition that the confirmatory phase or Phase III trials had taken place elsewhere earlier (21). These regulations were important safeguards that prevented the country’s population from being treated as first-line trial subjects. With the 2005 amendment, the nature and scope of clinical trials in India was considerably altered. Data analysed from India’s clinical trial registry indicates an increase in the number of trials since 2005 and the strong and increased presence of the drug industry in clinical trial sponsorship. Before 2006 there were 29 pharmaceutical sponsors of clinical trials in India compared to 350 in the year 2009 (22).

There is little information in the public domain on reasons why people participate in clinical trials or the breakdown of trial subject populations by caste, class and gender. From media reports on ethical violations of clinical trials, we know that trial subjects are largely India’s poor, vulnerable and unsuspecting populations who are induced into trials by promises of free treatment, monetary incentives and an implicit faith in their doctor’s judgment (21). For example, journalist Jennifer Kahn describes the physician of a hospital in Sevagram, in Maharashtra, as “uneasy about his clinical success” because, according to the doctor, “Nine out of 10 times...the patient will just ask me to make the decision about the trial for him” (23:p 3). The asymmetry inherent in every doctor–patient relationship is further exacerbated by India’s healthcare system. According to Rao et al, 71% of spending on health is out-of-pocket and this expenditure pushes 4% of India’s population into poverty every year (24). With healthcare expenses being

one of the leading causes of poverty in India, clinical trials hold the promise of healthcare for many patients, and perhaps even a cure. At the hospital in Sevagram, the sponsor of a stroke prevention trial promised trial subjects two free physical examinations in a year during the course of the trial (23). Even if a drug does prove beneficial to a patient in a trial, it is most likely that the trial subject will not be able to afford the drug after the trial is over. The doctor at the Sevagram hospital gave the example of a trial conducted to test an anti-clotting drug, at a cost of Rs 800 a day that would not be affordable to his patients (23). Moreover, media coverage of doctors covertly accepting monetary payments to recruit patients for trials stand testimony to unscrupulous practices adopted by the medical community in conducting clinical trials (25).

The emergence of a clinical trial industry in India has thus raised many complex ethical issues that overshadow the clinical trial process and those that ethics committees must confront in an ethical review.

Research methods

Seventeen IEC members were individually interviewed across five hospitals located in New Delhi. Since there is no centralised registry of IECs or a systematic means of identifying medical institutions that have ethics committees, the selection of hospitals was purposive or based on the researchers’ judgment of which institutions would be the most appropriate to the study’s aims. Of the five hospitals, two were public institutions; two were private hospitals and one a trust-managed hospital. Differently-run medical institutions were selected in an attempt to observe differences and similarities, if any, in the respective IECs.

With the exception of one IEC, the researcher made initial contact with the member secretaries or secretariats of the ethics committees. These individuals were identified either through the hospital’s website or via the researcher’s personal contacts. Details of other IEC members were provided by the member secretary, through the institution’s website or with the help of personal contacts.

The synopsis and research tools of the study were approved by the ethics committee constituted by the Centre of Social Medicine and Community Health at Jawaharlal Nehru University (JNU). Before the interview, all interviewees were informed in writing by the researcher and the research supervisor about the objectives of the study. All interviews were conducted by the student researcher at the interviewee’s place of work, with the exception of three members. The identities of all interviewees and their institutions were kept confidential by the researcher. The interviews conducted were semi-structured and divided into two broad themes: the operational and functional aspects of the IECs, and the opinions and views of IEC members on a range of topics such as member appointments, ethics training, workload and other challenges faced by IEC members. Additionally, findings of this study are also based on the non-participant observation of an IEC meeting at one of the private hospitals, where the researcher was a silent observer at the

meeting. An IEC meeting was observed to primarily understand the nature of deliberations of such a meeting, the IEC inter-group dynamics and the nature of interaction between the IEC and investigators, who were invited to present their protocols. Additionally, three SOPs that were made available to the researcher by the respective IECs were examined to assess whether these ethics committees had articulated their terms of reference for members and if the institution had an established policy on the IEC selection process. An interview with the manager of a private hospital's department of clinical research was also conducted in order to understand the department's role in functioning as the IECs secretariat. All interviews were recorded in writing as answers to questions based on the interview guide. Individual interviews were transcribed on the basis of responses to the interview guide and grouped according to institution. The findings were then organized by the researcher into different themes based on the interview guide and also examined for similarities and differences in the workings of the IECs. The themes used are not mutually exclusive of each other and each topic must be read in relation to the others.

Findings

Arbitrariness in member selection

The non-affiliated members – or those external to the institution – interviewed for this study were selected to their respective IECs by a seemingly arbitrary process based on an informal network of contacts and affiliations. Across hospitals, there appears to be no written policy on member selection. Instead, non-affiliated members are appointed to the IEC through word-of-mouth referrals in order to fulfil the requirement of forming a multidisciplinary team. For example, a non-affiliated, non-medical/non-scientist member from the IEC of a public hospital was unsure of the reasons why the hospital approached him for IEC membership. "They must have heard about me," the member stated. A non-affiliated, non-medical/non-scientist member of a private hospital was appointed to the institution's IEC because of an informal recommendation by his cardiac surgeon who is a practising doctor at the hospital. According to an affiliated member from a private hospital, the hospital "found out who the experts are in the industry." In some cases, the non-affiliated, medical members had a former association with the concerned hospital. Thus, doctors from both within and outside the hospital – who constitute about half the IEC – can frequently have an institutional affiliation.

For affiliated doctors, membership on an IEC was a burden and an additional responsibility to their already busy schedules. "I did not have a choice," said one doctor and another contended that he "was not asked" if he "would like to become a member" or if he "was willing." From the majority of responses of non-affiliated and non-medical/non-scientist members, it was not clear whether they joined the IEC because of individual career prospects or to fulfil an obligation. "It is a big honour to be a part of an elite group of doctors," stated a non-affiliated/non-medical member. The response of only one non-affiliated and

non-medical/non-scientist member implied reflection on the need of an IEC in the context of the global clinical trial. The member expressed the importance of having a "working position" on transnational corporations because "they are here and you have to deal with them" as his reason for joining an ethics committee.

Lack of training on the ethics of clinical research

While the majority of IEC members interviewed for this study emphasised the importance of ethics training, only members from private hospitals had undergone any form of training. A non-affiliated, non-medical/non-scientist member from a private hospital's IEC found the training to be "very useful." On the other hand, a non-affiliated, non-medical/non-scientist member on the IEC of a public hospital expressed the difficulties faced by new IEC members due to the lack of training: "in the first two to three meetings we are like dumb people. But we are not showpieces," the member stated. While untrained members are a concern, the member secretary of a public hospital's IEC pointed out that organising training programmes is difficult due to the busy schedules of doctors.

An affiliated member of a public hospital's IEC implied that doctors do not require "intensive training" as "they are already sensitised" to patient issues. The member however stated the importance of developing discerning clinicians so that they can read between the lines of drug company-sponsored research protocols that "could be hiding information and not revealing everything." Another doctor on the IEC of a private hospital was also of the opinion that ethics training was not such a necessity for doctors on the committee because these individuals "are well aware of the role of ethics in clinical research," the member said. While admitting that "sometimes clinicians may not see things from a layman's perspective" and "there can be oversight which is not intentional," this member "takes ethics for granted."

Ethical dilemmas

Ethical dilemmas are not only inherent to clinical research but are also the reason why an independent ethics review is imperative. However, it is evident that there is a dearth of debate and discussion on weighty ethical questions. For example, a medical member who favoured the use of control groups in an experiment was of the opinion that the IEC is in fact a "big hurdle" to conducting scientific experiments because "we need more controls (groups)...statistical evaluation is not up to the mark. This is the constant dilemma." Thus, the scientific design of a clinical trial such as a randomised control trial—in which patients that are randomly assigned to the placebo arm of the trial will be denied treatment—can in itself raise ethically complex questions, especially when effective treatment exists. It is in these difficult situations that in fact the role of the multidisciplinary IEC must come into play to arrive at morally acceptable solutions that do not endanger the safety of trial subjects.

Challenges faced by the non-affiliated, non-medical/non-scientist member

The findings of this study indicated that while on paper IECs are multidisciplinary bodies, in spirit the intention of diversity in ethical review is not apparent in either private or public institutions. The medical/scientist members on the IEC are the most assertive voices in ethics committee deliberations. There is little room for the non-medical/non-scientist members to express an opinion, and their presence on an IEC appears to be merely obligatory. Barriers to the effective participation of non-medical/non-scientist members include the inherent hierarchy that exists between the medical expert and the non-medical expert, as well as the highly technical nature of clinical trial protocols.

A non-affiliated, non-medical/non-scientist member describes her experience at IEC meetings of a public hospital:

We can't ask the doctors. Doctors are not conducive; they assert their knowledge of medical technology... It is a closed circle; they [the doctors] don't open up. At times I feel I am not doing justice. Three of us are from outside. We don't usually say anything. You have to be well studied if you say anything.

A non-affiliated, non-medical/non-scientist member of a private hospital's IEC described the inability of investigators in adapting protocols for an ethics review thus:

Although there is a separate technical committee, for an ethics committee they [the investigators] present the same information. It's a huge amount of literature and none of it makes sense. Nothing in the proposal says what the ethical issues are. There is no effort to make it easier.

While voices of non-medical/non-scientist members are not adequately represented in IEC meetings, a social scientist member from the IEC of a private hospital also stated, "that it is easier in a way for unaffiliated members to make a point" than for a clinician affiliated to the institution. Non-affiliated members, he explained, have less at stake in raising an objection than affiliated members, whose disapproval could offend both the institution and the investigator, who might possibly be a colleague of the doctors on the IEC.

Interestingly, even when non-affiliated, non-medical/non-scientist members have the confidence to voice an opinion, there is very little they can do to impact the ethics of the clinical trial process. For example, an outside member raised a question in an IEC meeting about the objectivity of the appraisal process by which it was declared that the death of a research subject was unconnected to the trial. The member was informed that an expert committee had reviewed the matter and reached this conclusion. However, the member learnt that the expert team had comprised doctors who were affiliated to the institution.

Institutional bias in ethical review

The likelihood that affiliated IEC members will prioritise institutional interests over the safety of the research subject

was evident during the deliberations of an IEC meeting of a private, super-specialty hospital where trial investigators – with institutional affiliation – were presenting their research protocols. In response to an investigator proposing the use of a placebo arm in the clinical trial, an affiliated member of the IEC advised the investigator to practice caution in his use of a placebo as an established treatment was known. The medical member expressed concern on placebo use in a hospital where patients "are paying for everything—in public hospitals it is different" and therefore the institution must "protect" itself in case the patient holds it responsible for any trial-related injuries. The reasons cited by the IEC member for reconsidering the use of a placebo did not express the moral dilemma that using a placebo raises, but rather indicated a concern for providing the hospital protection from any liability. In this instance, safety of the trial subject was only a byproduct of the hospital safeguarding the institution's legal accountability.

Workload

The findings of this study indicated a significant difference in the number of protocols reviewed per meeting in the IECs of public hospitals compared to private hospitals. For example, a public hospital that meets once a month reviews about 50 protocols per meeting compared to a private hospital that also meets once a month but reviews two to six protocols in a meeting. The IEC of this particular public hospital also undertakes the scientific review of the protocol in addition to the ethical review. This adds an additional burden to the workload. An affiliated member of this IEC stated that its members "had a debate about the scientific review being separate. Some of us think it should be separate but there are clinicians in the group so it continues to be combined". According to an affiliated member, the three to four hour-long meetings of this public hospital's IEC are still not enough to include the review of amendments made to older protocols.

Lack of administrative support

The work pressure experienced by an IEC of a public hospital is heightened by the lack of administrative support for the committee from the hospital. The IEC's member secretary, who also chairs a hospital department, has to rely on the services of an assistant assigned to the department to keep minutes of IEC meetings and for other administrative tasks of the IEC. A major administrative challenge for the IEC "is filing and how well you can retrieve documents. These are important if an ethics committee has to function properly," stated the member secretary. While another public hospital's IEC does have dedicated office space, the support staff is limited to only one clerical position. "That is all I have," complained the member secretary who needs a "full-fledged office and different levels of clerical staff to set the agenda, set dates for the meeting and look at the proposals."

The IECs of private hospitals appeared to have more institutional support than the public hospitals. For example, one of the private hospitals has a clinical research department that is dedicated to the management of its IEC.

Inadequate monitoring of ongoing clinical trials

None of the five IECs in this study had been visiting clinical trial sites. The shortage of manpower and already overworked ethics committees were the reasons given for the lack of on-site review. All the IECs thus solely rely on the investigator to provide them with progress reports, reports on serious adverse events and information on protocol amendments. While the member secretary of an IEC expressed that random checks of trial sites was very important, she was of the opinion that monitoring should ideally be done by a third party. The member secretary of another IEC was also of the opinion that a third party should be responsible for visiting the clinical trial site, unless a member on the IEC was specifically assigned the task of on-site monitoring. An affiliated IEC member of a private hospital was of the opinion that the responsibility of monitoring a trial's progress must lie with the sponsors and investigators.

While reporting the progress of a clinical trial to the IEC is the mandate of investigators and/or sponsors, the objectivity of an ongoing review is questionable if it is left to individuals who are not entirely independent of the research (2). In fact, the member secretary of a public hospital's IEC expressed difficulties in negotiating with drug companies because of their evasiveness in providing an accurate picture of adverse events. "Information on adverse events is the main issue," the member secretary stated, "but the sponsors try to make it seem not so serious."

The influential presence of the drug industry in the clinical trial process

Dealings with the pharmaceutical industry presented a challenge for some IEC members. The member secretary of a public hospital's IEC expressed how pharmaceutical companies try to get things done their way and attempt to manipulate the clinical trial agreement drawn-up among the sponsor, the investigator and the institution.

The member secretary also expressed concern about the public health relevance of the drugs being tested in industry-sponsored clinical trials in India. "They [drug firms] are making India a dumping ground.... studying drugs of all types that we don't use," he remarked.

Another member—from the IEC of a public hospital—while agreeing with the member secretary's concern regarding the global pharmaceutical industry's disregard for India's public health needs, justified the industry's clinical research priorities. He argued that foreign sponsors should not be responsible for public health in India when the state itself had failed to deliver healthcare to the majority of its people.

But why should a pharma company do malaria drug trials? They are commercial, looking for profit. It's the government's responsibility, world over governments are giving up their role of social responsibility so why should a pharma company care?

"Of course then one can say that physicians should not do trials of diseases that are not relevant," stated this member, who further explained the reason why physician-investigators are willing to participate in trials that may not necessarily be relevant to India's disease burden:

For a doctor's career, for promotional aspects it is important to be published in an international journal... these won't be publishing on malaria unless it is a path breaking study but 80-90 percent of studies are not.

A social scientist member on a private hospital's IEC stated that his time on an ethics committee had given him an insight into the pressure that the industry imposes on investigators: "It is apparent that this is corporate driven research. Ethical issues are commercial considerations...I sensed the pressure that researchers are under."

Discussion

Historically, medical experimentation has exploited human vulnerability and targeted the most disadvantaged and impoverished sections of society for research purposes (6, 26). Presently, what has changed is not the desperation of the trial subject or the risks and uncertainties inherent in drug development, but the very structure and scope of the clinical trial. The clinical trial enterprise today is built on the foundation of a global business model driven largely by drug companies. It transcends national boundaries and can involve multiple trial sites using thousands of trial subjects across the world. "Treatment saturated" populations of the developed world are not ideal candidates for clinical trials and neither are they easily available in adequate numbers to provide data for a drug to pass the marketability test. Increasingly, it is the clinical trial industry in developing countries such as India that is meeting the demand of transnational pharmaceutical companies for running clinical trials and recruiting trial subjects as quickly as possible.

Clinical trials being conducted in India do not necessarily offer any direct benefit to trial subjects nor cater to the health needs of the country. Only 10% of research on drugs is focused on conditions that comprise 90% of the global disease burden (7). An analysis done by Clinical Trials Watch of trials that were registered on India's clinical trial registry found that in the month of June 2010, for example, only 16 of the total 1078 registered trials (1.48%) were on lower respiratory tract infections and only seven of 1078 (0.6%) were on tuberculosis, with 13.4% of trials dedicated to cancer research (27).

The IEC in India, thus operates in a competitive business environment in which responsibility to the trial subject and the community at large can often be lost in the individual interests of different groups. The safety of trial subjects is further jeopardised if IEC members are not adequately equipped to confront ethically complex situations and if they are deprived of a supportive environment in which they must carry out their role. The findings of this study indicate that IECs face many challenges that need urgent consideration and reform.

The lack of transparency in appointing members, limited training opportunities, the invasion of institutional interests in an ethical review, inadequate continuing review and the non-participatory presence of non-medical members are among the structural and functional deficiencies of IECs found across both private and public hospitals. Some of these issues are discussed in greater detail in the following paragraphs.

Institutions need to place greater emphasis on ethics training for all their IEC members. The SOP of every ethics committee must specify the nature and extent of training to be provided and also clearly state its definition of ethical expertise. Training programmes should sensitise medical professionals to the role of non-medical members, who must become equal partners in the ethical review process. A collaborative approach to the understanding of ethics must be attempted by educational initiatives in order to bridge the current divide within the IEC that vitiates its overall goal of protecting the trial subject. Globally, research conducted specifically on non-medical IEC members has also revealed the dominating presence of medical members in IEC meetings. For example, Sengupta and Lo in their study on non-medical/non-scientist IEC members in the US, found that 88% of the non-medical/non-scientist participants had negative experiences with their scientist colleagues (28). A US Government report issued in 1998 by the Office of the Inspector General stated that the tendency to limit an ethics review to technical inputs could negatively impact ethical deliberations. Investigators who would rather focus on the scientific outcomes of the trial may choose to disregard issues such as trial-related risks and the equitable selection of subjects. Effective participation of non-medical IEC members who can counteract the tendency to neglect the ethical components of a research protocol is thus integral to the review process. Based on their study, Sengupta and Lo recommended a mentoring programme for newly appointed IEC members that would require them to work closely with more experienced members on the committee while reviewing protocols (28).

Even so, an educated and cohesive IEC alone will not strengthen an ethical review process unless its members are selected with transparency and the ethical decisions they make are independent of institutional interests. There is limited guidance for institutions in ensuring an appointment process that is bias-free and representative of the interests of trial subjects (13). For instance, research in the US on IECs indicates that institutions face practical impediments in identifying individuals who have both the time and necessary qualifications to attend ethics committee meetings (14, 29). Institutions may therefore use the easier option of selecting members who are amenable to the rest of the committee (29). The findings of this study indicate that IEC members are either employees of institutions or are likely to have a personal affiliation. Investigators of clinical trials in many cases also belong to institutions where the trial is being conducted. For these individuals, clinical trials represent the progress of scientific knowledge as well as a means of advancing their own personal careers. The nature of IEC composition could thus

lend itself to institutional bias and undermine the autonomy of the ethical review process, a concern that was evident from the findings of this study. A discussion at an IEC meeting on the use of placebo when a known treatment existed primarily centred on the need to protect the institution from liability charges. For another IEC, distancing a trial subject's death from the trial was a decision exclusive to doctors associated with the concerned institution. Additionally, a non-affiliated, non-medical member observed that members like him—who are distanced from the institution—have less at stake if they challenged ethically problematic issues of a protocol. The crucial policy questions on IEC composition that therefore arise are: should all IEC members be unaffiliated to the institution to ensure an unbiased protocol review? Should the IEC be an autonomous, public-funded body that is not dependent on institutional support?

An untrained, unsupported and overworked IEC bound by obligations to the institution and the investigator stands powerless in the face of the global clinical trial enterprise. Such an IEC will be unable to do justice to an ethics review and neither will it be able to carry out its additional role of on-site monitoring of trials. Without a supervisory mechanism in place that is independent of research, in all likelihood, a breach in protocol by investigators will remain unnoticed, or serious violations will become public knowledge only after the unethical practice has occurred. Should a third party monitor clinical trials as some IEC members of this study suggested? Or would another review body only add to the bureaucracy of the clinical trial process and further distance trial subjects from the people who are entrusted to protect their interests? These are critical questions that need the attention of the country's regulatory authorities.

Fixing the fundamental systemic issues that interfere with an IEC's daily operations and affect the quality of an ethics review needs immediate remedy if the IEC has to fulfil its responsibility towards the trial subject. Nonetheless, the dilemma remains—are we expecting too much from a group of individuals whose autonomy in an ethics review is questionable in the face of institutional interests and the formidable global framework of the clinical trial industry?

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References

1. Jesani A. Ethics in ethics committees: time to share experiences, discuss challenges and do a better job. *Indian J Med Ethics*. 2009 Apr-Jun;6(2):62–3.
2. Central Drugs Standard Control Organisation. Schedule Y, The Drugs and Cosmetics Rules, 1945 (as amended upto 30th June, 2005). New Delhi:CDSCO;2005 Jun 30[cited 2013 Jun 15]. Available from: http://cdsco.nic.in/html/D&C_Rules_Schedule_Y.pdf
3. The Nuremberg Code. *JAMA*. 1996 Nov;276(20):1691.
4. Shuster E. The Nuremberg Code: Hippocratic ethics and human rights. *Lancet*. 1998 Mar;351(9107):974–77.
5. Levine RJ. *Ethics and regulation of clinical research*. New Haven,

- Connecticut: Yale University Press; 1988.
6. Beecher HK. Ethics and clinical research. *N Engl J of Med.* 1966 Jun;274(24):367–72.
 7. Petryna A. *When experiments travel: clinical trials and the global search for human subjects.* Princeton: Princeton University Press; 2009.
 8. Hoffman S. Beneficial and unusual punishment: an argument in support of prisoner participation in clinical trials. *Indiana Law Review.* 2009 Feb;33(2):475–515.
 9. Williams JR. The Declaration of Helsinki and public health. *Bulletin WHO.* 2008 Aug;86(8):650–651.
 10. Council for International Organizations of Medical Sciences. International ethical guidelines for biomedical research involving human subjects. Geneva: CIOMS; 2002.
 11. Indian Council of Medical Research. Ethical guidelines for biomedical research on human participants. New Delhi: ICMR; 2006 Oct [cited 2013 Jun 15]. Available from: http://icmr.nic.in/ethical_guidelines.pdf
 12. Allen P, Waters WE. Attitudes to research ethical committees. *J Med Ethics.* 1983 Jun;9(2):61–5.
 13. De Vries RG, Forsberg CP. What do IRBs look like? What kind of support do they receive? *Account Res.* 2002 Jul-Dec; 9 (3–4):199–216.
 14. Department of Health and Human Services, Office of Inspector General. Institutional review boards: their role in reviewing approved research. Boston: The Office of Evaluation and Inspections; 1998 Jun. Report No.: OEI-01-97-00190. Available from: <https://oig.hhs.gov/oei/reports/oei-01-97-00190.pdf>
 15. Indian Council of Medical Research. WHO-ICMR Summary report: status of ethical review of ICMR funded projects in clinical research/clinical trials. New Delhi: ICMR; 2007. p14.
 16. Kamath G. Making the grade. *Business World* [Internet]. 2007 November 16 [cited 2011 Jan 2]. Available from: <http://www.businessworld.in>
 17. Brahme R, Mehendale S. Profile and role of the members of ethics committees in hospitals and research organizations in Pune, India. *Indian J Med Ethics.* 2009 Apr–Jun; 6(2):78–84.
 18. Petryna A. Ethical variability: drug development and globalizing clinical trials. *Amer Ethnologist.* 2005 May; 32(2):183–197.
 19. Thiers FA, Sinskey AJ, Berndt ER. Trends in the globalisation of clinical trials. *Nat Rev Drug Discov.* 2008 Jan;7(1):13–14.
 20. Sunder Rajan K. Experimental values: Indian clinical trials and surplus health. *New Left Review.* 2007 May-Jun; (45):67–88.
 21. Nundy S, Gulhati CM. A new colonialism? – Conducting clinical trials in India. *New England J Med.* 2005 Apr;352(16):1633–6.
 22. Ravindran D, Nikarge S. Clinical trials watch. *Indian J Med Ethics.* 2010 Oct–Dec;7(4):259–62.
 23. Kahn J. A nation of guinea pigs. *Wired* [Internet]. 2006 March 14 [cited 2013 Jun 3]. Available from: <http://www.wired.com/wired/archive/14-03/indiadrug.html>
 24. Rao M, Rao KD, Shiva Kumar AK, Chatterjee M, Sundararaman T. Human resources for health in India. *Lancet.* 2011 Feb; (377):587–98.
 25. Nagarajan R. Indore docs flout clinical trial norms, earn lakhs. *Times of India* [Internet]. 2011 Jun 3:17. Available from: http://articles.timesofindia.indiatimes.com/2011-06-03/india/29616513_1_clinical-trials-quintiles-research-doctors
 26. Baader G, Lederer SE, Low M, Schmaltz F, Schwerin AV. Pathways to human experimentation, 1933–1945: Germany, Japan, and the United States. *Osiris.* 2005;20(2):205–31.
 27. Ravindran D, Ingle G. Clinical trials in India: the needs of the country and the focus of sponsors. Paper presented at: Third National Bioethics Conference; 2010 Nov 17–20; New Delhi.
 28. Sengupta S, Lo B. The roles and experiences of nonaffiliated and non-scientist members of Institutional Review Boards. *Acad Med.* 2003 Feb;78(2):212–18.
 29. Anderson EE. A qualitative study of non-affiliated, non-scientist institutional review board members. *Account Res.* 2006 Jun;13(2):135–55.

National Vaccine Policy: ethical equity issues

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Abstract

The ministry of health and family welfare published the national vaccination policy in April 2011. The policy document drew severe criticism from several public health experts. A review of the print and web-based literature on the national vaccine policy was done and the issues of ethics and equity involved in introducing new vaccines under the Universal Immunisation Programme (UIP) were studied.

The average coverage of the UIP vaccines at the national level is below 50%. Despite this, the policy document did not state any concrete strategy for increasing the coverage. The main stumbling block for evidence-based vaccine policy in India is the lack of reliable epidemiological data, which makes it difficult for the National Technical Advisory Group on Immunisation to offer sound technical advice to the government. No attempts have been made to prioritise diseases or the selection of vaccines. The policy suggests the introduction of the following vaccines in the UIP: Haemophilus influenzae type b, pneumococcal vaccine, rotavirus vaccines and human papillomavirus (HPV). This selection is on the grounds of the vaccines' availability, not on the basis of epidemiological evidence or proven cost-effectiveness. This is a critical review of the current vaccination policy and the move to include the rotavirus and HPV vaccines in the UIP.

Introduction

Vaccines are important preventive medicines for primary healthcare, are critical for a nation's health security and play a useful role in public health by reducing morbidity and mortality due to communicable diseases (1-3). Every country should have its own immunisation policy that states how the government proposes to universalise the benefits of immunisation to the large sections of the population which do not receive the basic vaccinations, and also describes how new vaccines are to be selected for introduction in the Universal Immunisation Programme (UIP)(3,4).

The ministry of health and family welfare (MOHFW) published the national vaccination policy in April 2011 (5). This policy was drafted by the National Technical Advisory Group on Immunisation (NTAGI), a government - constituted committee of experts. As for the context and framework of the policy, it states, "The document covers all categories of vaccines used in the UIP, vaccines available but not part of the UIP and those vaccines which are likely to become available in future." (5: p 4) The chapter on ethics and equity stresses, "The ethical use and equitable access to prevention and care should be the basic mantra of any programme meant for ameliorating