

Review article**Role of Ethics Committee and issues involved in Bio-medical research on human beings – an update.**

Rajkumari Ajita

Regional Institute of Medical Sciences, Imphal, Manipur, India.

Abstract

With the ever increasing and expanding in medical sciences and bio-medical research involving human beings, the role of Ethics Committee is becoming very important. It is mandatory that all proposals on biomedical research involving human subjects should be scrutinized and cleared by an appropriately constituted Institutional Ethics Committee (IEC) also referred to as Institutional Review Board (IRB) in many countries, to safeguard the welfare and the rights of the participants. The purpose of a Research Ethics Committee is to protect the dignity, rights, safety and well being of all actual or potential research participants and also to ensure that the privacy, safety, social sensitivities and welfare of participants are protected. This review paper makes an attempt to educate the medical fraternity about the role of Ethics Committee and share basic principles and contemporary issues of ethics guidelines with the physicians doing research on human beings.

Key Words: Ethics Committee, Research Protocol, Informed Consent, Declaration of Helsinki.

Introduction:

There have been considerable advances in medical sciences and bio-medical research in the recent past. Recent advances in the field of Assisted Reproductive Technologies, Organ Transplantation, Human Genome Analysis, Gene Therapy and Embryo and Fetal research promise unquestionable and hitherto undreamed of benefits to mankind. At the same time, they raise many questions of law and ethics, stimulating public interest and concern. Experimentation on human being is subject to ethical standards that promote respect for all and protect their health and rights. With the ever increasing and expanding in medical research especially increasing research facilities and availability of the state of the art equipment, there are newer challenges to ethical standards; as a result the ethical guidelines are frequently revised^[1]. In most cases noncompliance of ethical guidelines, is more out of ignorance than deliberate omission and in some, intense pressure to publish for continuance in positions of repute^[2].

The conduct of research with human participants is facing increased scrutiny from government, media, and academic sources^[3]. Every researcher who conducts research involving human subjects for their data has experiences with one or more Institutional

Review Boards. Some view their institutional review board experiences as helpful; others view them as painful and obstructive^[4]. Even lawsuits against investigators, institutional review boards, and academic institutions are becoming increasingly common in view of recent instances of serious injury to subjects at several major research institutions^[5].

It is mandatory that all proposals on biomedical research involving human subjects should be scrutinized and cleared by an appropriately constituted Institutional Ethics Committee (IEC) also referred to as Institutional Review Board (IRB) in many countries, to safeguard the welfare and the rights of the participants^[6,7,8,9]. The Ethics Committee are entrusted not only with the initial review of the proposed research protocols prior to initiation of the projects but also have a continuing responsibility of regular monitoring for the compliance of the ethics of the approved programmes till the same are completed^[1].

The need for uniform ethical guidelines for research on human subjects is of utmost importance in the present scenario of research on medical sciences or allied areas. The aim of this review paper is to educate the medical fraternity about the role of Ethics Committee and share basic principles and contemporary issues of ethics guidelines with the physicians doing research on human beings.

History:

History has shown that medical research has misused people. Research participants have been subject to unacceptable risk and have acted as a means to obtain a certain goal^[10]. The first International Code of Ethics for Research involving human subjects "The Nuremberg Code" was a response to the cruelties committed by Nazi research

physicians at the Nuremberg war crime trials. Thus, it was to prevent any repetitions by physician of such attacks on the rights and welfare of human beings that human research ethics came into being. The Nuremberg Code (1947) laid down standards for carrying out human experimentations, emphasizing the subject's voluntary consent. World Medical Association (1964) took a step further to reassure society by adopting the "Declaration of Helsinki", which laid down the ethical guidelines for research involving human subjects and is revised from time to time^[1].

Research Ethics Committee and its role and responsibilities:

Research Ethics Committee (RECs) are the committees convened to provide the independent advice to participants, researchers, funders, sponsors, employers, care organizations and professionals on the extent to which proposals for research studies comply with recognized ethical standards. The purpose of a REC in reviewing the proposed study is to protect the dignity, rights, safety and well being of all actual or potential research participants and also to ensure that the privacy, safety, social sensitivities and welfare of such participants are protected as envisaged in the Declaration of Helsinki^[11]. RECs are responsible for acting primarily in the interest of potential research participants and concerned communities, but they should also take into account the interests, needs and safety of researchers who are trying to undertake research of good quality. However, the goals of research and researchers, while important, should always be secondary to the dignity, rights, safety, and well being of the research participants.

A medical Research Ethics Committee is an upfront censoring committee that, in most

countries, has the mandate to stop research, including research that could have provided important results for many people^[8,10]. It is empowered to exempt, approve, disapprove or require modifications in the submitted protocol of proposed studies. The Committee should be aware of their responsibility to accept standard quality criteria for research. It should be fair in its judgement, and it should restrict its evaluation to ethical issues only. It should also provide coherent arguments for their decisions and communicate these to the applicants. Its main role is to assess both the scientific and ethical aspects of submitted protocols. Each Ethics Committee should have its own standard operating procedure. The role of an Ethics Committee is not to hinder research, but to make sure that it is performed accordingly to high ethical standard. The ethical review should be done through formal meetings with proper quorum^[12]. Thus the role of an Ethics Committee is crucial in the implementation of any research venture.

All the research involving human subjects should be conducted in accordance with the four basic ethical principles namely Autonomy or respect for person subject, beneficence (do good), Non-maleficence (do not harm) and Justice^[7]. Autonomy refers to the right of individuals to decide for themselves what is good for them. Beneficence concerns the benefits and risks of participating in research. According to the principles of non-maleficence and beneficence, we should minimize risks by using procedures, which are consistent with sound research design. We must ensure that benefits from the research outweigh the risks. It is unethical to ask a group to bear the burden of trial while the benefits are passed on to the advantageous group. The principle of justice requires that the benefits and burdens of research be distributed fairly among all groups and classes in society, taking into account in

particular age, gender, economic status, culture and ethnic considerations^[13,14].

The Ethics Committee, at the same time, should be in conformity with the laws and regulations of the country in which the research experiment is being performed. Most Institutions in India do not have Ethics Committees. These are mandatory for centres that conduct research, as per the Indian Council of Medical Research (ICMR) guidelines. These committees must play the role of the watchdog.

The responsibilities of an IEC can be defined as follows:

- i) To protect the dignity, rights and well being of the potential research participants.
- ii) To ensure that universal ethical values and international scientific standards are expressed in terms of local community values and customs
- iii) To assist in the development and the education of a research community responsive to local health care requirements.

Composition of REC:

RECs should be multi-disciplinary and multi-sectorial in composition. Independence and competence are the two hallmarks of REC. The composition of REC may vary from institution to institution depending on local circumstances. The REC should have members who can reflect community values. Lay (non-medical) membership is important if the community is to have confidence in the decisions of the REC. The REC should contain at least one specialist in the relevant discipline of research. Others like Bioethicists, theologians, philosophers and

Calicut Medical Journal 2008;6(2): e3

psychologists may be able to contribute greatly to the work of an REC. A nurse should also be included, especially for RECs dealing with clinical research. The number of persons in an ethical committee should be kept fairly small (7-9 members). It is generally accepted that a minimum of five persons is required to compose a quorum. There is no specific recommendation for a widely acceptable maximum number of persons but it should be kept in mind that too large a Committee will make it difficult in reaching consensus opinions. 12-15 is the maximum recommended number^[15].

The composition of the Committee may be as follows: (i) Chairperson, (ii) 1-2 basic medical scientists, (iii) 1-2 clinicians from various institutes, (iv) one legal expert or retired Judge, (v) one social scientist/representative of non-governmental voluntary agency, (vi) one philosopher/ethicist/theologian, (vii) one lay person from the community, (viii) Member-Secretary. The Chairman of the Committee should preferably be from outside the Institution and not the head of the same Institution to maintain independence of the Committee. The Member Secretary who generally belongs to the same Institution should conduct the business of the Committee^[15].

Research Protocol:

The research protocol should always contain a statement of the ethical considerations involved and should indicate that there is compliance with the principles enunciated in the Declaration of Helsinki. The design and performance of each experimental procedure involving human subjects should be clearly formulated in an experimental protocol. This protocol should be submitted for consideration, comment, guidance, and where appropriate, approval to a specially appointed ethical review

committee, which must be independent of the investigator, the sponsor or any other kind of undue influence. The IRB is not expected to examine the technical details and statistical design in depth. It considers mainly the interests of research subjects.

Medical research involving human subjects should be conducted only by scientifically qualified persons and under the supervision of a clinically competent medical person. The responsibility for the human subject must always rest with a medically qualified person and never rest on the subject of the research, even though the subject has given consent. Such research should only be conducted if the importance of the objective outweighs the inherent risks and burdens to the subject. This is especially important when the human subjects are healthy volunteers. Every precaution should be taken to respect the privacy of the subject, the confidentiality of the patient's information and to minimize the impact of the study on the subject's physical and mental integrity and on the personality of the subject. Both authors and publishers have ethical obligations. In publication of the results of research, the investigators are obliged to preserve the accuracy of the results. Negative as well as positive results should be published or otherwise publicly available. Sources of funding, institutional affiliations and any possible conflicts of interest should be declared in the publication. Reports of experimentation not in accordance with the principles laid down in the Declaration of Helsinki should not be accepted for publication.

Informed consent:

An important component of research involving human subjects is informed consent. Researchers need to be patient, meticulous and innovative to make sure that informed

Calicut Medical Journal 2008;6(2): e3

consent is truly voluntary, and that there is adequate understanding of the process among the participants^[16]. Informed consent is based on the principle that competent individuals are entitled to choose freely whether to participate in research or not. It protects the individual's freedom of choice and respect for individual's autonomy. Informed consent is not just a piece of paper – rather it is a whole process and the process has to be documented. The patient information sheet and informed consent document is reviewed meticulously by Ethics Committees and their input always enriches the informed consent document and protects the patient^[17]. Informed consent and ethics committee review are the two pillars on which the rights and welfare of participants in research programme rest^[18].

Each potential subject must be adequately informed of the aims, methods, anticipated benefits and potential hazards of the research and any discomfort it may entail. Any documentation given to potential participants should be comprehensible and there should be an opportunity for them to raise any issues of concern. The consent should be required in writing and records of consent should be maintained. Potential participants must be informed that they are free to withdraw consent to participation at any time. There should be a procedure for making complaints and participants should be made aware of this. All participants should be volunteers. The key to success in gaining informed consent lies in effective communication between researchers, families, associated professionals, professional bodies, research councils, charities, drug companies and educational institutions, and possibly parental or patient involvement in the design of the project^[19]. Informed consent ensures that individuals can decide to participate only when the research is consistent with their values, interests and preferences.

Unfortunately, for most clinical investigators in India, informed consent is a dispensable formality and few of them explain to patients what the trial is all about^[13].

Vulnerable groups:

Some research populations are vulnerable and need special protection. The particular needs of the economically and medically disadvantaged must be recognized. Research involving vulnerable groups includes children, the mentally ill, elderly people and the dying^[19]. Vulnerability is one of the least examined concepts in research ethics^[20]. Efforts should be made to ensure that individuals or communities invited for research be selected in such a way that the burdens and benefits of the research are equally distributed. Research on genetics should not lead to racial inequalities. Persons who are economically or socially disadvantaged should not be used to benefit those who are better off than them. Rights and welfare of mentally challenged and mentally differently able persons who are incapable of giving informed consent or those with behavioural disorders must be protected. Adequate justification is required for the involvement of subjects such as prisoners, students, subordinates, employees, service personnel etc who have reduced autonomy as research subjects^[7]. As a general rule, pregnant or nursing women should not be subjects of any clinical trials except such trials as are designed to protect or advance the health of pregnant or nursing women or fetuses or nursing infants, and for which women who are not pregnant or nursing would not be suitable subjects. Research in pregnant subjects should be undertaken only if pregnancy is an essential part of the research. Research on prisoners should not be undertaken unless the fact of being imprisoned

Calicut Medical Journal 2008;6(2): e3

is itself an essential component of the research topic.

Ethics Committee in Indian Scenario:

Constitution of a proper Ethics Committee in medical colleges is considered an essential requirement. However, most research institutions in India either do not have an Ethics Committee or, whenever formed lack adequate representation on it by lay persons. All Ethics Committee must be dynamic and vibrant, scrutinize research projects and confirm their ethical validity and take a stand on various ethical issues. Its work must be open to scrutiny. It must be responsive and responsible to the people. The ICMR Guidelines for Clinical Trials advocate the setting up of Ethics Committees at institutional levels. Despite these guidelines, more than 50% of institutions conducting research in India reportedly lack formal Ethics Committees. Ethics review mechanisms currently in position need drastic improvement, if India has to face the challenge of being projected as a "global hub" for clinical trials by the pharmaceutical industry. Institutional mechanisms for ethical reviewing of research involving human participants in India are weak and vulnerable. A concerted effort is required to strengthen them to fulfill their stated missions^[21-22].

Safeguarding confidentiality:

The right of research subjects to safeguard their integrity must always be respected. Every precaution should be taken to respect the privacy of the subject, the confidentiality of the patient's information and to minimize the impact of the study on the subject's physical and mental integrity and on the personality of the subject. The investigator must safeguard the confidentiality of research data, which might lead to the identification of the individual

subjects. Data of individual subjects can be disclosed only in the court of law under the orders of the presiding judge or in some cases may be required to communicate to drug registration authority or to health authority. Therefore, the limitations in maintaining the confidentiality of data should be anticipated and assessed. The identities of the patients or volunteers must be guarded in most studies. The institute and the IRB should insist that the study results are quoted only in scientific literature or technical reports submitted to regulatory authorities and not used for media publicity aimed at the lay public.

Conclusion:

There is an urgent need to educate the medical fraternity in India in basic research methodology and ethical principles if the level of research has to improve. Thankappan^[23] recommended that ethics should be a part of the medical curriculum. The ICMR must play a more proactive role in this process of education. Medical ethics must be taught at undergraduate or post graduate level. The teaching of research ethics for researchers and scientists should be part of Continuing Medical Education (CME) programmes^[18]. Medical Associations must promote good ethics by holding seminars, CMEs lectures and workshops.

Ethics Committee continues to be a vital safeguard for human experimentation. Many research projects, with good scientific content, get rejected on ethical grounds by review boards of institutions or funding agencies. Education and timely orientation of students to ethical issues and guidelines prior to taking up research projects will reduce delays and rejections from research and funding agencies^[2]. Every country, irrespective of its level of economic development, should have in

Calicut Medical Journal 2008;6(2): e3

place a functional research ethics review system in order to protect the dignity, integrity and safety of its citizens who participate in research^[24]. Despite the criticism that Ethics Committee hinders the human right of freedom of research; it is the need of the hour to

educate the medical researchers about the basic principles and contemporary issues of ethics guidelines.

References:

1. Shah N. Ethical guidelines for Biomedical Research on Human Subjects. *Trends in Biomaterials & Artificial Organs* 2005 Jan; **18(2)**:174-77.
2. Kanungo R. Ethics in research. *Indian Journal of Medical Microbiology* 2006; **24**: 5-6.
3. Candilis PJ, Arikan R, Noone SB, Holzer JC. The new research ethic: will oversight requirements sink forensic research? *J Am Acad Psychiatry Law* 2005; **33(3)**:361-7.
4. Lynn MR, Nelson DK. Common (mis)perceptions about IRB review of human subjects research. *Nurs Sci Q.* 2005 Jul; **18(3)**:264-70.
5. Mello MM, Studdert DM, Brennan TA. The rise of litigation in human subjects research. *Ann Intern Med* 2003 Jul 1; **139(1)**:40-5.
6. Borst-Eilers E. A welcome guide for evaluating medical research involving human subjects. *Ned Tijdschr Geneeskde* 2003 May 10; **147(19)**:898-900.
7. Indian Council of Medical Research. Ethical Guidelines for Biomedical Research on human Subjects. New Delhi, 2000.
8. Shrotri DS. Role of ethics committees in medical research. *Indian Journal of Medical Ethics* 2004 Oct-Dec; 12(4).
9. Ravindra RP. Ethics in human medical research: views of a non-medical person. *Issues in Med Ethics* 1994 May-Jul; **1(4)**: 6-7.
10. Olsen J, Mulvad G, Pedersen MS, Christiansen T, Sorensen PH. An ethics committee for medical research in Greenland: history and challenges. *Circumpolar health*, 2003: 144-146.
11. Krishna A. Editorial; The Ethics of Research in Children. *Indian Pediatrics* 2005; **42**: 419-423.
12. Tyebkhan G. Ethics Committee. *Indian J Dermatol Venereol Leprol* 2003; **69**:300-302.
13. Kalantri SP. Ethics in clinical research. *Indian J Anaesth* 2003; **47(1)**:30-32.
14. Goodyear-Smith F, Lobb B, Davies G, Nachson I, Seelau SM. International variation in ethics committee requirements: comparisons across five Westernised nations. *BMC Med Ethics* 2002 Apr 19; **3:E2**.Epub 2002 Apr 19.
15. Indian Council of Medical Research: Guidelines for preparing Standard Operating Procedures (SOP) for Institutional Ethics Committee for Human Research available at http://www.icmr.nic.in/ethics_SOP.pdf accessed on 1 Feb, 2008

Calicut Medical Journal 2008;6(2): e3

16. Bhan A, Majd M and Adejumo A. Informed consent in international research: perspectives from India, Iran and Nigeria. *Medical Ethics* 2006; **3(1)**:36-41.
17. Thatte UM. Do all projects require ethics committee clearance? *Journal of Postgraduate Medicine* 2002; **48**:91-91.
18. Kumar NK. Bioethics activities in India. *Eastern Mediterranean Health Journal* 2006; **12** (Supplement 1): S56-S65.
19. Eckstein S. Training for research ethics committees in the UK. *Indian Journal of Medical Ethics* 2001 Apr-Jun; **9(2)**.
20. Levine C, Faden R, Grady C, Hammerschmidt D, Eckenwiler L, Sugarman J. Consortium to Examine Clinical Research Ethics.: The limitations of "vulnerability" as a protection for human research participants. *Am J Bioeth* 2004 Summer; **4(3)**:44-9.
21. Muthuswamy V. Editorial: Status of Ethical Review and challenges in India. *Indian Pediatrics* 2005; **42**:1189-1190.
22. Nair VM, Martin DK. Concerns about ethical review of health research in India. *Indian Journal of Medical Ethics* 2004 Oct-Dec; **12 (4)**.
23. Thankappan KR, Cash RA. Ethical issues in biomedical research on human beings. *Indian Pediatrics* 2001; **38**:514-517.
24. Kirigia JM, Wambebe C, Baba-Moussa A. Status of national research bioethics committees in the WHO African region. *BMC Med Ethics* 2005 Oct 20; **6:E10**.
-

Corresponding author
Dr. Rajkumari Ajita, MS

Assistant Professor
 Department of Anatomy,
 Regional Institute of Medical Sciences
 Imphal, Manipur-795004, INDIA.

e-mail: rajkumariajita1@yahoo.co.in

Mobile No. 09436027602