

Ethical Aspects In Clinical Research

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An experiment is an attempt to discover something unknown or to test a supposition or principle, but we cannot be sure of the outcome. By definition, an experiment involves chance and it is because of this chance that ethics become paramount in the experiments, more so if they involve human subjects.(1)

All innovative scientific interventions whether diagnostic, prophylactic or therapeutic should ultimately involve human subjects. The need of safeguards in human experimentation should incorporate several important codes and regulations for the protection of human subjects.

The three human principles are(2)

- **Beneficence**, which requires that good should result, and harm should not result because of the experimentation.
- **Respect for rights** including the free choice of the subject and protection of the autonomy.
- **Justice**, which requires an equal distribution of burden and benefits.

The Nuremberg code of 1947 was developed in response to the criminal experimentation on captive persons by the Nazis during the World War II and it clearly emphasized on the ethical conduct and the use of consent during experimentation. Consent should be given only after a proper understanding of the procedure and the risks involved. The current practice of obtaining consent prior to initiation of a study also addresses the competence of the investigator.

The declaration of Helsinki(3) was adopted by the world medical association in 1964 and was revised in 1975 and this document addresses for the first time the concept of independent review of the research protocols by a committee of individuals who are not associated with the study.

Declaration of Helsinki(3,4,5)

The international code of ethics for biomedical research- Helsinki II.

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Basic principles in the Declaration of Helsinki revised and extended after revision in the 29th world medical assembly in Tokyo, 1976.

- The design and performance of each experimental procedure including human subjects should conform to existing scientific principles.
- The design of the study must be clearly mentioned in the experimental protocol which should be forwarded to an independent review committee.
- The study must be conducted only by persons adept at conducting the study after assuming full responsibility towards any problem arising because of the study.
- The study should be carried out legitimately.
- Every biomedical research should be preceded with a carefully conducted study of the biases, effects and the feasibility of the study.
- The right of the research project to safeguard the privacy of an individual is paramount.
- Human trials must be conducted only when an investigator is satisfied about the predictability of the side effects, hazards etc.
- Investigators must preserve the accuracy of the results in the event that the results are published.
- The subjects must be informed about the aims, objectives and the potential hazards of the study.
- The consent can be obtained from the subject's doctor or relatives provided that the subject legally cannot give the consent and if the study is of real use to him.

- In the case of legal incompetence, a legal guardian can give consent.
- The protocol must always contain a statement of ethical considerations involved and that the regulations have been complied with.

Respect your subject's rights(6)

The principle of medical ethics (autonomy) requires us to respect people and their rights. Informed consent ensures that individuals can decide to participate only when the research is consistent with their values, interests and preferences. Though written consent forms are used to document the consent, the process of informed consent is more important than a subject's signature on the form.

Elements of informed consent(6,7)

- **Purpose of the research project:** A clear explanation why the study is being done and the reason why an individual has been selected.
- **Procedures:** A clear explanation of what will be done with the individual.
- **Risks and Discomforts:** in a truthful statement.
- **Benefits:** a description of all the benefits if any including monetary benefits.
- **Alternatives to participation:** with a description on all the alternative methods of treatment.
- **Confidentiality:** ensuring the anonymity of the individual.
- **Request for more information:** in the form of statement ensuring further discussions with the patient.
- **Refusal or withdrawal:** The right of the patient to withdraw from the study at any point of time.
- **Injury statement:** describing the measures to be taken in case of injury.
- **Consent statement:** indicating the consent of the patient with the treatment procedure.
- **Signature of the patient, guardian in case of a minor]**
- Consent of the Subjects is mandatory in all the cases including
 - ◆ Children
 - ◆ Pregnant and Nursing women
 - ◆ Mentally ill and deficient patients
 - ◆ **Other vulnerable social groups** such as medical and nursing students, laboratory personnel and employees of pharmaceutical companies and armed forces.
 - ◆ **Community based research**

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. The consent forms are lengthy, complicated and difficult to understand. Obtaining

consent from a patient is often delegated, in public hospitals, to the junior most nurses or a resident. Also, the patients are poor and even if they do not want to enter the trial they do not refuse. They believe that this would displease their treating clinicians who may deliberately ignore them during their hospital stay. On the other hand, doctors in the private sector are worried that on hearing the very term 'trial' patients might choose to get treated elsewhere. Investigators often shorten the consent form or deliberately omit some 'offensive' parts that might deter patients from agreeing to participate.(8)

Review procedures(1,2,5)

In a highly centralized administration a national review committee may be constituted to review research protocols from both scientific and ethical view point. They may be appointed locally also. Their functions are

- To verify that all proposed interventions particularly the administration of drugs under development have been assessed by a competent expert body as safe for administration in humans.
- To ensure that all other ethical considerations arising from a protocol are satisfactorily resolved both in principle and practice.

For projects funded by federal agencies or conducted in institutions there must be the formation of an institutional review board. It should comprise of at least 5 members consisting of competent institutional members, a lawyer and a member not affiliated with the institution. The function of the institutional review board is to review proposal of research, accept or reject the proposal based on its feasibility.

Whatever the pattern of the procedure adopted for ethical review, it should be based on a detailed protocol comprising of steps outlined in the Helsinki declaration. Care should be taken to ascertain the criteria to determine admission and withdrawal of individuals including full details of the informed consent procedures.

Biomedical Research has acquired dimensions which are at once exciting and awesome. It raises some delicate and difficult issues of ethics which need to be dealt with sensitivity to human values and with great circumspection. While research which promises to mankind the great blessings of Science should not be stifled by too restrictive an approach, however, great care should be taken to ensure that something does not go out of hand. Therefore, any system of ethical guidelines on research needs to be cognizant of, and informed by, a sensitive balance of the risks and benefits.

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References

1. Health Research methodology, A guide for training in research methods. Oxford University Press 1993.
2. Portney LV, Watkins MP. Foundations of clinical research, applications to practice. Connecticut:Appleton and Lange press;2000: 1st edition.
3. World medical association declaration of Helsinki. Ethical principles for medical research involving human subjects. Finland 1964. Available from : URL: http://www.wma.net/e_policy (accessed on 23 september 2004).
4. Beauchamp TL, Childress J. The Principles of Biomedical Ethics. New York, NY: Oxford University Press; 2001: 5th edition. Chap 3.
5. Emanuel EJ, Wendler D, Grady C. What makes clinical research ethical? *JAMA* 2000;**283**(20):2701-11.
6. Calman KC. Communication of risks: choice, consent, and trust. *Lancet* 2002;**360**:166-68.
7. Farthing MJG. Ethics of publication. In: How to write a paper. Ed. Hall GM. Delhi: Byword Publishers, 2000: 2nd edition.
8. Kalantri SP. Ethics of drug trials in India. *Natl Med J India* 2002;**15**(3):179.
9. Indian Council of Medical Research. Ethical Guidelines for Biomedical research on Human Subjects. New Delhi 2000.