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# ETHICAL GUIDELINES FOR BIOMEDICAL RESEARCH ON HUMAN SUBJECTS

The need for uniform ethical guidelines for research on human subjects is universally recognised. Indeed, it has acquired a new sense of urgency as the critical issues in the areas of genomic research involving human subjects have become acute. Apart from the mandatory clinical trials on new drugs, a number of diagnostic procedures, therapeutic interventions and preventive measures including the use of vaccines are being introduced which involve human subjects. Further, the advent of new medical devices and radio-active materials, and therapeutic benefits of recombinant DNA products have added a new dimension to the ethical issues that need to be considered before evaluating these for their efficacy, utility and safety.

With the ushering in of the era of biotechnology (including genetic engineering) medical procedures and therapeutics have undergone tremendous changes and many techniques based on these advances are no longer in the realm of science fiction, but have become a reality today. Recent advances in the field of assisted reproductive technologies, organ transplantation, human genome analysis and gene therapy 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. On the one hand, there is a need to address legitimate public concern, and on the other, there is a need to appreciate and encourage and not unduly deter new scientific innovations for the benefits of mankind. The new advances in science and medicine are a cause for celebration, at the same time they need careful evaluation of risk benefit. It is imperative that specific guidelines for such research are provided from time to time, taking into consideration all these new and ever changing dimensions. It is, however, to be emphasized that in their very nature and in view of the innate complexity of the subject the guidelines formulated can be neither exhaustive nor static. They need to be updated, consistent with the speed of change in science and technology.

The Indian Council of Medical Research (ICMR) had brought out in February 1980, a document entitled '*Policy statement on ethical considerations involved in research on human subjects*' prepared by the ethics committee under the chairmanship of Honourable Justice Shri H.R. Khanna. This document is being widely used by not only ICMR but also by other government agencies, research institutions and scientists. The document, however, needed to be updated in view of the recent developments in modern biology as also in different branches of medical science so as to add to its contemporary relevance.

The ICMR, therefore, constituted a Central Ethics Committee on Human Research (CECHR) under the chairmanship of Honourable Justice Shri M.N. Venkatachaliah to consider various issues related to the ethical, legal and social dimensions of research involving human subjects. The Committee identified the following major areas for drawing up guidelines:

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(i) Clinical evaluation of drugs/devices/diagnostics/ vaccines/herbal remedies.

(ii) Epidemiological research.

(iii) Human genetics research.

(iv) Transplantation research, including foetal tissue transplantation.

(v) Assisted reproductive technologies.

A draft consultative document was prepared for wide circulation and subsequent regional/national debates before finalisation. The process of public debates highlighted the regional and cultural differences in our country. These guidelines will be updated periodically *pari passu* with the developments in the area of biomedical sciences. It is expected that all institutions in the country which carry out any form of biomedical research involving human beings should follow these guidelines in letter and spirit to protect the safety and well being of all individuals who participate in such research for the progress of science through acquisition of new knowledge.

In the subsequent pages some salient features of the general principles of ethical guidelines for biomedical research on human subjects, are highlighted.

## General Principles in Biomedical Research Involving Human Subjects

Medical and related research using human beings as subjects must ensure that

(i) The purpose of such research is that it should be directed towards the increase of knowledge about the human condition in relation to its social and natural environment, and that such research is for the betterment of all, especially the least advantaged.

(ii) Such research is conducted under conditions that no person or persons become a mere means for the betterment of others and that human beings who are subject to any medical research or scientific experimentation are dealt with in a manner conducive to and consistent with their dignity and well being, under conditions of professional fair treatment and transparency; and after ensuring that the subject is placed at no greater risk other than such risk commensurate with the well being of the subject in question in the light of the object to be achieved.

(iii) Such research must be subjected to a regime of evaluation at all stages of the study and that each such evaluation shall bear in mind the objects to be achieved, the means by which they are sought to be achieved, the anticipated benefits and dangers, the potential uses and abuses of the experiment and its results, and above all, the premium that civilised society places on saving and ensuring the safety of each human life as an end in itself.

Any research using human beings as subjects of medical or scientific research or experimentation should bear in mind the following principles –

(i) **Principles of essentiality.** The research is considered to be absolutely essential after due consideration of all alternatives in the light of existing knowledge in the proposed area of research and after the proposed research has been duly vetted and considered by an appropriate and responsible body of persons who are external to the particular research and who, after careful consideration, come to the conclusion that the research is necessary for the advancement of knowledge and for the benefit of all members of the human species and for the ecological and environmental well being of the planet.

(ii) **Principles of voluntariness, informed consent and community agreement.** The research subjects are fully apprised of the research and the impact and risk of such research on the subject and others; and the subjects retain the right to abstain from further participation in the research irrespective of any legal or other obligation that may have been entered into by such subjects or someone on their behalf, subject to only minimal restitutive obligations of any advance consideration received and outstanding. When such research entails treating any community or group of persons as a research subject, these principles of voluntariness and informed consent shall apply, *mutatis mutandis*, to the community as a whole and to each individual member who is the subject of the research or experiment. Where the subject is incapable of giving consent and it is considered essential that research or experimentation be conducted on such a person incompetent to give consent, the principle of voluntariness and informed consent shall continue to apply and such consent and voluntariness shall be obtained and exercised on behalf of such subjects by someone who is empowered and under a duty to act on their behalf. The principles of informed consent and voluntariness are cardinal principles to be observed throughout the research and experiment, including its aftermath and applied use so that research subjects are continually kept informed of any and all developments in so far as they affect them and others. However, without in any way undermining the cardinal importance of obtaining informed consent from any subject involved in any research, the nature and form of the consent and the evidentiary requirements to prove that such consent was taken, shall depend upon the degree and seriousness of the invasiveness into the concerned subject's person and privacy, health and life generally, and, the overall purpose and the importance of the research.

(iii) **Principles of non-exploitation.** As a general rule, research subjects are remunerated for their involvement in the research or experiment; and, irrespective of the social and economic condition or status, or literacy or educational levels attained by the subjects they are kept fully apprised of all the dangers arising in and out of the research so that they can appreciate all the

(v) **Principles of precaution and risk minimisation.** Due care and caution is taken at all stages of the research and experiment (from inception to its applicative use) to ensure that the subject and those affected by the research are put to the minimum risk, suffer from no irreversible adverse effects and, generally, benefit from and by the research or experiment; and that requisite steps are taken to ensure that both professional and ethical reviews of the research are undertaken at appropriate stages so that further and specific guidelines are laid down, and necessary directions given, in respect of the conduct of the research or experiment.

(vi) **Principles of professional competence.** The research is conducted at all times by competent and qualified persons who act with total integrity and impartiality and who have been made aware of, and are mindful of, the ethical considerations to be borne in mind in respect of such research or experiment.

physical and psychological risks as well as moral implications of the research whether to themselves or others, including those yet to be born. Such subjects should be selected so that the burdens and benefits of the research are distributed without arbitrariness, discrimination or caprice. Each research should include an in-built mechanism for compensation for the human subjects either through insurance cover or any other appropriate means to cover all foreseeable and unforeseeable risks by providing for remedial action and comprehensive after-care, including treatment during and after the research or experiment, in respect of any effect that the conduct of research or experimentation may have on the human subject and to ensure that immediate recompense and rehabilitative measures are taken in respect of all affected, if and when necessary.

(iv) **Principles of privacy and confidentiality.** The identity and records of the subjects of the research or experiment are as far as possible kept confidential; and no details about the identity of these subjects, which would result in the disclosure of their identity, are disclosed without valid scientific and legal reasons which may be essential for the purposes of therapeutics or other interventions, without the specific consent in writing of the subject concerned, or someone authorised on their behalf; and after ensuring that the said subject does not suffer from any form of hardship, discrimination or stigmatisation as a consequence of having participated in the research or experiment.

(vii) **Principles of accountability and transparency.** The research or experiment will be conducted in a fair, honest, impartial and transparent manner after full disclosure is made by those associated with the research or experiment, of each aspect of their interest in the research, and any conflict of interest that may exist; and subject to the principles of privacy and confidentiality and the rights of the researcher, full and complete records of the research inclusive of data and notes are retained for a reasonable period as may be prescribed or considered necessary for the purposes of post-research monitoring, evaluation of the research, conducting further research (whether by the initial researcher or otherwise) and in order to make such records available for scrutiny by the appropriate legal and administrative authority, if necessary.

(viii) **Principles of the maximisation of the public interest and of distributive justice.** The research or experiment and its subsequent applicative use are conducted and used to benefit all human kind and not just those who are socially better off but also the least advantaged; and in particular, the research subject themselves.

(ix) **Principles of institutional arrangements.** It will be the duty of all persons connected with the research to ensure that all the procedures required to be complied with and all institutional arrangements required to be made in respect of the research and its subsequent use or application are duly made in a bonafide and transparent manner; and to take all appropriate steps to ensure that research reports, material and data connected with the research are preserved and archived.

(x) **Principles of public domain.** The research and any further research, experimentation or evaluation in response to, and emanating from such research is brought into the public domain so that its results are generally made known through scientific and other publications subject to such rights as are available to the researcher and those associated with the research under the law in force at that time.

(xi) **Principles of totality of responsibility.** The professional and moral responsibility, for the due observance of all the principles, guidelines or prescriptions laid down generally or in respect of the research or experiment in question, devolves on all those directly or indirectly connected with the research or experiment including the researchers, those responsible for funding or contributing to the funding of the research, the institute(s) where the research is conducted and the various persons, groups or undertakings who sponsor, use or derive benefit from the research, market the product (if any) or prescribe its use so that, inter alia , the effect of the research or experiment is duly monitored and constantly subject to review and remedial action at all stages of the research and experiment and its future use.

(xii) **Principles of compliance.** There is a general and positive duty on all persons, conducting, associated or connected with any research entailing the use of a human subject to ensure that both the letter and the spirit of these guidelines, as well as any other norms, directions and guidelines which have been specifically laid down or prescribed and which are applicable for that area of research or experimentation, are scrupulously observed and duly complied with.

These 12 principles are common to all areas of biomedical research.

### Ethical Review Procedures

It is mandatory that all proposals on biomedical research involving human subjects should be cleared by an appropriately constituted Institutional Ethics Committee (IEC) to safeguard the welfare and the rights of the participants. The Ethics Committee is entrusted not only with the review of the proposed research protocols prior to initiation of the projects but also has a continuing responsibility of regular monitoring for the compliance of the ethics of the approved programmes till the same are completed.

### Basic Responsibilities

The basic responsibility of an IEC is to ensure a competent review of all ethical aspects of the project proposals received and execute the same free from any bias and influence that could affect their objectivity. IECs should provide advice to the researchers on all aspects of the welfare and safety of the research participants after ensuring the scientific soundness of the proposed research through appropriate scientific committees. In smaller institutions the Ethics Committee may take up the dual responsibility of scientific and ethical review. It is advisable to have separate committees for each taking care that the scientific review preceeds the ethical scrutiny.

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

IECs should be multidisciplinary and multisectorial in composition.

The ethic committee should usually have 5 - 8 members. It is generally accepted that a minimum of five persons is required to complete a quorum. There is no specific recommendations 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 a consensus; 12 to 15 is the maximum recommended number.

The Chairperson of the Committee should preferably be from outside the institute and not head the same institute to maintain the independence of the Committee. The Member Secretary who generally belongs to the same institute should conduct the business of the Committee. Other members should be a mix of medical/non-medical, scientific and non-scientific persons including lay public to reflect the differed viewpoints. The composition may be as follows:

Chairperson; 1-2 basic medical scientists; 1-2 clinicians from various institutes; one legal expert or retired judge; one social scientist/representative of non-governmental voluntary agency; one philosopher/ethicist/theologian; one lay person from the community; and the Member Secretary.

There should be adequate representation of age, gender, community, *etc.* in the Committee to safeguard the interests and welfare of all sections of the community/society. Members should be aware of local, social and cultural norms, as this is the most important social control mechanism. If required, subject experts could be invited to offer their views, for example for drug trials a pharmacologist, preferably a clinical pharmacologist, should be included. Similarly, based on the requirement of research area, for example HIV, genetic disorders, *etc.*, specific patient groups may also be represented in the Committee.

### Terms of Reference

The IEC members should be made aware of their role and responsibilities as committee members. Any change in the regulatory requirements should be brought to their attention and they should be kept abreast of all national and international developments in this regard. The Terms of References should also include a statement on Terms of Appointment with reference to the duration of the term of membership, the policy for removal, replacement and resignation procedure ,*etc.* Each committee should have its own operating procedures available with each member.

### Review Procedures

The Ethics Committee should review every research proposal on human subjects. It should ensure that a scientific evaluation has been completed before ethical review is taken up. The Committee should evaluate the possible risks to the subjects with proper justification, the expected benefits and adequacy of documentation for ensuring privacy, confidentiality and justice issues. The ethical review should be done through formal meetings and should not resort to decisions through circulation of proposals.

of existing knowledge; (ii) recent curriculum vitae of the investigators indicating qualification and experience; (iii) subject recruitment procedures; (iv) inclusion and exclusion criteria for entry of subjects in the study; (v) precise description of methodology of the proposed research, including intended dosages of drugs, planned duration of treatment and details of invasive procedures if any; (vi) a description of plans to withdraw or withhold standard therapies in the course of research; (vii) the proposed statistical analysis of the study; (viii) procedure for seeking and obtaining informed consent with sample of patient information sheet and informed consent forms in English and vernacular languages; (ix) safety of proposed intervention and any drug or vaccine to be tested, including results of relevant laboratory and animal research; (x) for research carrying more than minimal risk, an account of plans to provide medical therapy for such risk or injury or toxicity due to overdosage; (xi) proposed compensation and reimbursement of incidental expenses; (xii) storage and maintenance of all data collected during the trial; (xiii) plans for publication of results – positive or negative – while maintaining the privacy and confidentiality of the study participants; (xiv) a statement on probable ethical issues and steps taken to tackle the same; (xv) all other relevant documents related to the study protocol including regulatory clearances; (xvi) agreement to comply with national and international GCP protocols for clinical trials; and (xvii) details of funding agency/sponsors and fund allocation for the proposed work.

### Decision Making Process

The IEC should be able to provide complete and adequate review of the research proposals submitted to them. It should meet at frequent intervals to review new proposals, evaluate annual progress of ongoing ones and assess final reports of all research activities involving human beings through a previously scheduled agenda, amended wherever appropriate.

(i) The decision must be taken by a broad consensus after the quorum requirements are fulfilled to recommend / reject / suggest modification for a repeat review or advice appropriate steps. The Member Secretary should communicate the decision in writing

**Submission of Application**

The researcher should submit an appropriate application in a prescribed format along with the study protocol at least three weeks in advance. The protocol should include the following : (i) Research objectives and rationale for undertaking the investigation in human subjects in the light

(iii) If one of the members has her/his own proposal for review, then the member should not participate when the project is discussed.

(iv) A negative decision should always be supported by clearly defined reasons.

(v) An IEC may decide to reverse its positive decision on a study in the event of receiving information that may adversely affect the benefit / risk ratio.

(vi) The discontinuation of a trial should be ordered if the IEC finds that the goals of the trial have already been achieved midway or unequivocal results are obtained.

(vii) In case of premature termination of a study, notification should include the reasons for termination along with the summary of results till date.

(viii) The following circumstances require the matter to be brought to the attention of IEC: (a) any amendment to the protocol from the originally approved protocol with proper justification; (b) serious and unexpected adverse events and remedial steps taken to tackle them; and (c) any new information that may influence the conduct of the study.

(ix) If necessary, the applicant/investigator may be invited to present the protocol or offer clarifications in the meeting. Representative of the patient groups or interest groups can be invited during deliberations to offer their viewpoint.

(x) Subject experts may be invited to offer their views, but should not take part in the decision making process. However, her / his opinion must be recorded.

(xi) Meetings are to be minuted which should be approved and signed by the Chairperson.

**Interim Review**

Each IEC should decide the special circumstances and the mechanism when an interim review can be resorted to instead of waiting for the scheduled time of the meeting. However, decisions taken should be brought to the notice of the main committee. This can be done for the following reasons : (i) re-examination of a proposal already examined by the IEC; (ii) research study of a minor nature such as examination of case records, *etc.*; and (iii) an urgent proposal of national interest.

Secretary should communicate the decision in writing.

(ii) A member must voluntarily withdraw from the IEC while making a decision on an application which evokes a conflict of interest, which should be indicated in writing to the chairperson prior to the review and should be recorded so in the minutes.

**Record Keeping**

All documentation and communication of an IEC are to be dated, filed and preserved according to written procedures. Strict confidentiality is to be maintained during access and retrieval proceudres.

All records must be safely maintained after the completion/ termination of the study for at least a period of 15 years if it is not possible to maintain the same permanently.

**Special Considerations**

While all the above requirements are applicable to biomedical research as a whole irrespective of the speciality of research, there are certain specific concerns pertaining to specialised areas of research which require additional safe guards/protection and specific considerations for the IEC to take note of. Examples of such instances are research involving children, pregnant and lactating women, vulnerable subjects and those with diminished autonomy besides issues pertaining to commercialisation of research and international collaboration. The observations and suggestions of IEC should be given in writing in unambiguous terms in such instances.

**General Ethical Issues**

All the research involving human subjects should be conducted in accordance with the four basic ethical principles, namely autonomy (respect for person / subject) beneficence, non-maleficence (do no harm) and justice. The guidelines laid down are directed at application of these basic principles to research involving human subjects. The Principal Investigator is the person responsible for not only undertaking research but also for observance of the rights, health and welfare of the subjects recruited for the study. She/he should have qualification and competence in biomedical research methods for proper conduct of the study and should be aware of and comply with the scientific, legal and ethical requirements of the study protocol.

**Informed Consent Process**

**(i) Informed consent of subject :** For all biomedical research involving human subjects, the investigator must obtain the informed consent of the prospective subject or in the case of an individual who is not capable of giving informed consent, the consent of a legal guardian. Informed consent protects the individual's freedom of choice and respect for individual's autonomy.

When the research design involves not more than minimal risk (*eg* where the research involves only collecting data from subject's records) the IEC may waive some of the elements of informed consent.

Waiver of informed consent could also be considered during conditions of emergency. However, this would be permissible only if the IEC has already approved the study or use of drug. However, the patient or the legal guardian should be informed after she/he regains consciousness or is able to understand the study.

**(ii) Obligations of investigators regarding informed consent :** The investigator has the duty to (a) communicate to prospective subjects all the information necessary for informed consent. There should be no restriction to the subject's right to ask any questions related to the study as any restriction would undermine the validity of informed consent. (b) Exclude the possibility of unjustified deception, undue influence and intimidation. Deception of the subject is not permissible. However, sometimes information can be withheld till the completion of the study, if such information would jeopardize the validity of research; (c) Seek consent only after the prospective subject is adequately informed. The investigator should not give any unjustifiable assurances to the prospective subject, which may influence the subject's decision to participate in the study; (d) As a general rule obtain from each prospective subject a signed form as an evidence of informed consent (written informed consent) preferably witnessed by a person not related to the trial, and in case of incompetence to do so, a legal guardian or other duly authorised representative; (e) Renew the informed consent of each subject, if there are material changes in the conditions or procedures of the research or new information becomes available during the ongoing trial; (f) Not use intimidation in any form which invalidates informed consent. The investigator must assure prospective subjects that their decision to participate or not will not affect the patient-clinician relationship or any other benefits to which they are entitled.

**(iii) Essential information for prospective research subjects :** Before requesting an individual's consent to participate in research, the investigator must provide the individual with the following information in the language he or she is able to understand which should not only be scientifically accurate but should also be sensitive to their social and cultural context: (a) the aims and methods of the research; (b) the expected duration of the subject's participation; (c) the benefits that might reasonably be expected as an outcome of research to the subject or to others; (d) any alternative procedures or courses of treatment that might be as advantageous to the subject as the procedure or treatment to which she/ he is being subjected; (e) any foreseeable risk or discomfort to the subject resulting from participation in the study; (f) right to prevent use of his/her biological sample (DNA, cell-line, *etc.*) at any time during the conduct of the research; (g) the extent to which confidentiality of records could be maintained *ie.*, the limits to which the investigator would be able to safeguard confidentiality and the anticipated consequences of breach of confidentiality; (h) responsibility of the investigators; (i) free treatment for research related injury by the investigator/institution; (j) compensation of subjects for disability or death resulting from such research related injury; (k) freedom of individual/family to participate and to withdraw from research any time without penalty or loss of benefits which the subject would otherwise be entitled to; (l) the identity of the research teams and contact persons with address and phone numbers; (m) foreseeable extent of information on possible current and future uses of the biological material and of the data to be generated from the research and if the material is likely to be used for secondary purposes or would be shared with others, clear mention of the same; (n) risk of discovery of biologically sensitive information; (o) publication, if any, including photographs and pedigree charts.

The quality of the consent of certain social groups requires careful consideration as their agreement to volunteer may be unduly influenced by the investigator.

**Compensation for Participation**

Subjects may be paid for the inconvenience and time spent, and should be reimbursed for expenses incurred in connection with their participation in research. They may also receive free medical services. However, payments should not be so large or the medical services so extensive as to induce prospective subjects to consent to participate in research against their better judgement. All payments, reimbursement and medical services to be provided to subjects should be approved by the IEC. Care should be taken (i) when a guardian is asked to give consent on behalf of an incompetent person, no remuneration should be offered except a refund of out of pocket expenses; (ii) when a subject is withdrawn from research for medical reasons related to the study the subject should get the benefit for full participation; and (iii) when a subject withdraws for any other reasons he/ she should be paid in proportion to the amount of participation.

Academic institutions conducting research in alliance with industries/commercial companies require a strong review to probe possible conflicts of interest between scientific responsibilities of researchers and business

research and in case she decides to do so, harm of cessation of breast feeding to the nursing child should be properly assessed except in those studies where breast feeding is harmful to the infant. Pregnant women who desire to undergo medical termination of pregnancy (MTP) could be made subjects for research related to termination of pregnancy. In pregnant women research related to prenatal diagnostic techniques should be limited to detect the foetal abnormalities or genetic disorders and not for sex determination of the foetus.

**(ii) Children:** Before undertaking a trial in children the investigator must ensure that (a) children will not be involved in research that could be carried out equally well with adults; (b) the purpose of the research is to obtain knowledge relevant to health needs of children. For clinical evaluation of a new drug the study in children should always be carried out after the

interests. In cases where the review board committee determines that a conflict of interest may damage the scientific integrity of a project or cause harm to research participants, the board should advise accordingly. Institutes need self-regulatory processes to monitor, prevent and resolve such conflicts of interest. Prospective participants in research should also be informed of the sponsorship of research, so that they can be aware of the potential for conflicts of interest and commercial aspects of the research. Undue inducement through compensation for individual participants, families and populations should be prohibited. This prohibition, however, does not include agreements with individuals, families, groups, communities or populations that foresee technology transfer, local training, joint ventures, provision of health care reimbursement, costs of travel and loss of wages and the possible use of a percentage of any royalties for humanitarian purposes.

**Selection of Special Groups as Research Subjects**

(i) **Pregnant or nursing women:** Pregnant or nursing women should in no circumstances be the subject of any research unless the research carries no more than minimal risk to the foetus or nursing infant and the object of the research is to obtain new knowledge about the foetus, pregnancy and lactation and for which women who are not pregnant or nursing would not be suitable subjects. The justification for participation of these women in clinical trials would be that they should not be deprived arbitrarily of the opportunity to benefit from investigations, drugs, vaccines or other agents that promise therapeutic or preventive benefits. Women should not be encouraged to discontinue nursing for the sake of participation in phase III clinical trials in adults. It can be studied earlier only if the drug has a therapeutic value in a primary disease of the children; (c) a parent or legal guardian of each child has given proxy consent; (d) the assent of the child should be obtained to the extent of the child's capabilities such as in the case of mature minors, adolescents, *etc.*; (e) research should be conducted in settings in which the child and parent can obtain adequate medical and psychological support; (f) interventions intended to provide direct diagnostic, therapeutic or preventive benefit for the individual child subject must be justified in relation to anticipated risks involved in the study and anticipated benefits to society; (g) the child's refusal to participate in research must always be respected unless there is no medically acceptable alternative to the therapy provided/tested, provided the consent has been obtained from parents/ guardian; (h) interventions that are intended to provide therapeutic benefit are likely to be at least as advantageous to the individual child subject as any available alternative interventions; and (i) the risk presented by interventions not intended to benefit the individual child subject is low when compared to the importance of the knowledge that is to be gained.

(iii) **Vulnerable groups :** Effort may 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. It should also be ensrued that research on genetics should not lead to racial inequalities. Individuals who are economically or socially disadvantaged should not be used to benefit those who are better off than them. The rights and welfare of the mentally challenged and mentally differently able persons who are incapable of giving informed consent or those with behavioural disorders must be protected. For studies involving prisoners, students, subordinates, employees, service personnel, *etc.* who have reduced autonomy as research subjects, adequate justification is to be provided.

**Essential Information on Confidentiality for Prospective Research Subjects**

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 a 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.

**Compensation for Accidental Injury**

Research subjects who suffer physical injury as a result of their participation in a study are entitled to financial or other assistance to compensate them equitably for any temporary or permanent impairment or disability. In case of death, their dependents are entitled to material compensation.

The sponsor whether a pharmaceutical company, the government, or an institution, should agree, before the research begins, to provide compensation for any physical or mental injury for which subjects are entitled to compensation or agree to provide insurance coverage for an unforeseen injury whenever possible.

**International Collaboration/Assistance in Biomedical/ Health Research**

Research in biomedical and health areas has been a part of international interaction over the centuries. However, it was only in the second half of the 20th century, especially since 1960s, that the scope of co-operation and collaboration assumed such proportions as to have exploitative connotations with commercial and human dimensions. Different levels of development in terms of infrastructure, expertise, social and cultural perceptions, laws relating to intellectual property rights, *etc.*, necessitate an ethical framework to guide such collaboration. The same concerns are applicable even when there is no formal collaboration between countries, but research is undertaken with the assistance from sponsors in the form of international organisations (Governmental, non-Governmental or others *eg.* WHO, UNICEF, UNAIDS, *etc.*).

*Special Concerns*

(i) Given the magnitude and severity of the health problems in different countries, capacity building to address ethical issues that arise out of collaborative research must be promoted on a priority basis.

(ii) Strategies should be implemented to build capacity in various countries and communities so that they can practise meaningful self-determination in health development, can ensure the scientific and ethical conduct of research, and can function as equal partners with sponsors and others in a collaborative process. Community representatives should be involved in an early and sustained manner in the design, development, implementation, and distribution of results of research.

(iii) Careful consideration should be given to protect the dignity, safety and welfare of the participants when the social contexts of the proposed research can create foreseeable conditions for exploitation of the participants or increase their vulnerability to harm and the steps to be taken to overcome these should be described.

(iv) As different kinds of research (epidemiological studies, clinical trials, product development, behavioural and social science oriented research, *etc.*) have their own particular scientific requirements and specific ethical challenges, the choice of study populations for each type of study should be justified in advance in scientific and ethical terms in all instances, regardless of where the study population is found. Generally, early clinical phases of research, particularly of drugs, vaccines and devices, should be conducted in communities that are less vulnerable to harm or exploitation. However, for valid scientific and public health reasons, if sufficient scientific and ethical safeguards are ensured it may be considered to conduct research in any phase.

(v) The nature, magnitude, and probability of all foreseeable harm resulting from participation in a collaborative research programme should be specified in the research protocol and explained to the participants as fully as can be reasonably done. Moreover, the modalities by which to address these, including provision for the best possible nationally available care to participants who experience adverse reactions to a vaccine or drug under study, compensation for injury related to the research, and referral for psychosocial and legal support if necessary, need to be described.

(vi) The research protocol should outline the benefits that persons / communities / countries participating in such research should experience as a result of their participation. Care should be taken so that these are not presented in a way that unduly influences freedom of choice in participation. The burden and the benefit should be equally borne by the collaborating countries.

(vii) Guidelines, rules, regulations and laws of all countries participating in collaborative research projects should be respected, especially by researchers in the host country and the sponsor country. These could be with reference to intellectual property rights, exchange of biological materials (human, animal, plant or microbial), data transfer, security issues, and issues of socially or politically sensitive nature.

**Researcher's Relations with the Media and Publication Practices**

Researchers have a responsibility to make sure that the public is accurately informed about results without raising false hopes or expectations, or unnecessarily scaring the people. Researchers should take care to avoid talking with journalists or reporters about preliminary findings as seemingly promising research that subsequently cannot be validated could lead to misconcepts if reported prematurely. In such circumstances, retractions most often do not appear in the media. Therefore, it is important to avoid premature reports and publicity stunts.

The investigator's publication plans should not threaten the privacy or confidentiality of subjects, for example publication of pedigrees in the report on research in genetics can result in identification of study participants. It is recommended that a clear consent for publication should be obtained besides the consent for participation in research or treatment and such a consent should preferably be obtained on two different occasions and not at the commencement of the study. Maintenance of confidentiality while publishing data should be taken care of. In case there is need for publication / presentation of photographs/ slides / videos of subject (s), prior consent to do so should be obtained.

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Excerpts from the document entitled "Ethical Guidelines for Biomedical Research on Human Subjects", which is available with the Division of Basic Medical Sciences, ICMR, New Delhi, and at the web site http://www.icmr.nic.in/vsicmr/ethical.pdf.