INDIAN SOCIETY OF ERGONOMICS

Guidance on Ethics

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1.0 BACKGROUND

In February 1980, the Indian Council of Medical Research released a **'Policy Statement on Ethical Considerations involved in Research on Human Subjects'** for the benefit of all those involved in clinical research in India. In 1982, the World Health Organization (WHO) and the CIOMS issued the **'Proposed International Guidelines for Biomedical Research involving Human Subjects.'** Subsequently the CIOMS (Council for International Organizations of Medical Sciences) brought out the **'International Guidelines for Ethical Review in Epidemiological studies'** in 1991 and **'International Ethical Guidelines for Biomedical Research involving Human Subjects'** in 1993. Over the years, various bioethics advisory bodies in national jurisdictions like Nuffield Council of Bioethics and European Commission on Ethics have also laid down general and specific principles in specific areas of scientific research involving human beings as subjects in health research. These codes drawn from the international codes and the universal principles therein provide the 'guidelines' that should be followed in the relevant jurisdictions. **It is emphasized that this is a guidance document, and the actual details and procedures would vary from case to case and must be tailored accordingly.**

2.0 INTRODUCTION

Health and related research using human beings as research participants must necessarily 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, mindful that the human species is one of the many species in a planet in which the well-being of all species is under threat, no less from the human species as any other, 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 health 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 participant is placed at no greater risk other than such risk commensurate with the well-being of the participant in question in the light of the object to the achieved. (iii) Such research must be subjected to a regime of **EVALUATION** at all stages of the proposal i.e., research design and experimentation, declaration of results and use of the results thereof, 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.

3.0 STATEMENT OF GENERAL PRINCIPLES

Any research using the human beings as participants shall follow the principles given below –

3.1 Principles of essentiality
3.2 Principles of voluntariness, informed consent and community agreement
3.3 Principles of non-exploitation
3.4 Principles of privacy and confidentiality
3.5 Principles of precaution and risk
3.6 Principles of professional competence
3.7 Principles of accountability and transparency
3.8 Principles of the maximisation of the public interest and of distributive justice
3.9 Principles of institutional arrangements
3.10 Principles of public domain
3.11 Principles of totality of responsibility
3.12 Principles of compliance

These are detailed as under.

3.1 Principles of essentiality whereby the research entailing the use of human participants is considered to be absolutely essential after a due consideration of all alternatives in the light of the 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 said 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.

3.2 Principles of voluntariness, informed consent and community agreement whereby research participants are fully apprised of the research and the impact and risk of such research on the research participant and others; and whereby the research participants 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 human participants or someone on their behalf, subject to only minimal restitutive obligations of any advance consideration received and outstanding. Where any such research entails treating any community or group of persons as a research participant, 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 participant of the research or experiment. Where the human participant 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 research participants 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 participants 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 human participant 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 human participant's person and privacy, health and life generally, and, the overall purpose and the importance of the research. Ethics committee shall decide on the form of consent to be taken or its waiver based on the degree of risk that may be involved.

3.3 Principles of non-exploitation whereby as a general rule, research participants 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 research participants kept fully apprised of all the dangers arising in and out of the research so that they can appreciate all the physical and psychological risks as well as moral implications of the research whether to themselves or others, including those yet to be born. Such human participants should be selected so that the burdens and benefits of the research are distributed without arbitrariness, discrimination or caprice. Each research shall include an in-built mechanism for compensation for the human participants either through insurance cover or any other appropriate means to cover all foreseeable and unforeseeable risks by providing for remedial action and comprehensive aftercare, 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 participant and to ensure that immediate recompense and rehabilitative measures are taken in respect of all affected, if and when necessary.

3.4 Principles of privacy and confidentiality whereby the identity and records of the human participants of the research or experiment are as far as possible kept confidential; and that no details about identity of said human participants, 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 human participant concerned, or someone authorised on their behalf; and after ensuring that the said human participant does not suffer from any form of hardship, discrimination or stigmatisation as a consequence of having participated in the research or experiment.

3.5 Principles of precaution and risk minimisation whereby due care and caution is taken at all stages of the research and experiment (from its inception as a research idea, its subsequent research design, the conduct of the research or experiment and its applicative use) to ensure that the research participant and those affected by it including community are put to the minimum risk, suffer from no known 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.

3.6 Principles of professional competence whereby 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, preferably through training, the ethical considerations to be borne in mind in respect of such research or experiment.

3.7 Principles of accountability and transparency whereby 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 whereby, 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 such 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.

3.8 Principles of the maximisation of the public interest and of distributive justice whereby 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 participants themselves and or the community from which they are drawn.

3.9 Principles of institutional arrangements whereby there shall be a duty on 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, materials and data connected with the research are duly preserved and archived.

3.10 Principles of public domain whereby 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.

3.11 Principles of totality of responsibility whereby 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 institution or institutions 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.

3.12 Principles of compliance whereby, there is a general and positive duty on all persons, conducting, associated or connected with any research entailing the use of a human participant 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 laid down under Statement on General Principles are common to all areas of biomedical research. The specific issues are mentioned under relevant topics.

4.0 ETHICAL REVIEW PROCEDURES

The need for evaluation of research proposals has been emphasized under the Statement of General Principles at item no. 3.5 pertaining to precaution and risk minimisation. It is mandatory

that all proposals on biomedical research involving human participants should be cleared by an appropriately constituted Institutional Ethics Committee (**IEC**), also referred to as Institutional Review Board (**IRB**), Ethics Review Board (**ERB**) and Research Ethics Board (REB) in other countries, to safeguard the welfare and the rights of the participants. There are also independent ethics committees [**IEC(Ind)**] functioning outside institutions for those researchers who have no institutional attachments or work in institutions with no ethics committee. The Ethics Committees 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 of the approved programmes to foresee the compliance of the ethics during the period of the project. Such an ongoing review shall be in accordance with the international guidelines wherever applicable and the Standard Operating Procedures (**SOP**) of the WHO available at www.who.int

5.0 BASIC RESPONSIBILITIES

The basic responsibility of an Institutional Ethics Committee (IEC) is to ensure a competent review of all ethical aspects of the project proposals received by it in an objective manner. 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 Review Committee. In institutions where this is lacking, the IEC may take up the dual responsibility of review of both, the scientific content and ethical aspects of the proposal. It is advisable to have separate Committees for each, taking care that the scientific review precedes the scrutiny for ethical issues. The scientific evaluation should ensure technical appropriateness of the proposed study. The IECs should specify in writing the authority under which the Committee is established.

5.1 Special situations

Small institutions could form alliance with other IECs or approach registered IEC(ind). Large institutions/Universities with large number of proposals can have more than one suitably constituted IECs for different research areas for which large number of research proposals are submitted. However, the institutional policy should be same for all these IECs to safeguard the research participant's rights. A sub-committee of the main IEC may review proposals submitted by undergraduate or post-graduate students or if necessary, a committee may be separately constituted for the purpose, which will review proposals in the same manner as described above. The responsibilities of an IEC can be defined as follows :-

1. To protect the dignity, rights and well being of the potential research participants.

2. To ensure that universal ethical values and international scientific standards are expressed in terms of local community values and customs.
3. To assist in the development and the education of a research community responsive to local health care requirements.

6.0 COMPOSITION

The IECs should be multidisciplinary and multi-sectorial in composition. Independence and competence are the two hallmarks of an IEC. The number of persons in an ethics committee should be kept fairly small (8-12 members). It is generally accepted that a minimum of five persons is required to form the quorum without which a decision regarding the research should not be taken. The IEC should appoint from among its members a Chairman who should be from outside the Institution and not head of the same Institution to maintain the independence of the Committee. The Member Secretary should be from the same Institution and should conduct the business of the Committee. Other members should be a mix of scientific and non-scientific persons including lay persons to represent the differed points of view. The composition may be as follows:-

1. Chairperson (legal expert or retired judge)
2. One - ~~two~~ one persons from basic health science area
3. One - ~~two~~ one clinicians from various Institutes
4. ~~One legal expert or retired judge~~
5. One social scientist/ representative of non-governmental voluntary agency
6. ~~One philosopher/ ethicist/ theologian~~
7. One lay person from the community
8. Member Secretary

7.0 TERMS OF REFERENCE

The Terms of References should include Terms of Appointment with reference to the duration of the term, the policy for removal, replacement, resignation procedure, frequency of meetings, and payment of processing fee to the IEC for review, honorarium/ consultancy to the members/ invited experts *etc.* and these should be specified in the SOP which should be made available to

each member. Every IEC should have its own written SOPs according to which the Committee should function. The SOPs should be updated periodically based on the changing requirements. The term of appointment of members could be extended for another term and a defined percentage of members could be changed on regular basis. It would be preferable to appoint persons trained in bioethics or persons conversant with ethical guidelines and laws of the country. Substitute member may be nominated if meetings have been continuously missed by a member due to illness or other unforeseen circumstances. For this the criteria for number of missed meetings may be defined in the SOP.

8.0 TRAINING

The EC members should be encouraged to keep abreast of all national and international developments in ethics through orientation courses on related topics by its own members or regular training organized by constituted body(ies), so that they become aware of their role and responsibilities. For drug trial review it is preferable to train the IEC members in Good Clinical Practice. Any change in the regulatory requirements should be brought to their attention and they should be aware of local, social and cultural norms, as this is the most important social control mechanism. .

9.0 TYPES OF REVIEW

The IEC should review every research proposal on human participants before the research is initiated. 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 participants with proper justification, the expected benefits and adequacy of documentation for ensuring privacy, confidentiality and the justice issues. The IEC's member-secretary or secretariat shall screen the proposals for their completeness and depending on the risk involved categorise them into three types, namely, exemption from review, expedited review and full review (see below for explanation). Minimal risk would be defined as one which may be anticipated as harm or discomfort not greater than that encountered in routine daily life activities of general population or during the performance of routine physical or psychological examinations or tests. However, in some cases like surgery, chemotherapy or radiation therapy, great risk would be inherent in the treatment itself, but this may be within the range of minimal risk for the research participant undergoing these interventions since it would be undertaken as part of current everyday life. An investigator cannot decide that her/his protocol falls in the exempted category without approval from the IEC. All proposals will be scrutinised to decide under which of the following three categories it will be considered :

9.1 Exemption from review

Proposals which present less than minimal risk fall under this category as may be seen in following situations: Research on educational practices such as instructional strategies or effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.

Exceptions:

9.1.1 When research on use of educational tests, survey or interview procedures, or observation of public behavior can identify the human participant directly or through identifiers, and the disclosure of information outside research could subject the participant to the risk of civil or criminal or financial liability or psychosocial harm.

9.1.2 When interviews involve direct approach or access to private papers.

9.2 Expedited Review

9.2.1 Minimal Risk

The proposals presenting no more than minimal risk to research participants may be subjected to expedited review. The Member- Secretary and the Chairperson of the IEC or designated member of the Committee or Subcommittee of the IEC may do expedited review only if the protocols involve -

9.2.1.1 Minor deviations from originally approved research during the period of approval (usually of one year duration).

9.2.1.2 Revised proposal previously approved through full review by the IEC or continuing review of approved proposals where there is no additional risk or activity is limited to data analysis.

~~9.2.1.3 Research activities that involve only procedures listed in one or more of the following categories :~~

~~Clinical studies of drugs and medical devices only when -~~

~~9.2.1.3.1 research is on already approved drugs except when studying drug interaction or conducting trial on vulnerable population or~~

~~9.2.1.3.2 adverse Event (AE) or unexpected Adverse Drug Reaction (ADR) of minor nature is reported.~~

9.2.1.4 Research involving clinical materials (data, documents, records, or specimens) that have been collected for non-research (clinical) purposes.

9.2.1.5 When in emergency situations like serious outbreaks or disasters a full review of the research is not possible, prior written permission of IEC may be taken before use of the test intervention. Such research can only be approved for pilot study or preliminary work to study the safety and efficacy of the intervention and **the same participants should not be included** in the clinical trial that may be initiated later based on the findings of the pilot study. ~~a. Research on interventions in emergency situation When proven prophylactic, diagnostic, and therapeutic methods do not exist or have been ineffective, physicians may use new intervention as investigational drug (IND) / devices/ vaccine to provide emergency health care to their patients in life threatening conditions.~~ Research in such instance of health care could be allowed in patients –

9.2.1.5.1 when consent of person/ patient/ responsible relative or custodian/ team of designated doctors for such an event is not possible. However, information about the intervention should be given to the relative/ legal guardian when available later;

9.2.1.5.2 when the intervention has undergone testing for safety prior to its use in emergency situations and sponsor has obtained prior approval of DCGI;

9.2.1.5.3 only if the local IEC reviews the protocol since institutional responsibility is of paramount importance in such instances.

9.2.1.5.4 if Data Safety Monitoring Board (DSMB) is constituted to review the data.

9.2.2 Research on disaster management

A disaster is the sudden occurrence of a calamitous event at any time resulting in substantial material damage, affecting persons, society, community or state(s). It may be periodic, caused by both nature and humans and creates an imbalance between the capacity and resources of the society and the needs of the survivors or the people whose lives are threatened, over a given period of time. It may also be unethical sometimes not to do research in such circumstances. Disasters create vulnerable persons and groups in society, particularly so in disadvantaged communities, and therefore, the following points need to be considered when reviewing such research:

9.2.2.1 Research planned to be conducted after a disaster should be essential culturally sensitive and specific in nature with possible application in future disaster situations.

9.2.2.2 Disaster-affected community participation before and during the research is essential and its representative or advocate must be identified.

9.2.2.3 Extra care must be taken to protect the privacy and confidentiality of participants and communities.

9.2.2.4 Protection must be ensured so that only minimal additional risk is imposed.

9.2.2.5 The research undertaken should provide direct or indirect benefits to the participants, the disaster-affected community or future disaster- affected population and *a priori* agreement should be reached on this, whenever possible, between the community and the researcher.

9.2.2.6 All international collaborative research in the disaster-affected area should be done with a local partner on equal partnership basis.

9.2.2.7 Transfer of biological material, if any, should be as per Government rules taking care of intellectual property rights issues.

9.3 Full Review

All research presenting with more than minimal risk, proposals/ protocols which do not qualify for exempted or expedited review and projects that involve vulnerable population and special groups shall be subjected to full review by all the members. While reviewing the proposals, the following situations may be carefully assessed against the existing facilities at the research site for risk/benefit analysis:

9.3.1 Collection of blood samples by finger prick, heel prick, ear prick, or venipuncture:

9.3.1.1 from healthy adults and non-pregnant women who weigh normal for their age and not more than 500 ml (not correct; minimal quantity, as may be required for the test procedure or estimation) blood is drawn in an 8 week period and frequency of collection is not more than 2 times per week;

9.3.1.2 from other adults and children, where the age, weight, and health of the participants, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected has been considered and not more than 50 ml or 3 ml per kg, (Aninda, please see how we can avoid this contagious issue) whichever is lesser is drawn in an 8 week period and not more than 2 times per week;

9.3.1.3 prospective collection of biological specimens for research purposes by noninvasive means.

9.3.2 Collection of data through noninvasive procedures routinely employed in clinical practice:

Where medical devices, procedures, methods and practices are employed, they must be cleared/ approved for marketing, implementation or use, for instance -

9.3.2.1 physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the participant or an invasion of the participant's privacy;

9.3.2.2 weighing or testing sensory acuity;

9.3.2.3 magnetic resonance imaging;

9.3.2.4 electrocardiography, echocardiography; electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow,

9.3.2.5 moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.

9.3.3 Research involving clinical materials

Such as data, documents, records, or specimens that will be collected solely for non-research purposes.

9.3.4 Collection of multi-media data

Such as from voice, video, digital, or image recordings made for research purposes.

9.3.5 Research on individual or group characteristics or behavior

not limited to research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies.

10.0 SUBMISSION OF APPLICATION

The researcher should submit an application in a prescribed format along with the study protocol as prescribed in SOP of IEC concerned. The protocol should include the following:

10.1 The title with signature of Principal Investigator (PI) and Coinvestigators as attestation for conducting the study.

10.2 Clear research objectives and rationale for undertaking the investigation in human participants in the light of existing knowledge.

10.3 Recent curriculum vitae of the Investigators indicating qualification and experience.

10.4 Participant recruitment procedures and brochures, if any.

10.5 Inclusion and exclusion criteria for entry of participants.

10.6 Precise description of methodology of the proposed research, including sample size (with justification), type of study design (observational, **experimental, pilot, randomized, blinded** *etc.*), intended intervention, dosages of drugs, route of administration, duration of treatment and details of invasive procedures if any.

10.7 Plan to withdraw or withhold standard therapies in the course of research.

10.8 Plan for statistical analysis of the study.

10.9 Procedure for seeking and obtaining informed consent with sample of patient information sheet and informed consent forms in English and local languages.

10.10 Safety of proposed intervention and any drug or vaccine to be tested, including results of relevant laboratory, animal and human research.

10.11 For research involving more than minimal risk, an account of management of such risk or injury.

10.12 Proposed compensation and reimbursement of incidental expenses and management of research related and unrelated injury/ illness during and after research period.

10.13 An account of storage and maintenance of all data collected during the trial.

10.14 Plans for publication of results - positive or negative - while maintaining the privacy and confidentiality of the study participants.

10.15 A statement on probable ethical issues and steps taken to tackle the same like justification for washout of standard drug, or the use of placebo control.

10.16 All other relevant documents related to the study protocol like investigator's brochure for trial on drugs/ devices/ vaccines/ herbal remedies and statement of relevant regulatory clearances.

10.17 Agreement to comply with national and international Good Clinical Practices (GCP) protocols for clinical trials.

10.18 Details of Funding agency/ Sponsors and fund allocation.

10.19 For international collaborative study details about foreign collaborators and documents for review of Health Ministry's Screening Committee (HMSC) or appropriate Committees under other agencies/ authority like Drug Controller General of India (DCGI)

10.20 For exchange of biological material in international collaborative study a MoU/ Material Transfer Agreement between the collaborating partners.

10.21 A statement on conflict-of-interest (COI), if any.

11.0 DECISION MAKING PROCESS

The IEC should be able to provide complete and adequate review of the research proposals submitted to them. It should meet periodically at frequent intervals to review new proposals, evaluate annual progress of ongoing ones, review serious adverse event (SAE) reports and assess final reports of all research activities involving human beings through a previously scheduled agenda, amended wherever appropriate. The following points should be considered while doing so:

11.1 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 to the PI.

11.2 If a member has conflict-of-interest (COI) involving a project then s/he should submit this in writing to the chairperson before the review meeting, and it should also be recorded in the minutes.,

11.3 If one of the members has her/his own proposal for review or has any COI then s/he should withdraw from the IEC while the project is being discussed

11.4 A negative decision should always be supported by clearly defined reason

11.5 An IEC may decide to reverse its positive decision on a study if it receives information that may adversely affect the risk/ benefit ratio.

11.6 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.

11.7 In case of premature termination of study, notification should include the reasons for termination along with the summary of results conducted till date.

11.8 The following circumstances require the matter to be brought to the attention of IEC:

11.8.1 any amendment to the protocol from the originally approved protocol with proper justification;

11.8.2 serious and unexpected adverse events and remedial steps taken to tackle them;

11.8.3 any new information that may influence the conduct of the study.

11.9 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.

11.10 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.

11.11 Meetings are to be minuted which should be approved and signed by the Chairperson/ alternate Chairperson/ designated member of the committee.

12.0 REVIEW PROCESS

The method of review should be stated in the SOP whether the review should be done by all reviewers or by primary reviewer(s) in which case a brief summary of the project with informed consent and patient information sheet, advertisements or brochures, if any, should be circulated to all the other members.

The ethical review should be done in formal meetings and EC should not take decisions through circulation of proposals. The committee should meet at regular intervals and should not keep a decision pending for more than 3 - 6 months, which may be defined in the SOP.

12.1 PERIODIC REVIEW

The ongoing research may be reviewed at regular intervals of six months to one year as may be specified in the SOP of the ethics committee.

12.2 CONTINUING REVIEW

The IEC has the responsibility to continue reviewing approved projects for continuation, new information, adverse event monitoring, follow-up and later after completion if need be.

12.3 INTERIM REVIEW

Each IEC should decide the special circumstances and the mechanism when an interim review can be resorted to by a sub-committee instead of waiting for the scheduled time of the meeting like re-examination of a proposal already examined by the IEC or any other matter which should be brought to the attention of the IEC. However, decisions taken should be brought to the notice of the main committee.

13.0 MONITORING

Once IEC gives a certificate of approval it is the duty of the IEC to monitor the approved studies, therefore an oversight mechanism should be in place. Actual site visits can be made especially in the event of reporting of adverse events or violations of human rights. Additionally, periodic status reports must be asked for at appropriate intervals based on the safety concerns and this should be specified in the SOP of the IEC. SAE reports from the site as well as other sites are reviewed by EC and appropriate action taken when required. In case the IEC desires so, reports of monitoring done by the sponsor and the recommendations of the DSMB may also be sought.

14.0 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 procedures. The following records should be maintained for the following:

14.1 the Constitution and composition of the IEC;

14.2 signed and dated copies of the latest the curriculum vitae of all IEC members with records of training if any;

14.3 standing operating procedures of the IEC;

14.4 national and International guidelines;

14.5 copies of protocols submitted for review;

14.6 all correspondence with IEC members and investigators regarding application, decision and follow up;

14.7 agenda of all IEC meetings;

14.8 minutes of all IEC meetings with signature of the Chairperson;

14.9 copies of decisions communicated to the applicants;

14.10 record of all notification issued for premature termination of a study with a summary of the reasons;

14.11 final report of the study including microfilms, CDs and video recordings.

It is recommended that all records must be safely maintained after the completion/ termination of the study for a period of 3 years if it is not possible to maintain the same for more than that due to resource crunch and lack of infrastructure.

15.0 SPECIAL CONSIDERATIONS

While all the above requirements are applicable to biomedical research as a whole irrespective of the specialty of research, there are certain specific concerns pertaining to specialized 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 participants and those with diminished autonomy besides issues pertaining to commercialization of research and international collaboration. The observations and suggestions of IEC should be given in writing in unambiguous terms in such instances.

Non-maleficence (do no harm) and justice. The guidelines laid down are directed at application of these basic principles to research involving human participants. The Principal Investigator is the person responsible for not only undertaking research but also for observance of the rights, health and welfare of the participants recruited for the study. S/he should have qualification and competence in biomedical research methodology for proper conduct of the study and should be aware of and comply with the scientific, legal and ethical requirements of the study protocol.

15.1 INFORMED CONSENT PROCESS

15.1.1 Informed Consent of Participants : For all biomedical research involving human participants, the investigator must obtain the informed consent of the prospective participant 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 and is given voluntarily to participate in research or not. Adequate information about the research is given in a simple and easily understandable unambiguous language in a document known as the **Informed Consent Form with Participant/ Patient Information Sheet**. The latter should have following components as may be applicable:

15.1.1.1 Nature and purpose of study stating it as research

15.1.1.2 Duration of participation with number of participants

15.1.1.3 Procedures to be followed

15.1.1.4 Investigations, if any, to be performed

15.1.1.5 Foreseeable risks and discomforts adequately described and whether project involves more than minimal risk

15.1.1.6 Benefits to participant, community or health profession as may be applicable

15.1.1.7 Policy on compensation

15.1.1.8 Availability of medical treatment for such injuries or risk management

15.1.1.9 Alternative treatments if available

15.1.1.10 Steps taken for ensuring confidentiality

15.1.1.11 No loss of benefits on withdrawal

15.1.1.12 Benefit sharing in the event of commercialization

15.1.1.13 Contact details of PI or local PI/Co-PI in multi-centric studies for asking more information related to the research or in case of injury

15.1.1.14 Contact details of Chairman of the IEC for appeal against violation of rights

15.1.1.15 Voluntary participation

15.1.1.16 If test for genetics and HIV is to be done, counseling for consent for testing must be given as per national guidelines

15.1.1.17 Storage period of biological sample and related data with choice offered to participant regarding future use of sample, refusal for storage and receipt of its results

A copy of the participant/patient information sheet should be given to the participant for her/ his record. The informed consent should be brief in content highlighting that it is given of free will or voluntarily after understanding the implications of risks and benefits and s/he could withdraw without loss of routine care benefits. Assurance is given that confidentiality would be maintained and all the investigations/ interventions would be carried out only after consent is obtained.

When the written consent as signature or thumb impression is not possible due to sensitive nature of the project or the participant is unable to write, then verbal consent can be taken after ensuring its documentation by an unrelated witness. In some cases an ombudsman (a third party) can ensure total accountability for the process of obtaining the consent. Audio-visual methods could be adopted with prior consent and adequate precaution to ensure confidentiality, but approval of EC is required for such procedures. For drug trials, if the volunteer can give only thumb impression then another thumb impression by the relative or legal custodian cannot be accepted and an unrelated witness to the project should then sign.

15.1.2 Fresh or re-consent is taken in following conditions :

15.1.2.1 Availability of new information which would necessitate deviation of protocol.

15.1.2.2 When a research participant regains consciousness from unconscious state or is mentally competent to understand the study. If such an event is expected then procedures to address it should be spelt out in the informed consent form.

15.1.2.3 When long term follow-up or study extension is planned later.

15.1.2.4 When there is change in treatment modality, procedures, site visits.

15.1.2.5 Before publication if there is possibility of disclosure of identity through data presentation or photographs (which should be camouflaged adequately).

15.1.3 Obligations of investigators regarding informed consent : The investigator has the duty to -

15.1.3.1 communicate to prospective participants all the information necessary for informed consent. Any restriction on participant's right to ask any questions related to the study will undermine the validity of informed consent;

15.1.3.2 exclude the possibility of unjustified deception, undue influence and intimidation. Although deception is not permissible, if sometimes such information would jeopardize the validity of research it can be withheld till the completion of the project, for instance, study on abortion practices;

15.1.3.3 seek consent only after the prospective participant is adequately informed. The investigator should not give any unjustifiable assurances to prospective participant, which may influence the her/his decision to participate;

15.1.3.4 obtain from each prospective participant 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 the participant is not competent to do so, a legal guardian or other duly authorised representative;

15.1.3.5 take verbal consent when the participant refuses to sign or give thumb impression or cannot do so. This can then be documented through audio or video means;

15.1.3.6 take surrogate consent from the authorized relative or legal custodian or the institutional head in the case of abandoned institutionalized individuals or wards under judicial custody;

15.1.3.7 renew or take fresh informed consent of each participant under circumstances described earlier in this chapter;

15.1.3.8 if participant loses consciousness or competence to consent during the research period as in Alzeimer or psychiatric conditions, surrogate consent may be taken from the authorized person or legal custodian.

15.1.3.9 the investigator must assure prospective participants that their decision to participate or not will not affect the patient - clinician relationship or any other benefits to which they are entitled.

15.1.4 Essential information for prospective research participants: Before requesting an individual's consent to participate in research, the investigator must provide the individual with the following information in the language she or he is able to understand which should not only be scientifically accurate but should also be sensitive/ adaptive to their social and cultural context:

15.1.4.1 the aims and methods of the research;

15.1.4.2 the expected duration of the participation;

15.1.4.5 the benefits that might reasonably be expected as an outcome of research to the participant or community or to others;

15.1.4.4 any alternative procedures or courses of treatment that might be as advantageous to the participant as the procedure or treatment to which s/he is being subjected;

15.1.4.5 any foreseeable risk or discomfort to the participant resulting from participation in the study;

15.1.4.6 right to prevent use of her/ his biological sample (DNA, cell-line, etc.) at any time during the conduct of the research;

15.1.4.7 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;

15.1.4.8 responsibility of investigators;

15.1.4.9 free treatment for research related injury by the investigator and/ institution and sponsor(s);

15.1.4.10 compensation of participants for disability or death resulting from such injury;

15.1.4.11 insurance coverage if any, for research related or other AEs;

15.1.4.12 freedom of individual / family to participate and to withdraw from research any time without penalty or loss of benefits which the participant would otherwise be entitled to;

15.1.4.13 the identity of the research teams and contact persons with address and phone numbers;

15.1.4.14 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;

15.1.4.15 risk of discovery of biologically sensitive information and provision to safeguard confidentiality;

15.1.4.16 publication, if any, including photographs and pedigree charts. The quality of the consent of certain social and marginalized groups requires careful consideration as their agreement to volunteer may be unduly influenced by the Investigator.

15.2 COMPENSATION FOR PARTICIPATION

Participants 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 health services. When this is reasonable then it cannot be termed as benefit. During the period of research if the participant requires treatment for complaints other than the one being studied necessary **free ancillary care** or appropriate referrals may be provided. However, payments should not be so large or the health services so extensive as to make prospective participants consent readily to enroll in research against their better judgment, which would then be treated as undue inducement. All payments, reimbursement and health services to be provided to research participants should be approved by the IEC.

Care should be taken :

15.2.1 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;

15.2.2 when a participant is withdrawn from research for health reasons related to the study the participant should get the benefit for full participation;

15.2.3 when a participant withdraws for any other reasons s/he should be paid an amount proportionate to the amount of participation.

15.3 CONFLICT OF INTEREST

A set of conditions in which professional judgment concerning a primary interest like patient's welfare or the validity of research tends to be or appears to be unduly influenced by a secondary interest like non-financial (personal, academic or political) or financial gain is termed as Conflict of Interest (COI).

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/ committee should advise accordingly. Significant financial interest means anything of monetary value that would reasonably appear to be a significant consequence of such research including salary or other payments for services like consulting fees or honorarium per participant; equity interests in stocks, stock options or other ownership interests; and intellectual property rights from

patents, copyrights and royalties from such rights. The investigators should declare such conflicts of interest in the application submitted to IEC for review. Institutions and IECs need self-regulatory processes to monitor, prevent and resolve such conflicts of interest. The IEC can determine the conditions for management of such conflicts in its SOP manual. 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. Those who have also to be informed of the secondary interest in financial terms should include the institution, IEC, audience when presenting papers and should be mentioned when publishing in popular media or scientific journals.

15.4 SELECTION OF SPECIAL GROUPS AS RESEARCH PARTICIPANTS

15.4.1 Pregnant or nursing women: Pregnant or nursing women should in no circumstances be the participant of any research unless the research carries no more than minimal risk to the fetus or nursing infant and the object of the research is to obtain new knowledge about the foetus, pregnancy and lactation. As a general rule, pregnant or nursing women should not be participants of any clinical trial 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 participants.

15.4.2 Children: Before undertaking trial in children the investigator must ensure that -

15.4.2.1 children will not be involved in research that could be carried out equally well with adults;

15.4.2.2 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 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;

15.4.2.3 a parent or legal guardian of each child has given proxy consent;

15.4.2.4 the assent of the child should be obtained to the extent of the child's capabilities such as in the case of mature minors from the age of seven years up to the age of 18 years.;

15.4.2.5 research should be conducted in settings in which the child and parent can obtain adequate health and psychological support;

15.4.2.6 interventions intended to provide direct diagnostic, therapeutic or preventive benefit for the individual child participant must be justified in relation to anticipated risks involved in the study and anticipated benefits to society;

15.4.2.7 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;

15.4.2.8 interventions that are intended to provide therapeutic benefit are likely to be at least as advantageous to the individual child participant as any available alternative interventions;

15.4.2.9 the risk presented by interventions not intended to benefit the individual child participant is low when compared to the importance of the knowledge that is to be gained.

15.4.3 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.

15.4.3.1 research on genetics should not lead to **racial inequalities**;

15.4.3.2 persons who are **economically or socially disadvantaged** should not be used to benefit those who are better off than them;

15.4.3.3 rights and welfare of **mentally challenged and mentally differently able persons** who are incapable of giving informed consent or those with behavioral disorders must be protected. Appropriate proxy consent from the legal guardian should be taken after the person is well informed about the study, need for participation, risks and benefits involved and the privacy and confidentiality procedures. The entire consent process should be properly documented;

15.4.3.4 adequate justification is required for the involvement of participants such as prisoners, students, subordinates, employees, service personnel etc. who have **reduced autonomy** as research participants, since the consent provided may be under duress or various other compelling reasons.

15.5 ESSENTIAL INFORMATION ON CONFIDENTIALITY FOR PROSPECTIVE RESEARCH PARTICIPANTS

Safeguarding confidentiality - The investigator must safeguard the confidentiality of research data, which might lead to the identification of the individual participants. Data of individual participants can be disclosed under the following circumstances :

15.5.1 only in a court of law under the orders of the presiding judge or

15.5.2 there is threat to a person's life or

15.5.3 in cases of severe adverse reaction may be required to communicate to drug registration authority or

15.5.4 if there is risk to public health it takes precedence over personal right to privacy and may have to be communicated to health authority.

Therefore, the limitations in maintaining the confidentiality of data should be anticipated and assessed and communicated to appropriate individuals or authorities as the case may be.

15.6 COMPENSATION FOR ACCIDENTAL INJURY

Research participants who suffer physical injury as a result of their participation 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.

15.7 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. It should also not unnecessarily scare 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 or could lead to misconceptions if reported prematurely. Or, the results of research may be reported in such a way that it would seem that the human application is round the corner, only to be told later by the researchers that considerable time has to pass before these findings can be translated into tools for human use. In such circumstances, retractions most often do not appear in the media. Therefore, it is important to avoid premature reports and publicity stunts. The best safeguard against inaccurate reporting is for the researcher to talk to media on condition that the reporter submit a full written, rather than oral version, of what will be reported, so that it enables the researcher to make necessary corrections, if needed, prior to publication. Investigator's publication plans should not threaten the privacy or confidentiality of participants, 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 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 as a blanket one 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 participant (s), prior

consent to do so should be obtained. Identification features should be appropriately camouflaged. The same safeguard should be observed for video coverage.

With regard to authorship, the International Committee of Medical Journal Editors (ICJME) has laid down criteria based on credit and accountability. Only those who make substantial contribution to the article and take responsibility for the published matter can be co-authors.

Plagiarism constitutes representing the work of another person, in whole or in part, as one's own. Conceptual or paraphrased material from another person or source should be acknowledged through citation, and exact wording should be indicated by quotation marks.

Plagiarism or falsification of data and authorship are important ethical issues in publications. The term 'misconduct in research' means fabrication, falsification, plagiarism, selective omission of data and claiming that some data are missing, ignoring outliers without declaring it, not reporting data on side effects/ adverse reactions in a clinical trial, publication of post-hoc analysis without declaring it, gift authorship, not citing others' work, not disclosing conflict of interest, redundant publication, and failure to adequately review existing research.

BIBLIOGRAPHY

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