

GENERAL ETHICAL ISSUES

2.0 All research involving human participants should be conducted in accordance with the basic and general ethical principles as outlined in section 1. The researcher and the team are responsible for protecting the dignity, rights, safety and well-being of the participants enrolled in the study. They should have the appropriate qualifications and competence in research methodology and should be aware of and comply with the scientific, medical, ethical, legal and social requirements of the research proposal. The ECs are responsible for ensuring that the research is conducted in accordance with the aforementioned principles.

2.1 Benefit-risk assessment

Benefits to the individual, community or society refer to any sort of favourable outcome of the research, whether direct or indirect. The social and scientific value of research should justify the risk, which is the probability of causing discomfort or harm anticipated as physical, psychological, social, economic or legal.

2.1.1 The researcher, sponsor and EC should attempt to maximize benefits and minimize risks to participants so that risks are balanced to lead to potential benefits at individual, societal and/or community levels.

2.1.2 The EC should assess the inherent benefits and risks, ensure a favourable balance of benefits and risks, evaluate plans for minimizing the risk and discomfort and decide on the merit of the research before approving it.

2.1.3 The EC should also assess any altered risks in the study at the time of continuing review.

2.1.4 The type of EC review based on risk involved in the research, is categorized as given in Table 2.1. Also see Table 4.2 for further details.

2.2 Informed consent process

Informed consent protects the individual's autonomy to freely choose whether or not to participate in the research. The process involves three components – providing relevant information to potential participants, ensuring the information is comprehended by them and assuring voluntariness of participation. Informed consent should explain medical terminology in simple terms and be in a language that the participant understands.

Table 2.1 Categories of Risk

Type of risk	Definition/description
Less than minimal risk	Probability of harm or discomfort anticipated in the research is nil or not expected. For example, research on anonymous or non-identified data/samples, data available in the public domain, meta-analysis, etc.
Minimal risk	Probability of harm or discomfort anticipated in the research is not greater than that ordinarily encountered in routine daily life activities of an average healthy individual or general population or during the performance of routine tests where occurrence of serious harm or an adverse event (AE) is unlikely. Examples include research involving routine questioning or history taking, observing, physical examination, chest X-ray, obtaining body fluids without invasive intervention, such as hair, saliva or urine samples, etc.
Minor increase over minimal risk or Low risk	Increment in probability of harm or discomfort is only a little more than the minimal risk threshold. This may present in situations such as routine research on children and adolescents; research on persons incapable of giving consent; delaying or withholding a proven intervention or standard of care in a control or placebo group during randomized trials; use of minimally invasive procedures that might cause no more than brief pain or tenderness, small bruises or scars, or very slight, temporary distress, such as drawing a small sample of blood for testing; trying a new diagnostic technique in pregnant and breastfeeding women, etc. Such research should have a social value. Use of personal identifiable data in research also imposes indirect risks. Social risks, psychological harm and discomfort may also fall in this category.
More than minimal risk or High risk	Probability of harm or discomfort anticipated in the research is invasive and greater than minimal risk. Examples include research involving any interventional study using a drug, device or invasive procedure such as lumbar puncture, lung or liver biopsy, endoscopic procedure, intravenous sedation for diagnostic procedures, etc.

2.2.1 The informed consent document (ICD), which includes patient/participant information sheet (PIS) and informed consent form (ICF) should have the required elements (see Box 5.1 for further details) and should be reviewed and approved by the EC before enrolment of participants. For all biomedical and health research involving human participants, it is the primary responsibility of the researcher to obtain the written, informed consent of the prospective participant or legally acceptable/authorized representative (LAR). In case of an individual who is not capable of giving informed consent, the consent of the LAR should be obtained. If a participant or LAR is illiterate, a literate impartial witness should also be present during the informed consent process.

- 2.2.2 In certain circumstances audio/audio-visual recording of the informed consent process may be required, for example in certain clinical trials as notified by CDSCO.
- 2.2.3 Verbal/oral consent/waiver of consent/re-consent may be obtained under certain conditions after due consideration and approval by the EC. See section 5 for further details.

2.3 Privacy and confidentiality

Privacy is the right of an individual to control or influence the information that can be collected and stored and by whom and to whom that information may be disclosed or shared. Confidentiality is the obligation of the researcher/research team/organization to the participant to safeguard the entrusted information. It includes the obligation to protect information from unauthorized access, use, disclosure, modification, loss or theft.

- 2.3.1 The researcher should safeguard the confidentiality of research related data of participants and the community.
- 2.3.2 Potential limitations to ensure strict confidentiality must be explained to the participant. Researchers must inform prospective participants that although every effort will be made to protect privacy and ensure confidentiality, it may not be possible to do so under certain circumstances.
- 2.3.3 Any publication arising out of research should uphold the privacy of the individuals by ensuring that photographs or other information that may reveal the individual's identity are not published. A specific re-consent would be required for publication, if this was not previously obtained.
- 2.3.4 Some information may be sensitive and should be protected to avoid stigmatization and/or discrimination (for example, HIV status; sexual orientation such as lesbian, gay, bisexual, and transgender (LGBT); genetic information; or any other sensitive information).
- 2.3.5 While conducting research with stored biological samples or medical records/data, coding or anonymization of personal information is important and access to both samples and records should be limited. See section 11 for further details.
- 2.3.6 Data of individual participants/community may be disclosed in certain circumstances with the permission of the EC such as specific orders of a court of law, threat to a person's or community's life, public health risk that would supersede personal rights to privacy, serious adverse events (SAEs) that are required to be communicated to an appropriate regulatory authority etc.

2.4 Distributive justice

- 2.4.1 Efforts must be made to ensure that individuals or communities invited for research are selected in such a way that the benefits and burdens of research are equitably distributed.
- 2.4.2 Vulnerable individuals/groups should not be included in research to solely benefit others who are better-off than themselves.
- 2.4.3 Research should not lead to social, racial or ethnic inequalities.
- 2.4.4 Plans for direct or indirect benefit sharing in all types of research with participants, donors of biological materials or data should be included in the study, especially if there is a potential for commercialization. This should be decided a priori in consultation with the stakeholders and reviewed by the EC.

2.5 Payment for participation

- 2.5.1 If applicable, participants may be reimbursed for expenses incurred relating to their participation in research, such as travel related expenses. Participants may also be paid for inconvenience incurred, time spent and other incidental expenses in either cash or kind or both as deemed necessary (for example, loss of wages and food supplies).
- 2.5.2 Participants should not be made to pay for any expenses incurred beyond routine clinical care and which are research related including investigations, patient work up, any interventions or associated treatment. This is applicable to all participants, including those in comparator/control groups.
- 2.5.3 If there are provisions, participants may also receive additional medical services at no cost.
- 2.5.4 When the LAR is giving consent on behalf of a participant, payment should not become an undue inducement and to be reviewed carefully by the EC. Reimbursement may be offered for travel and other incidental expenses incurred due to participation of the child/ward in the research.
- 2.5.5 ECs must review and approve the payments (in cash or kind or both) and free services and the processes involved, and also determine that this does not amount to undue inducement.

2.6 Compensation for research-related harm

Research participants who suffer direct physical, psychological, social, legal or economic harm as a result of their participation are entitled, after due assessment, to financial or other assistance to compensate them equitably for any temporary or permanent impairment or disability. In case of death, participant's dependents are entitled to

financial compensation. The research proposal should have an in-built provision for mitigating research related harm.

- 2.6.1 The researcher is responsible for reporting all SAEs to the EC within 24 hours of knowledge. Reporting of SAE may be done through email or fax communication (including on non-working days). A report on how the SAE was related to the research must also be submitted within 14 days.
- 2.6.2 The EC is responsible for reviewing the relatedness of the SAE to the research, as reported by the researcher, and determining the quantum and type of assistance to be provided to the participants.
- For clinical trials under the purview of CDSCO, the timeline and procedures as notified from time to time may be followed.
 - All research participants who suffer harm, whether related or not, should be offered appropriate medical care, psycho-social support, referrals, clinical facilities, etc.
 - Medical management should be free if the harm is related to the research.
 - Compensation should be given to any participant when the injury is related to the research. This is applicable to participants in any of the arms of research, such as intervention, control and standard of care.
 - While deliberating on the quantum of compensation to be awarded to participants who have suffered research-related injury, the EC should consider aspects including the type of research (interventional, observational, etc.), extent of injury (temporary/permanent, short/long term), loss of wages, etc.
 - For other sponsored research, it is the responsibility of the sponsor (whether a pharmaceutical company, government or non-governmental organization (NGO), national or international/bilateral/multilateral donor agency/institution) to include insurance coverage or provision for possible compensation for research related injury or harm within the budget.
- 2.6.3 All AEs should be recorded and reported to the EC according to a pre-planned timetable, depending on the level of risk and as recommended by the EC.
- 2.6.4 In investigator initiated research/student research, the investigator/institution where the research is conducted becomes the sponsor.
- It is the responsibility of the host institution to provide compensation and/or cover for insurance for research related injury or harm to be paid as decided by the EC.

- The institution should create in-built mechanism to be able to provide for compensation, such as a corpus fund in the institution.
- In the applications for research grants to funding agencies – national or international, government or non-government agencies – the researcher should keep a budgetary provision for insurance coverage and/or compensation depending upon the type of research, anticipated risks and proposed number of participants.

2.7 Ancillary care

2.7.1 Participants may be offered free medical care for non-research-related conditions or incidental findings if these occur during the course of participation in the research, provided such compensation does not amount to undue inducement as determined by the EC.

2.8 Conflict of interest

Conflict of interest (COI) is a set of conditions where professional judgement concerning a primary interest such as participants welfare or the validity of research tends to be unduly influenced by a secondary interest, financial or non-financial (personal, academic or political). COI can be at the level of researchers, EC members, institutions or sponsors. If COI is inherent in the research, it is important to declare this at the outset and establish appropriate mechanisms to manage it.

2.8.1 Research institutions must develop and implement policies and procedures to identify, mitigate conflicts of interest and educate their staff about such conflicts.

2.8.2 Researchers must ensure that the documents submitted to the EC include a disclosure of interests that may affect the research.

2.8.3 ECs must evaluate each study in light of any disclosed interests and ensure that appropriate means of mitigation are taken.

2.8.4 COI within the EC should be declared and managed in accordance with standard operating procedures (SOPs) of that EC.

2.9 Selection of vulnerable and special groups as research participants

Vulnerable groups and individuals may have an increased likelihood of incurring additional harm as they may be relatively (or absolutely) incapable of protecting their own interests.

2.9.1 Characteristics that make individuals vulnerable are legal status – children; clinical conditions – cognitive impairment, unconsciousness; or situational conditions –

including but not limited to being economically or socially disadvantaged, (for example, certain ethnic or religious groups, individuals/communities which have hierarchical relationships, institutionalized persons, humanitarian emergencies, language barriers and cultural differences).

- 2.9.2 In general, such participants should be included in research only when the research is directly answering the health needs or requirements of the group. On the other hand, vulnerable populations also have an equal right to be included in research so that benefits accruing from the research apply to them as well. This needs careful consideration by researchers as well as the EC.
- 2.9.3 The EC should determine vulnerability and ensure that additional safeguards and monitoring mechanisms are established. It should also advise the researcher in this regard. See section 6 for further details.

2.10 Community engagement

Community can be defined as a social group of people of any size sharing the same geographical location, beliefs, culture, age, gender, profession, lifestyle, disease, etc. The community should be meaningfully engaged before, during and after the research to mitigate culturally sensitive issues and ensure greater responsiveness to their health needs and requirements.

- 2.10.1 The community can be engaged in many ways and can provide valuable opinions. The degree of community engagement should depend on the type of research that is being conducted.
- 2.10.2 Community advisory board/group (CAB/CAG) can act as an interface between the community (from which participants are to be drawn), the researchers and the concerned EC. Members of the CAB should be such that they do not coerce the members of the community to participate in the research and also protect the rights and serve the requirements of the group.
- 2.10.3 Members of the community can also be represented in the EC either as members or special invitees.
- 2.10.4 Community engagement does not replace individual informed consent. It ensures that the community's health needs and expectations are addressed, informed consent is appropriate, and access to research benefits are provided through research that is designed and implemented in the best interests of science and the community.
- 2.10.5 After the study is completed, the researcher may communicate with the community

representative, local institution or the government department from where the data was collected to help in dissemination of the results to the entire community.

See sections 8 and 9 for further details.

2.11 Post research access and benefit sharing

The benefits accruing from research should be made accessible to individuals, communities and populations whenever relevant. Sometimes more than the benefit to the individual participant, the community may be given benefit in an indirect way by improving their living conditions, establishing counselling centres, clinics or schools, and providing education on good health practices.

- 2.11.1 Efforts should be made to communicate the findings of the research study to the individuals/communities wherever relevant.
- 2.11.2 The research team should make plans wherever applicable for post-research access and sharing of academic or intervention benefits with the participants, including those in the control group.
- 2.11.3 Post-research access arrangements or other care must be described in the study protocol so that the EC may consider such arrangements during its review.
- 2.11.4 If an investigational drug is to be given to a participant post-trial, appropriate regulatory approvals should be in place.
- 2.11.5 The EC should consider the need for an a priori agreement between the researchers and sponsors regarding all the points mentioned above (from 2.11.1 to 2.11.3).
- 2.11.6 In studies with restricted scope, such as student projects, post study benefit to the participants may not be feasible, but conscious efforts should be made by the institution to take steps to continue to support and give better care to the participants.