Ethical Conduct of Human Studies- Basis for Good Clinical Practices

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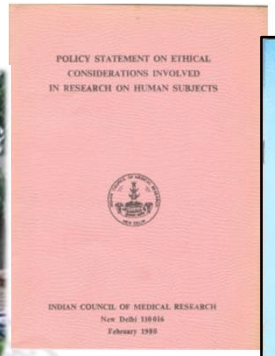

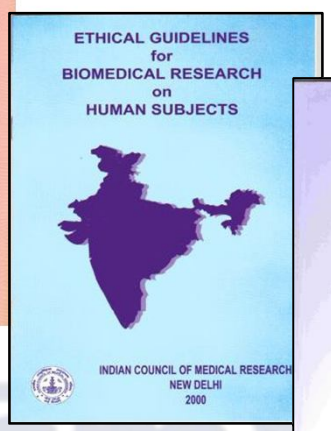

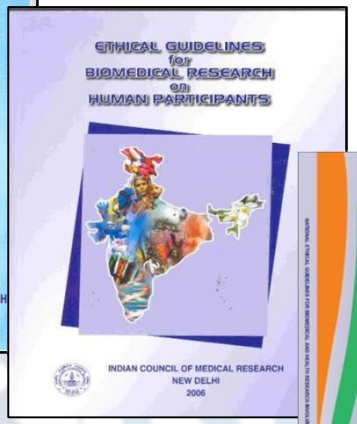

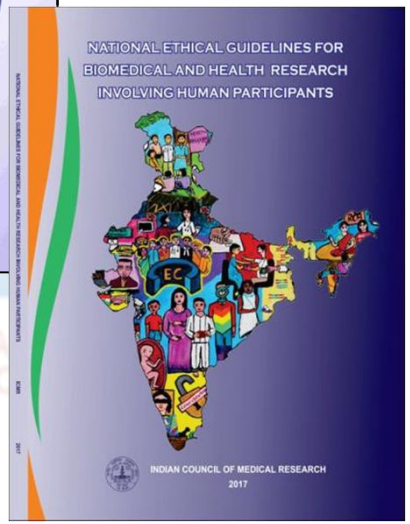

Apex organization to formulate, conduct, coordinate, fund and promote biomedical research

http://icmr.nic.in/guidelines/ICMR_Ethical_Guidelines_2017.pdf

Ethics Review of Health Research

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Principles

- Autonomy of participant/ respect for persons
- Beneficence & Non maleficence
- Justice

Scope

- These guidelines are applicable to all **biomedical, socio-behavioural and health research** conducted in India involving human participants, their **biological material and data**

- **Includes all regulatory studies- Drugs, Devices, Cells, *Foods, Food ingredients, Software, Methodologies* etc**

General Principles

1. Principle of essentiality
2. Principle of voluntariness
3. Principle of non-exploitation
4. Principle of social responsibility
5. Principle of ensuring privacy and confidentiality
6. Principle of risk minimization
7. Principle of professional competence
8. Principle of maximization of benefit
9. Principle of totality of responsibility
10. Principle of institutional arrangements
11. Principle of transparency and accountability
12. Principle of environmental protection

General Ethical Issues

Benefit-Risk assessment

Categories of risk:

- **Less than minimal risk**
- **Minimal**
- **Low risk**
- **High risk**

Risk Categories

Less than minimal risk- data/samples,

Minimal risk - routine questioning or history taking, observing, physical examination, chest X-ray, obtaining body fluids without invasive intervention

Minor increase over minimal risk or Low risk

Routine research on children and adolescents

Randomisation or Placebo

Persons incapable of giving consent

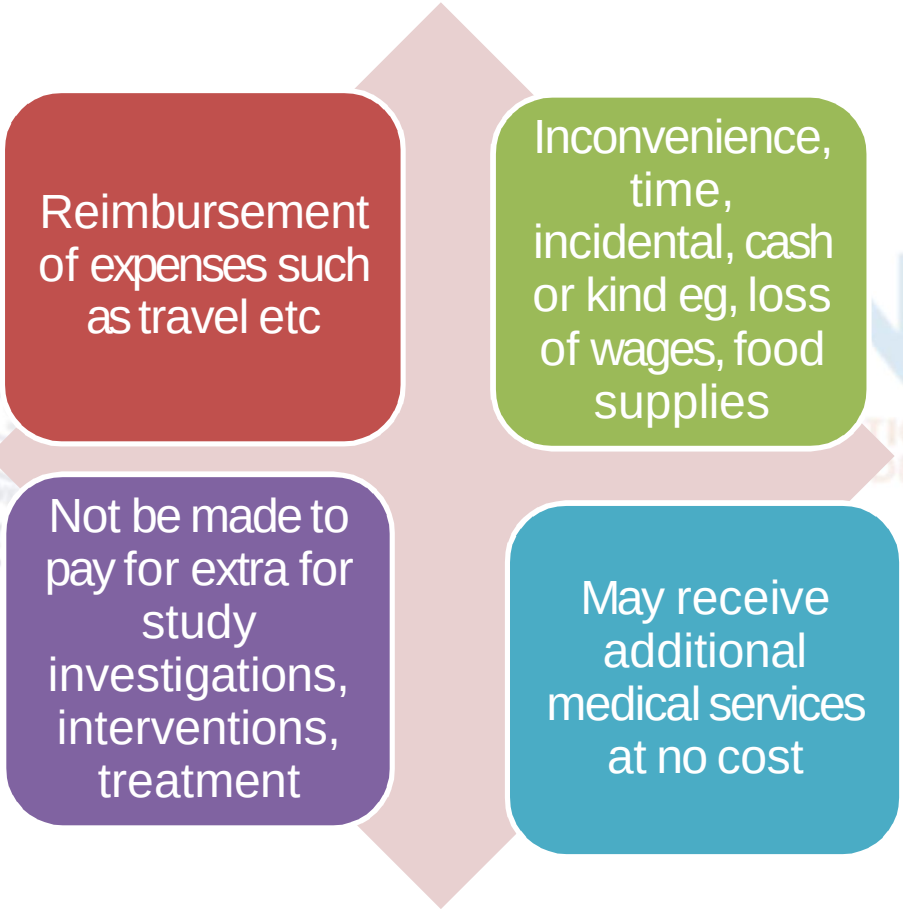
Minimally invasive procedures that might cause no more than brief pain

Social risks, psychological harm

More than minimal risk or High risk

Research involving any interventional study
using a drug, device, a novel ingredient or invasive procedure

Payment for participation



Privacy and confidentiality

Privacy - right of an individual to control what information can be collected and stored and by whom and to whom disclosed or shared

Confidentiality is obligation of the researcher/ team to safeguard information from unauthorised access, use, disclosure, modification, loss or theft

The investigator should safeguard participant's information and data

The limits to ensure strict confidentiality must be explained to the participant

Publication should consider upholding the privacy of the individuals by not publishing any photographs or revealing the individual's identity without consent

Compensation for research related harms

A direct physical, psychological, social, legal, economic harm due to participation in research - compensated by financial/other assistance for any temporary/permanent disability -medical care, referrals, clinical facilities etc

- In case of death, their dependents are entitled to financial compensation

Investigator to report all SAE along with report on relatedness to EC

- EC should review relatedness of the SAE to research & determine quantum of compensation to be paid

Research project/ Institution should have an in-built mechanism to be able to provide for compensation e.g. corpus fund created in institution/ Insurance or grants from agencies

Conflict of interest (COI)

COI is a set of conditions where professional judgment concerning a primary interest like participants welfare or validity of research tends to be unduly influenced by a secondary interest, non-financial (personal, academic or political) or financial

COI can be at the level of researchers, EC members, institutions or sponsors and always present, it is important to declare & manage them

Research institutions must develop and implement policies and procedures and educate their staff

Researchers to make a disclosure of interests to EC that may affect research

ECs must evaluate any disclosed interests and ensure that appropriate means of mitigation are taken

Distributive justice

Individuals or communities selected in such a way that the burdens and benefits of research are equitably distributed

Economically or socially disadvantaged or with any disability should not be used to benefit others who are better off

Research should not lead to social, racial or ethnic inequalities

Plans for benefit sharing should be included a priori in the study which has potential for commercialization

Community engagement

Community should be meaningfully engaged before, during and after research to mitigate culturally sensitive issues and ensure more responsiveness

Can be represented as CAB/CAG or EC member/special invitee

Community engagement does not replace individual informed consent

After study completion, can help in meaningful dissemination/translation of the results

Inclusion, Sensitivity, Understanding, partnership to the needs and requirements

Responsible Conduct of Research (RCR)

- Responsibility, sensitivity, mentoring
  - Scientist as a responsible member of society
- Institutional policies, SOPs, COI, monitoring, misconduct
- Data acquisition, management, sharing, ownership
- Reviewing, reporting, authorship (ICMJE), peer review
- Clinical Trial Registry of India (CTRI)
- Collaborative research: Communication between EC, exchange of biological material, MoU, MTA, International Collaboration

Actively promote honesty, accuracy, efficiency, objectivity and transparency in research

Composition and functions

- Multi-disciplinary/ age/ gender /including non-affiliated
- The Head of the Institution should not be part of the EC
- EC can have alternate members/ subject experts/ patient representative
- Every EC should have written SOPs
- Protect research participants, ethical & community values, customs
- Development and education of the research community
- Independence, selection, appointment, training

- **Special situations:** More than one EC, use other EC, Multicentre, Independent EC, subcommittees

Members of EC	Definition/description
Chairperson/ Vice Chairperson (optional) Non-affiliated Qualifications - A well-respected person from any background with prior experience of having served/ serving in an EC	• Conduct EC meetings and be accountable for independent and efficient functioning of the committee • Ensure active participation of all members (particularly non-affiliated, non-medical/ non- technical) in all discussions and deliberations • Ratify minutes of the previous meetings • In case of anticipated absence of both Chairperson and Vice Chairperson at a planned meeting, the Chairperson should nominate a committee member as Acting Chairperson or the members present may elect an Acting Chairperson on the day of the meeting. The Acting Chairperson should be a non-affiliated person and will have all the powers of the Chairperson for that meeting. • Seek COI declaration from members and ensure quorum and fair decision making. • Handle complaints against researchers, EC members, conflict of interest issues and requests for use of EC data, etc.
Member Secretary/ Alternate Member Secretary (optional) Affiliated Qualifications - • Should be a staff member of the institution • Should have knowledge and experience in clinical research and ethics, be motivated and have good communication skills	• Organize an effective and efficient procedure for receiving, preparing, circulating and maintaining each proposal for review • Schedule EC meetings, prepare the agenda and minutes • Organize EC documentation, communication and archiving • Ensure training of EC secretariat and EC members • Ensure SOPs are updated as and when required • Ensure adherence of EC functioning to the SOPs • Prepare for and respond to audits and inspections • Ensure completeness of documentation at the time of receipt and timely inclusion in agenda for EC review. • Assess the need for expedited review/ exemption from review or full review.
Social scientist/ philosopher/ ethicist/theologian Affiliated/ non-affiliated Qualifications - • Should be an individual with social/ behavioural science/ philosophy/ religious qualification and training and/or expertise and be sensitive to local cultural and moral values. Can be from an NGO involved in health-related activities	• Ethical review of the proposal, ICD along with the translations. • Assess impact on community involvement, socio-cultural context, religious or philosophical context, if any • Serve as a patient/participant/ societal / community representative and bring in ethical and societal concerns.
Lay person(s) Non-affiliated Qualifications - • Literate person from the public or community • Has not pursued a medical science/ health-related career in the last 5 years • May be a representative of the community from which the participants are to be drawn • Is aware of the local language, cultural and moral values of the community • Desirable: involved in social and community welfare activities	• Ethical review of the proposal, ICD along with translation(s). • Evaluate benefits and risks from the participant's perspective and opine whether benefits justify the risks. • Serve as a patient/participant/ community representative and bring in ethical and societal concerns. • Assess on societal aspects if any.

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Ethical review procedures

- Social Value
- Scientific design & conduct
- Benefit risk assessment
- Selection of participants
- Payment for participation
- Privacy and confidentiality
- Community considerations
- Qualifications & site assessment
- Disclosure of COI
- Medical management & Compensation
- Informed consent form/ process

Review of multi-centric research

- To save time, duplication of effort and streamline the review process, ECs of all sites should establish communication with one another
- Identify one main designated EC whose decision may be acceptable
- Local concerns, translations, monitoring locally
- Good communication between EC secretariats

Concept of Common Review by one EC introduced

Informed consent

Responsibility of researchers
Documentation
Electronic Consent
Waiver of Consent, re-consent,
After consent
Special Situations- Gatekeepers, community consent, Vulnerable
Using Deception- de briefing

- Statement- Research
- Purpose & methods
- Duration of participation
- Benefits
- Risks & Discomforts
- Confidentiality
- Payment reimbursement
- Compensation
- Freedom to participate/ withdraw
- Contact Info
- Additional
  - Alternatives
  - Stigmatization
  - Insurance
  - Future use of biological material
  - Period of storage, sharing
  - Confidentiality,
  - Benefit sharing
  - Publication

Vulnerability

- **Definition:** *Relatively or absolutely incapable of protecting their own interests*
- Key principles of research:
  - Others will be responsible for protecting their interests because they cannot do so or are in a compromised position
  - Right to inclusion so benefits accruing apply
  - For solely recruiting, research to answer health needs of the group
  - Additional safeguards
- Obligations of researchers, ECs, sponsors

- **Economically/ socially disadvantaged**
- **Unduly influenced**
- **Children**
- **Women in special situations**
- **Tribals and marginalized**
- **Refugees, migrants, homeless, conflict zone, riot, disaster hit**
- **Mental illness, differently abled**
- **Terminally ill**
- **Stigmatizing or rare diseases**
- **Diminished autonomy due to hierarchy**

Clinical trials

General - Risk benefit assessment, GCP, therapeutic misconception, qualifications, site facilities, EC and regulatory approval, SAE reporting, medical management, compensation for related injury, ancillary care, Institutional mechanisms

Specific - Phases of Drug development, Vaccine trials, BA/BE studies, Placebo use, Phytopharmaceuticals, Devices, biological, biosimilars, stem cells, Surgical interventions, Community Trials, HIV/AIDS trials, Traditional medicine, diagnostic agents, radio active and X ray, Investigator initiated, Contraceptives, pregnancy and Clinical trials, oncology trials, new technology, synthetic biology etc

All clinical trials for regulatory approval must be conducted in accordance to the Drugs and Cosmetics Act and Rules and applicable amendments from time to time

FSSAI ?

Ethics Review of Health Research

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A Case Study- 1

Industry wants to make a claim that its food product prevents muscle loss in critically ill patients (FSMP)

Plans to conduct the study in hospital workers

Wrong – Vulnerable subjects. Not intended for them

Case study 2

Industry wants to make a claim that its food product prevents muscle loss in critically ill patients (FSMP)

Plans to conduct the study in a hospital ICU patients

Does not take consent since patients are critically ill but takes consent of the ICU doctors

Wrong – Legally Acceptable Representatives consent required followed by consent of patient when fit to give consent

Case study 3

Industry wants to make a claim that its food product prevents muscle loss in critically ill patients (FSMP)

Plans to conduct the study in a hospital ICU patients

Principle investigator is a senior physician who also holds shares in the same industry

Wrong- Conflict of Interest

Case study 4

An industry wants to conduct a study on its iron fortified wheat flour in a village

PI is a doctor in a nearby hospital- Takes EC approval from his hospital to do the study

Wrong – Should take community approval through the District admin, Village Panchayat.
If product found beneficial , it should be accessible to the same community who took part in the study

Case Study 5

An industry tests a beverage that shows distinct benefit in cognition and scholastic improvement in school children.

Publishes in a journal mentioning the name , location and address of the school as well as the classes and year of study

Wrong – breach of confidentiality. Students could be identifiable with this information.

Case Study 6

An industry tests a beverage that shows distinct benefit in cognition and scholastic improvement in school children.

During the study there is a mild incident of food poisoning in some of these children unrelated to the test beverage or the study. The sponsor is not willing to meet the costs of the treatment.

Wrong – Ancillary care to be provided during study period.

Case Study 7

An industry conducts a study with an ingredient of proven pre- clinical safety on a group of volunteers. One of them has a serious reaction and needs emergency treatment.

PI or CRO says he was only conducting the study and not responsible for the ingredient

Sponsor says during the study period the safety of the study participants is with the CRO and PI

Ethics committee says they only gave the approval based on the documents

Wrong- Principle of totality of responsibility

Case study 8

A study is to be conducted in a hospital by a Physician who is willing to take the responsibility and the needed resources from the sponsor without the management's approval and management is not willing to make any provisons fo the study

Wrong- Institutional responsibility and arrangements are essential

Need to Develop a Quality Culture
in
Ethical Conduct and Review

Thank you