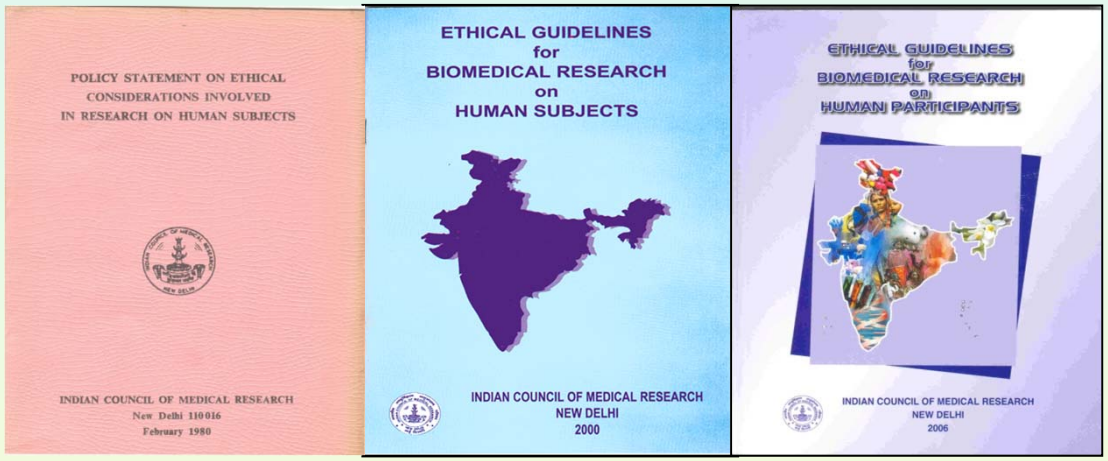
ICMR Ethical Guidelines for Biomedical Research in India



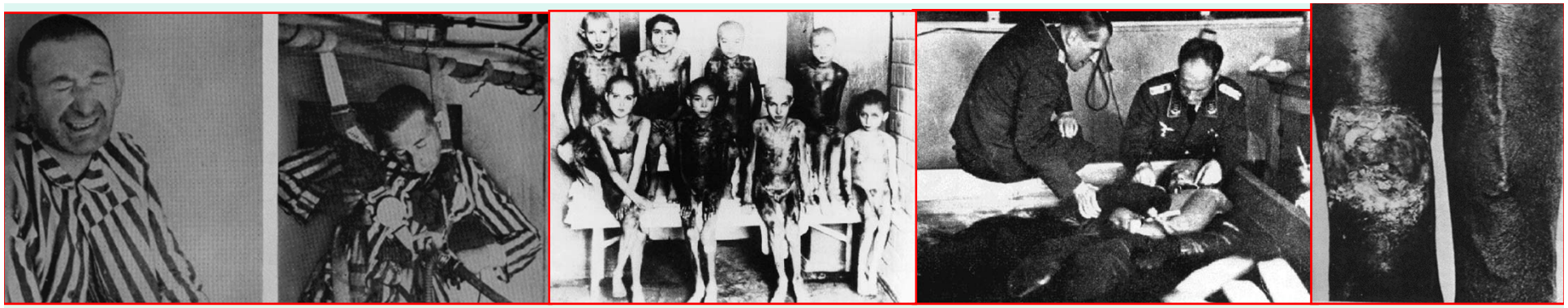
Dr. Roli Mathur

Scientist 'D'

Program Officer for Bioethics, Animal Ethics, Human Genetics, Anthropology, Anatomy, Hematology, Short Term Studentship

Indian Council of Medical Research, New Delhi- 110029

mathurr@icmr.org.in



Need for ethical guidelines ?

Reasons: Historical and Modern

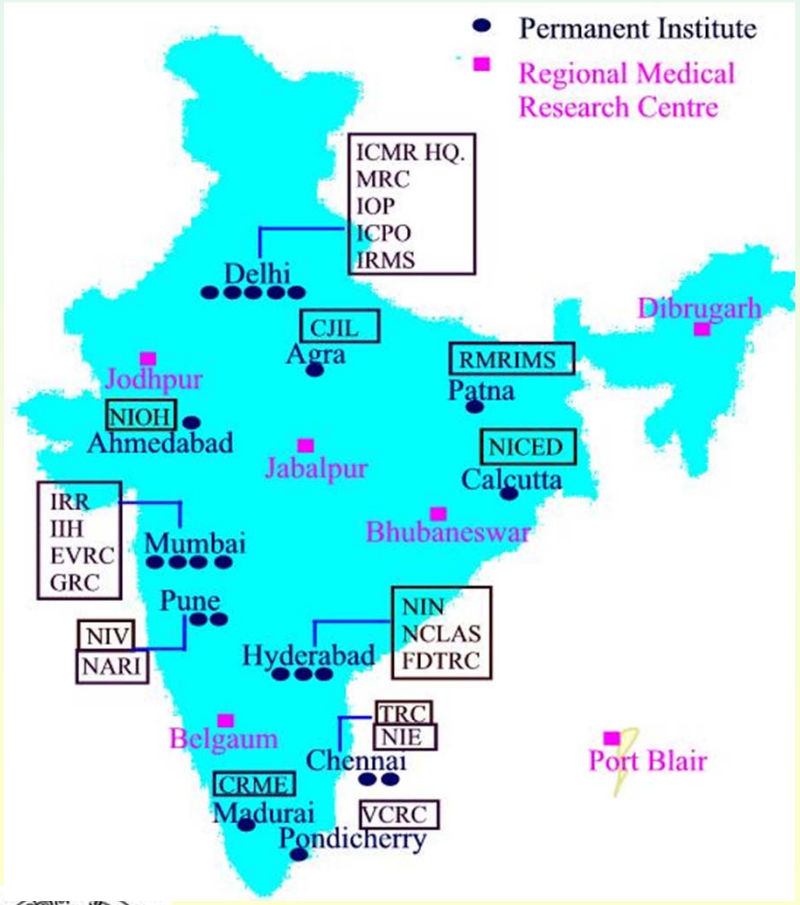
Past Misuse of Research

Present Day Technology

WHY ETHICAL GUIDELINES ARE IMPORTANT?

- Research to integral to creation/ improvement in scientific knowledge in medicine
- Thin line of distinction between research and practice
  - Most often done on patients with or without their knowledge
  - Patient data collected for patient care often used for research
- Avoid exploitation and protect human rights
- Guidelines provide appropriate direction / reference

Indian Council of Medical Research



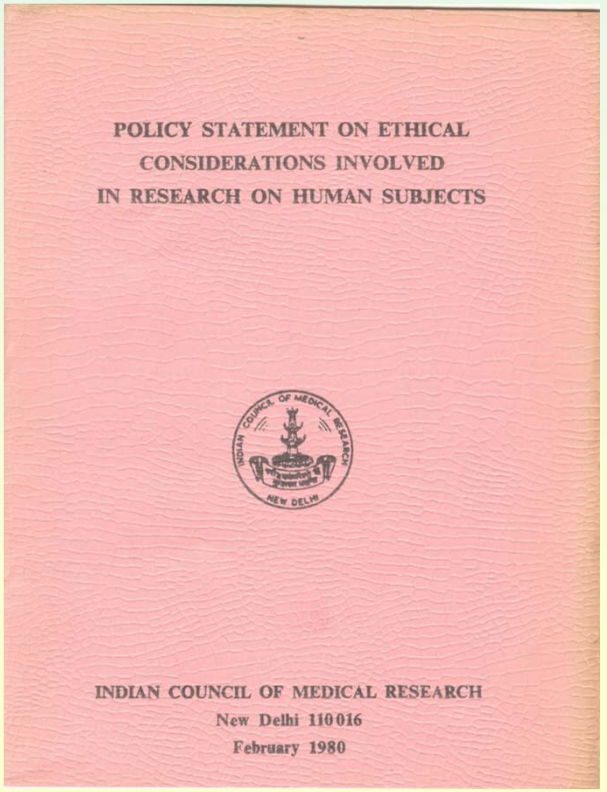
- Apex body to formulate, conduct, coordinate and promote biomedical research
- Founded in 1911 - Indian Research Fund Association, Renamed as ICMR in 1949
- Intramural & extramural – 28 Institutes & 6 Regional Medical Research Centres + medical colleges, universities, research institutions
- Mandate: To undertake and support research

  Basic, Applied, Epidemiological, Operational in the areas of national public health importance

1980 ICMR Guidelines

Policy Statement on Ethical Considerations involved in research on Human Subjects

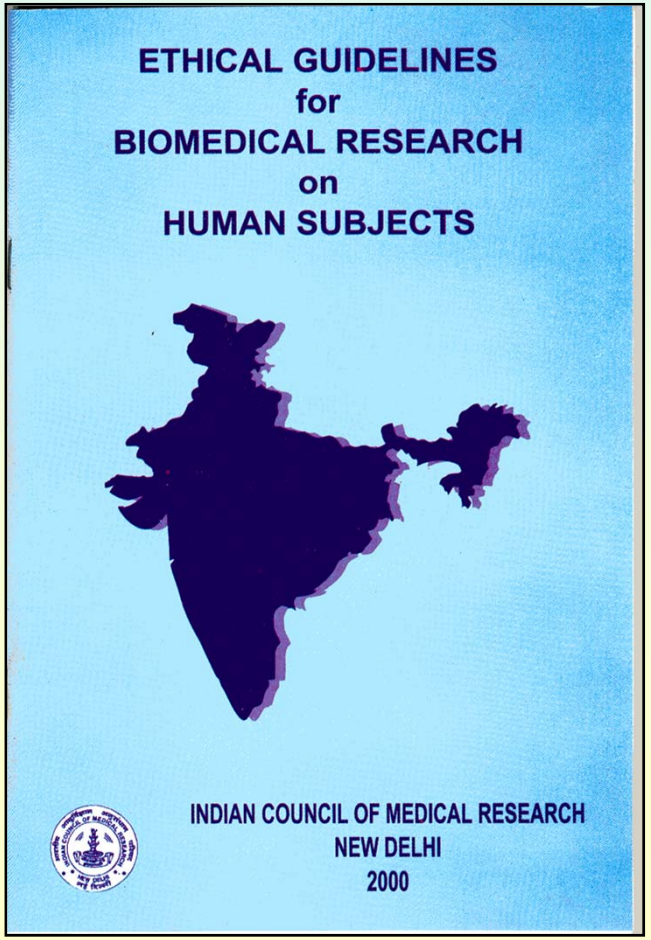
- Ethics Committee
- Informed consent
- Clinical trials
- Research on children, mentally disadvantaged, those with diminished autonomy
- Traditional Medicine
- Publications



Ethical Guidelines for Biomedical Research on Human Subjects, 2000

- All institutions in the country which carry out any form of biomedical research involving human beings should follow these guidelines in letter and spirit to protect safety and well being of all individuals.

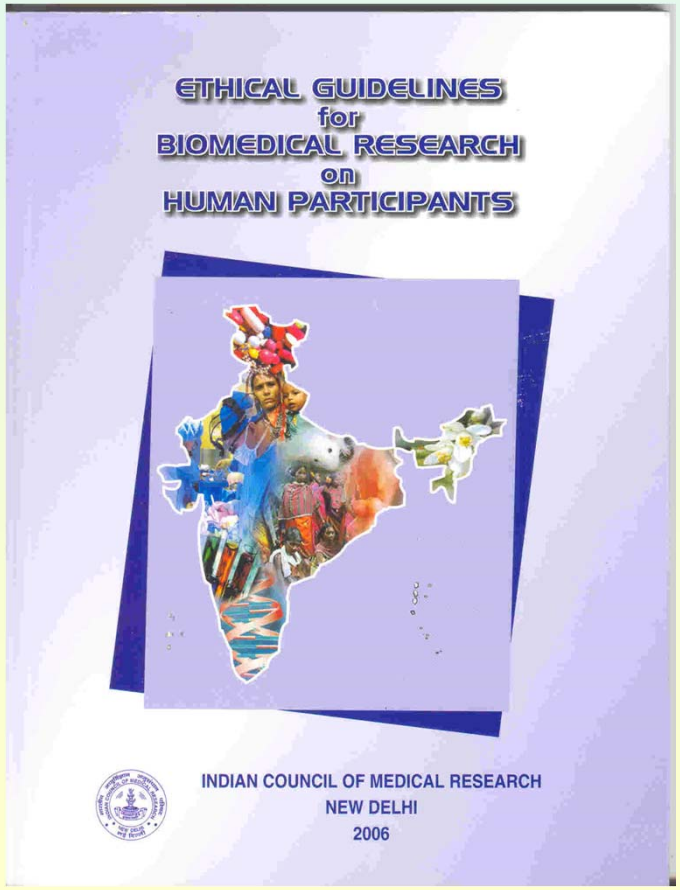
- All proposals on biomedical research involving human subjects should be cleared by an Institutional Ethics Committee (IEC)



Ethical Guidelines for Biomedical Research on Human participants - 2006

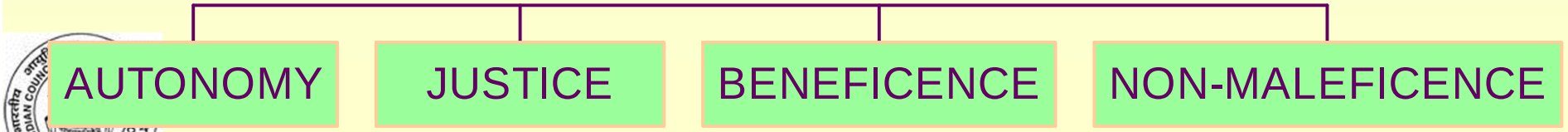
- All institutions which carry out any form of biomedical research involving human beings should follow these guidelines to protect safety & well being of participant.

- Priced at Rs 250/- and can be downloaded at no cost from website (www.icmr.nic.in)



Principles

- Autonomy of participant/ respect for persons
  - informed consent, confidentiality, rights to biological material, data, use of samples for another purpose, research on children, vulnerable
- Beneficence & Non maleficence
  - benefit and harm, direct or indirect benefit, personal vs social benefit, degree of forseeable risks and discomforts, benefits during and after the study, conflict of interest issues
- Justice
  - selection of participants, non discrimination, stigmatization, protection of vulnerable, coercion, Equal distribution of burdens and benefits of research, Post trial benefits / prior agreements



General Statement

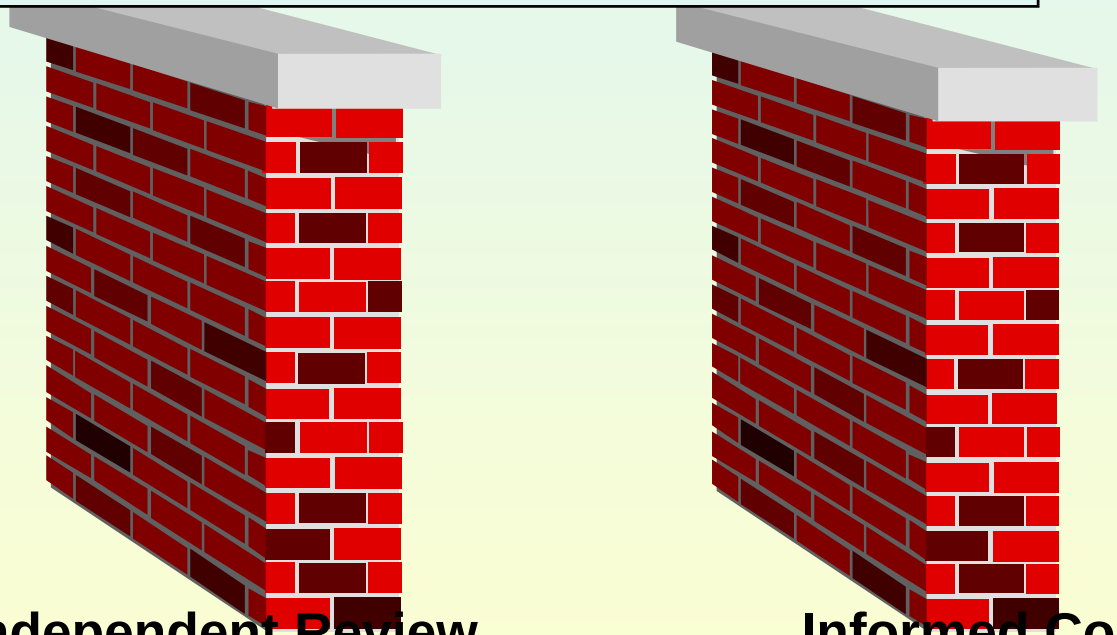
- Research on human participants must ensure that :
  - PURPOSE : increase in knowledge, betterment of all
  - CONDUCTED : under conditions that no person becomes mere means, respect dignity and well being, transparency, avoiding risks
  - EVALUATION : at all stages, design, experimentation, declaration of results ensuring safety of human life

Statement of General Principles

- Essentiality
- Voluntariness, informed consent and community agreement
- Non-exploitation
- Privacy and confidentiality
- Precaution and risk minimisation
- Professional competence
- Accountability and transparency
- Maximisation of the public interest and of distributive Justice
- Institutional arrangements
- Public domain
- Totality of responsibility
- Compliance

“The Twin Pillars of Protection” in Biomedical research

Rights and Welfare of Human Subjects



Independent Review **Informed Consent**

Basic Responsibilities

- Competent, timely Review
- Advice to researchers on all aspects of welfare and safety of participants
- Ensuring scientific soundness and technical appropriateness
- Specify authority under which committee is established
- Small institutions could form alliance with other IECs
- Large Institutions can have more than one IECs
- Responsibilities
  - To protect dignity, rights, well being of research participants
  - Ensure universal ethical values and international scientific standards are expressed in terms of local community values and customs
  - Assist in development and education of research community responsive to health care requirements.

ICMR Ethical Guidelines

- Chairperson
- One - two persons from basic medical science area
- One - two clinicians from various Institutes
- One legal expert or retired judge
- One social scientist/ representative of non-governmental voluntary agency
- One philosopher/ ethicist/ theologian
- One lay person from the community
- One member Secretary

Schedule Y (2005)

- One basic medical scientist (preferably one pharmacologist).
- One clinician
- One legal expert or retired judge
- One social scientist/ representative of non-governmental organisation/philosopher/ ethicist/ theologian or a similar person
- One lay person from the community

Adequate representation of age and gender

Ethical Review Procedures

Basic responsibilities of IECs – Special situations

Composition –Schedule Y of Drugs & Cosmetics Act

Terms of Reference

Training

Regulation

Review Procedures – Exemption, expedited review, full review

Submission of Application

Decision Making

Review Process

Periodic Review

Continuing Review

Interim Review

Monitoring

Record Keeping

Administration and Management

Special Considerations

Types of review

- Full Review
- Expedited Review
- Exemption from Review
- Periodic Review
- Continuing Review
- Interim Review
- Monitoring

TERMS OF REFERENCE

- Should include Terms of Appointment with reference to the duration of term, policy for removal, replacement, resignation procedure, frequency of meetings, payment of fee for review, honorarium/ consultancy / invited experts etc.
- Term of appointment of members could be extended for another term and a defined percentage of members could be changed.
- 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. For this the criteria for number of missed meetings may be defined in the SOP

Standard Operating Procedures (SOPs)

- All IEC functions, procedures and details should be written up in detail.
- SOPs should also have all forms and checklists to be used by IEC for its functions.
- All functions 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.

TRAINING

- Members should receive an initial training as well as ongoing training on a regular basis to keep them updated
- Abreast of all national and international developments in ethics through orientation courses on related topics by its own members or regular training so that they become aware of their role and responsibilities.
- 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.

SUBMISSION OF APPLICATION

• Title	• Compensation
• Objectives	• Storage and Maintenance records
• Curriculum Vitae	• Publication
• Procedures	• Ethical Issues
• Inclusion and exclusion	• Relevant Documents (IB)
• Methodology	• Guidelines
• Withdrawal	• Sponsors
• Statistical Analysis	• HMSC / DCGI
• Informed Consent	• MoU/ MTA
• Safety of Proposed Intervention	• Conflict-of-Interest (COI)
• Management of Risk	

RECORD KEEPING

- All documentation and communication of an IEC are to be dated, filed and preserved according to written procedures.
- Strict confidentiality maintained during access and retrieval procedures.
  - the Constitution and composition of the IEC;
  - signed and dated copies of the latest the curriculum vitae of all IEC members with records of training if any;
  - standing operating procedures of the IEC;
  - national and International guidelines;
  - copies of protocols submitted for review;
  - all correspondence with IEC members and investigators regarding application, decision and follow up;
  - agenda of all IEC meetings;
  - minutes of all IEC meetings;
  - copies of decisions communicated;
  - record of all notification issued ;
  - final report of the study

ADMINISTRATION AND MANAGEMENT

- A full time secretariat and space for keeping records is required for a well functioning IEC.
- The members could be given a reasonable compensation for the time spared for reviewing the proposals.
- A reasonable fees can be charged to cover the expenses related to review and administrative processes.
- Every institution should allocate reasonable amount of funds for smooth functioning of the IEC.

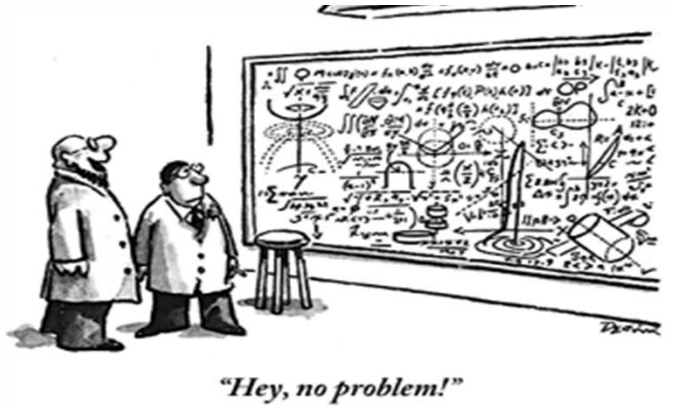
General Ethical Issues

- Informed consent of subject – Fresh /re-consent
- Waiver of consent
- Obligations of investigators
- Essential information for prospective research
- Compensation for participation
- Conflict of interest
- Selection of special groups as research participants
- Essential information on confidentiality for prospective research
- Compensation from accidental injury
- Post – trial access
- International Collaborative Research/ Assistance in Biomedical / Health Research
- Special Concerns
- Researcher's relations with the media and publication practices

Elements of Informed Consent

Nature and purpose
Duration & procedures
Benefits
Alternative procedures
Risks and discomforts
Use of biological sample
Confidentiality
Benefit sharing
Compensation for injury
Voluntary participation/withdrawal
Contact information
Future use of data/samples

How and Who ?



- PI/ Co-PI/ Counselor / staff - knowledgeable & can spare time
- Language, manner clear & understandable
- Small sentences, simple words, short paragraphs
- Remove technical jargon/medical terms
- Opportunity to say 'no', time for Q's
- Non-directive, open ended discussion
- Undue influence/ coercion

- Kind of consent- verbal/written/ language/translations
- Audiovisual/ telephone/ media
- Educational video designed to enhance the IC process

Oral consent Waiver of Consent

- Participants who do not read, or understand the language of the written consent form
- Ethics review committee must approve the script which is read to the individual
- A witness is required to sign

May be granted by an IEC

- Minimal risk study
- Obtaining informed consent is not ‘practicable’
- Publicly available information, documents
- Will not adversely affect rights and welfare
- Subjects to be provided with additional pertinent information after participation
- Emergencies: Incapacity of patient – surrogate consent
- Data / Case record studies

Secondary Use

- Use of Stored tissue/left over Anonymous samples

Compensation for Accidental Injury

- For temporary / permanent impairment or disability
- For any physical or mental injury Obligation of the Sponsor/ Institution
- May provide insurance coverage for an unforeseen injury

Post Trial Benefits

- *a priori agreement*
- Distribution of burden & benefit of research
- After completion of trial product availability free/ subsidized cost
- Care of participants during and after the trial
- Affordability and accessibility issues

Protection of Confidentiality / Privacy

- Disclosure during informed consent
- risk due to breach of confidentiality
- Means of ensuring data security/ Limiting data access
- Anonymization, coding, delinking etc
- Investigator integrity
- Sample sharing by researchers
- Samples from deceased or non-traceable persons
- Benefit sharing in commercialisation
- Right to information
- Type of information - personal /sensitive/readily available
- Consent for stored biological material / database

Conflict of Interest

Situations in which financial or other personal considerations may compromise, professional judgment in conducting or reporting research

IEC member	Investigator
• Speaking fees, consultation fees, stock, equities	• Financial incentive, investment/partnership
• Academic interest	• Primary interest
• Announce & leave room during review	• Not participate in review except to give information

•Publications, promotions, project grants

•enrollment of ineligible subjects

•EC to limit to amount of investment & Disclosure

•Threatens research design, data integrity, patient safety, dissemination of results

Special & Vulnerable Groups

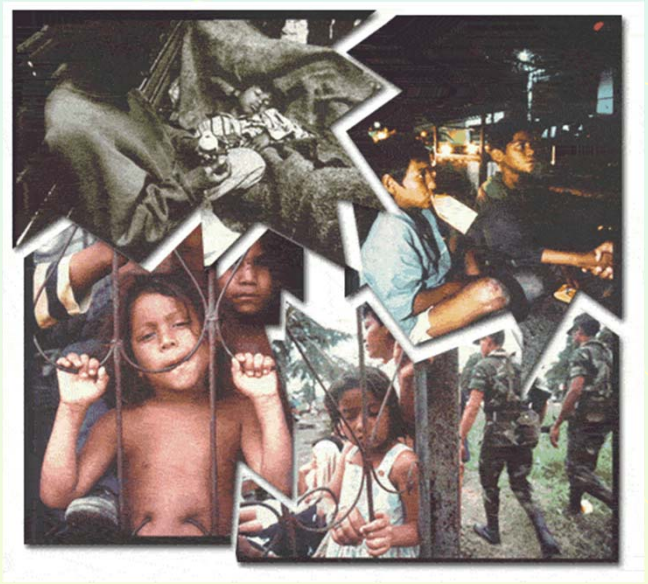
disease/condition

age

poor

students

institutionalised



mentally ill

uneducated

employee

military

pregnant

children

prisoners

tribals

Selection of Special Groups as Research Subjects

Pregnant or Nursing Women

- Only if objective of research to obtain new knowledge about foetus, pregnancy and lactation
- No more than minimal risk to the fetus or nursing infant.

Vulnerable Groups

- No racial inequality
- Economically/socially disadvantaged not used for benefit of the better off
- Protection of Mentally challenged
- Do not involve Prisoners, Students, Subordinates, Employees, Service Personnel- reduced autonomy

Specific Principles

- Clinical Trials of Drugs,Devices,Vaccines,Diagnostic agents, Herbal Drugs
- Epidemiological Studies
- Human Genetics Research
- Transplantation Research including Fetal tissue and Xeno-transplantation
- Assisted Reproductive Technologies

ISSUES IN CLINICAL TRIALS

- DRUG TRIALS – special considerations as per Schedule Y, 2005
  - Phases of clinical trials – Combined Phase I & II
  - Special Studies
  - Multicentric trials - special concerns
  - Contraceptive trials
  - RCTs
  - Monitoring & reporting Adverse reactions or events

- Vaccine trials including r-DNA and combination vaccines - special concerns
- Devices/ Surgical procedures
- Traditional ASU remedies and Medicinal plants
- Quality Control

EPIDEMIOLOGICAL STUDIES

- Definition/Types of studies
- General Principles
- Specific Principles - Informed consent –individuals & communities, inducements, risks, benefits, ethical review procedures, conflict of interest – community participation
- Privacy/ Confidentiality
- Research and Programme Evaluation

HUMAN GENETICS RESEARCH

- General Guidelines
- Pedigree studies
- Privacy/confidentiality
- Genetic screening
- Therapeutic trials including Gene therapy
- Human Genome Project
- DNA and cell line Banking/ repository – Repository, Biobanking
- DNA diagnosis
- Pre- natal diagnosis

Biological specimens- Types of Samples

- Left over samples, collected in past – research/ clinical purpose, donor, prospective
- Precious material
- Samples collected for clinical purpose not be used for research e.g., tissue, biopsy, histopathology samples, blood, serum, DNA etc

  – **Anonymous:** No personal identifiers
  – **Anonymized:** Personal identifiers removed completely
  – **Coded:** Linked to personal identifiers
  – **Identified:** Personal identifiers attached

TRANSPLANTATION

- Definitions
- Live donor transplants
- Cadaver donor transplants
- Research on recipients
- **Embryonic and Fetal tissue transplantation**
- Xeno-transplantation
- Transplantation for cosmetic purposes
- **Stem cell research & therapy**
- **Umbilical Cord Blood**

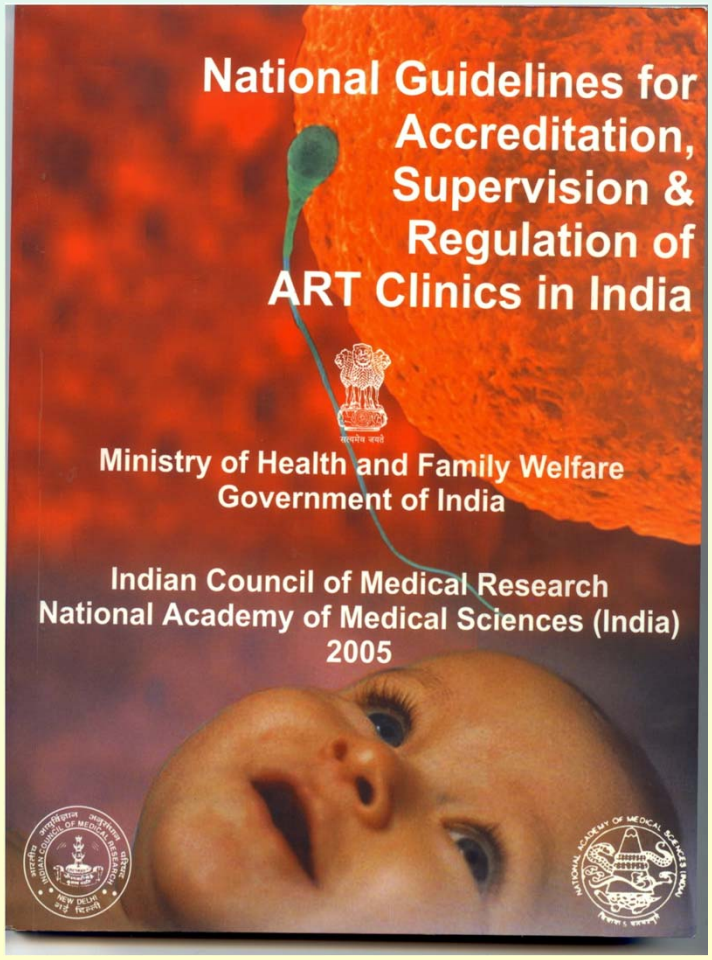
ART

General Principles

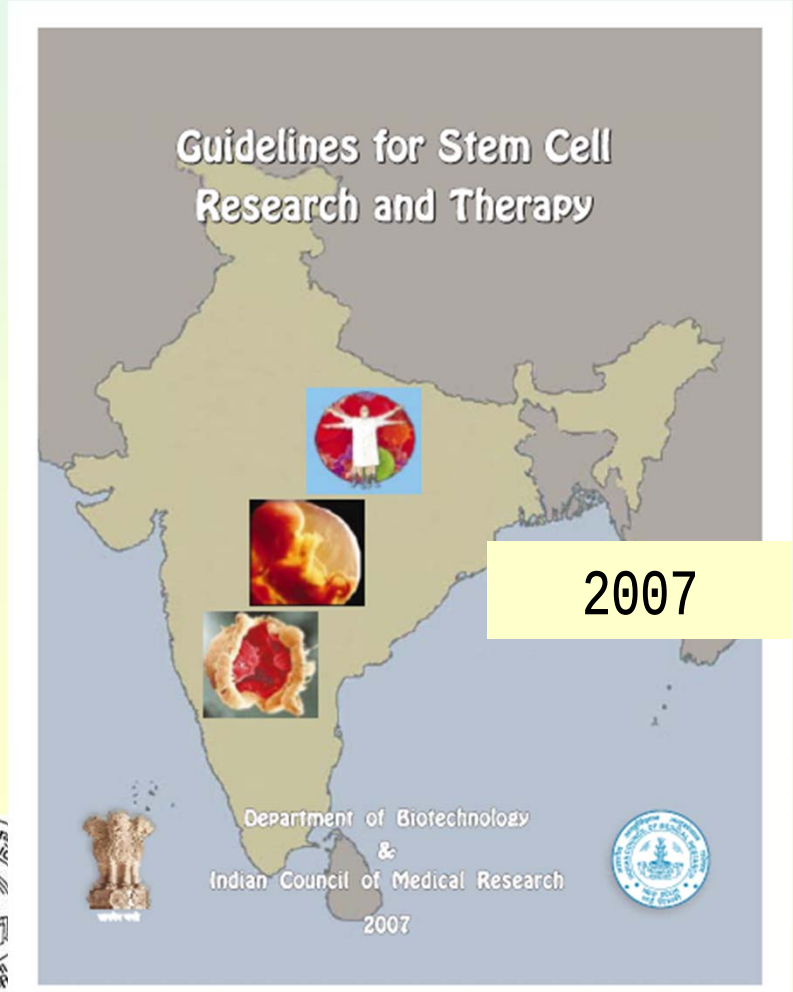
- Informed Consent
- Selection of donor
- Gametes & embryo
- Cloning prohibited

Specific Principles

- Legitimacy of child
- Surrogate motherhood
- Preservation, utilisation & destruction of embryos
- Use of Spare embryos
- Right of children/parents



Stem Cell Research in India



2007

2014

Ministry of Health & F.W. GOVERNMENT OF INDIA
19th November, 1997
OFFICE MEMORANDUM
Subject :Guidelines for Exchange of Human Biological Material for Biomedical Research Purposes

- International Collaboration
  - Exchange of biological material permitted as per existing procedures of funding agencies (DST, DBT, ICMR etc) and the Health Ministry's screening committee (as per GOI Guidelines)
- Capacity Building
- Community participation
- Protection of vulnerable population
- Assessment of burden and benefit
- Equal respect for rules & regulations of both countries
- Transfer of biological samples
  - MTA
  - MoU

Clinical Trial Registry of India (CTRI)

Joint ICMR-DST-WHO activity for registering clinical trials in India

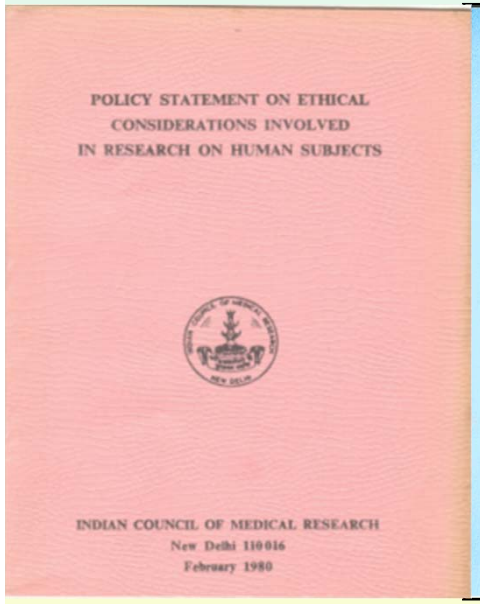
Objectives of NCTR

1. To establish a public record system by registering all clinical trials on health products that are drugs, devices, vaccines, herbal drugs etc.
2. To create a more complete, authentic, public and readily available data of all ongoing and completed clinical trials.
3. Increase awareness and accountability of all the participants of the clinical trials and also for public access

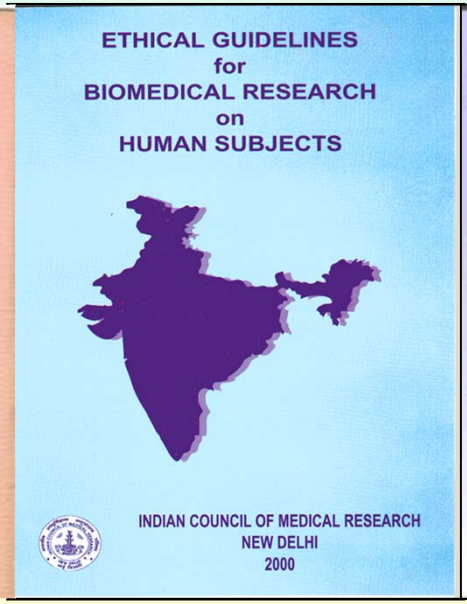
Since 15th June, 2009 it is mandatory to register any clinical trial with CTRI.

Encourages all clinical trials conducted in India to be prospectively registered before the enrollment of the first participant

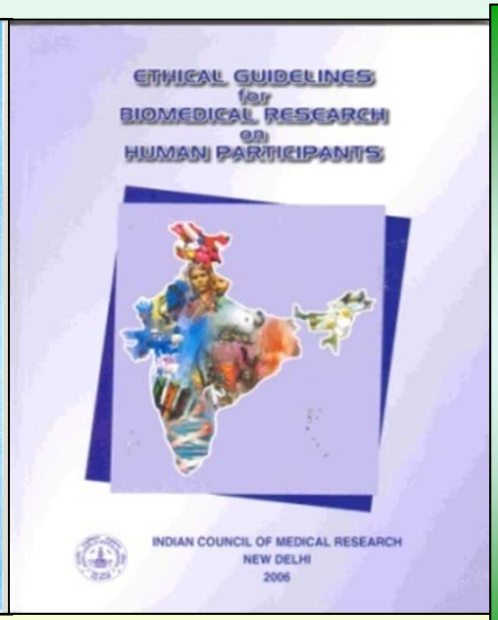
Ethical Guidelines for Biomedical Research



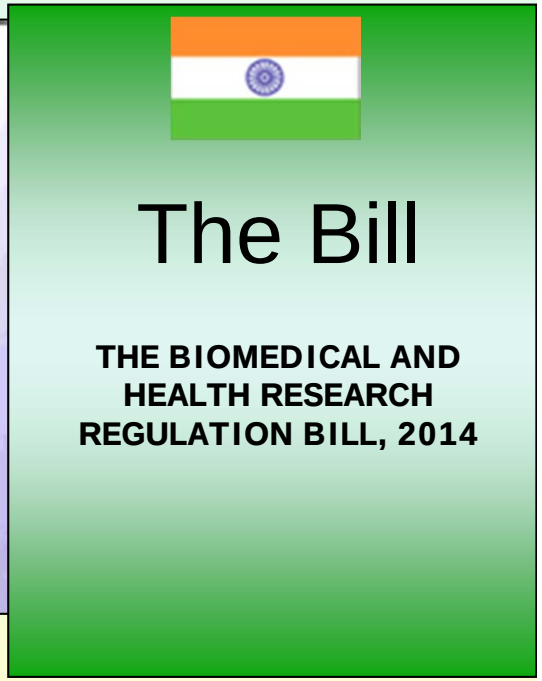
1980



2000

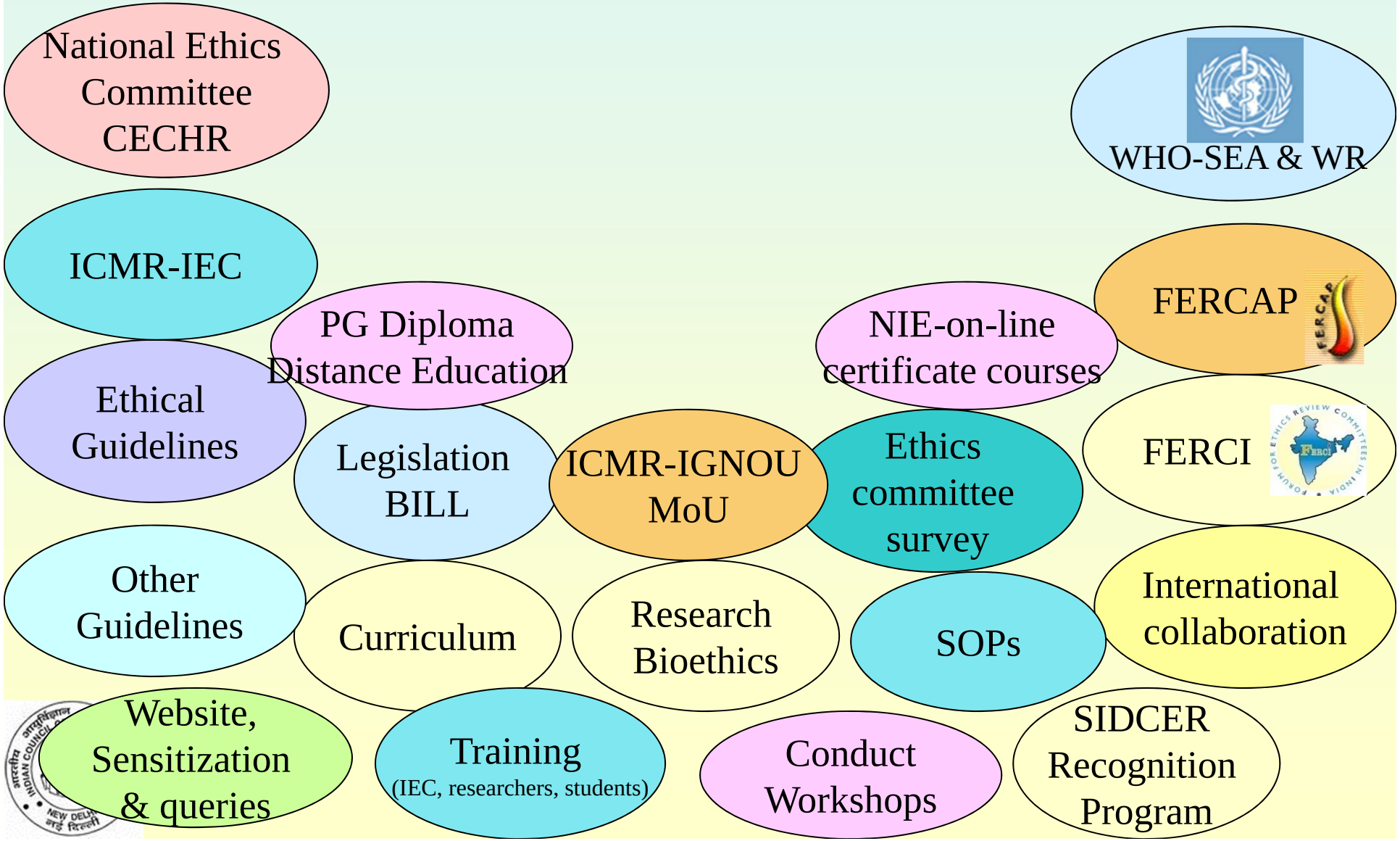


2006



2014

BIOETHICS ACTIVITIES



Capacity Building

ICMR has partnered with various agencies/ organizations

- FERCAP Courses
- FERCI
- SIDCER Recognition Program
- WIRB Long Term Training
- NIH preparation of curriculum & training
- WHO-SEARO
- WHO-WR
- IGNOU Distance Education
- AIIMS- CREATE (Clinical Research Advancement Towards Excellence)
- AYUSH
- Various other Institutions/ medical colleges, Universities, hospitals (One-three day WSs)

Challenges Today

- Rights, welfare, safety of participants
- Regulatory uncertainty
- Investigator concerns
- Ethical concerns
- Protection of Vulnerable
- Privacy and Confidentiality
- Conflicts of Interest
- Societal concerns
- Clinical Trials
- Ethics Committee review
- Bioethics Education
- Specific Guidelines

Thank you

Code of Ethics

Encourage respect for the law and the administration of justice;

Observe rules governing privileged communications and confidential information;

Promote and exemplify high standards of loyalty, cooperation and courtesy;

Perform all duties of the profession with integrity and competence;

and

Pursue a high order of professional attainment.