Ethical Issues in Clinical Research:
Informed Consent and IRBs

Dr. Urmila Thatte
Prof. and Head
Dept. of Clinical Pharmacology
TNMC & BYL Nair Hospital
Participants in Clinical Research

- Regulators
  - Sponsor
  - Monitor
- Patient/Society
- Institute
- Investigator
- Ethics Committee
- Administrator
Right of the human subject to understand

- the *nature* of research,
- *risks & benefits* involved
- to *agree* or *not agree* to participate.
"Medical experiments of the 20th Century"

Sea Water Experiments

High Altitude Experiments
The Declaration of Helsinki
1964

Adopted by the 18th World Medical Assembly
Revised 5 times
Latest version 2000, Edinburgh, Scotland
32 principles

Para 13: protocols must be submitted to an Ethics Committee for review, which must be independent of the investigator, the sponsor or any other kind of undue influence.
The Belmont Report

Ethical Principles and Guidelines for the Protection of Human Subjects of Research

The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research

April 18, 1979
Basic Principles of Ethics

- Autonomy
- Justice
- Beneficence
- Non-malfeasance

- Informed Consent
- Equitable Selection
- Protocol
- Protocol

Ethics Committee Oversight
ICMR Ethics Guidelines

- Released in 2000; second version 2006-07
- Guidelines on website http://www.icmr.nic.in
- To be legislated - The Biomedical Research on Human Subjects (Promotion and Regulation) Bill, 2007
2001 Indian GCP

2005 Schedule Y of Drugs and Cosmetics Act Amendment: pertinent to clinical trials
“The Twin Pillars of Protection”

Rights and Welfare of Human Subjects

Independent Review

Informed Consent
Informed consent

- Consent given by a **competent** individual who
- Has **received** the necessary **information**
- Has **understood** the information
- And having understood the information has **arrived** at a **decision** without having been under any coercion, undue influence or inducement or intimidation
Informed consent

- **Written**
- **Voluntary**
- from **every** subject
- **before** any study related procedure
- and **documented** on EC approved form
- adhere to GCP, based on Helsinki Declaration
Informed Consent: Children

- Approval of older children: understand the concepts: *assent*
- Consent from parents/legally acceptable representative
“The Twin Pillars of Protection”

Rights and Welfare of Human Subjects

Independent Review

Informed Consent
Composition of the EC

A *reasonable* number of members who *collectively* have the qualifications and experience to review and evaluate the *science, medical aspects and ethics* of the proposed trial.
What does an EC do for Clinical Research?

- Before the study begins:
  - Submission of research proposal
  - Review of proposal
  - Decision making process
  - Issuing an approval
  - Record keeping
During the study:

- Review of amendments (Protocol, ICD)
- Review of Serious Adverse Events
- Protocol deviations
- Progress (study status)
- Record keeping
What does an EC do for Clinical Research?

» After the study:
  - Study report,
  - Post trial management
  - Publishing
  - Record keeping
Criteria For Approval

- Suitability of Investigator
- Suitability of Protocol
- Equitable Selection Of Subjects
- Time management
- Confidentiality of subjects and data
- Informed consent process
Some Issues .....
What requires Ethical Clearance?

- Retrospective studies
- Studies on nutraceuticals/diets
- Surgical procedures, devices, radiation and imaging
- Student’s thesis
- Phase IV studies
- Medical records/HP slides
- Samples of body fluids which will be discarded
- Embryos, stem cells
- Epidemiological, social and psychological studies

Drug studies sponsored by pharmaceutical companies
What studies to submit to the Ethics Committee?

WHO is a research participant?

The human participant is a living individual about whom a researcher obtains either:

1. data through intervention or interaction with the individual; or

2. identifiable private information.
What studies require Ethics Committee Clearance?

Research involving

1. tissue specimens, medical records, genetic material, behavioral and/or biomedical assessments, and treatments.
2. cells, blood or urine, tissues, organs, and hair or nail clippings, even if the researcher did not collect these materials.
3. residual diagnostic specimens, including specimens obtained for routine patient care that would have been discarded if not used for research.
What studies require Ethics Committee Clearance?

Research involving

4. Private information, such as medical data, that can be readily identified with individuals, even if the information was not specifically collected for the study in question.

5. Research on cell lines or DNA samples that can be associated with individuals falls into this category.
Regulatory Clearance?

- DCGI permission for Phase 1-3 studies
- **Definition of a “new drug”** – new indication/new route of administration/new dosage form
- Sending samples abroad: DGFT, MOH (ambiguity: “collaborative”)
- Biotech products: multiple agency approvals
- **Devices??????**
WHY are you looking at the science?

- Incomplete protocols only CRF submitted
- Safety emphasis is low: interim analysis, lab tests
- No controls: level of evidence very low
- “Me-too” studies
- Efficacy and failure end points not specified

Poor science is poor ethics
Special Considerations

- Vulnerable populations
- Commercialization of research results
- International collaborations: protection of IPR, rights of patients and investigators
- Multi-centric studies
- Standard of care for controls
- Use of Placebo
Investigator

- Multiple studies: conflict of interest and bias in allocation
- Qualifications and expertise
- Communication between Investigator and EC: Skills of the Secretary!
- Continued communication during trial
Subjects in Study

- Incentives?
- Management of trial related injury
- Advertisements/recruitment methods
- How will the patient be looked after the end of study?
- Methods for retention of patients
Consent Forms

- Generic forms used
- Size of the consent forms, vernacular – meaning
- Language
- Is the modified, approved version being administered?

Incorrect documentation
Permissions

- Retrospective permissions!!!!
- Expedited reviews
- Content of the permission letter
Herbal/Traditional Medicines

- Need for Ayurveda specialist as co-investigator
- Regulatory clearances: confusions
Research has been called a good business, a necessity, a gamble, a game. It is none of these, It is a state of the mind

Martin H. Fischer