Basics for EC Members

Pharmawisdom Consultant 2013

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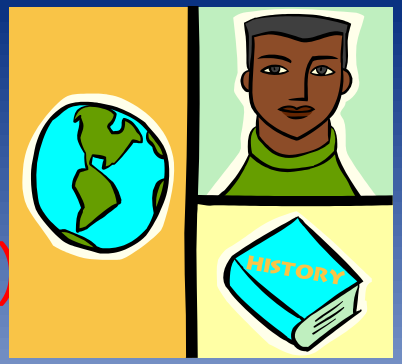
History of Research



- Nazi Medical War Crimes (1939–1945)
- Tuskegee Syphilis Study - Alabama
  - The study was stopped in 1973 by the U.S. Department of Health, Education, and Welfare only after its existence was publicized and it became a political embarrassment. In 1997, President Clinton apologized to the study subjects and their families
- 1963 -- Brooklyn - Jewish Chronic Diseases Hospital:
  - Cancer cells were injected into debilitated elderly patients to see if they would immunologically reject the cells.
- 1972 - Willowbrook State Hospital in New York:
  - Retarded children were deliberately infected with viral hepatitis to study its natural history.

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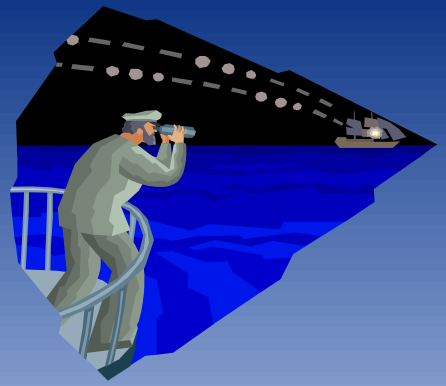
Nuremberg Code



- The Nuremberg Code
  - Voluntary informed consent
  - Likelihood of some good resulting based on prior research (animal models)
  - Avoidance of physical or psychological injury or harm
  - Benefits should outweigh risks
  - Proper experience of researcher
  - Right to withdraw consentResearch must stop if harm is resulting

(no specific mention of children, unconscious people, or others who may not be competent to give consent)

Helsinki Declaration

- The World Medical Association (WMA) has developed the Declaration of Helsinki as a statement of ethical principles for medical research involving human subjects, including research on identifiable human material and data. The first version was adopted in 1964 and has been amended six times since, most recently at the General Assembly in October 2008. The current (2008) version is the only official one.
- Still the controversy about use of placebo and post-trial access of medication,as described in it, is being debated

Other International Guidelines

- 1982 - International Ethical Guidelines for Biomedical Research Involving Human Subjects by World Health Organization (WHO) and Council for International Organizations of Medical Sciences (CIOMS)
- This 2002 text supersedes the 1993 Guidelines. It is the third in the series of biomedical-research ethical guidelines issued by CIOMS since 1982. Its core consists of 21 guidelines with commentaries.

Ethical principles– Belmonte Report

1979 report called the *Belmont Report,* is named after the Commission's Chairperson,

Identified three basic principles of research involving humans:

- Respect for persons
- Beneficence
- Justice

These three principles correspond to the fundamental requirements for ethically acceptable research:

- Consent that flows from the principle of respect for autonomy;
- Appropriate risk-potential benefit ratio that flows from the principle of beneficence;
- Equitable selection of research participants that flows from the principle of justice

IRB vs IEC

- Institutional review Board
- Members attached to the institution
- Meetings held in institution
- Review projects from that institute only, unless specified in SOPs
- Fees may not be charged unless sponsored

- Independent Ethics Committee
- Members from > one organisation
- Venue decided by members
- Review projects for any organisation, or individual
- Charge a fee for review

Composition ICH

- The IRB/IEC should consist of a reasonable # of members, who collectively have the qualifications and experience to review and evaluate the science, medical aspects, and ethics of the proposed trial. It is recommended that the IRB/IEC should include:
  - At least five members.
  - At least one member whose primary area of interest is in a nonscientific area.
  - At least one member who is independent of the institution/trial site.
- Only those IRB/IEC members who are independent of the investigator and the sponsor of the trial should vote/provide opinion on a trial-related matter

Composition FDA

IRB Membership (21 CFR 56.107)

- At least five members of varying backgrounds. Sufficiently qualified
- Not solely of one profession
- Gender diversity
- At least one non-scientist and one non-affiliated member
- Expertise with “vulnerable populations” if the IRB reviews research involving these populations
- Outside consultants as needed

Conflicted person does not need to leave the room but can’t vote: minutes should reflect that they did not vote!

FDA does not prohibit compensation/payment for IRB members although it should not be contingent on approvals

Composition Sch Y

- The quorum of EC should be at least 5 members
  - basic medical scientists (preferably one pharmacologist).
  - clinicians
  - legal expert
  - social scientist / representative of non-governmental voluntary agency /philosopher / ethicist / theologian or a similar person
  - lay person from the community.
- At least one member (**non scientific background**) and at least one member who is **independent of the institution** / trial site.
- Appropriate **gender** representation
- **Subject experts** may be invited if necessary.
- For special research areas, e.g. HIV AIDS, genetic disorders etc. **specific patient groups** may also be represented in the EC
- Only those Ethics Committee members who are independent of the clinical trial and the Sponsor of the trial should vote / provide opinion in matters related to the study.

Composition GCP Guidelines CDSCO

- EC should be multidisciplinary and multi-sectorial
- The number of members -(5-7 members). Corum = 5
  - 1. Chairperson preferably not from the institution
  - 2. 1-2 basic medical scientists (preferably one pharmacologists).
  - 3. 1-2 clinicians from various Institutes
  - 4. One legal expert or retired judge
  - 5. One social scientist / representative of NGO/ volunt agency
  - 6. One philosopher / ethicist / theologian
  - 7. One lay person from the community
  - 8. Member Secretary
- EC can have, individuals from other institutions or communities. There should be adequate representation of age, gender, community; Members should be aware of local, social and cultural norms, as this is the most important social control mechanism. If required subject experts could be invited to offer their views.
- **Very similar to ICMR**

Roles & responsibilities - Chairman

The chairperson is responsible for the overall proper functioning of the EC. The chairperson plays a significant role in the deliberations, often acting as **the facilitator or mediator** of discussions that take place during the evaluation of a given research project.

Rules of deliberation

- Listening and openness;
- Expressing one's opinion;
- Taking all factors into consideration;
- Reaching out for those who don't participate in discussion;
- Highlighting discrepancies and analyzing them;
- Helping the group to progress

Roles & responsibilities - Members

- All members - ethical evaluation of the project, & based on their expertise can contribute in other areas
- Community members - provide a value base beyond that of the institution, of researchers or of experts.
- Member knowledgeable in ethics - additional expertise that helps to identify and address ethical issues.
- Member knowledgeable in law - legal implications of research and protects the research participants' interests, but does NOT provide formal legal opinions for the EC.
- Although members contribute differently, collectively they all have the common role of protecting research participants.

Roles & responsibilities - Secretary

- Secretary has a major administrative role that includes but is not limited to:
  - developing agendas,
  - sending documents to the EC members,
  - preparing minutes of all meetings,
  - and preparing correspondence.

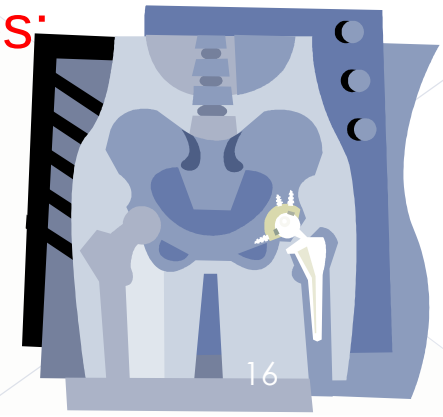
- Secretary maintains EC records including a database of research projects and the number of participants involved in each project.
- Secretary in collaboration with the Chairman also prepares the annual report

Standard Operating Procedure

- The SOPs address the evaluation of research projects and their activities, the transparency of the process, the protection of persons and functions of the EC

SOPs must at least contain norms pertaining to the following :

- Protection of persons;
- Mandatory declaration of research activities;
- Management of cases of scientific and ethical misconduct;
- Management of conflict of interests, double remuneration, and incorporation of researchers;
- Financial management of research and costs of research activities;
- Management of databanks and research files;
- Control of experimental drugs; and
- Functioning of the EC.



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Functioning – documents to be screened

In practice, as a minimum, this list usually includes:

- Submission form, dated and signed by the researcher
- Proposed project
- Any documentation that is to be presented or given to prospective participants (e.g., questionnaires, participants' agenda)
- all pertinent information on the agent or device regarding safety profile, and toxicities (e.g. investigator brochure, publications)
- Recruitment strategies and Informed Consent procedures The consent document
- In addition. the EC can ask to review any document it sees as relevant to the ethical acceptability of any project

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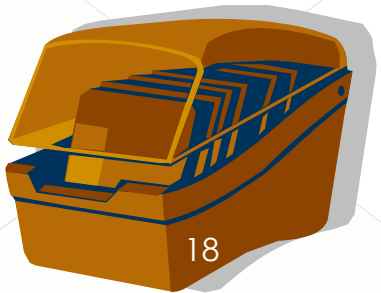
Record keeping

WHO (section 10) provides a list of documents that should be filed and archived that include, but are not limited to:

- The EC's constitution, written SOPs, and regular (annual) reports;
- The curriculum vitae of all EC members;
- The published submission guidelines established by the EC;
- Agendas and minutes of the EC meetings;
- One copy of all materials submitted by an applicant;
- Correspondence to researchers or concerned parties regarding application, decisions, advice or requirements and follow-up;
- All written documentation received during the follow-up;
- The notification of the completion, premature suspension, or premature termination of a study; and
- The final report of the research project.



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Expedited reviews

- The following could undergo expedited review:
- Research protocols that involve no more than minimal risk;
- Annual review of approved projects in which there has been little or no change in the ongoing research;
- Research involving review of patient records by hospital personnel;
- Affirmations that conditions laid down by the EC as condition of approval have been met.

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Appeals of EC decisions

- In order to make the decision making process fair & impartial, the EC should allow researchers to reply to unfavourable decisions
- There should be a provision to review the decision through an appeals committee from same or other institution
- The researcher can submit to another EC but ideally it should inform that there was rejection for specified reasons

Thanks