Research Ethics
Part II

Module 3 Topic 2

Ethics Committee

The Declaration of Helsinki- 1975
First proposes IRB/IEC

The design and performance of each experimental procedure involving human subjects should be clearly formulated in an experimental protocol which should be transmitted to a specially appointed independent committee for consideration, comment and guidance.

DOH (1975)

Institutional Ethics committee

The National Research Act 1974

- "Sec. 474. (a) The Secretary shall by regulation require that each entity which applies for a grant or contract under this Act for any project or program which involves the conduct of biomedical or behavioral research involving human subjects submit in or with its application for such grant or contract assurances satisfactory to the Secretary that it has established (in accordance with regulations which the Secretary shall prescribe) a board (to be known as an 'Institutional Review Board') to review biomedical and behavioral research involving human subjects conducted at or sponsored by such entity in order to protect the rights of the human subjects of such research."

Ethics Committee (Institutional Ethics Committee)

- An IEC should safeguard the rights, safety and well being of all trial subjects.
- Special attention should be paid to trials that include vulnerable subjects.

The IEC

- Every Institute involved in clinical research shall have its own IEC
- The IEC shall have a roster of Membership
- The IEC shall have a set of Standard Operating Procedures
- The IEC shall review all research proposals and maintain records of the same.

Responsibilities of the IEC

- Contribute to the continuing definition of the organization's standards and procedures.
- Assume responsibility for overall compliance with those standards and procedures.
- Oversee the use of due care in delegating discretionary responsibility.

Responsibilities

- Communicate the organization's standards and procedures, relating to clinical research and ensuring the effectiveness of that communication.
- Monitor and audit compliance.
- Oversee enforcement, including the assurance that discipline is uniformly applied.
- Take the steps necessary to ensure that the organization learns from its experiences.

Responsibilities

- Ensure that the research proposal fulfils the three principles as laid down in the Belmont Report-
- Autonomy
- Beneficence
- Non-malfeasance
- Justice

Responsibilities

- Approve and permit continuation of studies which:
  - Are scientifically sound.
  - Protect the rights of subjects
- Ask for modification in submitted studies if required.
- Reject proposals which violate any rights of subjects

Responsibilities

- Grant waivers to studies from:
  - IEC review
  - Full board review
  - Informed consents
  - Relaxation of inclusion exclusion criteria
  - Protocol violations
- Report SAEs to regulators
- Recommend compensation for injuries/death.

Autonomy

- Vulnerability of subjects
- LAR
- Impartial witness
- The third parties chosen should be those who are most likely to understand the incompetent subject's situation and to act in that person's best interest.

Beneficence

- Do good for people
- The IEC ensures that the trial is in benefit of the subjects
- That the benefits to the subjects are maximized and the risks minimized.
- Some risks are inherent to trials, balance the possibility of risk and benefits.

Justice

Equal distribution of burden and benefit

(1) to each person an equal share,

(2) to each person according to individual need,

(3) to each person according to individual effort,

(4) to each person according to societal contribution, and

(5) to each person according to merit.

Appointment

- The head of the institute shall appoint the members of the Ethics Committee
- During appointment the terms of office are clearly spelled out.
- Letters of appointment and consent letters from members are a part of the IEC documents
- The letter of appointment spells out the role and responsibilities of the members.

Composition of the IEC

- The IEC shall have a reasonable number of members who collectively have the qualifications and experience to review and evaluate the science, medical and ethics of the proposed trial.
- (An unscientific trial is always unethical though every scientific trial is not ethical)
- The IEC has a minimum of five members (seven in India)

Composition of the IEC

- Clinicians who can understand the science of trials.
- Members shall not be solely of one gender (at least one woman)
- At least one member who is a lay person (non scientific)
- At least one member who is not affiliated to the institute (nor is in any way related to an employee or functionary of the institute)

Composition of the IEC

- Indian rules:
- The chairperson of the IEC shall not be from the institute
- There shall be a representative of the legal profession
- There shall be a social worker/NGO representative
- There shall be a theologist/philosopher/member of a religious order.
- One clinician and one basic medical scientist (MD in pharmacology).

Chairperson of IEC

- An eminent person who is able to guide and add value to the deliberations of the committee
- Under Indian Laws shall not be a member of the Institute
- The Chairperson is responsible for the conduct of the meetings, and the decisions taken
- The Chairperson is authorized to demand interim reports from the investigators

Chairperson

- The Chairperson is authorized to decide about the type of review that needs to be conducted for a particular protocol.
- In case of dispute the Chairman may decide to put the issue to vote.
- The Chairperson is responsible to ensure that members attend meetings regularly

Member Secretary (MS)

- MS is the administrator of the IEC
- Ensures maintenance of all records
- Circulates project proposals and trial related documents to all members prior to meeting
- Maintains minutes of the meetings
- Is over all in charge of the functioning of the IEC.

Non Scientific Member

- ICH and FDA rules mandate a non scientific person.
- Indian rules use the term “lay person” and at times “non scientific” person
- These terms are not synonymous, IECs should appoint intelligent non scientific persons (Chartered Accountant, retired Armed Forces Officer, Architects, Engineers etc)

Term of office

- Every member has a definite term of office
- At the end of the term the member may be reappointed
- In case the member resigns or leaves the IEC another member shall be nominated in his/her place.
- In case a member's attendance or performance is not satisfactory the chairperson may replace such a member.

Meetings

- The IEC shall hold regular meetings to consider proposals for trials
- Members of the IEC shall meet and discuss proposals before accepting or rejecting them
- IEC members shall ensure that they religiously attend meetings
- Failure to attend meetings should be taken seriously and members can be dropped for this.

Meetings

- Members with Conflict of Interest shall not discuss and vote.
- If a member of the investigation team is also the member of the IEC, he/she shall abstain from discussion when the project is discussed.
- The minutes of the IEC meeting shall specifically state that Dr. X, who is a part of the investigation team did not take part in discussing the project, nor did he/she vote on the project.

Powers of the IEC

- The IEC shall review research proposals put before it, for approval
- In certain circumstances the IEC may hold an expedited review of the proposal
- The IEC shall review all changes (other than administrative) to the protocol before the same are implemented.

Powers of the IEC

- The IEC is authorized to approve/recommend changes or reject a research proposal
- While giving its decision the IEC shall provide reasons for taking the action (esp. in case of rejection)
- The IEC shall review trials in progress and recommend their continuation (with or without changes) or even demand discontinuation.

Powers of the IEC

- The IEC is authorized to review all SAEs and demand additional data on SAEs. May recommend the discontinuation of a subject.
- The IEC is authorized to question PIs if the rights and well being of subjects is jeopardized.
- The IEC can question sponsors on adequacy of data and risk to subjects.

Academic Research

- Academic research projects need not go to DCGI for approval, EC approval is adequate.
- Addition of a new site/PI to an approved proposal can be granted by the EC, DCGI permission not required.
- Approval of a PI is now the prerogative of the EC.

Expedited Reviews

- When research involves minimum risk to subjects or the amendment to the protocol is minor in nature, it may be subjected to an expedited review.
- When the Chairperson agrees to an expedited review he/she may depute a senior member of the IEC to do so.

IEC Review

The IEC shall review the following documents:

1. Protocol
2. Informed Consent Forms (ICF) & Translations
3. Patient Information Brochure (PIB)
4. Clinical Trial Agreement
5. Insurance policies covering the trial
6. Investigator's Brochure
7. Materials used for patient recruitment
8. Any other material required to take a decision

IEC Review

- The IEC may demand
- The resumes of the investigators
- Additional data on the investigational product
- Details of methods of patient procurements
- Details of payments to be made to patients
- Probe conflict of interests of investigators

Records

- The IEC shall maintain a copy of all research projects received for approval.
- The IEC shall maintain all correspondence with investigators
- The IEC shall maintain a roster of membership
- The IEC shall maintain a copy of minutes of every meeting held

SOPs

The IEC shall have SOPs covering the following:

1. Membership
2. Documents required for review
3. Procedure for receipt and review of proposals
4. Procedure for disposal of proposals
5. Procedures for expedited reviews

Sponsor and IEC

- The sponsor is responsible to ensure that the selected site has an IEC compliant with regulatory requirements and that the IEC is registered with CDSCO
- Sponsor should collect IEC roster and satisfy himself that the IEC is compliant with all requirements.

Regulations

- All IECs functioning in India must be compliant with the rules laid down in New drug rules 2019
- If the projects are funded by or are on products to be registered in the US the IEC must be compliant with 21 CFR part 56.

IEC Approval

- The IEC in its approval letter must mention the following:
- Protocol title, version and date
- ICF version and date
- All documents with version and date
- Members who reviewed the above documents
- Members who voted/did not vote
- Clear cut decision of the IEC

Trial related injury

- All SAE (injuries) should be managed at the cost of the sponsor for as long as required.
- If SAE is considered as due to trial drug or procedure, financial compensation will be paid to subject (or nominee) in addition to medical management.
- Chairman and IEC to recommend amount of compensation.

New Clinical Trial rules 2019

- CT to be in compliance to new drug rules and CDSCO GCP
- CT should be approved before beginning a study.
- CT sites, sponsors and CRO should allow inspections and audits by regulators.
- In case of violations, regulators may stop trials and blacklist sponsors or CRO or site.

New Clinical Trial rules 2019

- No trial shall begin unless approved by an Institutional Ethics Committee registered with the CDSCO
- Institutional Ethics Committees will be allowed to approve Clinial studies and BA/BE studies, and continuation of any study approved in the past.
- Ethics Committee on Biomedical research will approve non interventional studies not involving medications

Ethics Training

- Available from NIH – Online Certification
- Go to http://phrp.nihtraining.com

Click register and complete registration form to go to NIH Training and certification test.
A free, Web-based course developed at the National Institutes of Health for physicians, nurses, and other members of clinical research teams. This online course satisfies the NIH human subjects training requirement for extramural researchers obtaining Federal funds.

Quis custodiet ipsos custodes?

-Juvenal

Who will guard us from the guards?

QUESTIONS ?

E mail me @

ravindra.ghooi@gmail.com

9922918967