



Institutional Review Boards (IRB) and Their Requirements

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For CALGB Participants Only

Overview

- Why do we have IRBs?
- What is involved (definitions and CFR)?
- When do we obtain IRB approval?
- What do we do with approvals?
- When is our IRB activity audited?
- What is the Central IRB?
- Tips
- Resources

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Why Do We Have IRBs?

- Brief history
- Mandate of IRBs
- Definitions

The Right to Say “No”

- Nuremberg Code of 1946
- Ten code requirements were developed for human subject trials

The Right to Say “No”

- Belmont Report of 1979

The Belmont Report

- April 1979 - Belmont Report
- Summarizes basic ethical principles and guidelines to assist in resolving ethical problems of research involving human subjects. It was a statement of the DHHS policy.

The Belmont Report

- Three basic ethical principles:
 - 1) Respect for persons
 - 2) Beneficence
 - 3) Justice

The Belmont Report

- **Beneficence:** Actions do not harm (The Hippocratic Maxim) and the rule to maximize possible benefits and minimize possible harm.
- Justice
- Fairness in distribution.

The Belmont Report

- Informed Consent
- Assessment of risks and benefits
- Selection of subjects

Mandate of IRBs

The major mandate of IRBs is to *protect the rights and safeguard the welfare of research participants*

- *Prospective review of research activities involving human subjects*
- Continuing review
- Review of research-related activities on an ongoing basis, especially *adverse events*

All research involving human subjects must be reviewed and approved by the IRB prior to initiation of the project.

Definitions

- Office for Human Research Protections (OHRP), formerly OPRR, under the Department of Health and Human Services
- *...will monitor programs for the protection of human subjects at institutions who receive NIH funding for research.*

Definitions

- Institutional Review Board (IRB)
- *... any board, committee, or other group formally designated by an institution to review, approve the initiation of, and conduct periodic review of, biomedical research involving human subjects.*
 - » (21 CFR 56.102)

IRB Membership

(21 CFR 56.107)

"Each IRB shall have at least 5 members, with varying backgrounds to promote complete and adequate review of research activities commonly conducted by institutions."

Definitions

Subjects

. . . a human who participates in an investigation, either as a recipient of the investigational new drug or as a control. A subject may be a healthy human or a patient with a disease.

(21.CFR 312.3(b))

What is Involved?

Code of Federal Regulations

Code of Federal Regulations

- **The CFR** (*Our Research Bible*):
 - Federal regulations for IRBs, sponsors, investigators, and research institutions come from the Code of Federal Regulations (CFR)

IRB Records

(21 CFR 56.115)

- An IRB shall prepare and maintain adequate documentation of IRB activities, including the following:
 - Copies of all research proposals reviewed.
 - Copies of all correspondence between the IRB and the investigators.

IRB Records

(21 CFR 56.115)

- Detailed minutes of IRB meetings to show attendance at the meetings; actions taken by the board; the vote on these actions including the number of members voting for, against, and abstaining.
- Records of continuing review of activities.

Criteria for IRB Approval of Research (21 CFR 56.111)

- In order to approve research covered by these regulations, the IRB shall determine that all of the following requirements are satisfied:
 - Risks to subjects are minimized:
 - By using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk.
 - Whenever appropriate, by using procedures already being performed on subjects for diagnosis or treatment purposes.
 - Risks to subject are reasonable in relation to anticipated benefits.

Criteria for IRB Approval of Research (21 CFR 56.111)

1. Selection of subjects is equitable.
2. Informed consent will be sought.
3. Informed consent will be appropriately documented.

Suspension or Termination of IRB Approval of Research *(21 CFR 56.113)*

An IRB shall have authority to suspend or terminate approval of research that is not being conducted in accordance with the IRB's requirements or that has been associated with unexpected serious harm to subjects.

When Do We Obtain IRB Approval?

- Before the initiation of any research activity
- Updates or changes to the study or consent
- At least annually
- Serious Adverse Events (SAE) and External IND safety reports (ESAER)

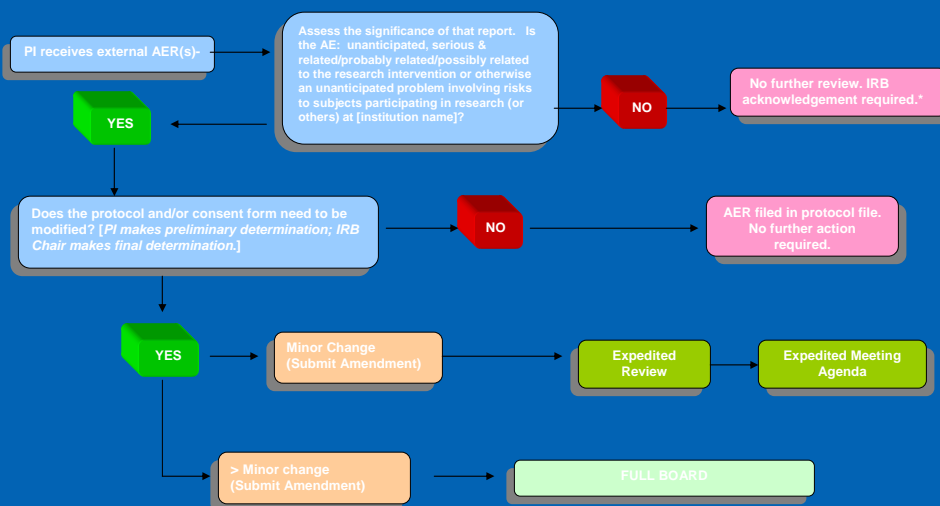
ESAER

- Once the CALGB Central Office posts the ESAER, the **90-day** clock starts ticking for required IRB acknowledgement.
- Local PIs should triage the ESAER reports to determine which need full board IRB review vs. IRB acknowledgement according to local IRB policies.

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REVIEW OF EXTERNAL ADVERSE EVENT REPORT FLOW CHART



Documentation of an established IRB policy regarding criteria for non-review may serve in lieu of an acknowledgement in some cases.

What Do We Do With Approval?

- Fax to Cancer Trials Support Unit (CTSU):
 - Initial approval prior to any registration + consent
 - Required amendments for continued enrollment + consent when applicable
 - Annual reviews of active studies
- Fax the approvals along with a CTSU transmittal sheet and certification form to (215) 569-0206.

CALGB Audits of IRB

- IRB is one of 3 main audit categories
- Auditors will review:
 - Initial approval
 - Consent content
 - All required IRB amendments
 - All required consent changes
 - Annual Reviews of active and closed studies with patients on follow up
 - Adverse event approvals and ESAERs

What Is The Central IRB?

- Sponsored by the NCI for cooperative group projects
- Approval replaces the need for local IRB approval
- The CIRB becomes the “IRB of record”

Tips to Maintain Complete IRB Records

- Keep copies of all submissions to and from the IRB including attachments.
- Use cover letters to clearly identify all documents being submitted to the IRB.
- Document all contacts with IRB – “get it in writing.”
- Use tickler files/flow sheets/tracking logs.
- Request more detail in approval notices if needed.
- Organize your files.

Tips to Facilitate the IRB Process

- Know the IRB submission deadlines.
- Know IRB Adverse Event reporting rules.
- Obtain a copy of IRB rules and guidelines.
- Periodically review file for completeness.
- Maintain rapport with IRB Administrator and staff.

General Resources

- OHRP Web Site
<http://ohrp.osophs.dhhs.gov/index.htm>
 - Belmont Report (ethical principles)
 - IRB Guidebook and Investigator 101 CD
 - Training Videotapes and Workshops
 - Common Findings in Noncompliance
 - Links to Other Web sites

General Resources

- CTSU Web Site
 - www.ctsuo.org
- CIRB Web Site
 - www.ncicirb.org

