HUMAN SUBJECTS
RESEARCH
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Timeline of historical key events

Development of human research regulations
  - Belmont Report
  - 45 CFR 46

Purpose of the Institutional Review Board (IRB)

Structure of the IRB Committee

Activities that require IRB review
  - QI-activities vs QI-research

Levels of IRB review
  - Definition of “Minimal Risk”

Submission of an IRB Application
  - Common submission errors

Post Approval Investigator Responsibilities
  - Common compliance issues

Q&A
BELMONT REPORT
Ethical Principles for Research

BELMONT PRINCIPLES

- RESPECT FOR PERSONS
  - Individual autonomy
  - Protect those with diminished capacity

- BENEFICENCE
  - Do no harm
  - Maximize benefits
  - Minimize harms

- JUSTICE
  - Fairness in distribution of burdens & benefits

CRITERIA FOR IRB APPROVAL

- Minimize Risk
- Risk to Benefit Ratio
- Equitable Selection of Subjects
- Written Informed Consent (or waiver)
- Obtain Informed Consent
- Ensure Privacy and Confidentiality

Minimize Risk

Risk to Benefit Ratio

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I. IRB Organization

1. What is an Institutional Review Board (IRB)?

Under FDA regulations, an IRB is an appropriately constituted group that has been formally designated to review and monitor biomedical research involving human subjects. In accordance with FDA regulations, an IRB has the authority to approve, require modifications in (to secure approval), or disapprove research. This group review serves an important role in the protection of the rights and welfare of human research subjects.

The purpose of IRB review is to assure, both in advance and by periodic review, that appropriate steps are taken to protect the rights and welfare of humans participating as subjects in the research. To accomplish this purpose, IRBs use a group process to review research protocols and related materials (e.g., informed consent documents and investigator brochures) to ensure protection of the rights and welfare of human subjects of research.

IRBs and Assurances

Registering an institutional review board (IRB) and obtaining a Federalwide Assurance (FWA) are related but separate processes.

- An institution must have an FWA in order to receive HHS support for research involving human subjects. Each FWA must designate at least one IRB registered with OHRP.

- Before obtaining an FWA, an institution must either register its own IRB, (an "internal" IRB), or designate an already registered IRB operated by another organization, (an "external" IRB), after establishing a written agreement with that other organization.

- An IRB is a committee that performs ethical review of proposed research.

- A graphic summarizing the decision sequence can be seen and printed in PDF format here - PDF, and is available in text form here.

- Other federal departments and agencies that conduct or support human subjects research permit use of the FWA as the assurance required by their regulations.
  - Some require use of their own assurance for research not appropriate for an FWA

§ 107.107 IRB membership.

(a) Each IRB shall have at least five members, with varying backgrounds to promote complete and adequate review of research activities commonly conducted by the institution. The IRB shall be sufficiently qualified through the experience and expertise of its members (professional competence), and the diversity of its members, including race, gender, and cultural backgrounds and sensitivity to such issues as community attitudes, to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects. The IRB shall be able to ascertain the acceptability of proposed research in terms of institutional commitments (including policies and resources) and regulations, applicable law, and standards of professional conduct and practice. The IRB shall therefore include persons knowledgeable in these areas. If an IRB regularly reviews research that involves a category of subjects that is vulnerable to coercion or undue influence, such as children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons, consideration shall be given to the inclusion of one or more individuals who are knowledgeable about and experienced in working with these categories of subjects.

(b) Each IRB shall include at least one member whose primary concerns are in scientific areas and at least one member whose primary concerns are in nonscientific areas.

(c) Each IRB shall include at least one member who is not otherwise affiliated with the institution and who is not part of the immediate family of a person who is affiliated with the institution.

(d) No IRB may have a member participate in the IRB's initial or continuing review of any project in which the member has a conflicting interest, except to provide information requested by the IRB.

(e) An IRB may, in its discretion, invite individuals with competence in special areas to assist in the review of issues that require expertise beyond or in addition to that available on the IRB. These individuals may not vote with the IRB.
Research is as a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.

A human subject is as a living individual about whom an investigator conducting research obtains (1) data through intervention or interaction with the individual; or (2) identifiable private information.
**QI Activities**

- **INTENT**
  - Specific to improving the performance of institutional practice in relationship to an established standard; *aimed at improving local systems of care (non-generalizable / not widely applicable)*; i.e., promote the betterment of a process of care, clinical outcome, etc
  - There are no additional risks/burdens beyond the standard practice
  - Does not involve randomization, nor (an) element(s) that may be considered less than standard of care

- **LEVEL OF CARE**
  - *exception: 45 CFR 46.101(c)*

- **RISKS**

*Note: Publication must describe the activity as a *QI Project* (and not as “research”)*

DOI: 10.1177/1556264615575513
https://www.research.uci.edu/forms/docs/irb-forms/request-determination-non-human-subjects.doc
Levels of IRB Review

- **Exempt**
  - Less than “minimal risk”
  - Fits one of the 6 Exempt Categories*
  - Example: Research with de-identified records, anonymous surveys

- **Expeditied**
  - Not greater than minimal risk
  - Fits one of the 9 Expeditied Review Categories*
  - Examples: Collection of biospecimens by noninvasive means, Research with existing documents/record collected for non-research purposes in which subjects are identifiable

- **Full Board**
  - More than “minimal risk” to subjects
  - Not covered under other review categories
  - Example: interventions involving physical or emotional discomfort or sensitive data

*Defined by federal regulation (45 CFR 46)
(j) *Minimal risk* means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

[https://www.federalregister.gov/d/2017-01058/p-1352](https://www.federalregister.gov/d/2017-01058/p-1352)
SUBMISSION OF AN IRB APPLICATION

IRB SUBMISSION

- APPLICABLE SUPPORTING DOCUMENTS, APPENDICES, ANCILLARY COMMITTEE REVIEW
- CITI TRAINING (HIPAA TRAINING WHEN APPLICABLE)
- ONLINE APPLICATION (PRINT / SIGN)
- PROTOCOL NARRATIVE
- RECRUITMENT MATERIAL(S) (WHEN APPLICABLE)
- HIPAA AUTHORIZATION FORM (WHEN APPLICABLE)
- CONSENT FORM (WRITTEN, ASSENT, VERBAL) (WHEN APPLICABLE)

Common IRB application errors

- Inconsistency in Documents
- Missing CITI Training
- Missing Ancillary Committee Review
- Missing Off Site Approvals
- Missing Other Documentations and Materials
- Incomplete Narrative and Consent Form
- IRB Submission Errors

POST APPROVAL INVESTIGATOR RESPONSIBILITIES

- Follow approved protocol
- Maintain records, per protocol
- When applicable, submit modification application
- When applicable, submit unanticipated problems report
- When applicable, submit continuing review application
- Upon completion of study, submit a closing report application

https://www.research.uci.edu/compliance/human-research-protections/researchers/lead-researcher-recordkeeping-responsibilities.html
https://www.research.uci.edu/compliance/human-research-protections/researchers/modification-to-approved-research.html
https://www.research.uci.edu/compliance/human-research-protections/researchers/continuing-review-process.html
Common IRB compliance issues

- Not following approved protocol
- Missing documentation/record keeping
- Post approval compliance issues
- Implementing unapproved procedures
- Not obtaining consent and HIPAA authorization
- Lapse in IRB approval
- Not reporting of unanticipated problems

https://www.research.uci.edu/compliance/human-research-protections/researchers/equip.html
RECOMMENDED BOOKMARKS

Human Research Protections

Guidance for Researchers

Applications & Forms
http://www.research.uci.edu/forms/index.html

IRB Calendar

HRP Staff Directory
http://www.research.uci.edu/compliance/human-research-protections/about-the-irb/hrp-contact-list.html
KEEP CALM AND ZOT ON