The IRB Process for Resident Research

Kimberly R. Barber, PhD
Genesys Regional Medical Center
AH Mid Michigan Region

Background of Human Protections

• Nuremberg Code
  • Developed from Nuremberg trials of Nazi war criminals
    – Included those involved in medical experiments
  • Principles
    – Voluntary consent
    – Freedom from coercion
    – Ability to withdraw at any time
    – Appropriate research design
    – Consideration of risk/benefit ratio
    – Qualified investigators

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Background, cont.

• Declaration of Helsinki
  • Developed by world Medical Assembly, Helsinki, Finland 1964
  • Research versus clinical care
  • Principles
    – Health of patient is first consideration
    – Well being of subject takes precedence over interests of science and society
    – Patient refusal to participate in research must never interfere with physician-patient relationship
    – Refers to ethical committees

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Tuskegee Syphilis Study, 1932-1972

• Purpose
  – Study progression of syphilis.
• Research population
  – 300 mostly indigent African-American sharecroppers in Macon County, Alabama.
  – Subjects did not know they were part of a study.
  – Thought they received beneficial medical care.
  – Were followed, untreated, many years after penicillin was known to cure syphilis.
• Results
  – Stopped in 1972 after high profile stories in national media generated public outrage.

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Development of Federal Regulations

- Congressional Hearings on the Quality of Health Care and Human Experimentation (1973)
  - Held in response to public concern about problems in way medical and social science research was conducted
- National Research Act passed (1974)
  - Required Dept. of Health, Education and Welfare to promulgate regulations for IRBs
  - Established National Commission for Protection of Human Subjects of Biomedical and Behavioral Research

Development of Federal Regulations, cont.

- 1974 – 1978 National commission for Protection of Human Subjects of Biomedical and Behavioral Research met:
  - Goal – clarify ethical guidelines applying to research on human subjects.
  - Issued the Belmont Report (1979).
## The Belmont Report - 1979

<table>
<thead>
<tr>
<th>Principle</th>
<th>Application</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respect for Persons</td>
<td>Informed Consent</td>
</tr>
<tr>
<td>Beneficence</td>
<td>Assessment of Risks &amp; Benefits</td>
</tr>
<tr>
<td>Justice</td>
<td>Equitable Selection of Subjects</td>
</tr>
</tbody>
</table>

These principles remain the basis for HHS human subject protection regulations.

*Informing a patient about research differs from informing them about a procedure.*

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## Institutional Review Boards (IRBs)

- **Committee makeup:**
  - Diverse membership
    - Scientific
    - Non-scientific
    - Non-affiliated
  - Reviews
    - Exempt
    - Expedited
    - Full
    - Continuing

- **Protect welfare by:**
  - Risks and benefits
  - Subject Selection
  - Informed consent
  - Privacy
    - Confidentiality
    - Anonymity
  - Conflict of interest
    - Address Potential

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Who has to obtain IRB approval?

- Anyone involved in a human subject research project who has contact with human subjects or their identifiable data.
- Scientific conference requirement for presenting.
- Scientific journal requirement for publication.

The IRB Process

- Proposal Submitted for Review.
  - Application
  - Data collection sheet
  - Consent form / Consent waiver
  - HIPAA Authorization / HIPAA waiver
- Committee makes determination.
- Modifications and revisions made.
- Letter of Approval provided.
- You can start your study.
Submission Items for Prospective Studies

• Prospective Study issues:
  – Individual risks and protections
  – Data protections
  – Protocol details
  – CONSENT
    • Obtaining
    • Informing

Prospective Issues

• Individual Harm / Risk
  – Physical
    • Is harm or risk increased from the intervention?
    • Is it greater than harm / risk from a typical blood stick?
  – Psychological
    • Mental health, mental stability, effects of deception?
    • Increased anxiety, anger, sadness?
    • Increased confusion?
Prospective Issues, cont.

• Address the harm / risk
  • Understand the potential for harm or risk:
    – Consult with faculty or an expert.
  • Acknowledge and describe the potential for harm or risk:
    – Physical, physiological, psychological (including deception).
  • Describe how the harm or risk will be mitigated:
    – Provide details on what you will do to avoid, minimize, or alleviate the harm or risk.

Prospective Issues, cont.

• Protocol Details
  – Identify the study team.
  – Study Population:
    • Define the broad group from which your subjects will be drawn.
  – Study Sample:
    • Define the specific group of subjects:
      – Inclusion criteria
      → Exclusion criteria
Prospective Issues, cont.

• Data Protections:
  – How will data be collected in a secure way?
    • Use secure systems.
    • Share with secure systems.
  – How will data be kept safe?
    • Use secure storage applications.
    • Share with minimal partners.
    • Keep hard copies locked up.

Prospective Issues: The Consent Process

• Consent Document:
  – Form
    • Details and explanations
      – Intervention, randomization, alternatives, voluntary, withdrawal, risks/benefits, HIPAA
    • Reading level
      – Simple and 6th grade level
  – Documentation
    • Witnessed and signed by all parties
    • Subject keeps a copy. Study copy kept for 3 years.
Prospective Issues: The Consent Process

• The Process of consenting:
  – The PI responsibility
    • To inform and secure patient understanding
    • Can be delegated [2-step process]:
      – PI introduces study
      – Other party explains study and provides the form and secures the signatures.
  – PI commitment to participants is to safeguard their interests throughout the study.
  – PI role in research consent differs from clinical consent.

Prospective Issues, cont.

• Risks / Benefit Balance:
  – Do individual benefits outweigh the harms?
    • If yes, explain how.
  
  – If no individual benefit:
    • Do benefits to science or society outweigh the individual risks?
Submission Items for Retrospective Studies

• Retrospective studies
  – Privacy protections
  – Data protections
  – Aggregate benefit

Retrospective Studies

• Privacy Protections:
  – De-identify any data that contains PHI
  – Assign study numbers for non-PHI data
    • Surveys, assessments, etc.
  – Master List

<table>
<thead>
<tr>
<th>Subject #</th>
<th>Patient Name</th>
<th>DOB</th>
<th>MR #</th>
</tr>
</thead>
<tbody>
<tr>
<td>001</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>002</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

– Data sheets will have only subject # and variables.
Retrospective Studies, cont.

• Data Protections:
  – How will data be collected in a secure way?
    • Use secure systems.
    • Share with secure systems. \textit{e.g.} Redcap
  – How will data be kept safe?
    • Use secure storage applications.
    • Share with minimal partners.
    • Keep hard copies locked up.

Retrospective Studies, cont.

• Risk / Benefit Balance:
  – Describe risks and/or inconveniences in relation to the potential benefits.
    – \textit{All research has risks. You don’t need to eliminate the risks, you do need to describe them.}
  – What are the benefits to science or society given the potential risk to privacy?
    – \textit{Describe how the benefits might outweigh the potential risks.}
Quality Improvement Projects

- Internal quality projects not need IRB.
- If publishing, journals expect an IRB determination.
- Submit for IRB letter of determination that it not need approval.

The IRB Submission Process

- Submission requirements
- Application requirements
- HIPAA requirements
- ClinicalTrials.gov
- Analytic Plans
Submission Requirements

- Human Protections training.
  - https://about.citiprogram.org
- CITI (Collaborative Institutional Training Initiative)
  - AH & MSU have accounts
  - Intense reading involved and long
- Certificate of Training:
  - Save copy to submit with application

Application Requirements

- Complete! Clear!
- No spelling or grammar errors.
- Application and other documents (e.g., consent) are consistent.
- Obtain signatures.

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Application Requirements, cont.

- **Background / Introduction Section:**
  - Rationale for the study
    - New or adds new information to medical field.
  - Reference the current literature
    - Other study findings suggest our proposal is needed.
  - Clinical relevance or importance
    - Patients or the medical field would benefit from the findings and why.

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Application Requirements, cont.

- **Methodology:**
  - Describe the protocol plan.
  - Provide details of the process.
  - Provide details of patient:
    - Identification
    - Enrollment
    - Consent.
  - Describe it so that a new person could pick up your protocol, implement the study, and get the same results that you would get if you did the study.

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Application Requirements, cont.

• Research Risks and Benefits
  – Describe benefits in relation to risks.
  – There are always risks with research!
    • Some are minimal but need to be addressed.
    • Privacy risks:
      – “Although minimal, there is a slight risk of loss of confidentiality”
  – Benefits may or may not be to the individual.
    • If not, describe benefits to society as a whole, to the scientific community, or to the medical field.

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Application Requirements, cont.

• Consent Process:
  – How consent is obtained:
    – Where patients will be approached.
    – How they are identified for consent.
  – Who will obtain consent:
    – Who will approach patients.
    – Who will explain study and consenting to patients.
    – Who will obtain consents.
  – What will be done with the consent forms:
    – Patient gets to keep a signed copy.
    – You keep copy in a secure file.
Application Requirements, cont.

• Plan of Analysis:
  – Sample size determination
    • Power calculation
      – Include estimate for number of subjects needed.
      – Survey rule of thumb
        » Not less than 100 up to 200.
  – Statistics
    • What statistic will be used to test your hypothesis.
    • What the primary outcome is.
    • What the independent / dependent factors are.
    • Other descriptive metrics.

HIPAA Requirements

• HIPAA Authorization
  • Obtain permission to use PHI from individual patients.
  • May be within consent form or a separate document.

• HIPAA Waiver
  • Request permission to waive HIPAA authorization.
  • Separate waiver form.
    – Sections describing why you not able to seek permission.
ClinicalTrials.gov Registration

• Requirement (FDAAA 801):
  – Intervenotional studies of FDA-regulated drugs, biological products, or devices that meet one of the following conditions:
    – Is done in the US.
    – Has an FDA#: IND or IDE.
    – Involves a drug, biologic, or device that is manufactured in the US.
  • Regardless of sponsorship or number of arms.
  • Otherwise it is N/A.

• Why Register?
  • Journals will not publish you if you don’t have the NCT# issued prior to enrollment.

'Continuing' Responsibilities

• Revisions
  • Obtain approval for changes before implementing them

• Renewals
  • Obtain renewal for your study before approval expires

• Unanticipated Problems and Adverse Events
  • Report those that may involve risks to subjects or others immediately to IRB

• Closures
  • Communicate completion of study to IRB

• Audits
  • Keep records for at least 3 years.