RESEARCH ETHICS, THE IRB & INVESTIGATIONAL DRUGS

Presentation for the Auburn University, Harrison School of Pharmacy Inpatient Pharmacotherapy Continuing Education Program

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Disclosure/Conflict of Interest

I, Bernie Olin, have no actual or potential conflict of interest in relation to this program.
Objectives

At the end of this presentation, the audience should be able to:

• Describe the foundation of the “Common Rule” and the Institutional Review Board (IRB).
• Apply the concepts and regulations for human drug research affecting medical/ drug research.
• List the updates on revisions to the “Common Rule” affecting medical/ drug research.
• Name at least three pharmacy-specific issues relating to research and the IRB.
Ethical Treatment of Subjects

• Nuremberg Code, 1949
  • Addresses the voluntary consent of human subjects
  • http://www.hhs.gov/ohrp/references/nurcode.htm

• Declaration of Helsinki, 1964 (rev. last 2004)
  • http://www.wma.net/e/policy/b3.htm

• U.S. Surgeon General policy statement, 1966
  • Origins of informed consent, IRBs

• National Research Act, 1974
  • Established the National Commission for the Protection of Human Subjects in Biomedical and Behavioral Research
  • Established the IRB through the CFR (45 CFR 46)

• Belmont Report, 1979
  • Further delineates ethical principles of medical research on human subjects
  • http://ohsr.od.nih.gov/guidelines/belmont.html

• Common Federal Policy for Protection of Human Subjects ("Common Rule")
  • 16 agencies adopt the regulations of 45 CFR 46 subpart A.
Ethical Treatment of Subjects (cont.)

• Belmont Principles
  • Respect for persons
  • Beneficence
  • Justice
Institutional Review Board (IRB)

• Definition
  • A committee of reviewers that evaluates the ethical implications of a clinical study protocol
    • At least five members
    • One member must be in a specialized scientific area (usually a physician)
    • One member must be a specialist in a nonscientific area (eg, law, ethics, religion)
    • One member must be nonaffiliated with the institution conducting the research
### Institutional Review Board (Auburn)

<table>
<thead>
<tr>
<th>Health/Biomedical Sciences</th>
<th>Social/Behavioral Research</th>
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<tbody>
<tr>
<td>Nurse (Chair)</td>
<td>Pharmacy (Chair)</td>
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<td>Physician (x2)</td>
<td>Psychology (x2)</td>
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<td>Communication Disorders</td>
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<td>Human Develop/Family Studies</td>
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<td>Sociology/Anthropology</td>
<td>Curriculum and Teaching</td>
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<td>Anatomy, Physiology, Pharmacology</td>
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<td>Community (x2)</td>
<td>Attorney</td>
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<td>Attorney</td>
<td>Prisoner Advocate (consultant)</td>
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Definitions: Research

• means a **systematic investigation**, including research development, testing and evaluation, designed to develop or contribute to **generalizable knowledge**.

• Activities which meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program which is considered research for other purposes.

• ...some demonstration and service programs may include research activities.
HUMAN SUBJECT

means a living individual about whom an investigator (whether professional or student) conducting research obtains:

• (1) data through intervention or interaction with the individual,

or

• (2) identifiable private information.
Human Subject (cont.)

Intervention
• includes both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.

Interaction
• includes communication or interpersonal contact between investigator and subject.
Private information includes information about:

(1) behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place

(2) information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, an educational or medical record).

Private information must be individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects.
Levels of IRB Review

• **Exempt** (from 45 CFR 46 Regulations)
  - Data are collected or recorded in anonymous fashion – includes pre-existing data

• **Expedited** – minimal risk studies (physical, emotional or social)
  - Data collected via survey, educational testing, or non-invasive procedures commonly conducted in medical exams
  - Data collected via new procedures where minimal risk can be substantiated and no higher than routine testing
  - Vulnerability of Participants must be considered (mental abilities, social situation, educational level, subjectivity to coercion)

• **Full Board** – risk is higher than that encountered in daily life and routine testing; also may include vulnerable subject populations
Criteria for IRB Approval

1. Risks have been minimized
2. Risk/benefit ratio favorable
3. Subject selection equitable
4. Informed consent
5. Adequate safety monitoring
6. Protection of privacy
7. Additional safeguards for vulnerable subjects
Investigator Expectations

• Specific training in human subjects protections
  • Collaborative Institutional Training Initiative (CITI)
  • National Institutes of Health (NIH) program

• Biomedical journals require proof of IRB review
Changes/Problems!?!?

• Required reporting of unanticipated problems.
• Any modification of protocol is required to be approved by the IRB.
• Protocols generally expire after one year. A renewal request must be submitted and approved.
  • Exempt protocols expire after three years.
• When study is completed, a final report is required.
• “At Risk” protocols may require a Data Safety Monitoring Committee and more frequent reporting.
Informed consent is a process, not just a form.
If interaction with subject occurs – must use informed consent process.
Signed written consent for any procedures or experimental work.
Wording must be clear and understandable; reading level appropriate for the audience.
Information letter may be used if conditions exist for waiver of signed consent.
Waiver of consent possible if certain conditions apply (e.g. data extracted anonymously from medical records).
Consent Requirements: Informed of ...

- Purpose of research.
- Description of procedures/identify those experimental.
- Description of risk.
- Description of benefit.
- Disclosure of alternatives.
- Extent confidentiality will be maintained.
- Compensation? Treatment for injury available?
- Participation is voluntary; refusal will involve no penalty, prejudice or recriminations; may withdraw at any time.
- Contact for research rights, subject rights, AR issues.
Waivers to signed consent

**IRB may waive requirement for written consent:**
- Consent implied by return of questionnaire
- Protection of anonymity
- The research involves no more than minimal risk to the subjects
- The waiver or alteration will not adversely affect the rights and welfare of the subjects
- The research could not practicably be carried out without the waiver or alteration
- Whenever appropriate, the subjects will be provided with additional pertinent information after participation.
De-identified Data Should Not Include:

- Names
- Geographic subdivisions smaller than state
- All dates related to the subject (e.g., birth date)
- Telephone, fax, e-mail, SSNs, student/employee ID
- Medical record and health plan numbers
- Account numbers
- Certificate/license numbers
- VIN and license plate numbers
- Device identifiers and serial numbers
- URLs and IP addresses
- Fingerprints, voice prints, images, etc

- or some identifiable combination ...
Conflict of Interest?

- Conflict of Interest
If IRB regulations are not followed, consequences could include:

• Suspension of research project.
• Suspension of all of a PI's research projects.
• Inability to use data or publish results.
• Notification of sponsors, regulatory agencies and funding agencies of noncompliance.
• Debarment by FDA from using investigational products.
• Inability to receive funding from federal grants.
• Additional monitoring and oversight by the IRB and/or third party monitoring of research activities.
• Termination of employment.
• Loss of licenses.
• Immediate shut-down of ALL research at an organization.
45 CFR 46 Subpart A = The Common Rule

- Highlights of Proposed Changes (NPRM)
  - Informed consent for all biospecimens (including broad future use)
  - Informed consent streamlining
  - Single IRB of record for multi-site (US) studies
  - Continuing review eliminated for Expedited studies; ongoing data analysis
  - Published list of activities that are minimal risk
  - IRBs no longer review grant applications or contract proposals
  - Longer list of excluded categories (Not subject to IRB review)
    - Some public health surveillance and quality assurance activities
    - Low risk social science research (survey, interview, focus group, oral history, journalism)
    - Data subject to other oversight (eg, HIPAA) such as medical records or claims data
  - Web-based decision tool to be available to self-select exemptions
  - Identifiable information with proper safety/security measures in place
  - Biospecimen and data repositories with previous broad consent
Roles & Reasons for Pharmacy Involvement with the IRB

Pharmacy involvement as a member of the IRB

• Protocol review before approval can be invaluable
  • Communication with investigators; identify/fix medication-related issues; improve study methodology or consent documents based on drug knowledge; contribute to overall resources utilization in the institution; better contribute to related policies/procedures;

• Keep abreast of current drug investigations

• Regulatory compliance; assure IRB review of studies; blinding/randomization; placebos; study monitoring; ADR monitoring; potential drug interactions; special storage and record-keeping

Roles & Reasons for Pharmacy Involvement with the IRB (cont.)

Pharmacy involvement as a member of the IRB (cont.)

• FDA audits assistance

• Liaison between institutions, other IRBs, other investigators, etc

• Enhance pharmacy activity and involvement in clinical trials (eg, PI, $).


Considerations of Research in Medical Environment

• Use of medical records and when HIPAA applies
  • Many entities do not have separate privacy boards; IRB often serves that function
• Drug clinical trials and FDA regulations
• QI vs. QA vs. Research
  • Check with local IRB as to how activity will be classified
Forms & Documents – Protocol Forms

• Determination Form
• Exempt Form
• Expedited Form
• Full Board

https://cws.auburn.edu/OVPR/pm/compliance/irb/forms
Forms & Documents – Reporting Forms

• Continuing Review Forms
  • Renewal
  • Modification
  • Final Report

• Reporting Forms
  • Noncompliance reporting
  • Event Notification
  • Anonymous Data Collection Assurance

https://cws.auburn.edu/OVPR/pm/compliance/irb/forms
Forms & Documents – Sample Documents

• Consent Documents
  • Informed Consent, Information Letter, parental permission, child assent, electronic vs. print

• Release Information
  • Video release; Audio release; Photo release (adults and minors)

• Recruitment Documents
  • Flyers, script, newspaper, email

• Site Authorizations
  • Research at schools; on-campus; off-campus

• Precautions
  • Referral; Emergency Plan; Debriefing form

https://cws.auburn.edu/OVPR/pm/compliance/irb/sampledocs
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• Mutnick AH, Miller LS. The pharmacist as an active member of the institutional review board. Top Hosp Pharm Mgt. 1993;13(1):55-59.