IRB Basics at BMC and BU Medical Campus

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BU Medical Campus Clinical Research Resources Office (CRRO)

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CRRO Clinical Research Resources Office

Clinical Research Resources Office

Supported by the BU CTSI and Office of Human Research Affairs (OHRA),
Serving all BMC/BU Medical Campus Clinical Researchers

Human Research Consultation Services and Education Program

- Consultation services
  - Study implementation
  - IRB application submission
- Education programs for all levels of the research team
- Support for sponsor-investigators of FDA-regulated research
- Tools and Resources *(web- based)*
- Quality Assurance Reviews

See our website: www.bumc.bu.edu/crro
See BU CTSI website: https://www.bu.edu/ctsi/

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Modern Ethical Research Principles

- Violations of ethical principles contributed to the development of our current regulatory framework.
- Belmont Principles: Respect, Beneficence, Justice
  - Ethical underpinnings of our regs
- Emphasis on:
  - Informed consent prior to research participation
  - Voluntary participation
  - Independent ethics review

Regulations Guiding Clinical Research

Subpart A: Protection of Human Subjects

45 CFR 46

OHRP

- Assurance
- Oversight
- Engagement

Informed Consent

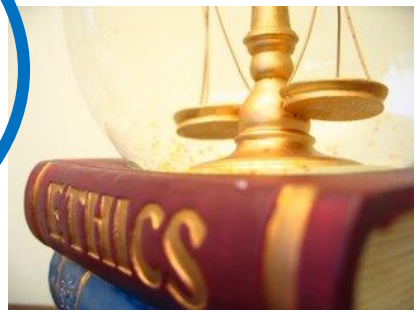
IRB Review/ Functions/ Operations

21 CFR 312, 812, 50, 54, 56

FDA

- Sponsor/investigator roles and conduct
- Drug/device dev't & testing process

- Subpart B: Pregnant women, Fetuses, neonates
- Subpart C: Prisoners
- Subpart D: Children
- Subpart E: IRB Registration



45 CFR 160, 162, 164

HIPAA (Health Insurance Portability and Accountability Act of 1996)

- Privacy and Security of protected health information

Institutional Review Board (IRB)

- Formally designated committee
  - Function as an ethics committee
  - Primary responsibility: protect rights and welfare of research subjects
- Review, approve, conduct periodic review (at least annually) of biomedical and behavioral research
- Document that reviews take place in compliance with regs
- Empowered to approve, require modifications or disapprove research
- Provide advice

111: Criteria for Approval

- Federal criteria for IRB approval of research
- "In order to approve research covered by these regulations the IRB shall determine that all of the following requirements are satisfied…"

(45 CFR 46.111 and
21 CFR 56.111)

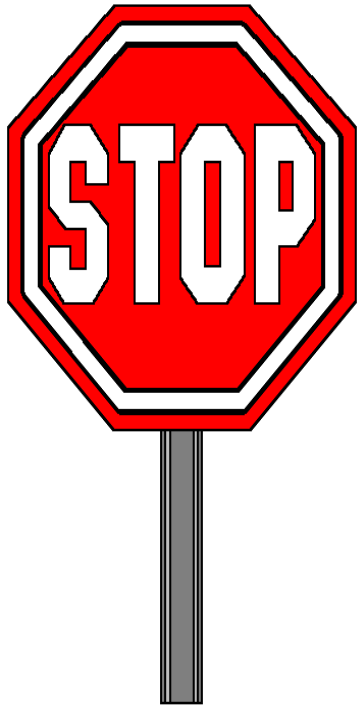
The 111 Criteria

1. Risks to subjects are minimized.
2. Risks to subjects reasonable in relation to benefits.
3. Selection of subjects is equitable.
4. Informed consent process.
5. Informed consent documentation.
6. Adequate provision for monitoring the data.
7. Provisions to protect privacy /maintain confidentiality.
8. Safeguards for vulnerable populations.

- 45 CFR 46.111 (HHS)
- 21 CFR 56.111 (FDA)

Deferral Decision

- Usually because insufficient information provided to the IRB for them to make a determination for one or more of the 111 criteria.
- If reviewed by the board, protocol will have to be revised and resubmitted and come back to the full board.



What requires IRB Review?

1) Is it research?

2) Are there human subjects?

Definitions

- Research (OHRP regs: 45 CFR 46.102 (d))
  - *"… a* systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge."

- Clinical Investigation (FDA regs: 21 CFR 312.3 (b))
  - "… any experiment in which a drug is administered or dispensed to, or used involving, one or more human subjects. For the purposes of this part, an experiment is any use of a drug except for the use of a marketed drug in the course of medical practice."

Definitions

- Human Subject (OHRP regs: 45 CFR 46.102 (f))
  - *"… a living individual about whom an investigator (whether professional or student) conducting research obtains:*
    - *Data through interventions or interactions with the individual, or*
    - *Identifiable private information."*
- Subject (FDA regs: 21 CFR 312.3 (b))
  - "…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."

Definitions

- Interaction/Intervention (45 CFR 46.102 (f))
  - Both physical procedures by which data are gathered… 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.

Definitions

- Private information (45 CFR 46.102 (f))
  - … info about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and 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, a 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."

(**See OHRP guidance on coded data/specimens, 2008: http://www.hhs.gov/ohrp/policy/cdebiol.html)

Exempt determination... 45 CFR 46.101 (b)*

1. **Normal educational practices** in established educational settings
2. Educational tests, **surveys, interviews**, or observation of public behavior -unless identified & sensitive**
3. Research on elected or appointed public officials or candidates for public office
4. Research using existing data, if publicly available or recorded without identifiers (existing = at time of submission to IRB)
5. Evaluation of public benefit service programs
6. Taste and food quality eval./consumer acceptance studies

*None of the categories apply to Prisoner research (Subpart C).

** does not apply to research with children except for research involving observation of public behavior when investigator(s) do not participate in the activities being observed.

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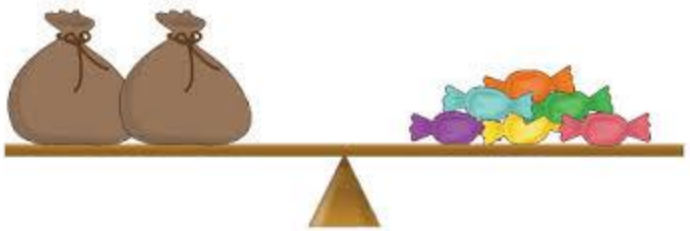
NHSR determination

2 types:

1. **Does not meet the definition of research (such as QI-only)**
2. **Does not involve human subjects according to the definition at 45 CFR 46.102(f)**
   - Tissue that was collected for some purpose other than this new research that has no link back to the individual (ANONYMOUS)
   - Data that was collected for some purpose other than this new research that has no link back to the individual (ANONYMOUS)

Equivalent protections

- Minimal risk research that does not receive federal funding
- Additional flexibility to requirements
- Lesser requirements still protects subjects for low risk research



Determining when HHS Regs Apply…

(and if you need to submit to the IRB)

1) Does the activity involve Research? (46.102(c))

If yes, then…..

2) Does the research involve Human Subjects? (46.102(f))

If yes, then….

3) Does the human subjects research meet criteria for Exempt from 45 CFR 46? (46.101(b))

Decision Trees: http://www.hhs.gov/ohrp/policy/checklists/decisioncharts.html

So … you have a research question!

- What you need to get started:
  - Up-to-date Human Subjects Protections Training
  - If your research is a clinical trial you will need up-to-date GCP training
  - INSPIR II access (BU username and Kerberos password)
  - If a trainee or student:
    - Get a faculty advisor experienced in clinical research
    - Decide what your role is…
      - Will you be working on somebody else's protocol as staff member?
      - Or, do you have a new research question?
        - » New Submission with you as PI and your advisor listed as "Faculty Sponsor."
        - » Amendment to an already-approved study if appropriate

Know the tools available to help you

- Examples:
  - IRB policies and guidance
  - Training in human subjects protection and GCP
  - Clinical Data Warehouse
  - IRB submission system
  - Pre-reviews of your application
  - Investigator-requested “audits” to ensure compliance
  - Assistance in study design and analysis
  - CTSI support

Tools/Services to Help You

- Human Research Protection Program Policies and Procedures
- CTSI: https://www.bu.edu/ctsi/
  - Biomedical informatics, GCRU, statistical support, etc.
  - **REDCap** (Research Electronic Data Capture): secure web application for building and managing online surveys and databases.
  - **StudyTRAX:** electronic data capture system for clinical research
  - **Profiles**: web-based research networking tool
  - **Recruitment Services**
  - **StudyFinder:** a web-based recruitment tool
  - i2b2
  - Much more!!!!

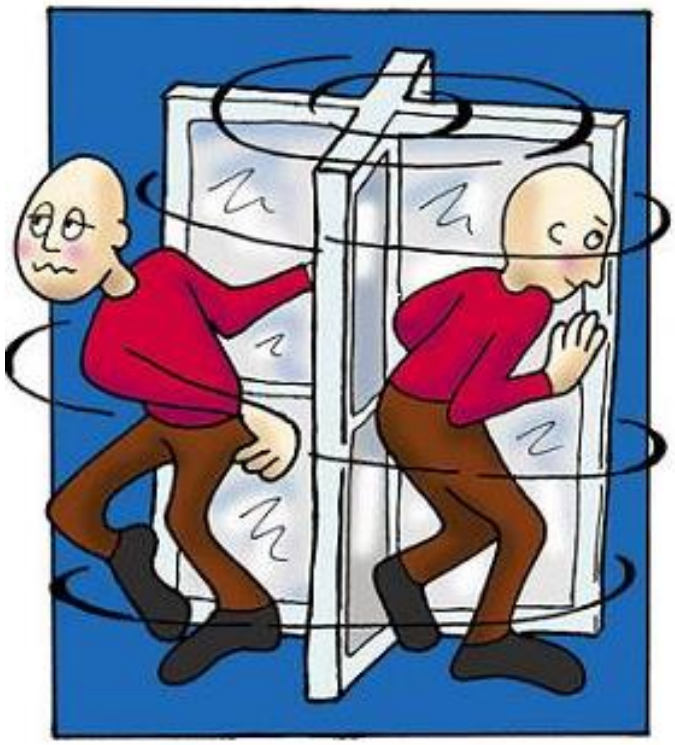
Tools/Services to Help You

- [Research] Clinical Data Warehouse: Linda Rosen
  - http://www.bumc.bu.edu/ocr/clinical-research-clinical-warehouse-data-access/
  - Submit a data request form
- Clinical Research Resources Office (CRRO): www.bumc.bu.edu/crro
- Biospecimen Archive Research Core:
  - http://www.bu.edu/cores/cores/biospecimen-archive-research-core-barc/

From many IRB letters……

"Administrative deferral:

This protocol has been administratively deferred because it is incomplete and not ready for IRB review."



- SOC procedures vs. research procedures are unclear.
- The Background does not justify why the study should be done.
  - There is no clear answer to the “So what?” question.
  - There is no supporting evidence or justification from the literature.
- If new to research…. not seeking mentorship and guidance from experienced faculty.

- Informed Consent Form is too complicated or the justification for why informed consent should be waived is missing/incomplete.
- Inappropriate recruitment plans or recruitment plans that are just not well-described.
- Key documents are missing.
  - e.g. surveys; data collection forms; the grant, project prospectus or thesis proposal.
- Study data collection forms have direct identifiers on them, such as name or MRN.
- Insufficient justification of sample size
- Insufficient detail in regards to analysis of the data to support aims

- Research design is not appropriate to answer the research question(s)
- Research design entails too much risk to subjects without balancing benefits
- Monitoring plan incomplete or insufficient
- Not all investigators up-to-date with Human Subjects Protection Training and/or GCP training
- Insufficient safeguards to protect subjects
- Inconsistent terminology
  - Anonymous, de-identified, coded

Questions?