BUMC Clinical Research Seminar:
What would YOU do?
Put your IRB hat on!

Mary-Tara Roth, RN, MSN, MPH
BUMC Clinical Research Resources Office (CRRO)

Mary Banks, RN, BSN
Senior Analyst II, BUMC IRB

September 10, 2014

CRRO Clinical Research Resources Office

CRRO Clinical Research Resources Office

Supported by the BU CTSI and Office of Clinical Research (OCR)
Serving all BUMC Clinical Researchers

Regulatory Service and Education Program	Recruitment Services Program

• Consultation services
  • Study implementation
  • IRB application submission
• Tools and Resources *(web-site based)*
• Education programs for all levels of the research team
• Support for sponsor-investigators of FDA regulated research
• Quality Assurance Reviews
	• Consultation services
	  • Study implementation
	  • IRB application submission
	• ReSPECT Registry
	  • Community Outreach
	• StudyFinder
	• Resources
	  • Web-based templates, tools, plans, etc.

See our website: www.bumc.bu.edu/crro

FDA Drug and Device Application Workshop

"Best Practices for Preparation and Maintenance of Sponsor-Investigator INDs and IDEs"

Featuring:

Jelena P. Berglund, PhD, RAC, Assoc. Director, Regulatory Affairs
Erin O'Reilly, PhD, RAC, Assoc. Director, Regulatory Affairs
Duke Translational Medicine Institute

Wednesday October 15, 2014

BU Trustee Ballroom

One Silber Way, 9th Floor

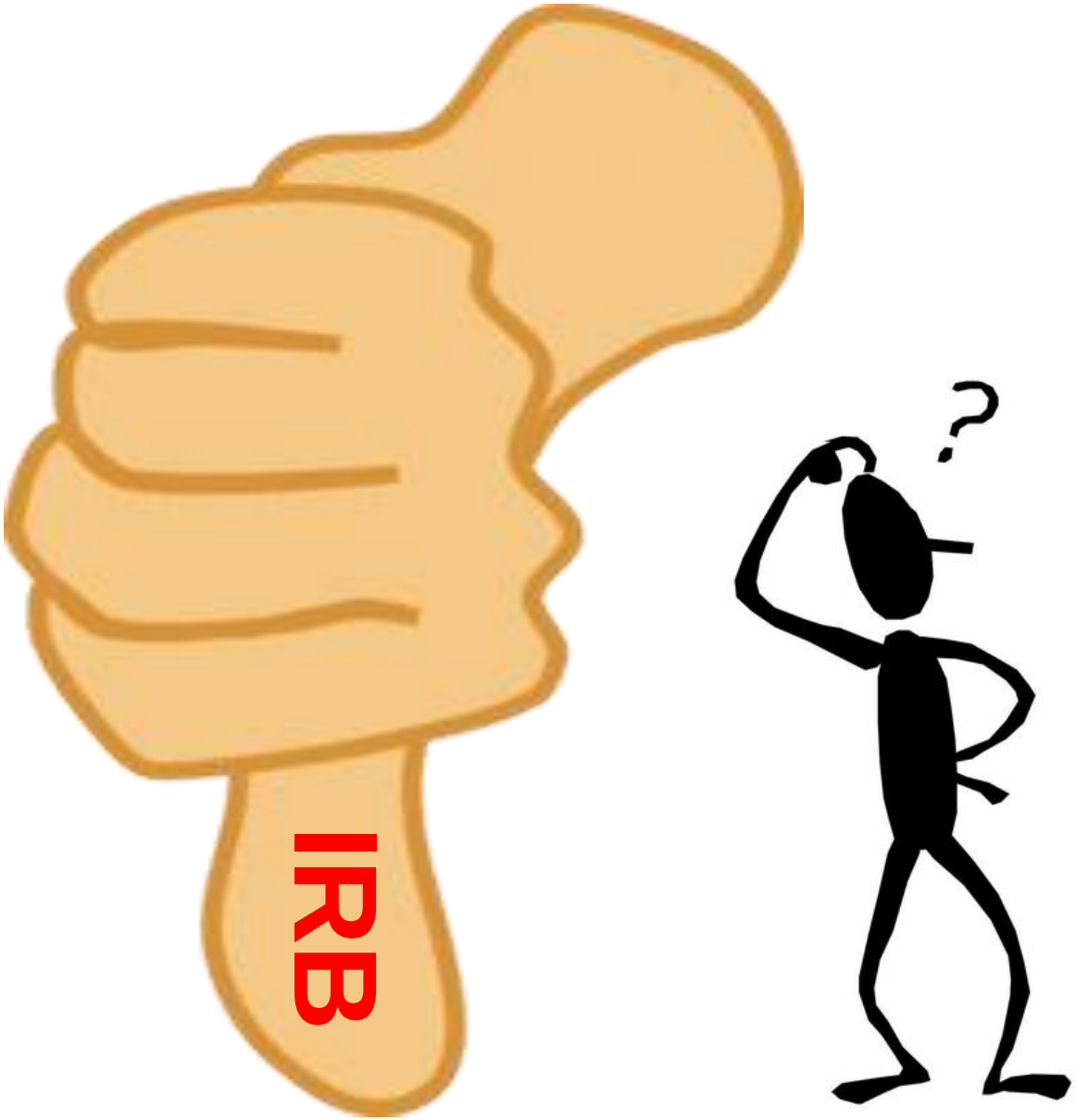
8:30 am: Check in and breakfast
9 am – 12 pm: IND Application Process
12:45 pm – 4 pm: IDE Application Process

Sponsored by the BU Center for Future Technologies in Cancer Care and the Clinical Research Resources Offices (CRRO)

To register for free, visit: www.tinyurl.com/bufdaworkshop2014

Objectives

- Define


IRB

Role of IRB

Keep in mind….

IRBs are rule ***enforcers*** <u>*not*</u> rule ***creators***

Leonard Glantz, JD

Associate Dean Emeritus, Academic Affairs

Professor, Health Law, Bioethics & Human Rights

Re-used with permission; Dr. Jim Feldman
Clinical Research Seminar presentation 4/17/13

Regulations Guiding Clinical Research

<u>Subpart A</u>: 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

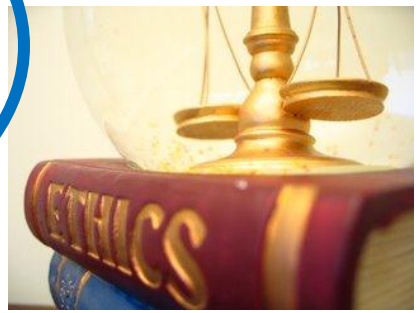
- Sponsor/investigator roles and conduct
- Drug/device dev't & testing process

- 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



The 111 Criteria:
Criteria for IRB Approval

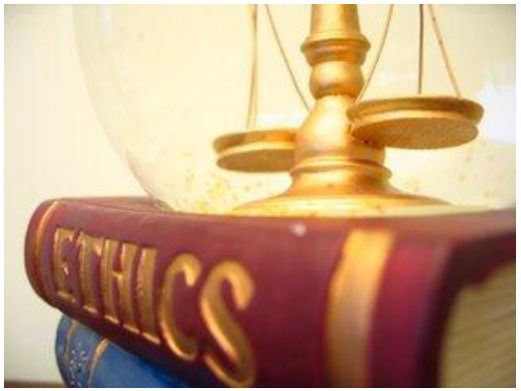
"In order to approve research covered by these regulations the IRB shall determine that all of the following requirements are satisfied…"

21 CFR 56.111

45 CFR 46.111

The 111 Criteria

for IRB review of research



1. Risks to subjects are minimized
   - Sound research design
   - Don't unnecessarily expose subjects to risk
2. Risks to subjects reasonable in relation to possible benefits
3. Selection of subjects is equitable
4. Informed consent process
5. Informed consent documentation
6. Adequate provision for monitoring the data to ensure subject safety
7. Provisions to protect privacy /maintain confidentiality
8. Safeguards for vulnerable populations

Conditional Approval vs. Deferral

- Simple Concurrence: There are issues, but the issues can be satisfied by "simple concurrence": *The IRB tells you the change – you agree to it.*
  - Ex: PI accepts IRB-suggested consent form wording change.

Vs.

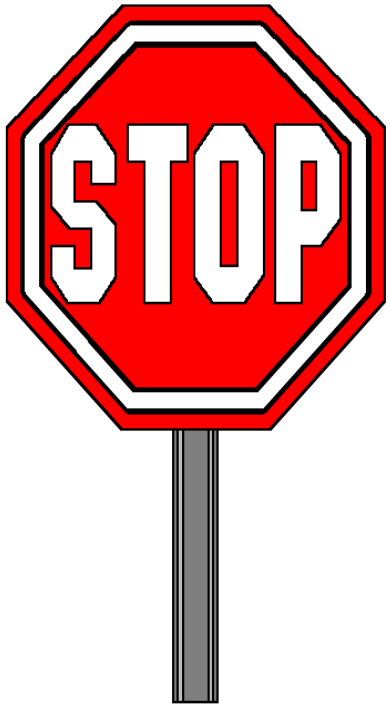
- Substantive clarifications or modifications of the research design or procedures.
  - Ex: The consent forms needs to be re-written to clearly describe what is the research and what is the SOC.

Deferral letter

- This is not an approval letter. This protocol has been deferred. Please note that no human subjects research activities (including recruitment, consenting, enrollment, randomization, screening, data collection, study interventions, data analysis, or follow-up) may be initiated until FULL IRB APPROVAL has been obtained. A deferral does NOT constitute full IRB approval.

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.
- Administrative Deferral: Not complete enough to make it to the board (or be fully reviewed if expedited or exempt).



Put your IRB Hat on!

Examples 1a/b

- **IRB item (retro chart review):** Describe in detail how the research population will be identified and your methods for contacting potential subjects. If this study is a chart review or medical record review, explain how you will identify potential records to be reviewed.
- Response (study 1):

  "No identification from the charts reviewed - they will NEVER be linked back to the subjects."
- Response (study 2):

  "As this is a retrospective chart review, there is no recruitment for this study. "

Example 2

- **IRB item (anonymous survey study):** Describe in detail how the research population will be identified and your methods for contacting potential subjects. If this study is a chart review or medical record review, explain how you will identify potential records to be reviewed.
- Response:

  "Households will be selected from within each community using a simple random sampling design. Heads of each household will be recruited for the study by visiting each household and requesting their participation in the study."

"A unique study ID will be created for each subject. This will allow subjects to complete surveys anonymously, and it will allow change to be tracked over time. The key linking the study ID to identifying information will be kept separate from study materials on a secure computer. The principal investigator will be the only one with access to the key. The chart review will be conducted by the principal investigator in one sitting using a secure electronic medical record. Data from the chart review will be kept in a spreadsheet using the anonymous study ID with no identifying information."

Example 3

- Protocol says:
  - "The subjects will voluntarily fill out the anonymous survey during their clinic visit, and return the survey upon leaving. The survey will assess presence and, if present, the severity of xxxxx in the subject's life…."
- Questionnaire says:

B. Please fill in the following information:

Examiner Name:_____ Patient Name:_____

Today's Date:_____ Sex:_____ Date of Birth:_____

Year Symptoms Began:_____

Medications:_____ Dosage:_____

_____ _____

_____ _____

_____ _____

Example 4

Study enrolling newborn infants with [the study condition] and babies born without the condition (normal controls).

Study objectives

"- To measure the blood and urine level of biomarkers xxxx, xxxx and xxxx in newborns with [study condition] and age-matched controls

- To identify the correlations between levels of biomarkers proposed above with short-term and long-term outcomes of mild, moderate and severe [study condition]"

Example 4 (cont'd.)

Procedures section:

"Sample collection: 1ml blood will be collected within 6 hours of birth. This 1 ml blood will be drawn for the study when blood is being obtained for other purposes as a part of standard clinical care. It is currently standard of care to obtain blood for various biochemical tests in these infants within 6 hours of birth. 5ml urine will be collected within 24 hours of birth. This will be a part of discarded sample from baby. Cord blood (2ml) will be obtained from the pathology lab. Cord blood is routinely obtained in babies with [the study condition] for biochemical analysis. Biomarkers xxxx, xxxx, xxxxx and xxxx will be measured with ELISA technique in the above samples."

(The attached protocol also describes a neurological exam at birth, 12, and 18 months as well as collection of data about the mother.)

Example 5

Study evaluating SOC group medical visits for xxxx condition via survey, focus groups, and medical record data collection to assess outcomes.

Recruitment Section

"Once a patient has indicated interest in participating in the xxxxxxx groups, the PI will contact the participant by telephone to find out if the patient is interested in participating in the study. If so, informed consent will be obtained on the day of the first xxxxxxx group medical visit. If the participant is unable to be reached by telephone prior to the first visit, the participant will be invited to participate in the study on the day of the first visit. Informed consent will be obtained then."

Example 5

Study evaluating [optional SOC visits] for xxxx condition via survey, focus groups, and medical record data collection to assess outcomes.

Consent Section

"Once patients are recruited to participate in the [SOC visit], the PI will follow up with a phone call describing the study purpose, protocol, potential risks and benefits to the patient. If the patient does not want to participate in the study, he will be offered a [SOC visit] at a later date. If the patient does want to participate …."

Example 6

Medical record review for patients at BMC dept. of xxxxx who received [SOC drug for their condition] during a specified timeframe. Link to individuals must be retained to collect any prospective data.

Waiver of Consent Section

"We will not obtain informed consent. Since the study involves an observational medical record review, it is impractical, both in terms of time and cost, to locate and consent subjects who may have moved or are deceased to participate in this research."

Example 7

Pilot study testing if there is any effect of a medication approved for a different condition with similar underlying cause.

Consent Background section

"Recently, a new medicine called [study drug] has been FDA approved for the treatment of a condition which shares the same underlying problem as a [the study condition]. The condition is [condition drug is approved to treat] and the underlying problem is thickened collagen. Collagens are proteins found in the flesh or "connective tissue" of humans and animals. This medication is approved by the FDA to be used to break up the collagen in patients who have [condition the drug is approved to treat]. This is a condition that causes the [physical effects of condition described]. Since the underlying condition of excess collagen is shared by [condition the drug is approved to treat] and [study condition], we think that [study drug] may also be used to help lessen [study condition]. [Study drug] is not FDA approved for treatment of [study condition]."

Example 7 (cont'd.)

Pilot study testing if there is any effect of a medication approved for a different condition with similar underlying cause.

Consent Background section

"Recently, a new medicine called [study drug] has been FDA approved for the treatment of a condition which shares the same underlying problem as [study condition]. This underlying problem is excess collagen, or "connective tissue." So, we would like to test whether this medicine could be used to lesson [study condition symptoms]. [Study drug] is not FDA approved for treatment of [study condition]."

Example 8

Protocol Purpose: Phase 1, first in human trial of a new drug being tested as a possible treatment for [debilitating/life-threatening condition]; designed to find the maximum tolerated dose.

- No “effectiveness” endpoints as a part of the primary or secondary purpose.
- Exploratory purpose: “We will also explore whether [drug name] leads to changes in [disease name] disease activity and symptoms.”

Example 8

Consent Purpose section:

"The main purpose of this research study is to test the safety, tolerability, and effectiveness of the drug, [drug name] when used to treat [disease]."

Thank you!

Any questions?

HIPAA

- **CR Times Feature Article March 2013 www.bu.edu/crtimes**
- ***Privacy and Confidentiality Requirements in the Use and Disclosure of Information for Research***
- **In order to approve research, the IRB must make a number of determinations in accordance with the Health and Human Services (HHS) "Common Rule" regulations and the FDA regulations. Two of these determinations relate specifically to privacy and confidentiality: That risks to subjects (including risks to privacy and confidentiality) are minimized; and that there are adequate provisions within the research plan to protect the privacy of subjects and to maintain the confidentiality of the data. These determinations, while not exactly the same as the regulations in the HIPAA Privacy Rule, are consistent with and overlap significantly with the Privacy Rule.**

CASE #1

- Student research: There is a correlation condition X and syphilis. We would like to explore this further by identifying all patients at BMC who have had a diagnosis of syphilis and then have the investigators (students) review their medical records and to abstract relevant data points.
- Submitted as Exempt Category 4 (retrospective chart review, research data will be abstracted and recorded without identifiers)
- Submitted a HIPAA Prep to research to identify the potential subjects from 2000-2013 who were patients at BMC (name, MRN, dx)
- Submitted a HIPAA Waiver of Authorization to abstract the data from the medical records
  - Date of birth
  - Lab values
  - Other conditions
  - Medication lists
  - Clinical presentation

What do you think?

- HIPAA Prep appropriate?
- HIPAA Waiver appropriate?
- Research plan appropriate?
- Any suggestions to minimize risks ?

Preparatory to Research ("Prep to Research")

- Under the HIPAA rule, investigators ***who are part of the covered entity*** are allowed to gain access to PHI in order to identify potentially eligible subjects.
- Under the HIPAA *Prep to Research,* investigators may NOT remove PHI from the covered entity or any of the covered entity's data sources, including medical records and electronic records. **A researcher who is not a part of the covered entity may not use the Prep to Research provision to access PHI**.
- Prep to Research cannot be used to collect research data. It is only used to identify potentially eligible subjects who would meet certain criteria:
- A Prep can only be used by members of the covered workforce.
- A Prep must be limited to the minimum necessary information needed.
- PHI obtained via a Prep to Research cannot be released outside the covered entity.
- Prep to Research information must be destroyed once the recruitment has been completed.

Waiver of HIPAA Authorization

- Research requires PHI identifiers beyond a De-identified or LDS and HIPAA Authorization can't be obtained. A Waiver is not needed if only obtaining a a De-identified Data Set or a Limited Data Set.
- To approve a Waiver, the IRB must determine that the research use of PHI does not represent greater than minimal risk to privacy/ that there exists:
  - An adequate plan to protect PHI identifiers from improper use & disclosure, to destroy identifiers at the earliest opportunity, and assurances the PHI will not be re-used or disclosed to any other entity or person(s)
  - That the research could not be done without the requested health information.
  - That it would not be practical to obtain signed authorizations from the subjects.
  - That the specific elements of health information that are requested are not more than the minimum necessary to accomplish the goals of the study. (Protocol must clearly state why and how the data elements being requested are necessary for research.)
- The minimal risk determination will often be affected by the sensitivity of the information. Identifiable research data that contains especially sensitive information (e.g., alcohol and drug use/treatment; psychiatric illness; HIV and sexually transmitted diseases, etc.) may not qualify for a HIPAA Waiver of Authorization.
-

Case #2

- This study involves chart reviews for retrospective and prospective data. Protocol says that investigators (MDs) will abstract de-identified data onto CRFs and which will be linked to identifiers via a mastercode.
- CRF includes the following data points ; study ID, diagnosis, lab values, age in years, date of surgery, infection noted (Y/N), antibiotic (Y/N)
- Submitted as HIPAA de-identified

De-identified Data Sets

- **Have been stripped of *all 18 HIPAA identifiers*.**
- Names, addresses (subdivisions smaller than state), telephone numbers, fax numbers, email addresses, SSN, MRN, and health plan beneficiary numbers.
- Also, any other unique account numbers, certificate or license numbers, VIN, medical device identification or serial numbers, personal website URLs, internet (IP) addresses, fingerprints, voiceprints, or other biometric identifiers, and full-face photographic images.
- ***IMPORTANT information about dates***: *Dates beyond year (such as month/year or day/month/year) are HIPAA identifiers.* This includes dates of birth or death, dates of procedures, dates of treatment, date of admission /discharge, etc.
- Ages beyond 89 are HIPAA identifiers.
- Other unique identifying numbers, characteristics, or codes are considered HIPAA identifiers if they are created from other HIPAA identifiers. So, a unique study ID that is linked to study data via a master code is not a HIPAA identifier unless it is created from another identifier.
- Geographic subdivisions smaller than a state are considered HIPAA identifiers except for the initial three digits of the zip code if, according to the current publicly-available data. from the Census Bureau, the geographic unit contains more than 20,000 people. This means, in most cases, demographics including city or zip code are considered HIPAA identifiers and cannot be included in a HIPAA de-identified data set.
- Patient initials are considered identifiers.

HIPAA Limited Data Set (LDS)

- Very similar to a De-identified Data Set because most HIPAA identifiers must be stripped from the dataset.
- A common descriptive term for an LDS is “facially” de-identified because the data are not identifiable to the casual observer.
- The difference is that a few specific HIPAA identifiers can be included in an LDS, namely dates and some geo-location information.
- A LDS must be stripped of all HIPAA identifiers noted above, except those related to ages, dates and locations as described below.
- A LDS can include dates of admission, discharge and other services; dates of birth/death.
- A LDS can include ages of subjects (including those over 89).
- A LDS can include full five-digit zip codes and other geographic subdivisions such as county, city, precinct, and equivalent geo-code (except street address).

Case #3

- Investigators are receiving tissue specimens from BARC repository (HIPAA covered entity).
- Protocol states that they will not receive any identifiers or PHI about the specimens.
- Only information provided by BARC about the specimens will be; age, gender, and diagnosis
- Submitted as Not Human Subjects Research
- HIPAA Exempt