BANKS ON BANKS

Clinical Research Seminar

March 20, 2013

Mary A. Banks

Director

BUMC IRB

TODAY

- Part II – following up on last month's presentation by Patricia Bass, JD
- Today's presentation will focus specifically on IRB review of repository research
- At the conclusion of today's presentation, the participants will be able to:

1. Identify which studies the IRB considers to be REPOSITORY studies.
2. State how the 45 CFR 46.111 are used by the IRB to review REPOSITORY research.
3. Utilize special template language related to REPOSITORIES appropriately in research consent forms.

TOPICS TO BE COVERED

- IRB review of protocols that involve collection of data/samples **for placement and storage in** a repository
- IRB review of research protocols that involve obtaining data/samples **from** a repository
- IRB requirements for maintaining a data/specimen repository
- Informed consent requirements for data/specimen repositories
- HIPAA requirements related to repositories

REPOSITORIES

For this presentation:

- Any collection of **data, human tissue, or information derived from human data or human tissue,** that you have saved or set aside for future use or research purposes
- Aka: tissue banks, biospecimen banks, registries
- **Regulations use global term of "repositories" to cover data and specimens**
- Repositories can be formal or informal; large or small; not for profit or commercial
- Data refers to information from or about individual human beings; can be identified or de-identified
- Can include genetic information or not
- Human tissue includes blood, tissue samples such as fat cells or skin cells, saliva, urine, breast milk, semen, isolates, DNA, cell lines, and other materials derived from humans
- Can also include diagnostic information and materials such as x-rays, CT scans, MRIs, laboratory results, etc.

IRB PROTOCOLS

OLD SCHOOL

- One study
- Collect data /samples
- Answer study question
- Complete analysis
- Destroy data /samples

- Start again

NEW SCHOOL

- Data/specimens are valuable vast resource
- Expensive to collect
- Multiple potential future uses /secondary analyses
- Genetic data
- Maximize the potential of the samples and data

CHALLENGES FOR IRB REVIEW

- Data and samples exist that people didn't specifically agree to be used in a repository or for future uses. What do we do with those?

- Science is developing rapidly – at times faster than the regulations

- Varied opinions about the potential risks associated with participation in research repositories and genetic research. How anonymous is anonymous? What are the chances of future re-identification of data/samples that contain genetic information even if they have no identifiers?

- How can a complex topic such as research repositories be explained to subjects in a way that they can give truly informed consent?

IN RESPONSE TO THE CHALLENGES

- Increased Federal focus on repository research
- Institutions are developing additional policies and procedures related to repositories
  - Focused IRB applications
  - Audits of repositories
- Many institutions recognizing need for expertise in addressing these issues – some now have specific IRB Panels and sub-committees
  - As of September 2011, BUMC officially added a new IRB Panel (Panel Orange) to review repository research and genetic research
  - Panel Orange
    - Chair is David Kaufman, PhD
    - Meets first and third Wednesday of each month
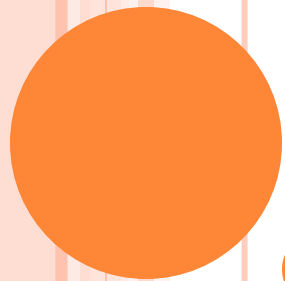
IRB REVIEW

Establishing a Repository

BEFORE WE BEGIN: CLARIFICATION REGARDING TERMINOLOGY

- These terms are frequently used/misused when describing repository data/specimens
  - Anonymous
  - De-identified
  - Coded
  - Limited Data Set (LDS)
  - Not Human Subjects Research (NHSR)
- Misuse of the terms causes confusion
- Confusion comes from OHRP and HIPAA having different terminology

OHRP (HHS)

- OHRP talks about identification in terms of **"able to ascertain the identities of the subjects"**
- For samples obtained **from a** repository: If the identity of the subjects cannot be readily ascertained, then under OHRP the data/sample may meet the criteria of "not human subjects research"
- In general, there are 3 ways by which the identities of subjects' data/specimens can be ascertained
  - **Direct identifiers:** name, medical record number, address, social security number, photographs
  - **Indirect identifiers:** data/specimens assigned a study ID that can be linked to identifiers via a master code or key
  - **Deductive Disclosure:** no direct or indirect identifiers but identity can be reasonably ascertained from the data itself (small population or specific data elements)

OHRP (COMMON RULE 45CFR46)

- **"Anonymous"**- (unofficial term) usually meaning that NO ONE is able to associate the data/specimens with individual subjects, neither the holders of the data/specimens nor the recipients
  - The data/specimens don't contain direct identifiers
  - There are no indirect identifiers (linkage by master code)
  - There isn't a reasonable risk of deductive disclosure
  - *Anonymous is not a HIPAA term

- **Not Human Subjects** (NHS) – if samples are obtained from a repository (not directly from subjects) and the recipients of data/samples cannot reasonably ascertain the identities of the subjects, because
  - Data/samples are truly anonymous   OR
  - Data /samples are coded and recipients never get access to master code/key and promise to never try to ascertain the identities of the subjects

HIPAA RULE   (45CFR 160 & 164)

- Uses different terminology than OHRP
- HIPAA: looks at data in terms of 18 "safe harbor" identifiers
  - Name, address, SS#, MR#, demographic info, etc.
  - **Dates**, ages >89, geographic information <state
- **De-identified:** stripped of **ALL 18** " safe harbor identifiers"
  - The master code is not one of the identifiers unless it is derived from an identifier
  - Data sets that contain dates (admission, discharge, surgery, birth, death, specimen collection, etc.) can't be called de-identified because dates are identifiers
- **Limited data set (LDS):** is like a de-identified dataset as most identifiers must be stripped except dates, ages >89 and some geographic information

Possibilities

"**Coded**" data/specimens in a repository

- May be de-identified (if no HIPAA identifiers)
- May not be de-identified if contains dates or other identifiers (might be LDS)
- Data/specimens in the repository are NOT anonymous
  - presumably someone (the investigators or keepers of the repository) has the master code to link the data/specimens to subjects
  - In most cases, only coded data without the master key will be RELEASED to investigators, but the repository itself is NOT anonymous

RECIPIENTS

- Data released **to recipients** could be
  - Coded and de-identified (HIPAA)
  - Coded and LDS (HIPAA)
  - Coded and contain a HIPAA identifier (e.g., contain subjects' initials)
  - Anonymous (**no one** can link to identifiers) and de-identified
  - Coded data released to recipients from a repository can qualify as NHSR under OHRP
    - if the recipient will never have access to the master code AND
    - If the recipient agrees to never try to ascertain the identities of the subjects OR
    - If policy/regulation prohibits release of the master code

Beware

- Data cannot be
  - Anonymous and coded
  - De-identified and include dates
  - De-identified and LDS

- These distinctions will be important later in the discussion

RETROSPECTIVE VS. PROSPECTIVE

- IRB considers "retrospective" to be if the data/samples exist at the time of the IRB submission (not at the time of use)
- Prospective sample collection for a Repository
  - Collecting data/samples for primary study use but also saving for future use
  - Collecting data/specimens from future research subjects for a repository only
  - Collecting data/samples going forward from "patients" for repository use (e.g., leftover surgical samples)
- Retrospective Samples for a Repository
  - Investigator closing his/her study but now wants to keep the data/specimens for repository (not previously considered for future use)
  - Department wants to retain data/samples collected by multiple researchers from multiple projects into a repository
  - Collecting existing data/samples obtained for non-research purposes (clinical care, billing, school data, laboratory discards, clinical databases, etc.) for research repository

IMPORTANT POINT

- According to OHRP
  - Research repositories are considered research that requires IRB oversight
  - Human subjects definition is met if
    - Investigators interact or intervene for the purpose of collecting research data/specimens OR
    - Obtain identifiable private information

  - Therefore, if data/samples are prospectively collected with the intent of use for research /placement in repositories, then this is human subjects research that requires IRB oversight

BUMC

- General rule: Research use or disclosure of identifiable private information or identifiable human specimens by BUMC employees or agents or from their databases, repositories, data banks, tissue banks, or registries requires review and oversight by the BUMC IRB.

- Non-research repositories (e.g., clinical, billing) do not require IRB oversight. **However, IRB oversight is required for research use of data/specimens from these repositories .**

- In some instances, additional institutional approvals may also be necessary.

IRB Protocol

1. Establishing a repository will usually require either expedited or full board IRB review
2. When completing the IRB application in Section 10.3 (Review Path Determination), select the **LAST option, "this protocol requires expedited or full board review"**
3. Review path depends on risk level, and that will be determined by IRB when protocol submitted
4. Often initial review is Full Board, and then IRB determines that it can be Expedited in the future

INSPIR APPLICATION

- Section 10 – review path determination
- Section 10.3 – last option
  - Complete all resulting questions
- Section 10.6 – HIPAA (will usually be YES)
- Section 10.7 – select if the repository involves genetic information
- Section 10.8 – select if the repository involves the collection of specimens/samples
- **Section 10.11- select to include repository specific questions**
- This is necessary for research projects with repositories as component or for stand-alone repositories
- IRB protocol must address 3 components of the repository

ESTABLISHING A REPOSITORY
THE BANK ANALOGY

3 MAJOR COMPONENTS OF BANKS & REPOSITORIES

Bank

- **Deposits**
  - Verification
  - Deposit slips
  - Appropriate tracking
- **Infrastructure**
  - Bank management
  - Security (physical)
  - IT security
  - Audits, accounting of transactions
  - SOPs
  - Emergency procedures
- **Withdrawals**
  - Verification
  - Tracking
  - Documentation & Accounting

Repository

- **Obtaining data/specimens for repository**
  - Consent
  - HIPAA Authorization
  - Eligibility criteria
  - IRB approval for the repository
  - Other approvals (e.g., NIH)
- **Infrastructure of repository**
  - Person responsible for the repository oversight
  - Security: physical
  - Security : IT
  - SOPs for acceptance and release of data/specimens
  - Accounting and auditing
  - Emergency procedures (e.g., power failure)
- **Data/specimen release to recipients**
  - Verification of approvals
  - Appropriate documentation
  - Tracking
  - What and when by whom

HOW THE IRB LOOKS AT REPOSITORIES

- IRB review is based on the 45 CFR 46.111 criteria

- And FDA 21 CFR 56.111 when applicable

- At BUMC, the IRB also conducts the review to ensure compliance with HIPAA

- The above is true whether the repository is a component of the research project or whether the repository is a stand-alone project

- *Next series of slides will address how these review criteria apply specifically to repositories*

Risks

- **45 CFR 46.111 (a)(1) Risks to subjects are minimized**
- Must consider all reasonably foreseeable risks - not just risks of physical harm
- IRB looks at "what" data/specimens will be obtained and considers
  - **Physical risks**
    - Clearly specify which are related to the research (research sample collection) vs. risks related to the clinical procedure
    - List all potential physical risks from each procedure
    - Be sure to include risks of taking "extra" samples (e.g., extra tissue beyond clinical biopsy, additional collections from bronchoscopy for research, etc.)
  - **Other (non-physical) risks**
    - Risk of criminal or civil liability (i.e., legal trouble)
    - Damage to financial standing
    - Impact on employability, insurability or reputation.

RISKS RELATED TO SENSITIVE DATA

- Is there a plan to collect/retain data about
  - use of illegal drugs, underage drinking or alcohol abuse
  - child or elder abuse, sexual behavior
  - "sensitive" diseases, conditions, treatments related to HIV, psychiatric conditions, sexually transmitted diseases
  - genetic testing and test results
- Does the sensitivity of the information reasonably place repository "donors" at risk of non-physical harms?
- Genetic information: Repositories that involve genetic samples or genetic information or samples for future genetic testing are potentially greater risk due to
  - Incidental findings
  - Social family connections / associations
  - Potential impact on insurability and employability
  - Potential future re-identification even if the sample does not contain identifiers

HOW ARE RISKS MINIMIZED

- All potential risks related to the research repository should be clearly identified in the research protocol
  - Don't forget risks for "additional" sample collection beyond clinical care
  - Don't forget additional data collection for research only
- The protocol must then specify how each of the risks will be minimized
  - Data use committees
  - SOP for ensuring that data /samples will only be released to recipients for use consistent with intent of subjects
  - Controlled access of well-designed repositories
  - Tightly controlled access to identifiable information – especially when it includes sensitive information

Risk/ Benefit

- **45 CFR 46.111 (a)(2) Risks to subjects are reasonable in relation to anticipated benefits…**
- Benefits shouldn't be overstated
- Ordinarily repositories are not expected to have direct benefit to subjects - value is to science
- If collection of repository specimens involves greater than minimal risk, then the potential benefit must be proportional to the risk (e.g., planned analysis rather than storage for "maybe" future use)
- Potential benefit to "science"- implications for repository infrastructure - must be sufficient to protect the specimens so they have some future research value
  - If samples are improperly stored or destroyed and not usable, then the risks outweigh the benefits because there are no benefits to subjects or science

SUBJECT ELIGIBILITY

- **45CFR 46.111 (a)(3) (3) Selection of subjects is equitable**
- The repository protocol should describe:
  - What are the eligibility criteria for repository?
  - How will potential subjects (donors) be identified and recruited?
  - If samples/data will not be obtained directly from subjects, then where are data/specimens coming from?
  - Will there be screening of potential donors?
  - Will subjects be approached by their clinicians or by the researchers?
  - Will non-English speaking subjects be recruited? If not, why not?
- HIPAA Prep to Research may be needed if clinical records are reviewed to identify potentially eligible subjects
- How is the repository set up to ensure that "deposits" meet the eligibility criteria?

CONSENT

- 45CFR 46.111 (a)(4) Informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by §46.116.

- Obtaining informed consent from individual subjects is the "gold standard"

- IRB recognizes that sometimes this isn't possible
  - Previously collected samples from non-research situations such as clinical care
  - Previously collected samples from other research
  - Research previously approved where future use of data/specimens was not considered at the time of consent

- Informed consent - by regulatory definition, means research consent that has been IRB-approved and contains all the required elements of consent under 46.116 unless certain elements have been waived by the IRB

- A general statement in a clinical/surgical consent that says "we can keep your samples for research" does NOT qualify as research informed consent

Protocol should address

- Who will obtain consent from subjects and under what circumstances?
  - Obtaining informed consent for research is a research activity - should not be delegated to clinical staff
- Subjects must be given sufficient time to consider participation
- How will repository be set up to ensure that:
  - Data/specimens are only collected /retained from those who gave consent
  - When consent has multiple Opt-in/Opt-out options – How will repository be managed to ensure these selections are honored?
  - Example: Framingham Heart Study tracking

CONSENT LANGUAGE

- Required elements of informed consent -"Usual stuff" familiar to all research consents
- Institution-specific language and format
  - Background, purpose, what happens
  - Spell out research vs. clinical care/standard care
  - Risks, benefits, alternatives
  - Subjects rights, payments, compensation for injury, etc.
  - Confidentiality protections & HIPAA
  - Signature lines

- **Combo Consents**: Sometimes repository consent is included in the main consent form, and sometimes it is separate - both must include repository-specific information such as:
  - Risks of participating in the repository
  - Benefits, if any; alternatives
  - Confidentiality protections for the repository

ADDITIONAL REPOSITORY SPECIFIC LANGUAGE

- General description of a repository and genetics
- Purpose of this repository - why they are being asked to participate
- Potential uses (opt-in/opt-out options)
  - Other BUMC investigators
  - Researchers at other academic institutions
  - National repositories; e.g., NIH dbGaP, NCI
  - Commercial entities/industry
- GINA language
- Certificate of Confidentiality (CoC) language
- Research results should not be expected to be returned to them
- What would happen if "incidental findings"
- Commercial use language

WAIVER OF INFORMED CONSENT

- IRB must consider what the potential subject expected when they provided the data/specimens
  - Consent - silent about future use
  - Consent - promises about future use
  - No consent obtained
- IRB may waive consent for single specified use for research
- More concern about waiving consent for repository placement for unspecified future use
- Additional concern when involves
  - genetic material/information
  - Sensitive information
  - Commercial use

IRB DISCUSSION ABOUT WAIVER

- Must meet regulatory criteria for waiver
  - Minimal risk (risks of physical and non-physical harms)
  - Does not adversely affect subject's rights /welfare
  - Impracticable to obtain consent – consider re-consenting
  - When appropriate, subjects will be provided with additional pertinent information after participation
- IRB carefully considers previous consent and what was promised
- Example: Subjects told their data would NEVER be released to others, then IRB can't approve release to dbGaP
- **Caution – do not "overpromise" in consent forms

Doc of Consent

- **45CFR 46.111 (a)(5) Informed consent will be appropriately documented, in accordance with, and to the extent required by §46.117**
- Usually for repositories, signature is required (not verbal consent) for repositories
- Signature of subject or subject's Legally Authorized Representative (LAR)
- LAR consent - specific IRB approval needed. IRB protocol should explain why data/specimens are needed from subjects who can't give consent.
  - **Research proxy** – previously designated by subject for consenting for research participation
  - **Next of Kin** –"assumed" to be best person to give consent by substituted judgment
  - In most cases, IRB is reluctant to allow consent by next of kin for repository research because there is no direct benefit to subjects, but will often allow consent by research proxy.

DATA AND SAFETY MONITORING

- 45CFR 46.111 (a)(6) When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects
- Data and Safety Monitoring plan depends on the risks related to the collection of data/samples for the repository
- Repositories themselves usually do not require a DSMB or Independent Data Monitor
  - Some larger repositories (e.g., FHS, NIH dbGaP) have data use committees
- **Minimally, each repository should have a Data and Safety Monitoring Plan (DSMP)** that addresses such items as:
  - procedures for overseeing and monitoring data/specimens
  - Security procedures
  - Emergency protections for samples/specimens (e.g., power loss)
  - Delegation of responsibilities for oversight, monitoring, reporting unanticipated problems to the IRB, etc.
- Any violations of privacy (e.g., failure to obtain informed consent) or breaches in security/confidentiality must be immediately reported to the IRB as an unanticipated problem
- Loss or misuse of samples or data also represent a reportable unanticipated problem

DATA AND SAFETY MONITORING PLAN

- How are samples protected?
- How are data protected?
- What is the oversight plan for the repository?
- Who, by name, is accountable for the repository?
- Minimum requirements for reporting Unanticipated Problems to IRB
  - Breaches in confidentiality/security
  - Violations in privacy (didn't get consent, consent not properly obtained, etc.)
  - Unexpected destruction of samples (freezer malfunction)
  - Accidental release of data not in accordance with IRB approval

Confidentiality

- **45CFR 46.111 (a)(7) When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.**

- Important repository consideration

- Protocol must specify:
  - Types of data and specimens to be included in repository
  - Must be specific so the IRB can determine the risks
  - Must explain how confidentiality will be protected (data security, stored where and how, transmitted to recipients how, who has access to identifiers, etc.)

CONFIDENTIALITY PROTECTIONS

- This is where the correct use of terms is important (anonymous, de-identified, coded, etc.)
- **Most repositories collect and store data/specimens with some identifiers/identifiable data**
- In most instances **only release coded samples**
  - May be de-identified or LDS or rarely other HIPAA identifiers
  - Specify why exceptions needed
- Repository protocol should describe confidentiality rules for
  - Collecting and storing data/specimens (e.g., collected with consent and HIPAA authorization)
  - Releasing data/specimens (e.g., recipient has HIPAA LDS and Data Use Agreement)

CONFIDENTIALITY PROTECTIONS

- Certificate of Confidentiality (CoC)
- GINA (Genetic Information Non-Discrimination Act) language
- HIPAA
  - Authorization is the gold standard
  - Consent usually will require HIPAA authorization language with specific details about the planned repository use
  - If data will not be obtained via HIPAA authorization, then protocol must describe mechanism for obtaining data for the repository under
    - De-identified data
    - LDS
    - Waiver of Authorization

Vulnerable subjects

- **45CFR 46.111(b) When some or all of the subjects are likely to be vulnerable to coercion or undue influence (such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons), additional safeguards have been included in the study** to protect the rights and welfare of these subjects.
- Protocol must identify vulnerable subjects
- Describe the additional protections that will be in place to protect these subjects
- Repositories often involve difficult concepts - How will subjects be made to understand the risks?
- Will assent be obtained from children? Is there a plan to re-consent children when they reach age of majority?
- When are subjects at risk for identification; e.g., NHLBI's determination about FHS - vulnerable to identification/association, so extra protections

Obtaining samples from an established repository

OBTAINING DATA/SPECIMENS FROM AN ESTABLISHED RESEARCH REPOSITORY

- Usually much easier process
- Most common request: CODED or ANONYMOUS
- Recipient investigators request use of data and/or specimens from an established research repository to conduct their research
- Assumptions
  - Repository is IRB-approved to release data/samples
  - Recipients were not involved in the collection of the specimens and are not part of the repository
  - If recipients will receive "coded" data, will not have access to identifiers or the master code
  - There is no plan to add the information (from the recipients' analyses) back into the repository
  - HIPAA – the recipients may receive some HIPAA identifiers (de-identified data or a LDS)

IRB APPROVAL

- Project will most likely qualify for review as a Not Human Subjects Research (NHSR) protocol
  - As long as the recipients will not receive information that would allow the subjects' identities to be ascertained
  - If the data is "coded" – the recipients must sign an agreement indicating that they do not have access to the master code/key and that they will not, now or in the future, make any attempts to ascertain the identities of the subjects
  - If the data is anonymous (then the protocol should state this) - this means that no one, even repository, knows the identities of the subjects or that the data will be scrambled or released in such as way that even the repository can't link it back

DOES **NOT** QUALIFY AS NHSR

- If the recipients are part of the registry or data collection or have access to the master code
- If the recipients will be giving results back that will be added to individual subjects' repository data
- If the recipient investigators will be directly going into patient's medical records to collect the data (i.e., not getting data from a research repository)

NHSR PROTOCOL IN INSPIR

- Complete sections 1-10 of the INSPIR application
- Section 10 (review path determination) of INSPIR
    - Section 10.3 – **select FIRST option – this project meets the regulatory definition of NHSR**
    - Section 10.6 – select yes if repository contains Protected Health Information (PHI) under HIPAA
        - Even if you will be getting de-identified data
    - **Sections 10.7, 10.8, 10.9, 10.10 should be "no"-** these questions are for establishing a repository and collecting data/samples to put into a repository

ADDITIONAL TIPS FOR INSPIR

- Complete the application – only a few questions:
  - Provide an explanation of the project, the proposed study population, the goals etc.
  - Explain how project meets criteria as NHSR
  - **Be sure to specify data/samples being requested – must be specific as the IRB must be able to determine based on the information provided that the identities of the subjects cannot be ascertained**
    - Attach data collection form (CRF)
  - Describe any potential risks. Be sure to consider non-physical risks
  - Attach the grant, if applicable
  - Use the right terminology
  - Complete HIPAA question and HIPAA form

ADDITIONAL ISSUES

- If recipient is receiving CODED DATA: Must sign the "not engaged in human subjects research" agreement
  - Form is posted on IRB website
  - Recipient agrees to not have access to master code and will make no attempt, now or ever to determine the identity of the data/specimens
- Obtaining samples - MTA may be required, especially if samples leaving the institution
- Data Use Agreement (DUA) must be done between recipient and "covered entity" if repository releasing a Limited Data Set (LDS)

Examples of Repositories

- BMC Clinical Data Warehouse CDW – from BMC clinical records
- BMC I2b2
- Biospecimen Archive Research Core (BARC)
- Some departments; e.g., Endocrine
- Some investigators may create a repository to store samples from all their studies
- Framingham Heart Study
- NIH dbGaP

RECIPIENT ISSUES

- Sometimes recipient investigators need identifiers that may allow subjects' identities to be ascertained
- This may not be a deal breaker, but will not usually qualify for NHSR or Exempt review
- Need to complete a "full" IRB application (selecting the final option in section 10.3 for expedited or full board review)
- May require consent waiver or re-consenting subjects
- HIPAA waiver may be needed – be sure to complete Section 10.6 and HIPAA questions

RESOURCES

- CR Times Archives has feature articles about these topics www.bu.edu/crtimes
  - BARC
  - i2b2
  - dbGaP
  - Respect Registry
  - CDW –Clinical Data Warehouse
  - GINA
  - Certificates of Confidentiality
  - Respect Registry
- HIPAA module- coming soon !!
- [Clinical Research Resources Office CRRO](#)
- [IRB website](#)

Commercial message

- Repository reviews are still evolving
- Interested in participating as IRB member?
  - Community members: non-affiliated with BUMC
  - Scientists: MDs, DMDs, PhDs, RNs, statisticians, etc.
  - Non-scientists: attorneys, clergy, administrators, etc.

Disclosure: There is no regulation against coercing IRB members to participate
- **Risks** - involves some work; time commitment; must be available to participate in 2x/month meetings
- **Benefit**s - catered lunches; interesting work; great people; better understanding of the IRB process
- **Alternatives** - not participate

Questions?