Network for Clinical Research Professionals (NCRP) Seminar

Program Director: JoNell Potter, PhD, RN
Program Manager: Marisabel Davalos, MSEd, CIP
Launched on November 3rd

- Clinical service to the ~500,000 patients of UHealth

- Empowering our patients with the choice to be contacted about future research opportunities

- Increases opportunity for patients to participate in clinical studies at our academic medical center

- Coincided with ‘Make Time for Research’ campaign

UHEALTH CONSENT-TO-CONTACT INITIATIVE

Enrollment Form for Future Contact About Clinical Studies at UHealth - the University of Miami Health System

Thank you for taking advantage of one of the unique services that UHealth has to offer its patients. Agreeing to be contacted regarding future clinical studies for which you may qualify and that may interest you is completely voluntary. This is an optional service offered by UHealth and your decision will never affect the medical care you receive at UHealth.

What you need to know before signing this form:
1. Right now, you are not being asked to be in any clinical study.
2. You are agreeing that a UHealth researcher can contact you in the future about clinical studies for which you might qualify.
3. All studies that you may be contacted about will first be approved by a special committee that protects people who participate in clinical studies.

What if I later change my mind and don’t want to be contacted?
You can change your mind at any time. Just call us at (305) 243-8888 and we will no longer contact you about future clinical studies. This will not affect your medical care at UHealth.

What happens when I am contacted for a clinical study?
You will be told about a particular clinical study for which you might qualify. You can then decide whether you want to join the study or not. Please feel free to ask any questions you wish.

Formal acceptance:
Please sign your name on this form if you agree to be contacted about future clinical studies.

Name ____________________________________________

SIGNATURE _______________________________________

Name of Personal Representative (if applicable) ____________

Relationship to Patient ____________________________

Date _________
PARTICIPANT RECRUITMENT ENHANCEMENT

Make Time for Research: brochures and videos are now available in patient waiting areas of all UHealth clinics.

Questions can be sent to contactforresearch@miami.edu or call 305-243-8888
PARTICIPANT RECRUITMENT ENHANCEMENT

Make Time for Research: Videos now available in patient waiting areas of all UHealth clinics.

Steps to Clinical Trial Enrollment

Will I Get a Placebo?

Safety and Well-being of Research Participants
Study Plan Folders

- Inventory available for distribution
- If your department needs for study participants, please place your request.
- Once inventory depleted, unsure CTSI will reorder.

Next NCRP: Tentatively scheduled for February 1, 2017
Efforts to Create Flexible Yet Compliant IRB Review: Collaborative Relationship with Investigators and Research Staff

Khemraj Hirani, PhD, RPh, CPh, CCRP, CIP, RAC, MBA
Associate Vice Provost for Human Subject Research
Office of Vice Provost for Research
Dominion Tower, 12th Floor
www.hsro.med.miami.edu

HSRO Update - 12/7/2016
DISCLOSURE STATEMENT

I have no conflict of interest in relation to this program/presentation.

The content is solely the responsibility of the presenter and does not necessarily represent the official views of my employers/alma maters, or my professional associations/affiliations.
Outline

- Mission & Guiding Principles of IRB
- Non-Human Subject vs. Human Subject Research
- IRB Reviews and Categories
- Regulations and legal framework
  - Reporting Obligations
- IRB Pre-review and IRB Review
- Current Volume and Productivity
- Operational Flexibility for Review
- Collaboration with Research Community
- NIH Mandate and Single IRB (Central IRB)
- Future Direction and Goals
- References
• The mission of an IRB is to ensure the protection, safety, and welfare of human subjects

45 CFR 46
• Subpart A (Basic DHHS Policy)
• Subpart B (Pregnant women, Fetuses & Human IVF)
• Subpart C (Prisoners)
• Subpart D (Children)

The Common Rule adopted by agencies (To standardized across federal agencies)

21 CFR PARTS
• 50 and 56 (IRB and ICF)
• 312 (IND)
• 320 (BA/BE)
• 812 (IDE)
The Guiding Ethical Principles of IRB Review: "Belmont Report"

- Respect for Persons ("Be Courteous")
  - Informed consent
  - Protection for the vulnerable
  - Individual autonomy

- Beneficence ("Do good")
  - Maximize possible benefits
  - Minimize possible harms

- Justice ("Be fair")
  - Fair distribution of research burdens vs. benefits
What is Human Subject Research?

- **Is it Research?**
  - Systematic Investigation
  - Research development
  - Testing
  - Evaluation etc.
  - Generalizable Knowledge

- **Is it Human Subject Research?**
  - **HHS.gov**
  - **U.S. FOOD & DRUG ADMINISTRATION**

  - **Clinical Investigation** - any experiment that involves a **test article** and one or more human subjects…

  - **Test article** - any drug (including a biological product for human use), medical device for human use, human food additive, color additive, electronic product, or any other article subject to regulation under the [Public Health Service Act].

  - **Human subject** - an individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may be either a healthy human or a patient.

  (…includes a human on whose specimen an investigational device is used.)

  - **Access to identifiable private information**
    - Viewing records or using data from a medical chart
    - Reasonably expect not to be observed, recorded or made public

  - **Interacting /Interventions with Individuals**
    - Including
      - non-invasive activities
      - Questionnaires
      - Surveys & procedures

  - **Use of Data or Specimens**
    - If they can be linked to an individual
## Differentiating Research From QI Projects

<table>
<thead>
<tr>
<th></th>
<th>Quality Improvement Project</th>
<th>Research</th>
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<tbody>
<tr>
<td><strong>Intent</strong></td>
<td>Apply known solutions to a limited problem</td>
<td>Discovery of new information that creates generalizable knowledge applicable at more than 1 institution</td>
</tr>
<tr>
<td><strong>Starting point</strong></td>
<td>To improve performance</td>
<td>To answer a question or test a hypothesis</td>
</tr>
<tr>
<td><strong>Design</strong></td>
<td>Theoretical framework may not be included, speaks to problem at hand</td>
<td>Rigorous theoretical framework, adheres to accepted design</td>
</tr>
<tr>
<td><strong>Setting</strong></td>
<td>A single setting and situation</td>
<td>Single or multiple setting</td>
</tr>
<tr>
<td><strong>Timeline</strong></td>
<td>Shorter</td>
<td>Longer</td>
</tr>
<tr>
<td><strong>Benefit</strong></td>
<td>Subjects in the project and institution where the project was conducted</td>
<td>Greater scientific community and clinicians, generalizable to larger populations and institutions</td>
</tr>
<tr>
<td><strong>Outcome Measurement</strong></td>
<td>Statistical analysis is optional</td>
<td>Statistically appropriate measures</td>
</tr>
<tr>
<td><strong>Extraneous variables</strong></td>
<td>May acknowledge but not controlled</td>
<td>Variables are controlled and measured</td>
</tr>
<tr>
<td><strong>Generalizable findings</strong></td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Plan for dissemination</strong></td>
<td>Internal communications, flyers, posters</td>
<td>External publication, podium presentation</td>
</tr>
<tr>
<td><strong>Oversight</strong></td>
<td>Institution where the project is conducted</td>
<td>Institution, IRB, sponsors, government agencies</td>
</tr>
<tr>
<td><strong>Subject risk (including use of PHI)</strong></td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Informed Consent</strong></td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>IRB</strong></td>
<td>Not always</td>
<td>Yes</td>
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</table>
What Does NOT require Review

• **Non-Human Subject Research**
  - Case report or case series
  - Quality improvement projects
  - Quality assessment projects
  - Medical practice and innovative therapy
  - Public health practice (disease monitoring or program evaluation)

• **HSR Self-Certification Tool (three basic Yes or No Questions)**
  https://umiami.qualtrics.com/SE/?SID=SV_4Iz2NPEhX1kdN1x

• **Question 1: Will the project involve evaluating the safety or effectiveness of any of the following:**
  - Drugs, Medical Device or biological product for human use
  - Foods or dietary supplements that include a nutrient content claim or a health claim
  - Infant formulas
  - Food and color additives

*Under development (beta testing/validation phase)*
What Does NOT require Review

• **Question 2:** Will you, a member of your research team or a collaborator observe, interact with, or intervene with individuals to gather information that will be used for research?
  - Surveys, questionnaires, focus groups, interviews
  - Games experiments in physical or in electronic environments
  - Physical or biomedical procedures (imaging, scanning, blood collection, anthropomorphic procedures)
  - Diet, nutrition studies, taste tests
  - Studies examining effectiveness of educational tools or curricula
  - Use of instruments or devices, including phones, to collect data or monitor or influence behavior
  - Passive observation of public behavior (in physical or online environments, including social media)
  - Studies examining individuals' responses to manipulation of their physical or online environment
  - Another activity that involves observation of, or interaction with, individuals to gather information for research

• **Question 3:** Are the data/specimens about or from individuals who are or may still be living?
  - If all “NO”
    - Project is Not Human Subject Research. No application to the IRB office needed.
  - If any “YES”
    - Continue to eProst for project submission
IRB Review and Categories

- Research involving existing or prospectively collected human specimens or data
- Review of medical records
- Educational research
- Research involving surveys, interviews or focus groups
- Clinical trials of investigational drugs and devices

RISK

Exempt from IRB Review
- No Risk

Expedited IRB Review
- No More Than Minimal Risk

Full Board (convened) IRB Review
- Greater than Minimal Risk
Exempt – ‘no risk’ activities

- The IRB must certify the exemption
- Involves only activities from an exemption list:
  - Research involving normal education practices.
    - e.g., instructional strategies/curriculum evaluation
  - Tests, surveys, interviews, or observation
    - e.g., data de-identified, or no harm if disclosure
  - Study of existing records or specimens if not identifiable/linkable, or if from public source
A study is *Minimal Risk* when both probability and magnitude of possible harm or discomfort are not greater than that ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.
Expedit ed – *no more than ‘minimal risk’*

- IRB Chair or IRB designee may approve
- Involves only activities from an expedited list, such as:
  - Data / materials collected solely for non-research purposes
  - Non-invasive recordings in adults (e.g., MRI, EKG)
  - Survey of individual/group characteristics (if no manipulation)
  - Collect samples non-invasively (e.g., saliva, sputum, excreta)
  - Blood draws (e.g., finger/heel stick, limited venipuncture)
- Not eligible if identification would expose subjects to risk of damage or stigmatization
- Standard informed consent requirements apply
IRB Review of Research – Full Board Review

- **Convened Board Review**
  - Required for research involving greater than minimal risk
  - Pre-review – Insures submission is ready for IRB
    29-35 average submissions per day
  - IRB primary reviewer may contact PI for clarifications
  - IRB approval must be obtained prospectively
    Before you start your research
  - The IRB does not grant retroactive approval
    Research that has already taken place

<table>
<thead>
<tr>
<th>DHHS</th>
<th>45 CFR 46</th>
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<tbody>
<tr>
<td>DoD</td>
<td>DoD policies &amp; procedures</td>
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<tr>
<td>HSRO/IRB/UM/FL</td>
<td>Institutional SOPs, FL State Laws</td>
</tr>
<tr>
<td>Belmont Report</td>
<td>Ethical Principles in the Belmont Report</td>
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From Lab to Label - The Outcome of Drug Development is the Negotiated Language of the Prescribing Information
US Drug Regulations: Legal Framework

CONGRESS

LAWs

Regulations

Guidelines

U.S. FOOD & DRUG ADMINISTRATION

CLINICAL RESEARCHERS
Definitions

• **Laws:** legislation passed by the United States Congress and signed by the President.
  
e.g. FDCA (Food Drug and Cosmetic Act, 1938)
  
  
  FDAMA (FDA Modernization Act, 1997)

• **Regulations:** rules issues by FDA consistently with Laws, published in the Federal Register and contained in Code of Federal Regulations (CFR)
  
  IRBs: 21 CFR Part 56.101-124
  
  IRB and Informed Consent (21 CFR 50 and 56)

• **Guidelines:** “informal” documents issued by FDA to clarify requirements; often specific to therapeutic areas or technical disciplines
  
  ▪ Information Sheet Guidance for Institutional Review Boards (IRBs), Clinical Investigators, and Sponsors
  
  ▪ Sponsor - Investigator - IRB Interrelationship - Information Sheet: Guidance for Institutional Review Boards and Clinical Investigators
The Difference...

(Credit: Steve Wilson, FDA)
Non-Compliance is really Expensive!
Submit RNI...

- Unanticipated Problems
- Breach of Confidentiality
- Complaint of a Subject
- Incarceration of a Subject while enrolled in a study
- Pregnancy if study excludes pregnant subjects
- Protocol Violations
- Medical License/ Credentialing issue of study staff
- Voluntary suspension/restrictions/hold
- Change in COI
- Change in risk/benefit ratio
  - Interim analysis/DSMB
  - Awareness of a paper published from another study
- FDA 483
- Any other event that PI believes need to be reported to the IRB
Unanticipated Problem = Any incident, experience, or outcome that meets all of the following criteria:

1. **Unexpected**
   - in terms of nature severity or frequency given
     - the research procedures that are described in the protocol-related documents, and
     - the characteristics of the subject population being studied;

2. **Related** or **possibly related** to participation in the research; and

3. Suggests that the research places **subjects or others at a greater risk of harm** including
   - physical
   - psychological
   - economic or
   - social harm

than was previously known or recognized.

All 3 criteria should be met.

Report PROMPTLY (within 10 days) to the IRB
Unanticipated Problems and Adverse Events

- **Safety Related**: Do not report adverse events that are not UPs
- **Safety Related**: Must report adverse events that are UPs
- **Non-Safety Related**: Must report UPs that are not adverse events

Adapted from HHS Guidance, *Guidance on Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events* (January 15, 2007); See also FDA Guidance.
Example:

In a phase II study testing an investigational drug for Hepatitis C, a subject experiences hepatic injury. In addition to the investigational drug, the subject was continuing her standard Hepatitis C therapy at the time of hepatic injury.

Is this reportable to the IRB as an individual occurrence?
Example:

In a phase II study testing an investigational drug for Hepatitis C, a subject experiences hepatic injury. In addition to the investigational drug, the subject was continuing her standard Hepatitis C therapy at the time of hepatic injury.

Is this reportable to the IRB as an individual occurrence?

NO
Example:

A subject with extrapulmonary small-cell carcinoma receiving an investigational chemotherapy agent experiences a bowel perforation during his second cycle of chemotherapy.

Is this reportable to the IRB as one occurrence?
Example:

A subject with extrapulmonary small-cell carcinoma receiving an investigational chemotherapy agent experiences a bowel perforation during his second cycle of chemotherapy.

Is this reportable to the IRB as one occurrence?

NO
Example:

17 oncology sites are participating in a research study comparing an investigational chemotherapy agent to standard therapy in subjects ages 60-85. Of those subjects receiving the investigational drug, an average of 35% of subjects across the 17 sites experience deep vein thrombosis.
Example:

17 oncology sites are participating in a research study comparing an investigational chemotherapy agent to standard therapy in subjects ages 60-85. Of those subjects receiving the investigational drug, an average of 35% of subjects across the 17 sites experience deep vein thrombosis.
Unanticipated Problems

Examples:

• Failure to obtain informed consent
• Omitting study procedure(s) required by the approved protocol
• Study personnel misconduct that adversely impacts the study
• Adverse findings by a regulatory agency, medical board, or other relevant body

Are these UPs?

* Whether these are UPs depends on the type of study and the specific factors surrounding each event or incident.
An Investigator is conducting a psychology study evaluating decision making and response times when persons are listening to music at various decibel levels. In order to perform the study, participants are placed in a small, windowless, soundproof booth. The IRB-approved protocol and consent form describe claustrophobic reactions as one of the research risks. The 12th subject enrolled in the research experiences significant claustrophobia, resulting in the subject withdrawing from the study.

Is this event reportable to the IRB as a UP?

NO
As a result of a processing error by a pharmacy technician, a subject enrolled in a multi-center clinical trial receives a dose of an experimental agent that is 10-times higher than the dose dictated by the IRB-approved protocol. While the dosing error increased the risk of toxic manifestations of the experimental agent, the subject experienced no detectable harm or adverse effect after an appropriate period of careful observation.

Is this error reportable to the IRB as a UP?
Unanticipated Problems
Example:

As a result of a processing error by a pharmacy technician, a subject enrolled in a multi-center clinical trial receives a dose of an experimental agent that is 10-times higher than the dose dictated by the IRB-approved protocol. While the dosing error increased the risk of toxic manifestations of the experimental agent, the subject experienced no detectable harm or adverse effect after an appropriate period of careful observation.

Is this error reportable to the IRB as a UP?  

YES
An investigator is conducting behavioral research and collects individually identifiable sensitive information about illicit drug use by surveying college students. The data is stored on a laptop computer that is password protected. The laptop is stolen from the investigator’s car.

Is this reportable to the IRB as a UP?
An investigator is conducting behavioral research and collects individually identifiable sensitive information about illicit drug use by surveying college students. The data is stored on a laptop computer that is password protected. The laptop is stolen from the investigator’s car.

Is this reportable to the IRB as a UP?

**Yes**
Different stages of Review once the study is submitted

- **Pre-Review is NOT IRB Review**
- Pre-Review is meant to review of documents to ensure they are
  - Complete
  - Correct
  - Consistent
## What makes Pre-review different from IRB Review

<table>
<thead>
<tr>
<th></th>
<th>Pre-IRB Review</th>
<th>IRB Review</th>
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<tbody>
<tr>
<td>Study population</td>
<td>Ensures that there is consistency in study populations and accrual through all documents</td>
<td>Evaluates whether the study population is appropriate for the design of the study</td>
</tr>
<tr>
<td>Data and safety monitoring</td>
<td>Ensure that monitor, plan and stop rules are identified</td>
<td>Evaluates the content of what is written</td>
</tr>
<tr>
<td>Compensation</td>
<td>Ensures that the protocol and consent identify if compensation is provided</td>
<td>Evaluates whether the compensation level is appropriate or whether it may create undue influence</td>
</tr>
</tbody>
</table>

- **A Good Pre-Review Enhances a Thorough IRB Review**
  - Checklist/templates/Standard language
  - Beneficial for both Investigators and IRBs
Number of active studies = 3479 (includes exempt studies)
Data as of Oct 1, 2016
Current Volumes: Department Data

Data from medical studies

- Medicine (non Hem/Onc): 25%
- Cancer (includes Hem/Onc, Surgical Hem/Onc, Radiation Oncology and Pediatric Hem/Onc): 19%
- Ophthalmology: 9%
- Pediatrics (non-Hem/Onc): 6%
- Neurology: 6%
- All other: 35%
Average Turnaround Time

- **Mod/CR**
  - Pre-review
  - Changes Requested
  - Pre-review2

- **Modifications**
  - Pre-review
  - Changes Requested

- **Continuing Review**
  - Pre-review
  - Changes Requested

- **New Studies**
  - Pre-review
  - Changes Requested
  - Pre-review2

Time in hours: 0 to 60
Top 10 Factors Increasing Turnaround Time

• **Study Design**
  Inadequate study design leads to increased pre-review time

• **Risk/Benefit Ratio**
  Insufficient information to determine risk/benefit
  Benefit > Risk not made explicit

• **Elements of the ICF**
  Informed consent elements missing or incomplete

• **Privacy/Confidentiality Sections**
  Incomplete/wrong HIPAA B form
  Missing elements of privacy/confidentiality sections

• **Subject selection**
  Not equitable as described
Top 10 Factors Increasing Turnaround Time

• **Continuing Review Submission Incomplete**
  - Incomplete supplemental form
  - Missing DSMB report
  - Missing progress report

• **Reportable New Information**
  - Incomplete information about deviation
  - Corrective and preventive action either incomplete or missing

• **Research and Standard of Care**
  - Difficult to distinguish research and SOC procedure/treatment from submitted documents

• **Incomplete Training**
  - CITI, COI and NIH-mandated GCP

• **Ancillary Review**
  - Pending ancillary review
Improved Measures; Flexible Yet Compliant

- Creation of Central IRB (Mandated by NIH)
- Re-evaluation of IRB Rosters based on therapeutic portfolios
- Self-Certification Tool for Human Subject Research determinations
- Simplified CITI selections for Biomedical Researchers
- Continual review and revision of SOPs when opportunities for increased efficiency are identified
- Competency and levels of Staffing
- FWA: Uncheck the box
- Continued eProst Mentoring Sessions (scheduled via Ulearn)
• IRB Tip of the Week

• HSRO Regulatory Staff Education program redesigned
  • Serve as alternate members

• Partnership with PRIM&R for more robust training for IRB Members/HSRO Staff

• Investigator Manual linked to the front page of the website

• Direct contact for subjects provided on front page of HSRO website

• Flexibility in allowing PI to determine who may serve as their Proxy

• Responsiveness: Emphasis on HSRO staff availability via phone/email
## Matters Pertaining to...  

<table>
<thead>
<tr>
<th>Matters Pertaining to..</th>
<th>Contact</th>
<th>Phone</th>
<th>Email</th>
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</thead>
<tbody>
<tr>
<td><strong>BOARDS</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Biomedical Board A</td>
<td>Joseph Datko</td>
<td>305-243-9769</td>
<td><a href="mailto:jad123@med.miami.edu">jad123@med.miami.edu</a></td>
</tr>
<tr>
<td>Biomedical Board B</td>
<td>Rachel Garcia</td>
<td>305-243-8314</td>
<td><a href="mailto:rxg286@med.miami.edu">rxg286@med.miami.edu</a></td>
</tr>
<tr>
<td>Biomedical Board C</td>
<td>Natalie Francis</td>
<td>305-243-7088</td>
<td><a href="mailto:nfrancis@med.miami.edu">nfrancis@med.miami.edu</a></td>
</tr>
<tr>
<td>UM Central IRB</td>
<td>Evelyne Bital</td>
<td>305-243-9977</td>
<td><a href="mailto:ebital@med.miami.edu">ebital@med.miami.edu</a></td>
</tr>
<tr>
<td>SBS Board</td>
<td>Vivienne Carrasco</td>
<td>305-243-9925</td>
<td><a href="mailto:vcarrasco@med.miami.edu">vcarrasco@med.miami.edu</a></td>
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<tr>
<td><strong>HIPAA &amp; Regulatory issues</strong></td>
<td>Thomas Street</td>
<td>305-243-6494</td>
<td><a href="mailto:t.street@med.miami.edu">t.street@med.miami.edu</a></td>
</tr>
<tr>
<td><strong>Administrative Matters/IRB Affairs</strong></td>
<td>Kenia Viamonte</td>
<td>305-243-9672</td>
<td><a href="mailto:kviamonte@miami.edu">kviamonte@miami.edu</a></td>
</tr>
<tr>
<td><strong>UM as Central IRB (Inflow)</strong></td>
<td>Evelyne Bital</td>
<td>305-243-9977</td>
<td><a href="mailto:ebital@miami.edu">ebital@miami.edu</a></td>
</tr>
<tr>
<td><strong>Education &amp; UM relying on External IRB (Outflow)</strong></td>
<td>Joey Casanova</td>
<td>305-243-9232</td>
<td><a href="mailto:jcasanova@miami.edu">jcasanova@miami.edu</a></td>
</tr>
<tr>
<td><strong>IRB Quality &amp; Compliance Issues</strong></td>
<td>Saloni Vahia</td>
<td>305-243-1599</td>
<td><a href="mailto:sxv297@miami.edu">sxv297@miami.edu</a></td>
</tr>
<tr>
<td><strong>All other matters Urgent Issues</strong></td>
<td>HSRO Helpline (Mireya)</td>
<td>305-243-3195</td>
<td><a href="mailto:HSRO@miami.edu">HSRO@miami.edu</a></td>
</tr>
<tr>
<td></td>
<td>Raj Hirani</td>
<td>813-454-7872</td>
<td><a href="mailto:Khirani@med.miami.edu">Khirani@med.miami.edu</a></td>
</tr>
</tbody>
</table>
Human Subject Research Office – www.hsro.med.miami.edu

Cancer - Protocol Review Committee (PRC)

Pathology – Pathology Protocol Review Committee (PPRC)

Tip of the Week

10/29/2016: Are you using data or samples from another institution?

Click here to submit new items to or manage existing items at the IRB.

The UM Investigator Manual describes all requirements for the conduct of human subject research at UMIRB.
TRADITIONAL IRB REVIEW – Changing Landscape

- Multiple IRBs evaluating one protocol
  - Inconsistencies in IRB assessments between sites (Hirshon et al, 2002)

- Start-up time for NIH-funded trials
  - Often exceeds one year

- Research teams
  - Spend too much time on bureaucratic tasks

- Patients
  - Frustrated with the slow pace of translational & clinical research

Discoveries → Health Benefits

- How can this be translated to benefit others?
REGULATORY POSITION (FDA, OHRP, HHS, NIH)

- 2006 Food and Drug Administration Guidance on “Centralized IRB Process”
  - “The agency hopes that sponsors, institutions, Institutional Review Boards (IRBs), and clinical investigators involved in multicenter clinical research will consider the use of a single central IRB (centralized IRB review process), especially if using centralized review could improve the efficiency of IRB review”.

- Other regulatory adoptions
  - OHRP allows for use of central IRB (April 30, 2010, letter)
  - HHS ANPRM for Revisions to the Common Rule (July. 2011)
  - HHS NPRM for Revisions to the Common Rule (Sept. 2015)

- Final NIH Single IRB Policy (June 21, 2016)
  - Effective date - May 25, 2017
DEVELOPMENT OF UM CENTRAL IRB

LEAD INVESTIGATOR (PI)

- Ensures mechanism for communication (Central IRB & Replying Sites).
- Ensures authorization agreements are in place.
- Each Lead Investigator must designate a Coordinating Center to facilitate the process.

COORDINATING CENTER (CC)

- Manages the flow of documents between the Lead PI, participating sites (Relying Institutions), and the Central IRB.
- Works with the Lead Investigator and Relying Institutions to obtain documents required for submission to the Designated IRB, completes the IRB application, and disseminates IRB approval documents to Relying Institutions.
- The point of contact for Relying Institutions and the Designated IRB, thus reducing the burden on all parties.
CReATe: Clinical Research in ALS and Related Disorders for Therapeutic Development

- University of Kansas Medical Center (KUMC)
- Wake Forest University
- University of Texas Southwestern Medical Center (UTSW)
- University of Texas Health Science at San Antonio (UTHSCSA)
- Cleveland Clinic
- California Pacific Medical Center (CPMC)
- University of Pennsylvania (UPENN)
- University of Virginia (UVA)
- Ohio State University (OSU)
- University of California San Diego (UCSD)
- University of Iowa

Reliance agreements completed

CC = USF

Sites joined the study
Type 1 Diabetes TrialNet*: International network of researchers who are exploring ways to prevent, delay and reverse the progression of type 1 diabetes.

*Jointly funded by NIDDK, NIAID, NICHD, NIH-GCRC, JDRF and ADA

- University of Florida
- University of Minnesota
- Stanford University
- University of California of San Francisco (UCSF)
- University of Texas Southwestern Medical Center
- Columbia University
- University of Colorado Denver
- Vanderbilt University
- University of Chicago
How to Understand What AAHRPP accredits?

- Organization
- Research Review & Support Units
- Investigators and Study Teams

A shared responsibility

AAHRPP
Association for the Accreditation of Human Research Protection Programs, Inc.
SUBJECT SAFETY & RIGHTS - IT TAKES A VILLAGE

- Strategic Initiatives
- Ethics/CITI Programs
- IRBs
- HSRO
- Grants & Contracts
- Ancillary Review
- ORC
- Institution
- Sponsor
- Clinical Investigator
- Study Team
- Compliance
- Innovation

Subject Safety and Rights
REFERENCES

- FDA Guidance for Clinical Investigators, Sponsors, and IRBs, Adverse Event Reporting to IRBs—Improving Human Subject Protection (January 2009)
- **Making Sense of Reporting Obligations to the IRB** (Claire Carbary, JD, CIP & Mitchell Parrish, JD, CIP)
- [www.ctti-clinicaltrials.org](http://www.ctti-clinicaltrials.org) (CTTI) / [www.FDA.gov](http://www.FDA.gov) (FDA)
- [www.aahrpp.org/](http://www.aahrpp.org/) (AAHRPP)
- [https://catalyst.harvard.edu/services/irbcede/](https://catalyst.harvard.edu/services/irbcede/) (Harvard Catalyst)
- [https://www4.vanderbilt.edu/irb/](https://www4.vanderbilt.edu/irb/) (IRB Share/Choice models)
- Central IRBs in Multicenter Studies, Adrian Hernandez, July 17, 2015 with NIH Laboratory & pcornet and IRBshare, Todd Rice MD, MSc presentation
- [https://www.diabetestrialnet.org/](https://www.diabetestrialnet.org/) (TrialNet) and its coordinating center
- [https://www.rarediseasesnetwork.org/](https://www.rarediseasesnetwork.org/) (Rare Disease Clinical Research Network)
Your vital role in protecting subject safety and rights is a significant contribution toward the University’s efforts to comply with federal regulations.

It’s about “U”

The Clinical Investigators and Study Coordinators are integral part of HRPP