Overall Agenda for Orientation

• **Module 1:**
  Introduction to Clinical Research, Education, and IRB

• **Module 2:**
  Informed Consent, Documentation and GCP, and Study Start up

• **Module 3:**
  Contracting, ClinicalTrials.gov, Billing Coverage Analysis, Essential Documents

• **Module 4:**
  Recruitment, Budgets and Accounting, Preparing NIH Grant Budgets and Drug/ Device Policies

• **Module 5:**
  Conflict of Interest, From CDA to Study Close Out
CONFLICT OF INTEREST

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Who is Covered by the Policy on Individual Conflicts of Interest (COI) and Commitment?

Eight sections for Conflict of Interest, including Research
What is a COI?

Conflict of interest is a situation in which financial or other personal considerations:

- may compromise,
- may involve the potential for compromising, or
- may have the appearance of compromising

an employee’s (covered individual’s) objectivity in meeting University duties or responsibilities, including research activities.

UNC Board of Governors Policy Manual
Visualizing COI at UNC

- External or Personal Interests
- Institutional (aka University) Duties

- Actual Conflict of Interest
- Potential Conflict of Interest
- Appearance of a Conflict of Interest
What is a COI?
(continued)

The bias that such conflicts may impart can affect many University duties, including:

- decisions about personnel,
- the purchase of equipment and other supplies,
- the collection, analysis and interpretation of data,
- the sharing of research results,
- the choice of research protocols,
- the use of statistical methods,
- and the mentoring and judgment of student work.
Why the Conflict of Interest (COI) Process?

Comply with:
- UNC Board of Governors’ Policies and Regulations
- North Carolina State Statutes and Regulations
- Federal requirements (funding, human subjects)
- DHHS 42 CFR Part 50, 45 CFR Part 94 effective 08/24/2012
- NSF Grant and Administrative Guidelines January 2013

Mantra:
Disclose and Manage
Terms to know

• **COI**: Conflict of Interest

• **FCOI**: Financial Conflict of Interest means a Financial Interest that could directly and significantly affect the design, conduct, or reporting of research.

• **Disclosure**: to submit to the University the details of any interests, financial or personal, that might be a potential conflict of interest

• **Disclosure**: to share details of a conflict of interest with subjects, a research team or in presentations or publications as necessary
How Does the Research COI Process Work?

• COI Training  coi-training.unc.edu – Valid four years
• Event-based Disclosure
  • - Sponsored Research
  • - IRB Protocols
• Evaluation and Review
• Management
• Report to Sponsor
• Submit Event Specific Disclosure Annually OR on Change of Circumstances
Research COI Disclosures

Not trigger COI disclosures:
- Fellow, Graduate Research Assistant, Other Key Participant, Project Manager, Technical Staff, Undergraduate Student, Administrative Contact, Administrative Assistant, Faculty Advisor

Not trigger COI disclosures:
- Research Assistant, Regulatory Associate, Other (Read Only Access)
Why is a Disclosure Required for Each Study and Reviewed for a “Known” Conflict?

- Federal regulation
- University Policy
- Each study is different even if the “conflict” appears to be the same
  - Different drugs
  - Different protocol
  - Different people
    - For human subjects research, informed consent text must be context specific
What Happens Next?

No conflicts indicated
- System filters immediately
- IRBIS/Ramses automatically updated

Potential conflicts indicated
- Initial Evaluation at COI Office, usually further information is needed
- Next Step
  - Expedited Review with Committee Chair(s) (Existing Management plans or <$10K) OR
  - Full Committee (New conflict, >10K)

NOTE: Five Standing COI Committees – Medicine, Public Health, Dentistry, Pharmacy and College of Arts & Sciences. Some committees meet 1x per month; others every 2-3 months.
What are Financial Interests?

**Tangible**
- Personal Income - real or potential value
- Equity/Stock/Options (mutual funds excluded)
- Royalties/licensing fees/copyrights
- Indirect – family member
- Gifts (for self or others)
What are Non-Financial Interests?

- Board membership
- Executive position
- Scientific or technical advisor
- Trustee
- Volunteer position
  - (such as fundraising)
Management Principles

**Principles**
- Transparency
- Honoring the Student/Trainee Experience
- Protection of the credibility of the individual doing the work
Management Tools

**Tools**

- Management Plans
  - Public Disclosure
  - Independent Review of Data
  - Change in Roles
  - Monitoring Committees
- Alternative Options for Trainees
- Alternative Administrative Routing

**NOTE:** Significant financial interests presumed not allowable in human subjects research, particularly for a principal investigator. “Rebuttable” but like anything with human subjects research, higher standard.
Federal Anti-Kickback Statute

**Purpose:** To protect patients and federal health care programs from fraud and abuse

**Summary:** Prohibits the solicitation, receipt, offer or payment of remuneration “in return for” or “to induce” the referral of program related business, arranging for, or recommending, the purchase, lease, or ordering of any item or service reimbursed by a federal healthcare program

**Penalties**
- Civil: Fines up to $50,000; Exclusion from federal health care programs
- Criminal: Felony; Up to five years in prison; Fines up to $25,000
Anti-Kickback: Clinical Trial Risks & Solutions

Risks

- Direct payments to investigators
- Incentives for investigators (exotic meeting locations)
- Unbudgeted payments
- Financial COI
- Study biases (site selection, prescribing)
- Excess funds
- Study merit

Potential Solutions

- Institutional financial management
- Institutional contracting
- Institutional financial management
- Published and enforced COI policies
- IRB and training
- Published Policy on Excess Fund Disposition
- Internal review and approval
UNC-CH CONFLICT OF INTEREST POLICY IS STRICTER THAN FDA

• Stricter definition of significant financial interest
• Project-by-project disclosure of financial and other conflicts of interest
• Any changes to financial and other interests must be reported within 30 days.
• University rules regarding compensation from Sponsors
UNC Policy regarding Compensation from Sponsors

• University employees may not accept gifts, payments, or in-kind support (including but not limited to financial payments, gift certificates, books, conference attendance and payment of travel expenses)
  • as inducements for performance in a University project
  • except as expressly included in budgeted project costs in a contract between the University and the project sponsor.
FDA Investigator Financial Disclosure

• This disclosure requires that the Principal Investigator certifies that s/he does not have a significant financial holding in the company with which he wishes to contract.

• This helps to avoid conflict of interest situations in which the Investigator’s data may be called into question because of financial interest in the company.
COI in the News

Doctors Downplaying Drug’s Suicide Risks Attract FDA’s Scrutiny

Anna Edney
annaedney
September 13, 2016 — 10:46 AM EDT
Updated on September 13, 2016 — 12:20 PM EDT

The U.S. Food and Drug Administration has a message for doctors: The money you’re taking from pharmaceutical companies may be clouding your judgment.

(https://www.insidehighered.com)

U of Maryland chocolate milk research investigation released

Submitted by Josh Logue on April 4, 2016 - 3:00am

More than a few people probably chuckled a little, back in January [1], when the University of Maryland at College Park came under fire for a press release about research that linked drinking a brand of chocolate milk to recovery from concussions. Many said at the time that the press release seemed like unpaid advertising, given that the findings were never subject to peer review.
Websites & Email

Activities, Interests and Relationships:  air.unc.edu
All COI disclosures, External Activities for Pay

COI Training:  coi-training.unc.edu

Conflict of Interest Program:  research.unc.edu/offices/coi

Compliance Line - contact anonymously

General Email for questions:  coi@unc.edu,  epap@unc.edu
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FROM CDA TO STUDY CLOSURE

Panel Members:

Christine Nelson
Val Buchholz
Objectives

- Review the steps for successful clinical trial implementation beginning with first sponsor contact through study closure
So it begins...
Site Survey

- Site information form
- Site Qualification form
- Site Feasibility form
- Sponsors and CROs track turn around times
CDA

• CDA must be submitted via CRMS
• Cannot be signed by PI
• Quick turn around
• Not every CDA results in receiving a protocol
• Sponsors and CROs track turn around times
CRMS

- Protocol – final or draft?
  - May just send protocol until you are selected as a site
  - May send someone out to do site qualification visit
- Draft ICF
- Draft CTA
- Draft Budget
- Investigator brochure
- Pharmacy manual
- Lab manual
Feasibility

- Conduct a preliminary feasibility assessment
  - Read the draft ICF
  - Read the protocol
    - Potential enrollment
    - Study schedule (practical, reasonable)
    - Study duration
    - Non-routine care items
    - Imaging
    - Pharmacy
    - Lab/specimens
    - Resources (study coordinator, data manager, 24/7)
    - Adequate staffing
    - Training requirements
    - Special vendor requirements
Budget

- Billing Coverage Analysis
  - Spreadsheet from CRMS
  - Deemed and Qualified
  - Epic Billing calendar
- Funding source (federal or industry)
- Consistent approach
- Ensure start up fees are sufficient and invoiced
- Standardized fees
- Screen fails
- Monitoring visits
- Monthly invoicing
- IDS
- CTRC
CTA

- Submit CTA to OCT via CRMS
  - Complete review request form (RRF)
- Contract manager assigned
- Only the assigned contract manager negotiates the CTA
- Open communication with your contract manager
- The CTA can be negotiated while you negotiate your budget
- Once budget has been finalized with sponsor we can execute the CTA
IRB

- Submit when you are sure the PI wants to participate
- UNC local IRB or Central IRB
- ICF and contract must be consistent in respect to subject injury, stipends and what has been promised for free to the subjects
CTA and IRB

- IRB Approval
- ICF and CTA must be consistent
- OCT will check but you should also check
- If inconsistent the ICF will need to be revised
Ramses

- eIPF
- Internal budget
- Need an account
  - Set up by OCT
- COI
  - Individual
  - Institutional
Study Start Up

- When can I enroll! It's been months and I am already tired…
Study Start Up

• More to do!
  • SIV – Site Initiation Visit
  • Study supplies
  • CRMS – Clinical Research Management System
  • Epic
  • IDS – Investigational Drug Services at UNC Healthcare
  • Subject binders
  • Source documents
  • Logs
  • Study visit checklist
Study Conduct

- Enroll your first subject
  - Inclusion/exclusion criteria
  - ICF
    - Documentation of the informed consent process
  - Complete screening
  - Randomize
  - IVRS
  - CRMS
  - Epic
  - HIPAA form - HIM
Ongoing conduct of study

- Study visit checklists
- Case report forms
- Epic Billing review
- Investigational product accountability
- SAE/AE reporting
- Monitor Access
- Annual IRB renewal
- Amendments
- Modifications
- Deviations
Audits –FDA or Sponsor

• Who do you call?

• Hint – it’s not Ghost Busters!
Close-out

• All study subjects complete
• Data lock
• IRB closure
• Pack up the records
• Pat yourself on the back
Questions
Upcoming Training:

IRB Safety and UP Reporting

May 4, 2017, 12 noon – 1:30pm
Brinkhous-Bullitt Bldg, Room 219