ORIENTATION FOR NEW CLINICAL RESEARCH PERSONNEL

MODULE 3

Presented by

NC TraCS Institute
UNC Office of Clinical Trials
UNC Network for Research Professionals
Overall Agenda for Orientation

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

- **Module 2:**
  Informed Consent, Documentation, GCP, Study Start-up and Roles of Research Personnel

- **Module 3:**
  Contracting, ClinicalTrials.gov, Billing Coverage Analysis, Budgets and Accounting, and Essential Documents

- **Module 4:**
  COI, Epic & HIPAA Training, Preparing NIH Grant Budgets, IDS / Device Policy

- **Module 5:**
  Recruitment, From CDA to Close Out
CLINICAL TRIAL CONTRACTS

Nina Cannon, JD, CPCM / Erin Edwards
Office of Industry Contracting
Learning Objectives

• What are Clinical Trial Agreements (CTA’s) and why do we need them?
  What is inside of a CTA?
  Why is the CTA important to us?

• What does the Office of Industry Contracting (OIC) and the Office of Clinical Trials (OCT) do with regards to the CTA’s?
Basic Definition

- An agreement between two or more parties outlining the responsibilities, duties, and rights of each party.
- Sponsor agreements typically have standard, template language for uniformity that may be difficult to change.
Clinical Trial Contracts

Agreements Associated with Clinical Trials

- Clinical Trial Agreement (CTA)
  - Sponsor-initiated
  - Investigator-initiated
- Confidential Disclosure Agreement (CDA)
- Consortium/Network/Collaboration Agreements
- Material Transfer Agreement (MTA)
- Equipment Loan Agreement
- Subcontracts to sub-Sites and collaborators
- All negotiated and signed by Office of Industry Contracting (OIC); important to get an early start, and involve OIC from the beginning!
CTA

Reviewing and Negotiating CTAs

• OIC, under the Vice Chancellor for Research, provides review and negotiation for CTAs: http://research.unc.edu/offices/clinical-trials/index.htm

• Location:
  – 720 Martin Luther King Jr. Blvd, Suite 100, CB# 1651
  – General phone: 919-843-2698
Which office does what?

- **Office of Industry Contracting (OIC)** – Facilitates UNC-CH faculty contracting with industry focusing on industry specific needs, and all University clinical research contracts, confidentiality agreements, and data use agreements

- **Office of Clinical Trials (OCT)** – Facilitates UNC-CH faculty with clinical trial regulatory compliance and study implementation

- **Office of Sponsored Research (OSR)** – Facilitates UNC-CH faculty with non-profit grant submissions, proposals, and contracting with non-profit entities and the US federal and state government, and foreign governments
Content of Typical CTA (not an exhaustive list)

- Parties to the Contract
- Preamble
- Purpose, Protocol/Statement of Work
- Use of CRO’s
- Conformance with Applicable laws, Enrollment, Reporting/ Meeting Requirements
- Communication of results to site/subject
- Confidential Information
- Ownership & Use of Data/ Biological Specimens
- Intellectual Property/ Copyrights
- Publications
- Ethics Committee
- Debarment Certification
- Access to Premises/Audits
- Code of Ethics (CIA’s)
- Changes/Amendments
- Recordkeeping, Retention/Destruction
- Electronic Data/Signatures
- Indemnification by Sponsor
- Cross Indemnification by Site
- Subject Injury and MSP Reporting
- Insurance
- Breach, Remedies and Waivers
- Return/Destruction of Study Materials
- Purchase/Supply, Shipping, Use, Maintenance, Risk of Loss & Disposition of Equipment
- HIPAA
- Noncompetition/ Freedom to Contract
- Term and Termination/ Payment in Event of Termination/ Closeout
- Notices and Notice Timelines
- Publicity/Use of Names and Personal Information, Advertising
- Assignment/ Delegation
- Survival of Obligations
- Choice of Law, Venue, Arbitration, Mediation
- Billing, Invoicing, Adjustments
- Budget and Payment Schedules
Parties to the Contract

• Parties are the sponsor and University
  - PI is NOT a party to the agreement

  - PI signs agreement only as acknowledging (or as “read and understood”) his/her obligations outlined in the agreement
  - The PI does not acknowledge/sign Confidentiality Agreements
Protocol/Statement of Work

• Investigator conducts study according to the protocol
  – Need enough detail for very clear understanding of research, conduct and deliverables (e.g., data, reports, milestones).

• Investigator-initiated studies: PI is sponsor
  – Do not share your protocol prior to obtaining a confidentiality agreement
  – Has all the regulatory and oversight obligations of a sponsor (investigator (II) = sponsor)
  – Make sure the protocol/statement of work (SOW) is very clear! Who, what, when, where, why, how.
Protocol/Statement of Work

Potential Issues:
Why won’t the company pay me what I expected?

Why does the company want me to do EXTRA work?

Why did the company think they could use my data for their regulatory submission?

WHY NOT?
Communication of Results to Site/Subject

SPONSOR ↔ SITE → SUBJECTS

- Notification requirements between sponsor and site where information found during monitoring or data collection may impact subject safety/ participation.
  - Even after study has ended
- PI is required to notify subjects
  - Such communication is subject to IRB approval
The cost of bringing the average new drug to market is between $4 billion to $11 billion, taking into account failure rates. (Forbes, 2-10-2012)

In such a costly and highly competitive market, the industry trial sponsor is very serious about protecting their confidential information.
Control and Use of Data/ Biospecimens

Important issue: Who can do what with the information related to the study?

• Sponsor “owns” and prevents University from sharing with 3rd parties:
  – Case Report Forms (CRFs)
  – Study results (University carves out right to use results/data to publish)

• University “owns” and gives Sponsor limited right to use:
  – Subject medical records
  – Research notebooks
Control and Use of Data/ Biospecimens

• For industry-initiated studies, University gets to use results/data for:
  - Own internal research, educational, and patient care purposes
  - Publication, in accordance with terms of the contract

• For investigator-initiated studies, important to know:
  - Who owns the data or how can we use it?
  - Can PI use the data to seek funding for future studies?

• If Biospecimens are collected:
  - Can we use them for other research?
  - Can we put samples in a repository?
Let OIC know...

• If you want to use the data or bio-specimens collected under the study/protocol for future funded research (RRF).
Intellectual Property (IP)

Protected by patents

- **Industry-initiated studies**
  - Important goal is to protect UNC-CH/PI’s background IP

- **Investigator-initiated studies**
  - OIC will seek input from PI.
  - PI may have rights in IP.

Please make sure OIC is aware if you have additional funding for your study from other sources (e.g., Federal, Industry, Foundation) because the other funders may have study-related IP rights!
Publications

• Importance of publication to University:
  - Closely linked to “academic freedom”/tax exempt mission
  - Helps to establish PI’s expertise in field and build connections

• Sponsor cannot have editorial control (academic freedom)

• Registry requirement must be met in order to preserve ability to publish
  - Clinicaltrials.gov
Recordkeeping, Retention/Destruction

Contract specifies:

• How long records must be kept
• How they will be stored
• When they can be given to sponsor or destroyed
• Sponsors typically want long retention and storage obligations. Ask for funding for it in your budget!
Indemnification by Sponsor

- Protects Institution and employees from study-related claims/lawsuits

BUT...
- You must give “Notice” as required in the contract.
- You must follow the Protocol.
- You must properly report adverse events.
- You must comply with applicable laws and regulations for the study.
- You must keep good study records.
Subject Injury in Industry-Initiated Trials

• Sponsor covers cost of care and treatment of research-related injuries to subjects
  – Covers Injuries directly related to use of investigational product or protocol procedures

• Subject injury payment wording in CTA and informed consent must be consistent!
  – Consent using Central IRB - Work with your assigned Contract Manager in OIC. They will help you with the language until there is agreement on final language between sponsor and UNC.
Subject Injury

Medicare Secondary Payor (MSP) Reporting Requirements

- Medicare Reporting:
  - **Medicare Secondary Payer (MSP):** Medicare is secondary to sponsor obligation to pay for injuries in a clinical trial contract.

- Sponsor’s obligations to verify Medicare status and report subject-identifiable information (e.g., social security number [SSN]) to CMS are only triggered when:
  - Sponsor has agreed to be responsible for medical expenses
  - Research subject is injured; and
  - Claim is made for payment of expenses relating to injury

- Sponsor must then collect subject’s SSN for reporting purposes
Term and Termination/Payment in Event of Termination

• **Term**: How long is the agreement in effect?
  - Fixed with provisions for extension
  - Open, based on duration of study

• **Termination**: Who can quit and under what conditions?
  - Termination rights may not always be mutual

• **Payment** in the event of early termination
  - Nonrefundable start-up costs
  - Expenses incurred
  - Non-cancellable obligations
Notices and Notice Timelines

• Even though you notify sponsor of important events, it may not legally count as notice under your contract
  – The contract language matters!

• Notices: Who to notify, who to copy, how to notify

• Throughout contract: When to notify
  – Events trigger timelines (e.g., you become aware of a study related legal claim, subject is injured, someone working on the study is debarred, you find out you are going to be audited, there is a breach of a confidentiality obligation, you have a discovery or invention). You may work through UNC to notify in some cases.
Final Helpful Hints About Clinical Trial Contracts

• Start with filling out a new clinical trial record in CRMS

• (Contact oic@unc.edu (919) 962-3630)

• Work with OIC to provide important information as necessary for your study

• Before signing, read, paying close attention to:
   – Final budget to ensure it is the one you agreed to!
   – Any study specific revisions you may have requested of OIC
   – Your obligations under the agreement
Don’t Forget…

• READ THE CONTRACT before signing!

Call OIC if you have questions!

919-962-3630 (Ginger Morgan)
TRIAL REGISTRATION AT CLINICALTRIALS.GOV: FDA, ICMJE, NIH, AND CMS

Monica Coudurier
Office of Clinical Trials
What is ClinicalTrials.gov?

- Web based registry that provides regularly updated information about federally and privately supported clinical trials
- First version publicly available February 29, 2000
- Some information provided in ClinicalTrials.gov records includes the following:
  - Disease or condition and experimental treatments studied
  - Title, description, and design of study
  - Requirements for participation
  - Location(s) where the study is available
  - Overall study status
  - Recruitment contact information
  - Links to relevant information at other health Web sites, such as MedlinePlus and PubMed
What Trials *Must* be Registered?

There are 4 *independent* reasons requiring trial registry:

- ICMJE (International Committee of Medical Journal Editors)
- FDA - FDAAA Section 801/Code of Federal Regulations
- NIH (National Institutes of Health)
- CMS (Centers for Medicare & Medicaid Services)
The International Committee of Medical Journal Editors (ICMJE) Policy

Per the ICMJE, any trial meeting their definition of “clinical trial” must be registered to be considered for publication: “any research project that prospectively assigns people or a group of people to an intervention, with or without concurrent comparison or control groups, to study the cause-and-effect relationship between a health-related intervention and a health outcome.”

- **Health-related interventions** include any intervention used to modify a biomedical or health-related outcome (e.g., drugs, surgical procedures, devices, behavioral treatments, dietary interventions, and process-of-care changes). **Health outcomes** include any biomedical or health-related measures obtained in patients or participants, including pharmacokinetic measures and adverse events.
ICMJE Policy

• **Purely observational studies** (those in which the assignment of the medical intervention is not at the discretion of the investigator) will not require registration?
HHS/Code of Federal Regulations (CFRs)

- Pertains to trials using an FDA-regulated intervention

- Trials that must be registered are called “Applicable Clinical Trials” (ACTs), these trials generally include:

  - Trials of **Drugs** and **Biologics**: Controlled, clinical investigations, (other than Phase 1 investigations), of a product subject to FDA regulation (*If efficacy is an endpoint of Phase I study, it must be registered*).

  - Trials of **Devices**: Controlled trial with health outcomes, other than small feasibility studies, and pediatric postmarket surveillance.
National Institutes of Health (NIH)

- NIH requires **Registration** of trials meeting FDA requirement;

- NIH requires **Results reporting** for all NIH supported clinical trials registered in ClinicalTrials.gov, regardless of whether or not they are required to do so under FDAAA
Effective January 1, 2014 CMS began requiring the NCT number on claims submitted to Medicare

- Dummy numbers no longer optional (since Jan 1, 2015)

- NCT must be entered into CRMS
Recent HHS/NIH Initiatives

• Federal register release Sept 21, 2016: Effective January 18, 2017

• Must submit full protocol and statistical analysis plan along with results submission

• ACT definition expanded to include unapproved products

• NIH will post records within specified time despite QC status (disclaimer citing concern may be posted)

• All single & multi-group studies with prespecified outcome measures considered “controlled.”
New Rule--Useful Links

• Federal Register Notice: HHS Final Rule

• Federal Register Notice: NIH Policy

• Summary of Changes: HHS Final Rule and NIH Policy
Which Studies Require Data Results?

- FDAAA 801 (effective Sept. 27, 2008) expanded registry and added results database to include:
  results reporting for those trials meeting the definition of “Applicable Clinical Trial” or ACT (*regardless of whether the study has an IND or IDE*)

- Serious Adverse Event reporting (effective Sept. 27, 2009)

- Combined DHHS + NIH Final Rule (effective Jan. 18, 2017)
  All Federally funded studies meeting “clinical trial” definition
Who is Responsible for Registering Trials?

Clinicaltrials.gov registration is the responsibility of the trial Sponsor:

- UNC Investigator initiates and sponsors trial – **PI registers**
  - Trial in which PI obtains industry funds
  - NIH or other grant funded trial (external or internal grants)
  - UNC PI holds an IND or IDE

- Industry initiated trial – **Industry sponsor registers**
Getting Started
CT.gov User Account Set-Up

If UNC PI must register on CT.gov:

- CT.gov user account set-up and record assistance available through the UNC Office of Clinical Trials—contact Monica Coudurier at (919) 843-2333 or m_coudurier@unc.edu

- Mary O’Dwyer for LCCC/Oncology studies mary_odwyer@med.unc.edu
Deadlines for Registering Trials

- **ICMJE Policy** – Study must be registered prior to enrollment of first subject. 
  
  *If an investigator would like to publish the data*

- **HHS/CFRs: FDAAA, Section 801** – Study must be registered no later than 21 days after enrollment of the first subject. 
  
  *Required by US Public Law and must be done to avoid $$ penalties*

- **NIH** – Unspecified

- **CMS** – Prior to claims submission
Record Upkeep: Following Registration

• Ensure the information is complete, accurate, and updated every 6 months or as changes occur
  • Review the record and update as necessary
  • Active trials (Not yet recruiting; Recruiting; Enrolling by Invitation; Active, not recruiting)
  • Update status when enrollment ceases

• Provide Results within 1 year of Actual Primary Completion Date
  • i.e., date that the last primary outcome measure data was collected
## Registration Overview

<table>
<thead>
<tr>
<th></th>
<th>Phase I</th>
<th>Phase II-IV</th>
<th>Other Interventional Trials</th>
<th>Registration timeline</th>
<th>Posting of Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>NIH</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>Unspecified</td>
<td>Yes</td>
</tr>
<tr>
<td>ICMJE</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>Prior to enrollment of 1st subject</td>
<td>NO</td>
</tr>
<tr>
<td>Applicable Clinical Trial (ACT) per CFRs: FDAMA, FDAAA, Public Law 110-85</td>
<td>NO (unless reporting efficacy)</td>
<td>YES</td>
<td>NO</td>
<td>Within 21 days of 1st subject’s enrollment</td>
<td>YES</td>
</tr>
<tr>
<td>CMS</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>Prior to claims submission</td>
<td>NO</td>
</tr>
</tbody>
</table>
**Monetary Penalties**

- **What are the penalties for failing to register an “Applicable Clinical Trial?”**

Penalties for responsible parties who fail to register, or provide false or misleading information in connection with, applicable clinical trials are significant and may include civil monetary penalties (up to $10,000 per day) and, for federally-funded trials, the withholding or recovery of grant funds. See PL 110-85, Sections 801(a), (b), (adding new 42 U.S.C. 282(j), and new 21 U.S.C. 331(jj).
Questions
BILLING COVERAGE ANALYSIS (BCA)

Andrea Eiring, MSM, CCRA, CPHRM
Office of Clinical Trials
DEFINITION

A systematic review of research-related documents to determine the (Medicare) billing status of both the study itself and the items and services provided to the research subjects over the course of the study.
A.K.A. Medicare Coverage Analysis

• Medicare ?#$%&*/!??

• Primary BCA objective -- to ensure that all clinical trial costs are billed to the appropriate payer (i.e., Sponsor, a third-party payer (including Medicare), or the patient.

• Almost every study has the potential to enroll Medicare/Medicaid patients as participants.

• Medicare rules tend to set the trend for the payer industry.
The Billing Coverage Analysis should:

- **Lead budget development process:**
  - to allow negotiators to identify what items and services can appropriately be billed to third party payers,

- **Be completed:**
  - before negotiating budget to ensure the sponsor adequately covers study costs, and
  - prior to enrolling study subjects and performing clinical research procedures,

- **Be communicated:**
  - to the charge capture and billing systems (Epic) in order to prevent inappropriate billing.
Which studies require BCA?

A billing coverage analysis is required for **ALL** trials involving any kind of Hospital billing - even those studies wherein the sponsor pays for everything.

- Drug trials
- Device trials
- Otherwise, any trial (e.g., behavioral) that includes hospital billed charges of any kind.
Current Medicare Clinical Trial Policy

• **National Coverage Determination (NCD) 310.1**
  “Medicare covers the routine costs of qualifying clinical trials, as well as reasonable and necessary items and services used to diagnose and treat complications arising from participation in all clinical trials.”

• All other Medicare rules apply.
“Qualifying” Clinical Trials

Determined by 2-step process:

- **Step 1**: Determine if trial is one that CMS has “deemed” to meet the 7 desirable characteristics
  - Funded by, or Supported by center or cooperative group funded by NIH, CDC, AHRQ, CMS, DOD, or VA - OR -
  - Conducted under an IND application - OR -
  - Determined IND-exempt according to FDA regulations

AND

- **Step 2**: Confirm that trial meets all 3 of the following criteria:
  1. Evaluates an item or service that falls within a benefit category - AND -
  2. Study designed with therapeutic intent - AND -
  3. Enrolls patients with diagnosed disease
“Qualifying” Trials-Device Trials (cont)

- Medicare pre-review required for Category A (experimental) and Category B (Nonexperimental/investigational) IDE device protocols
- IDE holder responsible for submitting to CMS
- Cannot bill routine costs of a Cat B device trial unless the trial is approved (Cat A costs can be billed under certain criteria with approval)
- CMS website lists all approved IDE protocols
If the study is a qualifying clinical trial, then “routine costs” in the trial can be billed to Medicare, provided the item or service is otherwise covered by Medicare.

In simple terms, a “routine cost” is one of the following:

- Conventional care
- Administration of the investigational item
- Detection, prevention, and treatment of side effects or complications

“Routine costs” do not include items like data collection, quality of life assessments, or tests done more often than “routinely” outside the trial.
“Qualifying” Clinical Trials (cont)

If trial fails either part of the two-part test, or has not been pre-approved by CMS if it is an IDE protocol, it is **not** a qualifying clinical trial and none of the protocol-required items and services are billable to Medicare, even if the item or service would be covered outside the trial.
“Qualifying” Clinical Trials (cont)

• An item or service that is NOT covered outside a clinical trial will not be covered when performed or given as part of a qualifying trial, even if the item or service is “standard of care.”

• Most self-administered drugs are such non-covered items. Example: P.O. (orally administered)
Exclusions from Medicare Coverage

We cannot bill Medicare for routine costs that are:

- paid for by the sponsor,
- promised free in the informed consent document,
- not ordinarily covered by Medicare, or
- performed solely to determine trial eligibility, data collection, or analysis.

In other words….. If the sponsor pays for an item or service; or an item or service is provided “free of charge” to an enrollee, then Medicare cannot be billed for that service.

Practical Implications

- If a “deal” (i.e., free service) is given to an enrollee in a research study, then Medicare must receive the same “deal” (i.e., a free service) and can’t charge Medicare.
Pre-Study Financial Workflow

Coordinator builds schedule of events in Excel template

Budget goes to OCT for Coverage Analysis Verification

Integrated Billing Office supplies codes and research prices

Budget and contract finalized

Office of Clinical Trials or Lineberger CPO creates billing protocol for study in Epic

Coordinator attaches billing calendar to study record in Epic.
Performing a Billing Coverage Analysis

Gather necessary items:

- **FINAL** Protocol;
- Draft contract + budget;
- Informed Consent (Sponsor’s model is fine);
- Investigational brochure;
- Lab manual;
- FDA correspondence;
- Miscellaneous: IND/IDE number, NCT number.
**Completing the BCA workbook**

**Determine if a BCA is needed, and which worksheets are needed if one is required**

<table>
<thead>
<tr>
<th>Payer</th>
<th>Definition</th>
<th>Required BCA Worksheets</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bill to sponsor only</strong></td>
<td>Procedures/Services are being done for research purposes only and all will be paid for by the research sponsor.</td>
<td>Instructions, Coverage Analysis, Billing Calendar, and Integrated Billing Tabs.</td>
</tr>
<tr>
<td>BCA Fee Not Req’d</td>
<td></td>
<td>[Deemed &amp; Qualifying is optional]</td>
</tr>
<tr>
<td><strong>Bill to sponsor and patient’s insurance</strong></td>
<td>Procedures/Services are being done for a mix of research and routine care purposes only. This may include procedures/services which are done for research purposes or for routine purposes that are paid for by the sponsor or the patient’s insurance.</td>
<td>Instructions, Deemed &amp; Qualifying, Coverage Analysis, Billing Calendar, Integrated Billing Tabs.</td>
</tr>
<tr>
<td><strong>$2K BCA Fee is Required except for Federally funded trials</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Bill to patient’s insurance only</strong></td>
<td>All procedures/services are routine care and would be done whether or not the participant was in the trial.</td>
<td>Instructions, and Deemed &amp; Qualifying Tabs</td>
</tr>
<tr>
<td>BCA Fee Not Req’d</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>There is nothing to bill</strong></td>
<td>Study team effort only, no billable procedures/services.</td>
<td>BCA Worksheet completion is not required.</td>
</tr>
<tr>
<td>BCA Fee Not Req’d</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Completing the BCA workbook (cont)

Download BCA workbook template from CRMS

Instructions tab and other various tabs as applicable (see Billing Coverage Analysis Instructions document at http://researchcentral.tracs.unc.edu)

Upload protocol and consent

Deemed & Qualifying tab

- Assess trial type: Drug, Device, other (e.g., service)
- Apply criteria to qualify & determine trial’s billing status ([NCD 310.1] Deemed & Qualifying; CMS coverage website)
Completing the BCA workbook (cont)

Determining the “qualifying” status is done by answering a series of questions as shown below:

1. Does the investigational item/service fall into a Medicare benefit category?

2. Does the study have therapeutic intent?

3. Does the study enroll patients with diagnosed disease?

4. Is the study a deemed trial?
Completing the BCA workbook (cont)

Coverage Analysis tab

- List all billable procedures
- Match visit headings to protocol
- Identify items/services provided “free” by Sponsor
- Indicate billing category type (Routine, Study, Effort) for each visit at which the procedure is performed
- Choose justification for procedures designated as ‘Routine’ Care based on Medicare acceptable guidelines

- Avoid acronyms
- List procedures separately
- Multiple possible procedures
- Lab analytes

Separate, Include all
Completing the BCA workbook (cont)

**Integrated Billing (IB) tab**

- Specify location(s) where each procedure will be performed
- For labs, specify who is collecting the sample
- Include any other details to help identify correct procedure code
- Enter CPT code (if known)

⭐️ *Route BCA to OCT within CRMS*

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**CRMS Step 2: OCT Coverage Analysis Review**

- OCT reviews for completeness then ⭐️ *Routes to Integrated Billing*

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**CRMS Step 3: Integrated Billing (IB) Coding & Pricing**

- Integrated Billing enters codes and pricing information then ⭐️ *Routes back to BCA creator*
Completing the BCA workbook: (cont)

CRMS Step 4: Research Coordinator Budget Finalization

- BCA creator receives email from CRMS
- Check proposed budget/contract to determine if offer covers items and services that are not billable
- Negotiate with sponsor to finalize budget terms
- Make sure BCA matches final budget
- **Finalize** “Will it cost you anything to be in this study?” section of Informed Consent

- **Send final negotiated budget to Office of Industry Contracting (OIC) for inclusion in final contractual agreement**

Route BCA to PI within CRMS
Completing the BCA workbook: (cont)

CRMS Step 5: Lead Principal Investigator BCA Certification

- Principal Investigator (PI) receives email from CRMS
- Ensure that PI is aware that action is required

⭐ PI routes final BCA to OCT within CRMS
Completing the BCA workbook (cont)

CRMS Step 6: OCT Budget Review and Contract Finalization

- OCT checks off in Alice that all BCA steps have been completed
- If any charges will be made through Epic:

⭐ OCT Routes final BCA for calendar build within CRMS

CRMS Step 7: OCT or Lineberger Creates Epic Calendar

- CRMS creator notified of calendar readiness
All research proposals which involve drugs, devices, or billing for items or services from UNC Hospitals, whether technical or professional charges must complete the Billing Coverage Analysis (BCA) within CRMS. This includes: Deemed & Qualifying Questionnaire, Coverage Analysis Schedule of Events Grid, and Billing Calendar, and Integrated Billing sheet will be available in CRMS with any hospital and professional billing codes provided. After you finalize the Staff Time & Other Fees, Internal Budget, and Sponsor Cost authorization and approval by the Principal Investigator and OCT.

[More detailed instructions are provided on the first sheet of the Excel Workbook.]

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### CRMS Budget Spreadsheet

<table>
<thead>
<tr>
<th>Steps</th>
<th>Status</th>
<th>Approver</th>
<th>Date</th>
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<tbody>
<tr>
<td>1</td>
<td>Research Coordinator Saved Initial Budget</td>
<td>Tyrone Wade</td>
<td>05/19/2015</td>
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<tr>
<td>2</td>
<td>OCT Coverage Analysis Review</td>
<td></td>
<td></td>
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<tr>
<td>3</td>
<td>Integrated Billing (IB) Coding &amp; Pricing</td>
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<td></td>
</tr>
<tr>
<td>4</td>
<td>Research Coordinator Budget Finalization</td>
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<td>5</td>
<td>Lead Principal Investigator BCA Certification</td>
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<td></td>
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<tr>
<td>6</td>
<td>OCT Budget Review and Contract Finalization</td>
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<tr>
<td>7</td>
<td>Integrated Billing (IB) Creates Calendar</td>
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<td>8</td>
<td>Complete (Calendar Not Needed)</td>
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<td></td>
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<tr>
<td>9</td>
<td>Complete (Calendar Created)</td>
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</table>

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It is important that you read the instructions in order to complete the Billing Coverage Analysis correctly for your study. Please click to review the instructions.
Role of Informed Consent Form

- Every research study must have a section in the Informed Consent Document that discloses added costs the subject may incur while participating in the trial.
  
  EXAMPLE: “You or your health plan must provide payment for hospital, clinic, and other medical costs that are considered routine care for patients with your disease. The sponsor of the study “XYZ Company” will provide the study drugs at no cost to you. Those procedures done solely for the purposes of the study will also be provided to you by “XYZ Company” at no charge.”

- Make sure the Sponsor budget and Informed Consent Document match for items billed to insurance or covered by Sponsor
Non-Compliance or Improper Billing

• Failure to comply with applicable laws, regulations, and Informed Consent documents
  ❖ Intentional or unintentional
  ❖ Serious and “continuing” non-compliance is reportable to federal funding agencies and FDA (for studies subject to their authority)

• Why does this happen?
  ❖ Decentralization
  ❖ Unfamiliar with the rules
  ❖ Not paying attention
  ❖ Lack of Coordination, Collaboration, and Communication
False Claims Act (31 USC §§3729-33)

Enacts liability against a person or entity who knowingly ignores CMS regulations (as demonstrated by “reckless disregard” or “deliberate ignorance”) by:

- Submitting a false claim,
- Using a false record or statement to get a claim paid or approved,
- Causing a 3rd party to do either of the above
False Claims Act (31 USC §§3729-33) (cont)

• Civil penalties: $5K-$11K per submitted claim plus up to 3x damages incurred by government

• Possible exclusion from participation in Federal health care programs

• Regardless of the funding source (i.e., applies to Industry sponsors and Federal grants alike)
Risks of Non-Compliance

Properly performed BCA is necessary to protect researchers and the institution against violations of the False Claims Act and other regulations. Inappropriate Medicare billing is considered fraud and can lead to large fines. The rules do not allow billing for services:

- that are part of a non-qualifying clinical trial
- promised free in the informed consent
- already paid by the sponsor (double-dipping)
- performed for research-purposes only
  - without providing the NCT number
  - to Part C (Medicare Advantage Plans) rather than the Medicare Administrative Contractor (MAC)
  - DEVICES: without CMS prior approval

Systems & processes are needed to apply proper billing and diligence to ensure charges go to the correct party and are not billed incorrectly or to multiple payers.
BCA Training Opportunities

• Training needed to properly complete the Billing Coverage Analysis process.

• Research 100 provides detailed BCA spreadsheet information.

• CITI training provides information on evolution of the need for coverage analysis and includes sample scenarios in the questions.
BUDGETING AND ACCOUNTING OF RESEARCH FUNDS

Jillyan Cunnup
Administrator, Division of Endocrinology
The Financial Struggle
Process of Building a Budget

1. Review most recent protocol and study activity listings (Protocol Feasibility)
2. Review Contract and current budget (if provided)
3. Identify procedures required and determine cost
4. List all other fees, direct and indirect

Diagram:
- Review most recent protocol and study activity listings (Protocol Feasibility) → Identify procedures required and determine cost → List all other fees, direct and indirect → Review Contract and current budget (if provided) → Review most recent protocol and study activity listings (Protocol Feasibility)
Budget Development

• Clinical Trial Agreement
  • Start up and Advance payment
    • When and How much?
  • Payment Cycle
    • How often will they pay?
  • Withholding %
    • How much are they going to hold back?
• Length of Storage
  • 10-20-30 years?
• Final Payment
  • Timing of Payment?
Billing Compliance and IRB Review Fees Invoiced by the Office of Clinical Trials

<table>
<thead>
<tr>
<th></th>
<th>Industry-Funded Studies using a Central IRB</th>
<th>Industry-Funded Studies using UNC’s IRB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial IRB Review Fee</td>
<td>N/A</td>
<td>$3,000</td>
</tr>
<tr>
<td>Initial Preparation Fee</td>
<td>$1,000</td>
<td>Included in above</td>
</tr>
<tr>
<td>IRB Renewal Fee</td>
<td>N/A</td>
<td>$750</td>
</tr>
</tbody>
</table>

**IRB Fees** (not subject to F&A) *IRB fees invoiced by the Office of Clinical Trials.*

IRB review fees shall be incurred upon IRB review, even if a study contract has not yet been executed. The IRB review fees are assessments for a portion of the real costs associated with protocol review and related study requirements by the IRB. The actual costs of the review process are still incurred if subjects are never enrolled, if the study terminates before milestones are met, if expenditures exceed revenue, or if a contract is never finalized. The invoice is therefore due and payable upon receipt. *The investigator and/or department will be responsible for all costs not covered by the sponsor, specifically including the IRB (and BCA) review fees.*
Billing Compliance Fees

- **Billing Compliance (for conduct of BCA) fee** (not subject to F&A)
  
  *BCA fees invoiced by the Office of Clinical Trials*

- A fee of $2,000 will be charged to the sponsor as a Billing Compliance Fee to cover the cost of conducting a BCA, and should be included in budgets submitted to the sponsor as of March 1, 2014. This fee is incurred upon conduct of the BCA, even if a study contract has not yet been executed.

- The purpose of the BCA is to determine deemed and qualifying status as well as which routine care costs may be billed to Medicare or other insurers and which costs must be paid by the sponsor. The Billing Coverage Analysis is required to be performed prior to the initiation of the clinical trial to ensure proper billing of services and financial feasibility.
External Budget

• Direct Costs
  • Labs
  • EKG
  • CT Scans

• Effort Costs
  • Informed Consent- Creation of CF as well as consenting subject
  • Physical Exams, Vitals and History
    • Coordinator and PI Time
  • Drug Dispensing
  • Review of Labs
    • Coordinator and PI Time
  • Scheduling of Patients
    • How long does it take to transport that patient for a CT Scan etc?
• Recruitment
• Monitor Visits
Effort Based Costs

Effort Based Procedures
- Informed Consent
- Physical Exams
- Vitals and History
- Drug Dispensing

PI and CRC Time
- Review of Labs, Scheduling of patients, recruitment of patients monitor visits etc.

F&A
- Ensure correct University F&A rate is being applied
Invoiced Items

- Start Up Fee
- Advertising
- Document Storage
- Rent
- Screen Fails
- Adverse Events
- FDA/Sponsor Audits
- IRB/BCA Fee

- IRB Renewal
- IDS
- Dry Ice
- Protocol Amendment
# Facilities and Administration Rate

<table>
<thead>
<tr>
<th>Activity</th>
<th>On-Campus</th>
<th>Off-Campus (10-mile radius)</th>
<th>Off-Campus (Remote)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Organized Research</td>
<td>52%</td>
<td>28.00%</td>
<td>26.00%</td>
</tr>
<tr>
<td>Instruction</td>
<td>50%</td>
<td>28.00%</td>
<td>26.00%</td>
</tr>
<tr>
<td>Other Sponsored Activities</td>
<td>36.%</td>
<td>28.00%</td>
<td>26.00%</td>
</tr>
<tr>
<td>Clinical Trials (Federal)**</td>
<td>52.00%</td>
<td>28.00%</td>
<td>26.00%</td>
</tr>
<tr>
<td>Clinical Trials (Non-Federal)**</td>
<td>28.00%</td>
<td>28.00%</td>
<td>26.00%</td>
</tr>
</tbody>
</table>
Successful Negotiation

• What is negotiation?
  • Negotiation is the process of two parties or individuals reaching an agreement and actively participating in making decisions

• Successful Negotiation?
  • Succeeding means that you work with the other party to reach a solution to the issue you are all happy with it does not mean viewing negotiation as a battle to be won!
Federally Funded Budgets

RFA-Request for Application

- All Federal Funded applications are linked to a RFA which details the requirements for the application.

SF424

- Common packet used for NIH submissions will include budget, bio sketches, research plans, science of grant etc.

Salary Cap/Cost Share

- The current NIH Salary Cap is 185,100 anyone being paid from the grant making over that amount must have a cost shared effort.

- Cost Sharing is the portion of the project that is contributed by the University for example if you have a salary of 200,000 and are going to spend 10% of your efforts (20,000) you are only allowed to charge the grant for 10% of 185,100 (18,510) the difference must be charged to a University account and paid for by the University. Using this example you would need approval to cost share $1,490
Modular Budget Vs. Detailed Budget

Modular Budget

- Used only in certain types of NIH applications provides a less detailed budget with a maximum of 25,000 per module (250,000 per project)
- Does NOT list out salary and fringe benefit rates though the salary cap does still apply

Detailed Budgets

- Effort must be shown in Calendar months not % of effort
  - (10% effort = 1.20 calendar months)
- Fringe Benefits
- Senior/Key Personnel
- Equipment
- Travel
- Publication
- Other costs related to project
- Maximum depends on the information in the RFA
"Wow this is a great budget they are giving up more money than we need"

Said no one ever.
Accounting of Research Funds

- The tracking of research funds can make or break a research project. This is often done by various people in the department but is crucial to success.

Visits  Payment  Expenses
Visit Tracking

- Industry Sponsored Trials
  - Log of completed, skipped or incomplete visits
  - Track when data entry is completed per visit
  - Keep a log of each visit completed by the subject and make note if certain parts of the visit were not completed or if a visit was skipped.

- Federal Funded
  - Tracking subject visits is equally important on a federal funded studies. Depending on how the study is set you up may have already received a set amount based on the number of patients. If you fail to recruit or skip a visit you could end up paying back money at the end of the grant.
Patient Data Invoicing - Why and How?

• Why should we invoice?
  • To ensure ACCURATE payment of completed work.
  • To ensure TIMELY payment of completed work
  • To ensure QUALITY reconciliation can occur

• How do we invoice?
  • Send invoice to the sponsor with visit data
  • Send invoice to managers with visit data
Payment and Expenses

• Checks
  • Ensure checks are sent in a timely manner based upon contract
  • Always verify that the amount of money received matched the amount of work completed.

• Expenses
  • Track procedure, patient payments, salary, supplies as well as other study related costs.
Financial Compliance

ARMED ROBBERY, EH? I'M IN FOR BEING OUT OF COMPLIANCE WITH A FEDERAL GUIDELINE.
Effort Certification and Reporting Technology

- Effort is the portion of time spent on a given professional activity and expressed as a percentage of the total 100% professional activity for which an individual is employed by UNC.

**Important points:**
- The government recognized that it is a “reasonable estimate”
- Total effort must equal 100%
- Effort is not based on a standard (e.g. 40-hour) work week, instead based on whatever was worked
- 100% effort considers all professional activities related to the individual UNC appointment.
- Effort does not include outside activities (external consulting etc)

**Certifying Effort**
- Effort is certified on a regular basis via ecrt.unc.edu
- All employees paid from sponsored activities are required to certify the effort spent
- Effort is calculated based on the information in the payroll system
- The investigational item or service itself, unless otherwise covered outside the clinical trial
Closing of Account

• All money received?
  • Make sure all visits, invoiced items,
  • Always verify that the amount of money received matched the amount of work completed as well as the amount on the contract.

• Expenses
  • Verify IRB, IDS and other University expense have been paid. Often with UNC bills are delayed and it is your responsibility to check this before closing a study.

• Residual Funds
  • If you have money leftover you will be allowed to transfer the funds into a residual. Residual accounts are managed at the Department/Division level. You will need to be aware of what the policy is on spending and accountability. Federal funded grants will require written communication and approval from the NIH for carryover or no-cost extensions.
ESSENTIAL (REGULATORY) DOCUMENTS

Valorie Buchholz
Associate Director for Quality Assurance
Office of Clinical Trials
Mornings in the Regulatory World
What Types of Trials Should Meet GCP Guidelines?

- FDA Regulated Trials
  - IND / IDE trials

- Federal funded (NIH) Trials

- PI Initiated Trials with External Funding

- PI Initiated Trials – No Funding

- “A quality research site complies with the ICH Good Clinical Practice guidelines, the accepted international ethical and scientific quality standards for designing, conducting, recording, and reporting trials involving human participants.”

American Society of Clinical Oncology Statement on Minimum Standards and Exemplary Attributes of Clinical Trial Sites; R. Zion et al; Journal of Clinical Oncology; April 7, 2008
What are Essential Documents?

GCP defines Essential Documents as:
- the documents which individually and collectively permit the evaluation of the conduct of a trial and the quality of the data produced

Many researchers refer to these documents as Regulatory Documents OR Reg Docs

(ICH GCP E6 8.1)
GCP Essential Documents
Guidance

• Categorizes documents into 3 sections

• Defines whether the sponsor, site or both are responsible for maintenance of the documents
  • Reminder – If your investigator holds and IND or IDE, he/she also has sponsor responsibilities
BEFORE STUDY IS INITIATED:

Investigative Site

Sponsor/Funding Agency
<table>
<thead>
<tr>
<th>IND trials – 1572</th>
<th>Statement of Investigator</th>
</tr>
</thead>
<tbody>
<tr>
<td>IDE Trials – Investigator Agreement</td>
<td></td>
</tr>
</tbody>
</table>
Documentation for Investigators and Sub-Investigators

**Curriculum Vitae**
- Documents qualifications and eligibility to conduct trial

**Licensure**
- Documents eligibility to provide medical supervision of subjects

**Certifications**
- Documents qualifications to perform tasks as delegated
## APPROVAL DOCUMENTS

- Institutional Review Board
- Regulatory Authorities
  - Protocol Review Committee
  - Institutional Biosafety Committee
- Others as required

## AGREEMENTS

- Site and Sponsor
- Site and CRO
- Financial Aspects
  - Disclosure Forms (FDA)
- Both Site and Sponsor keep copy of CTA
AND MORE……
• IRB Committee Rosters
• Investigational Product Shipping and Accountability Records
  • Applicable for both Drugs and Devices
  • Procedures for Decoding Blinded Trials
    – used in case of emergency – doesn’t break blind for others
• Study Initiation Report
  – Document questions asked during SIV!
READY, SET, GO!
DOCUMENTS UPDATED DURING THE STUDY

1572
/Investigator Agreement
Only required by FDA if a new protocol is added to the IND and the Investigator is participating OR a new investigator is added

Laboratory Accreditations (CLIA/CAP)

Investigator’s Brochures

Normal values to lab ranges

Revisions to Protocols
Update

IRB renewals / modifications

Regulatory Authorities
- Biosafety Committee
- Protocol Review Committee

CV’s / Licensures / Certifications for New Investigators
ADD

LOGS

DELEGATION OF AUTHORITY LOG / SIGNATURE SHEET

SCREENING LOG

SUBJECT ENROLLMENT LOG

SUBJECT ID CODE LIST

TRAINING LOGS
Protocol IB Equipment CRF Completion / Correction

RETAI NED BODY FLUID / TISSUE SAMPLES
# SAFETY

## Serious Adverse Events
- Report to sponsor and IRB

## Unanticipated / Unexpected Adverse Events
- Report to Sponsor and IRB

## Safety Information / Reports
- Sponsors Notify Sites
STUDY COMPLETION

- Logs
  - Investigational Product Accountability
  - Subject Identification Code

- Final Close-out monitoring report
  - Includes where site documents will be stored

- Termination of study with IRB

- Clinical Study Report
Inspections and Essential Documents

Sponsors and other regulatory agencies look to these documents as part of their processes to confirm the validity of the conduct of the trial and the data collected.
Record Retention Requirements

Depends on the Type of Trial

• FDA: 21CFR312.62 (IND) OR 21CFR812.140 (IDE)

• Funding source contracts

  (see Section 6 – Grants and Research Records)

![Pediatric Studies](image)
TAKE AWAY POINTS

- Organized
- Consistent
For Additional Information


It's QUESTION TIME!!
PLEASE VISIT

TRACS.UNC.EDU / RESEARCH CENTRAL

FOR A COPY OF THIS PRESENTATION & ADDITIONAL HELPFUL INFORMATION