Reliance on Independent/Central IRBs for Multicenter Clinical Trials

October 15, 2013
Outline

• Background
• New policy and process
• Non-IRB reviews
• Revised fee structure
• Workflow
• Demo of IRBIS application items
• Q&A
Background

- Academic institutions increasingly relying on independent IRBs
  - “Sole provider” model employed by most centers has its own drawbacks
  - Few data to guide decisions
- In 2012-13, UNC conducted novel pilot project
  - Randomized, controlled comparison of local vs central IRB review
  - Assessed feasibility and acceptability of relying on any central/independent/commercial IRB already involved with a multicenter trial, provided certain criteria were met
Pilot Project

• Results
  • Quality of review by central IRBs was good
  • Time savings of ~20 days per trial, if master service agreements already in place
    • Little advantage if no standing agreement
  • 8 central IRBs utilized for 22 protocols randomized to the “experimental” arm
    • Reinforced our hypothesis that “sole provider” model misses many opportunities to streamline
  • Data supported informed policy change
New Policy and Process

• Effective October 15, 2013, UNC will rely on the approval and oversight of the central/independent IRB already involved with an industry-sponsored, multicenter trial, provided certain criteria are met
  – Sponsor/CRO has contracted with independent IRB to provide central review for any/all sites in that study
  – IRB is on UNC’s pre-approved list
Which IRBs?

- Alpha IRB
- Aspire IRB
- Chesapeake IRB
- Compass IRB
- Copernicus IRB
- Ethical & Independent IRB
- IntegReview IRB
- IRB Company
- IRB Service, LTD
- Quorum IRB
- Schulman and Associates
- Sterling
- WIRB

Additional IRBs may be added over time, on request.
What is this NOT?

• Use of central IRB under these circumstances is allowed, encouraged, should be desirable but is NOT mandatory
  – You still have the option to use UNC IRB

• This is NOT a mechanism to involve a commercial IRB in “homegrown” single site studies in which that IRB is not already involved
  – These will remain under UNC IRB oversight
Your interaction with central IRB will shift from protocol review to site registration

(think “add personnel”)

UNC IRB

Protocol
Personnel & Facilities
Non-IRB Issues

Central IRB

Protocol

Sponsor/CRO

Site
Site
Site
Site
Site
Important to Realize

• Even when *IRB review* is “outsourced”
  – UNC is still responsible
  – There are other University-based reviews and obligations that are not transferred to central IRB, and must still be satisfied
    • HIPAA
    • Conflict of Interest (COI)
    • Investigational Drug Service (IDS)
    • Radiation safety
    • Institutional biosafety
    • Data security
    • Institutional consent language → congruence with CTA

• OHRE and IRBIS will remain central relay station
Revised Fee Structure

Industry-Funded Multisite Clinical Trials WITH Central IRB

• IRB Preparation Fee - $1,000

All Other Industry-Funded Clinical Trials

• IRB Preparation & Review Fee - $3,000
• IRB Renewal Fee - $750
1. Submit IRB application requesting reliance on Independent IRB
2. Receive IRB “stipulation” letter with permission to use Independent IRB & CF injury language
3. Register site with Independent IRB
4. Satisfy all Independent IRB & UNC requirements
5. Respond to UNC IRB stipulation letter
6. Receive UNC reliance letter documenting permission to begin study
The vast majority of IRBIS application questions have been suppressed.

Approx 10-20 questions remain, depending on circumstances of individual study.
## Abbreviated IRBIS Application

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<th>Section</th>
<th>Questions</th>
<th>Purpose Served</th>
</tr>
</thead>
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<tr>
<td>General Info</td>
<td>Personnel, Sponsor, Multisite?</td>
<td>COI, training, REQUEST RELIANCE ON CENTRAL IRB</td>
</tr>
<tr>
<td>A.4.A.2</td>
<td>Biomedical- drugs, devices?</td>
<td>IDS</td>
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<tr>
<td>A.4.A.3</td>
<td>Stem cells, clinical labs, radiation, gene transfer?</td>
<td>ESCRO, UNC-HCS, RSC, IBC</td>
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<tr>
<td>A.9</td>
<td>Identifiers?</td>
<td>Data security</td>
</tr>
<tr>
<td>A.10</td>
<td>Confidentiality, sensitivity?</td>
<td>Data security</td>
</tr>
<tr>
<td>B.2</td>
<td>Protected Health Info (PHI)?</td>
<td>HIPAA waiver or authorization</td>
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<td>Collecting SSN for payments?</td>
<td>SSN collection form</td>
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<tr>
<td>C.4</td>
<td>Sources of data?</td>
<td>Data security</td>
</tr>
</tbody>
</table>
Demo of IRBIS Application for Central IRB Scenarios
Create New Submission
- New Study
- Modification
- Renewal
- Unanticipated Problem
- Closure

Submissions In Progress
- In Draft (17)
- Being Routed
- Submitted to IRB (1)
- Waiting PI Response

All My Studies
- My Studies
- Studies in My Dept

Routing Inbox
- PI Certification
- Dept Approval
- Dept Review

IRB
University of North Carolina - Chapel Hill
Medical School Building 52
Mason Farm Road
CB #7897
Chapel Hill, NC 27599-7097
(919) 966-3113
## 3. Funding Sources

<table>
<thead>
<tr>
<th>Sponsor Name</th>
<th>UNC Ramese Number</th>
<th>Sponsor Type</th>
<th>Prime Sponsor Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abbott Laboratories</td>
<td>Currently Not Available</td>
<td>Industry</td>
<td></td>
</tr>
</tbody>
</table>

1. Is this project funded (or proposed to be funded) by a contract or grant from an organization EXTERNAL to UNC-Chapel Hill? *
   - Yes  
   - No

Funding Source(s) and/or Sponsor(s)

- Click here to add funding source and/or sponsor

2. Is this study funded by UNC-CH (e.g., department funds, internal pilot grants, trust accounts)? *
   - Yes  
   - No

3. Is this research classified (e.g. requires governmental security clearance)? *
   - Yes  
   - No

4. Is there a master protocol, grant application, or other proposal supporting this submission (check all that apply)?
   - [ ] Grant Application
   - [X] Industry Sponsor Master Protocol
   - [ ] Student Dissertation or Thesis Proposal
   - [ ] Investigator Initiated Master Protocol
   - [ ] Other Study Protocol

Required document(s): Master Protocol

To navigate the Application, press continue or any link.
The following questions will help you determine if your project will require IRB review and approval.

The first question is whether this is RESEARCH.

1. Does your project involve a systematic investigation, including research development, testing and evaluation, which is designed to develop or contribute to generalizable knowledge? PLEASE NOTE: You should only answer yes if your activity meets all the above. *

   - Yes

The next questions will determine if there are HUMAN SUBJECTS.

2. Will you be obtaining information about a living individual through direct intervention or interaction with that individual? This would include any contact with people using questionnaires/surveys, interviews, focus groups, observations, treatment interventions, etc. PLEASE NOTE: Merely obtaining information FROM an individual does not mean you should answer "Yes," unless the information is also ABOUT them. *

   - Yes

3. Will you be using identifiable private information about a living individual collected through means other than direct interaction? This would include data, records or biological specimens that are currently existing or will be collected in the future for purposes other than this proposed research (e.g., medical records, ongoing collection of specimens for a tissue repository). *

   - Yes

The following questions will help build the remainder of your application.

4. Will subjects be studied in the Clinical and Translational Research Center (CTRAC, previously known as the GRC) or is the CTRC involved in any other way with the study? If yes, this application will be reviewed by the CTRC and additional data will be collected. *

   - Yes

5. Does this study directly recruit participants through the UNC Health Care clinical settings for cancer patients or does this study have a focus on cancer or a focus on a risk factor for cancer (e.g., increased physical activity to reduce colon cancer incidence) or does this study receive funding from a cancer agency, foundation, or other cancer related group? (If yes, this application may require additional review by the Oncology Protocol Review Committee). *

   - Yes

6. Are any personnel, organizations, entities, facilities or locations in addition to UNC-Chapel Hill involved in this research (e.g., In this a multi-site study or does it otherwise involve locations outside UNC-CH, including foreign location(s)? You should also click “Yes” if you are requesting reliance on an external IRB, or that UNC’s IRB cover another site or individual. See guidance. *

   - Yes

IMPORTANT:
YOU MUST RESPOND “YES” SCREENING QUESTION #6
5. Multi-site Study Information  Reference Id: 128345

1. Will this study be conducted in locations outside the United States? *
   - Yes  - No

2. Is UNC-CH taking or being asked to take responsibility for the oversight of research by individuals, groups or organizations outside of UNC-CH sites? *
   - Yes  - No

Are you requesting that UNC-CH rely on an external IRB for continuing review and approval of this study?
   - Yes  - No

Required document(s): External IRB Approval Letter

Researchers are reminded that additional approvals may be needed from relevant "gatekeepers" to access subject.
Select External IRB:

- National Cancer Institute Central IRB (NCI CIRB)
- Independent/Central IRB already designated for this study by Sponsor/CRO
- Institutional IRB (e.g., another university)
Select IRB from dropdown menu
1. Is this a Clinical Trial?
Check YES if this is a prospective study of an intervention (drugs, treatments, devices, or new ways of using drugs, treatments or devices). Do NOT check yes merely because your study is going to involve human subjects.

Click here for additional definition of "Clinical Trial".

- Yes
- No

Will this clinical trial be listed in ClinicalTrials.gov, either by you or the sponsor?

- Yes
- No

Choose the appropriate Phase designation for this clinical trial.

- Pilot Study
- Phase 0
- Phase I
- Phase II
- Phase III
- Phase IV
- Other

If other, please explain:

2. Will this study involve drugs, biologics or other substances (such as a botanical or dietary supplement)?
For guidance on dietary supplements, see Section VI, C FDA guidance document UCM229175.pdf

- Yes
- No

Required document(s): IDS Approval, Investigator Brochure and/or Drug Package Insert
<table>
<thead>
<tr>
<th>Option</th>
<th>Required document(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Embryonic stem cells</td>
<td>ESCRO Approval</td>
</tr>
<tr>
<td>Fetal tissue</td>
<td></td>
</tr>
<tr>
<td>Genetic testing (see GINA and GWAS)</td>
<td></td>
</tr>
<tr>
<td>Clinical laboratory tests</td>
<td></td>
</tr>
<tr>
<td>Testing for communicable diseases that have mandated reporting</td>
<td>link to state guidance</td>
</tr>
<tr>
<td>Testing done by hospital, clinic or research personnel (not by</td>
<td></td>
</tr>
<tr>
<td>subject). Examples include urine pregnancy testing, glucose</td>
<td></td>
</tr>
<tr>
<td>monitoring, etc.</td>
<td></td>
</tr>
<tr>
<td>Diagnostic or therapeutic ionizing radiation, or radioactive</td>
<td>Radiation Safety Committee Approval</td>
</tr>
<tr>
<td>isotopes, which subjects would not receive otherwise if not</td>
<td></td>
</tr>
<tr>
<td>participating in this research study</td>
<td></td>
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<tr>
<td>Gadolinium administered as a contrast agent</td>
<td></td>
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<tr>
<td>Recombinant DNA or gene transfer to human subjects</td>
<td>Institutional Biosafety Committee Approval</td>
</tr>
</tbody>
</table>

To navigate the Application, press continue.
Information used to determine data security level

1. Check all of the following identifiers you already have or will be receiving. This does not apply to information on consent forms.

- [ ] Names
- [x] Telephone numbers
- [ ] Any elements of dates (other than year) for dates directly related to an individual, including birth date, admission date, discharge date, date of death. For ages or dates that cross a threshold into a single category of age 90 and older
- [ ] Any geographic subdivisions smaller than a State, including street address, city, county, precinct, zip code and their equivalent geocodes (e.g. GPS coordinates)
- [ ] Fax numbers
- [ ] Electronic mail addresses
- [ ] Social Security numbers
- [ ] Medical record numbers
- [ ] Health plan beneficiary numbers
- [ ] Account numbers
- [ ] Certificate/license numbers
- [ ] Vehicle identifiers and serial numbers (VIN), including license plate numbers
- [ ] Device identifiers and serial numbers (e.g., implanted medical device)
- [ ] Web universal resource locators (URLs)
- [ ] Internet protocol (IP) address numbers
- [ ] Biometric identifiers, including finger and voice prints
- [ ] Full face photographic images and any comparable images
- [ ] Any other unique identifying number, code, or characteristic, other than dummy identifiers that are not derived from actual identifiers and for which the re-identification risk cannot be assessed.
Request limited waiver of HIPAA

Triggers HIPAA authorization form

B.2. Protected Health Information (PHI) Reference Id: 128345

Protected Health Information (PHI) is any identifiable information about the subject's health that relates to their participation in studies such as medical records, health care providers, insurance plans, etc. more

1. Are you requesting a limited waiver of HIPAA authorization?
   - Yes
   - No
   
   Please provide a response to each of the following questions:

   Under this limited waiver, you are allowed to access and use only the minimum amount of PHI necessary to review eligibility criteria and otherwise planning to collect for this purpose *
   
   Name, MRN, telephone number, Dx. of X, Dx. data, current medications
   
   Describe how confidentiality/privacy will be protected prior to ascertaining the patient's willingness to participate *
   
   data entered into password protected department server
   
   Describe when and how you will destroy the contact information if an individual declines participation *
   
   file will be deleted

2. Will you need to access PHI for reasons OTHER than the identification of potential subjects (e.g., ongoing use of medical records to conduct Authorization. *
   
   Required document(s): HIPAA Authorization

   Triggers HIPAA authorization form
1. Are you collecting Social Security numbers for payment and/or tax-related purposes? *

- Yes
- No

Check all that apply

- Processing payments greater than $200 per year, to support IRS reporting
- Processing payments of any amount through UNC-CH Accounts Payable

**Required document(s):** SSN Collection for payments

Triggers SSN collection form
1. Generate HIPAA Authorization and SSN forms

2. Do not upload consent form until AFTER your site (and all site documents) have been approved
The Application can be submitted at this time by clicking the yellow submit button located on the bottom left of the screen.

Application Attachments Reference Id: 128345

Based on your responses in the application, the materials listed below are expected to be attached. If not currently available, you may be required to provide the steps below.

>>> 1. REVIEW REQUIRED ATTACHMENTS:

- [x] Master Protocol
- [x] External IRB Approval Letter
- [x] ESCRO Approval
- [x] IDS Approval
- [x] Investigator Brochure and/or Drug Package Insert
- [x] Radiation Safety Committee Approval
- [x] Institutional Biosafety Committee Approval

>>> 2. UPLOAD ATTACHMENTS:

Use this section to upload attachments listed above. Select the appropriate Document Type for the attachment you want to upload. Click Browse to locate each document a unique file name. (Why is this important?) You can also upload additional materials not listed or multiple versions of items already listed. Do not use this section to replace documents already listed below under "Revise/Replace Previously Uploaded Attachments."

Document Type: 

Attachment: 

New Documents Only

Upload Attachment
The Application can be submitted at this time by clicking the yellow submit button located on the bottom left of the screen.

Optional Cover Memo Reference Id: 12345

This section serves as a cover memo from the Investigator to the IRB, if needed. Provide any additional information here that is not already addressed above. You are not required to submit a cover memo.

Application Cover Memo:

Please note, I am requesting reliance of Copernicus IRB for this study.

To navigate the Application, press any link in the Item List to your left.

Save and Continue
To: <PI NAME>
<DEPT>
From: Biomedical IRB

Date: <NOW>

RE: Notification of Permission to Rely on Independent IRB
Submission Type: Initial
Study #: <IRB STUDY #>
Study Title: <STUDY TITLE>

This serves as permission to register your site with <INDEPENDENT IRB>, which has been selected by the study sponsor/CRO as the central IRB for your study. The study itself has already been approved by the central IRB, but you must still register your site. Site registration provides the central IRB with information about the researchers, study population, and the University. We have compiled guidance documents to assist you with the registration process.

Please be aware that, although the UNC IRB will not be overseeing this study, you are still obligated to comply with all applicable University requirements (e.g., radiation safety, COI, IDS, OCT). All required approval letters must be attached to your application in IRBIS before reliance on <INDEPENDENT IRB> is approved.

In addition, <INDEPENDENT IRB> will expect to see UNC-specific language in selected parts of the consent form, including:

**Subject Injury:** This pre-approved template language must be incorporated into your consent form. This language must reflect subject injury provisions in the Clinical Trial Agreement with Sponsor, and should not be modified without approval by the Office of Clinical Trials.

All research involves a chance that something bad may happen to you. This may include the risk of personal injury. In spite of all safety measures, you might develop a reaction or injury from being in this study. If such problems occur, the researcher will help you get medical care, but The University of North Carolina at Chapel Hill has not set aside funds to pay you for any such reactions or injuries, or for the related medical care.

The Sponsor of the study, [INSERT SPONSOR NAME], has agreed to pay all reasonable medical expenses for the treatment of injuries related to the administration of the study drug/device, defects in the manufacture of the study drug/device, or as a direct result of properly performed study tests and procedures.

Any costs for medical expenses not paid by Sponsor will be billed to you or your insurance company. You do not give up any of your legal rights by signing this form.

**Conflict of Interest Disclosure:** If a potential conflict of interest has been identified, please insert the disclosure language that was provided to you by the COI Office. Please note that...
Step-by-step instructions for registering with Alpha IRB

1. Submissions may be sent to Alpha IRB as hard-copy, via email to Sites@alphairb.com, or through OASIS (Online Access Study Information System). The preferred method is online using OASIS. For access to OASIS, go to http://www.alphairb.com. Click on the OASIS icon at bottom right of the screen (recommend using Internet Explorer or Mozilla Firefox). At the Login Screen, enter the following:
   - **Username:** newpi
   - **Password:** newpi
   - **Client:** AlphaIRB

You will be taken to the Investigator Registration Screen. Or you may email Sites@alphairb.com with a request to provide you with your Oasis log-in information. You will need to provide your first name, last name, email address and telephone number in the email sent.

For additional guidance, see Investigator OASIS Userguide.

2. Complete the Alpha IRB application forms. All Alpha IRB Forms are available on their website at http://www.alphairb.com/forms.asp. An annotated copy of the electronic application which includes institution-specific information is available here. **Please review this document before completing the submission forms detailed below.**
   - Site Submission Form (Multicenter)
   - Site Submission Form (Additional Study Location), if conducting study at other locations
   - Financial Disclosure Form, if applicable

3. The following supporting documents should be uploaded with the site submission:
   - UNC IRB Notification of Permission to rely on Alpha IRB
   - UNC COI Disclosure email (whether or not there is a conflict)
   - Principal Investigator’s Medical license(s)
   - Principal Investigator’s Current Credentials (CV), including human subjects’ research experience (specific study information and dates).
   - Consent form with site specific revisions as required (in word format, changes tracked on the most current IRB approved template). You may request a copy of the most current IRB approved template by sending your request to Sites@alphairb.com.
   - Site specific advertising and recruitment materials, if applicable
   - FDA Audit Information (if applicable)

4. In addition, you will need to attach the following NC-specific documents to your application. They are provided in the “**General Documents**” folder:
   - Current North Carolina race/ethnicity information (see application Section 3A)
Recipients:
To:
CC:
Subject: AIR COI #  IRBIS#

Dear XXXX,

Thank you for reporting on a potential and/or appearance of a conflict for the following study:

Study Title:
AIR #
IRBIS#
Sponsor:
Role:

You have identified an external relationship with the study sponsor, XXXX. This conflicting issue is allowed under your overall management plan.

Management for this study includes:
- disclosure in the informed consent
- disclosure in any publications or presentations arising from this study
- disclosure to the research team
- no participation in the informed consent process (delete if not applicable)
- no involvement in final AE adjudication (delete if not applicable)
- no participation in data analysis (delete if not applicable)

The disclosure language in all the informed consents should read as follows. The IRB does retain final approval over all language in any informed consent:

Who is sponsoring this study?

This research is funded by Inc. (the Sponsor). This means that the research team is being paid by the sponsor for doing the study. In addition, XXXX, the ROLE of this study, receives money from XXXXX for work that is not a part of this study. These activities may include consulting, service on advisory boards, giving speeches, or writing reports. OR In addition, XXXX, the ROLE of this study owns shares of XXX. If the approach used in this study is successful, at some point in the future, Dr. XXXX may receive financial benefits.

A committee at the University of North Carolina at Chapel Hill has reviewed these arrangements. They concluded that the possible benefit to the person listed above does not appear to affect your safety or the scientific quality of the study. If you would like more information, please ask the researchers listed in the first page of this form.

UNC COI Information letter is emailed directly to each member of the research team who identified an external relationship with the study sponsor.
FINAL STEPS:

- Respond to IRB stipulations
- Upload current Central IRB approved consent form
- Upload a copy of the Central IRB approval letter
- Upload any outstanding attachments (i.e., institutional approvals)
- Click “Proceed to Submit”
RE: Agreement to Rely on External IRB
External Organization: [External IRB]
Study #: [IRB_ID]
Study Title: [TITLE]

This confirms that an IRB Authorization Agreement with the organization identified above has been executed to rely on their IRB for continuing oversight of this study. This agreement specifies the roles and responsibilities of the respective entities.

[DESCRIPTION]
[SUBMISSION_DESCRIPTION]

It is your responsibility to:
• Inform the UNC IRB about any actions by the external IRB affecting their approval to conduct the study, including suspension or termination of approval.
• Submit a modification to the UNC IRB (via IRBIS) if/when new personnel are to added the study team or the study is modified in such a way that additional institutional approvals are required (e.g., radiation safety, biosafety).
• Submit a copy of the external IRB approval letter and current approved consent document to the UNC IRB (via IRBIS) when the study is renewed; you will continue to receive reminder notices from the UNC IRB for renewal, and should provide external approvals at that time.
• Report all Unanticipated Problems to the UNC IRB in addition to the external IRB
• Maintain compliance with all other UNC policies (e.g., data security, Investigational Drug Service (IDS), conflict of interest)