WORKING WITH CENTRAL IRBS

A step-by-step review of the process

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Discussion Points

• Introduction
• Why use a central IRB?
• History of central IRB utilization at UNC
• What you need to know about UNC Central IRB service agreements
• Step-by-step process
• Who to contact for help
Talking the talk

• Central IRB = Independent IRB = Commercial IRB = For-profit IRB
• Rely on = Defer to = Cede to
• Permission to Register = Permission to submit to Central IRB
• Approval = Approval from Central IRB
• Final Reliance = UNC acknowledgement to fully rely-on Central IRB for oversight
  • Investigators must have final reliance from UNC IRB to start study activities
Why use a Central IRB?

- National effort to utilize a central IRB since 2006
- Reduce time to approval
- Reduce staff effort
- Streamlining across multiple sites
- Reduce duplicative efforts
- Sponsor request/requirement
Approved Central IRBs

- Chesapeake
- Quorum
- Schulman
- Sterling
- Copernicus Group
- Western (WIRB)

{ WIRB–Copernicus Group (WCG) }
Research that qualifies…

UNC allows investigators to utilize a Central IRB when…

• The research is an industry-sponsored, multi-center, clinical research study

• One of the UNC-approved Central IRBs has been appointed as the *Central IRB of Record* by the Sponsor or CRO

• The study has been approved (or is in the process of being approved) by the Central IRB
Research that qualifies…

The IRB **may allow** the use of a Central IRB in other situations. The use of a Central IRB is **optional**.
Research that does not qualify

This is NOT a mechanism to involve a commercial IRB in “homegrown” single site studies in which the central IRB is not already involved.

– These will remain under UNC IRB oversight
The Office of Human Research Ethics/IRB conducted a pilot study from June to December 2012 to assess the feasibility and acceptability of reliance on central IRBs. Utilized 20 eligible Central IRBs (AAHRPP accredited; in good standing with FDA and OHRP.)
Randomized 43 multicenter, industry studies were randomized into one of two groups:

- **Control** – Remained under the oversight of UNC IRB. Reviewed in the usual manner.
- **Experimental** – IRB oversight ceded to Central IRB. UNC IRB (sham) review served as an internal quality control measure.
- UNC investigators, IRB members and staff were all blinded to group assignment.
What did we learn from the pilot project?

- Approximately 1/3 of initial reviews by convened biomedical IRB are potentially eligible for outsourcing.
- Of the 20 approved central IRB’s, only 8 were utilized.
- Potential time-savings of ~20 days/study
Background…

- No quality issues identified; UNC IRB contingencies were administrative in nature
- Problems encountered were related to:
  - Consent form language (injury, COI)
  - Navigating the registration process
  - Miscommunications with CRO
From Pilot Project to Policy

- June-December 2012 - Pilot Project
- October 2013 - Institutional policy permitting reliance on 13 Central IRBs
- October 2014 - Revision of institutional policy limiting reliance to 6 Central IRBs.
Year 1 (October 2013-2014) Data for All Central IRBs with MSA in Place

Western: 32
Quorum: 10
Copernicus: 9
Shulman: 11
Chesapeake: 13
Sterling: 2
Aspire: 2
Compass: 1
Ethical: 1
IntegReview: 1
New England: 1
Alpha: 0
IRB Co.: 0
IRB Services: 0
## I-IRB Utilization Data

**Years 1 (October 2013-2014) & 2 (October 2014-2015)**

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<thead>
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<th>Year 1</th>
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**Legend:**
- **Blue Bar Chart:** Year 1
- **Dark Blue Bar Chart:** Year 2
Master Service Agreements with Central-IRBs

“Institution shall assure that the Clinical Trials Agreement (CTA), if any, and the approved consent form do not conflict with each other regarding compensation for injury.”

“Institution shall provide to IRB subject injury language and conflict of interest language to be included in the informed consent form(s) for each study. IRB shall not change Institution’s subject language or conflict of interest language without the express written permission of the Institution.”

- Issues related to subject injury language should be provided to the Office of Industry Contracting (OIC).
- Issues related to conflict of interest language should be directed to the Conflict of Interest Office (COI).
Master Service Agreements with Central-IRBs

“IRB agrees to defer to Institution’s IRB for any HIPAA related analysis and to use Institution’s HIPAA Authorization form as an addendum to the informed consent form.”
Workflow

1. Submit CTA to Office of Industry Contracting (OIC)
2. Complete IRB application requesting reliance on Central IRB
3. IRB issues stipulation/“Permission to Register” letter
4. Submit application to Central-IRB
5. Satisfy all Central-IRB & UNC requirements
6. Respond to UNC IRB stipulation letter. Must include current approved ICF and Central IRB approval letter
7. IRB issues “Official” reliance letter documenting permission to begin study
Submission Process – Office of Industry Contracting

Step 1: Submit the Clinical Trials Agreement (CTA), model consent form and current version of the protocol to the Office of Industry Contracting (OIC) prior to submitting your study in IRBIS.

The OIC Contract Manager needs to ensure that the subject injury language in the Sponsor/CRO-provided draft consent form is consistent with the language in the Clinical Trial Agreement (CTA).
## Submission Process – IRB

### Step 2: Complete *Abbreviated* IRB application requesting reliance on Central IRB

<table>
<thead>
<tr>
<th>Section</th>
<th>Questions</th>
<th>Purpose Served</th>
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</thead>
<tbody>
<tr>
<td>General Info</td>
<td>Personnel, Sponsor, Multisite?</td>
<td>COI, training, REQUEST RELIANCE ON CENTRAL IRB</td>
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<tr>
<td>A.4.A.2</td>
<td>Biomedical- drugs, devices?</td>
<td>IDS</td>
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<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>
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<tr>
<td>A.10</td>
<td>Confidentiality, sensitivity?</td>
<td>Data security</td>
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<tr>
<td>B.2</td>
<td>Protected Health Info (PHI)?</td>
<td>HIPAA waiver or authorization</td>
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<tr>
<td>B.4</td>
<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>
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</tbody>
</table>
1. **Project Title**

Rely on Central IRB
UNC maintains oversight of "institutional" responsibilities only.

2. **Brief Summary.** Provide a brief non-technical description of the study, which will be used in IRB documentation as a description of the study. Typical summaries are one to two paragraphs. Each item below, retaining the subheading labels already in place, so that reviewers can readily identify the content. PLEASE NOTE: THIS SECTION MAY BE EDITED BY THE LENGTH. ✴

Purpose: To identify questions in the application to be asked for studies in which UNC relies on an external IRB.

Participants:

Procedures (methods):

[Tips and Techniques on using the HTML Editor](#)

3. Is this new study similar or related to an application already approved by a UNC-Chapel Hill IRB? Knowing this will help the IRB in reviewing your new study.

- [ ] Yes
- [ ] No
CURRENT PROGRAMMING CANNOT SUPPRESS "REQUIRED DOCUMENT". RESPOND "N/A" IN ATTACHMENT SECTION.
The following questions will help you determine if your project will require IRB review and approval.

The first question is whether this is RESEARCH (click for details)

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 or No]  

The next questions will determine if there are HUMAN SUBJECTS (click for details)

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 or No]  

3. Will you be obtaining 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 or No]  

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

4. Will subjects be studied in the Clinical and Translational Research Center (CTRC, previously known as the GCRC) 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 or No]  

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 or No]  

6. Are any personnel, organizations, entities, facilities or locations in addition to UNC-Chapel Hill involved in this research (e.g., is this a multi-site study or does it otherwise involve locations outside UNC-Chapel Hill, including foreign locations)? You should also click "Yes" if you are requesting reliance on an external IRB, or that UNC's IRB cover another site or individual.  
   [Yes or No]  

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

2. Is UNC-CH the lead site or is the lead PI a UNC-CH employee? *
   - Yes  ○ No

3. Is UNC-CH taking or being asked to take responsibility for the oversight of research by individuals, groups or organizations outside of UNC-CH? *
   - 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.
**NEW ADDITION TO IRBIS APPLICATION WHEN REQUESTING RELIANCE ON ANY EXTERNAL IRB**

Please be aware that reliance on an external IRB obligates you to review and adhere to the reviewing IRB’s Human Research Protection Program (HRPP) policies (i.e., SOPs) so that you understand your responsibilities as an Investigator. To obtain a copy of the external institution’s policies, contact your collaborator/colleague or the external IRB directly. If you have questions about the policies, you should contact the external IRB directly.

☐ I agree to obtain and review the external IRB’s policies PRIOR to conducting research
1. 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)

If you are planning to use a central IRB please submit your CTA to OCT at your earliest convenience. By doing so, the OCT Contract Manager assigned to your study can help to ensure acceptable subject injury language is negotiated in the contract and consent form.

Select one: *

- Chesapeake IRB
- Copernicus Group IRB
- Quorum Review IRB
- Schulman Associates IRB
- Sterling IRB
- Western IRB
- Other

* Required.

Press continue or any link in the Item List to your left.

Save and Stay  Save and Continue
REQUEST A LIMITED WAIVER OF HIPAA

1. Are you requesting a limited waiver of HIPAA authorization?

Under this limited waiver, you are allowed to access and use only the minimum amount of PHI necessary to review eligibility criteria and planning to collect for this purpose.

- Name, MRN, telephone number, Dx of X, Dx data, current medications
- Data entered into password protected department server
- Describe when and how you will destroy the contact information if an individual declines participation

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?

A YES RESPONSE 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

CHECKING EITHER TRIGGERS SNN 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: 12345

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 them at the steps below.

**1. REVIEW REQUIRED ATTACHMENTS:***
- Master Protocol
- External IRB Approval Letter
- ESCRO Approval
- IRB Approval
- Investigator Brochure and/or Drug Package Insert
- Radiation Safety Committee Approval
- Institutional Biosafety Committee Approval

**2. UPLOAD ATTACHMENTS:**
Use this section to upload attachments listed above. Select the appropriate Document Type for the attachment you wish to upload. Click "Browse" to locate each document using a unique file name. (Why is this important?) You may 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 "Review/Replace Previously Uploaded Attachments."

**Document Type:** 

**Attachment:**
- Now Documents Only
- Browse

Upload Attachment
EXCEPTIONS: You may check “Not Yet Available/Not Applicable” for Master Protocol, Investigator Brochure, Certificate of Confidentiality

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<tr>
<th>Attachment</th>
<th>Reason</th>
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<tr>
<td>Master Protocol</td>
<td>Not Yet Available / Not Applicable</td>
<td>Why is this form required?</td>
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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.

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

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

Save and Continue
Submission Process

首位 3: 跟踪后审批你的申请，IRB 将会发送一个Permission to Register信件。按照信件中的指示进行操作:

- 完成所有成员的COI过程
- 如果没有完成，则提交给OIC
- 修改赞助商的模型同意书，并将HIPAA语言放入单独的文件中
- 提交到中央IRB
Submission Process

Step 4: Following notification of Central-IRB approval, Investigator re-submits application to UNC IRB for ‘Final-Reliance’

- Respond to any outstanding UNC IRB contingencies
- Finalize process with UNC IRB:
  - Submit final approved consent form,
  - Central IRB approval letter and
  - Confirmation email from OIC
Step 5: The IRB will review your responses and if no outstanding institutional requirements have been identified and COI and injury language are acceptable, the UNC IRB will email you an “official” reliance letter, permitting research to begin.

If applicable, the UNC IRB will grant a limited waiver of HIPAA. A limited waiver of HIPAA allows you to review medical records for the purpose of identifying and contacting potential eligible subjects.
References:

- Using a Centralized IRB Review Process in Multicenter Clinical Trials
  [Link](http://www.fda.gov/RegulatoryInformation/Guidances/ucm127004.htm)

- The Paradoxical Problem with Multiple-IRB Review, Menikoff, J, N Engl J Med 2010; 363;17, October 21, 2010

- IRB Guidance Document: How to Request Reliance on an External IRB
  [Link](https://research.unc.edu/files/2016/02/How-to-Request-a-Reliance-Agreement-2016-03-01.pdf)