UNC THE NORTH CAROLINA TRANSLATIONAL & CLINICAL SCIENCES INSTITUTE

THE UNIVERSITY of NORTH CAROLINA at CHAPEL HILL NRP Network for Research Professionals

UNC OFFICE OF CLINICAL TRIALS

ORIENTATION FOR NEW CLINICAL RESEARCH PERSONNEL

MODULE 2

Presented by

NC TraCS Institute

UNC Office of Clinical Trials

UNC Network for Research Professionals

Online Logistics

- I will be monitoring the chat window for questions and will ask those questions to the presenter at the end of each talk, or during breaks in the conversation when the presenter invites questions.

- Slides will be emailed to everyone after the presentation, along with the evaluation link and any announcements.

- If you would like a certificate for ACRP/SOCRA credit, please complete the evaluation at the end of the presentation and send me an email – marie_rape@med.unc.edu

- Feel free to reach out to me either in the chat window or by email, I'm happy to help with anything you need.

Overall Agenda for Orientation

- **Module 1:** Introduction, NRP/ Education, and Office of Clinical Trials
- **Module 2:** IRB Processes, Conflict of Interest
- **Module 3:** GCP, Documentation, Informed Consent, Research Monitor Access
- **Module 4:** Contracts, Clinical Trial Agreements, Planning/Accounting of Funds, NIH Budgets, Billing Coverage Analysis
- **Module 5:** Recruitment, Study Start-up, Roles of Research Personnel, UNC Investigational Drug Services, UNC Device Policy
- **Module 6:** Introduction to RedCap, Investigator-Initiated Study Process, ClinicalTrials.gov, Documenting AEs & SAEs, IND and IDE studies

INTRODUCTION TO THE UNC IRB

3/24/2021

Office of Human Research Ethics

Institutional Review Board

- Cassandra Myers– OHRE Director
- John Roberts- Associate Director, Regulatory Affairs & Compliance
- Mike Matamoros– Associate Director, Operations and Education

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Discussion Topics

- IRB Process & Function
- IRB Application Submission Process, Waivers
- New Safety Information
- Reliance Agreements
- Navigating the IRB Website

Objectives

- Become familiar with:
  - IRB review process
  - IRB applications
  - Investigator responsibilities following IRB approval
  - Research-related institutional responsibilities
  - Understanding waivers
  - Reporting of New Safety Information (NSI)
  - Reliance agreements
  - The IRB website

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IRB PROCESS & FUNCTION

Cassandra Myers, CIP

History of Human Subject Research

- Nuremburg Trials*
- Tuskegee Syphilis Trial*
- Cold War Radiation Experiments
- Willowbrook State School*
- Henrietta Lack's and Follow-up Family Studies
- San Antonio Contraception Study*
- Jesse Gelsinger
- U of MN Dan Markingson*

What do they all have in Common?

Regulations and Protections

- Nuremberg Code-1947
- Declaration of Helsinki-1964
- Belmont Report-1979
  - Respect for Persons (Autonomy)
  - Beneficence (Risk/Benefit Assessment)
  - Justice (Equitable Selection)
- Common Rule-1991/2019
- FDA/OHRP

What is an OHRE?

- The **Office of Human Research Ethics (OHRE)** is responsible for ethical and regulatory oversight of research at UNC-Chapel Hill that involves human subjects. The OHRE administers, supports, and guides the work of the Institutional Review Boards (IRBs) and all related activities.

- 6800+ Active Studies
- 15,000+ Submissions a Year (25000 in 2020)
- 38,000+ Actions a Year
- 400+ Executed Reliance Agreements
- Quality, Reliance, Compliance and Education Areas
- 22 Staff
- IRB for UNC and UNC Health System

What is an IRB?

An **Institutional Review Board (IRB)** is a committee mandated by federal regulations.

Protects the rights and welfare of human subjects in research activities through independent review of proposed research.

Independent committee formally designated to review, approve, and monitor research involving humans.

*Many are generalist and may not have specific expertise in community engagement as the community representative member is often not related.

IRB Membership

- 6 Biomedical/Nonbiomedical Boards
- Not all members of one profession
- Diverse background
- At least one scientist, one non-scientist
- At least one unaffiliated member
- Expertise appropriate to review research

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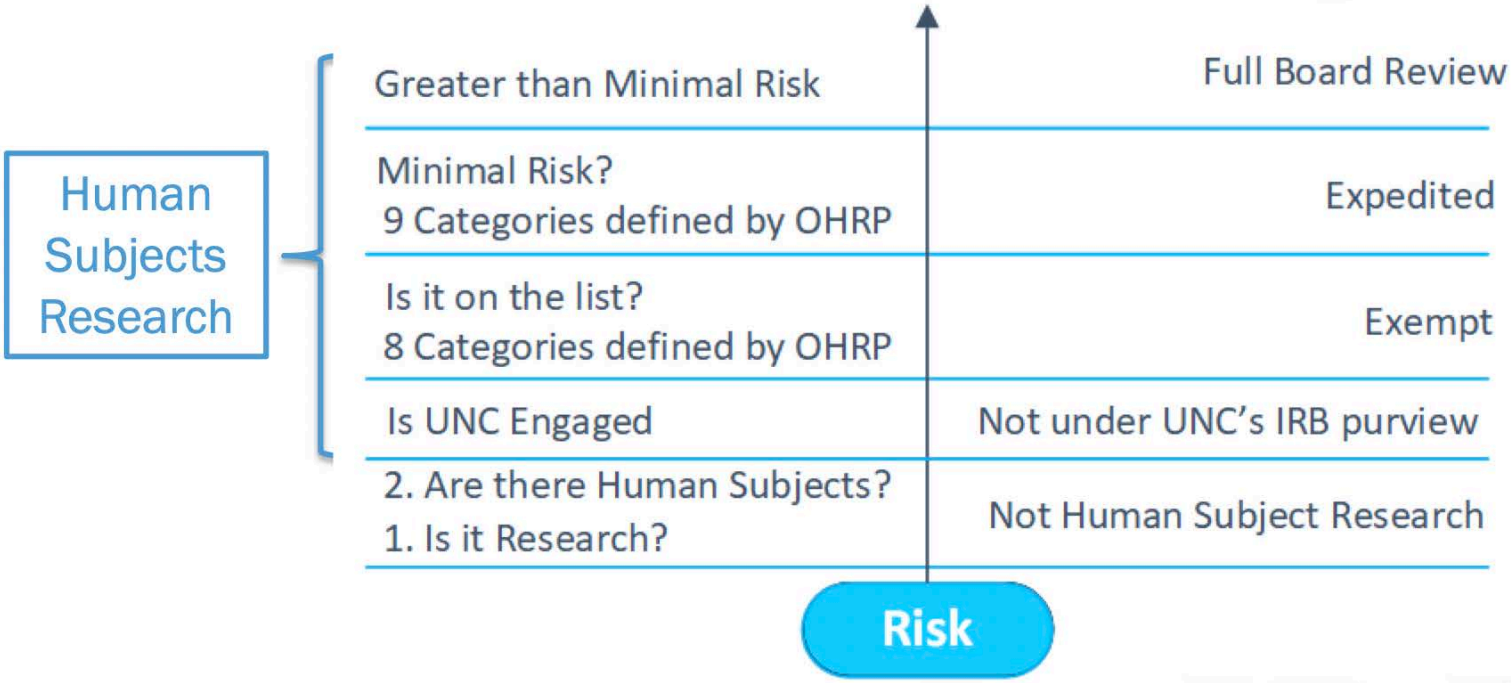
TYPES OF REVIEW

IRB Levels of Review



Human Subjects Research

A project is under the oversight of the IRB when it qualifies as **human subjects research**.

In order to qualify as human subjects research, the project must meet both criteria (#1 and #2, or #1 and #3, or #1, #2, and #3):

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. *

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

2. Will you be obtaining information or biospecimens through intervention or interaction with the individual, and use, study, or analysis of the information or biospecimens? This would include any communication or interpersonal contact between investigator and subject such as using in-person or online 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. *

3. Will you be obtaining, using, studying, analyzing, or generating identifiable private information or identifiable biospecimens 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).
   OR
   Will you be using human specimens that are not individually identifiable for FDA-regulated in vitro diagnostic (IVD) device investigations? *

Not Human Subjects Research (NHSR)

If a project does not meet definition of human subjects and/or research =**Not Human Subjects Research (NHSR)**

IRB review is not required to make a NHSR determination, however, researchers are encouraged to complete and submit an application to the IRB if they are unsure.

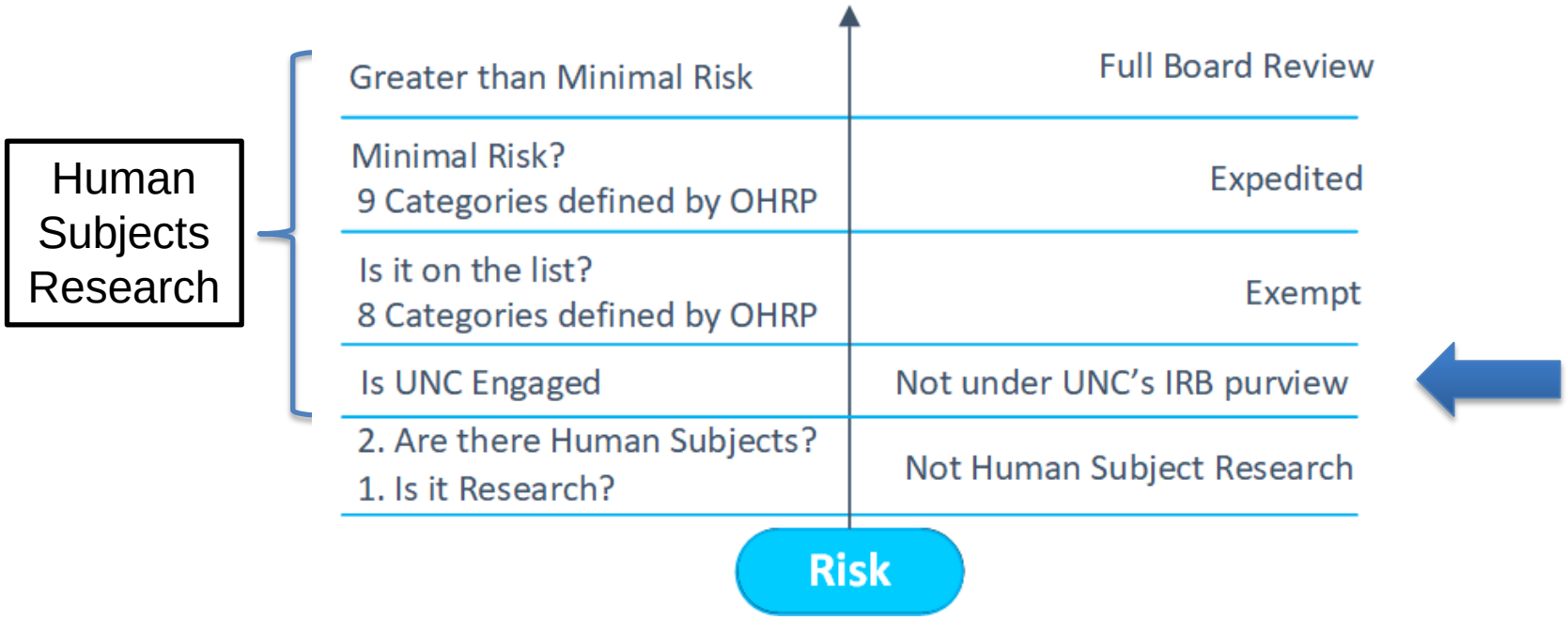
- Includes projects such as…
  - Interview for campus newspaper
  - Analysis of de-identified data
  - Research of leftover cadaver specimens
  - Case study
  - Quality Improvement projects

Case Study #1

A project is designed to increase pharmacy consultations at UNC to improve how many children complete all courses of antibiotics utilizing EPIC flags.

“Is it Human Subject Research?”

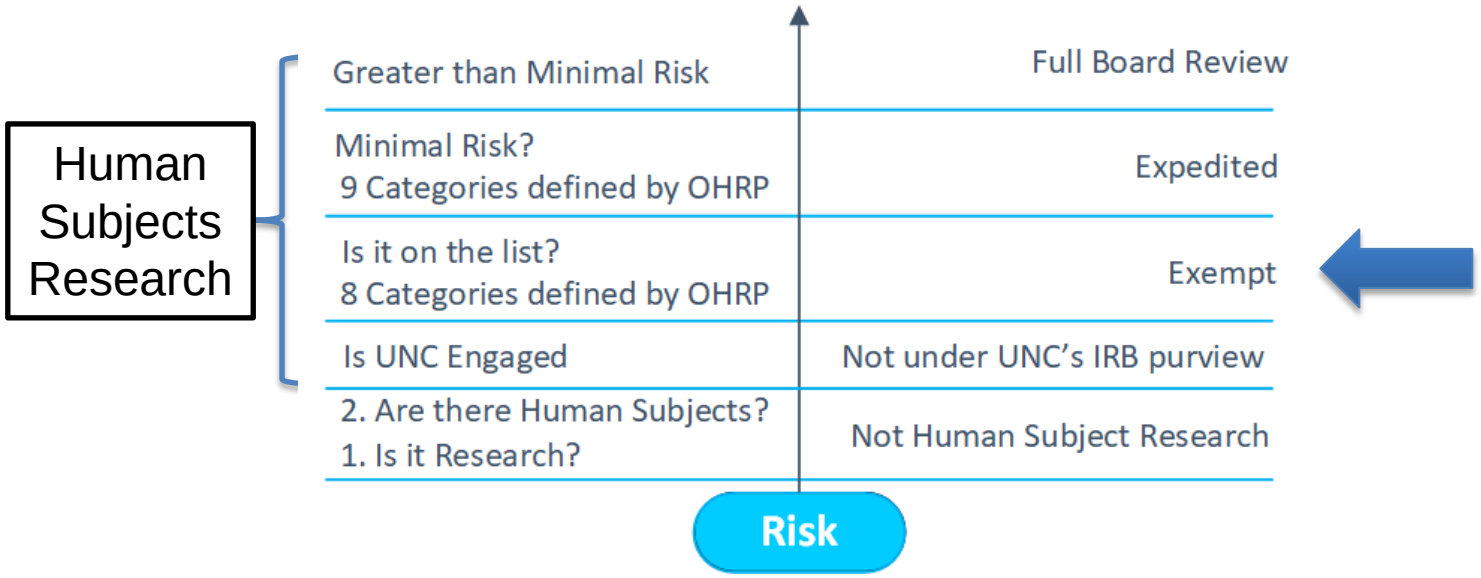
UNC & Engagement



Exempt

Reminder

- Exempt ≠ Not Human Subjects Research (NHSR). Exempt are human subjects research and require a determination by the IRB prior to beginning research.



Exempt Review

- Qualifies as human subjects research
- Involves no greater than *minimal risk**
- Must be “on the list” of exempt categories (45 CFR 46.101(b)(1)-(6))
- Determination concurrence by IRB Chair or designee
- IRB may choose to provide additional measures of protection

**Minimal risk* means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. 21 CFR 56.102 (i)

Exempt Review Categories

1. Normal educational practices in established educational settings
2. Educational tests, surveys, interviews, or observation of public behavior -unless identified & sensitive**
3. Benign Behavioral Interventions
4. Research using secondary data and/or biospecimens (includes medical records)
5. Evaluation of public benefit service programs
6. Taste and food quality evaluation and consumer acceptance studies

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EXPEDITED AND FULL BOARD REVIEW

Case Study #2

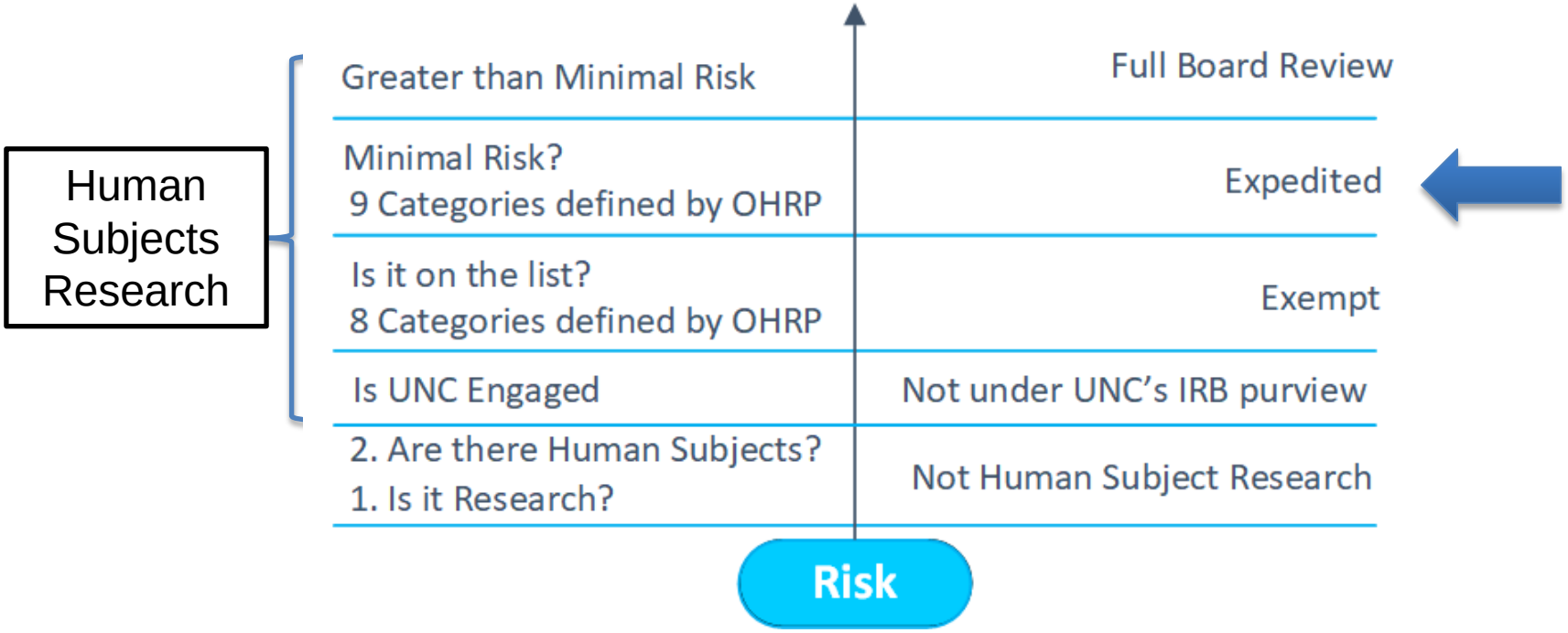
A psychiatric research study enrolled individuals that had been diagnosed with Borderline Personality Disorder (BPD) for a 24-week investigational drug study who are in a locked psychiatric unit. The individuals were closely monitored by both clinical and research staff for the first 12 weeks. If a participant was willing to enroll in the study the participant would not be recommended for an involuntary commitment. Due to the sensitive nature of the diagnosis extra precautions had been put into place, such as not documenting participation in electronic health records.

What should the IRB consider?

111 Criteria for Approval

1. Risks are Minimized
2. Favorable Risk to Benefit Assessment
3. Equitable Selection of Subjects
4. Informed Consent Sought
5. Informed Consent Documented
6. Monitoring Plan for Safety
7. Privacy and Confidentiality Protected
8. Additional Safeguards for Vulnerable Population

Expedited Review



Expedited Review

- Involves no greater than minimal risk or…
- Involves a minor change in previously approved research
- May be carried out by IRB Chair or designee
- IRB may choose to provide additional measures of protection
- Described in (45 CFR 46.110 and 21 CFR 56.110)—must be “on the list” (63 FR 60364-60367, November 9, 1998)

*AVERAGE TURNAROUND TIME APROXIMATELY 10-16 DAYS

Expedited Review Categories

1. Studies of drugs and medical devices when no IND or IDE is needed.
2. Blood samples by finger stick, heel stick, ear stick, or venipuncture.
3. Biological specimens for research purposes by “noninvasive” means.
4. Data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves.
5. Materials (data, documents, records, or specimens) that have been collected, or will be collected solely for nonresearch purposes. Evaluation of public benefit service programs
6. Data from voice, video, digital, or image recordings made for research purposes.
7. Research employing survey, interview, oral history, focus group, etc.
8. 8.Continuing review where: (a) only-follow-up remains, (b) no subjects enrolled, or (c) only data analysis remains.
9. Continuing review where: (1) not conducted under an IND/IDE, (2) other expedited categories n/a, and (3) Board considers minimal risk.

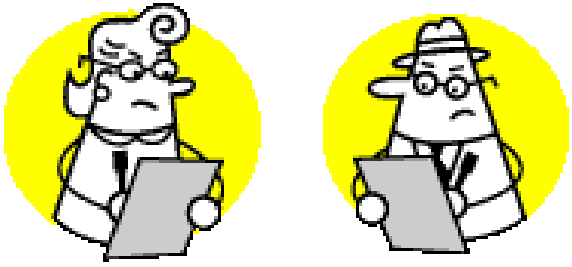
Possible Action of Expedited Review

Approved

Minor contingencies required for approval

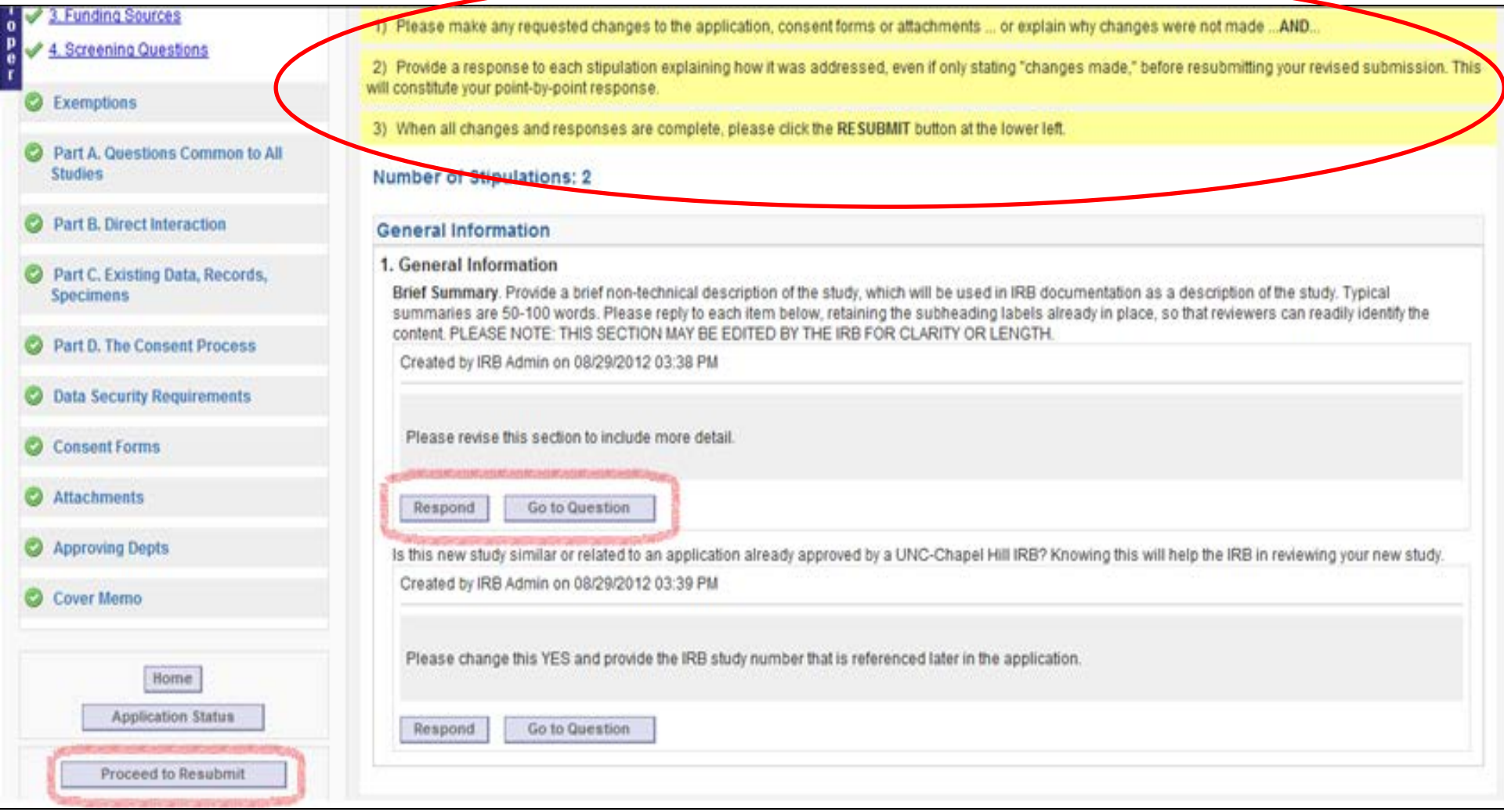
Refer to Full Board

When You Get a Contingency Memo…

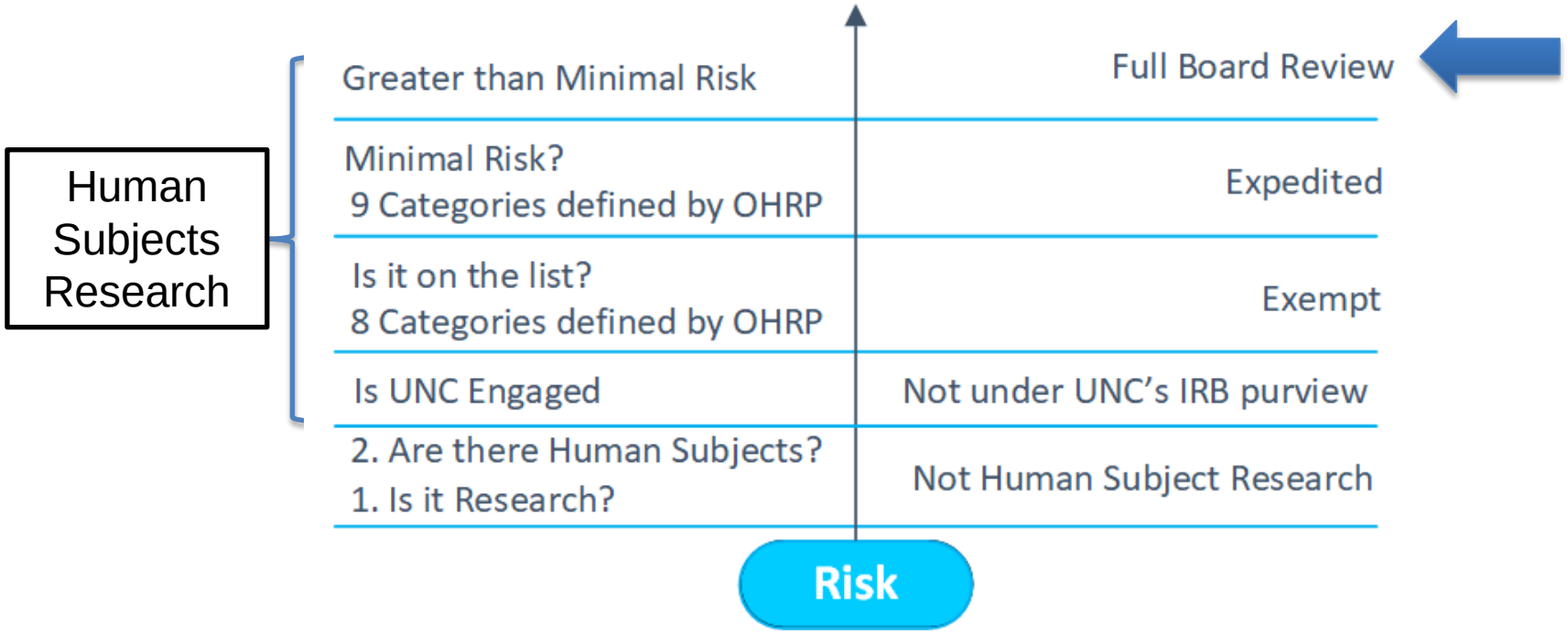


- Don’t despair
- Don’t take it personally
- It is rare for an initial proposal not to raise at least one question from the IRB
- The PI should respond to each contingency by responding to the stipulation AND making the corresponding changes to the application and/or consent forms.
- If you believe that the IRB misinterpreted or did not fully understand the information you provided, or you don’t understand a stipulations; you should call the office. Ask to speak with the IRB Analyst at whose meeting your study was reviewed

When You Get a Contingency Memo:



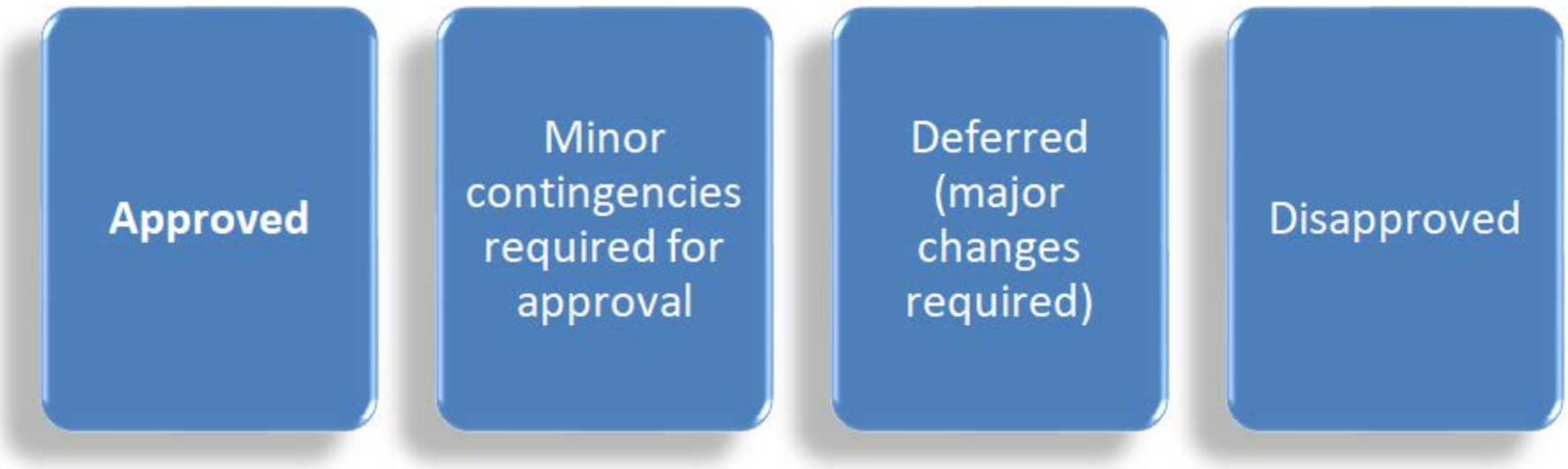
Full Board Review



Full Board Review

- Human subjects research involves procedures or issues that do not qualify for exempt or expedited review
  - Requires full Board review as the entire study does not fit any prescribed exempt or expedited categories
  - Requires full Board as the study presents greater than minimal risk
    - IND or IDE's always require initial full board review.
      - If studying the safety and effectiveness of drug and devices include appropriate worksheet.
- Published calendar on OHRE website.

Possible Action of Convened Board



Informed Consent and Recruitment

How, When, from Whom, and by Whom will consent to be obtained

Waivers as appropriate

Is there compensation and how is it allocated

Compensation/Coercive vs. Paid as “Subcontractor”

Is there a conflict of interest (COI) and how will it be managed

What is the strategy to emphasize voluntariness

Consent Form Elements

*TIP-USE CONSENT BUILDER

Basic Elements of Informed Consent (new elements in the 2018 rule in bold)	Citation
○ Statement that study involves research, ○ Explanation of the purposes of the research and the expected duration of the subjects' participation, ○ A description of the procedures to be followed, and ○ Identification of any procedures that are experimental	_.116(b)(1)
○ Description of any reasonably foreseeable risks or discomforts to the subject	_.116(b)(2)
○ Description of any benefits to the subject or to others that may reasonably be expected from the research	_.116(b)(3)
○ Disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject	_.116(b)(4)
○ Statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained	_.116(b)(5)
○ For research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained	_.116(b)(6)
○ Explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject	_.116(b)(7)
○ Statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled; and	_.116(b)(8)
○ **Statement that identifiers might be removed from the identifiable private information or identifiable biospecimens and that, after such removal, the information or biospecimens could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from the subject or the LAR, if this might be a possibility - OR -** ○ **Statement that the subject's information or biospecimens collected as part of the research, even if identifiers are removed, will not be used or distributed for future research studies**	**_.116(b)(9) (i) and (ii)**
Additional Elements of Informed Consent (as appropriate to the research) (new elements in the 2018 rule in bold)	**Citation**
○ Statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are currently unforeseeable	_.116(c)(1)
○ Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent	_.116(c)(2)
○ Any additional costs to the subject that may result from participation in the research	_.116(c)(3)
○ Consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject	_.116(c)(4)
○ Statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject	_.116(c)(5)
○ Approximate number of subjects involved in the study	_.116(c)(6)
○ **Statement that the subject's biospecimens (even if identifiers are removed) may be used for commercial profit and whether the subject will or will not share in this commercial profit**	**_.116(c)(7)**
○ **Statement regarding whether clinically relevant research results, including individual research results, will be disclosed to subjects, and if so, under what conditions; and**	**_.116(c)(8)**
○ **For research involving biospecimens, whether the research will (if known) or might include whole genome sequencing (i.e., sequencing of a human germline or somatic specimen with the intent to generate the genome or exome sequence of that specimen)**	**_.116(c)(9)**

Criteria for Waivers

- The research involves no more than minimal risk to the subjects;
  - Expedited and Exempt studies only
  - If greater than minimal risk, call the IRB/OHRE
- The waiver or alteration will not adversely affect the rights and welfare of the subjects;
- The research could not practicably be carried out without the waiver or alteration; and
- Whenever appropriate, the subjects will be provided with additional pertinent information after participation

Limited Waiver of HIPAA Authorization

- Allows for access to existing medical records for the purpose of identifying and making initial contact with potential subjects (e.g. recruitment)
- Data collection limited to minimum necessary information to allow identification of potential subjects.
- Records must be destroyed for all subjects who decline participation. All other subjects must sign a HIPAA Authorization form.

>> B.2. Protected Health Information (PHI) Reference Id: 138148

Current Application: Quick View (HTML) PDF Delete Subm

Protected Health Information (PHI) is any identifiable information about the subject's health that relates to their participation in this research and is obtained from sources other than the subject, such as medical records, health care providers, insurance plans, etc. more

1. Are you requesting a limited waiver of HIPAA authorization?
If you need to access Protected Health Information (PHI) to identify potential subjects who will then be contacted, you will need a limited waiver of HIPAA authorization (see SOP 29.3). This does not apply to situations where you will never contact subjects directly (e.g., retrospective chart review), in which case you should request a full waiver under section D. *

(•) Yes ( ) No

Will you access the records of 50 or more patients under this limited waiver? *

( ) Yes (•) No

If you access the records of fewer than 50 patients under this waiver, submit a copy of your IRB approval letter and a completed Research Disclosure Form to Health Information Management (HIM). Do not submit this information to the IRB. For additional information about this process, you should contact HIM directly at 595-5691 or 966-1255.

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 contact potential subjects. Describe the information you are planning to collect for this purpose *

Describe the specific data elements you will need to identify potential subjects: ex., name, diagnosis, date of treatment, age, contact information.

Describe how confidentiality/privacy will be protected prior to ascertaining the patient's willingness to participate *

HOW WILL PRIVACY BE PROTECTED BEFORE SUBJECT IS CONTACTED FOR PARTICIPATION: ex., storing recruitment list in a secure manner

Describe when and how you will destroy the contact information if an individual declines participation *

IF POTENTIAL PARTICIPANT SAYS NO OR CAN'T BE CONTACTED, WHAT WILL YOU DO WITH CONTACT INFORMATION?

When do I need to submit to the IRB?

Initial

Modifications

Personnel Changes

Renewals

NSI's

Closures

***If the IRB has not approved the submission, change, or the study is expired, and unapproved activities occur this is considered noncompliance.**

Types of Annual Review

No annual review

- Exempt & NHSR
- Includes studies re-reviewed under the revised Common Rule

Administrative Review

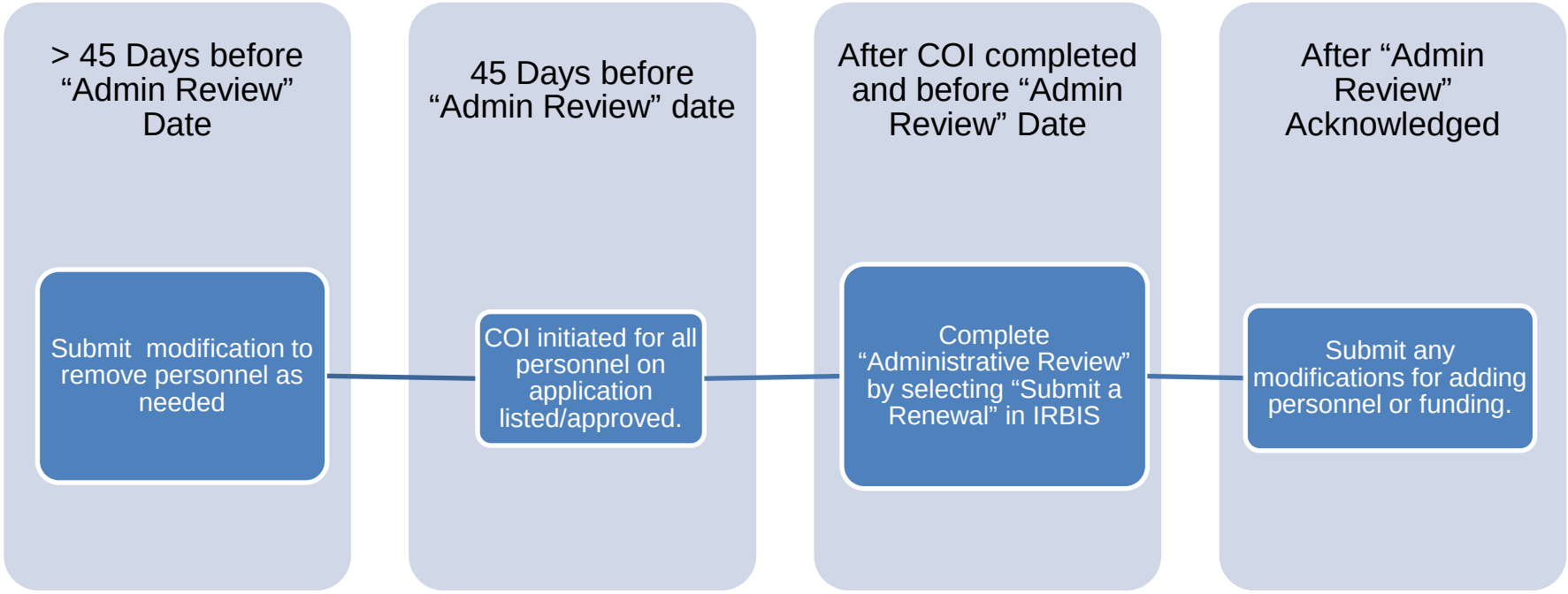
- Non-FDA regulated minimal risk (expedited studies) under the revised "Common Rule"
- Abbreviated form with automatic acknowledgement*
- Required by AAHRPP
- See Next Slide for Timeline

Continuing Review

- Greater than minimal risk/FDA regulated/studies remaining under old "Common Rule
- Previous renewal processes
- Required by Regulations
- 30 Days Prior Recommended

* Provided there are no study concerns and COI has been completed.

Administrative Timeline



How will I know which one?

No Review

RE: Notice of IRB Exemption
Exemption Category: 2.Survey, interview, public observation
Study #: 18-0607

Study Title:

This submission has been reviewed by the Office of Human Research Ethics and was determined to be exempt from further review according to the regulatory category cited above under 45 CFR 46.101(b).

Administrative Review

Approval Date: January 29, 2019
UNC Administrative Review Due Date : January 29, 2020
RE: Notice of IRB Approval by Expedited Review (under 45 CFR 46.110)
Submission Type: [Initial, Renewal]
Expedited Category: 2.Minimal blood draw, 4.Noninvasive clinical data
Study #: [IRB_ID]

Study Title:

This submission, [REFERENCE_ID], has been approved by the IRB. It has been determined that the risk involved in this research is no more than minimal. **This research requires annual UNC administrative review.** Under the revised 'Common Rule' of 2018, this study does not require continuing review and IRB approval will not expire.

Renewal/
Continuing Review

Approval Date: January 29, 2019
Expiration Date of Approval: January 28, 2020
RE: Notice of IRB Approval by Full Board Review
Submission Type: [Initial, Renewal]
Study #: [IRB_ID]

Study Title: [TITLE]

This submission, [REFERENCE_ID], has been approved by the IRB for the period indicated. It has been determined that the risk involved in this research is no more than minimal. **This research requires IRB continuing review. IRB approval will expire on January 28, 2020.**

When can I close my study?

- Renew the study as long as data analysis of **identifiable** data is on-going *(Don't forget publication reviews)*
- When you are completely done with all interventions, follow-up and data analysis, the study should be closed
- If IRB approval of a study expires, no new subjects may be enrolled and all ongoing research activities must stop

118/JIT

- A 118/JIT submission is for federally funded projects that have received a Just-in-Time notice and is an approval in concept, when a full research plan has not been developed.

- Submissions typically completed in 1-3 business days
  - JIT Notice from Program Officer Attached/e-commons system
  - Ramses Submission# linked

- Require a new submission and 111 approval before human subject research activities begin

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ANCILLARY REVIEWS

Mike Matamoros, MS, CIP

The IRB and Ancillary Reviews

Serves as the “gate keeper”/monitor to ensure compliance with Institutional Responsibilities:

- Radiation Safety
- Investigational Drug Services
- Institutional Bio-safety
- Ethics training
- Conflict of Interest
- Privacy Office
- Office of University Counsel (OUC)
- Scientific Review Committee

Scientific Review Process at UNC

- **Any new study, classified as greater than minimal risk*, submitted for IRB review will be required to have scientific review completed and documented prior to the review.**

- ***Office of Clinical Trials (OCT) can give you guidance on risk level. They may consult with IRB, as needed.**

https://research.unc.edu/clinical-trials/src/review-required/

Annual COI Review

- Submission will be created 45 days prior to expiration (or administrative review due) date.

IMPORTANT: We highly recommend all personnel changes be made before the 45 day COI submission is created to avoid delays.

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NAVIGATING THE IRB WEBSITE

OHRE.UNC.EDU

Call IRB Analyst with questions @ 919-966-3113

IRB and the Office of Human Research Ethics

About OHRE and the IRBs

Getting Started

Required Ethics Training

Review Process Overview

Review Process FAQ

Dates and Deadlines

Just-in-Time / 118 Process

IRBIS Online Submission

Sample Consent Forms

Additional Forms

Reliance Agreements

Regulatory Documents

Revised Common Rule

Resources Related to UNC Research

For Research Participants

Training and Education Resources

News

OHRE Staff Intranet

IRB Member Intranet

Getting Started

Prior to initiating an IRB application, new researchers are expected to complete an introductory online course in human research ethics, as well as to familiarize themselves with the IRB submission and review process. Please follow the links below to the relevant webpages:

Required Ethics Training: includes course information and links to the required CITI Human Research Ethics online training course, and UNC's training data base; UNC's policy on human research ethics training and certification; and FAQs.

Review Process Overview: contains brief descriptions of the types of IRB review; the typical timeframe for IRB application submission and review; how IRB decisions are communicated; the approval period; and post-approval submission and review procedures.

Review Process FAQ: provides guidance on how to determine whether research requires IRB review; what first steps to take in applying to the IRB; data gathering requirements; whether informed consent may be needed; and the IRB submission and review process.

CONTACT

CB 7097
720 Martin Luther King Jr. Blvd.
Bldg # 385, Second Floor
Chapel Hill, NC 27599-7097

Ph: 919-966-3113
Fax: 919-966-7879
Help/Questions

UPCOMING EVENTS

IRB Events Schedule

QUICK LINKS

Online Applications

Ethics Training

Dates and Deadlines

UNC OHRE SOP

Follow us on Twitter:

@UNC_IRB

Association for the Accreditation of Human Research Protection Programs, Inc. Full Accreditation

Dates and Deadlines

Upon receipt of your application, the IRB will determine level of review. Most reviews are **expedited**, i.e., reviewed in-office, on an ongoing basis, by the Chair and selected reviewers. Only those proposals subject to **full board** review, i.e., by full board review, are required to meet submission deadlines (see table, below).

IRB Board Meeting Schedules

- Boards A, B, C, and D of which one meets on **each of the first four Mondays of the month**, unless the Monday is a holiday.
- Board E meets the **second Tuesday of each month**.
- Board F meets the **second Thursday of each month**.
- New studies requiring **dental or oncology** expertise are reviewed by the Board B or D (meet **second and fourth Monday**, except holidays). Once approved, a renewal or modification of a dental or oncology study can often be reviewed by any of boards.

Notes:

- The "Deadline" date in the table below is the date the submission is accepted for review by the IRB. The "Meeting" date is when the board meets.
- An application accepted by the published deadline will *generally* be assigned to the corresponding meeting. However, there may be circumstances when this is not possible, in which case it will be assigned to the next available board meeting. ***Please be advised that receipt by submission deadline does not guarantee review at the corresponding meeting.***
- Dates are subject to change.

IRB Board Meeting Dates and Submission Deadlines

Search:

Board	Deadline Date	Meeting Date
A	December 20, 2019	January 6, 2020
F	December 23, 2019	January 9, 2020
B	January 2, 2020	January 13, 2020
E	January 2, 2020	January 14, 2020

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Help/Questions

UPCOMING EVENTS

IRB Events Schedule

QUICK LINKS

- Online Applications
- Ethics Training
- Dates and Deadlines
- UNC OHRE SOP

Follow us on Twitter:

Sample Consent Forms

Consent Form Templates

These consent form templates have been posted for your reference. When completing and IRB submission in IRBIS, please fill in the application and use the consent form builder specific to your project. For more information, please find instructions here.

Summary of Changes to the Regulations for Informed Consent: Revised Common Rule Changes to Informed Consent and Waiver Requirements

Summary of Changes to Consent Documents:

- Informed Consent Documents – Version 2.0 Summary of Changes
- Informed Consent Documents – Version 2.1 Summary of Changes – Coming Soon!

Consent Document Type	Last Updated
Adult Consent Form	2020-01-17
Stored Specimens with Identifiers	2020-01-17
Stored Specimens without Identifiers	2020-01-17
Parental Permission Form	2020-01-17
Assent Form Ages 15-17	2020-01-17
Information or Fact Sheet	2020-01-17
Focus Group Consent Form	2020-01-17
The following documents are samples. IRBIS does NOT generate these documents with application-specific information.	

Just-in-Time / 118 Process

§46.118 Applications and proposals lacking definite plans for involvement of human subjects.

46.118 Determinations can be granted to satisfy federal sponsor requirements (e.g., Just-In-Time) to allow investigators to have access to funding to begin aspects of the project that do not involve human subjects. **Human subject research activities cannot begin until a full application and all applicable material (e.g., consents, surveys, tools) have been developed, submitted, and IRB approval (§46.111) has been obtained.**

Under the federal regulations (§46.118) certain types of applications for grants are submitted with the knowledge that subjects may be involved, but definite plans would not normally be set forth in the application or proposal. These can fall under three categories:

- institutional type grants when selection of specific projects is the institution's responsibility;
- research training grants in which the activities involving subjects remain to be selected; and,
- projects in which human subjects' involvement will depend upon completion of instruments, prior animal studies, or purification of compounds.

Many of the request for a .118 determination will fall under the third category. Research instruments refers to measurement devices and can include surveys, tests, questionnaires, etc. It is important to distinguish if the release of funds are required for the completion of instruments, prior animal studies, or purification of compounds.

CONTACT

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Fax: 919-966-7879
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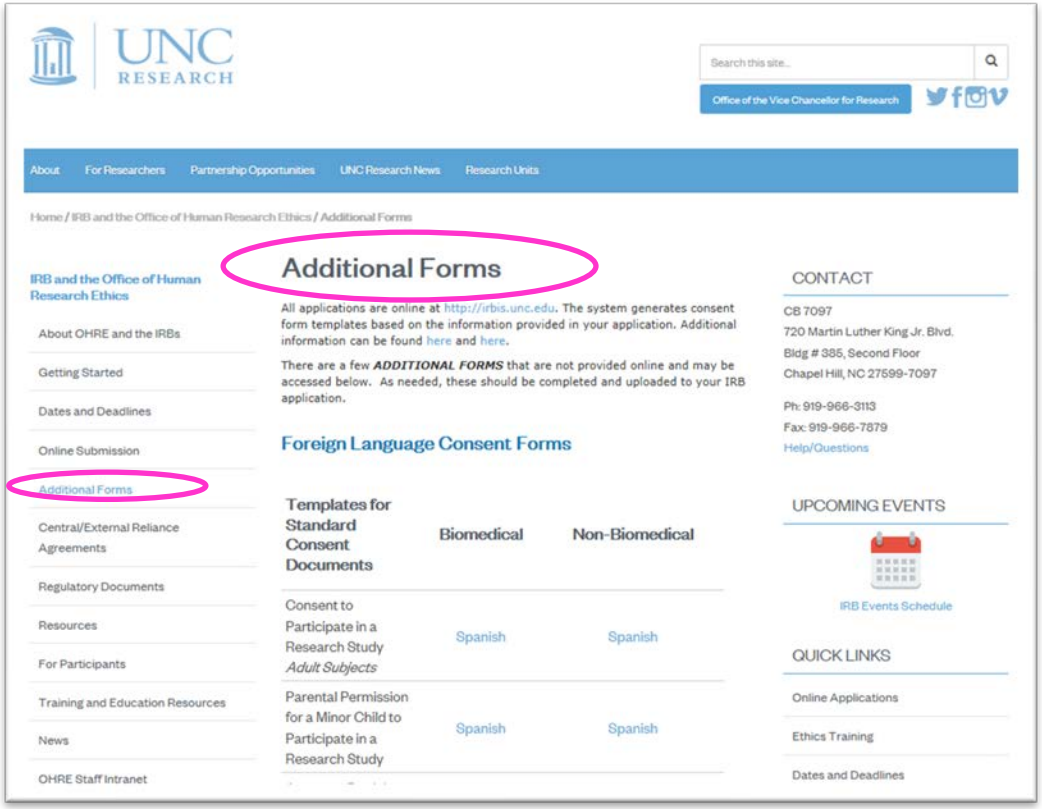
UPCOMING EVENTS

IRB Events Schedule

QUICK LINKS

Online Applications
Ethics Training
Dates and Deadlines
UNC OHRE SOP

Follow us on Twitter:



Miscellaneous

Report of Emergency Use of a Test Article to the IRB

Verification of Foreign Language Translation

Protocol Exception Request Form

Device Related

HUD Addendum Completion Instructions
Humanitarian Use Device (HUD) Application Addendum

Investigational Device Guidance Document
Investigational Device (IDE) Worksheet

Expanded Access Drugs/Devices Addendum Instructions
Expanded Access Devices Addendum
Expanded Access Devices Informed Consent Form Template

Drug Related

IND Exemption Checklist

Expanded Access Drugs/Devices Addendum Instructions
Expanded Access Drugs Addendum
Expanded Access Drugs Informed Consent Form Template

IRB and the Office of Human Research Ethics

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Additional Forms
Reliance Agreements
Regulatory Documents
Revised Common Rule
Resources Related to UNC Research
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IRB Member Intranet

Regulatory Documents

The documents listed below are commonly needed regulatory or informational documents for the University of North Carolina at Chapel Hill Office of Human Research Ethics (OHRE) and the Institutional Review Boards (IRBs). Also included on this page is information about proposed regulatory reforms, and UNC comments to these proposals. Access to other related documents can be found on our Resources page.

Standard Operating Procedures (SOP)

The *University of North Carolina at Chapel Hill Human Research Protection Program Standard Operating Procedures* (SOP) describes the policies and procedures that govern human subjects research at this University. These are intended for use by IRB chairs and members, the staff of the Office of Human Research Ethics and investigators and research team members.

Federal Wide Assurance (FWA)

The University of North Carolina at Chapel Hill has committed to uphold regulatory and ethical standards through a Federal Wide Assurance (FWA) approved by the federal Office for Human Research Protections (OHRP). Our assurance with OHRP is FWA #4801. OHRP no longer provides paper copies of these agreements. To view our OHRP assurance records, Click here for the OHRP database and follow these steps:

1. Click the TAB FOR "FWAs";
2. Enter "4801" in the FWA number field; and
3. Click the Search button.

Statement of Compliance

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Reliance Agreements

How to Request a Reliance Agreement

Guidance Document: Requesting Reliance on an External IRB or Extending UNC IRB Oversight to an External Group or Individual

A reliance agreement may be required when you are collaborating with researchers external to UNC who are engaged in research. This document describes how to complete the IRBIS application to request one of the following:

- UNC provide IRB oversight for institutions, groups or organizations external to UNC
- UNC provide IRB oversight for individuals (whose collaboration is NOT on behalf of an external institution, group or organization) external to UNC
- UNC rely on an Institutional IRB
- UNC rely on an Independent/Commercial IRB
- UNC rely on the NCI CIRB

Reliance documents for collaborations with organizations or institutions

These are samples of the forms the IRB uses to document reliance arrangements. The UNC Reliance Team will be responsible for preparing these forms when specific reliance requests are made. They are provided here for informational purposes, and should not be completed by the study team unless during consultation with the Reliance Team.

- UNC's IRB Authorization Agreement (IAA) template may be used when both parties have a Federal Wide Assurance (FWA).
- Smart IRB Authorization Agreement may be used when both parties have an FWA and are Smart IRB Participating Institutions.
- Smart IRB Letter of Acknowledgement (LOA) may be used to document a Smart IRB reliance arrangement (alternative to the online reliance system)

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IRB and the Office of Human Research Ethics

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Training and Education Resources

Training and Education Resources

IRB Guidance Information

Researcher Resources

Research Ethics Resources

Research Regulation Resources

Non-Governmental Organizations (NGOs)

Newsletters and Additional Materials

Other

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UPCOMING EVENTS

Researcher Resources

- OHRE Overview of Research Subjects' Protections at UNC-CH (TBA)
- UNC Responsibilities of Staff in Human Subjects Research
- UNC IRB Process
  - CITI Training Requirements
  - Conflict of Interest Program
  - Office of Human Research Ethics (OHRE) SOPs
  - IRBIS (UNC on-line submission e-system)
    - On-line submission guide

(Other Links at UNC-CH Related to Human Subjects Research—drop title, left in as a guide of where to find on webpage)

- IRB Review Fee for Industry-Sponsored Studies
- NRP New Coordinator Orientation (recordings of 5 workshops sponsored by NC TraCS, UNC OCT, and NCRP)
- Environment, Health and Safety
- Radiation Safety and the Radiation Safety Committee
- Biological Safety and the Institutional Biosafety Committee
- Oncology Protocol Review Committee
- Investigational Drug Service (IDS) Note: This web site is on an intranet, and access may not be possible from some locations.
- UNC Hospitals Policy on Investigational Devices
- Office of Clinical Trials
- Registering an Investigator-Initiated Clinical Trial in a Public

IRB Guidance Information

Documents

- Requesting a reliance agreement
- Unanticipated Problems and Adverse Events
- 10 Things Directors of Undergraduate Studies at UNC-CH Should Know about the IRB
- IRB Guidance for Student Research & Class Projects
- Navigating the IRB Process: Steps for Faculty Advisors
- Navigating the IRB Process: Steps for Students
- IRB Essentials' Fact Sheet
- Relying on Central IRBs
- Data Use Agreement Guidance
- Review Process FAQ

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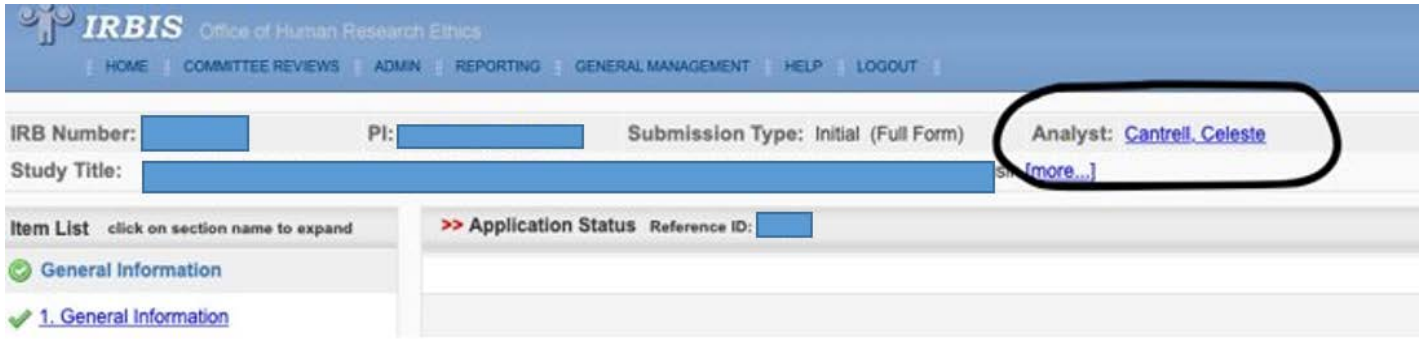
IRB Resources

- **Website**: *IRB and Office of Human Research Ethics - UNC Research*
- **Telephone:** 919-966-3113
- **Address:** Bolin Creek, 720 Martin Luther King, Jr. Blvd, CB # 7097 Second Floor
- OHRE Did You Know? Section: https://research.unc.edu/human-research-ethics/news/did-you-know/
- **IRB Staff** (see website for listing of staff names): http://research.unc.edu/offices/human-research-ethics/
  - See Analyst assigned to any open submission.



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IRB APPLICATION SUBMISSION PROCESS

Mike Matamoros, MS, CIP

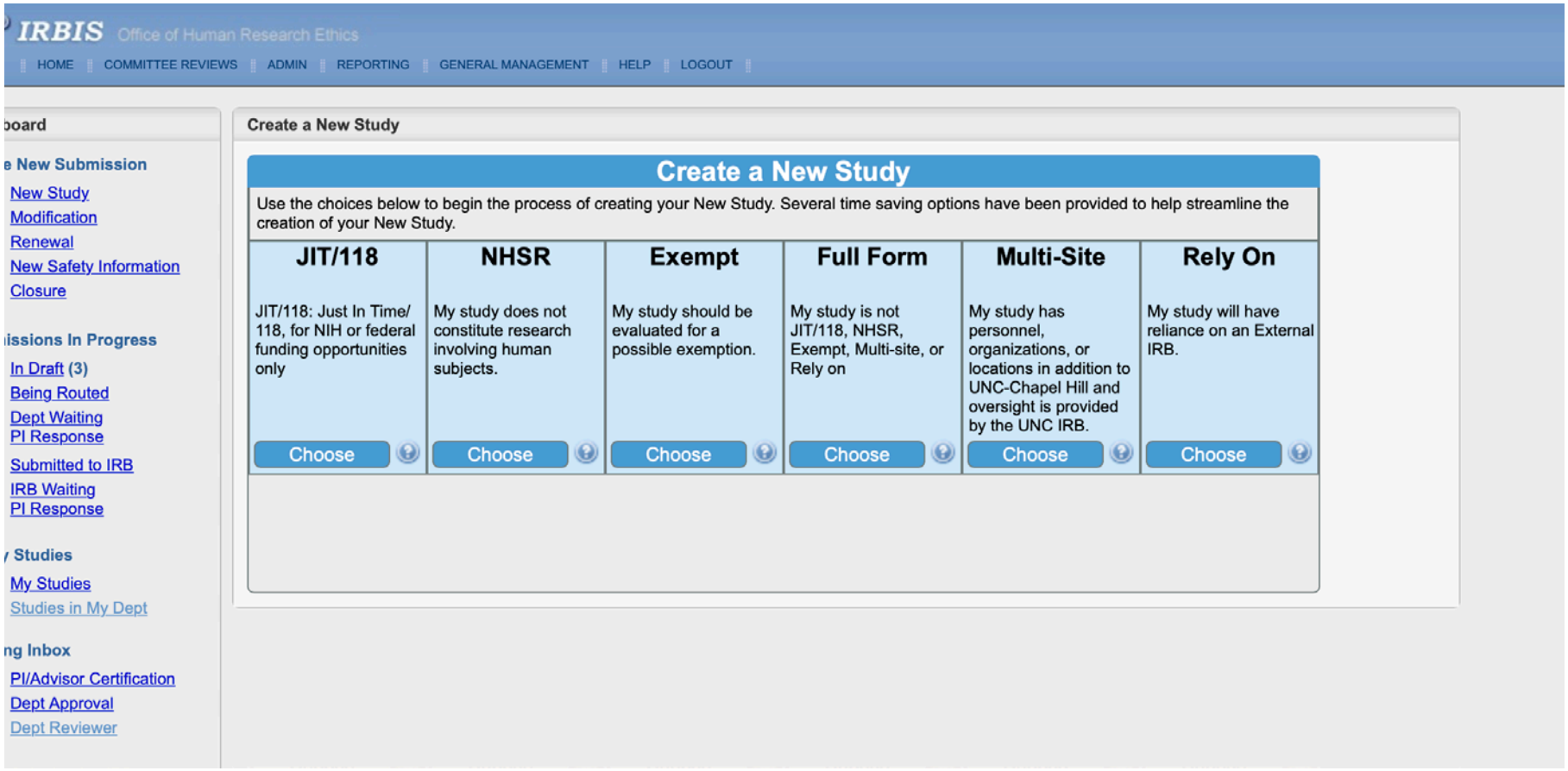
Plan Ahead!

- Your application may be one of 100's submitted that week (on average 350-450 submitted a week)
- Pay attention to dates and deadlines (tentative)
- Complete the application as directed
- Provide consents; recruitment materials; and supporting documents
- Familiarize yourself with the "IRB" SOPs
- If you have **questions** while completing the application or consents, please
    - **call 919-966-3113 or**
    - **email irb_questions@unc.edu**

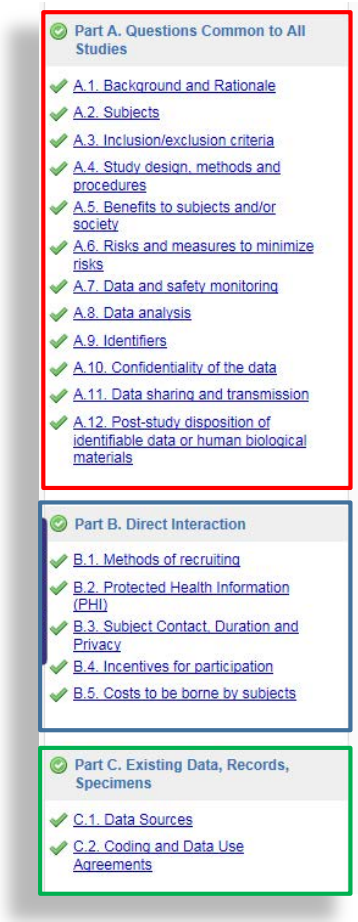
On-line Submissions

- Smart form approach
- Selection of type of initial submission (e.g., NHSR, Exempt, Full Form)
- System builds consent forms
- Electronic Routing and Approvals
- On-line communication to and from the IRB
- Include a cover memo that explains special circumstances

Application Type-Create a New Study



The Application Proper



The online IRB Application proper consists of three primary Parts:

A: Questions Common to All Studies
B: Direct Interaction
C: Existing Data Records, Specimens

- Parts **A** and **C** are always present, if sometimes conditionally abbreviated.
- Part **B** is displayed only if the researcher is collecting personal information through subject interaction.
- The number of constituent sections may vary, depending on: the nature of the research (e.g., whether the study uses biomedical or behavioral methodology); or the level of review requested (e.g., Exempt or NHSR).

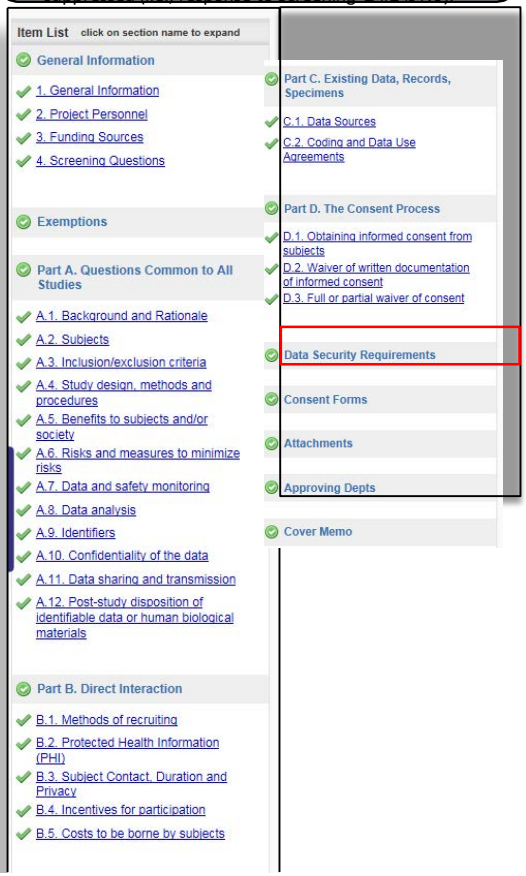
IRBIS Orientation: Initial Application types (As reflected in the ITEM LIST)

A completed application:

- The PI is prevented from submitting until all sections/parts of the IRB application are complete (as denoted by **green checkmarks**).

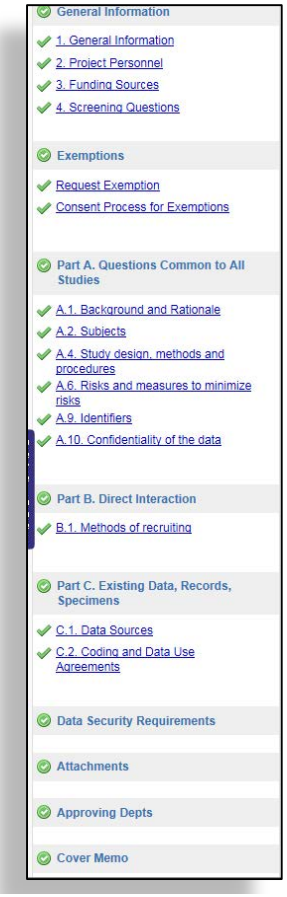
The full IRB Application:

- Consent Form templates are tailored specifically to each application, but are not presented until all preceding sections are complete.
- An application is considered "full" even if Part B is suppressed (i.e., response to Screening Q #2 is *No*).

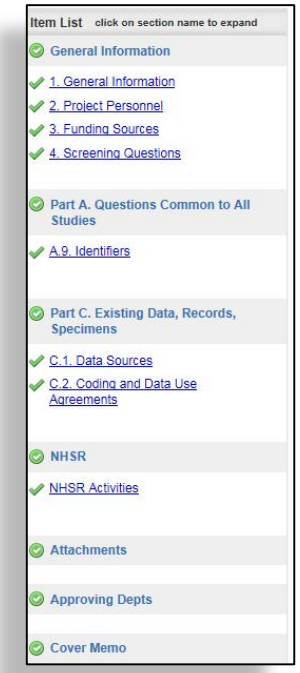


Exempt Request

- Consent forms are neither required nor presented

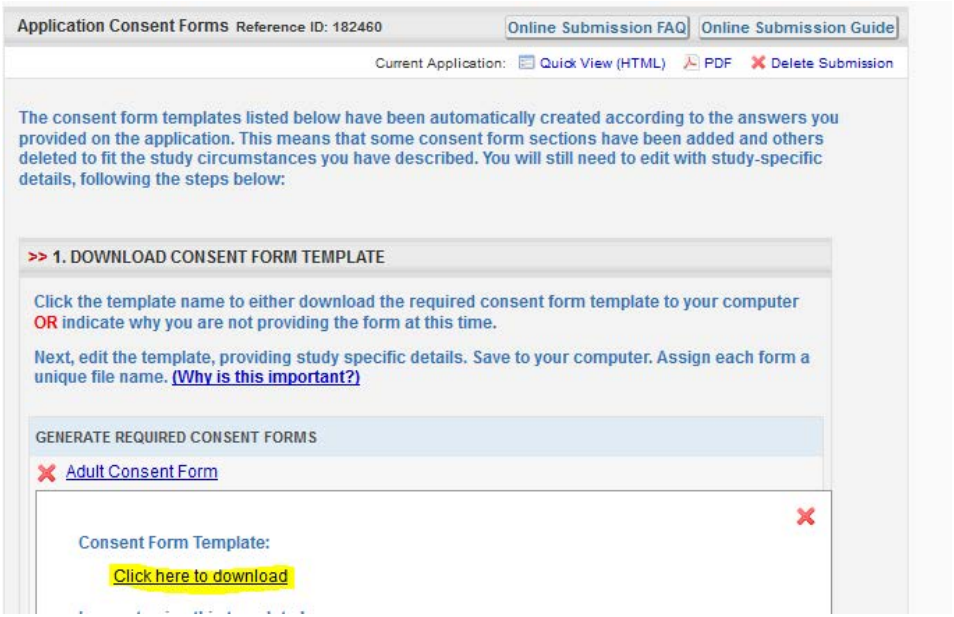


NHSR Request



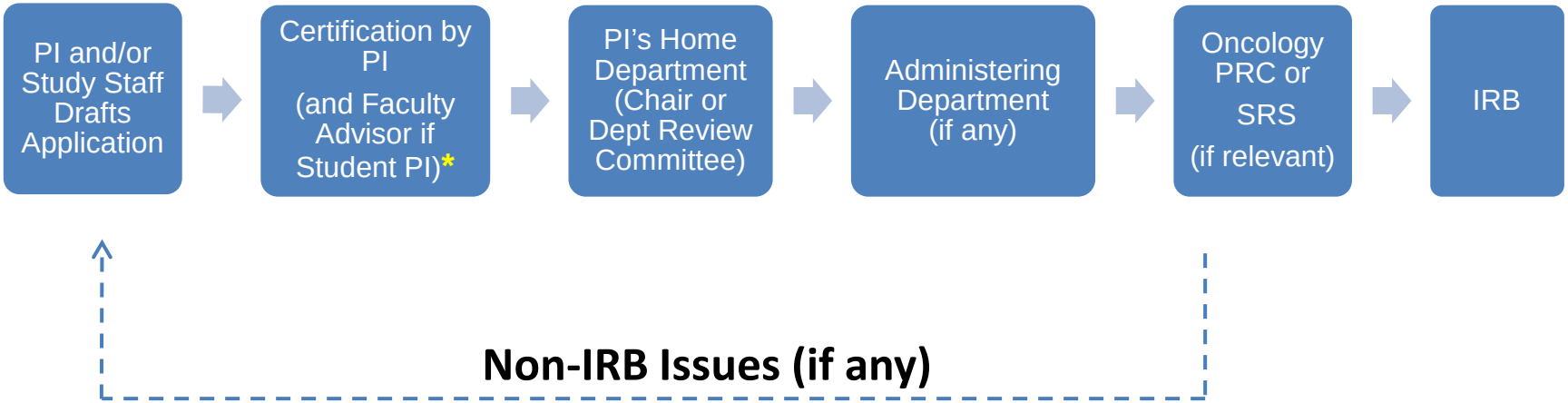
Consent Templates

- Study specific templates are generated in IRBIS.



- Sample templates are available on the OHRE website at https://research.unc.edu/human-research-ethics/common-rule/consent-forms/

Routing of IRB Submissions



Research Data Security Grading System

Subject IDs	Sensitive Questions	Security Level	Requirements*
---	---	I	Password protection
YES	---	II	Level I plus secure network
---	YES	II	Level I plus secure network
YES	YES	III	Level II plus encryption, vulnerability scans, security audits

** Note that schools and departments will be expected to play a more central role in ensuring security requirements are met. Investigators should consult with IT managers for their units.*

IT Expert within the Approving Department

(Department Responsible for the Study)

Level II Data Security Requirements:

Based on the information the PI provided in the IRB application, this study will be collecting sensitive data that require additional security measures to ensure that they are adequately protected from inadvertent disclosure. Due to the nature of these data, the PI is required to implement the following security measures on any computer(s) that will store or access information collected for this study. The PI should coordinate efforts in this area with the unit's IT data security personnel receiving this email.

Required Measures for Level II Data Security

1. Access to study data must be protected by a username and password that meets the complexity and change management requirements of a UNC ONYEN.
2. Study data that are accessible over a network connection must be accessed from within a secure network (i.e., from on campus or via a VPN connection).
3. Computers storing or accessing study data must have Endpoint Protection (AntiVirus/AntiSpyware) installed and updated regularly where technologically feasible.
4. Patch management and system administration best practices should be followed at all times on systems storing or accessing your data.
5. Users should be granted the lowest necessary level of access to data in accordance with ITS Security's Standards and Practices for Storing or Processing Sensitive Data (when technologically feasible).

**These requirements do not replace or supersede any security plans or procedures required by granting agencies or sponsors. Questions or concerns about compliance with these requirements should be directed to the administering department's IT support staff.

Additional IT Security Resources

- ITS Security
- Carolina Population Center Security Guidelines
- SOM Information Security
- ITS Research Computing

Due to the nature of this research study, the senior IT official in the administering department is receiving this email about the study and may contact the PI or technical contact(s) to discuss any data security questions on concerns they may have. If the PI has indicated that the research will take place in another unit on campus (i.e., a Center or Institute), that group will also be notified.

The Data Security Level contact(s) for your administering department (Computer Science - 318400):

- Rob Noel (rob@unc.edu)
- Timothy Hensley (thensley@email.unc.edu)
- Barbara Olszanowski (barboski@email.unc.edu)

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IRB RELIANCE AGREEMENTS

John Roberts, CIP

Associate Director of Regulatory Affairs & Compliance

What is an IRB Reliance Agreement?

- Formal document that provides a mechanism for an institution **engaged in research** to delegate IRB review to an independent IRB or an IRB of another institution, *or* allows an IRB to accept primary review responsibilities regarding the research on behalf other institutions or individuals.
- Used when **non-exempt human subjects** research is conducted at multiple sites, when a participating research entity does not have its own IRB, or when the research requires specialized IRB expertise.
- Expected benefits include reduction in duplication and variation, decrease in activation time, and foster collaboration between sites.
- NIH single IRB review policy https://grants.nih.gov/policy/humansubjects/single-irb-policy-multi-site-research.htm
- As of January 2019 the Revised Common Rule expanded the sIRB requirement to most federally funded multisite collaborative research

Adapted from: http://www.niaid.nih.gov/LabsAndResources/resources/toolkit/Pages/faq.aspx

OHRP Federalwide Assurance (FWA)

Documents an institution's commitment to comply with federal regulations governing human subjects research.

- Covers all research supported or conducted research involving human subjects
- **Requires written formal agreement of compliance from all non-affiliated investigators

- ***The institution*** bears full responsibility for ensuring that all human subject research is conducted in accordance with Federal regulations.

- ***The IRB*** must review and approve or disapprove research involving human subjects according to guidelines set forth in 45 CFR 46.

- ***The investigators*** acknowledge and accept their responsibility for protecting the rights and welfare of human subjects and for complying with the FWA.

- **NOTE:** *Without an FWA, Federally Funded research can not be conducted at an institution. An FWA can be cancelled by the Office for the Protection of Human Subjects (OHRP)*

NIH Single IRB Review Mandate

Effective January 25, 2018

For applications with due dates on or after January 25, 2018, and contract solicitations published on or after January 25, 2018, NIH expects that all sites participating in multi-site studies, which involve non-exempt human subjects research funded by the NIH, will use a single Institutional Review Board (sIRB) to conduct the ethical review required for the protection of human subjects.

This policy applies to the domestic sites of NIH-funded multi-site studies where each site will conduct the same protocol involving non-exempt human subjects research. It does not apply to career development, research training or fellowship awards. Implementation of the NIH sIRB policy is expected to reduce unnecessary administrative burdens and systemic inefficiencies while maintaining appropriate human subjects protections.

Applicants will be expected to include a plan for the use of a sIRB in the grant applications and contract proposals they submit to the NIH (for due dates on or after January 25, 2018).

NIH Single IRB Review Mandate

https://smartirb.org/

- Currently 800+ Participating Institutions, all 64 CTSA hubs
- Smart IRB: a platform designed to ease common challenges associated with initiating multisite research and to provide a roadmap for institutions to implement the NIH Single IRB Review policy
- Smart IRB Agreement: a standardized reliance agreement, does not require negotiating of agreement terms, may be cited for multisite collaborative arrangements sponsored by any funding type
- Reviewing IRB = IRB of Record = Lead IRB = sIRB
- Relying Institution = participating site ceding review

4 Types of Agreements

- **IAA**: IRB authorization agreements (e.g., UNC relies on Duke IRB, Wake Forest relies on UNC IRB; can be executed between institutions when both have an FWA) ←→ (e.g. Smart IRB)

- **IIA**: Independent Investigator Agreements (e.g., Bob Smith relies on UNC IRB; typically consultants, subcontractors, former students; UNC IRB extends our FWA to a small non-profit that does not have an FWA) →

- **Central or Commercial** IRB Agreements: IAAs (e.g., UNC relies on WIRB, UNC relies on the NCI CIRB; typically refers to a commercial IRB or the NCI CIRB) →

- **Broad** Agreements: IAAs (e.g. the joint NCSU/UNC biomedical engineering dept, EPA relies on UNC IRB for all HSR reviews) →

UNCs most common agreements when providing regulatory oversight for those external to UNC

- UNC's IRB Authorization Agreement (IAA) template may be used when both parties have a Federal Wide Assurance (FWA).
- Smart IRB Authorization Agreement may be used when both parties have an FWA and are Smart IRB Participating Institutions.
- UNC Individual Investigator Agreement (IIA Institutional) is used when the external group or organization does NOT have a Federal Wide Assurance (FWA)
- UNC Individual Investigator Agreement (IIA Individual) is used when an Independent Investigator will be covered by the UNC IRB.

Independent Investigators

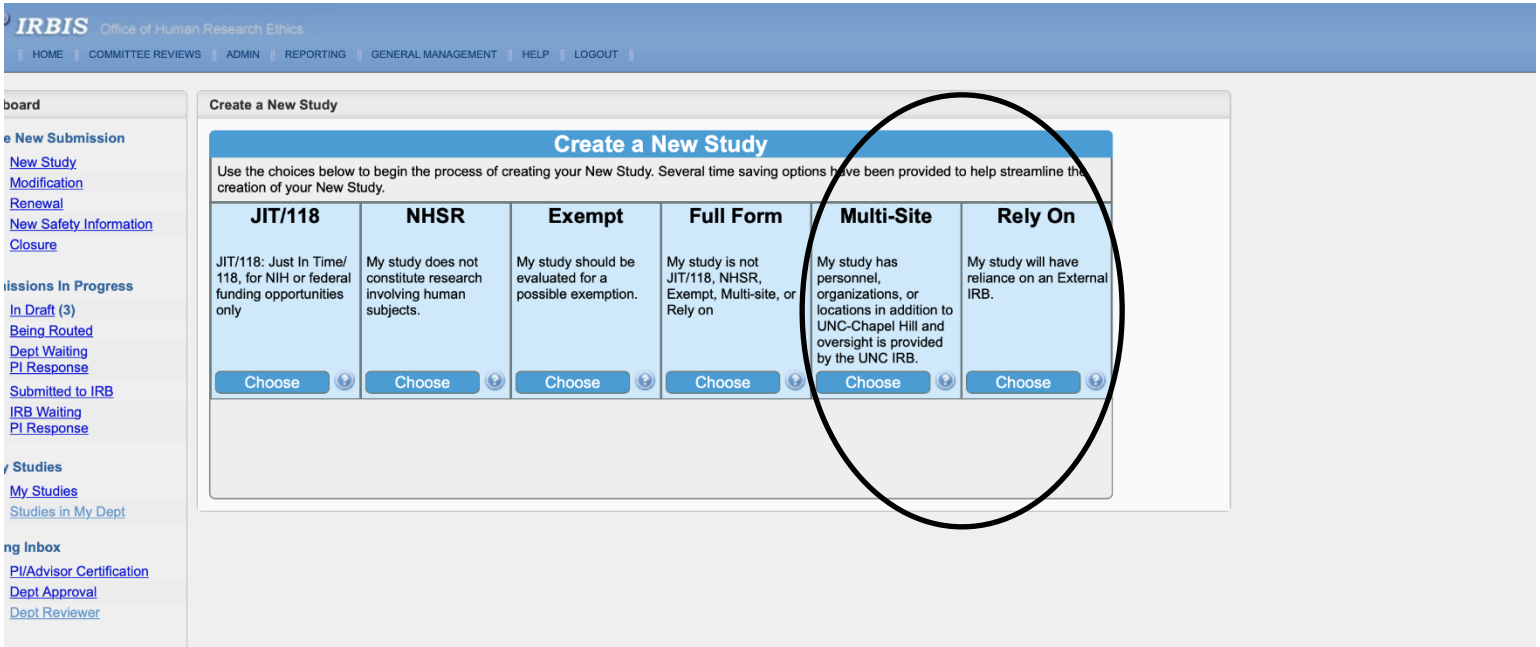
- When a collaborator outside of UNC-CH is not acting as an employee of another group or organization with respect to their involvement in the research, they may be considered an Independent Investigator. Typically independent investigators are volunteers, recent graduates or former staff who are no longer affiliated with UNC, or independent consultants contracted to work on the research. In order to be considered an independent investigator, this person is required to complete an ‘Independent Investigator Confirmation Form’, provide evidence of qualifications (CV etc), complete the UNC ethics training and complete a UNC COI disclosure

Process for Requesting a Reliance Agreement

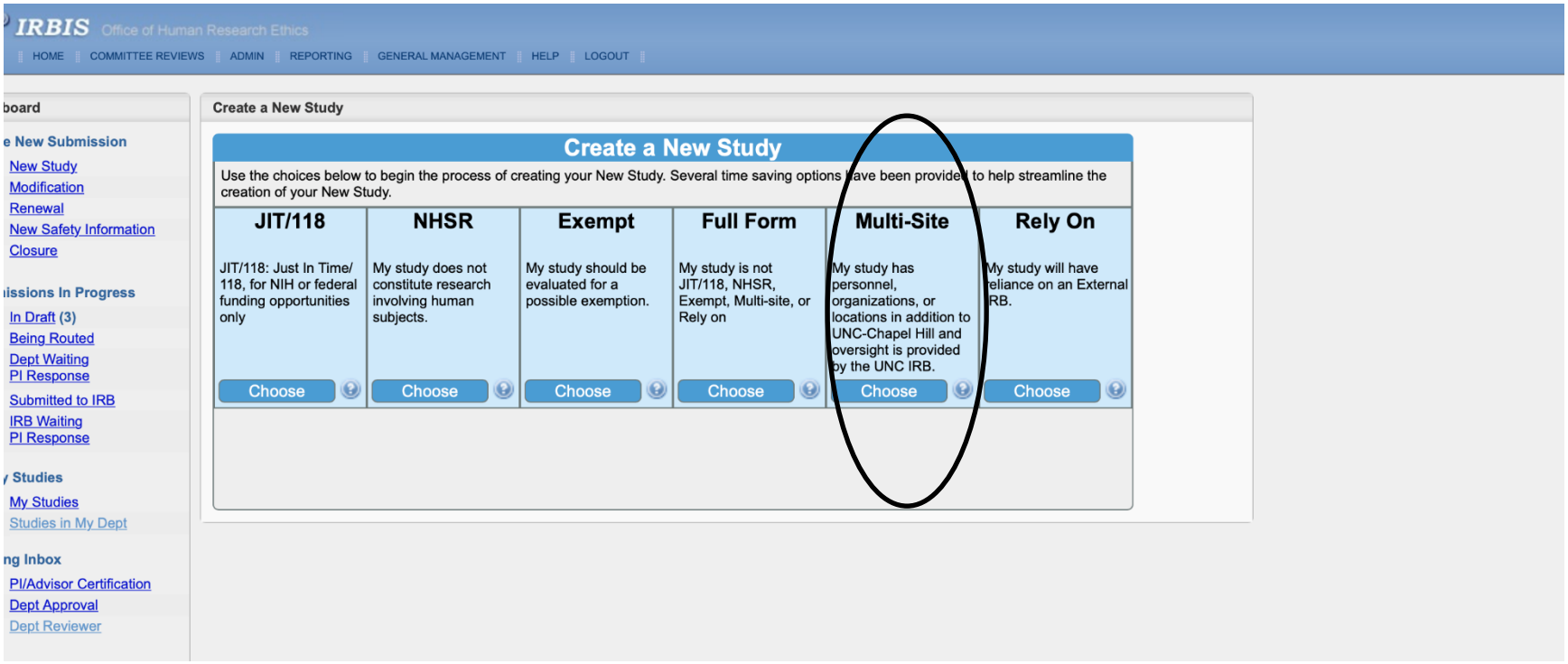
Guidance documents are located on the OHRE website here: http://research.unc.edu/human-research-ethics/reliance/

NOTE: updates to guidance coming

All requests for reliance agreements are submitted through IRBIS.



UNC is the IRB of Record for Others

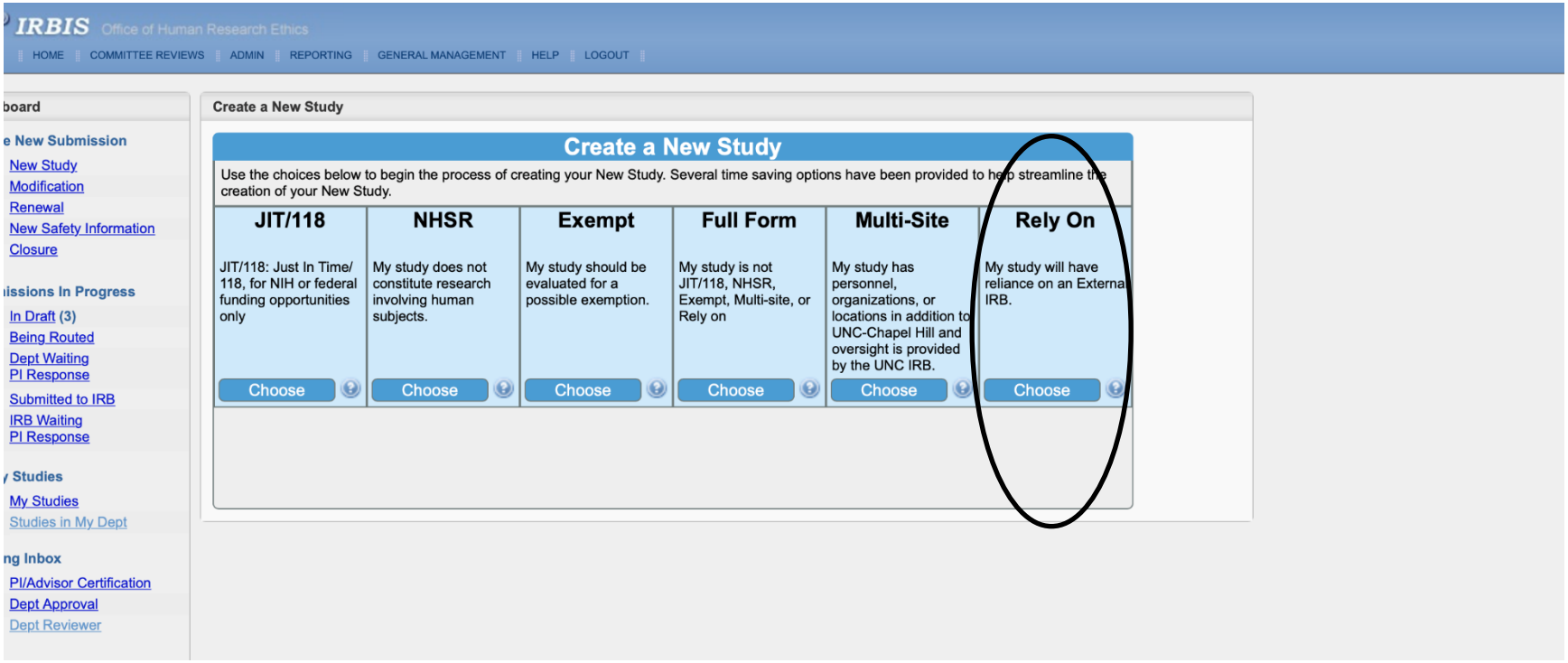


Multisite = UNC IRB is reviewing IRB

- External individuals or sites and their personnel added to IRBIS application
- UNC gathers local context information from the sites in order to review appropriately, incorporate local requirements into review and approve site's study documents
- Personnel requirements determined by whether or not the site holds an FWA
- If site is consenting subjects locally, we typically tailor a consent for the site based upon the UNC IRB approved model consent form

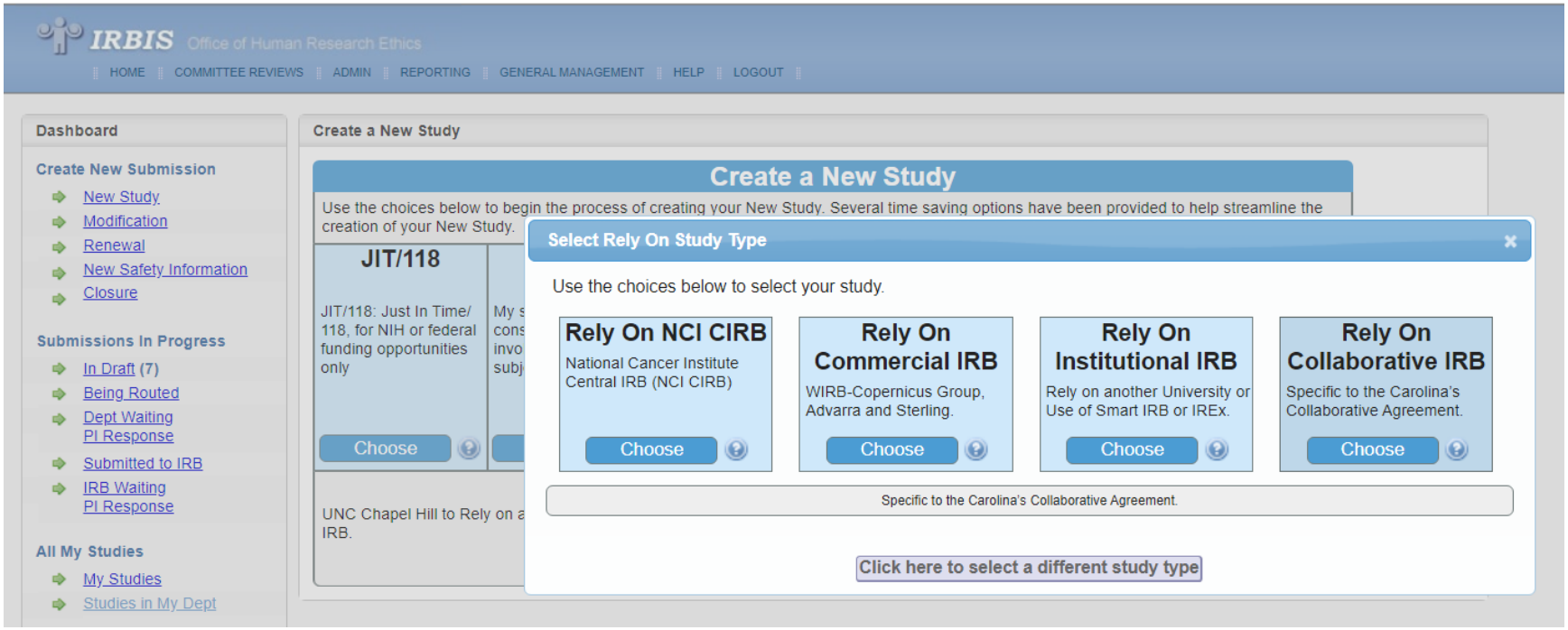
UNC is relying on another IRB

If the intent is for UNC to rely on another IRB for review (cede review):



UNC is relying on another IRB

- Select appropriate reviewing IRB type:



Relying on Commercial IRBs

- Required for all industry sponsored multi-site clinical trials, unless exception by OHRE Director or Associate Director is given.

- UNC has MSA's with:
  - WIRB
  - Advarra
  - Sterling

- Must obtain Permission to Register from UNC OHRE through IRBIS before submitting to commercial IRB, a Cover Letter will be provided with UNC rules.

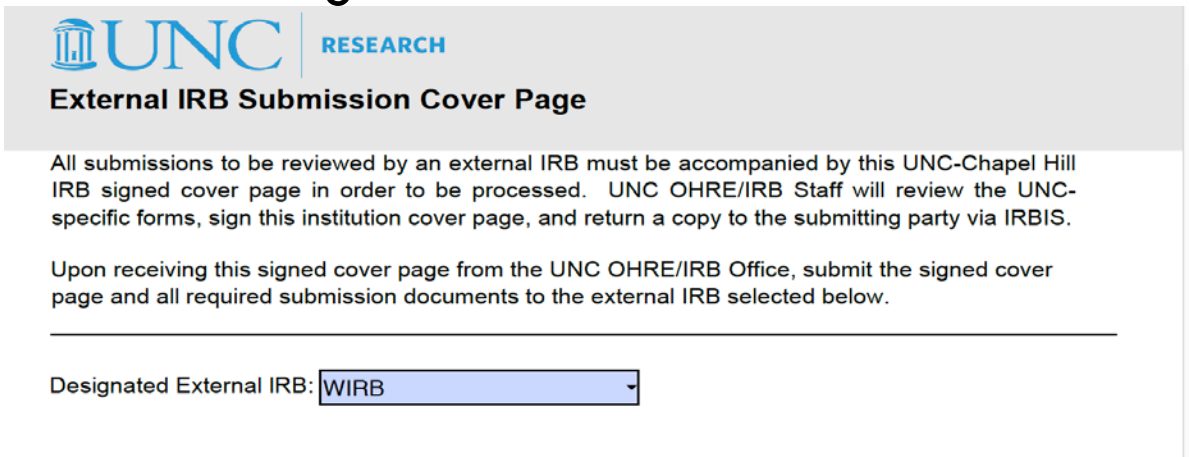
Commercial IRB Submission Req.

- Initial Submission using the **Rely on External IRB** application type in IRBIS
- External IRB approval letter (with date of expiration) for the overall study/protocol*
- Master Protocol
- Sponsor's Model Consent Forms
- UNC Standalone HIPAA Authorization form generated from IRBIS (if applicable)
- Recruitment materials, only for MyChart/Join the Conquest/Research for Me
- Documentation of any applicable UNC based ancillary review, as well as any resulting language requirements (IDS, radiation safety, PRC, IBC, etc)
- Documentation of the approved Subject Injury Language from OIC/Chris Nelson
- Completed Conflict of interest Review**:** The standard UNC process for COI disclosure still applies. Registration with the Commercial IRB cannot occur until the UNC COI process has been completed for all applicable members of the research team.
- Confirmation of required ethics training for all UNC personnel

*If the commercial IRB is acting as a single IRB of record then the approval letter can be provided. If UNC is a standalone site there will be no existing approval letter and can be noted in the IRBIS Submission

Commercial IRB Cover Page

- A Commercial IRB "Cover Page" will be provided along with a Permission to Register letter



UNC | RESEARCH

External IRB Submission Cover Page

All submissions to be reviewed by an external IRB must be accompanied by this UNC-Chapel Hill IRB signed cover page in order to be processed. UNC OHRE/IRB Staff will review the UNC-specific forms, sign this institution cover page, and return a copy to the submitting party via IRBIS.

Upon receiving this signed cover page from the UNC OHRE/IRB Office, submit the signed cover page and all required submission documents to the external IRB selected below.

Designated External IRB: WIRB

- Local context items covered in Cover Page will include:
  - Subject Injury Language for UNC consent
  - HIPAA Determinations (UNC-Full, WIRB Partial)
  - HIPAA Authorization (if applicable)
  - COI Language
  - UNC ancillary review requirements or site-specific language

Broad Agreements

Executed to provide IRB coverage for multiple protocols, when the collaborator and reviewing IRB have special arrangements, typically to accommodate substantial collaborations.

- Environmental Protection Agency (EPA) – UNC IRB is the IRB of record for the EPAs HSR, has broad agreement to cover EPA research conducted at EPA facilities on campus, as well as other EPA/UNC collaborations.

IRB Contacts for Reliance Agreements:

http://research.unc.edu/human-research-ethics/reliance/

OHRE main line 919-966-3113

- For questions about commercial IRBs:

Jamie Kauwell jamieb@email.unc.edu

- For questions about all other reliance agreements:

IRBReliance@unc.edu or

John Roberts jtr@unc.edu

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NEW SAFETY INFORMATION (NSI) SOP 1401

Cassandra Myers, CIP

Objectives

- Identify information that is reportable as New Safety Information (NSI)
- Submit comprehensive New Safety Information reports within the required time frame
- Describe the IRB's NSI review process

*TIP-READ SOP 1401

NSI Reporting Obligation

- FDA and HHS regulations require the IRB to promptly receive safety and other information throughout to ensure the criteria for approval is still met and to ensure the safety, rights, and welfare of subjects are protected

  - *45 CFR 46.109 and 46.111; 21 CFR 56.109 and 56.111*

What is Reported to the IRB

The PI is required to notify the IRB, within *7 days*, of any of the following events by submission of an NSI:

- **An unanticipated problem involving risks to subjects or others**
- **An event that, as dictated by the protocol, requires urgent reporting to the sponsor**
- **Non-compliance with protocol requirements (including protocol deviations) or IRB policies.**
- **Any other reported event where the PI is unsure if the event represents an unanticipated problem involving risk to subjects or others**

What is a UPIRTSO/UPIRSO

- The phrase “unanticipated problems involving risks to subjects or others” is found but not defined in the HHS regulations at 45 CFR part 46. OHRP considers *unanticipated problems*, in general, to include any incident, experience, or outcome that meets **all** of the following criteria:
  - ***unexpected (in terms of nature, severity, or frequency)*** given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied;
  - ***related or possibly related to participation in the research*** (in this guidance document, *possibly related* means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and
  - ***suggests that the research places subjects or others at a greater risk of harm*** (including physical, psychological, economic, or social harm) ***than was previously known or recognized.***

What is risk?

Risk is not harm:

it is the ***possibility of harm***, and an analysis of the risks must take into account including both the ***magnitude*** of the possible harm and the ***probability*** that the harm may occur.

(The National Commission 1979 and Common Rule)

What is unexpected?

The nature, severity, or frequency of the adverse event is not consistent with either:

- the risk information described in study product documents, the protocol or the informed consent document

or

- the characteristics of the subject population being studied

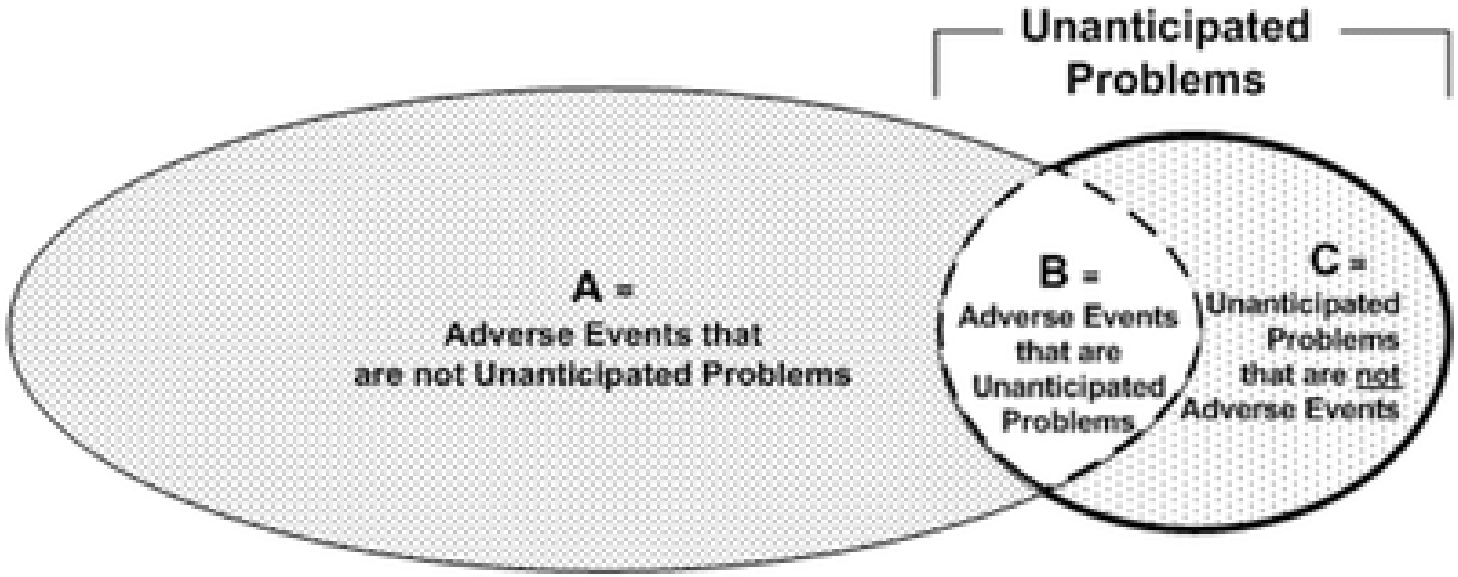
What is related?

That participation in the research caused or may have been related to the event

Examples may include:

- Storage of data
- Study drug
- Investigational device malfunction

UP Diagram



Under 45 CFR part 46: Do not report A; Report B and C.

What is Noncompliance

Intentional or unintentional failure to follow applicable federal human subject protection regulations, the requirements or determinations of the IRB, the IRB-approved study protocol, or University policies when that failure adversely affects the rights or welfare of participants, such as:

- Conducting human subjects research without an IRB-approved protocol or exemption
- Starting research prior to meeting the conditions required by the IRB and receiving an IRB notification of approval, or conducting research during a lapse in approval
- Failure to obtain informed consent or deviating from the approved process
- Initiating changes without IRB approval, unless immediate risk of harm.
- Failure to follow GCP requirements in regard to conduct of the research.

Serious Noncompliance

Serious Noncompliance: “Noncompliance” that adversely and significantly affects the rights or welfare of participants.

Continuing Noncompliance

Continuing Noncompliance: Any “Noncompliance” that occurs after implementation of an IRB-approved CAPA plan that is due to the failure of the investigator and/or research team to comply with that CAPA plan OR repeated instances of noncompliance within one study or across multiple studies that has a high likelihood of resulting in Serious Noncompliance.

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HOW DO I SUBMIT?

Reporting Timeframe

- Within 7 days of event being identified in IRBIS

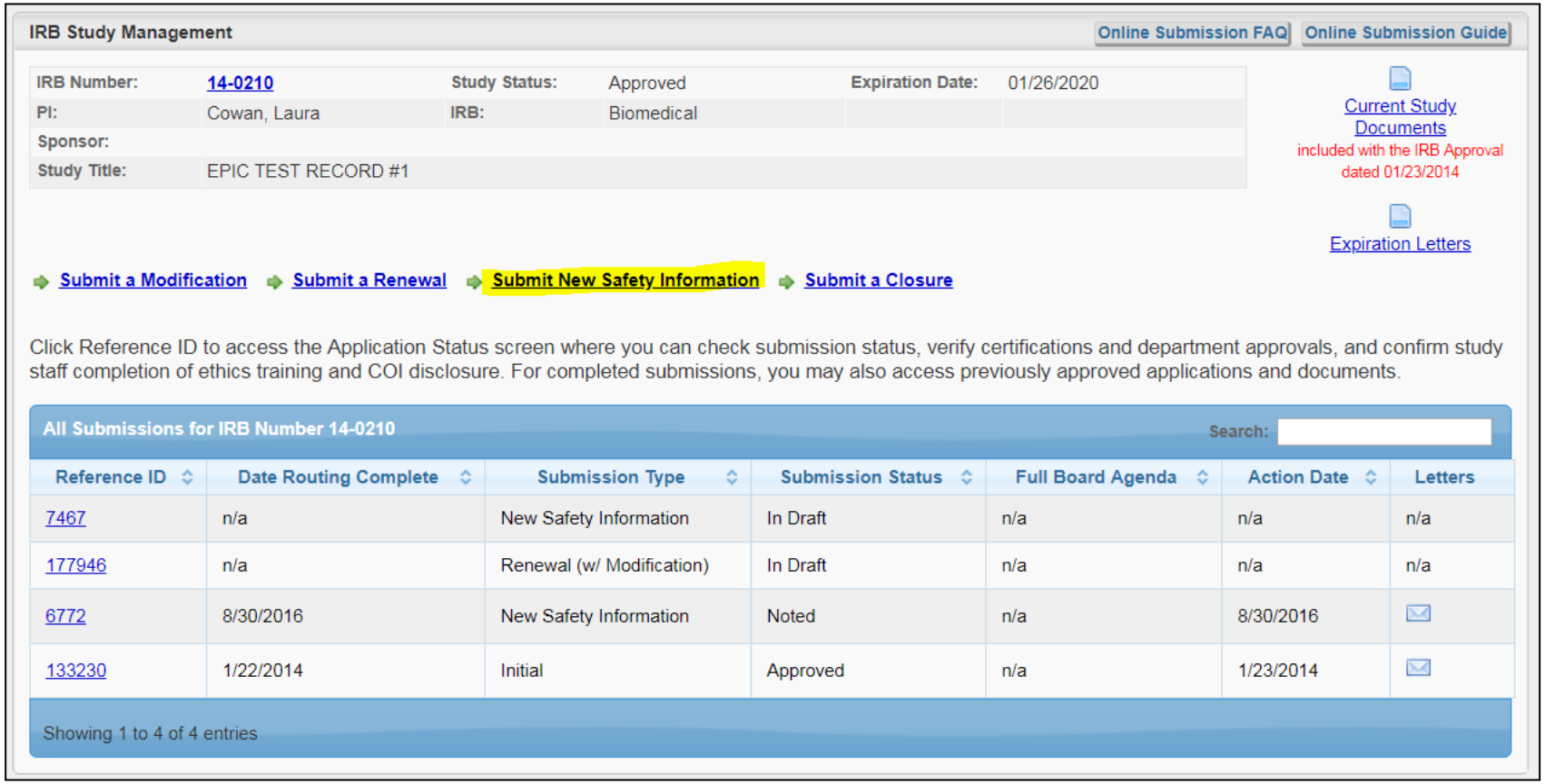
Event vs. Outcome

Ensure that your describing the event, and not just the outcome

E.g. Administered 4 extra capsules of study drug, but no subject complaints.

What is the event vs. outcome?

Submit in IRBIS



IRB Study Management

Online Submission FAQ | Online Submission Guide

IRB Number:	14-0210	Study Status:	Approved	Expiration Date:	01/26/2020
PI:	Cowan, Laura	IRB:	Biomedical		
Sponsor:					
Study Title:	EPIC TEST RECORD #1				

Current Study Documents
included with the IRB Approval dated 01/23/2014

Expiration Letters

Submit a Modification | Submit a Renewal | Submit New Safety Information | Submit a Closure

Click Reference ID to access the Application Status screen where you can check submission status, verify certifications and department approvals, and confirm study staff completion of ethics training and COI disclosure. For completed submissions, you may also access previously approved applications and documents.

All Submissions for IRB Number 14-0210 — Search:

Reference ID	Date Routing Complete	Submission Type	Submission Status	Full Board Agenda	Action Date	Letters
7467	n/a	New Safety Information	In Draft	n/a	n/a	n/a
177946	n/a	Renewal (w/ Modification)	In Draft	n/a	n/a	n/a
6772	8/30/2016	New Safety Information	Noted	n/a	8/30/2016	
133230	1/22/2014	Initial	Approved	n/a	1/23/2014	

Showing 1 to 4 of 4 entries

What information should I include?

- Detailed information about the event or issue, including relevant dates.
- The report should identify the affected subjects by their study codes and not by their names or other personal identifiers.
- An assessment of whether any subjects or others were placed at risk or suffered any harm (e.g., physical, social, financial, legal or psychological) as a result of the event.
- If the event involves noncompliance, describe the result of the root cause analysis.
- Any corrective and preventative actions, planned or already taken.
- Any other information requested by OHRE, if applicable.
- If the report cannot be completed in its entirety within the required time period, the report should describe what information is still needed and when the investigator anticipates that a follow-up report will be submitted.

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WHAT HAPPENS NEXT?

NSI Lifecycle

SWAG vs. Board Review

Safety Welfare Analysis Group

- Reviews NSI Information
- Requests additional information
- Develops and approves CAPA Plans
- Refers information to Safety Committee

Board Review

- IRB Committee
- Makes regulatory determinations
- Develops and approves CAPAs
- Makes recommendations to IO

Notification Process

- PI Notification Letter Sent to PI
  - Determinations
  - CAPA
  - Includes Department Chair and other central compliance officers depending upon determination
- External Reporting Requirements

When is a determination reported to OHRP/FDA/Other Reporting Agencies

OHRP

- **Study is federally funded.**

FDA

- **Study is FDA regulated.**

Other Federal Agencies

- **When the research is overseen by those agencies and they require reporting separate from OHRP, such as NIH, NSF and DOD**

CONFLICT OF INTEREST

Joy Bryde, MSW
Conflict of Interest Officer
Director, Conflict of Interest Office
Institutional Integrity and Risk Management

UNC THE NORTH CAROLINA TRANSLATIONAL & CLINICAL SCIENCES INSTITUTE
THE UNIVERSITY of NORTH CAROLINA at CHAPEL HILL NRP Network for Research Professionals
UNC OFFICE OF CLINICAL TRIALS

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 Individual COI?

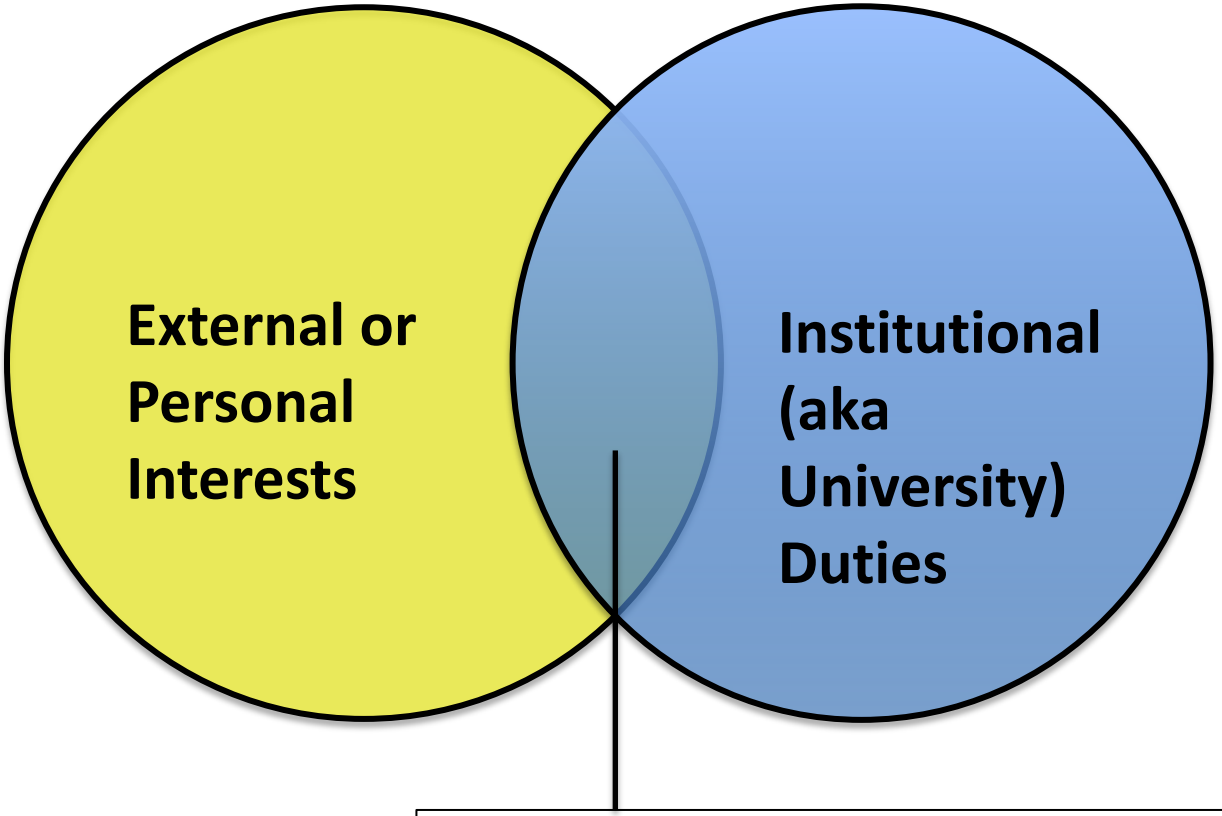
Conflict of interest is a situation in which financial or other personal considerations:

- 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 Individual COI at UNC



- Actual Conflict of Interest
- Potential Conflict of Interest
- Appearance of a Conflict of Interest

What is a Individual 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 (updated annually)

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

COI Snapshot

Steps of the Research COI Process?

Research COI Training coi-training.unc.edu – Valid four years

Event-based Disclosure

- Created from two areas
  - Sponsored Research (aka Ramses)
  - IRB Protocols (aka IRBIS)
- Submission
- Evaluation and Review
- Initiate Management Plan if needed
- Report to Sponsor if applicable
- Send out COI Finalization Letter to submitter, copy to PI if needed

Submit Event Specific Disclosure Annually OR on Change of Circumstances

Research COI Disclosures

IRB (IRBIS)

- Principal Investigator
- Co-investigator
- Faculty Advisor
- Project Manager or Study Coordinator
- UNC Faculty Member in any role

OSR (RAMSeS)

- Lead Principal Investigator
- Principal Investigator
- Investigator
- Faculty Advisor
- Fellow or Fellow NIH
- Postdoctoral Research Associate
- Clinical Research Coordinator
- Other Key Participant (UNC Faculty)
- Independent Consultant Investigator

<u>Not trigger COI disclosures</u>:
Research Assistant, Regulatory Associate, Other (Read Only Access)

<u>Not trigger COI disclosures:</u>
Graduate Research Assistant, Other Key Participant, Project Manager, Technical Staff, Undergraduate Student, Administrative Contact, Administrative Asst

Who Completes the Disclosure?

- Each person is responsible for submitting their own form – this means that the faculty MUST complete their own COI form.
- It a violation of multiple policies for an individual to login using another's ONYEN and PW to complete the form.

Policies Governing this Process (minimum):

- UNC CH ITS Password Policy and Standards for General Users
- UNC CH Individual COI Policy
- UNC CH Research Code of Conduct and Standards
- UNC System Policy on Individual Conflicts of Interest and Commitment

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

Human Studies: Specific Points of Concern

Review and/or Manage

- Study Design
- Obtaining Informed Consent
  - Referring Patients
  - Influence
- Adverse Event decisions
- Research specific decisions versus clinical care
- Access to research information
- Data Analysis involvement

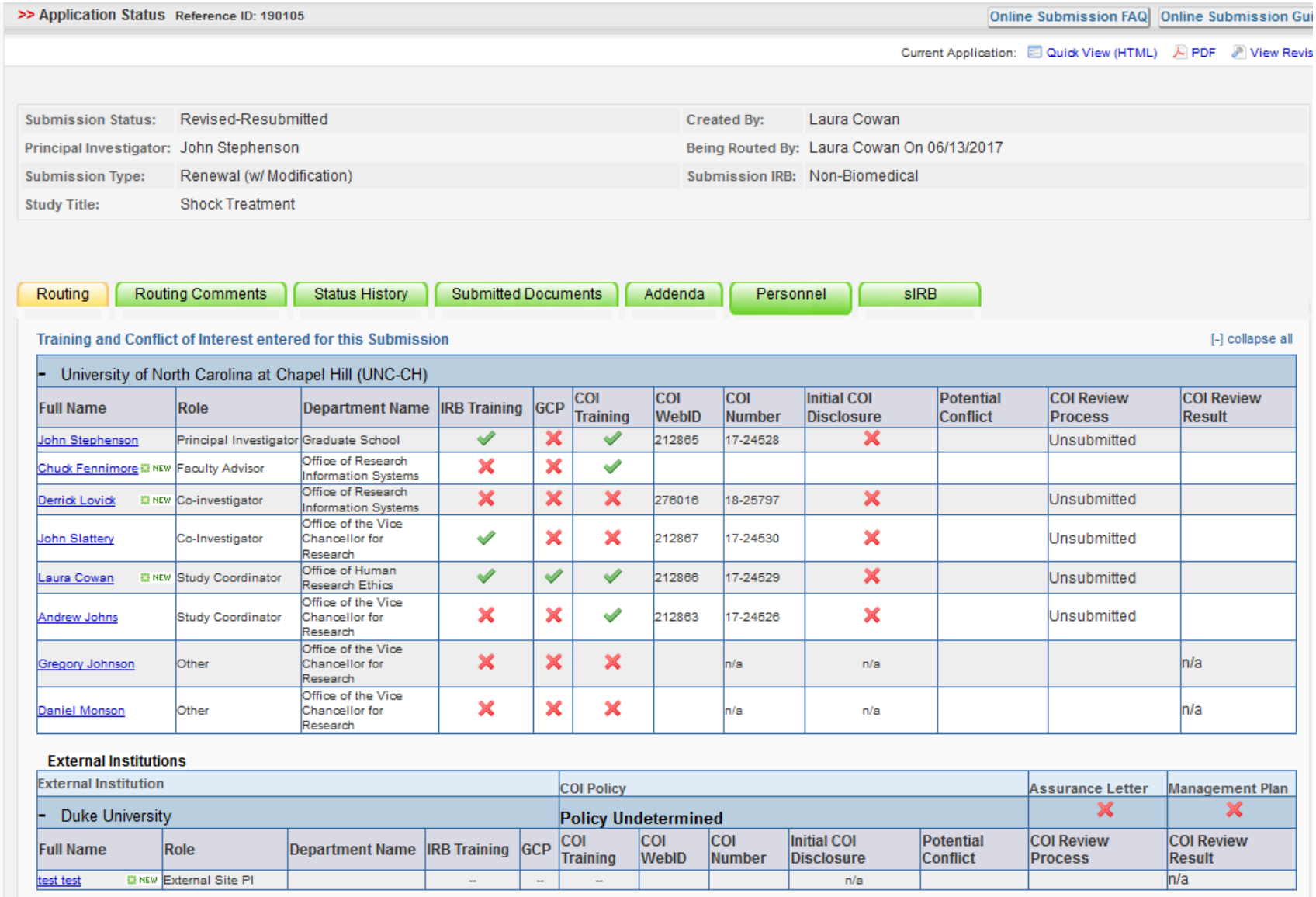
Management Tools

Tools

- Management Plans
  - Public Disclosure
  - Independent Review of Data
  - Change in Roles
  - Change in Activities
- Monitoring Committee
- 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.

How Can I Check the Review Status?



>> Application Status Reference ID: 190105

Online Submission FAQ | Online Submission Gui

Current Application: Quick View (HTML) | PDF | View Revis

Submission Status:	Revised-Resubmitted	Created By:	Laura Cowan
Principal Investigator:	John Stephenson	Being Routed By:	Laura Cowan On 06/13/2017
Submission Type:	Renewal (w/ Modification)	Submission IRB:	Non-Biomedical
Study Title:	Shock Treatment		

Routing | Routing Comments | Status History | Submitted Documents | Addenda | Personnel | sIRB

Training and Conflict of Interest entered for this Submission [-] collapse all

- University of North Carolina at Chapel Hill (UNC-CH)

Full Name	Role	Department Name	IRB Training	GCP	COI Training	COI WebID	COI Number	Initial COI Disclosure	Potential Conflict	COI Review Process	COI Review Result
John Stephenson	Principal Investigator	Graduate School	✓	✗	✓	212865	17-24528	✗		Unsubmitted	
Chuck Fennimore NEW	Faculty Advisor	Office of Research Information Systems	✗	✗	✓						
Derrick Lovick NEW	Co-investigator	Office of Research Information Systems	✗	✗	✗	276016	18-25797	✗		Unsubmitted	
John Slattery	Co-Investigator	Office of the Vice Chancellor for Research	✓	✗	✗	212867	17-24530	✗		Unsubmitted	
Laura Cowan NEW	Study Coordinator	Office of Human Research Ethics	✓	✓	✓	212866	17-24529	✗		Unsubmitted	
Andrew Johns	Study Coordinator	Office of the Vice Chancellor for Research	✗	✗	✓	212863	17-24526	✗		Unsubmitted	
Gregory Johnson	Other	Office of the Vice Chancellor for Research	✗	✗	✗		n/a	n/a			n/a
Daniel Monson	Other	Office of the Vice Chancellor for Research	✗	✗	✗		n/a	n/a			n/a

External Institutions

External Institution	COI Policy	Assurance Letter	Management Plan
- Duke University	Policy Undetermined	✗	✗

Full Name	Role	Department Name	IRB Training	GCP	COI Training	COI WebID	COI Number	Initial COI Disclosure	Potential Conflict	COI Review Process	COI Review Result
test test NEW	External Site PI		--	--	--			n/a			n/a

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	Potential Solutions
Direct payments to investigators	Institutional financial management
Incentives for investigators (exotic meeting locations)	Institutional contracting
Unbudgeted payments	Institutional financial management
Financial COI	Published and enforced COI policies
Study biases (site selection, prescribing)	IRB and training
Excess funds	Published Policy on Excess Fund Disposition
Study merit	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.

Pages 6-7

UNC Health System & UNC School of Medicine -- The Search for Balance

- Belief in Benefits of Industry Engagement
  - Positively influence the development of products and services to benefit patients and society
  - Opportunities to develop collaborations

- Activities Prohibited under Vendor Relations Policy Due to Perceived Influence:
  - Ghostwriting
  - Speakers' Bureaus
  - Any personal gifts
  - Meals/hospitality

Travel to any study or investigator meetings must be included in contract!

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.

And the latest COI in the News….

https://www.nytimes.com/2018/09/08/health/jose-baselga-cancer-memorial-sloan-kettering.html?emc=edit_th_180909&nl=todaysheadlines&nlid=348776000909

Top Cancer Researcher Fails to Disclose Corporate Financial Ties in Major Research Journals

Sept. 8, 2018

This article was reported and written in a collaboration with ProPublica, the nonprofit investigative journalism organization.

One of the world's top breast cancer doctors failed to disclose millions of dollars in payments from drug and health care companies in recent years, omitting his financial ties from dozens of research articles in prestigious publications like The New England Journal of Medicine and The Lancet.

The researcher, Dr. José Baselga, a towering figure in the cancer world, is the chief medical officer at Memorial Sloan Kettering Cancer Center in New York. He has held board memberships or advisory roles with Roche and Bristol-Myers Squibb, among other corporations, has had a stake in start-ups testing cancer therapies, and played a key role in the development of breakthrough drugs that have revolutionized treatments for breast cancer.

According to an analysis by The New York Times and ProPublica, Dr. Baselga did not follow financial disclosure rules set by the American Association for Cancer Research when he was president of the group. He also left out payments he received from companies connected to cancer research in his articles published in the group's journal, Cancer Discovery. At the same time, he has been one of the journal's two editors in chief.

At a conference this year and before analysts in 2017, he put a positive spin on the results of two Roche-sponsored clinical trials that many others considered disappointments, without disclosing his relationship to the company. Since 2014, he has received more than $3 million from Roche in consulting fees and for his stake in a company it acquired.

Dr. Baselga did not dispute his relationships with at least a dozen companies. In an interview, he said the disclosure lapses were unintentional.

Foreign Influence?? Science & Security??

- Through a variety of mechanisms, the U.S. government has raised concerns about “foreign threats” to the integrity of research at national academic and research institutions.
- Also being referred to as National Security
- Webinar overview: NIH, AAU, Legal
  - https://www.youtube.com/watch?v=D-rvbGxQrq0

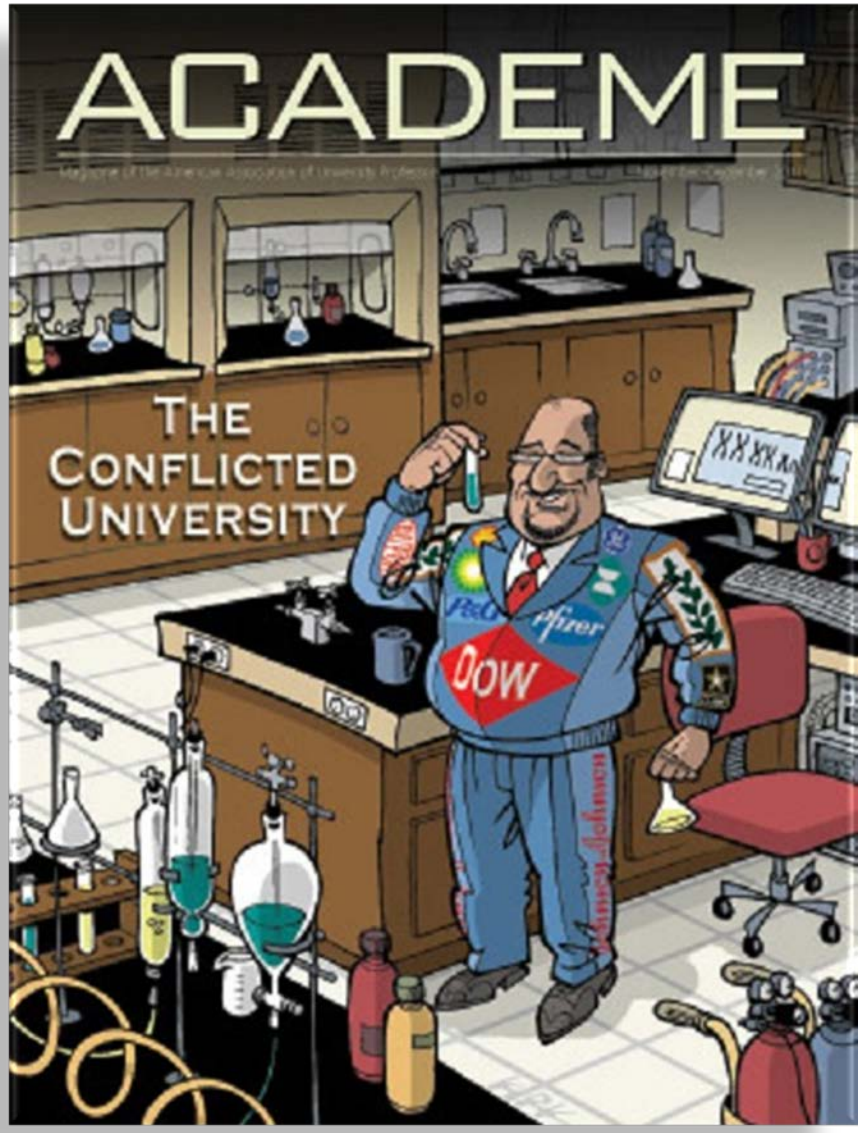
3 Main Areas of Concern

1. Diversion of intellectual property to foreign entities (govt, schools, other)
2. Disclosing confidential grant application information by NIH peer reviewers to third parties, which may or may not include foreign entities
3. Failure of researchers to disclose research resources and support provided by other organizations, including foreign entities

Some Sample Ways……

- Conduct computer intrusions via email or in person
  - Copy laptop data along with presentation
- Through possible COI activities – relationships with foreign entities or international activities
  - Conferences = collect sensitive research
  - Talent Programs
  - Teaching

FOR US GOVT "Intellectual property" also includes pre-publication data and sensitive information.


ACADEME
THE CONFLICTED UNIVERSITY
DOW

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 Office: https://iirm.unc.edu/coi/

Carolina Ethics Line - contact anonymously
www.unc.Ethicspoint.com or call 866-294-8688

General Email for questions: coi@unc.edu, epap@unc.edu

Contact Information

Joy M. Bryde, MSW

Conflict of Interest Officer

Mailing Address: Conflict of Interest Office
Institutional Integrity & Risk Management
UNC-CH CB 9103

Physical Address: Carolina Square, 6th Floor
123 W. Franklin St.

E-mail: jbryde@unc.edu

Phone: (919) 843-9953

Week 2
Evaluation Link:
https://go.unc.edu/orientwk2

OR

If you need a certificate of attendance, please email marie_rape@med.unc.edu after completing the evaluation survey.