NEW NIH Human Subjects & Clinical Trial Policies and Single IRB

December 12, 2017
Presenters

Stephanie F. Scott, MS, CRA
Director of Policy & Research Development
Sponsored Projects Administration (SPA)
sfs2110@columbia.edu

Alan Teller, CIP
Director of IRB Operations
Human Research Protection Office and IRBs
at2059@columbia.edu
## Summary of Changes

<table>
<thead>
<tr>
<th>Proposal Preparation</th>
<th>Does project meet Clinical Trial Definition?</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Selecting the appropriate FOA – 1/25/2018</td>
</tr>
<tr>
<td></td>
<td>Using new HS/CT Form – 1/25/2018</td>
</tr>
<tr>
<td></td>
<td>Single IRB (sIRB) Policy if multi-project. – 1/25/2018</td>
</tr>
<tr>
<td></td>
<td>New Clinical Trial-Specific Review Criteria – 1/25/2018</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>If Awarded</th>
<th>Good Clinical Practice (GCP) Training every three years.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Registering the study with ClinicalTrials.gov not later than 21 calendar days after the enrollment of the first participant.</td>
</tr>
</tbody>
</table>
Why All These Changes?

• And now a video that explains it all:

Why All These Changes?¹

• “NIH is the largest federal funder of clinical trials in the United States, with a $3 billion annual investment.”

• “We have known for years that many NIH-funded trials are completed, yet their main results are either never made public or made public in a timely manner.”

• “Additionally, historically NIH has had difficulty reporting how many clinical trials it has funded and results from many NIH-funded clinical trials are never published or reported in a public database. Consequently, the Government Accountability Office (GAO) recommended NIH improve clinical trial data collection and establish and implement a process for using this data effectively.”

Why all these changes?

• **Scientific and ethical obligation**: ensure that the burden and risk that volunteers assume as research participants ultimately contributes to scientific knowledge.

• **Transparency**: How are these dollars being spent? How are these trials being conducted?

• **Broader dissemination of data and conclusions**: What can we learn from these studies? Are they reproducible? How can we avoid the same mistakes? Avoid duplication of efforts?
Definition of Clinical Trial²

“A research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes.”

Definition of Clinical Trial$^{3,4}$

- “Includes some research approaches not traditionally considered clinical trials.”$^{3}$

- “Example, many behavioral or biobehavioral studies that focus on underlying mechanisms of development may now be considered clinical trials.”$^{3}$

- “Also, conducting experiments that involve human subjects may be considered a clinical trial.”$^{3}$

- “If you are conducting studies involving human subjects, it is very important that you understand this definition and determine whether it applies to your research.”$^{3}$

---


$^{4}$Wolfe, Jeremy M., and Nancy G. Kanwisher. 2017. “Not Your Parent’s NIH Clinical Trial.” Nature Human Behaviour, November, 1. [https://doi.org/10.1038/s41562-017-0262-7](https://doi.org/10.1038/s41562-017-0262-7).
Does the project meet NIH’s definition of a clinical trial?

- Correctly identify whether your study meets NIH’s definition of a clinical trial during proposal development.

- Use the decision tree, FAQs, and case studies (35 examples) to help you determine if the study meets the criteria.


- The PI should talk with an NIH Program Official if unsure. Talk to people referenced on the FOAs.

- Get confirmation in writing via email.

- Reference the name of the individual who confirmed eligibility in the proposal cover letter.
The Four Questions

If the answer to all four questions is “yes,” then the clinical study would be considered a clinical trial according to the NIH definition.

• Does the study involve human participants?
• Are the participants prospectively assigned to an intervention?
• Is the study designed to evaluate the effect of the intervention on the participants?
• Is the effect being evaluated a health-related biomedical or behavioral outcome?

In the next two slides, we dive deeper into the definitions for reference.
“Prospectively Assigned”

The term "prospectively assigned" refers to a pre-defined process (e.g., randomization) specified in an approved protocol that stipulates the assignment of research subjects (individually or in clusters) to one or more arms (e.g., intervention, placebo, or other control) of a clinical trial.
“Intervention”

• An "intervention" is defined as a manipulation of the subject or subject’s environment for the purpose of modifying one or more health-related biomedical or behavioral processes and/or endpoints.

• Examples include: drugs/small molecules/compounds; biologics; devices; procedures (e.g., surgical techniques); delivery systems (e.g., telemedicine, face-to-face interviews); strategies to change health-related behavior (e.g., diet, cognitive therapy, exercise, development of new habits); treatment strategies; prevention strategies; and, diagnostic strategies.
Q 4.2.c on new Form: Intervention Type

• Drug (including placebo)
• Device (including sham)
• Biological/Vaccine
• Procedure/Surgery
• Radiation
• Behavioral (e.g., Psychotherapy, Lifestyle Counseling)
• Genetic (including gene transfer, stem cell, and recombinant DNA)
• Dietary Supplement (e.g., vitamins, minerals)
• Combination Product
• Diagnostic Test
• Other
Health-related biomedical or behavioral outcome

Defined as the pre-specified goal(s) or condition(s) that reflect the effect of one or more interventions on human subjects’ biomedical or behavioral status or quality of life.

• Examples include: positive or negative changes to physiological or biological parameters (e.g., improvement of lung capacity, gene expression); positive or negative changes to psychological or neurodevelopmental parameters (e.g., mood management intervention for smokers; reading comprehension and/or information retention); positive or negative changes to disease processes; positive or negative changes to health-related behaviors; and, positive or negative changes to quality of life.
Source: https://grants.nih.gov/policy/clinical-trials.htm
Case Studies (#23)

• The study involves the recruitment of physicians who will be randomly assigned to use a new app or an existing app, which cues directed interviewing techniques. The study is designed to determine whether the new app is better than the existing app at assisting physicians in identifying families in need of social service support. The number of community service referrals will be measured.

• Does the study involve human participants? Yes, both the physicians and the families are human participants.

• Are the participants prospectively assigned to an intervention? Yes, physicians are prospectively assigned to use one of two apps, which are the interventions.

• Is the study designed to evaluate the effect of the intervention on the participants? Yes, the study is designed to evaluate the effect of intervening with physicians, on social service support referral for families.

• Is the effect being evaluated a health-related, biomedical, or behavioral outcome? Yes, the effect being evaluated, the number of referrals, is a health-related outcome.
Case Studies (#26)

• The study involves randomizing individuals to different processes for informed consent. It is designed to assess the effectiveness of interactive and multimedia components in enhancing participants’ understanding of the study’s purpose and procedures.

• Does the study involve human participants? Yes, the individuals assigned to the different consent processes are human participants.

• Are the participants prospectively assigned to an intervention? Yes, the participants are prospectively assigned to an intervention, different consent processes.

• Is the study designed to evaluate the effect of the intervention on the participants? Yes, the study is designed to evaluate the effect of different informed consent processes on understanding the study.

• Is the effect being evaluated a health-related biomedical or behavioral outcome? Yes, enhanced comprehension of information is a health-related behavioral outcome.
Case Studies (#30b)

- The study involves the recruitment of research participants in three different communities (clusters) to test three CPR training strategies. The rate of out-of-hospital cardiac arrest survival will be compared.

- Does the study involve human participants? Yes, the study involves human participants.

- Are the participants prospectively assigned to an intervention? Yes, the participants are prospectively assigned to receive one of three types of CPR training, which is the intervention.

- Is the study designed to evaluate the effect of the intervention on the participants? Yes, the study is designed to evaluate the effect of different CPR training strategies on patient survival rates post cardiac arrest.

- Is the effect being evaluated a health-related biomedical or behavioral outcome? Yes, out-of-hospital cardiac arrest survival is a health-related outcome.
Select the Appropriate FOA$^5$

• If any part of your study (the specific aims, components, studies, etc) meets NIH’s definition of a clinical trial, then you must select an FOA that allows for clinical trials.

• If none of the aims or studies within your project meet the definition, select an FOA that says “Clinical trials not allowed” or “Clinical trials optional”.

• “The participating organizations may vary between the “clinical trial not allowed” parent FOA and the “clinical trial required” parent FOA for the same activity code. Read the details of each FOA carefully.”

• “Note that some institutes that participate on a “Clinical Trial Required” parent may limit their participation to mechanistic studies.”

Mechanistic Study

“A mechanistic study is designed to understand a biological or behavioral process, the pathophysiology of a disease, or the mechanism of action of an intervention. A mechanistic study may be classified as a clinical trial if the study meets the NIH definition of a clinical trial.”

R01 FOA Example

For applications due **BEFORE** January 25\(^{\text{th}}\), 2018 (FORMS-D)

- Use [PA-16-160](#) for the January 7\(^{\text{th}}\), 2018 AIDS-related deadline.
  - “NIH Research Project Grant (Parent R01)”

For applications due **ON OR AFTER** January 25\(^{\text{th}}\), 2018 (FORMS-E)

- Use [PA-18-345](#) for the R01 clinical trial February 5\(^{\text{th}}\) deadline.
  - “NIH Research Project Grant (Parent R01 Clinical Trial Required)”

- Use [PA-18-484](#) for an R01 application that is NOT a clinical trial due February 5\(^{\text{th}}\).
  - “NIH Research Project Grant (Parent R01 Clinical Trial Not Allowed)”
Very Important!
PA-18-345 R01 Clinical Trial Required

• Not all NIH Institutes and Centers (ICs) participate in Parent Announcements.
• Applicants should carefully note which ICs participate in this announcement and view their respective areas of research interest at the R01 Clinical Trial Required IC-Specific Scientific Interests and Contact website.
• Applicants should also carefully note which ICs accept only mechanistic trials by viewing the Related Notices.
• ICs that do not participate in this announcement will not consider applications for funding.
• https://grants.nih.gov/grants/guide/contacts/Clinical-Trial-Parent-R01.html
Other Main Takeaways for Applications

• All clinical trial applications must be submitted to a Funding Opportunity Announcement (FOA) that allows clinical trials, effective with due dates on or after January 25, 2018.

• Read the FOA very carefully for additional criteria to be included in clinical trial proposals.

• Consider the NIH Single Institutional Review Board (sIRB) Policy if multiple sites are involved.
  • Talk to HRPO first. irboffice@columbia.edu
  • Even if Columbia does NOT serve as sIRB, still follow all same institutional policies, including submission of IRB protocols in Rascal.
If Awarded as a Clinical Trial

• All investigators and clinical research staff who work on NIH-funded clinical trials (funded in whole or in part) must complete Good Clinical Practice (GCP) Training every three years. Register for training in Rascal, and view these instructions.

• All NIH-funded clinical trials initiated and awarded on or after January 18, 2017 must register and submit results in ClinicalTrials.gov not later than 21 calendar days after the enrollment of the first participant.

• Submit summary results to ClinicalTrials.gov no later than one year after primary completion date.
FORMS-E: The New NIH Human Subjects and Clinical Trials Form
Proposal Deadlines

• This is not a normal forms transition!

• MSPH SPA strongly recommends you submit the full application to the SPA Project Officer no less than 7 business days prior to sponsor’s deadline.

• If still working on the research plan/science, SPA will review:
  • Rascal
  • Budget
  • Budget Justification
  • Subrecipients’ budgets, forms, etc.
  • Biosketches
  • Other administrative requirements

• Start this form early!!!

• Deadline day and electronic submissions.
These are GOALS
Proposal Development (in any system) & Submission Timeline (for any sponsor)

Months before sponsor deadline – Proposal Development Phase

4-8 weeks before deadline – application built in online proposal system

5 business days (7 for MSPH) before deadline – Sr. PO Receives the Application for Review

2 business days before deadline - Sr. PO hits the submit button

Sponsor Deadline!
The Recommended Target Dates - Example

• If preparing an R01 with Monday, February 5th, 2018 deadline date:

  • Goal (2 business days prior): Senior PO submits application to Grants.gov on Thursday, February 1st, 2018

  • Goal (5 business days prior): Senior PO has most administrative aspects of proposal to review on Monday, January 29th, 2018

  • MSPH (7 business days): Thursday, January 25th
Which System to Use?

NIH and AHRQ Proposals:
• Currently use NIH ASSIST?
  • Continue to use ASSIST until further notice.

• Currently use PD in InfoEd?
  • Training will be provided to current PD users on the new FORMS-E.
  • Scheduled for December 13th. SPA will contact those users.
Get Familiar with the Form

Register for some informal sessions via ZOOM:

- **Wednesday, December 13th, 12pm – 1pm**
- **Monday, December 18th, 11am – 12pm**
- **Tuesday, December 19th, 2pm – 3pm**
Applicability to Various Grant Mechanisms

• New PHS HS/CT form is a mandatory form in most NIH application packages.

• Exceptions:
  • Training grants - T15, T32, T34, T35, T36, T37, D71, U2R, T01, T02, T03, T14, T42, T90, T90/R90, TU2
  • Shared Instrumentation – S10
  • Construction – C06/UC6, G20
  • Resource Awards – X01

• Form optional in certain circumstances:
  • Admin Supp Type 3 – research, career dev, fellowship, institutional training (K12 and D43)
  • Type 6 & Type 7 - research, career dev, fellowship
Special Note on K-Awards

Three situations:

• No Clinical Trial at all – select the FOA that says “Independent Clinical Trial Not Allowed” in the title.

• Applicant proposes Clinical Trial Research Experience under a mentor – select the FOA that says “Independent Clinical Trial Not Allowed” in the title. Additional review criteria.
  • permitted to propose research experience in a clinical trial led by a mentor or co-mentor.

• Applicant proposes an Independent Clinical Trial - select the FOA that says “Independent Clinical Trial Required” in the title.
  • for applicants proposing to serve as the lead investigator of an independent clinical trial,
The Essentials for FORMS-E

• The FORMS-E application instructions:

• The annotated forms sets:

• Become familiar with the new PHS Human Subjects and Clinical Trials Information Form
  • Watch the 9-minute [video](https://www.youtube.com/watch?v=example_video) to walk you through the form.
# New SPA Checklist for Form

## Checklist for the PHS Human Subjects and Clinical Trials Form (FORMS-E)

Before doing **ANYTHING**, you must first determine if your study meets NIH's definition.

**Use the Clinical Trial Decision Tree**

You must then select the appropriate FOA, depending on whether it allows for clinical trials.

Parent Announcements

If unsure, reach out to an NIH Program Official, and get in writing whether your study meets the

### Resources:

- FORMS-E Annotated Form Set
- FORMS-E Annotated Form Set for Multi-Projects
- Video: PHS HS/CT Form
- R&R Other Project Information Form

### R&R Other Project Information Form

1. Are Human Subjects Involved? Yes/No

   1a. If YES to Human Subjects:

   Is the Project Exempt from Federal regulations? Yes/No

   If yes, check appropriate exemption number 1, 2, 3, 4, 5, 6, 7, 8
Quotes from the Instructions

• “Be especially careful to avoid redundancies with your research strategy.”

• Add a separate study record for each protocol involving human subjects proposed in your application. No duplicates. Each study should be unique and should have a unique study title.

• **STUDY** - Research protocol that supports or refutes a hypothesis.
• **STUDY RECORD** - A set of data elements about a research study involving human subjects. Each proposed protocol must have its own study record.
## PHS 398 Research Plan

### Introduction
1. Introduction to Application (Resubmission and Revision)
   - Limited to 1 page (except R25 Resubmission and Revision applications). Limited to 1 page.

### Research Plan Section
2. Specific Aims
   - Required attachment (except DP1, DP2, P20, R03). Limited to 1 page.
3. *Research Strategy
   - Adhere to page limits specified in Application Guide and/or FOA. Typically 6 or 10 pages; a small number of FOAs will specify 30 pages.
4. Progress Report Publication List

### Human Subjects Section
- Attachments typically required if Human Subjects is Yes on the Other Project Information form.

5. Protection of Human Subjects
   - Required if Human Subjects is Yes.
6. Data Safety Monitoring Plan
   - Required if Clinical Trials is Yes on the PHS 398 Cover Page Supplement form.
7. Inclusion of Women and Minorities
   - Required if Human Subjects is Yes and exemption number is not 4.
8. Inclusion of Children
   - Required if Human Subjects is Yes and exemption number is not 4.

### Other Research Plan Section
9. Vertebrate Animals
   - Required for all apps. (except S10), if Vertebrate Animals is Yes on the Other Project Information form.

---

This is a screen shot of FORMS-D. The entire Human Subjects section of the Research Plan is moving to the new PHS Form in FORMS-E.
The Basics of FORMS-E

• The Research & Related (R&R) Other Project Information Form must be completed first!

• Answers to that form drive the validations on the NEW form.

• Are Human Subjects Involved? Check Yes or No.

• If Yes, is the project exempt from Federal regulations? Check Yes or No.

• If yes, check appropriate exemption number
  • #s 1-8
  • For NOW, do not select exemptions 7 or 8 (due to possible delay in Common Rule)
## Screen Shot – R&R Other Project Information

### RESEARCH & RELATED Other Project Information

**Expiration Date:** 10/31/2019

1. **Are Human Subjects Involved?**
   - Yes [ ]
   - No [ ]

2. **Project Exempt from Federal regulations?**
   - Yes [ ]
   - No [ ]

3. **Human Subjects Involved?**
   - Yes [ ]
   - No [ ]

4. **Vertebrate Animals Used?**
   - Yes [ ]
   - No [ ]

---

**Human Subject Assurance Number:**

**IRB Approval Date:**

---

**IRB Approval Date** is not required at time of submission, but may be requested later in the pre-award process as Just-In-Time data. Date cannot be in the future.

---

**If Human Subjects = Yes, additional attachments may be required on the PHS Human Subjects and Clinical Trials Information form.**

---

**Don't use Exemption numbers 7 and 8 at this time.**

---

**If Human Subjects = Yes, the Human Subject Assurance Number or the text 'None' must be provided exactly as it appears in eRA Commons institution profile.**

---

(Columbia Research)
The New Form

• If said NO to Human Subjects (HS) on R&R Other Project Information Form, then you have to answer:

• Does the proposed research involve human specimens and/or data? Check Yes or No.

  • If you select YES here, then you’ll have to upload a justification of why the application does not involve human subjects research. This will be REQUIRED.

  • If NO, then done!
If NO to Human Subjects – New Form

PHS Human Subjects and Clinical Trials Information

Please complete the human subjects section of the Research & Related Other Project Information form prior to completing this form. The following items are taken from the Research & Related Other Project Information form and displayed here for your reference. Any changes to these fields must be made on the Research & Related Other Project Information form and may impact the data items you are required to complete on this form.

Are Human Subjects Involved?
- Yes
- No

Is the Project Exempt from Federal regulations?
- Yes
- No

Exemption number:
1 2 3 4 5 6 7 8

Information populated from R&R Other Project Information form.

If No to Human Subjects

Does the proposed research involve human specimens and/or data?
- Yes
- No

If Yes, provide an explanation of why the application does not involve human subjects research.

Required if Yes to human specimens/data question.

Skip the rest of the PHS Human Subjects and Clinical Trials Information Form.

Answer required and system enforced when human subjects is No.

When human subjects is No, applicants answer a single question, provide associated attachment (as applicable), and are done with the form unless instructed in announcement to include Other Requested Information attachment.
The New Form

• If said YES to Human Subjects (HS) on R&R Other Project Information Form, then you have to add either:

• **Add a Full Study Record**
  • Can have up to 150 separate Study Records

• **Delayed Onset Study(ies)** - Human subjects research is anticipated within the period of award but definite plans for this involvement cannot be described in the application, until other aspects of the research are completed.
  • Can have up to 150 delayed onset studies, but they can be grouped into a single record. Indicate if one or more clinical trials are anticipated.
  • Delayed onset does NOT apply to a study that can be described but will not start immediately (i.e., delayed start). NIH expects full study records for delayed start studies.
Full Study Record for Human Subjects (HS) and Clinical Trials (CT) – FIVE SECTIONS

• **Section I – Basic Information – required for both HS and CT**
  • Information is at the Study Level, not the application as a whole!
  • **Includes the CT Four Questions!** Will classify the study as a CT or not.
  • If CT, then parts of Sections 4 and 5 may be required.

• **Section II – Study Population Characteristics – required for both HS and CT, unless Exemption 4 applies.**
  • Inclusion of Woman, Minorities and Children
  • Recruitment and Retention Plan
  • Recruitment Status
  • Study TimeLine
  • Inclusion Enrollment Report – NIH will no longer use the stand alone report form
    • Data collection for up to 20 inclusion enrollment reports have been folded into EACH Study Record
• **Section III — Protection and Monitoring Plans**
  - Protection of HS – used to be in the Research Plan – CT & HS
  - Is this a multi-site study? – CT & HS
    - If yes, describe your sIRB plan
  - Data and Safety Monitoring Plan – required for CT Only
  - Will a Data and Safety Monitoring Board be appointed for this study? – CT Only
  - Overall Structure of the Study Team – required for CT only

• **Section IV — Protocol Synopsis – CT Only**
  - Lots of questions related to study design
  - Up to 50 outcome measures
  - Dissemination Plan

• **Section V — Other Clinical Trail-related Attachments – CT Only**
  - Only when requested in the FOA
sIRB Attachment

• Describe how you will comply with the NIH Policy on the Use of sIRB for Multi-Site Research.

• Provide the name of the IRB that will serve as the sIRB of record.

• Indicate that all identified participating sites have agreed to rely on the proposed sIRB and that any sites added after award will rely on the sIRB.

• Briefly describe how communication between sites and the sIRB will be handled.

• Refer to sIRB instructions in the application instructions. There is more!
Single IRB Process

Alan Teller
Director of IRB Operations
Upcoming Requirements

• NIH Policy on the Use of a Single IRB for Multi-Site Research
  • Final Policy effective January 25, 2018 (**NEW DATE!**)
    Required to use a single IRB of record for *NIH funded domestic multi-site studies* unless there is justification for an exception
    Multi-site = 2 or more sites

• Changes to the Common Rule (45CFR46) released January 2017
  • Creates a requirement for U.S.-based institutions engaged in cooperative research to use a single IRB for that portion of the research that takes place within the United States, with certain exceptions
  • This requirement becomes effective 3 years after publication of the final rule (January 2020)
Terminology (courtesy of TIN)

**Reviewing IRB**
- the IRB of record to which authority for IRB review and oversight for a study has been ceded [For a given study or multiple studies]
  - **Single IRB (sIRB)**
    - the Reviewing IRB for a given study
  - **Central IRB (CIRB)**
    - the Reviewing IRB designated to be the Reviewing IRB for a group of studies (e.g., for a research network)

**Independent IRB**
- an IRB organization that provides IRB review services

**Relying Institution**
- an institution that cedes IRB review to a Reviewing IRB for a study or studies
Delineation of Roles & Responsibilities

• Reviewing IRB
  - Review for multiple sites
  - Learning and applying local requirements for each Relying Site

• Relying Institution
  - Provide local context reviews
  - Ensuring local requirements are met and local policies & state law are followed
**Trial Innovation Network**

**CIRB MYTH:** Relying site study teams do not have to submit anything to the IRB for approval.

**FACTS:**
- The IRB review is only one of the elements of the Human Research Protection Program (HRPP)
- Each participating site’s institution must still complete the remaining institutional reviews that make up the HRPP

**Responsibilities given to the CIRB**

- IRB Review
- Review of investigator training and expertise
- Ancillary Reviews (Safety, Scientific, COI)
- Monitoring compliance with local, state laws; HIPAA
- Institutional Resources Review
- Grants and Contracts
**Trial Innovation Network**

*CIRB MYTH: Relying site study teams do not have to submit anything to the IRB for approval.*

It is important that relying site study teams talk to their local IRBs about how to initiate reliance and their submission requirements—the earlier the better!

**Prior to initial approval:** Your local institution has many responsibilities when relying on another institution (see pie chart on previous slide) and needs information from the local study team to complete those reviews.

**Submitting to the CIRB:** Relying site study teams have to provide information to the CIRB so it can review the study and consider the local context of each participating site. The mechanism for submitting to the CIRB will depend on the CIRB’s preferred process (e.g., directly to their electronic system, via survey, via email, via the lead study team, etc.).

**After initial approval:** Your local institution may still require information to be submitted, although not reviewed, at continuing review and for amendments. This will ensure your institution has the most up-to-date information in their systems.
Trial Innovation Network

CIRB MYTH: A single/CIRB will help get my study started more quickly.

Not necessarily. In order to use reliance, a reliance agreement has to be in place. This can take weeks or even months to get executed. However, even when a reliance agreement is already in place, implementing reliance requires input and communication with the local HRPP and the CIRB.

But it will get faster. The NIH mandate was announced in June 2016, and it requires a huge shift in the way institutional IRBs are structured. Given this, additional time will be needed for IRBs to adjust their processes and identify best practices for support CIRB review.

Continuing/annual review and study-wide amendments will be faster. All sites that have IRB approval when it is time for continuing review or for study-wide amendments, all sites can be reviewed and approved by the CIRB at once.
Process

- Discuss with HRPO before making commitments
- All studies need to be submitted in Rascal
  - Columbia as Reviewing IRB:
    - Master Protocol for all sites
    - Separate protocol for Columbia site
  - Columbia as Relying Site
    - Local context review; facilitate ancillary reviews
      - COI, Training, Personnel. Biosafety, radiation Safety, Cancer Center PRMC, etc.
- Fees
  - NIH policy allows Reviewing IRBs to charge for IRB review
  - IRB Fees for Industry Supported Protocols will be assessed for review for Relying Sites
Columbia to Serve as Single IRB

- Considerations
  - # of sites
  - Who are the Relying Sites?
  - Type of study
  - Funding (who is Prime?)
  - Role in study (i.e., study site, coordinating center, repository)
  - Requirement vs. preference for Single IRB?
  - Budget for IRB Fees
sIRB Attachment

Describe how you will comply with the [NIH Policy on the Use of sIRB for Multi-Site Research](#)

- **Provide the name of the IRB that will serve as the sIRB of record.**
- **Indicate that all identified participating sites have agreed to rely on the proposed sIRB and that any sites added after award will rely on the sIRB.**
- **Briefly describe how communication between sites and the sIRB will be handled.**
What should I do first?

Contact the HRPO
Researcher Reliance Request Form

• CU S/CIRB Request Form

• Elicits information from Research Team for consideration of IRB Reliance
  • Single or Central?
  • Reviewing IRB or Relying Site?
    • Who is Reviewing IRB
    • Who are Relying Sites
  • Summary of study procedures

• HRPO to issue Letter of Support to serve as sIRB once request is approved
sIRB Attachment

Describe how you will comply with the NIH Policy on the Use of sIRB for Multi-Site Research

• Provide the name of the IRB that will serve as the sIRB of record.

• Indicate that all identified participating sites have agreed to rely on the proposed sIRB and that any sites added after award will rely on the sIRB.

• Briefly describe how communication between sites and the sIRB will be handled.
Federally-funded Resources to Support sIRB (courtesy of TIN)

Sponsor
NCATS
(National Center for Advancing Translational Science)

Initiative
Trial Innovation Network
(3 central IRBs)
SMART IRB

sIRB Tools and Resources
SMART IRB Exchange
CIRB Letter of Indemnification
SMART IRB Reliance Agreement
Ambassadors & Working Groups
Online Reliance System

Tools used by TIN CIRBs
NCATS funded a CTSA IRB Reliance project to Dartmouth College, Harvard Medical School & University of Wisconsin

Initiative developed under an award from the National Center for Advancing Translational Sciences (NCATS) of the National Institutes of Health (NIH) to support single Institutional Review Board (IRB) review of multi-site human subjects research

A single national Authorization (reliance) Agreement that is pre-negotiated and signed by institutions once

- An umbrella agreement - No additional IRB authorization agreements required to enable reliance among institutions that have joined SMART IRB Reliance arrangements, however, need to be documented for each study
- Establishes an approach for roles and responsibilities of the single IRB and participating sites
# sIRB Roles and Responsibilities

<table>
<thead>
<tr>
<th>Agreement Term</th>
<th>Responsible Entity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Education/Training/Qualifications of Study Team and PI</td>
<td>Relying Site</td>
</tr>
<tr>
<td>Requiring Compliance with IRB determinations, regulations, state and local laws and institutional policy</td>
<td>Relying Site</td>
</tr>
<tr>
<td>Notifying Research Personnel of Sites Obligations under the Reliance Agreement</td>
<td>Relying Site</td>
</tr>
<tr>
<td>HIPAA Compliance and Obligations</td>
<td>Relying Site</td>
</tr>
<tr>
<td>Provide Site Specific Information for Insertion into Informed Consent Documents</td>
<td>Relying Site</td>
</tr>
<tr>
<td>Conduct Conflict of Interest Review and Notify IRB of Conflict Management Plan</td>
<td>Relying Site</td>
</tr>
<tr>
<td>Respond with comments on Draft Reports to Federal Agency within 5 Days of receipt</td>
<td>Relying Site</td>
</tr>
<tr>
<td>Communicating Local Considerations to IRB</td>
<td>Relying Site</td>
</tr>
<tr>
<td>Notify IRB of Unanticipated Problems or Injuries</td>
<td>Site PI and Relying Site</td>
</tr>
<tr>
<td>Notify IRB of Noncompliance or suspension/restriction of Personnel’s ability to conduct research</td>
<td>Site PI and Relying Site</td>
</tr>
<tr>
<td>Cooperate with Audit or Investigation</td>
<td>Site PI and Relying Site</td>
</tr>
<tr>
<td>HIPAA Determinations Including Waivers of Authorizations</td>
<td>CU IRB</td>
</tr>
<tr>
<td>Conducting Initial and Continuing IRB Reviews of Submitted Research</td>
<td>CU IRB</td>
</tr>
<tr>
<td>Providing Informed Consent Documents for submitted Research</td>
<td>CU IRB</td>
</tr>
<tr>
<td>Consider Conflict of Interest Management Plan In IRB review</td>
<td>CU IRB</td>
</tr>
<tr>
<td>Notify Site PI and Relying Institution of Unanticipated Problems, Injuries, Complaints, Suspensions or Terminations of Research</td>
<td>CU IRB</td>
</tr>
<tr>
<td>Notify Site PI and Relying Institution of Serious or Continuing Non-Compliance</td>
<td>CU IRB</td>
</tr>
<tr>
<td>Notify Relying Institution of Audit or Investigation related to Coded Review</td>
<td>CU IRB</td>
</tr>
<tr>
<td>Notify Relying Insitution of Required Reporting to Federal Agency</td>
<td>CU IRB</td>
</tr>
</tbody>
</table>
Post Award IRB Process

1. Circle back to HRPO
2. Reliance Agreement must be executed by all engaged institutions
   - Some sites may need multiple agreements if multi-institutional relationships
3. Submit Master Protocol in Rascal
4. Collect Local Context Information Sheet
   - Protocol Specific Information Sheet (PSIS)
5. Add Relying Sites in Rascal
6. Localize consent documents
7. Local Institution sign off (ancillary reviews, local IRB acknowledgment, etc.)
Columbia has been formally designated as the **Central IRB** for all sites in this multicenter study.

Formally Designated = Signed and Executed Reliance Agreement by IOs at all Sites
Notes and Reminder – CU as sIRB

- Each approved Relying Site will be individually listed on a CU IRB Approval Letter
- A Relying Site should not begin research related activities until that respective site has been approved
- Approval of the Master Protocol is NOT global approval for any site to begin research
Columbia as Relying Site – Pre Award

Indicate that all identified participating sites have agreed to rely on the proposed sIRB and that any sites added after award will rely on the sIRB

• Contact the HRPO

• CU S/CIRB Request Form
  • Who is Single IRB?
  • What are the terms of Reliance?

• Letter of Support from HRPO
Columbia as Relying Site – Post Award

- Execute Reliance Agreement
- Submit in Rascal once sIRB approves Master Protocol
- Complete Local Context Sheet and all forms with IRB
- Applicability of Columbia Policies & NYS Law
- Submit to sIRB to approve Columbia as a Research Site
- After sIRB approval, resubmit in Rascal with sIRB Approval Letter
- Rascal attachments:
  - S/CIRB Approval Letter adding Columbia as a Research Site
  - S/CIRB Approved Consent Form and study material
- Confirm all applicable Ancillary Reviews have been completed/approved and all Administrative requests have been addressed
Rascal – Attributes Page – Columbia as Relying Site

- Complete IRB Application in Rascal
- Attributes section appropriately reflects reliance on a sIRB

*IRB of record information: Will a Columbia IRB be the IRB that is responsible for providing review, approval, and oversight for this study? *

- [ ] Yes
- [ ] No
- [ ] I don't know

*Select the appropriate response:
- [ ] Columbia is relying on a Central IRB that has been designated for this study
- [ ] Columbia is relying on the IRB of a collaborating research institution. Note: This does not include formally relying on a Central IRB for all sites
- [ ] Columbia is relying on an independent or commercial IRB

*Select the name of the study or series of studies for which Columbia will rely on a Central IRB.

- [Select~]

- sIRB Approval Letter for Master Protocol
- sIRB Approved Protocol
- sIRB Approved Consent Form and study materials
Local Context Review

- Relying Institutions need to inform the Reviewing IRB about relevant local context issues
  - Applicability of Columbia Policies & NYS Law that could affect the IRB’s review
    - Incidental Findings in Research Studies
    - Enrollment of Non-English Speaking Subjects
    - Recruitment
    - Disclosure of SSNs for Research Purposes
    - Genetic Testing
  - Locally required consent form language in 3 areas
    - Availability of treatment and compensation for research-related injury
    - Payment or reimbursement of research costs incurred by subjects
    - Local contact information
  - Ensuring all applicable Ancillary Reviews are initiated
    - Any conflicts of interest relevant to study and applicable management plans throughout the life of the study
Budgeting for Single IRB Studies

- The additional costs associated with sIRB review may be charged to grants or contracts as direct costs provided that such costs are well-justified and consistently treated as either direct or indirect costs according to applicable cost principles in the NIH Grants Policy Statement and the FAR 31.202 (Direct Costs) and FAR 31.203 (Indirect Costs).

- Primary activities are charged as indirect costs because Institution has Federally approved F&A rate and is a participating site.

- Secondary activities related to the other participating sites may be charged as Institution’s direct costs.

- Fee structure being developed by HRPO with assistance from SPA and Controllers Office.
Recap

Contact the HRPO
Recap

- Discuss with HRPO before making commitments
- All studies need to be submitted in Rascal
- Approval of the Master Protocol is **NOT** global approval for any site to begin research
- NIH policy allows Reviewing IRBs to charge for IRB review for Relying Institutions
- When Columbia is Relying Site: do **not** begin any research related activities until approval has been granted by both the Reviewing IRB and by the Columbia IRB
- Must follow Columbia policies as well as any policies enforced by Reviewing IRB
- Discuss with HRPO before making commitments
Contacts

HRPO Office: 154 Haven Avenue, First Floor

Walk-in Consultations: Tuesdays, 10-11 am

Phone: 212.305.5883

Email: irboffice@columbia.edu

HRPO website: https://research.columbia.edu/irb
<table>
<thead>
<tr>
<th>Policy/Form/Training</th>
<th>Contact</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>FORMS-E</td>
<td>SPA</td>
<td>The application instructions are key.</td>
</tr>
<tr>
<td>NEW PHS Human Subjects and Clinical Trial Information</td>
<td>SPA</td>
<td>See NIH 9-minute video, use SPA checklist, and the application instructions are key.</td>
</tr>
<tr>
<td>Information Form</td>
<td></td>
<td></td>
</tr>
<tr>
<td>sIRB Policy</td>
<td>HRPO</td>
<td>Ask HRPO if Columbia should serve as sIRB.</td>
</tr>
<tr>
<td>Budgeting Guidance for sIRB</td>
<td>SPA</td>
<td>SPA and HRPO working on this. More to come.</td>
</tr>
<tr>
<td>GCP Training</td>
<td>CTO</td>
<td>For questions concerning the training requirement and how to complete the training.</td>
</tr>
<tr>
<td>ClinicalTrials.gov</td>
<td>CTO</td>
<td>Assists with trial registration and results reporting, and provides training</td>
</tr>
</tbody>
</table>
QUESTIONS?