# Human Subjects Research and Clinical Trials

## 2018 NIH POLICY AND PROPOSAL CHANGES

University of Colorado Boulder

# Topics

Overview of Changes

Policy Changes – How this affects IRB submission

Prepare for NIH Proposal Application

Changes to NIH Funding Opportunity Announcements (FOA)

Changes to NIH Proposal Documents

ClinicalTrials.gov

*Note: HS = human subjects*

*CT = clinical trials*

# Overview of Changes

# Policy Changes

***WHAT HAPPENED TO THE COMMON RULE?***

July 19, 2018: New effective date of Common Rule changes

# Policy Changes

***NEW DEFINITION OF CLINICAL TRIAL – NIH ONLY***

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.

*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.*

# Does your human subjects research study meet the NIH Definition of a clinical trial?

The NIH definition of a clinical trial is very broad. Some investigators conducting human subjects research may not be aware that NIH considers their study to be a clinical trial. Use this tool to help determine if your research meets the NIH definition of a clinical trial.

**For application due dates on/after January 25, 2018, identifying whether your study is a clinical trial will be important for:**

- picking the right NIH **funding opportunity**
- ensuring your application includes all the **information required for peer review**
- complying with the appropriate **policies and regulations**

## NIH Definition of a Clinical Trial

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. Learn more

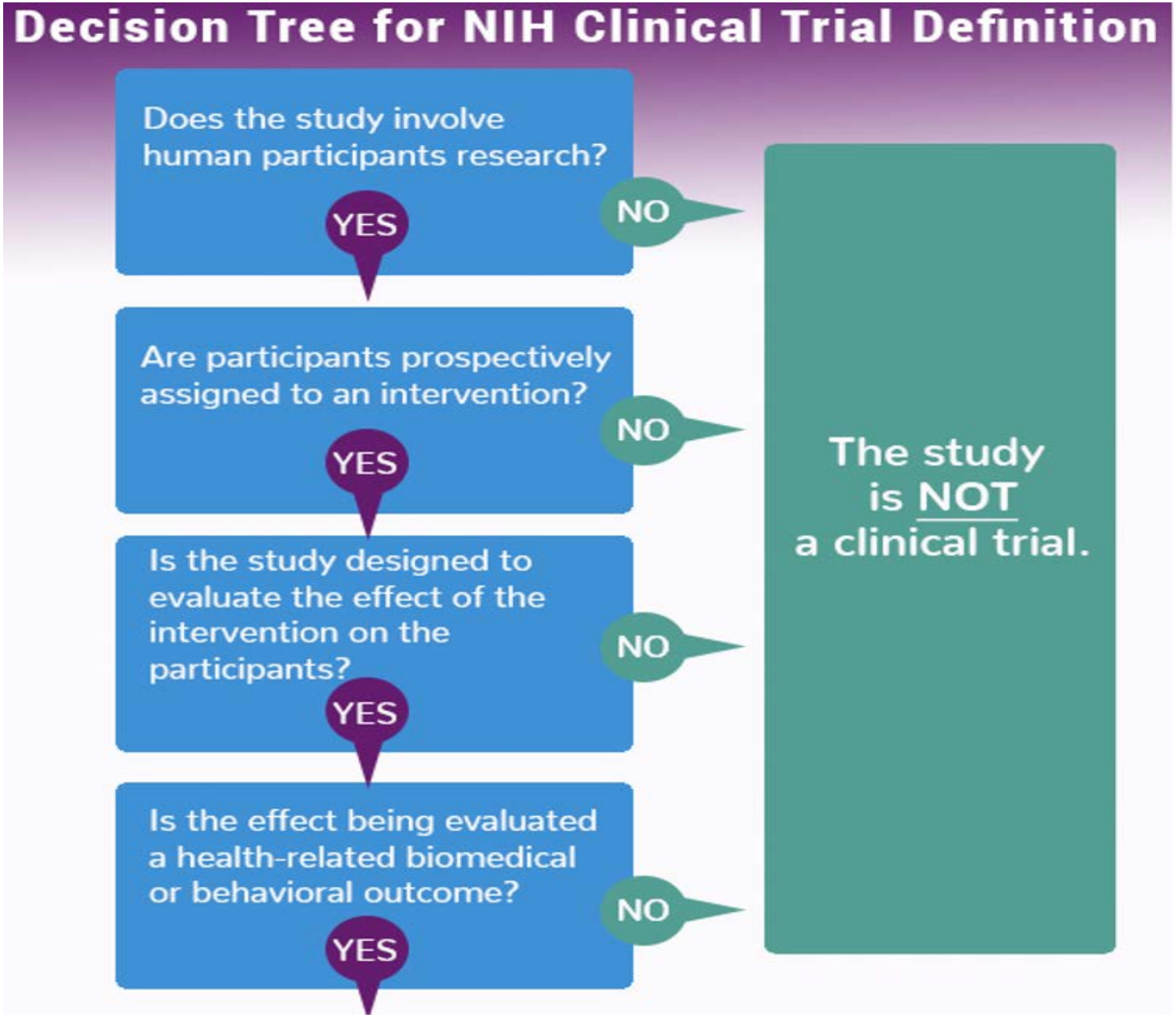
Answer a few simple questions below to help determine if your study is a clinical trial

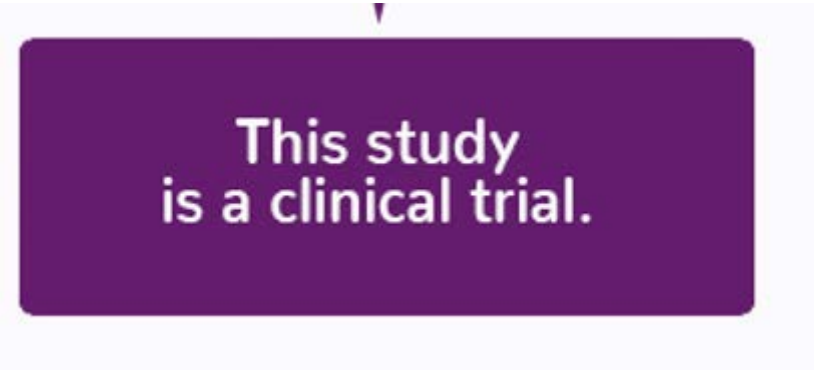
**Note for ancillary studies:**
When answering the following questions, take into account only the work being proposed in the ancillary study, not the work being done in the parent project.

### 1. Does the study involve human participants?

Unsure how to respond? Our case studies and FAQs may help you decide.

✓ X


Decision Tree for NIH Clinical Trial Definition
Does the study involve human participants research?
YES
NO
Are participants prospectively assigned to an intervention?
YES
NO
Is the study designed to evaluate the effect of the intervention on the participants?
YES
NO
Is the effect being evaluated a health-related biomedical or behavioral outcome?
YES
NO
The study is NOT a clinical trial.


This study
is a clinical trial.

# Policy Changes

***GOOD CLINICAL PRACTICE TRAINING***

- All NIH-funded clinical investigators and clinical trial staff who are involved in the design, conduct, oversight, or management of clinical trials can learn about the requirement to be trained in Good Clinical Practice (GCP). Effective date: January 1, 2017
- Recipients of GCP training are expected to retain documentation of their training. GCP training should be refreshed at least every three years in order to stay up to date with regulations, standards, and guidelines.
- GCP training is available through CITI – see the IRB website for the link.

# Policy Changes

***SINGLE IRB REQUIREMENTS***

- 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.

# Policy Changes

***SINGLE IRB REQUIREMENTS***

- 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).
- CU Boulder IRB plan to send NIH funded multi-site studies to WIRB for review.

# Policy Changes

***CERTIFICATE OF CONFIDENTIALITY***

- Effective October 1, 2017, all NIH funded research involving
  - human subjects and identifiable data,
  - bio-specimens or
  - genomic data,

    will automatically be issued a Certificate of Confidentiality as part of the terms and conditions of the award
- Investigators with NIH funded research need to update their consent forms by the next continuing review at the latest by submitting an amendment to the approved protocol.

# Policy Changes

***CERTIFICATE OF CONFIDENTIALITY***

- The new language to be added to consent forms is in our consent form template on the IRB website:
  - https://www.colorado.edu/researchinnovation/irb/investigator-resources/forms-templates

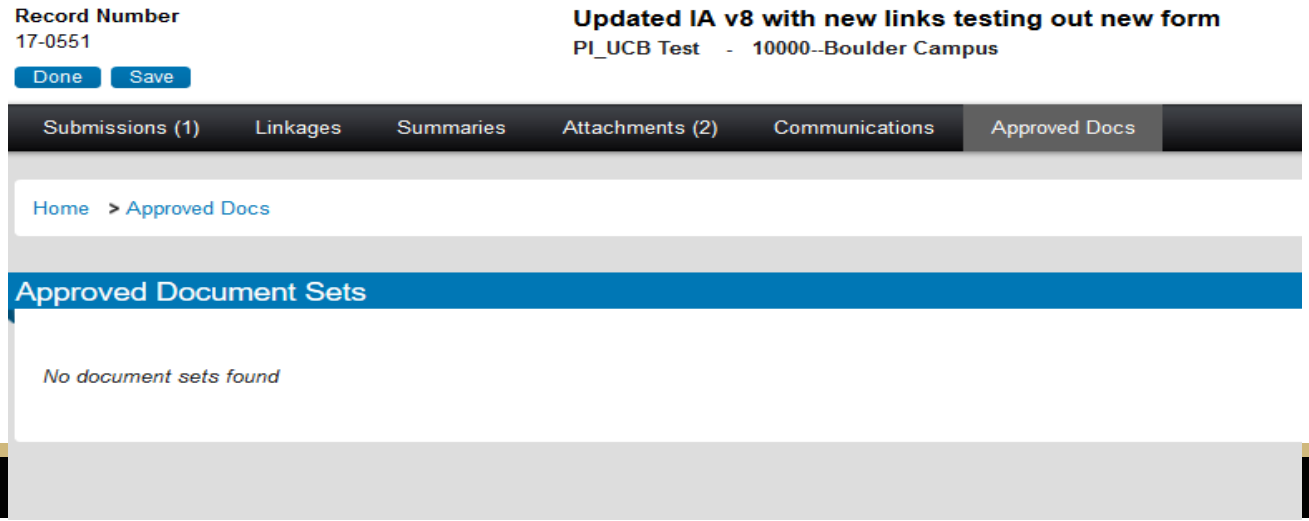
Include the following **only** if the study is funded by the National Institutes of Health or you have obtained a Certificate of Confidentiality specifically for this study.

This study has been issued a Certificate of Confidentiality from the federal government help protect your privacy. This certification means that the researchers cannot be forced to tell people who are not connected with the study, such as the court system, about your participation in this study. But, if you request that we do so, we will release information that is unique to you.

# Policy Changes

***CERTIFICATE OF CONFIDENTIALITY***

- Submitting an amendment:
- DO
  - Make sure you use the currently approved consent form document
  - Use the Track Changes function so we can see where the document has been updated



# Contact IRB Office

If you have questions please contact the IRB office:

irbadmin@Colorado.edu

303-735-3702

# Prepare for NIH Proposal Application

***Changes apply to all proposals due on or after***

***JANUARY 25, 2018***

***Details: General Application Guide for NIH and Other PHS Agencies***

# Prepare for NIH Proposal Application

***Is human subjects research proposed?***

IF NO:

- Does it involve research involving human specimens and/or data?

IF YES:

- Is it exempt?
- Is it a clinical trial?

# Changes to NIH FOAs

- New – FOAs now specify if clinical trails are or are not accepted or required
- This includes parent announcements
- Choose the correct FOA
- Provide FOA number or URL on OCG's Proposal Submission Request (PSR) form
- Application packages are specific to FOAs

# Changes to NIH Proposals

***NOT HUMAN SUBJECTS RESEARCH***

Very few changes to proposal documents UNLESS . . .

**Not HS, but research involves human specimens and/or data**

# Changes to NIH Proposals

***NOT HS, RESEARCH INVOLVES HUMAN SPECIMANS AND/OR DATA***

Provide justification document for claim that no human subjects are involved.

Include:

- information on who is providing the data/biological specimens and their role in the proposed research;
- a description of the identifiers that will be associated with the human specimens and data;
- a list of who has access to subjects' identities; and
- information about the manner in which the privacy of research participants and confidentiality of data will be protected.

# Changes to NIH Proposals

***HUMAN SUBJECTS RESEARCH - EXEMPT***

- NIH does not require IRB approval at the time of application.
- NIH understands that exemptions designated on proposal often represent the opinion of the PD/PI, and the justification provided for the exemption by the PD/PI is evaluated during peer review.
- Consult IRB if needed. IRB makes all final exemption determinations.
- Provide Exemption on PSR to Proposal Analyst
- Exemption 4 – NIH does not consider Clinical Research. Fewer proposal document requirements

# Changes to NIH Proposals

***NOTE ON DELAYED ONSET STUDIES***

Definition: Human subjects research is anticipated within the period of award but definite plans for this involvement cannot be described at time of application.

- **For delayed onset studies provide justification explaining why human subjects study information is not available at the time of application.**
- **No study record for delayed onset studies.**
- **Provide justification document with other proposal documents to Proposal Analyst.**

# Changes to NIH Proposals

***HUMAN SUBJECTS RESEARCH – NOT DELAYED ONSET OR CT***

- Complete *Study Record* for each proposed protocol involving HS with applicable required documents attached.
- All attachments must have unique file names
- Complete Sections 1, 2, 3

# Changes to NIH Proposals

***HUMAN SUBJECTS RESEARCH – NOT DELAYED ONSET OR CT***

Study Record: Section 1

- Basic Information
- Includes Clinical Trial Questionnaire

# Changes to NIH Proposals

***HUMAN SUBJECTS RESEARCH – NOT DELAYED ONSET OR CT***

Study Record: Section 2

- Study Population Characteristics (includes Inclusion Enrollment Report)
- Inclusion of Women, Minorities and Children Attachment
- Recruitment and Retention Plan Attachment
- Recruitment Status
- Study Timeline Attachment
- Enrollment of First Subject

Exemption 4 – Section 2 information and documents not required

# Changes to NIH Proposals

***HUMAN SUBJECTS RESEARCH – NOT DELAYED ONSET OR CT***

Study Record: Section 3

- Protection of Human Subjects Attachment
  - If claiming exemption, justify why research meets criteria of the exemption.
  - No exemption – Follow requirements in guide for this attachment.
- Multi-Site Study and Single IRB
  - Answer question about and required attachments for multi-site studies
  - When sIRB to be used, sIRB attachment required for each study within application.
  - Attach either the same sIRB plan with unique file name or attach document that refers to the sIRB plan in another study within the application.
- See guide for attachment requirements.

# Changes to NIH Proposals

***HUMAN SUBJECTS RESEARCH – NOT DELAYED ONSET OR CT***

Study Record: Section 3

Optional for non-CT HS:

- Data and Safety Monitoring Plan Attachment
- Question about Data and Safety Monitoring Board
- Overall Structure of the Study Team Attachment

# Changes to NIH Proposals

***HUMAN SUBJECTS RESEARCH – CLINICAL TRIAL(S)***

Provide all of the above AND

Study Record:  Section 3 – Required

- Data and Safety Monitoring Plan Attachment
- Question about Data and Safety Monitoring Board
- Overall Structure of the Study Team Attachment

# Changes to NIH Proposals

***HUMAN SUBJECTS RESEARCH – CLINICAL TRIAL(S)***

Study Record: Section 4

- ONLY for Clinical Trials
- Answer all questions and provide attachments

***DO NOT provide for non-CT HS. This will cause errors and prevent application from being accepted.***

# Changes to NIH Proposals

***HUMAN SUBJECTS RESEARCH – CLINICAL TRIAL(S)***

Study Record: Section 5

- ONLY for Clinical Trials
- ONLY if FOA specifies that an attachment needs to be included

***DO NOT provide for non-CT HS. This will cause errors and prevent application from being accepted.***

# Changes to NIH Proposals

***OTHER CHANGES***

Updated biosketch instructions: Scholastic performance requires only scientific/professional graduate courses to be listed

In Research Strategy do not duplicate information collected in the new PHS Human Subjects and Clinical Trials Information form.

Research Strategy, Approach section: New instruction to describe research methods for trials that randomize groups or deliver interventions to groups.

New review criteria questions for applications proposing clinical trials.

# Provide to PAs

At least **5 business days** before deadline:

- Budget
- PSR with FOA number or URL
- If human subjects research proposed, provide:
  - Study Record(s) for each human subject study
  - All required HS and CT attachments

# OCG Form Updates

- PSR to be updated with additional HS related questions
- NIH checklists updated

# ClinicalTrials.gov *PRS*

New Guidelines

- Trials must be registered within 21 days of trial start (NIH-funded and other studies subject to Section 801 of the Food and Drug Administration Amendments Act)
- For non-NIH and non-FDAAA studies, protocols can be registered at any time
- Trials that are already completed can be registered in ClinicalTrials.gov PRS (Protocol Registration and Results System)

Training materials: https://clinicaltrials.gov/ct2/manage-recs/present

# ClinicalTrials.gov *PRS*

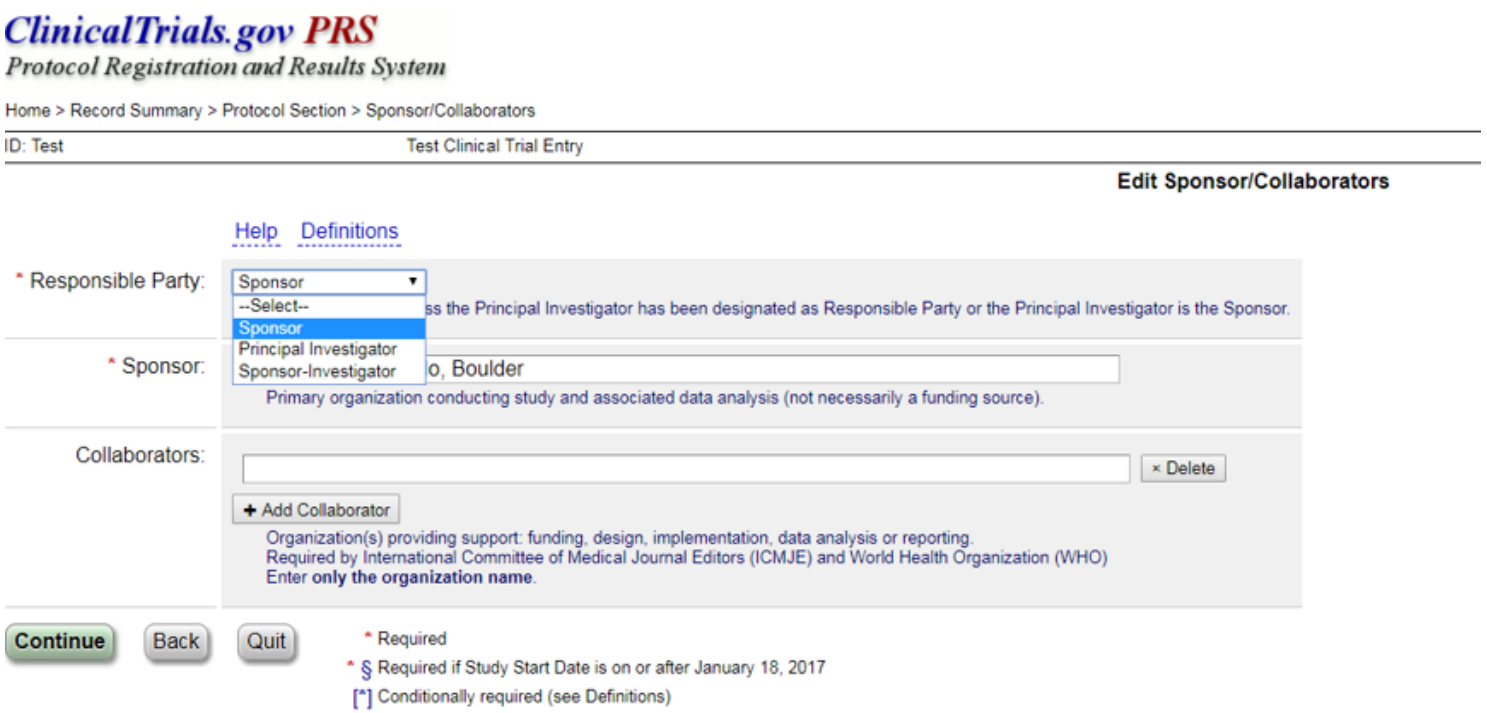
Step 1: Get registered

- Contact OCG to have account created
  - Who should have an account?
  - Responsible Party: PI
    - Authorization to submit
    - Other users can access as “record owners” (can be updated later as needed)

- Previously Responsible Party had been “Sponsor” now, will be PI

https://clinicaltrials.gov/ct2/manage-recs/how-apply

# ClinicalTrials.gov *PRS*



# ClinicalTrials.gov *PRS*

Step 2: Enter your study information

- Select “New Record”
- Complete four primary modules(https://clinicaltrials.gov/ct2/manage-recs/how-report)
  - Participant Flow
  - Baseline Characteristics
  - Outcome Measures and Statistical Analyses
  - Adverse Events
- Note protocol review criteria: http://prsinfo.clinicaltrials.gov/ProtocolDetailedReviewItems.pdf

**ClinicalTrials.gov PRS**
*Protocol Registration and Results System*

Contact ClinicalTrials.gov PRS
Org: UColoradoBoulder Admin: KSnider

**Create New Record**

**To avoid duplicate or invalid registration** of your study, check the following before proceeding with registration:

1. **Studies may only be registered by the Responsible Party.** The Responsible Party for a clinical study is the Sponsor, Sponsor-Investigator, or Sponsor-designated Principal Investigator who meets specific requirements.
   - When a study is subject to U.S. Food and Drug Administration regulations and conducted under an investigational new drug application (IND) or investigational device exemption (IDE), the IND or IDE Holder is considered the Sponsor or Sponsor-Investigator.
   - When a study is not conducted under an IND or IDE, the entity or single person who initiates the study, by preparing and/or planning the study, and who has authority and control over the study, is considered the Sponsor or Sponsor-Investigator.
2. **Use the PRS account of the Sponsor or Sponsor-Investigator to register the study.** If the Sponsor has designated the Principal Investigator to be the Responsible Party for a study, that study must be registered using the PRS account of the Sponsor.
3. **Multi-site studies are NOT registered by individual sites.** If this is a multi-site study it must be registered only once, by the Responsible Party (IND/IDE holder or the person or organization who initiates the study and who has authority and control over the study) or its designated principal investigator (PI).
4. **Coordinate with all collaborators before registering.** If the study has multiple collaborators, contact the other organizations to confirm that the study has not already been registered and to notify them that your organization (or designated PI), as Responsible Party is registering the study.
5. **Refer to the ClinicalTrials.gov Review of Protocol Submissions document** for a description of items evaluated by ClinicalTrials.gov after protocol information is submitted.

Help Definitions

* Organization's Unique Protocol ID:

* Brief Title:

Special Characters

[*] Acronym: (if any)

If specified, will be included at end of Brief Title in parentheses.

* Study Type:

- Interventional (or clinical trial) — participants assigned to intervention(s) based on a protocol
- Observational participants **not** assigned to intervention(s) based on a protocol; typically in context of routine care
- Expanded Access availability of an experimental drug or device outside of a clinical trial protocol

Continue Cancel

* Required
* § Required if Study Start Date is on or after January 18, 2017
[*] Conditionally required (see Definitions)

**ClinicalTrials.gov PRS**
*Protocol Registration and Results System*

Home > Record Summary > Protocol Section > Study Status

ID: Test  Test Clinical Trial Entry

**Edit Study Status**

Help  Definitions

* Record Verification Date: Month: November Year: 2017

* Overall Recruitment Status: --Select--

--Select--
Not yet recruiting
Recruiting
Enrolling by invitation
Active, not recruiting
Completed
Suspended
Terminated (Halted Prematurely)
Withdrawn (No Participants Enrolled)

ted or Withdrawn see the Overall Recruitment Status definition.

ated dates.

* § Study Start Date: Year: Type: --Select--

ticipated) or date first participant is enrolled (Actual).

* Primary Completion Date: Month: --Select-- Day: Year: Type: --Select--

Final data collection date for primary outcome measure.

* § Study Completion Date: Month: --Select-- Day: Year: Type: --Select--

Final data collection date for study.

Continue  Back  Quit

* Required
* § Required if Study Start Date is on or after January 18, 2017
[*] Conditionally required (see Definitions)

# ClinicalTrials.gov *PRS*

Step 3: Complete and Release Record

- View the “Protocol Section” – correct any error warnings
- Mark the record as “entry complete”
- Select “next step” to approve and release the record to PRS

# ClinicalTrials.gov *PRS*

Step 4: Record Published

- PRS staff will return any record with errors for correction or clarification
- Error-free records published on ClinicalTrials.gov within 5 business days

# ClinicalTrials.gov *PRS*

Step 5: Ongoing updates and maintenance

- Responsible Parties should update their records within 30 days of a change to any of the following:
  - Recruitment Status and Overall Recruitment Status data elements on ClinicalTrials.gov
  - Completion Date (See Primary Completion Date data element on ClinicalTrials.gov)
- Other changes or updates to the record must be made at least every 12 months.
- Record Verification Date: updated at least every 6 months for studies that are not yet completed (ClinicalTrials.gov recommendation, not requirement).
- Standard timeline for reporting results: 12 months

# Take Aways

- NIH Policies on Human Subjects and Clinical Trials are changing as of January 25, 2018.
- This affects IRB and proposals.
- Start IRB and Proposals early
- Email or call us!

# Resources

CU Boulder IRB
https://www.colorado.edu/researchinnovation/irb

General Instructions for NIH and other PHS Agencies: Forms E
https://grants.nih.gov/grants/how-to-apply-application-guide.html

NIH: Research Involving Human Subjects
https://humansubjects.nih.gov/

NIH: Clinical Trials Requirements
https://grants.nih.gov/policy/clinical-trials.htm

Video: Overview of New NIH Policies on Human Subjects Research
https://grants.nih.gov/policy/clinical-trials/tutorial/story.html

Video: Tour of New Forms
https://www.youtube.com/watch?v=nz9NWFhYOG8&list=PLOEUwSnjvqBJeHcb4yai7_fDnFZFPEmQK&index=1

# Resources

Contact your OCG Proposal Analyst

https://www.colorado.edu/ocg/directory