Requirements for Registration, Updating and Results Reporting for ClinicalTrials.gov

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Objectives

- Provide a brief history, scope and mission of ClinicalTrials.gov
- Explain the role of the ICMJE on the registration process and data sharing
- Discuss best practices and tips for registering, updating and posting results on clinicaltrials.gov
  - Understand how to gain access to CTgov as a new user, start a new record, and add users
  - Describe the role of the RP (responsible party) and institution/sponsor
  - Present when and how to update/edit existing records
  - Provide an overview of results reporting and submitting documents
- Discuss the penalties and enforcement for noncompliance
Why is Trial Registration Important?

- The registration of all interventional trials is considered to be a scientific, ethical and moral responsibility because:
- There is a need to ensure that decisions about health care are informed by all of the available evidence
- It is difficult to make informed decisions if publication bias and selective reporting are present
- The Declaration of Helsinki (1964) states that "Every clinical trial must be registered in a publicly accessible database before recruitment of the first subject".
- Improving awareness of similar or identical trials will make it possible for researchers and funding agencies to avoid unnecessary duplication
- Describing clinical trials in progress can make it easier to identify gaps in clinical trials research
- Making researchers and potential participants aware of recruiting trials may facilitate recruitment
- Enabling researchers and health care practitioners to identify trials in which they may have an interest could result in more effective collaboration among researchers. The type of collaboration may include prospective meta-analysis
- Checking study design and outcome measures as part of the registration process may lead to improvements in the quality of clinical trials by making it possible to identify potential problems (such as problematic randomization methods) early in the research process
What is ClinicalTrials.gov?

- ClinicalTrials.gov is a Web-based resource that provides patients, their family members, health care professionals, researchers, and the public with easy access to information on publicly and privately supported clinical studies on a wide range of diseases and conditions. *It is searchable* like PubMed and also maintained by the NLM at NIH.
- Studies are generally submitted to the Web site (registered) when they begin, and the information on the site should be **updated throughout the study**.
- For some but not all studies, results are submitted after the study ends. This Web site and database of clinical studies is commonly referred to as a "registry and results database."
- ClinicalTrials.gov contains information about clinical studies in human volunteers. Most of the records describe clinical trials (also called interventional studies).
- A clinical trial is a research study in which human volunteers are prospectively assigned to interventions (for example, a medical product, behavior, or procedure) based on a protocol (or plan) and are then **evaluated for effects** on biomedical or health outcomes.
ClinicalTrials.gov is a database of privately and publicly funded clinical studies conducted around the world.

Explore 271,595 research studies in all 50 states and in 205 countries.

ClinicalTrials.gov is a resource provided by the U.S. National Library of Medicine.

IMPORTANT: Listing a study does not mean it has been evaluated by the U.S. Federal Government. Read our disclaimer for details.

Before participating in a study, talk to your health care provider and learn about the risks and potential benefits.
### Locations of Registered Studies

The chart below shows the distribution of locations for all studies registered on ClinicalTrials.gov.

#### Percentage of Registered Studies by Location (as of January 14, 2019)

Total of 294,540 studies

<table>
<thead>
<tr>
<th>Location</th>
<th>Number of Registered Studies and Percentage of Total (as of January 14, 2019)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-U.S. only</td>
<td>141,377 (48%)</td>
</tr>
<tr>
<td>U.S. only</td>
<td>102,158 (35%)</td>
</tr>
<tr>
<td>Both U.S. and non-U.S.</td>
<td>15,691 (6%)</td>
</tr>
<tr>
<td>Not provided</td>
<td>35,314 (12%)</td>
</tr>
<tr>
<td>Total</td>
<td>294,540 (100%)</td>
</tr>
</tbody>
</table>

### Types of Registered Studies

The table below shows the number and types of studies that are registered and have results posted on ClinicalTrials.gov.

#### Study and Intervention Type (as of January 14, 2019)

<table>
<thead>
<tr>
<th>Type of Intervention*</th>
<th>Number of Registered Studies and Percentage of Total</th>
<th>Number of Studies With Posted Results and Percentage of Total***</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>294,540</td>
<td>34,384</td>
</tr>
<tr>
<td>Interventional</td>
<td>233,588 (79%)</td>
<td>32,399 (94%)</td>
</tr>
<tr>
<td>Drug or biology</td>
<td>134,620</td>
<td>25,690</td>
</tr>
<tr>
<td>Behavioral, other</td>
<td>73,298</td>
<td>5,817</td>
</tr>
<tr>
<td>Surgical procedure</td>
<td>24,781</td>
<td>1,787</td>
</tr>
<tr>
<td>Device**</td>
<td>29,246</td>
<td>4,100</td>
</tr>
<tr>
<td>Observational</td>
<td>59,814 (20%)</td>
<td>1,685 (8%)</td>
</tr>
<tr>
<td>Expanded Access</td>
<td>533</td>
<td>N/A</td>
</tr>
</tbody>
</table>

* A study may include more than one type of intervention, meaning that a single study may be counted more than once. Because of this, the sum of counts by type of intervention do not equal the total number of interventional studies.
** A total of 816 applicable device clinical trials were submitted as "delayed posting" under the Food and Drug Administration Amendments Act of 2007 (FDAAA). That is, the Responsible Party indicated that the trial includes a device not previously approved or cleared by the Food and Drug Administration (U.S. FDA) for any use. These trials are not included in the counts of trials with at least one device.
*** Results are required to be submitted only for certain studies. For example, results submission is generally not required for observational studies; trials completed before 2008, and trials that include drug, biological, or device products not previously approved by the U.S. FDA for any use (if the Primary Completion Date is before January 18, 2017). See FDAAA 811 and the Final Rule for further information.

https://clinicaltrials.gov/ct2/resources
Number of Registered Studies Over Time

The graph and table below show the total number of studies posted on ClinicalTrials.gov since 2000, based on the First Posted date. The first version of ClinicalTrials.gov was made available to the public on February 28, 2000.

Number of Registered Studies Over Time and Some Significant Events (as of January 14, 2019)

Number of Registered Studies With Posted Results Over Time

The graph and table below show the number of registered studies with results posted on ClinicalTrials.gov, based on the Results First Posted date. ClinicalTrials.gov launched its results database in September 2008, at which time sponsors or investigators could begin submitting results for their registered studies. The results database was first developed to accommodate the results submission requirements outlined in FDAAA. See About the Results Database for more information.

Source: https://ClinicalTrials.gov

Key:

ICMJE: Indicates when the International Committee of Medical Journal Editors (ICMJE) began requiring trial registration as a condition of publication (September 2005)

FDAAA: Indicates when the registration requirements of FDAAA began and were implemented on ClinicalTrials.gov (December 2007)
International Clinical Trials Registry Platform (ICTRP)

WHO ICTRP-The main aim of the WHO ICTRP is to facilitate the prospective registration of the WHO Trial Registration Data Set (24 items) on all clinical trials, and the public accessibility of that information. UTN (Universal Trial Number assigned- similar to the NCT for the US ClinicalTrials.gov register/registry)

www.who.int/ictrp/
BMC (BostonMC) 230 studies
BUMC (BostonU) 170 studies
CRC (BostonUCRC) about 60 studies -- PRS Administrator Cynthia Monahan (also CRC IRB Director)
ClinicalTrials.gov – Brief History

• ClinicalTrials.gov is a registry website maintained by the National Library of Medicine (NLM) at the National Institutes of Health (NIH)

• ClinicalTrials.gov was launched in 2000 in response to FDA Modernization Act of 1997, which required HHS, through NIH, to establish a clinical trials registry

• In 2005, International Committee of Medical Journal Editors (ICMJE) began requiring trial registration as a condition of publication
  • In June 2007 the ICMJE adopted the WHO’s definition of clinical trial: “Any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes.“

• In 2008, ClinicalTrials.gov released its results database in response to the FDA Amendments Act of 2007 (FDAAA), which expanded the requirements to include result reporting for trials involving FDA regulated products

• Effective January 1, 2014, CMS required mandatory reporting of NCT on claims for items and services provided in clinical trials that are qualified for coverage under the Medicare Clinical Trial Policy (“Qualifying Clinical Trials”)

• In 2014 NIH expanded the definition of CTs
ClinicalTrials.gov – brief history (cont.)

• On **September 16, 2016**, HHS issued the final rule for Clinical Trials Registration and Results Information Submission, which clarified and expanded the registration and results submission requirements in accordance with FDAAA (the “Final Rule”)
  

• On **September 16, 2016**, NIH published a Policy, which requires registration and result reporting of all NIH funded clinical trials (the “NIH Policy”)  
  

• The NIH Policy complements the Final Rule

• **Both the Final Rule and the NIH Policy went into effect January 18, 2017**

• Noncompliance enforcement began **April 18, 2017**

• Upgrades to the ClinicalTrials.gov system continue
  
  • **June 6, 2017** - **IPD** (Individual Participant Data) Sharing Statement module was added to the Protocol Section to document the plan for sharing and supporting materials.
  
  • **June 29, 2017** - The new **Document Section** requires uploading of the Study Protocol and Statistical Analysis Plan (SAP) as part of results information submission for studies with a Primary Completion Date on or after January 18, 2017. Informed Consent Forms (ICF) may optionally be uploaded.
What is a Clinical Trial Under the NIH Policy?

“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.”

• Includes clinical trials that are not “Applicable Clinical Trials”
  ✓ Phase 1 trials of FDA-regulated drugs and biologicals
  ✓ Small feasibility studies of FDA-regulated device products
  ✓ Study of an intervention that is not regulated by the FDA (i.e. behavioral interventions)

NIH Clinical Trial Decision Tree

If **yes** to all of the following, registration and results reporting is required

1. Does the study involve human participants?
2. Are the participants prospectively assigned to an intervention?
3. Is the study designed to evaluate the effect of the intervention on the participants?
4. Is the effect that will be evaluated a health-related, biomedical, or behavioral outcome?

*Does not include observational and natural history studies*

“NIH Policy on Dissemination of NIH-Funded Clinical Trial Information” Presentation to the Clinical Trials Registration Taskforce, December 15, 2016 by Sarah Carr and Valery Gordon
https://research.uic.edu/sites/default/files/Carr_Gordon_NIH.pdf
Is this a clinical trial?

The study involves the recruitment of research participants with disease X to receive either an investigational drug or a placebo. It is designed to evaluate the efficacy of the investigational drug to relieve disease symptoms.

1. **Does the study involve human participants?** Yes, the study involves human participants.
2. **Are the participants prospectively assigned to an intervention?** Yes, the participants are prospectively assigned to receive an intervention, the investigational drug or placebo.
3. **Is the study designed to evaluate the effect of the intervention on the participants?** Yes, the study is designed to evaluate the effect of the investigational drug on the participants’ symptoms.
4. **Is the effect being evaluated a health-related biomedical or behavioral outcome?** Yes, the effect being evaluated, relief of symptoms, is a health-related outcome.

This study is a clinical trial.
Is this a clinical trial?

The study involves the recruitment of research participants with disease X to be evaluated with an investigational in vitro diagnostic device (IVD). The study is designed to evaluate how knowledge of certain antibody levels impacts clinical management of disease.

1. Does the study involve human participants? Yes, the study involves human participants.
2. Are the participants prospectively assigned to an intervention? Yes, the participants are prospectively assigned to an intervention, measurement of an antibody level, with the idea that knowledge of that antibody level might affect clinical management.
3. Is the study designed to evaluate the effect of the intervention on the participants? Yes, the study is designed to evaluate how knowledge of the level of an antibody might inform treatment.
4. Is the effect being evaluated a health-related biomedical or behavioral outcome? Yes, the effect being measured, how blood antibody levels inform treatment, is a health-related outcome.

This study is a clinical trial.
Is this a clinical trial?

The study involves the recruitment of research participants with disease X to test an investigational in vitro diagnostic device (IVD). It is designed to evaluate the ability of the device to measure the level of an antibody in blood.

1. **Does the study involve human participants?** Yes, the study involves human participants.

2. **Are the participants prospectively assigned to an intervention?** No, in this context the IVD would not be considered an intervention. The IVD is being used to test its ability to measure antibody levels, but not to test its effects on any health-related biomedical or behavioral outcomes.

This study is not a clinical trial.
Is this a clinical trial?

Prior to a study of the effects of interference on working memory and brain function, an investigator wishes to test the study procedures and adjust the difficulty of the memory tasks for a range of individuals. To do so, the investigator runs a few healthy volunteers through the procedures and adjusts and finalizes the procedures prior to initiating the formal study.

1. **Does the study involve human participants?** Yes.

2. **Are the participants prospectively assigned to an intervention?** Yes, the participants are prospectively assigned to different interference conditions.

3. **Is the study designed to evaluate the effect of the intervention on the participants?** No, the purpose of these preliminary or practice runs is to evaluate and refine the study procedures, not the effect of the intervention on the participants.

**This study is not a clinical trial.**
Health-related biomedical or behavioral outcome

**Definition:** 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
- positive or negative changes to quality of life

**Clarification-**
- If procedures and tasks are being performed to measure and describe, but not to modify then the study is **NOT** a clinical trial
- Refer to case study # 18 a-f at: [https://grants.nih.gov/policy/clinical-trials/case-studies.htm](https://grants.nih.gov/policy/clinical-trials/case-studies.htm)
Which Trials Require Results Information

• Applicable Clinical Trials (ACT) under FDAAA (The Final Rule)
  – Studies with a **Primary Completion Date** on or after January 18, 2017, results information required regardless of whether FDA regulated product has been approved, licensed or cleared for marketing
  
  – **Primary Completion Date** is “the date that the final subject was examined or received an intervention for the purposes of final collection of data for the primary outcome, whether the clinical trial concluded according to the pre-specified protocol or was terminated.”

• NIH-funded clinical trials initiated (enroll first subject) after January 17, 2017 that are supported from grants submitted after that date.
What is an ACT?  Use The ACT Check List

<table>
<thead>
<tr>
<th>Question</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Is the study interventional (a clinical trial)?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study Type data element is “Interventional”</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Does the study evaluate at least one drug, biological, or device product regulated by the United States Food and Drug Administration (U.S. FDA)?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Studies a U.S. FDA-regulated Device Product data element is “Yes” and/or Studies a U.S. FDA-regulated Drug Product data element is “Yes.”</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Is the study other than a Phase 1 trial of a drug and/or biological product or is the study other than a device feasibility study?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>For drug product trials, Study Phase data element is NOT “Phase 1” and for device product trials, Primary Purpose is NOT “Device Feasibility.”</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. Do ANY of the following apply (is the answer “Yes” to at least one of the following sub-questions: 4a, 4b, OR 4c)?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>a. Is at least one study facility located in the United States or a U.S. territory?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Facility Location – Country data element is “United States,” “American Samoa,” “Guam,” “Northern Mariana Islands,” “Puerto Rico,” “U.S. Virgin Islands,” or other U.S. territory.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>b. Is the study conducted under a U.S. FDA Investigational New Drug application (IND) or Investigational Device Exemption (IDE)?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>U.S. Food and Drug Administration IND or IDE Number data element is “Yes.”</td>
<td></td>
<td></td>
</tr>
<tr>
<td>c. Does the study involve a drug, biological, or device product that is manufactured in and exported from the U.S. (or a U.S. territory) for study in another country?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Product Manufactured in and Exported from the U.S. data element is “Yes.”</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

If “Yes” is answered to all 4 questions, and the study was initiated on or after January 18, 2017, the trial would meet the definition of an ACT.
The ICMJE defines a clinical trial as any research project that prospectively assigns people or a group of people to an intervention, with or without concurrent comparison or control groups, to study the relationship between a health-related intervention and a health outcome.

- *Health-related interventions* are those used to modify a biomedical or health-related outcome; examples include drugs, surgical procedures, devices, behavioural treatments, educational programs, dietary interventions, quality improvement interventions, and process-of-care changes.
- *Health outcomes* are any biomedical or health-related measures obtained in patients or participants, including pharmacokinetic measures and adverse events.
- The ICMJE does not define the timing of first participant enrollment, but best practice dictates registration by the time of first participant consent.

The ICMJE recommends that journals publish the trial registration number at the end of the abstract. The ICMJE also recommends that, whenever a registration number is available, authors list this number the first time they use a trial acronym to refer either to the trial they are reporting or to other trials that they mention in the manuscript.
The purpose of clinical trial registration is to prevent selective publication and selective reporting of research outcomes, to prevent unnecessary duplication of research effort, to help patients and the public know what trials are planned or ongoing into which they might want to enroll, and to help give ethics review boards considering approval of new studies a view of similar work and data relevant to the research they are considering.

Retrospective registration, for example at the time of manuscript submission, meets none of these purposes. Those purposes apply also to research with alternative designs, for example observational studies. For that reason, the ICMJE encourages registration of research with non-trial designs, but because the exposure or intervention in non-trial research is not dictated by the researchers, the ICMJE does not require it.

The ICMJE recommends that journals publish the trial registration number at the end of the abstract. The ICMJE also recommends that, whenever a registration number is available, authors list this number the first time they use a trial acronym to refer either to the trial they are reporting or to other trials that they mention in the manuscript.
Registration and Results Reporting Requirements on ClinicalTrials.gov

<table>
<thead>
<tr>
<th>Element</th>
<th>Final rule</th>
<th>NIH Policy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention and phase type</td>
<td>Drug, biologic, device products regulated by FDA; <em>not phase 1</em></td>
<td>All, including behavioral interventions; all phases</td>
</tr>
<tr>
<td>Timeframe-registration</td>
<td>Not later than 21 days after enrollment of the first subject</td>
<td>Same</td>
</tr>
<tr>
<td></td>
<td>At BMC/BUMC BEFORE IRB approval</td>
<td></td>
</tr>
<tr>
<td>Registration data elements</td>
<td>Consists of descriptive information, recruitment information, location</td>
<td>Same</td>
</tr>
<tr>
<td></td>
<td>and contact information, and administrative data.</td>
<td></td>
</tr>
<tr>
<td>Timeframe- results reporting</td>
<td>Not later than 12 months after primary completion date</td>
<td>Same</td>
</tr>
<tr>
<td>Results data elements</td>
<td>Includes participant flow, demographic and baseline characteristics,</td>
<td>Same</td>
</tr>
<tr>
<td></td>
<td>outcomes and statistical analyses, adverse events, the protocol and</td>
<td></td>
</tr>
<tr>
<td></td>
<td>statistical analysis plan, and administrative information</td>
<td></td>
</tr>
<tr>
<td>Effective Date</td>
<td>Jan 18, 2017; Compliance by April 18, 2017</td>
<td>Jan 18, 2017</td>
</tr>
</tbody>
</table>


**ICMJE Policy** (effective 2005 updated 2017). Registration required for all phases of clinical trials of all interventions with any funding source prior to enrollment of the first participant. Enforcement is refusal to publish.
ICMJE Data Sharing Policy

1. As of July 1, 2018 manuscripts submitted to ICMJE journals that report the results of clinical trials must contain a data sharing statement.

2. Clinical trials that begin enrolling participants on or after January 1, 2019 must include a data sharing plan in the trial’s registration.

3. If the data sharing plan changes after registration this should be reflected in the statement submitted and published with the manuscript, and updated in the registry record.

4. Authors of secondary analyses using shared data must attest that their use was in accordance with the terms (if any) agreed to upon their receipt.
   • They must also reference the source of the data using its unique, persistent identifier to provide appropriate credit to those who generated it and allow searching for the studies it has supported.
   • Authors of secondary analyses must explain completely how theirs differ from previous analyses.
   • In addition, those who generate and then share clinical trial data sets deserve substantial credit for their efforts. Those using data collected by others should seek collaboration with those who collected the data. As collaboration will not always be possible, practical, or desired, the efforts of those who generated the data must be recognized.

Responsible Party’s (RPs) Obligations under the Final Rule and the NIH Policy

- **Register the clinical trial**
  - Final Rule + NIH Policy no later than 21 days after enrollment
  - **For ICMEJE prior to the enrollment of first participant**
    - BMC/BUMC Policy Requires that all CTs be registered (obtain the NCT) before the IRB review will be completed
  - For QCT (those that submit claims to CMS) prior to enrollment of first participant

- **Update the clinical trial (at least annually [prefer every 6 months] and as needed)**
  - For Final Rule and NIH Policy update on at least once every 12 months (some information within 15 or 30 days of change-- recruitment status, Primary Completion Date)

- **Report results of ACT and NIH funded clinical trials**
  - For Final Rule and NIH Policy, submit summary results, which includes adverse events information, *not later than 12 months after the Primary Completion Date* (delays allowed under certain circumstances)

- **Summary**
  - **ALL CTs** must be registered and updated as needed and at least annually
  - Results must be reported on all ACTs and any NIH grant with enrollment and funding after Jan 17, 2017
Required CT Results Information for ACTs and NIH Funded Clinical Trials

• Participant Flow
• Demographic and baseline characteristics
• Outcomes and statistical analyses
• Adverse event information
• Protocol and statistical analysis plan (new requirement)
• Administrative information
• Additional information for applicable device clinical trials of unapproved or uncleared devices

*Review instructions and the templates before the trial starts to make sure the data is collected to facilitate compliance with the results information requirements*
Navigating register.clinicaltrials.gov
(dashboard, protocol, results, and documents sections)
PRS- Protocol Registration and Results System

To obtain a ClinicalTrials.gov user account, contact your institutional CTgov administrator. You will be assigned a username (case/space sensitive) and CTgov will email instructions on how to set your password. Your/the RP/PR’s password can be reset as needed, just contact the PRS Administrator. The organization name will be either BostonMC or BostonU
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.

<table>
<thead>
<tr>
<th>Help</th>
<th>Definitions</th>
</tr>
</thead>
<tbody>
<tr>
<td>* Organization's Unique Protocol ID:</td>
<td>H-37777</td>
</tr>
<tr>
<td>* Brief Title:</td>
<td>Program to Reduce Obstetrical Problems and Prematurity</td>
</tr>
<tr>
<td>[*] Acronym: (If any) PROPP</td>
<td></td>
</tr>
<tr>
<td>If specified, will be included at end of Brief Title in parentheses.</td>
<td></td>
</tr>
<tr>
<td>* Study Type:</td>
<td>Intervventional (or clinical trial) — participants assigned to intervention(s) based on a protocol</td>
</tr>
<tr>
<td></td>
<td>Observational participants not assigned to intervention(s) based on a protocol, typically in context of routine care</td>
</tr>
<tr>
<td></td>
<td>Expanded Access availability of an experimental drug or device outside of a clinical trial protocol</td>
</tr>
</tbody>
</table>

* Required
* Required if Study Start Date is on or after January 18, 2017
* Conditionally required (see Definitions)
Program to Reduce Obstetrical Problems and Prematurity

Record Status
In Progress

Next Step: Finish Protocol section
Entry Complete

Record Owner: KHDamus
Access List: Edit
Last Update: 04/24/2018 05:18 by KHDamus
Upload: Allowed
Initial Release: [Not yet released]
PRS Review: [Not yet released]
FDAAA: Unknown (insufficient information entered)

Protocol Section

Identifiers:
[NCT ID not yet assigned] Unique Protocol ID: H-377777

Brief Title: Program to Reduce Obstetrical Problems and Prematurity (PROPP)

Module Status:
Study Identification: Yes
Study Status: Yes
Sponsor/Collaborators: Yes
Oversight: Information is required
Study Description: Information is required
Conditions: Information is required
Study Design: Information is required
Arms and Interventions: Information is required
Outcomes Measures: Information is required
Eligibility: Information is required
Contacts/Locations: Information is required

No Sharing Statement:

Document Section

Only certain studies need to have study documents uploaded.

- Full study protocol and statistical analysis plan - required with results information submission for studies with a Primary Completion Date on or after January 18, 2017
- Informed consent forms - optional for all studies

Uploaded PDF/A Documents:

Results Section

Results submission is required by FDAAA 801 for certain applicable clinical trials of drugs, biologics and devices. Note: other clinical trials may need to have results submitted based on other funder or sponsor policies.

[Record must have a ClinicalTrials.gov ID (NCT number) before results can be entered.]

For applicable clinical trials subject to FDAAA 801, results submission may be delayed (in limited circumstances) with a Certification or Extension Request.

For more information see: When Do I Need to Register and Submit Results?
**Study Identification**

- **Unique Protocol ID:** H-37777
- **Brief Title:** Program to Reduce Obstetrical Problems and Prematurity (PROP) (PRRPP)
- **Official Title:** Program to Reduce Obstetrical Problems and Prematurity in the Bronx
- **Secondary IDs:** [U.S. NIH Grant/Contract Award Number]

**Error(S) in Protocol Section:** See ERROR or information required messages below.

**Study Status**

- **Record Verification:** April 2018
- **Overall Status:** Enrolling by Invitation
  - **Study Start:** April 10, 2018 [Actual]
  - **Primary Completion:** July 2020 [Anticipated]
  - **Study Completion:** July 2020 [Anticipated]

**Sponsor/Collaborators**

- **Sponsor:** Boston University
- **Responsible Party:** Sponsor
- **Collaborators:**

**Oversight**

- **U.S. FDA-regulated Drug:**
- **U.S. FDA-regulated Device:**
- **U.S. FDA IND/IDE:**
- **Human Subjects Review:** Board Status:
- **Data Monitoring:** Information is required

**Study Description**

- **Brief Summary:**
- **Detailed Description:** Information is required
Record Verification Date:
- Month: April
- Year: 2018

Overall Recruitment Status:
- Enrolling by invitation

Tip: Day is not required for Anticipated dates.

Study Start Date:
- Month: April
- Day: 10
- Year: 2018
- Type: Actual

Date study is open for recruitment (Anticipated) or date first participant is enrolled (Actual).

Primary Completion Date:
- Month: July
- Day: [ ]
- Year: 2020
- Type: Anticipated

Final data collection date for primary outcome measure.

Study Completion Date:
- Month: July
- Day: [ ]
- Year: 2020
- Type: Anticipated

Final data collection date for study.

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

2. Study Status

Record Verification Date *
Definition: The date on which the responsible party last verified the clinical study information in the entire ClinicalTrials.gov record for the clinical study, even if no additional or updated information is being submitted.

Overall Recruitment Status *
Definition: The recruitment status for the clinical study as a whole, based upon the status of the individual sites. If at least one facility in a multi-site clinical study has an Individual Site Status of "Recruiting," then the Overall Recruitment Status for the study must be "Recruiting." Select one.

- Not yet recruiting: Participants are not yet being recruited
- Recruiting: Participants are currently being recruited, whether or not any participants have yet been enrolled
- Enrolling by invitation: Participants are being (or will be) selected from a predetermined population
- Active, not recruiting: Study is continuing, meaning participants are receiving an intervention or being examined, but new participants are not currently being recruited or enrolled
- Completed: The study has concluded normally; participants are no longer receiving an intervention or being examined (that is, last participant’s last visit has occurred)
- Suspended: Study halted prematurely but potentially will resume
- Terminated: Study halted prematurely and will not resume; participants are no longer being examined or receiving intervention
- Withdrawn: Study halted prematurely, prior to enrollment of first participant

Example

Study Status
Record Verification: December 2016
Overall Status: Recruiting
Study Start: December 18, 2016 [Actual]
Primary Completion: June 2018 [Anticipated]
Study Completion: January 2019 [Anticipated]

Data Entry Tips
- Review a record for an Active (not completed or terminated) study and update the Verification Date at least once per year, even if no additional or updated information was submitted during that year. Note: some data elements will need to be updated more frequently.
- When Overall Recruitment Status is Recruiting, the Recruitment Status must be specified for each Location.
- When the final participant has been examined or received an intervention for the purposes of final collection of data for the Primary Outcome Measure, update Primary Completion Date and change Type to Actual.
- When the final participant has been examined or received an intervention for the purposes of final collection of data for the overall study, update Study Completion Date and change Type to Actual.
- When a study is terminated, update Primary Completion Date and Study Completion Date to reflect when data collection ended. Change Type to Actual for both dates.

Additional Resources
- Protocol Review Criteria (PDF)
- Interventional Study Protocol Registration Template (PDF)
Completion Dates are based on data collection. They are NOT based on:

- data analysis
- publication
- IRB closure

If a date is 'anticipated' only provide a month and year. If a date is 'actual' you need to provide the full date.

Often the primary completion and the study completion date are the same but not always. Remember to go back into the record and update all 'anticipated dates before they become in arrears or the it is an error and the record becomes a problem record.
ClinicalTrials.gov PRS
Protocol Registration and Results System

Home > Recent Summary > Protocol Section > Outcome Measures

ID: N37777
Program to Reduce Obstetrical Problems and Prematurity

- **Primary Outcome Measure**
  - Title:
  - Description:
  - Time Frame:

- **Secondary Outcome Measures**
  - Title:
  - Description:
  - Time Frame:

Other Pre-specified Outcomes:
- Title:
- Description:
- Time Frame:

Save  Cancel
Group Activity

Editing Examples
Study Status Section

What is the record verification date?
How often do records need to be verified?
What is the overall status?
   What is the overall status if you have collected all study data on each participant but you are still analyzing identifiable data? ‘active, not recruiting’ or ‘completed’?
What is the difference between the primary completion date and the study completion date?
   Can they be the same date?
   What is the difference between the information provided for an ‘anticipated’ date and an ‘actual’ date?
   What would you do if you ‘anticipated’ that the primary completion date would be December 2019 but the ‘actual’ primary completion date turned out to be November 12, 2019?
Once the overall status is ‘completed’ what other information needs to be added to the record?
Outcome Measures

What three pieces of information are required for each outcome measure?
How many primary outcome measures and secondary outcome measures can you list?
If you are doing a study and depressive symptoms are to be collected using the Beck Inventory at baseline, 3mo and 6mo, propose an outcome measure title, a description and a time frame for the outcome measures
If you are doing a study and quarterly patient satisfaction is a primary outcome measure to be collected based on a survey, what title, description and time frame would you propose.
What would you do if your outcome measures change during the study?
Tips for Registering, Updating and Reporting Results on ClinicalTrials.gov
Some CTgov Tips

• All ERRORS and Major Comments (in pink) must be addressed in a timely manner
• You can ignore Warnings and Advisory Comments (in light orange)
• You can ignore Red flags on the overall record
• Do not use pronouns anywhere in the record (e.g. ‘the investigators’ instead of ‘our research team’)
• Use the ‘spelling check’ on the dashboard before submitting to PRS review
• Set up a tickler system for annual verification and for updating all ‘anticipated’ dates
• Note the each time the record is released for PRS review a PDF is made and attached and a log of all traffic on the record
Some Additional Tips

- Each time you submit an amendment and/or the annual review to the IRB, revise your protocol, modify your outcome measures, or have other changes to the research (e.g., early termination of the study) go into your record and edit as needed.
- If you have to report results, meet with the PRS Administrator (months in advance) to review the tables, format, and requirements for statistical testing.
- Before you begin to add results, check your outcome measures and make sure they are what you plan to report about as they flip to the results section.
- Submit results as soon as possible and within a year of the primary completion date (records can become ‘late results per FDAAA’ during the review period).
- Respond to PRS Administrator comments promptly.
- The public has full access to the posted information including changes that are made to the record so keep the record up to date, accurate, and consistent with the research study.
NIH Policy for Noncompliance

• Requirements for clinical trial registration and results submission will be included in the terms and conditions of the award

• Must certify compliance with registration and results requirements in progress report forms

• Failure to comply with terms and conditions of award may provide basis for enforcement actions (45 C.F.R. 75.371 – Remedies for noncompliance for HHS awarding agency or pass-through entity)
  – Temporarily withhold payments pending correction
  – Suspend or terminate award
  – Withhold further awards for the project or program
NIH-Funded ACT and Final Rule Noncompliance

- If NIH-funded clinical trial is also an ACT, non-compliant with 42 USC 282(j) (FDAAA) and 42 CFR Part 11.66 (Final Rule)
  - HHS agency will verify compliance, and if not compliant, any remaining funding for grant or funding for a future grant to such grantee will not be released
  - If HHS agency will provide notice to grantee of non-compliance and allow 30 days to correct

- ACT (Applicable Clinical Trial)
  - Failure to certify compliance and failure to submit required information are violations of Food, Drug and Cosmetic Act
  - Civil monetary penalties of up to $11,800+/day
  - Institutions had until April 17, 2017 to become compliant
Resources

- https://clinicaltrials.gov/
- www.bumc.bu.edu/ohra/clinicaltrials-gov/
- The hidden side of CTs-- https://www.youtube.com/watch?v=-RXrGLolgEc&feature=youtu.be
Site Specific Policies
Process AT BMC – BU Medical Campus

• Provide centralized support through the BMC – BU Medical Campus Office of Human Research Affairs (OHRA)
• Process is documented in a joint policy
• Studies to Register
  ▫ NIH-Funded Clinical Trials (results information needed)
  ▫ Applicable Clinical Trials (ACT) (results information needed)
  ▫ Qualifying Clinical Trials (QCT) (those that submit claims to CMS)
  ▫ Clinical trials Meeting ICMJE Definition
• Above studies should be registered in ClinicalTrials.gov concurrently with IRB submission
• NCT number must be provided to IRB and BMC CTO for trials using BMC clinical infrastructure
Process at BMC – BU Medical Campus

- BMC and BU Medical Campus each delegate PI as RP
- Departing PIs will need a transition plan for ongoing studies in ClinicalTrials.gov
- Registration through the PRS (Protocol Registration and Results System) institutional administrator
  - Karla Damus for both BMC and BU Medical Campus, if unavailable:
    - Fanny Ennever for BMC
    - Mary-Tara Roth for BU Medical Campus
- BMC non-compliance escalated to BMC Research Compliance officer then to BMC Institutional Official
- BU Medical Campus non-compliance escalated to Director, Human Research Protection Program, OHRA
- Training, education, and compliance monitoring will be provided by OHRA/CRRO/CTSI
Who is Responsible for Registering, Updating and Submitting Results?

• The Responsible Party is the awardee or investigator for NIH-funded clinical trial (subawardees and subinvestigators must coordinate with RP)

• When BMC or BU Medical Campus is the sponsor (no outside funding, NIH grantee) they will designate the PI as RP
  - To be the RP the PI must
    ✓ Be responsible for conducting the trial
    ✓ Have access to and control over the trial data
    ✓ Have the right to publish the trial results; and
    ✓ Have the ability to meet the ClinicalTrials.gov requirements for submitting and updating trial information
Supporting Researchers with the Process at BMC–BU Medical Campus

- Assist PIs in determining if their study is a CT and the type of trial
- Assist in registration, updating and reporting results
- Regular auditing and monitoring for compliance
- Training and education for RPs/PIs and research staff provided by OHRA_CRRO
  - Annually, present a CRRO Seminar on ClinicalTrials.gov
  - Integrate key information into CRRO trainings (PI and Fundamentals)
  - Educational venues developed for BMC/BU Medical Campus Research Professional Network (RPN) and the BMC Research Managers
  - Departmental presentations to research faculty on request
  - Website with ClinicalTrials.gov information, links, and resources (e.g. checklists, algorithms, templates, videos, publications)
  - CRRO consultations from the design of clinical trials throughout the registration, updating and results reporting process

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