

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

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Clinical Research Seminar 4-24-18

Objectives

- Review the Final HHS Rule and the NIH Policy regarding registration and results submissions to ClinicalTrials.gov
- Highlight the requirements for Responsible Party (RP/PI) when BMC or BU Medical Campus is the Sponsor
- Describe the process to facilitate ClinicalTrials.gov compliance at BMC or BU Medical Campus
- Discuss tips for registering, updating and results reporting
- Contact Karla Damus for any questions/concerns

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 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.

What is ClinicalTrials.gov

- ClinicalTrials.gov also contains records describing observational studies and programs providing access to investigational drugs outside of clinical trials (expanded access).
- Studies listed in the database are conducted in all 50 States and in 203 countries.
- ClinicalTrials.gov was created as a result of the Food and Drug Administration Modernization Act of 1997 (FDAMA).
- The ClinicalTrials.gov registration requirements were expanded after Congress passed the FDA Amendments Act of 2007 (FDAAA). Section 801 of FDAAA (FDAAA 801) requires more types of trials to be registered and additional trial registration information and results for certain trials to be submitted.
 - This led to the development of the [ClinicalTrials.gov results database](#), which contains summary information on study participants and study outcomes, including adverse events. The results database was made available to the public in September 2008.

ClinicalTrials.gov

NIH U.S. National Library of Medicine

ClinicalTrials.gov

Find Studies ▾

About Studies ▾

Submit Studies ▾

Resources ▾

About Site ▾

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 203 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](#).

Find a study (all fields optional)

Saved Studies (5)

Recruitment status ⓘ

Recruiting and not yet recruiting studies

All studies

Condition or disease ⓘ (For example: breast cancer)

Other terms ⓘ (For example: NCT number, drug name, investigator name)

Country ⓘ

Search

[Advanced Search](#)

[Help](#) | [Studies by Topic](#) | [Studies on Map](#) | [Glossary](#)

Patients and Families

Search for actively recruiting studies that you may be able to participate in or learn about new interventions/treatments that are being considered.

[Learn more](#)

Researchers

Search the database to stay up to date on developments in your field, find collaborators, and identify unmet needs.

[Learn more](#)

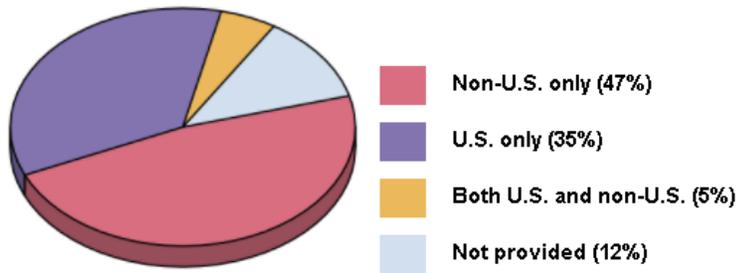
Study Record Managers

Learn about registering studies and about submitting their results after study completion.

[Learn more](#)

Percentage of Registered Studies by Location (as of April 17, 2018)

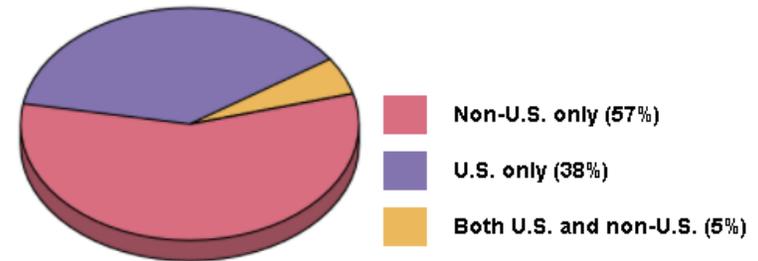
Total of 271,326 studies



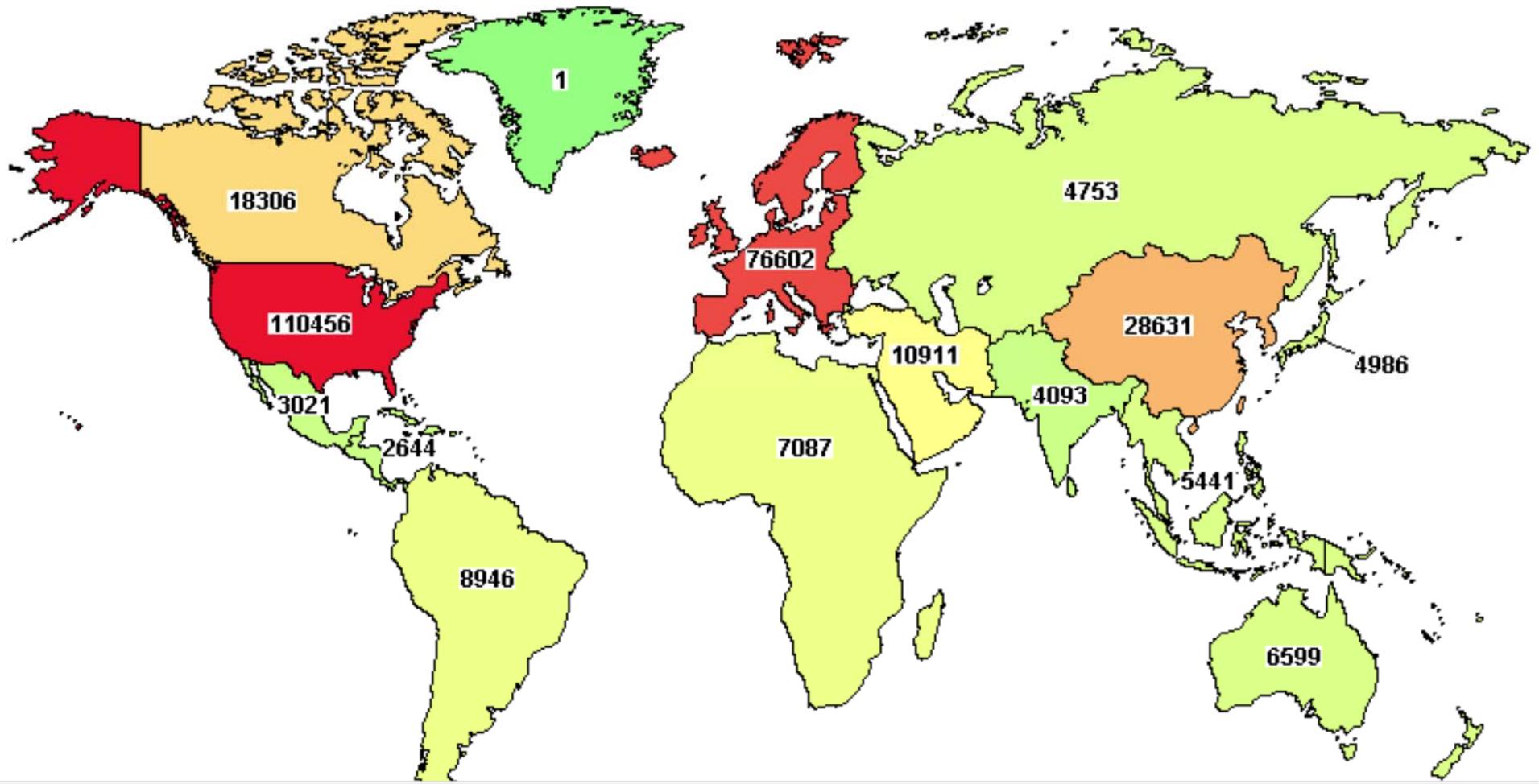
Location	Number of Registered Studies and Percentage of Total (as of April 17, 2018)
Non-U.S. only	128,651 (47%)
U.S. only	95,776 (35%)
Both U.S. and non-U.S.	14,680 (5%)
Not provided	32,219 (12%)
Total	271,326 (100%)

Percentage of Recruiting Studies by Location (as of April 17, 2018)

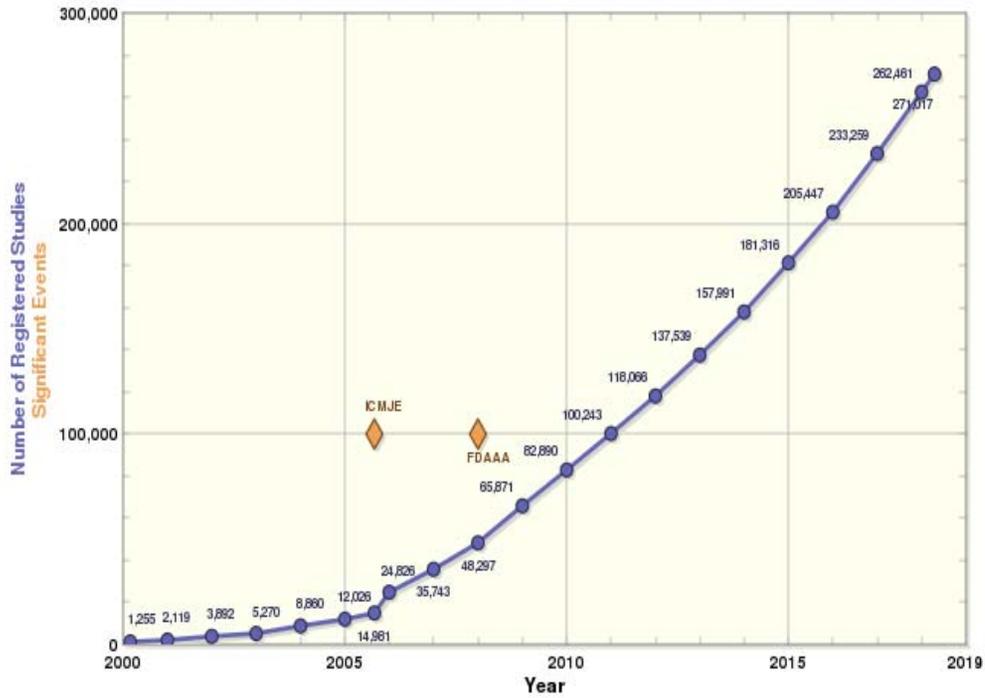
Total of 46,944 recruiting studies



Location	Number of Recruiting Studies and Percentage of Total (as of April 17, 2018)
Non-U.S. only	26,738 (57%)
U.S. only	17,756 (38%)
Both U.S. and non-U.S.	2,390 (5%)
Not provided	60 (0%)
Total	46,944 (100%)



**Number of Registered Studies Over Time
and Some Significant Events (as of April 17, 2018)**



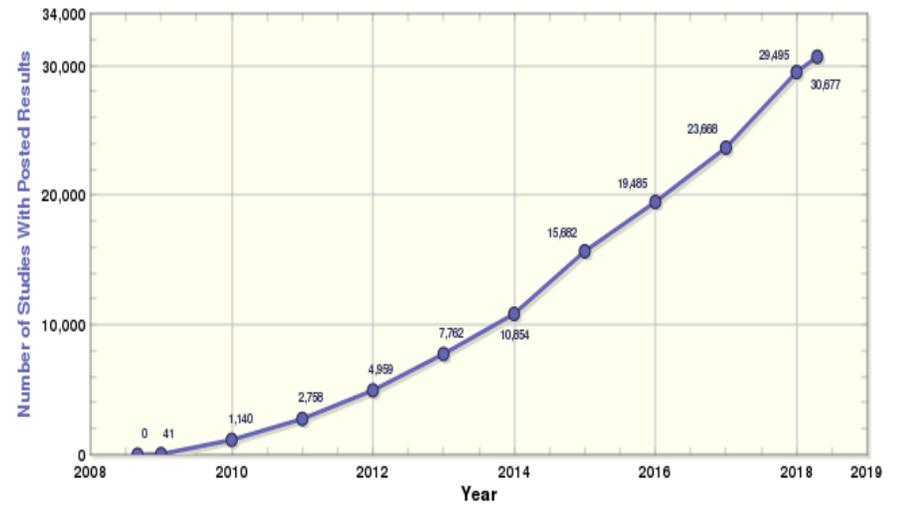
Source: <https://ClinicalTrials.gov>

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)

**Number of Registered Studies With Posted Results Over Time
(as of April 17, 2018)**



Source: <https://ClinicalTrials.gov>

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 April 17, 2018)		Number of Registered Studies and Percentage of Total	Number of Studies With Posted Results and Percentage of Total****
Total		271,326	30,735
<u>Interventional</u>		215,864 (80%)	28,899 (94%)
Type of <u>Intervention*</u>	Drug or biologic	127,012	23,047
	Behavioral, other	66,169	5,115
	Surgical procedure	23,013	1,590
	Device**	26,500	3,557
<u>Observational</u>		54,216 (20%)	1,836 (6%)
<u>Expanded Access</u>		475	N/A

* 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 771 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 801 and the Final Rule](#) for further information.

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)

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* 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
- Registries checking data 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

www.who.int/ictrp/

[Search tips](#) Search for [clinical trials in children](#)

[Phases](#) are

- All
- Phase 0
- Phase 1
- Phase 2
- Phase 3
- Phase 4

Welcome

- The Clinical Trials Search Portal provides access to a central database containing the trial registration data sets provided by the registries listed on the right. It also provides links to the full original records.
- To facilitate the unique identification of trials, the Search Portal bridges (groups together) multiple records about the same trial. [More information](#)
- Please note: This Search Portal is not a clinical trials registry. [How to register a trial](#)
- It is now possible to export the results of the search into XML. [More information](#)
- Crawling the ICTRP database now requires a username/password. To request access to the crawling pages please send an email to ictripinfo@who.int (**This service is now enabled**)
- A new field called 'Prospective registration' has been added to the ICTRP database, More details about this new field can be found [here](#)

Data Providers

Data sets from [data providers](#) are updated every Friday evening according to the following schedule:
Every week:

- Australian New Zealand Clinical Trials Registry, last data file imported on **16 April 2018**
- Chinese Clinical Trial Registry, last data file imported on **16 April 2018**
- ClinicalTrials.gov, last data file imported on **16 April 2018**
- EU Clinical Trials Register (EU-CTR), last data file imported on **16 April 2018**
- ISRCTN, last data file imported on **16 April 2018**
- The Netherlands National Trial Register, last data file imported on **16 April 2018**

Every 4 weeks:

- Brazilian Clinical Trials Registry (ReBec), last data file imported on **26 February 2018**
- Clinical Trials Registry - India, last data file imported on **26 March 2018**

Register.ClinicalTrials.gov

ClinicalTrials.gov PRS
Protocol Registration and Results System

Contact ClinicalTrials.gov PF
Org: BostonU Admin: KHDamus Log

- Quick Links
- [New Record](#)
 - [Admin Quick Reference](#)
 - [Problem Resolution Guide](#)

Records Accounts Help

Email: damusk@bu.edu [Update]

Help us improve: PRS Surveys

Record List

All Records (157) Problem Records (10) Custom Filter

Showing: 10 records Search: Show/Hide Columns

	Protocol ID	ClinicalTrials.gov ID	Brief Title	Overall Status	Verification Date	Primary Completion Date	Record Status	Results Status	Last Update	Last Updated by	Record Owner	Responsible Party	Central Contacts	Problems
Open	H-34609	NCT03014050	Bio Electro Stimulation Therapy for Parkinson's Disease (BEST)	Not yet recruiting	09/2017	05/2018	Approved		09/07/2017 01:17	KHDamus				<ul style="list-style-type: none"> Record Has 1 Error Update Not Released
Open	H-34579	NCT02775760	The Entorhinal Cortex and Aerobic Exercise in Aging (ECE)	Not yet recruiting	09/2017	04/2018	Approved		09/07/2017 01:16	KHDamus				<ul style="list-style-type: none"> Record Has 1 Error Update Not Released
Open	H-23184	NCT00491751	Clinical Utility of Endothelial Dysfunction in PAD	Terminated	05/2017	06/2012	In Progress	Released	08/14/2017 08:12	KHDamus				<ul style="list-style-type: none"> PRS Review Comments Entry Not Completed Update Not Released

BMC (BostonMC) 211 studies

BUMC (BostonU) 162 studies

CRC (BostonUCRC) about 60 studies-- PRS Administrator Cynthia Monahan (also CRC IRB Director)

ClinicalTrials.gov – Brief History and Updates

- 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 – (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”)
<https://www.federalregister.gov/documents/2016/09/21/2016-22129/clinical-trials-registration-and-results-information-submission>
- On **September 16, 2016**, NIH published a Policy, which requires registration and result reporting of all NIH funded clinical trials (the “NIH Policy”) <https://grants.nih.gov/grants/guide/notice-files/NOT-OD-16-149.html> NIH Policy on the Dissemination of NIH-Funded Clinical Trial Information
- 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 has been 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.

ICMJE Data Sharing Policy

1. As of 1 July 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 1 January 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.

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)

<https://grants.nih.gov/grants/guide/notice-files/NOT-OD-16-149.html>

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>

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

Question	Yes	No
1. Is the study interventional (a clinical trial)? <i>Study Type</i> data element is "Interventional"	<input type="checkbox"/>	<input type="checkbox"/>
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)? <i>Studies a U.S. FDA-regulated Device Product</i> data element is "Yes" and/or <i>Studies a U.S. FDA-regulated Drug Product</i> data element is "Yes."	<input type="checkbox"/>	<input type="checkbox"/>
3. Is the study <u>other than</u> a Phase 1 trial of a drug and/or biological product or is the study <u>other than</u> a device feasibility study? For drug product trials, <i>Study Phase</i> data element is NOT "Phase 1" and for device product trials, <i>Primary Purpose</i> is NOT "Device Feasibility."	<input type="checkbox"/>	<input type="checkbox"/>
4. Do ANY of the following apply (is the answer "Yes" to <u>at least one</u> of the following sub-questions: 4a, 4b, OR 4c)? <ol style="list-style-type: none"> Is at least one study facility located in the United States or a U.S. territory? <i>Facility Location – Country</i> data element is "United States," "American Samoa," "Guam," "Northern Mariana Islands," "Puerto Rico," "U.S. Virgin Islands," or other U.S. territory. Is the study conducted under a U.S. FDA Investigational New Drug application (IND) or Investigational Device Exemption (IDE)? <i>U.S. Food and Drug Administration IND or IDE Number</i> data element is "Yes." 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? <i>Product Manufactured in and Exported from the U.S.</i> data element is "Yes." 	<input type="checkbox"/>	<input type="checkbox"/>

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.

International Committee of Medical Journal Editors (ICMJE)

- 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.
- Although not a required item, the ICMJE encourages authors to include a statement that indicates that the results have not yet been published in a peer-reviewed journal, and to update the registration with the full journal citation when the results are published.

2018 Omnibus Spending Bill, March 2018

- \$3 billion boost, to \$37 billion, is the biggest percent increase NIH has received since a 5-year effort to double the agency's budget ended in 2003.
- \$414 million in new funding for Alzheimer's disease research, a 30% increase
- 'All of Us' precision medicine study gets a \$60 million increase, to \$290 million.
- \$40 million in new funds for research on a universal flu vaccine, for \$100 million in total.
- At least \$500 million in new funds will be targeted to research on opioid addiction.

- **Companion report** – also addressed new reporting requirements for clinical trials that would apply to basic research studies with humans that don't test treatments and were not considered trials until now.
- Cognitive and brain scientists have warned that [this expanded definition of a clinical trial didn't make sense and would stifle their research with red tape](#).
- The report echoes their views: “There is concern that policy changes could have long-term, unintended consequences for this research, add unnecessary regulatory burdens, and substantially increase the number of studies in the ClinicalTrials.gov database that are not clinical trials.”
- [It directs NIH to apply the new reporting rules only to studies that were already considered clinical trials](#) and to *delay adding basic studies while NIH consults with the community about more suitable ways to report their results.*
 - *NIH must seek input and update Congress on its plans by June 22, 2018.*

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
 - For QCT (those that submit claims to CMS) prior to enrollment of first participant

BMC/BUMC Policy Requires that all CTs be registered (obtain the NCT) before the IRB review will be completed
- **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

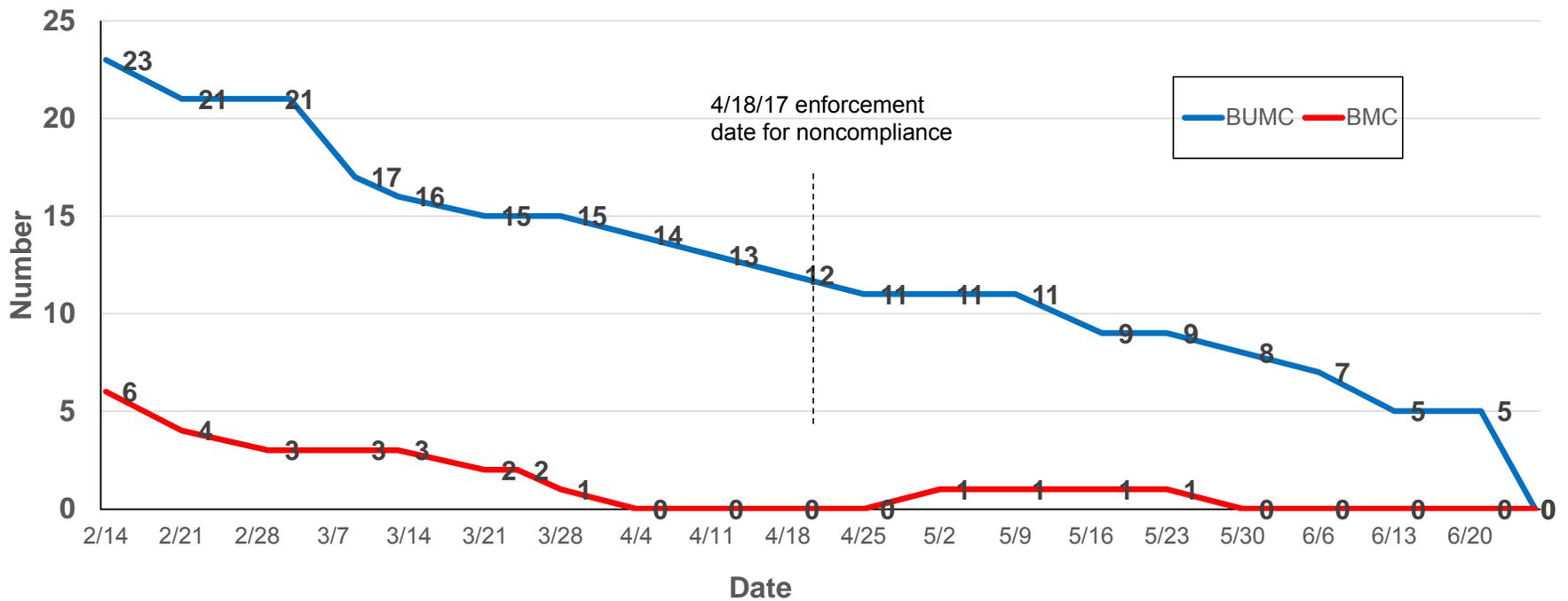
NIH Policy Compliance

- 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 New Rule Compliance

- 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
- Other ACT
 - Failure to certify compliance and failure to submit required information are violations of Food, Drug and Cosmetic Act
 - Civil monetary penalties of up to \$10,000/day
 - Had until April 17, 2017 to be compliant

Number of Trials in *ClinicalTrials.gov* with Late Results per FDAAA at BUMC and BMC February 14, 2017 to June 28, 2017



Some Tips for Registering, Updating and Reporting Results on *ClinicalTrials.gov*

PRS- Protocol Registration and Results System

To obtain a ClinicalTrials.gov user account, please contact Karla Damus damusk@bu.edu, 358-7382. 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**

CT ClinicalTrials.gov PRS: Login x

Secure | <https://register.clinicaltrials.gov>

Apps Home Clinicaltrials.gov Policies Standard Practices Training Other books

ClinicalTrials.gov PRS
Protocol Registration and Results System

Login

Welcome to the [ClinicalTrials.gov](https://clinicaltrials.gov) Protocol Registration and Results System (PRS). OMB NO: 0925-0598
EXPIRATION DATE: 02/29/2020
[Burden Statement](#)

Organization:

One-word organization name assigned by PRS (sent via email when account was created)

Username:

Password: [Forgot password](#)

See [Submit Studies](#) on ClinicalTrials.gov for information on how to apply for an account, how to register your study, and how to submit result
[Send email to ClinicalTrials.gov PRS Administration](#)

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

* Required

* § Required if Study Start Date is on or after January 18, 2017

[*] Conditionally required (see Definitions)

Record Status

In Progress → Entry Completed → Approved → Released → PRS Review → Public

Next Step: Finish Protocol section **Entry Complete** ⓘ

Record Owner: KHDamus ⓘ

Last Update: 04/24/2018 05:18 by KHDamus ⓘ

Initial Release: [Not yet released]

Access List: [] [Edit](#)

Upload: Allowed [Edit](#)

PRS Review: [Not yet released]

Public Site: [Not yet registered]

FDAAA: Unknown (insufficient information entered) ⓘ

[Spelling](#) [Preview](#) [Draft Receipt \(PDF RTF\)](#) [Download XML](#) [Delete...](#) [Admin Only: Copy Protocol](#) [Change Owner](#)

[Open](#)

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: ✓

Study Status: ✓

Sponsor/Collaborators: ✓

Oversight: **Information is required**

Study Description: **Information is required**

Conditions: **Information is required**

Study Design: **Information is required**

Arms and Interventions: **Information is required**

→ Outcome Measures: **Information is required**

Eligibility: **Information is required**

Contacts/Locations: **Information is required**

→ IPRD Sharing Statement:

→ References:

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.]

[Delay Results](#) 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?](#)

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

[Record Summary](#) [Preview](#) [Edit All](#) [Help](#) [Definitions](#)

[Edit](#)

Study Identification

Unique Protocol ID: H-37777

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

Official Title: Program to Reduce Obstetrical Problems and Prematurity in the Bronx

Secondary IDs: [U.S. NIH Grant/Contract Award Number]

ERROR: "" is not a recognized U.S. NIH grant/contract award number.

ERROR: Secondary ID is a required field.

[Edit](#)

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]

[Edit](#)

Sponsor/Collaborators

Sponsor: Boston University

Responsible Party: Sponsor

Collaborators:

[Edit](#)

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

[Edit](#)

Study Description

Brief Summary:

Detailed Description:

Information is required

[Help](#) [Definitions](#)

* Record Verification Date: Month: April ▼ Year: 2018

* Overall Recruitment Status: Enrolling by invitation ▼
Before selecting Suspended, Terminated or Withdrawn see the [Overall Recruitment Status definition](#).

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.

Continue Back Quit

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

▼ 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

Definitions

▼ 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.

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- **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)
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- 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

Help: Study Status

Introduction

The Study Status module contains key dates and Overall Recruitment Status of a study.

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 \(PDF\)](#)

Primary and Study Completion Dates

* Primary Completion Date:

Month: --Select-- ▾ Day: Year: Type: --Select-- ▾

Final data collection date for primary outcome measure.

❌ ERROR: Primary Completion Date has not been entered.

* § Study Completion Date:

Month: --Select-- ▾ Day: Year: Type: --Select-- ▾

Final data collection date for study.

⚠ WARNING: Study Completion Date has not been entered.

Completion Dates are based on data collection. They are NOT based on:

- data analysis
- publication
- IRB closure

If you use these as
Completion Dates, you may
have LATE RESULTS

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**.

ID: H-37777 Program to Reduce Obstetrical Problems and Prematurity

[Edit](#) **Conditions**
 Conditions:
 Keywords:
 Information is required

[Edit](#) **Study Design**
 Study Type: Interventional [\[Change...\]](#)
 Primary Purpose:
 Study Phase:
 Interventional Study Model:
 Number of Arms:
 Masking:
 Allocation:
 Enrollment: []
 Information is required

[Open](#) **Arms and Interventions**
 Information is required

[Edit](#) **Outcome Measures**
 Information is required

[Edit](#) **Eligibility**
 Minimum Age:
 Maximum Age:
 Sex:
 Gender Based:
 Accepts Healthy Volunteers:
 Criteria:
 Inclusion Criteria:
 -
 Exclusion Criteria:
 -
 Information is required

[Open](#) **Contacts/Locations**
 Central Contact Person:
 Central Contact Backup:
 Study Officials:
 ▼ Locations:
 Information is required

[Edit](#) **IPD Sharing Statement**
 Plan to Share IPD:

[Edit](#) **References**
 ▼ Citations:
 Links:
 Available IPD/Information:

[Record Summary](#)

[Help](#) [Definitions](#)

* Primary Outcome Measure: Outcome 1
 Title:
 Description:
 Time Frame:
 x Delete Outcome

+ Add Primary Outcome

[*] Secondary Outcome Measures: (if any)
 Outcome 2
 Title:
 Description:
 Time Frame:
 + Copy Outcome x Delete Outcome

Outcome 3
 Title:
 Description:
 Time Frame:
 + Copy Outcome x Delete Outcome

+ Add Secondary Outcome

Other Pre-specified Outcomes:
 Outcome 4
 Title:
 Description:
 Time Frame:
 + Copy Outcome x Delete Outcome

+ Add Other Outcome

[Save](#)

[Cancel](#)

* Required

* § Required if Study Start Date is on or after January 18, 2017

[*] Conditionally required (see Definitions)

Some Additional 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 (eg '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 that 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 (eg 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.

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

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

Contact Karla Damus damusk@bu.edu, 358 7382

Resources

- <https://clinicaltrials.gov/>
- www.bumc.bu.edu/ohra/clinicaltrials-gov/
- www.nih.gov/news-events/news-releases/hhs-take-steps-provide-more-information-about-clinical-trials-public
- www.nih.gov/news-events/news-releases/hhs-take-steps-provide-more-information-about-clinical-trials-public
- Zarin DA, et al. “Trial Reporting in Clinical Trials.gov– The Final Rule”. NEJM 2016,375:20, 1998-2004. www.nejm.org/doi/full/10.1056/NEJMs1611785
- Tse T, Bergeris A, Zarin DA. [Lockbox for Registered Trials of Unapproved Devices](#). *N Engl J Med*. 2018 March 15;378(11):1064.
- Bergeris A, Tse T, Zarin DA. [Trialists' intent to share individual participant data as disclosed at ClinicalTrials.gov](#). *JAMA*. 2018 Jan 23;319(4):406-8.
- www.nih.gov/news-events/summary-hhs-nih-initiatives-enhance-availability-clinical-trial-information
- http://www.bu.edu/researchsupport/2017/08/31/new-nih-requirements-for-registering-nih-funded-clinical-trials-on-clinicaltrials-gov-and-for-good-clinical-practice-gcp-training/?utm_source=RR&utm_medium=email&utm_campaign=0917
- The hidden side of CTs-- <https://www.youtube.com/watch?v=-RXrGLolGec&feature=youtu.be>

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