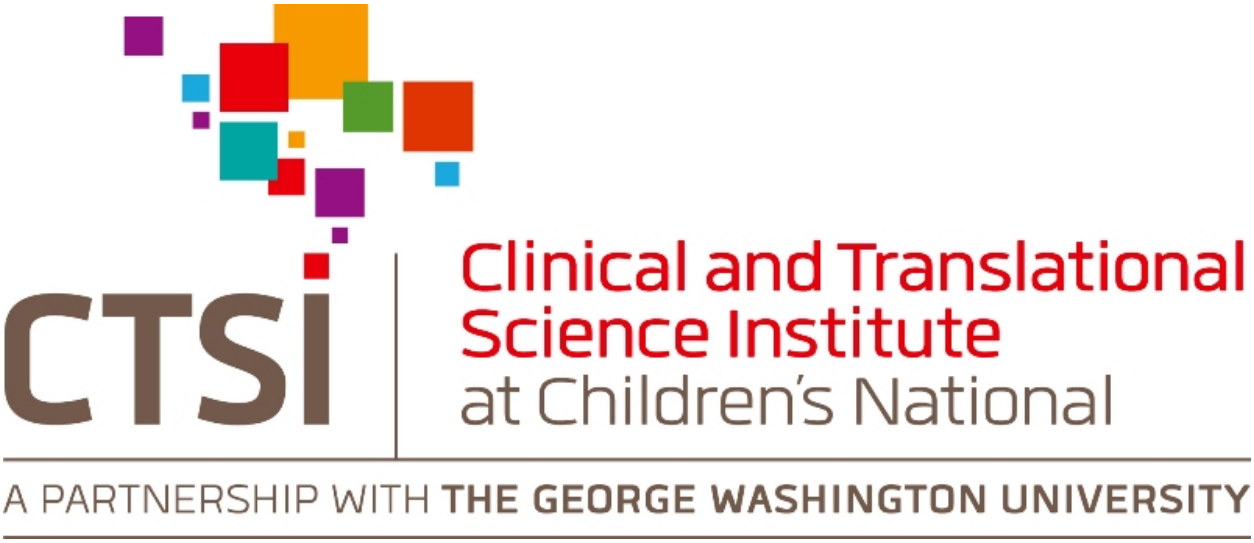


Guidelines for Registering with Clinicaltrials.gov

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 trials on a wide range of diseases and conditions. The website is maintained by the National Library of Medicine (NLM), which is part of the National Institutes of Health (NIH). Clinical trials are generally submitted (that is, registered on the website) when they begin. Information on Clinicaltrials.gov is provided by the sponsor or principal investigator (PI), who updates the information throughout the clinical trial. In some cases, results of the clinical trial are submitted after the clinical trial ends. Website commonly referred to as a "registry and results database", this website is a publicly available database of federally and privately supported clinical trials conducted in the United States.

The purpose of Clinicaltrials.gov is to share key information with the public about current and past clinical trials. Clinicaltrials.gov captures significant summary information before and during the clinical trial as well as summary results and adverse event information of a completed clinical trial. Federal laws and regulations as well as editors of prominent medical journals require registration of a clinical trial, as described below.

Why Do I Have to Register my Clinical Trial?

Over the years various regulations have affected the registration of clinical trials, beginning in 1997 with a mandate from Congress to the Food and Drug Administration (FDA) that clinical trials must be registered. In 2000, the NIH established Clinicaltrials.gov and began registering clinical trials. In 2005, the *International Committee of Medical Journal Editors (ICMJE)* began requiring clinical trial registration for article publication. The ICMJE supports many top tier journals and has significantly influenced the registration and publication of articles. Over the years, the federal requirements have broadened. In 2016, the “Final Rule” was published; it required that NIH-funded clinical trials must be registered through Clinicaltrials.gov. Additionally, summary results must be submitted and posted in a timely manner for every clinical trial funded in whole or in part by NIH.

What are the Consequences for NOT Registering a Clinical Trial?

Several issues can arise from not registering a clinical trial on the NIH website.

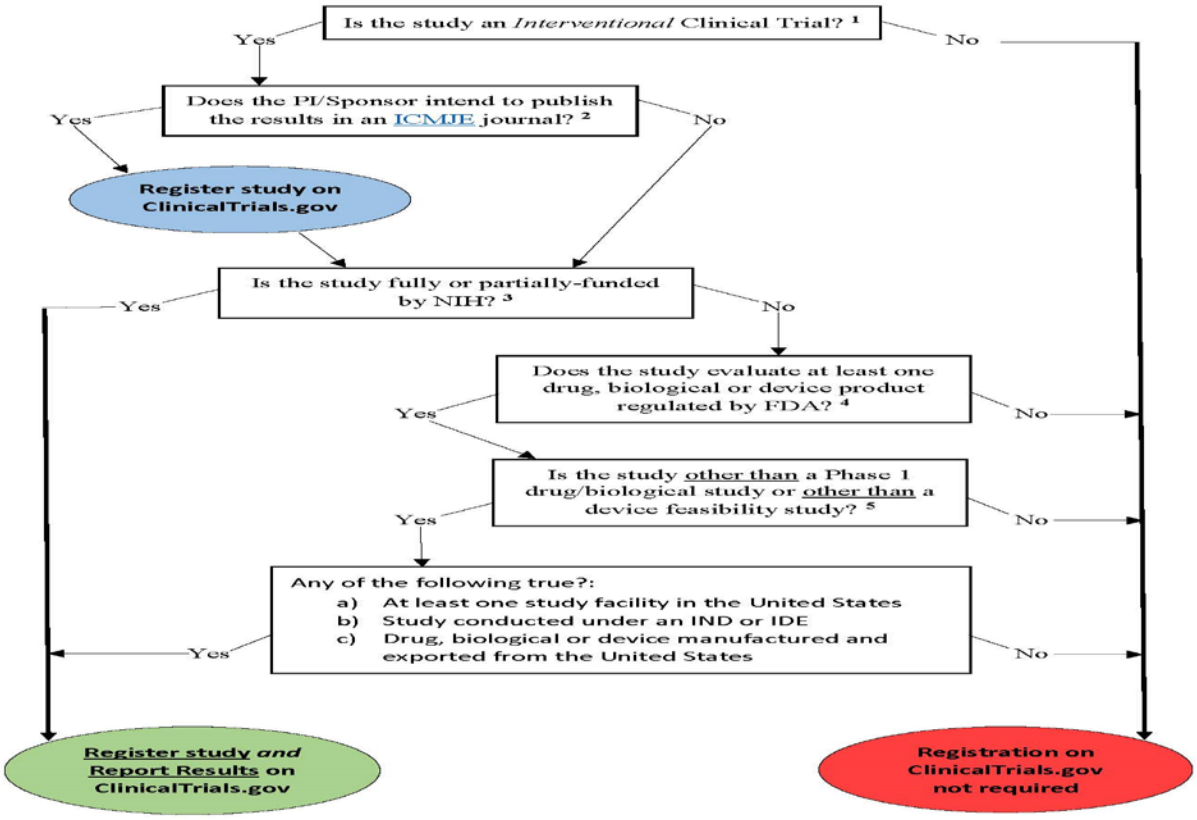
- The ICJME has a general requirement for registering clinical trials as part of their submission and review process. Therefore, many nationally and internationally recognized journals will not publish an article about a clinical trial that was not registered.
- The more serious penalties for failure to register clinical trials, keep the information up to date, or submit false or misleading information include:
  - Civil monetary penalties (allowed under FDA regulations)
  - For federally funded clinical trials, withholding or recovery of grant funds. These penalties not only apply to the investigator, but also can apply to the institution as a whole.

What is an Applicable Clinical Trial?

Given the various agencies that oversee clinical research, the definition of a clinical trial can vary. If a clinical trial meets any of these definitions, the clinical trial must be registered.

- The *FDA* requires registration for "applicable clinical trials" as follows:
  - For any clinical trials of drugs and biologics: controlled clinical investigations of a product subject to FDA regulation. Phase I investigations are excluded from this definition.
  - For clinical trials of biomedical devices: controlled clinical investigations with health outcomes of devices subject to FDA regulation and pediatric post-market surveillance. Small feasibility clinical trials are excluded from this definition.
- *ICMJE* defines a clinical trial as any research clinical trial that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes. This definition is included because some publications require the registration of a clinical trial as a registry such as Clinicaltrials.gov as one of the requirements for consideration in publication.
- The *NIH* defines a clinical trial *as* a prospective biomedical or behavioral research clinical trial of human subjects that is designed to answer specific questions about biomedical or behavioral interventions (for example, drugs, treatments, devices, or new ways of using known drugs, treatments, or devices).

This flowchart helps outline those studies that may require registration:



Clinicaltrials.gov has developed a checklist to help simplify these definitions/requirements and thus determine if your study falls under the registration requirements. The Applicable Clinical Trials Checklist can help investigators assess their clinical trial for registration. It asks the following questions:

1. Is the study interventional (a clinical trial)?
2. Does the clinical trial evaluate at least one drug, biologic, or device regulated by the FDA?
3. Is the clinical trial other than a Phase 1 clinical trial of a drug and/or biological product or is the clinical trial other than a device feasibility clinical trial?
4. Do any of the following apply?
    a. Is at least one clinical trial facility located within the US or a US territory?
    b. Is the clinical trial conducted under an FDA Investigational New Drug (IND) application or Investigational Device Exemption (IDE)?
    c. Does the clinical trial involve a drug, biologic, or device that is manufactured in or exported from the US or a US territory for clinical trial in another country?

If the answer to all 4 questions is YES then your clinical trial MUST be registered on Clinicaltrials.gov under Title 42 Section 11.22 under the Code of Federal Regulations.

Who is Responsible for Registering the Clinical Trial?

By law, the “responsible party” must register a clinical trial. The responsible party is defined as:

- The *sponsor* of the clinical trial

OR

- The PI of the clinical trial if so designated by a sponsor, grantee, contractor, or awardee. *For most clinical trials*, the PI should register the clinical trial, since it is the PI who is responsible for conducting the clinical trial, has access to and control over the data, has the right to publish the results of the clinical trial, and has all of the information necessary to complete the registration.
- For those clinical trials that involve an application for *an IND or IDE* the responsible party may be someone other than the PI. In the case of an industry sponsored clinical trial, the company may register the clinical trial. If the PI receives NIH or other government funding for a clinical trial, particularly those that do not include an IND or IDE application, the PI is the responsible party. To ensure that any extramurally funded clinical trial is properly registered, the PI should contact the sponsor for clarification.
- For multi-site clinical trials, the lead sponsor should take responsibility for registering the clinical trial. If the PI is not the lead sponsor, he or she should work with the other investigators and sponsors to ensure that the clinical trial is registered only once for the entire project.
- For *investigator-initiated clinical trials*, whether or not there is industry funding or, in fact, if there is no funding, the PI is considered the sponsor and is responsible for registering the clinical trial.

What is the Process for Registering a Clinical Trial?

When: Clinical trials should be registered before any subjects are enrolled. The FDA requires registration no later than 21 days after the first subject is enrolled; however, the ICMJE requires registration before the first subject is enrolled. To avoid publication restrictions imposed by the ICMJE, the responsible party (who may be the CN Investigator) should register the clinical trial before enrolling the first subject. Expect each registration to take approximately 1 to 2 hours.

How: Clinical trials are registered at Clinicaltrials.gov via a web-based data entry system called the Protocol Registration System (PRS). PRS users are responsible for ensuring that the information they provide on their clinical trial is correct, complete, readily understood by the public, and updated in a timely manner.

Children's National Health System

Who: Contact CTgov Liaison via email (ctgov@childrensnational.org) to set up a new account. The PCI Clinical Lead serves as the CTgov Liaison and PRS Administrator at Children's National.

Log in to the PRS: Once an account has been created, go to https://register.clinicaltrials.gov.

Complete the three fields on the Login screen:

- Organization: ChildrensRI
- Username: XXXXXX
- Password: XXXXXXXX

Create a Protocol Record: A clinical trial is registered in the system by creating a "protocol record." Under *Protocol Records* on the main menu, click the *Create* link and complete in a series of data entry screens. Clicking on the various fields will allow for access to instructions for that field. If researchers have any questions, they should email register@clinicaltrials.gov.

IMPORTANT NOTE: Using an electronic version of the protocol, researchers can copy and paste information into the requested data fields.

Review the Protocol Record: After filling in the last data entry screen, the *Edit Protocol* screen will appear. Review the information for accuracy and completeness and address any ERRORS, ALERTS, WARNINGS, or NOTES in the protocol record. If the record is incomplete or has errors, researchers cannot complete the registration process.

Mark the Protocol Record as Complete: If not, it will not be approved/released for publication, and the clinical trial will not be properly registered.

Keep the Protocol Record Current: An affirmative verification or update of the data in the protocol records is required every six months. Failing to login to the PRS and confirm or update the record(s) every six months, regardless of whether there has been a change to the clinical trial or not, may result

in a loss of funding and/or the inability to publish the results of a clinical trial in an ICMJE associated journal. If a study is closed to enrollment, terminated early, completed, etc., the PRS should be updated immediately.

IMPORTANT NOTE: Researchers will receive an email reminder from clinicaltrials.gov once every six months to update their clinical trial information.

Suggestions for Completing Certain Items: It will be helpful to have the protocol, the informed consent document, the IRB application, and the IRB approval letter on hand.

- ***Protocol Title:*** Record the title of the clinical trial exactly as it is listed on the protocol. This official title should be listed in both IRBear and ClinicalTrials.gov.
- ***Unique protocol ID***: Use your CNMC IRBear Protocol Registration Number – CNMCPro00xxxxxx (remember to add CNMC as part of this registration number).
- ***IND/IDE Number:*** If an IND or IDE is involved, enter the serial number. Refer to the IND/IDE letter from the FDA Review Board Approval Number.
- ***Board Name:*** Enter information for Children's National Health System IRB.
- ***Board Affiliation:***
  Office for the Protection of Human Subjects
  Children's National Health System
  111 Michigan Avenue, NW
  Washington, DC 20010-2970
- **Oversight Authority:** Institutional Review Board
- **Country:** United States

Record Verification Date: Update the record with the date of the most recent IRB approval. This date alerts the public as to whether the information is being kept current, particularly with reference to recruiting status and contact information.

Clinical Trial Start Date: Use the date of the first enrollment (or projected first enrollment), not the date of IRB approval.

Last Follow-up Date: Actual date that the last subject was examined or treated or the anticipated date when the last follow-up will occur.

George Washington University

Who: Contact the PCI Lead, Donna Embersit, to set up a new account via email: dembersit@mfa.gwu.edu.

Login to PRS: Once an account has been created go to https://register.clinicaltrials.gov

Complete the three fields on the Login screen:

- Organization: GWUniversity
- Username: XXXXXX
- Password: XXXXXXXX

Create a Protocol Record: A clinical trial is registered in the system by creating a "protocol record." Click on the *Create* link under *Protocol Records* on the Main Menu and fill in a series of data entry screens. Clicking on the various fields will allow for access to instructions for that field. If researchers have any questions, they should email: register@clinicaltrials.gov

IMPORTANT NOTE: Using an electronic version of the protocol, researchers can copy and paste information into the requested data fields.

Review the Protocol Record: After filling in the last data entry screen, the *Edit Protocol* screen will appear. Review the information for accuracy and completely and address any ERRORS, ALERTS, WARNINGS, or NOTES in the protocol record. If the record is incomplete or has errors, researchers cannot complete the registration process.

Mark the Protocol Record as Complete: If not, it will not be approved and released for publication and the clinical trial will not be properly registered.

Keep the Protocol Record Up-To-Date: An affirmative verification or update of the data in the protocol records that have not been closed or terminated is required every six months. Failing to login to the PRS and confirm or update the record(s) every six months, regardless of whether there has been a change to the clinical trial or not, may result in a loss of funding and/or the inability to publish the results of a clinical trial in an ICMJE associated journal.

IMPORTANT NOTE: Researchers will receive a reminder e-mail notification from clinicaltrials.gov once every six months to update their clinical trial information.

Suggestions for Completing Certain Items: Pertinent Source Information: It will be helpful to have the protocol, the informed consent document, the IRB application and the IRB approval letter on hand.

- ***Protocol Title:*** Record the title of the clinical trial exactly as it is listed on the protocol. This official title should be listed in both IRB and ClinicalTrials.gov.
- ***Unique protocol ID***: As a suggestion use your IRB Number – or, you may assign another ID that will identify the project.
- ***IND/IDE Number:*** If an IND or IDE is involved, enter the serial number. Refer to the IND/IDE letter from the FDA Review Board Approval Number.
- ***Board Name:*** Enter information for GWU IRB
- **Board Affiliation:**
  George Washington University
  Office of Human Research

2100 Pennsylvania Avenue NW Suite 300A
Washington, DC 20037

- **Oversight Authority:** Institutional Review Board
- **Country:** United States

Record Verification Date: The date of the most recent IRB approval. This date alerts the public as to whether the information is being kept current, particularly with reference to recruiting status and contact information.

Clinical trial Start Date: Use date enrollment began - not the date of IRB approval.

Last Follow-up Date: Actual date that the last subject was examined or treated or anticipated date when expected last follow-up will occur.

Do Adverse Events Need to be Posted?

Posting of adverse events (AE) is mandatory. AE posting is required for clinical trials of FDA-approved drugs, biologics, and devices. The following *must* be reported:

- Serious adverse events (SAE) and
- Non-serious AEs that exceed a frequency threshold of 5% in any arm of the clinical trial.

What Clinical Trial Results Need to be Posted?

The following results need to be posted:

- Posting basic clinical trial results is mandatory.
- Required for clinical trials of FDA-approved drugs and devices.
- Submission of results is required within twelve months after the primary endpoint completion date.

What is the Required Language for a Consent Form?

In the IRB consent form is a specific section about Clinicaltrials.gov for clinical trials that meet the requirement of an “applicable clinical trial” requiring registration as previously outline. The text from the sample template reads as:

ClinicalTrials.gov

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

The text in this statement must appear word-for-word as written. Only if the clinical trial does not meet the requirements for registration and is not listed on the Clinicaltrials.gov website should the text be deleted from the consent form.

Are there Additional Resources and Regulations Available?

Clinicaltrials.gov

- Clinialtrials.gov Main Website
- Protocol Registration System
- Factsheet
- Data Elements
- Frequently Asked Questions
- ACT Checklist (PDF)

Food and Drug Administration

- FDA Amendments Act (FDAAA) of 2007
- FDA Modernization Act (FDAMA) of 1997
- Public Law 111-85, Title VIII, Section 801

National Institutes of Health

- NIH Guide Notice NOT-OD-08-014 - Expand the Scope of ClinicalTrials.gov: Registration
- NIH Guide Notice NOT-OD-10-007 - Clarification to Date of Initiation and Status as an “Ongoing” Trial
- NIH Guide Notice NOT-OD-16-149 - Dissemination of NIH-Funded Clinical Trial Information