# University of Wisconsin

## Investigator Guidance to ClinicalTrials.gov

University of Wisconsin – Madison

Clinical Research Office

CT.gov_Help@clinicaltrials.wisc.edu

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# Quick Start to UW ClinicalTrials.gov Registration

Log into https://register.clinicaltrials.gov/ [CT.gov_Help@clinicaltrials.wisc.edu for user account]

- Organization: UWisconsin
- Username: per **Protocol Registration and Results System** (PRS, the data entry portal) email
- Password: temporary per PRS email, password can be changed by following the 'User Account' > 'Change Password'
- 'Help' menu and 'Definitions' in each section will assist in starting and populating a New Record, the Record Owner is ultimately the Study PI – per UW Policy

**Things to Keep in Mind While Registering Your Clinical Trial to ClinicalTrials.gov**

- NIH prefers 'Participant' to 'Subject' or 'Patient' in reference to trial participation
- CT.gov requires the record is written in the third person (do not use 'we' and 'our')
- Define all acronyms
- Avoid using symbols
- Subsequent protocol amendments must be reflected in the CT.gov record
- A full study protocol is required to be uploaded with results per FDAAA Law or NIH Policy

## ClinicalTrials.gov Protocol Section

### Study Identification

- **Unique Protocol ID:** Please use the UW IRB number
- **Brief Title:** Avoid using study design details (ie Phase II Crossover) in brief title
- **Secondary IDs:** Add all federal grant numbers here, other trial identifiers (ie. NCI CTRP), UDDS number will be added to assist in searching for department specific CT.gov records

### Study Status

- **Actual Study Start Date:** Date the first participant is enrolled (*Anticipated* until then)
- **Actual Primary Completion Date:** Date upon which data collection was complete to answer the Primary Outcome (*Anticipated* Primary Completion until that time)
- **Actual Study Completion Date:** From the participant perspective, it is the date upon which all study data collection is complete (*Anticipated* until that time, often the same as the Primary Completion Date)

### Sponsors/Collaborators

- **Sponsor:** University of Wisconsin, Madison
- **Responsible Party:** Sponsor
- **Collaborators:** include Funding Agencies

**Oversight**

- **U.S. FDA-regulated Drug or Device:** Required, UW guidance at this link
- **Human Subjects Review**
    - Board Name: Health Sciences or Minimal Risk Research Institutional Review Boards
    - Board Affiliation: University of Wisconsin – Madison
    - Phone: 608-263-2362
    - Email: AskTheIRB@HSIRB.wisc.edu
    - Address: 800 University Bay Drive, Madison, WI 53705

**Study Description - Brief Summary:** A layperson's description of the purpose, hypothesis, the participant, and how long they be will be on study. Aim for no more than 3 sentences.

**Conditions and Keywords:** important for trial search engines

**Study Design - Study Phase:** refers to Drug Interventions only, all other is N/A

**Arms and Interventions**

- Add all arms
- Add all interventions (any study drug, device, vaccine, procedure/surgery, radiation, behavioral, genetic, dietary supplement, combination product, diagnostic test, or other)
- Cross-reference Arms with their respective interventions

**Outcome Measures**

- All **Primary and Secondary Outcome Measures** listed in the Protocol are required to be registered and results reported (where relevant)
- The **Title** is required to indicate what will be reported, not the Aims of the study
- All scales / scoring systems are required to be defined in the **Description**, the total range of possible scores, what higher scores mean
- Only one measure per outcome measure, each measure has its own units
- The **Time Frame** is from the participant perspective, where a change is measured include all relevant time points

**Eligibility:** formatted in a bulleted list

**Contacts/Locations**

- **Study Contacts:** central contact person / email for study
- **Study Officials:** Required for ICMJE
- **Locations:** Required upon status change to 'Recruiting', individual sites have their own status in this section

**IPD Sharing Statement** – 'Yes' or 'No' is a requirement at registration per ICMJE (see page 13)

## What is ClinicalTrials.gov?

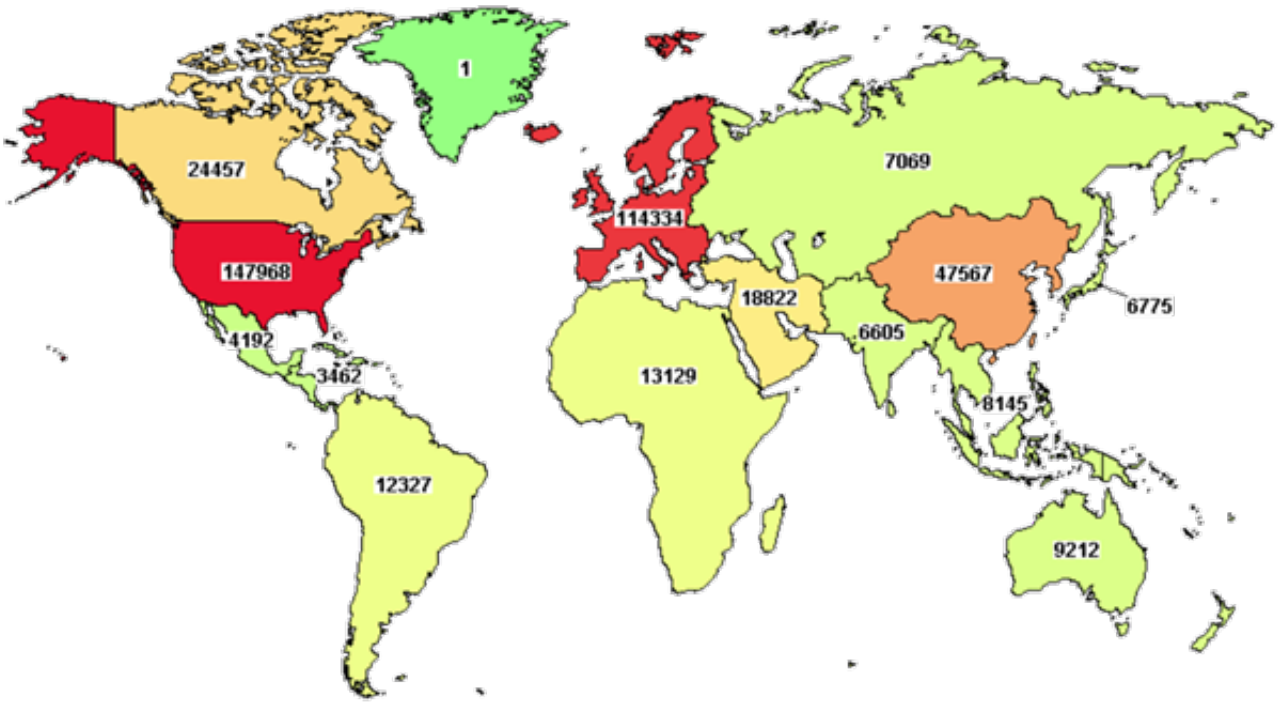
**ClinicalTrials.gov** is an online clinical study registry and results database for participants, their families, health-care professionals, researchers, and the public to access information about research studies involving human volunteers.

The intention of ClinicalTrials.gov is:

- To fulfill an ethical obligation to participants, their families, and the research community by providing timely study status updates, protocol amendments, and trial results
- To connect participants with clinical trial opportunities
- To provide a public mechanism to identify and understand the evidence base for specific biomedical questions
- To improve the evidence base by addressing publication bias; a large percentage of non-favorable trial results are not reported or refused publication
- To promote scientific integrity, transparency, and to build trust
- To house summary results for the purpose of leveraging existing volunteer efforts for additional study, particularly useful in trials underpowered for meaningful results
- To ensure appropriate allocation of research funds
- To help IRBs determine the appropriateness of a research study

## How can ClinicalTrials.gov benefit your research?

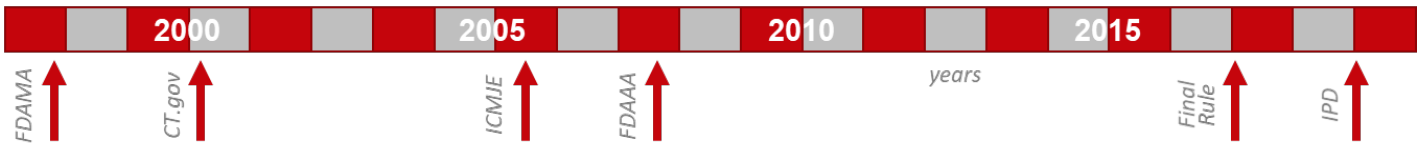
There are nearly 400,000 studies registered to ClinicalTrials.gov (**CT.gov**) from all 50 states and 220 countries (~52,500 with results reported as of Dec 2021 – click on the map below to drill down). This database is available to mine for information and will be of most use to those familiar with its evolution, structure, and rules that inform its content.




ClinicalTrials.gov provides a number of ways to search their database, by:

- Condition or Disease
- Country
- Recruitment Status
- Eligibility Criteria
- Study Type
- Results Posted
- Study Phase
- Funder Type
- Study Documents
- Related Terms
- Topic
- Map

*CT.gov Specialists often search the public site to see how specific trial-types have posted their results. It is a useful resource for understanding how best to report qualitative results, or how to customize experimental groups to allow for meaningful results reporting. There are literally tens of thousands of examples.*




## History of ClinicalTrials.gov

**November 1997:** Signed into law by President Clinton, the Food and Drug Administration Modernization Act (FDAMA) requires the NIH to create a database that is readily understood by the public for drug interventions treating serious or life-threatening diseases and conditions

**February 2000**: ClinicalTrials.gov launched in response to FDAMA

**July 2005**: International Committee of Medical Journal Editors (ICMJE) policy makes clinical trial registration to a public database a condition for publication. ICMJE is comprised of a core group of 15 member journals with ~6800 journals that follow their guidance (as of Dec 2021)

**September 2007**: Signed into law by President George W. Bush, the Food and Drug Administration Amendments Act (FDAAA) contains a legal mandate for a results database, requires registration and results reporting (all Primary and Secondary Outcomes per the Protocol) of non-phase I FDA-regulated interventional drug, biologic, and non-feasibility device trials (if FDA cleared/approved)

**January 2017**: Final Rule implementing FDAAA definition of Applicable Clinical Trials (ACTs) as non-phase I FDA-regulated interventional drug, biologic, and non-feasibility device trials (whether or not FDA approved, cleared, or licensed) with legal requirement for registration and results reporting

**January 2017**: NIH policy on the dissemination of NIH-funded clinical trials requires NIH-funded clinical trials (per their definition) to register and report results

**January 2019**: ICMJE policy to include Individual Participant Data (IPD) Sharing Plan at registration to ClinicalTrials.gov for the purposes of enabling secondary analysis

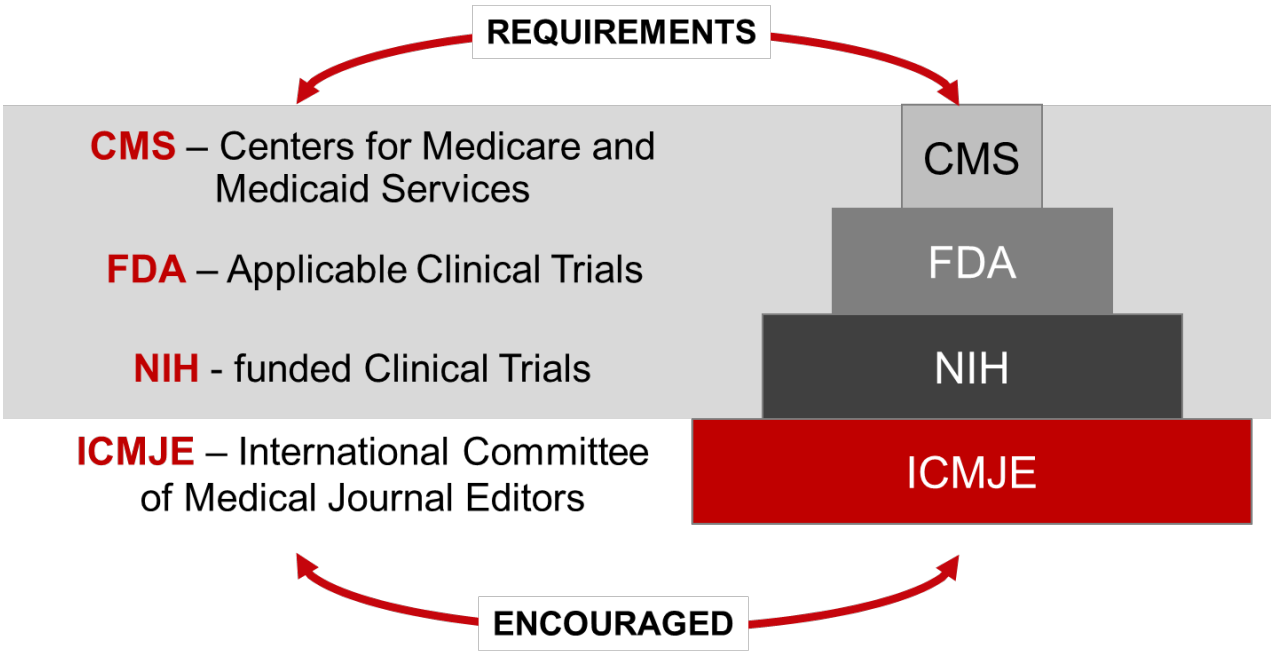
**January 2019**: The Revised Common Rule requires posting of consent forms to a public database for federally-funded studies initiated after this date and within 60 days of the date upon which all participant data collection is complete

**October 2020:** The Final NIH Policy for Data Management and Sharing was released. It was developed to 'promote the management and sharing of scientific data generated from NIH-funded or conducted research'. More guidance to follow as to if this Policy will affect CT.gov records.

**January 2023:** The Final NIH Policy for Data Management and Sharing will take effect.

## What Requires CT.gov Registration?

While any human research can be registered, the following requirements drive CT.gov Reporting at Academic Medical Centers.




**Centers for Medicare and Medicaid Services (CMS):** 'Qualifying Trials' of therapeutic intent that enroll participants diagnosed with disease that evaluate an item or service that falls within the Medicare benefit category require study protocols be registered to the public. At UW, protocol registration and NCT number assignment is required prior to SMPH Signoff in OnCore.

**Food and Drug Administration (FDA):** Applicable Clinical Trials (ACTs) must register and report results. ACTs (checklist next page, see 'Elaboration' for details) are interventional Phase 2-4 trials that study FDA-Regulated drugs, biologics, or device (with the exception of small feasibility device studies). Trial must have NCT number (be registered) within 21 days of first participant enrolled.

**National Institutes of Health (NIH):** Applicable to all clinical trials funded by NIH and IRB approved on or after January 18, 2017. NIH Policy requires public protocol registration and results reporting for all trials in which prospectively assigned human participants receive one or more intervention to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes. Trial must have NCT number (be registered) within 21 days of first participant enrolled. NIH ASSIST sources CT.gov to pre-populate annual reports due as a condition of funding.

**International Committee of Medical Journal Editors (ICMJE):** All clinical trials per WHO definition "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" require public protocol registration and *Individual Participant Data Sharing Plan* prior to first participant enrolled.

# Checklist for Evaluating Whether a Clinical Trial or Study is an Applicable Clinical Trial (ACT) Under 42 CFR 11.22(b) for Clinical Trials Initiated on or After January 18, 2017[1] (NOT FOR SUBMISSION[2])

Instructions: Answer the following questions to evaluate whether the study is an applicable clinical trial (ACT). Use the accompanying "Elaboration" for additional information to help answer the questions.

| Question | Yes | No |
|---|---|---|
| **1. Is the study interventional (a clinical trial)?**<br>*Study Type* data element is "Interventional" | ☐ | ☐ |
| **2. Do ANY of the following apply (is the answer "Yes" to at least one of the following sub-questions: 2a, 2b, OR 2c)?** | ☐ | ☐ |
| **a. Is at least one study facility located in the United States or a U.S. territory?**<br>*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. | | |
| **b. Is the study conducted under a U.S. FDA Investigational New Drug application (IND) or Investigational Device Exemption (IDE)?**<br>*U.S. Food and Drug Administration IND or IDE Number* data element is "Yes." | | |
| **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?**<br>*Product Manufactured in and Exported from the U.S.* data element is "Yes." | | |
| **3. Does the study evaluate at least one drug, biological, or device product regulated by the United States Food and Drug Administration (U.S. FDA)?**<br>*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." | ☐ | ☐ |
| **4. 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?**<br>For drug product trials, *Study Phase* data element is NOT "Phase 1" and for device product trials, *Primary Purpose* is NOT "Device Feasibility." | ☐ | ☐ |

**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 that is required to be registered under 42 CFR 11.22.**

[1] All pediatric postmarket surveillance studies of a device product as required by U.S. FDA under section 522 of the FD&C Act and for which FDA approved the plan on or after January 18, 2017 meet the definition of an ACT in 42 CFR Part 11.22(b) and are subject to the final rule requirements.

[2] The outcome generated by the checklist tool will not be retained by the Agency and will not be binding on either the user or any Government agency in any future actions.

## UW Expectations & Clinical Research Office Recommendations

- **UW expects** all clinical trial protocols that are required by FDAAA Law, NIH Policy, and CMS Policy to be registered, maintained in compliance, and results reported to CT.gov, as applicable
    - Requirement for clinical trial protocol registration is determined by the Principal Investigator in the IRB application via the Application for Review of Research Oversight at Wisconsin (ARROW) system and subsequently audited by a ClinicalTrials.gov Committee in the Vice Chancellor for Research and Graduate Education (VCRGE) Office of Research Compliance
    - UW Policy is for the Principal Investigator to be the CT.gov Record Owner, the Responsible Party is the 'Sponsor', and the Sponsor is the University of Wisconsin, Madison
- The **UW Clinical Research Office** recommends a best practice as follows
    - Registration of study protocol to CT.gov prior to opening to enrollment per ICMJE guidance, as a contingency for subsequent publication
    - List the NCT number on consent forms to connect participants with publicly available trial information. A trial may be registered to CT.gov prior to initial IRB approval to facilitate this.
    - Use OnCore to manage trial data in real time, CT.gov Specialists monitor OnCore for study status changes in order to keep UW CT.gov records compliant
    - If not otherwise required, consider voluntary protocol registration and summary results reporting for any trial that enrolls human **participants** in a good faith effort to meet ethical obligations to the participant, to grow the publicly available scientific evidence base, in the interest of scientific transparency, and to build trust in the community the study team is in service to.

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*CT.gov prefers the use of 'participant' to 'patient' or 'subject', and the UW CT.gov Specialists edit CT.gov Registration records to reflect this. The word 'participant' is empowering, the person feels voluntarily on study and able to make decisions about study participation. The words 'patient' and 'subject' connote a power dynamic where the person may feel disempowered and less engaged in their healthcare decisions.*

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## Who is Responsible for ClinicalTrials.gov Registration?

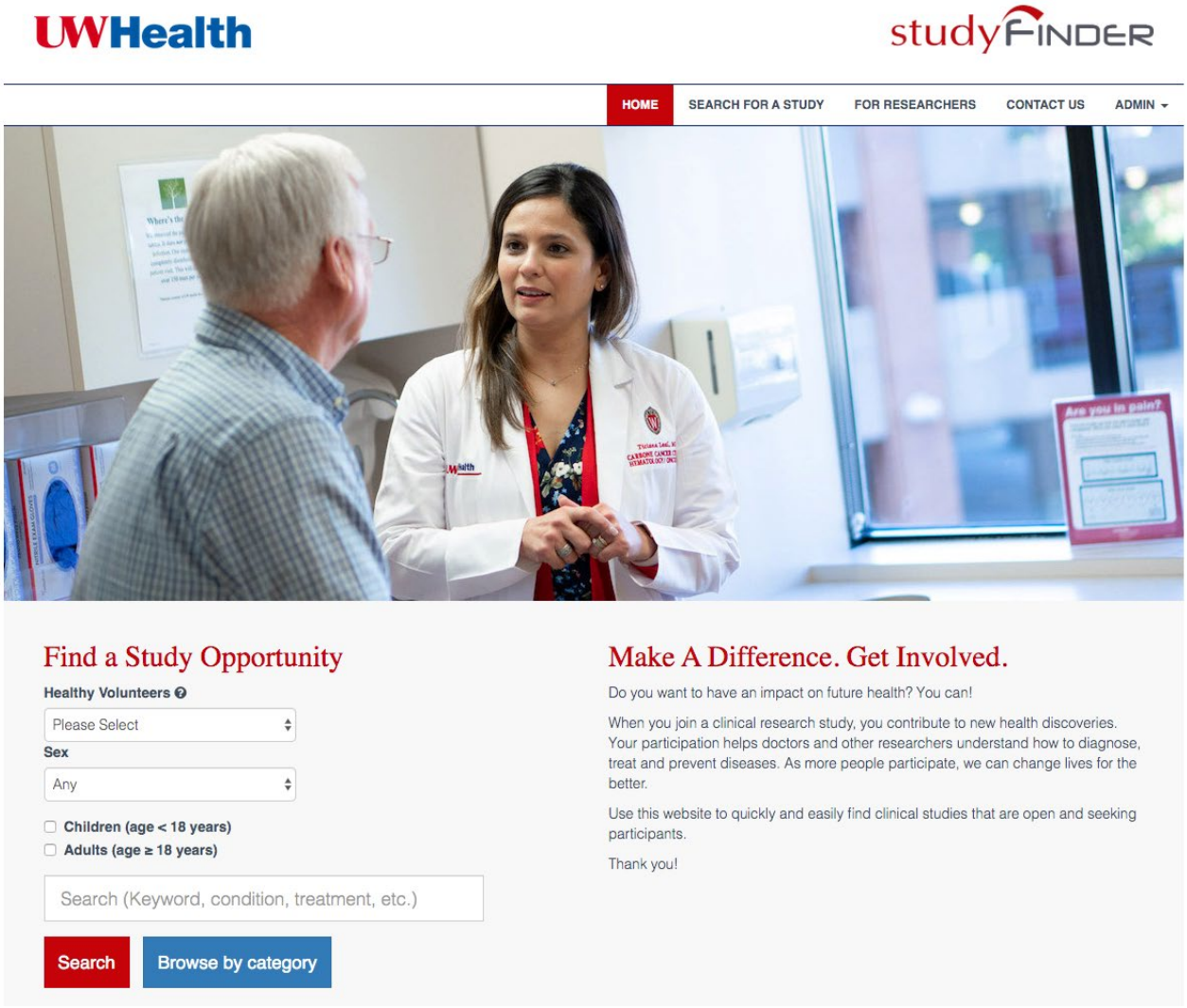
The **Study Sponsor** is responsible for registering the clinical trial protocol to CT.gov. This means if the study is Industry-Sponsored, the Industry-Sponsor is responsible for registration, maintenance, and results reporting to CT.gov.

The **UW-Madison Principal Investigator (or their delegate)** is responsible for ensuring CT.gov registration if one or more of the following apply:

- The trial is a UW Investigator-Initiated Trial (IIT)
- The trial is federally sponsored and UW-Madison is the only study site or the coordinating center
- The UW Investigator holds the IND for the agent being studied or the IRB has determined the agent is IND exempt
- The UW Investigator holds an IDE for the device being studied or the IRB has determined it to be of non-significant risk (NSR)

Find the Elaborations of Definitions of Responsible Party and Applicable Clinical Trials here.

If the PI (or delegated study team member) is responsible for registering the clinical trial to CT.gov and require a CT.gov user account, please contact the UW CT.gov Service Line for assistance.




## Who is Looking at ClinicalTrials.gov Records?

CT.gov has an average of 215 million page views a month and 145,000 unique visitors daily (data as of April 2019). Whether these visitors are researchers, physicians, funding agencies, concerned family members, potential participants, or clinical trials transparency advocates, the CT.gov database attracts attention. The UW is driven by scientific integrity and ethical obligation to participants to maintain accurate UW CT.gov records.

The UW launched **Study Finder** in Spring 2020 to connect potential participants to relevant UW clinical trials. Study Finder is an online tool to assist study teams with participant recruitment and will be located on the UWs public-facing website.

As CT.gov records are required to be up-to-date, Study Finder will source most trial data directly from CT.gov records. An OnCore record with the NCT number will be required to source PI, study contacts, keywords, and conditions. The PI is able to opt-out of Study Finder in OnCore.

**Note: If Industry-Sponsored, please confirm that UW is listed as a location on the Sponsor's CT.gov record in order for trial-relevant data to be pulled into Study Finder.*

## Individual Participant Data Sharing Plan

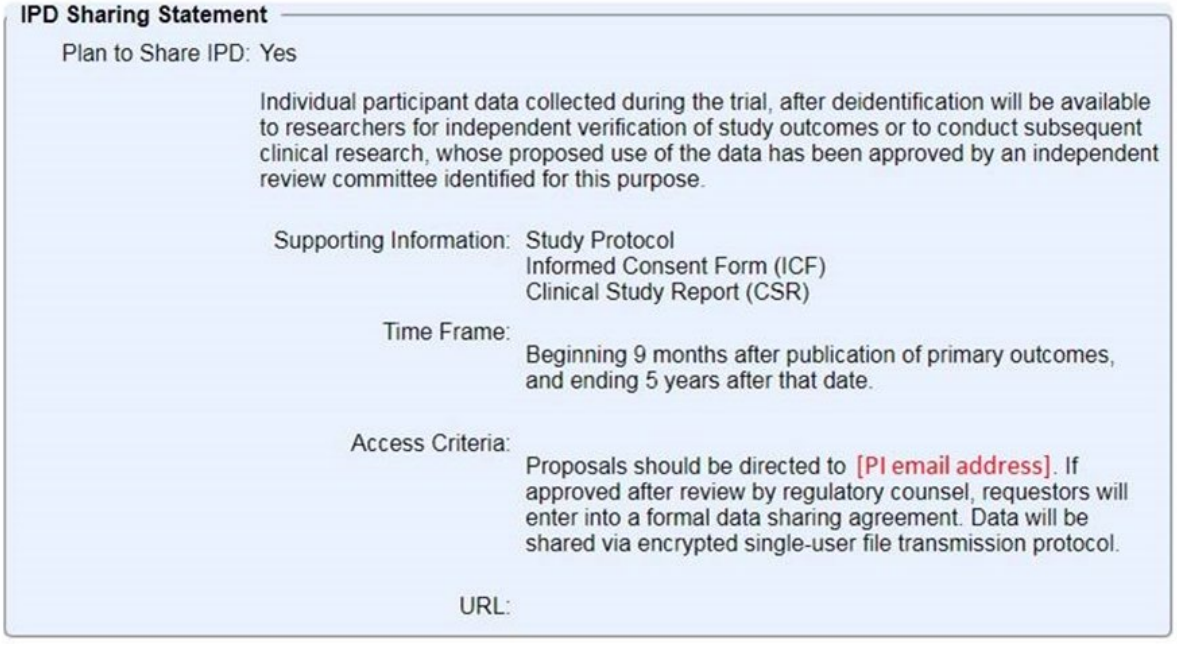
The CT.gov Protocol Registration Record has a section for an Individual Participant Data (IPD) Sharing Statement. The IPD Sharing Statement is required at CT.gov registration to as a contingency for future publication to journals that follow ICMJE guidelines (applicable for trials that began enrolling participants on or after 1/1/2019).

Find examples of IPD Sharing Plans at this link.

The guidance from ICMJE is that either **'yes' or 'no**' be selected to the 'Plan to Share IPD' question on the CT.gov Registration Record. **The option of 'undecided' is not acceptable**. Update the registration record in real time with any subsequent changes to the IPD Sharing Plan.

The following is a UW example of an IPD Sharing Statement that works well as template language.

- **Will IPD be available to other researchers?** Yes
- **What data will be shared?** Individual participant data collected during the trial, after deidentification.
- **What documents will be available?** Study Protocol, Informed Consent, Statistical Analysis Plan, Clinical Study Report
- **When will data be available?** Beginning 9 months after publication of primary outcomes, and ending 5 years after that date.
- **With whom will it be shared?** Researchers whose proposed use of the data has been approved by an independent review committee identified for this purpose.
- **For what types of analyses?** Independent verification of study outcomes or to conduct subsequent clinical research.
- **How will data be shared?** Proposals should be directed to [PI email here]. If approved after review by regulatory counsel, requestors will enter into a formal data sharing agreement. Data will be shared via encrypted single-user file transmission protocol.



**IPD Sharing Statement**

Plan to Share IPD: Yes

Individual participant data collected during the trial, after deidentification will be available to researchers for independent verification of study outcomes or to conduct subsequent clinical research, whose proposed use of the data has been approved by an independent review committee identified for this purpose.

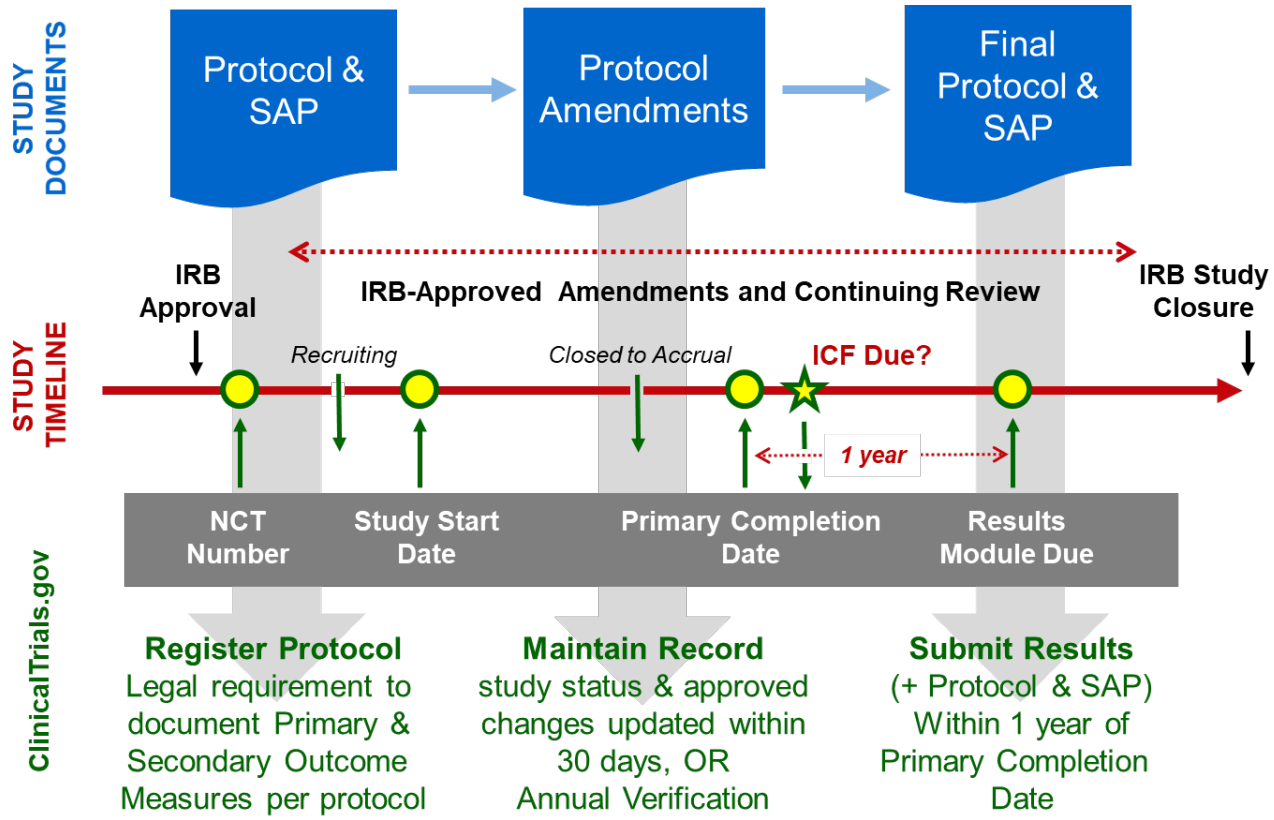
| | |
|---|---|
| Supporting Information: | Study Protocol<br>Informed Consent Form (ICF)<br>Clinical Study Report (CSR) |
| Time Frame: | Beginning 9 months after publication of primary outcomes, and ending 5 years after that date. |
| Access Criteria: | Proposals should be directed to [PI email address]. If approved after review by regulatory counsel, requestors will enter into a formal data sharing agreement. Data will be shared via encrypted single-user file transmission protocol. |
| URL: | |

## The Protocol Drives the ClinicalTrials.gov Record

In alignment with the intent of this database, CT.gov encourages all prospective clinical trials to have a protocol registration record and report summary results whether or not it is a legal or policy requirement.

While the PI is responsible for the accuracy of the CT.gov record (registration, maintenance, and results reporting), the UW has a **free** centralized ClinicalTrials.gov Service to assist in this process. The requirements for CT.gov record compliance are generally to submit study updates (protocol amendments, study status changes, results) to the public in real time.

The figure below illustrates the integration of study process, showing the evolution of study **documents** at the top, the study **timeline** in the middle, and the **CT.gov actions** below.




**Protocol Registration:**

- Recommended prior to first participant enrolled (**Study Start Date** on figure above) and include a statement about IPD Sharing Plan to meet the ICMJE policy (as a condition of publication)
- The protocol **can** be registered to CT.gov prior to IRB approval (protocol listed as 'submitted, approval pending' in the Oversight Section). This facilitates listing the NCT number on IRB-approved consent forms to help participants discover trial information.

- All Primary and Secondary Outcome Measures per the protocol are required to be listed in the CT.gov Registration record. It is important that outcome measures or endpoints for each study objective be clearly and individually defined in the protocol.
- UW CT.gov Specialists complete an initial review and edit of all new registration records per CT.gov Review Criteria and/or make recommendations to the study team to facilitate approval and assignment of a National Clinical Trial (NCT) number
- CT.gov Protocol Registration Quality Control reviews registration record, returns comments and/or assigns NCT number
- It can take up to 2 weeks from initial registration to assignment of an NCT number

**CT.gov Record Maintenance:**

- When the study is open to accrual, this status change must be updated in the public record within 30 days of the change. The Actual Study Start Date falls after the change in study status to 'Recruiting'.
- **Actual Study Start Date** is the date upon which the first participant is enrolled.
- All subsequent protocol amendments must be reflected in the public record within 30 days of IRB-approval. This includes changes in study team personnel who may be listed on the CT.gov record as a contact or otherwise have edit access to it.
- Final Enrollment is updated from *Anticipated* to *Actual* at Closed to Accrual
- Federally-funded studies require upload of consent form within 60 days of final data collection, or Actual Study Completion per CT.gov [Revised Common Rule]
- If there have been no changes to the CT.gov record in a year, the record will require **Annual Verification** to confirm that it is still up-to-date.
- Monitor and update of Anticipated and Actual **Primary and Study Completion Dates**

**Primary Completion Date** is the date on which the last participant in a clinical study was examined or received an intervention to collect final data for the primary outcome measure. Whether the clinical study ended according to the protocol or was terminated does not affect this date. For clinical studies with more than one primary outcome measure with different completion dates, this term refers to the date on which data collection is completed for all the primary outcome measures. **Primary Results are due within 1 year of this date.**

**Study Completion Date** is the date on which the last participant in a clinical study was examined or received an intervention/treatment to collect final data for the primary outcome measures, secondary outcome measures, and adverse events (the last participant's last visit). The study is complete from the participant's perspective.

The Primary and Study Completion Date are often the same date. For secondary measures or safety monitoring that require longer term follow-up, the Study Completion Date is a later date, and the remaining results are due within 1 year of this date.

**The duration of the Study registered to CT.gov is from the first participant enrolled to the last participant off study.**

**Results Reporting:**

- For Applicable Clinical Trials (ACTs) and relevant NIH-funded trials, results for Primary Outcome Measures are due within one year of the Primary Completion Date, results for all Primary and Secondary Outcome Measures are due within one year of the Study Completion Date. **Study Completion Date is not the IRB Closure Date**.
    - Ideally, results are submitted ~2 months in advance of the due date to allow for review, comment, and corrections
- Results data include: participant flow, baseline characteristics, outcome measures, adverse events data, and upload of **final study protocol with statistical analysis plan (SAP)**
    - Data for each section should be individually informative and internally consistent as there is no supporting text
- UW CT.gov Specialists complete an initial review of results per Results Review Criteria and make recommendations to the study team to facilitate CT.gov approval
- Additionally, subsequent manuscripts can be linked to the CT.gov record

| **Registration** | *NCT # assigned prior to first participant enrolled* | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | months | | | | | | | | | | | |
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 |
| **Maintenance** | *update record within X months of study change* | | | | | | | | | | | |
| Study Status Changes | X | | | | | | | | | | | |
| Protocol Amendments | X | | | | | | | | | | | |
| * Final Enrollment | X | | | | | | | | | | | |
| * Upload Consent Form | | X | | ** from date upon which all data collection* | | | | | | | | |
| Primary Completion Date | X | | | | *is complete* | | | | | | | |
| Study Completion Date | X | | | | | | | | | | | |
| Annual Verification | | | | | | | | | | | | X |
| **Results Reporting** | *months from Actual Primary/Study Completion Date* | | | | | | | | | | | |
| Open Results Module | | | | | | X | | | | | | |
| Populate Result Module | | | | | | | X | X | X | | | |
| Submit Results Module | | | | | | | | | | X | | |
| PRS Review Process | | | | | | | | | | X | X | |
| Results Posted | | | | | | | | | | | | X |

## Potential Consequences for Noncompliance

**International Committee of Medical Journal Editors (ICMJE):** The primary consequence of failure to comply with ICMJE Policy is refusal to publish. Increasingly, PIs are discovering that journals have their own interpretation of ICMJE Policy and as a result, the UW recommends contacting target journals in advance to understand their requirements to publish (ie, do they require submission of protocol? Do they require an observational study to have an NCT number?)

**Food and Drug Administration (FDA):** The FDA threatens civil monetary penalties (currently adjusted up to $12,462/day) for noncompliance. Failure to comply with FDAAA Law may also result in loss of US Department of Health and Human Service (HHS) funding, FDA Sanctions in the form of a 483 letter, and public notice of non-compliance. FDAAA Trials Tracker is a database that mines the ClinicalTrials.gov database to publicly share trials with overdue results.

**National Institutes of Health (NIH):** The primary consequence of failure to comply with NIH Policy is loss of NIH funding.

**Centers for Medicare and Medicaid Services (CMS):** CT.gov registration and input of NCT number into OnCore prior to SMPH Signoff is UW Policy for CMS trials. Therefore, the primary consequence for not having an NCT number assigned is delayed initiation of the trial.

| *Reporting Requirement* | ICMJE Guidance | NIH Policy | FDAAA Law | CMS |
|---|---|---|---|---|
| **Scope** | Registration | Registration & Results | Registration & Results | Registration |
| **Phase** | All | All | Phase II - IV | All |
| **Intervention Type** | All clinical trials per WHO definition | All clinical trials (per NIH definition) including behavioral interventions | Drug, biologic, & device products regulated by the FDA | "qualifying trial" of therapeutic intent evaluating Medicare benefit & enrolling participants with diagnosed disease |
| **Funding Source** | Any | NIH | Any | Any |
| **Register before** | first participant enrolled | within 21 day of first participant enrolled | within 21 days of first participant enrolled | SMPH signoff |
| **IPD Sharing Plan** | required at registration | N/A | N/A | N/A |
| **Report Results** | N/A | 1 year of Primary Completion | 1 year of Primary Completion | N/A |
| **Enforcement** | Refusal to Publish | Loss of NIH funding | Civil Monetary Penalties (up to $12,462*/day); Loss of HHS funding; FDA Sanctions (483 Letter); public Notice of Noncompliance | Delayed initiation; Billing delayed or denied |

** 2021 adjustment for inflation*

## UW ClinicalTrials.gov Service Line

The UW Clinical Research Office employs 2 full-time CT.gov Specialists. The UW has recognized the need for this centralized service to assist PIs with required CT.gov registration, maintenance, and results reporting process. **This service is free of charge to UW study teams who would like assistance.**

Below is an outline of the process:

**Registration** - UW recommends registration prior to first participant enrolled. It can take up to **2 weeks** from initial registration to assignment of an NCT number.

- The PI (or their delegate; hereafter 'study team') may choose to populate CT.gov record
  - For guidance into this process, follow this link
  - To see how CT.gov will review the registration record click here
  - CT.gov Specialists will review the registration record prior to releasing it to CT.gov and contact the study team to make changes as necessary
  - CT.gov Specialist releases record for Protocol Registration and Results System (PRS) Review
  - Review Comments may be returned, once review comments are addressed, CT.gov will assign an NCT number
- If the study team would like assistance from UW CT.gov Specialists:
  - Study team shares the protocol with CT.gov Specialist
  - Study team determines if study will ultimately require results reporting per FDAAA Law or per NIH Policy. Is this an Applicable Clinical Trial (ACT)?
    - If yes, please be aware of results reporting requirements (see below)
    - Consider using OnCore to assist in Record Maintenance and Results Reporting; CT.gov Specialists monitor status changes in OnCore
  - CT.gov Specialist populates a draft of the Protocol Registration Record
  - CT.gov Specialist provides the study team access to the CT.gov record
  - Study team confirms Oversight and Study Design sections are populated correctly
  - PI reviews registration record and approves or edits the record
  - CT.gov Specialist releases record for PRS Review
  - Review Comments may be returned, once review comments are addressed, CT.gov will assign an NCT number

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*The UW recognized the need for a centralized ClinicalTrials.gov service to assist Research Groups with ethical, legal, and policy-driven Registration, Maintenance, and Results Reporting requirements. The UW ClinicalTrials.gov Specialists participate in a nationwide CT.gov Taskforce to keep on top of evolving requirements and process changes.*

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**CT.gov Record Maintenance** (Status Changes, Protocol Amendments, Verification)

- **Status Changes**: Study team updates study status within **30 days** of change, OR requests CT.gov Specialist to do this on their behalf
    - Actual Study Start Date – date on which the first participant is enrolled
    - Federally-funded clinical trials require ICF is uploaded to a public database within **60 days** of date that all data collection is complete per the Revised Common Rule
    - Upon study completion, relevant manuscripts can be linked to the CT.gov record
- **Protocol Amendments:** CT.gov Specialist will have view access to ARROW records and are notified of IRB-approved protocol amendments
    - CT.gov Specialist will update CT.gov record to reflect protocol amendment (unless study team is actively maintaining the record)
    - Study team reviews and approves the record
    - CT.gov Specialist releases record to CT.gov
- **Verification:** CT.gov requires all CT.gov records to be verified annually
    - If there were no status changes or protocol amendments, verification involves careful review and relevant update of the public record and verification date
    - CT.gov Specialist will reach out to the study team to verify the record if deadline is approaching

**Results Reporting** (If Applicable Clinical Trial or per NIH Policy, as determined at registration)

- CT.gov Specialist will follow up with the study team after the Actual Primary Completion regarding Results Reporting requirements
    - Results are due for the Primary Outcome Measures within 1 year of the Primary Completion date –date upon which data collection was complete to answer all Primary Outcome Measures
    - Results are due for Secondary Outcome Measures within 1 year of the Study Completion date – the date upon which all data collection is completion to answer all outcome measures and adverse events (this is not the IRB closure date)
    - Summary Results submitted in tabular format to CT.gov are not considered as 'prior publication' by the ICMJE and will not be a barrier to journal publication
- Study team gets familiar with the Results Module
    - Participant Flow (data can be pulled from OnCore)
    - Baseline Characteristics (data can be pulled from OnCore)
    - Outcome Measures Data
    - Adverse Events Data (data can be pulled from OnCore)
    - **Full study protocol and statistical analysis plan must be uploaded with results**
- CT.gov Specialist will assist in this process
- Subsequent manuscripts can be linked to the CT.gov record

## Helpful Publications & Resources


Bergeris et al, 2018, *Trialists' Intent to Share Individual Participant Data as Disclosed at ClinicalTrials.gov*, JAMA, vol. 319, no. 4, p. 406-408, PMID 29362784.

Fain et al, 2018, *Results Reporting for Trials With the Same Sponsor, Drug, and Condition in ClinicalTrials.gov and Peer-Reviewed Publications*, JAMA, vol. 178, no. 7, p. 990-992, PMID 29532058.

Lynch et al, 2017, *Reaping the Bounty of Publicly Available Clinical Trial Consent Forms*, IRB, vol. 39, no. 6, p. 10-15 PMID 29881132.

Tse et al, 2018, *How to avoid common problems when using ClinicalTrials.gov in research: 10 issues to consider*, BMJ, vol. 362, PMID 29802130.

Zarin et al, 2017, *The role and importance of clinical trial registries and results databases*. In: Gallin JI, Ognibene FP, Johnson LL eds, Principles and Practice of Clinical Research. 4th ed. London: Academic Press, 111-25.


- Public database >>> ClinicalTrials.gov
- Register a study >>> https://register.clinicaltrials.gov/
- PRS Registration Review Criteria >>> https://prsinfo.clinicaltrials.gov/ProtocolDetailedReviewItems.pdf
- PRS Results Review Criteria >>> https://prsinfo.clinicaltrials.gov/ResultsDetailedReviewItems.pdf
- PRS Guided Tutorial for the Results Module
- FDAAA Trials Tracker >>> http://fdaaa.trialstracker.net/
- ICMJE >>> http://www.icmje.org/recommendations/browse/publishing-and-editorial-issues/clinical-trial-registration.html
- NIH Compliance >>> https://grants.nih.gov/policy/clinical-trials/reporting/steps.htm
- FDAAA Law >>> https://www.federalregister.gov/documents/2016/09/21/2016-22129/clinical-trials-registration-and-results-information-submission
- CMS Clinical Trial Policy >>> https://www.cms.gov/Medicare/Coverage/Coverage-with-Evidence-Development/Downloads/Mandatory-Clinical-Trial-Identifier-Number-QsAs.pdf
- UW Clinical Trials kb page >>> https://kb.wisc.edu/gsadminkb/34044
- UW Processing the Departure of a Principal Investigator Guidance >>> https://kb.wisc.edu/hsirbs/page.php?id=77592#closure


The ClinicalTrials.gov Specialists offer an Introduction to ClinicalTrials.gov Presentation and one-on-one training to help your team get familiar with Registration, Maintenance, and Results Reporting Requirements. We are happy to present at graduate seminars in an effort to train future investigators. Please reach out via email to schedule a time.