



MCW Office of Research Standard Operating Procedure

CLINICALTRIALS.GOV REGISTRATION & COMPLIANCE

Unit: Human Research Protections Program (HRPP), Office of Research

Applies to: Faculty and Staff involved in human subjects research at MCW

PURPOSE

The purpose of this SOP is to provide guidance to ensure consistency across MCW to properly register a study in the *ClinicalTrials.gov* Protocol Registration and Results System (PRS); to complete standard reporting fields and summary results information; and define Principal Investigator/study staff responsibilities after trial registration to maintain institutional compliance.

In accordance with Federal regulations FDAAA 801 and 42 CFR Part 11 (per the Final Rule, effective 1/18/2017), an applicable clinical trial (ACT) must be registered on *ClinicalTrials.gov* (CT.gov), the clinical trial registry and results data bank operated by the National Library of Medicine (NLM) of the National Institutes of Health (NIH). Further, NIH policy requires that NIH-funded awardees submit registration and results information for all NIH-funded clinical trials, whether they are covered by FDAAA requirements. It is critical that ACTs be registered not only to meet the needs of patients, the public and the research community, but also to avoid the civil and monetary penalties which may accompany failure to register applicable clinical trials.

SCOPE

This SOP applies to all faculty and staff involved in research at the Medical College of Wisconsin (MCW), Froedtert Hospital (FH), Children's Wisconsin (CW) and Versiti/Blood Center of Wisconsin, who will be adding and editing records in PRS under the MCW organizational username **MCWisconsin**

DEFINITIONS

- **Applicable Clinical Trial (ACT):** The World Health Organization (WHO) defines a clinical trial as "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. Interventions include but are not restricted to drugs, cells and other biological products, surgical procedures, radiological procedures, devices, behavioral treatments, process-of-care changes, preventive care, etc." Various organizations and entities require Applicable Clinical Trials be registered on ClinicalTrials.gov, including the NIH, ICJME and CMS. Please note that organizations may differ in their definition of an ACT and their requirements for registration (see table below).
- **ClinicalTrials.gov:** Also known as CT.gov, is a web-based resource designed to increase transparency in research and to provide public access to information on clinical trials. CT.gov was developed by the National Library of Medicine (NLM) as part of a mandate from the Food and Drug Administration Modernization Act (FDAMA) and further enhanced to include a results database as part of a mandate from FDAAA.

- **Departmental Subject Matter Expert (SME):** Individuals identified by each respective MCW department to facilitate RP and ROs with accurate CT.gov submissions, maintaining compliance by addressing queries and ensuring completion of annual updates.
 - **International Committee of Medical Journal Editors (ICMJE):** Requires clinical trial registration in a public registry as a condition for publication. ClinicalTrials.gov meets all the criteria they set forth for an acceptable public registry.
 - **NCT Number:** Each study registered on CT.gov receives an NCT number, or unique study identifier. The format for the ClinicalTrials.gov registry number is “NCT” followed by an 8-digit number, e.g.: NCT00000123.
 - **Primary Completion Date:** The date the final subject was examined/received an intervention for purposes of final collection of data for the primary outcome
 - **Protocol Registration and Results System (PRS):** A web-based data entry system used to register the clinical studies and submit results information to CT.gov. PRS staff will also review submissions before publishing to the public site or submit back to RO/RP for further clarification.
 - **Results Information:** Per CT.gov requirements, results information includes participant flow, demographic and baseline characteristics, outcomes and statistical analyses, adverse events, the protocol and statistical analysis plan.
 - **Record Owner (RO):** May be the Principal Investigator but is often his/her designee (i.e. study coordinator, regulatory specialist). The RO is responsible for data entry and updating the ClinicalTrials.gov record in a timely manner. They must communicate with the RP, so the record is released in the required time frame.
 - **Responsible Party (RP):** The entity or individual who is ultimately responsible for registering a clinical and submitting clinical trial information to PRS and releasing the record. The RP has the sole ability to release the record to PRS. The RP may be:
 - The sponsor of the clinical trial
 - The PI of the trial (providing the PI is responsible for conducting the trial), has access to and control over the data from the clinical trial and has the right to publish the results of the trial.
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PROCEDURES

A. ACT Determination

The Responsible Party (RP) will verify their trial needs to be registered on ClinicalTrials.gov per FDAAA, FDDAMA, CMS, ICMJE or NIH requirements. See table below for reference. The MCW Office of Research is reviewing ways to assist with ACT determination process.

PLEASE NOTE: For all ACTs, registration on ClinicalTrials.gov should be completed in parallel with the IRB submission. While NCT registration is not a requirement for initial IRB submission or approval, registration is required prior to the first subject enrollment.

B. Account Registration

To create an account in the Protocol Registration and Results System (PRS):

- Send an email to the MCW PRS administrators at mcwcto@mcw.edu
- Include the full name, role, email address and phone number of all study team members requiring access.
- Enter "Request CT.gov account" in the subject line.

The PRS administrator will create an account for the requested study team members. Study team members will receive an email from PRS with log-in information and a temporary password. After logging into PRS (<https://register.clinicaltrials.gov/>) the temporary password should be changed. Once you have a PRS account, it can be used for future study record submissions.

The CTSI PRS Administrators will assist with:

- Establishing user accounts and resetting passwords
- Department SME and study team education (i.e. initial record submission, annual maintenance and results submission)
- Changing the ownership of a study
- Transferring study(s) to or from other institutions
- Acting as a liaison between PRS and the investigator when necessary

C. Study Registration Criteria & Timeline

While registration timelines differ by various entities, MCW requires that all ACTs must be registered on ClinicalTrials.gov prior to enrollment of first study subject. This is in accordance with ICMJE requirements.

Entity	Phase I	Phase II-IV	Other Interventional Trials	Registration Timeline	MCW Required Timeline
ACT per FDAMA, FDAAA, Public Law 110-85	NO	YES	NO	Within 21 days of 1 st Subject enrollment	Prior to enrollment of 1 st subject
NIH	YES	YES	YES	Unspecified	Prior to enrollment of 1 st subject
ICMJE	YES	YES	YES	Prior to enrollment of 1 st subject	Prior to enrollment of 1 st subject
CMS	YES	YES	YES	Prior to claims submission	Prior to enrollment of 1 st subject

D. Data Element Standards

The study team (RO/RP) will complete the record for PRS review, with guidance from their Department SME. A list of data element standards follows:

1. Organization's Unique Protocol ID – use the MCW IRB number (i.e. PRO#####)

* Organization's Unique Protocol ID:

Full IRB Unique ID

2. If NIH funded, the "Secondary ID" will be the NIH Grant #.

[*] Secondary IDs:
(if any)

+ Add Secondary ID

3. Oversight Data Element

Board Name: Medical College of Wisconsin Institutional Review Boards
Affiliation: Medical College of Wisconsin
Phone: 414-955-8422
Email: IRBOffice@mcw.edu
Address: Institutional Review Board
Office of Research
8701 Watertown Plank Road
Milwaukee, WI 53226-0509

The Record Owner (RO) will complete the record in PRS. The Responsible Party (RP) will review AND release the record to PRS once it has been completed. The Department SME will review the record and ensure the PI/RP releases it. Once submitted, PRS staff will review the record submissions before publishing to the public site or submit back to RO/RP for further changes. The study team will be notified of "PRS Comments." Once the comments are addressed, the RP will be required to release the record again in what may be an iterative process. After PRS approves the record, an NCT number will be assigned within three to five days and the record will be made public. **Please note: a record may not be deleted once it is assigned an NCT number.**

E. Record Management

To remain in compliance with the regulations, the Responsible Party is accountable for the following:

- **Annual Record Verification:** CT.gov records are required to be reviewed and verification date updated yearly. It is strongly encouraged the RP/RO/Department SME log-in to PRS monthly to address any errors in their respective study records.
- **Change in Study Status:** For any changes in study status (i.e. open/closed to enrollment, primary completion date), the CT.gov record must be updated within 30 days of status change.
- **Change in PI and/or Faculty Departure:** If the PI/RP is leaving MCW, the record must be transferred to a new local PI or to their new institution prior to their departure. If the PI/RP is unavailable or unresponsive, the department/unit chair or chief becomes responsible for the record, including results reporting.

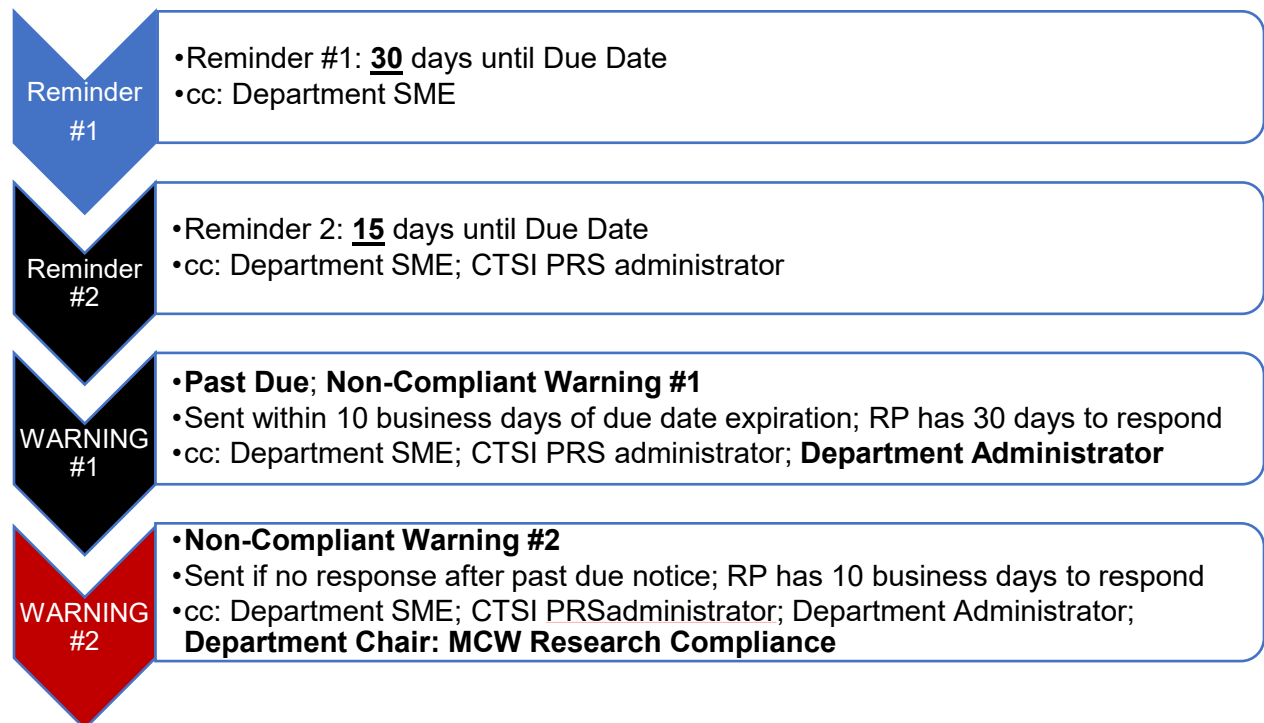
- **Study Results Submission:** Study results must be posted to the Ct.gov record within one year of the primary completion date, regardless if study closed prematurely. Please note that some statistical data may be required to meet PRS requirements.
- **Study Closure/Document posting:** Effective 1/21/2019 with the Common Rule, an IRB-approved version of the informed consent document must be uploaded to CT.gov upon study closure.

COMPLIANCE

All trials published on CT.gov under the MCW username (MCWisconsin) will be monitored by the MCW Office of Research for ongoing institutional compliance. Effective October 2023, ACT determination will be incorporated into the eBridge system to alert study teams when CT.gov reporting is required. The CPR SmartForm will remind study teams to review their records annually and the Final Report SmartForm will remind study teams to report results when the trial is closed, when applicable.

The RP/RO for CT.gov records that are due for annual review or appear on the MCW institutional problem list for failure to address outstanding queries will be notified based on the following escalation timeline:

NON-COMPLIANCE COMMUNICATION TIMELINE



Penalties for failing to register and/or maintain compliance

The federal law allows for significant civil monetary penalties, and for federally funded trials, the withholding or recovery of grant funds for Responsible Parties who fail to register or provide study results information for applicable clinical trials. As of July 2022, each PRS record that is delinquent for posting results may be assessed civil monetary penalties of over \$13,237 per occurrence and \$13,237 per day if the record is not brought into compliance within 30 days. Failure to maintain study records also has a direct impact on MCW's institutional compliance rate. Further, most medical journals will not publish clinical trial results unless the trial was registered before the first subject was enrolled.

Consequences for continued non-compliance may result in a hold on current study funding, or future funding opportunities may not be made available to the Principal Investigator. MCW Office of Research may also halt an investigator's future IRB and GCO reviews until all record corrections are completed. Departments are responsible for any financial penalties that might be levied against the institution for PI/RP non-compliance

REFERENCES

- [Clinical Trials Registration](#) (internal CTSI website)
- [ClinicalTrials.gov](#)
- NIH Clinical Trial Definition [FAQ](#)
- [NIH-Funded Trials in ClinicalTrials.gov](#)
- [42 CFR Part 11 Final Rule](#)
- [ICJME Registration Policy](#)
- [Medicare Clinical Trial Policies](#)
- [Checklist for Applicable Clinical Trials Under 42CFR11](#)
- [NIH Decision Tool for Applicable Clinical Trials](#)
- [FDA Guidance Document: Civil Money Penalties Relating to the ClinicalTrials.gov Data Bank \(August 2020\)](#)

SUPPORTING DOCUMENTS:

SOP Process Map: CT.gov Registration & Compliance

Effective Date:	10/05/2023
Version number:	2.0
Previous Version/date:	4/30/2019
Responsible Office:	Office of Research - Administration

Approval Date:	10/02/2023
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