

UC SAN DIEGO CLINICALTRIALS.GOV REQUIREMENTS

The Food and Drug Administration Amendments Act (FDAAA), National Institutes of Health (NIH) and International Committee of Medical Journal Editors (ICMJE) require registration of certain studies on a publicly accessible website (ClinicalTrials.gov). UC San Diego Principal Investigators should ensure registration of the applicable investigator initiated studies regardless of fund source (industry initiated clinical trials will be registered and maintained by the sponsor).

I. Principal Investigator Responsibilities:

At UC San Diego, the Principal Investigator is responsible for the registration and reporting of results on ClinicalTrials.gov as well as the accuracy and completeness of the submitted information. The Principal Investigator must establish an individual Protocol Registration and Results System (PRS) account in order to register and submit results information for their studies. Directions for the PRS account set up and registration are available at <https://clinicaltrials.gov/ct2/manage-recs/how-apply>.

Dissemination Plan:

Below is suggested language for the Principal Investigator to include in NIH grant applications regarding their dissemination plan. This language reflects what the Principal Investigator should complete as a minimum requirement and can be modified to meet the needs of the project.

XX (insert name or role, can be a designee) will be responsible for handling ClinicalTrials.gov requirements for this project under the Principal Investigator's oversight. S/he will register the trial prior to enrolling the first subject. Once a record is established, s/he will confirm accuracy of record content; resolve problems; and maintain records including content update and modifications. S/he will also be responsible for aggregate results and adverse event reporting at the conclusion of the project.

The Principal Investigator should also add the specifics related to the clinical trial as well as ensure that the informed consent form(s) for the clinical trial will include a specific statement relating to the posting of the clinical trial information and results at ClinicalTrials.gov.

II. Summary of the Requirements for each Authority:

The information below will provide a summary of the requirements for each authority. Please note that studies that do not meet the FDAAA requirements and are not NIH funded, may still meet the ICMJE requirements.

A. The Food and Drug Administration Amendments Act (FDAAA):

The FDAAA requires that all investigators who perform an "applicable clinical trial" must ensure that the study is registered on ClinicalTrials.gov. ClinicalTrials.gov is the national registry of federally and privately supported research studies conducted in the United States and around the world. ClinicalTrials.gov is meant to be utilized as a tool to improve transparency and reduce duplication of effort.

What is an Applicable Clinical Trial:

Studies considered to be an "applicable clinical trial" include:

- Trials of Drugs and Biologics: Controlled, clinical investigations, other than Phase 1 investigations, of a product subject to FDA regulation; and
- Trials of Devices: Controlled trials with health outcomes, other than small feasibility studies, and pediatric post-market surveillance.

Applicable clinical trials generally include interventional studies (with one or more arms) of drugs, biological products, or devices that are subject to FDA regulation, meaning that the trial has one or more sites in the United States (U.S.), involves a drug, biologic, or device that is manufactured in the U.S. (or its territories), or is conducted under an investigational new drug application or investigational device exemption.

Registration Timeline:

Applicable studies initiated after September 27, 2007, or initiated on or before that date and were still ongoing as of December 26, 2007, must be registered. In addition, applicable studies initiated after September 27, 2007, and that do not involve a serious or life threatening disease or condition must be registered in full by September 27, 2008. New studies must be registered within 21 days of enrollment of the first subject and updated at least on an annual basis.

Results Reporting:

Results must be submitted for applicable studies within 12 months after the completion date, which is defined as the date of the final data collection for the primary outcome measure. To view the data elements required for results reporting, please see http://prsinfo.clinicaltrials.gov/results_definitions.html.

Consequences for Failure to Comply with the FDAAA Requirements:

The consequences of noncompliance may include public notices of noncompliance and violations, withholding of federal funds, FDA sanctions and civil monetary penalties (up to \$10,000 per day).

B. NIH Funded Studies:

Effective January 2017, the NIH requires registration and results reporting for all NIH funded clinical trials, regardless of whether or not they are subject to the FDAAA. As part of the application or proposal process, applicants seeking NIH funding will be required to submit a plan for the dissemination of NIH funded clinical trial information that will address how the expectations of the NIH policy will be met. NIH funded awardees and investigators conducting clinical trials funded in whole or in part by the NIH will be required to comply with all terms and conditions of award, including following their plan for the dissemination of NIH-funded clinical trial information.

Registration Timeline:

Clinical Trials must be registered within 21 days of enrollment of the first subject and updated on an annual basis.

Results Reporting:

Results must be submitted within 12 months of the final data collection for the primary outcome.

Consequences for Failure to Comply with the NIH Requirements:

Compliance is a term and condition of an award. The consequences of noncompliance may include withholding of NIH funding.

C. The International Committee of Medical Journal Editors (ICMJE):

The ICMJE requires registration of clinical studies in order for results to be published in member medical journals and has adopted a broader definition of a clinical study, consistent with the definition developed by the World Health Organization. The ICMJE's definition of a clinical trial is, "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."

1. Health-related interventions: Include any intervention used to modify a biomedical or health-related outcome (for example, drugs, surgical procedures, devices, behavioral treatments, dietary interventions, etc.).
2. Health outcomes: Include any biomedical or health-related measures obtained in patients or subjects, including pharmacokinetic measures and adverse events.
3. Purely observational studies (those in which the assignment of the medical intervention is not at the discretion of the investigator) do not require registration.

Registration for applicable studies with ICMJE must be done prior to enrollment of the first subject. The ICMJE does not require submission of results.

Consequences for Failure to Comply with the ICMJE Requirements:

The information may not be accepted for publication in member medical journals following ICMJE policy.

D. Medicare Qualified Clinical Trials:

Effective January 1, 2014, the Centers for Medicare and Medicaid Services (CMS) require the mandatory reporting of the National Clinical Trial (NCT) number on claims for items and services provided in clinical trials that are qualified for coverage under the Medicare National Coverage Determination (NCD) Manual, Section 310.1. Any claim that does not include the NCT number will be returned to the billing provider and may not be paid. If the study has been determined to be a qualifying clinical trial under Medicare's NCD and the investigator intends to enroll Medicare beneficiaries, the study must be registered on ClinicalTrials.gov regardless if it meets the criteria for registration under the FDAAA, NIH and/or ICMJE requirements.

III. Compliance:

For clinical trials where the UC San Diego Principal Investigator is the responsible party, the Principal Investigator is responsible for the registration and reporting of results on ClinicalTrials.gov as well as the timeliness, accuracy and completeness of the submitted information. Upon receipt of notice of award from NIH, UC San Diego Office of Contract & Grant Administration will formally provide written notification to the named Principal Investigator (either directly or via project staff members) of their responsibilities to comply with all ClinicalTrials.gov requirements, including:

1. Registration of the clinical trial prior to enrolling the first subject,
2. Confirming accuracy of record content,
3. Resolution of problems,
4. Maintenance of records, including content update and modifications, and
5. Provide aggregate results reporting and adverse event reporting at the conclusion of the project.

Please note that UC San Diego is currently in the process of enhancing its ClinicalTrials.gov compliance oversight approach. There will however be periodic monitoring by the institution to ensure compliance with the ClinicalTrials.gov registration and reporting requirements.

IV. References and Resources:

1. FDA Amendments Act (related information): <https://clinicaltrials.gov/ct2/manage-recs/fdaaa>
2. ClinicalTrials.Gov: <https://clinicaltrials.gov/ct2/home>
 - a. How to Register a Study: <https://clinicaltrials.gov/ct2/manage-recs/how-register#StepsForRegistering>
 - b. Protocol Data Element Definitions (for registration purposes): <https://prsinfo.clinicaltrials.gov/definitions.html>
 - c. How to Submit Results: <https://clinicaltrials.gov/ct2/manage-recs/how-report>
 - d. Frequently Asked Questions: <https://clinicaltrials.gov/ct2/manage-recs/faq>
3. NIH Policy on the Dissemination of NIH Funded Clinical Trial Information: <https://grants.nih.gov/policy/clinical-trials/reporting/understanding/nih-policy.htm>
 - a. Steps to Compliance with ClinicalTrials.gov for NIH Awardees: <https://grants.nih.gov/policy/clinical-trials/reporting/steps.htm>
 - b. Frequently Asked Questions re FDAAA and NIH ClinicalTrials.gov Registration and Reporting Requirements: <https://grants.nih.gov/policy/clinical-trials/reporting/faq.htm>
4. ICMJE: <http://www.icmje.org/about-icmje/faqs/clinical-trials-registration/>
5. ICMJE FAQs: <http://www.icmje.org/about-icmje/faqs/> CMS Transmittal SE1344: <https://www.cms.gov/Outreach-and-Education/Medicare-Learning-Network-MLN/MLNMattersArticles/Downloads/SE1344.pdf>