Registration of Clinical Trials at ClinicalTrials.gov

Background

ClinicalTrials.gov is a databank or registry of federally and privately supported clinical trials conducted in the United States and worldwide. It is managed by the National Library of Medicine within the National Institutes of Health (NIH). ClinicalTrials.gov is the result of a federal law requiring that clinical trials be registered to improve public access to information about clinical research, promote public trust in research, and inform future research (Public Law 110-85). In some cases, registration is required for journal publication. This guidance document provides information about clinical trial registration requirements set forth by the Food and Drug Administration, the National Institutes of Health, and the International Committee of Medical Journal Editors.

Applicability

Food and Drug Administration Registration Requirements

The Food and Drug Administration (FDA) requires registration at ClinicalTrials.gov for all applicable clinical trials (ACTs) that were initiated after 9/27/2007, or were initiated before 9/27/2007, but were ongoing as of 12/26/2007. Applicable drug and device clinical trials are defined as follows:¹

- **Drugs and Biologics**: A controlled clinical investigation, other than a Phase 1 clinical investigation, of a drug or biologic product subject to FDA regulation.
- **Medical Devices**: A prospective clinical study of health outcomes comparing an intervention with a medical device against a control, or pediatric postmarket surveillance required by the FDA.

Registration is not required for small trials to determine the feasibility of a device or to test prototype devices where the primary outcome measure relates to feasibility, and not to health outcomes.

National Institutes of Health Registration Requirements

Effective January 18, 2017,² National Institutes of Health (NIH) requires registration at ClinicalTrials.gov for all clinical trials funded wholly or partially by NIH. NIH defines a clinical trial as 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


² For the NIH extramural program, the policy applies to applications for funding submitted on or after January 18, 2017 that request support to conduct a clinical trial initiated on or after January 18, 2017. For the NIH intramural program, the policy applies to all clinical trials initiated on or after January 18, 2017. The policy does not apply to clinical trials in ongoing, non-competing awards, but will apply if the grantee submits a competing renewal application that includes a new clinical trial, [https://grants.nih.gov/ClinicalTrials_fdaaa/faq.htm](https://grants.nih.gov/ClinicalTrials_fdaaa/faq.htm).
biomedical or behavioral outcomes. This includes Phase 1 clinical trials, and trials that do not involve any FDA-regulated products (such as trials involving only behavioral interventions).

ICMJE Registration Requirements

As of 2005, most medical journals, including member publications of the International Committee of Medical Journal Editors (ICMJE), require registry as a condition of publication. Thus, researchers who plan to publish in an ICMJE member journal must meet ICMJE guidelines for clinical trial registration. ICMJE defines a clinical trial as follows:

“…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. 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, and process-of-care changes). Health outcomes include any biomedical or health-related measures obtained in patients or participants, including pharmacokinetic measures and adverse events.

Frequently Asked Questions

Who is responsible for registration and reporting results?

Responsibility for registration falls to the individual designated to be the “responsible party.” In some cases, the sponsor of the trial is the responsible party. However, the lead principal investigator is the responsible party in cases where there is no sponsor (Investigator-initiated trials) or for NIH-funded clinical trials that do not involve FDA-regulated components. Additionally, the sponsor can delegate all registration and reporting responsibilities to the principal investigator under the following conditions:

- The trial is initiated by the investigator,
- The investigator has access to and control over the data from the clinical trial, and
- The investigator has the right to publish the results of the clinical trial.

For research involving an IND (Investigational New Drug Application) or IDE (Investigational Device Exemption Application) with the FDA, the holder of the IND or IDE is the responsible party unless responsibility has been delegated to the principal investigator.

It is very important for researchers to know who the “responsible party” is, related to these requirements. Substantial penalties (i.e., monetary fines, withholding federal funds, denial of publication in an ICMJE journal, etc.) can be levied against responsible parties for failure to meet these requirements. Beginning January 18, 2017, applications for NIH funding must include a plan describing how the registration and reporting requirements will be met.

Principal investigators who are the responsible party may designate an individual to register the trial and complete registration information. However, it is ultimately the responsibility of the PI to ensure that registration occurs and the information provided is accurate and current. Research teams should identify the responsible party and ensure their responsibilities are clearly articulated prior to starting a clinical trial.

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4 Many non-ICMJE medical journals have adopted similar registration requirements. Researchers are encouraged to consider publication plans prior to initiating clinical trials to ensure they meet journal requirements.

How are clinical trials registered?

Clinical trials are registered via a web-based protocol registration system (PRS). Instructions for completing registration can be found here.

ISU researchers who need an account may contact the PRS Account Administrator in the Office for Responsible Research (ORR) at cltrlgov@iastate.edu. Please be aware that setting up an account with the ClinicalTrials.gov federal office can take time, so plenty of advance notice is advised.

**Important**: The PRS Account Administrator’s role is to help establish an account for the responsible party. The PRS Account Administrator is *not* responsible for registering a study, ensuring a study is registered or results are entered in accordance with required timelines, or verifying the accuracy of information entered by the responsible party.

How is registration handled for research projects conducted at multiple institutions?

The lead sponsor should take responsibility for registering the trial. In cases where there is no sponsor, investigators involved in the research must work with each other to identify a responsible party and ensure the trial is registered only once for the entire project.

When must clinical trials be registered?

Federal regulations require that applicable clinical trials and NIH-funded clinical trials be registered no later than 21 days after enrollment of the first participant. However, researchers should be aware that ICMJE requires registration prior to enrollment of any subjects, and member journals may decline publication articles from studies that were not registered in accordance with this requirement.

When must results from clinical trials be reported to ClinicalTrials.gov?

Results from clinical trials must be reported to ClinicalTrials.gov no later than 12 months after the *primary completion date*. The primary completion date is defined as 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.6

What specific information must be provided to ClinicalTrials.gov?

Detailed information on the data elements required by FDA and the NIH for registration and results reporting can be found on the ClinicalTrials.gov PRS (Protocol Registration System) Information website:

- Data elements for protocol registration
- Data elements for results reporting

How often must data on ClinicalTrials.gov be updated?

For clinical trials initiated on or after January 18, 2017, information submitted to ClinicalTrials.gov must be updated at least once every 12 months. However, regulations require more frequent updates of certain information. See Table 3 in this document for details.

6 42 CFR 11.10 (a)
How does registration of clinical trials relate to IRB review and approval?

IRB review is a completely separate process from clinical trial registration. IRB approval is not required prior to initial registration at ClinicalTrials.gov, nor does the IRB review any information submitted for registration. However, IRB approval is needed before research activity with human subjects is initiated (including recruitment of subjects).

The Protocol Registration System requires some information about IRB approval of Clinical Trials. If your clinical trial was approved by the ISU IRB, you may use the following information:

Board Name: Iowa State U IRB #1 (or, for prisoner research, Iowa State U IRB #2)
Board Affiliation: Iowa State University
Board Contact: Email: IRB@iastate.edu
Address: Office for Responsible Research
2420 Lincoln Way, Suite 202
Ames, IA 50014

Do I need to inform research participants about ClinicalTrials.gov Registration?

Yes! Research participants must be informed of the availability of clinical trial information on ClinicalTrials.gov. Federal regulations require the following language to be included verbatim in informed consent documents for applicable clinical trials initiated on or after March 7, 2012 and for all NIH-funded clinical trials subject to registration:

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.

What are the consequences for failure to properly register a clinical trial?

Under federal law, penalties for failure to register, or for providing incomplete, false, or misleading registration information (including updates subsequent to initial registration) may include civil monetary penalties of up to $10,000 per incident and/or per day, non-compliance notices from the FDA, and, for federally-funded trials, the withholding or recovery of grant funds.

Compliance with ClinicalTrials.gov registration requirements will be a term and condition of NIH awards. NIH grantees are required to certify their compliance with registration and reporting requirements in grant applications and progress reports. Failure to comply may lead to suspension or termination of funding and publicly identifying the clinical trial record as noncompliant in clinicaltrials.gov. NIH may consider compliance with these requirements in decisions about future funding.

Additionally, unregistered or improperly registered trials risk not being accepted for consideration by ICMJE member or other journals.

Resources

Clinical Trials.gov
www.ClinicalTrials.gov
ClinicalTrials.gov FAQ’s
ClinicalTrials.gov Protocol Registration System
Food and Drug Administration
Food and Drug Administration Amendments Act (FDAAA 801) Information
Checklist for Evaluating whether a Clinical Trial or Study is an Applicable Clinical Trial (ACT)
Summary of Changes from Current Practice Effective January 18, 2017

National Institutes of Health
NIH Implementation of FDAAA
What NIH Grantees Need to Know about the Food and Drug Administration Amendments Act
FAQ’s for NIH Grantees