

INSTITUTIONAL REVIEW BOARD & HUMAN SUBJECTS OFFICE

ClinicalTrials.gov Investigator Guide

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1.0 INTRODUCTION

ClinicalTrials.gov is a public database of clinical trial and related research information. The purpose of ClinicalTrials.gov is to provide easily accessible information on clinical trials for the public. The Food and Drug Administration Modernization Act of 1997 (FDAMA) required the creation of a public site for storing and reporting of information about federally or privately funded clinical trials. In 2000, The National Libraries of Medicine (NLM) at the National Institute of Health (NIH) responded to this call by creating a publicly available website called ClinicalTrials.gov. In 2005, the International Committee of Medical Journal Editors (ICMJE) adopted a [policy](#) that began requiring trial registration as a condition of publication in ICMJE peer-reviewed journals. Registration requirements with ClinicalTrials.gov were expanded in 2007, including many more types of trials, expanded trial information, and the submission of summary results (including adverse events) as part of the Food and Drug Administration Amendments Act (FDAAA 801). In 2017, a final rule (42 CFR 11) regarding clinical trial registration and results reporting took effect. This update expanded the definition of clinical trials which are required to register, known as Applicable clinical trials (ACT), and further specified the penalties for non-compliance with the regulations.

In 2017, NIH adopted its own, separate [policy](#) regarding NIH-funded clinical trials. All NIH-funded clinical trials are required to register and report results on ClinicalTrials.gov under the policy. NIH further revised its definition of ‘clinical trial’ by indicating that any intervention with prospective assignment where the primary purpose is to evaluate the effect of the intervention on a health, biomedical, or behavior-related outcome would be considered a clinical trial. This clinical trial definition differs from FDAAA 801 in that a drug or device is not required to be considered a clinical trial. In order to facilitate compliance with these federal regulations, the University of Iowa provides education and assistance to investigators through a ClinicalTrials.gov working group. In addition, the University of Iowa Human Subjects Office facilitates in the registration of clinical trials and monitoring of ClinicalTrials.gov record.

2.0 DEFINITIONS

42 CFR 11 – Code of Federal Regulations requiring clinical trial registration and results submission

42 U.S.C 281(j) – United States Code Public Health and Welfare service regarding National Research Institutes.

ACT – Applicable Clinical Trial

ClinicalTrials.gov – Public database of clinical trial information created in 2000 as a result of the 1997 Food and Drug Administration Modernization Act (FDAMA)

FDAMA - Food and Drug Administration Modernization Act of 1997

FDAAA 801 - Food and Drug Administration Act of 2007

Final Rule – Update to FDAAA 801 expanding definitions of Applicable Clinical Trials and revising penalties of non-compliance

ICMJE - International Committee of Medical Journal Editors

IDE – Investigational Device Exemption

IND – Investigational New Drug

IRB – Institutional Review Board

NCT number – National Clinical Trials number assigned when the record is published for the first time

NIH – National Institutes of Health

PRS - Protocol Registration and Results System; where information published on ClinicalTrials.gov is entered

Record Owner - Person responsible for entering data in ClinicalTrials.gov PRS record

Responsible Party – Person or entity responsible for the oversight of a clinical trial and its records.

RO – Record Owner

RP – Responsible Party

Sponsor – Person or entity that initiates the clinical trial protocol.

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Sponsor-Investigator – an individual who both initiates and conducts, alone or with others, a clinical investigation, i.e., under whose immediate direction the test article is administered or dispensed to, or used involving, a subject. The term does not include any person other than an individual, e.g., corporation or agency. [21 CFR § 50.3]

UI – University of Iowa

VA – Veteran’s Affairs

3.0 Getting Started

Any study may register on ClinicalTrials.gov, not just ACTs or other clinical trials. However, investigators must know when reporting requirements apply, to assure that all required registrations are completed. To help make this determination, the Human Subjects Office provides multiple [tools](#) to assist investigators – including a guide on [Getting Started](#). While the IRB will formally determine whether a study meets the definition of an ACT, investigators can evaluate this determination at any time using the [ClinicalTrials.gov Checklist](#), a tool reviewed and evaluated by a [ClinicalTrials.gov Working Group Departmental Liaison](#) in conjunction with the Principal Investigator (PI). The HawkACT Determination Form can also be provided to the IRB if the investigator seeks to provide feedback on the formal ACT determination. One-on-one help for an individual or group can also be requested of a ClinicalTrials.gov Working Group Departmental Liaison by completing a [Help Request Form](#).

3.0.1 Protocol Registration and Results System (PRS)

To register a study or report results, investigators must use the [Protocol Registration and Results System \(PRS\)](#). To access the PRS, investigators should navigate to <https://register.clinicaltrials.gov> in their web browser. Registration in the University of Iowa’s PRS account for ClinicalTrials.gov requires a username and password. The username can be obtained by contacting the PRS Administrator at ct-gov@uiowa.edu. Once the account is created and investigators login for the first time, they will set a password. This password should not be shared with other users and does not require a periodic update. If a password is forgotten or needs to be reset, investigators can do so by selecting the ‘reset’ link in the PRS system, or by contacting the PRS administrator.

When requesting initial access from the PRS administrator, investigators should provide the name of the Responsible Party (RP), a Record Owner (RO) who will enter the data (if this is not the RP), and their department. By default, the person who starts the record will be named the RO. If an investigator would ever like to change the Record Owner designation, they should contact the PRS administrator. A PRS account can typically be created within 1-2 business days. Once an investigator is registered, they will receive an email detailing how to login and they will have access to this account as long as they are a UI investigator.

3.0.2. Applicable Deadlines

Federal regulations (FDAAA 801; 42 CFR 11) require registration within 21 days of enrollment of the first subject, but some funding agencies and journals have [different requirements](#). Researchers should become familiar with specific deadline requirements related to their study. Additional information can also be found on the [Human Subjects Office website](#). ClinicalTrials.gov records must be updated anytime significant changes are made to the protocol, and/or verified by the RP that the record is up to date at least once per year, even if nothing has changed. The University of Iowa IRB will facilitate in completing these changes by notifying investigators of the need to update their record when a modification is submitted to the IRB, and at the time of Continuing Review. Below is the timeline for updates to a record:

Data Element	Deadline for Updating (i.e., not later than the Specified Date)
Study Start Date	21 calendar days after the first subject is enrolled
Overall Recruitment Status	30 calendar days after a change in overall recruitment status <ul style="list-style-type: none">If the overall recruitment status is changed to "suspended," "terminated," or "withdrawn," the Why Study Stopped data element must be updated at that time as well

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Table 1. Deadlines for Updating Key Data Elements per Federal Law (42 CFR §11)	
Data Element	Deadline for Updating (i.e., not later than the Specified Date)
IRB Approval Status	30 calendar days after a change in status
Primary Completion Date	30 calendar days after the clinical trial reaches its actual primary completion date
Enrollment	At the time the primary completion date is changed to "actual," the actual number of participants enrolled must be submitted
Study Completion Date	30 calendar days after the clinical trial reaches its actual study completion date
Responsible Party, by Official Title	30 calendar days after a change in the Responsible Party or the official title of the Responsible Party
Responsible Party Contact Information	30 calendar days after a change in the Responsible Party or the contact information for the Responsible Party
Device Product not Approved or Cleared by US FDA	15 calendar days after a change in approval or clearance status has occurred
Record Verification Date	Any time the Responsible Party reviews the complete set of submitted clinical trial information for accuracy and not less than every 12 months, even if no other updated information is submitted at that time.
Good Cause Extension Request for Delayed submission of Result Information	Prior to the date, that the results information submission is due (1 year from the study's Primary Completion Date)

3.0.3. Institutional Review Board (IRB)

Investigators are strongly encouraged to submit their Institutional Review Board (IRB) application prior to initiating the ClinicalTrials.gov record, as the IRB will assist in the registration process. However, there is no requirement for the order in which these forms must be submitted. IRB approval of a New Project Application may be delayed until the ClinicalTrials.gov record has been created for UI investigator-initiated clinical trials.

To begin, an ACT determination must be made so that application of the registration requirement can be assessed. The IRB will make this determination using the [ACT Checklist](#), but investigators can also use the [HawkACT Determination Form](#) to provide the IRB with the investigator's rationale on the ACT determination. The form can also be used to evaluate an ACT determination before it is reviewed by the IRB. The form is reviewed by a ClinicalTrials.gov Working Group member, which is helpful when applying for federal funding.

For studies evaluating a drug, device, or biologic, the PRS administrator communicates with the IRB regarding the determination of an ACT. The IRB has been assigned the authority to make a determination of whether the research study meets the criteria to be an ACT requiring registration on ClinicalTrials.gov. The determination is communicated via the IRB meeting minutes. When the ACT determination is made and an investigator is required to register the study, a required action is made to enter the NCT number into the HawkIRB application. As part of ongoing review, the IRB will evaluate the compliance and status of your record with each IRB modification or continuing review submission. If the ClinicalTrials.gov PRS record is not up to date when submitting to the IRB, a required action may be made to set a meeting with a ClinicalTrials.gov Working Group Member so that the issues can be addressed. Once the meeting is set, the required action from the IRB is considered met.

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3.0.4. Identifying the Responsible Party

The IRB must decide who is responsible for registering the study – a sponsor or the investigator. The initiator of the study protocol is considered the ‘sponsor’ of the study. If this initiator is a University of Iowa (UI) investigator, he/she would be considered a Sponsor-investigator and required to register and report results on ClinicalTrials.gov. If an industry or investigator from another institution initiated the study, that sponsor would be responsible for registering and reporting results and should provide the registered NCT number to the research team. The IRB will not make an ACT determination for studies sponsored outside of UI.

3.0.5. Record Holder Designations and Responsibilities

There are two primary designations in each PRS record: The Record Owner (RO) and the Responsible Party (RP). Each role can be fulfilled by a single Principal Investigator (PI), or the RO designation can be granted to a member of the research team. The PRS record also allows for additional parties to be granted access via an ‘Access List.’ The Access List should only be used to grant access to the record to individuals who would require it, such as a statistician. PIs are encouraged not to add multiple team members to this list for the purpose of updating the record.

- **Responsible Party** is defined as the person or entity that initiated the protocol. Also called the ‘Sponsor’ of the study, this party is responsible for the content and compliance of the PRS record. The Responsible Party must assure that the record is kept up to date, and that changes to the study are reported within the specified time frame which is typically within 30 days of the change. The Responsible Party is also liable for the penalties of non-compliance, along with the Responsible Party’s institution.
- **Record Owner** is defined as the person responsible for entering data into the record. This person should have a working knowledge of the data they enter and are often listed as a primary or back-up contact in the study record. By default, the person who starts the record is named the RO.

3.0.6 Veteran’s Affairs (VA) Oversight of Clinical Trials

For IRB-03 studies where the Veteran’s Affairs (VA) institution is the primary study location or coordinating center of a study (listed in VII.A.10 of the IRB application), the study must be registered under the VA per their registration policy. Currently, the VA is requiring investigators who need to register at ClinicalTrials.gov under their institution to create and maintain their own institutional account in the PRS for any records where the VA is the lead site. Accounts can be created by emailing a request to register@clinicaltrials.gov. Any study with both an IRB 01 and an IRB 03 application for the same study should look to VII.A.10 to identify which institution, the VA or UI, is the coordinating center of the study. Questions can be directed to suzanne.kieffer@va.gov.

4.0 Registration and Results Reporting

The PRS consists of 3 sections: The Protocol (or Registration) Section, the Study Documents Section, and the Results Section. Each section is broken down into individual modules which can be opened and edited. The Results section is only required to be completed for Applicable Clinical Trials. **Additional information can be found by clicking on links in blue.**

4.0.1 Protocol (Registration) Section

The registration portion of your record. You will describe the study through the various modules presented. Detailed help on completing this section can be found on the [public site](#).

- [Study Identification](#)
Indicate your study title and a brief title. The brief title should be written in lay language. Other relevant information about the identification of the study such as study IDs and acronyms.

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The 'Unique Protocol ID' must list your HawkIRB number (digits only).

- [Study Status](#)

This section lists relevant study dates and marks the last date the Responsible Party verified the content of the record. Information on the study status, start date, and completion dates is collected.

- [Sponsor/Collaborators](#)

Responsible Party information will be identified here. Investigators should select 'Sponsor-investigator' as the Responsible Party type, unless otherwise directed by the PRS administrator. For studies using an Investigational New Drug (IND) product which is registered by a PI who is not the sponsor-investigator of the study, contact the PRS administrator at ct-gov@uiowa.edu.

- [Oversight](#)

IRB information will be identified here, as well as information on the FDA regulated drug or device product. The UI IRB information should be listed as:

Board Name: IRB-01

Board Affiliation: University of Iowa

Phone: 319-335-6564 Email: irb@uiowa.edu

Address:

Human Subjects Office/IRB

Hardin Library, Office 105

600 Newton Road

Iowa City, IA 52242-1098

- [Study Description](#)

A detailed and brief description of the study. The brief description should use lay language.

- [Conditions](#)

Conditions/diseases studied will be selected. Keywords can also be identified. This information is used by the search function on the public site.

- Study Design:

- [Interventional Study Design](#)

Participants are assigned prospectively to an intervention or interventions according to a protocol to evaluate the effect of the intervention(s) on biomedical or other health related outcomes. Using a drug or device in subjects outside of standard care treatment will always be considered interventional.

- [Observational Study Design](#)

Studies in human beings in which biomedical and/or health outcomes are assessed in pre-defined groups of individuals. Participants in the study may receive diagnostic, therapeutic, or other interventions, but the investigator does not assign specific interventions to the study participants. This includes when participants receive interventions as part of routine medical care, and a researcher studies the effect of the intervention.

- [Arms/Groups and Interventions](#)

Detailed information about the study arms (displayed on the site in rows) and interventions (displayed on the site in columns)

- [Outcome Measures](#)

The primary purpose for conducting the clinical trial. Information should be specific (e.g., effect being measured, scale or tool used, grades of the scale, etc.) Secondary outcomes can also be listed. For ACTs or NIH funded clinical trials, any primary or secondary outcome must have results reported.

- [Eligibility](#)

Information about the subjects being accepted in the study and any inclusion/exclusion criteria should be listed. This information is relevant to subjects using the site as a recruitment tool.

- [Contacts/Locations](#)

Primary contacts from the coordinating center, as well as a list of each site involved in the study.

- [IPD Sharing Statement](#)

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Yes/No statement about sharing individual participant data. If 'Yes' is answered, a plan must be described. This section meets the ICMJE requirement for disclosure of a data sharing plan.

- [References](#)
Currently optional. Use to link to previous research and other personal publications. This section is helpful for those using the public site to review previous research in a particular area.

4.0.2 Documents Section

The Document Section is for the uploading of study documents (Study Protocol, Statistical Analysis Plan (SAP), and/or Informed Consent Form) to the PRS. Each document must include a cover page with the Official Title of the study, NCT number (if available), and date of the document. Uploaded study documents should be the most recent version reviewed by a human subjects protection review board (if applicable). The full study protocol and SAP are required at the time Results information is submitted.

Uploaded study documents are made available publicly in the study record on the ClinicalTrials.gov website. All documents must be in English and must be converted to Portable Document Format Archive (PDF/A) files. If this format is unable to be obtained prior to uploading, a conversion tool will be used by the PRS. Any documents converted to a PDF/A format by the PRS should be reviewed prior to submitting the study record to assure there were no conversion errors.

All uploaded documents should be evaluated for content and any redacted if necessary. For information on how to redact a document, refer to the [Redaction Guide](#). A previously submitted study document can be deleted from a record even after being made publicly available. However, the deleted document(s) will remain accessible on ClinicalTrials.gov, in the record's History of Changes.

Document Upload Review Checklist

- Documents are in English.
- Documents are in PDF/A (not just PDF) format.
- Each uploaded document contains the original full text of the specified document type.
- Documents do not include any personally identifiable information (PII), such as a participant's name in an ICF.

4.0.3. Results Section

The Results portion of your record. All ACTs and NIH-funded studies must report results within 1 year of their primary completion date. Delayed results posting can be requested, but significant justification must be provided. All primary and secondary outcomes must report outcomes in a primary outcome table, as well as the relevant statistics used to examine the data. In addition to the results, information is gathered on participant demographics and movement through the trial, as well as on Adverse Events. Information is provided on [completing the results section](#), as well as [examples of various study designs](#).

- [Participant Flow](#)
Information to document the progress of research participants through each stage of a study in a tabular format, including the number of participants who started, completed, and dropped out of each period of the study based on the sequence in which interventions were assigned. (Identical in purpose to a [CONSORT flow diagram](#), but represented as tables). The tabular presentation may be separated into "periods," each of which comprises an interval of study activity. Each period consists of "milestones" for reporting numbers of participants at particular points in time within that period. This module provides information related to study design and description of key events after study enrollment but before group assignment. Simple participant flow template can be found here, [Participant Flow Template](#).

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- [Baseline Characteristics](#)
Demographic information about study subjects. Age, gender, and ethnicity must be reported. Users can also specify study-specific characteristics. More information on baseline characteristics data preparation can be found here, [Baseline Characteristics Data Preparation Checklist](#).
- [Outcome Measures and Statistical Analyses](#)
It is a tabular summary of Outcome measure values, by study arm and comparison group. Outcome measure data and relevant statistical analysis information for all primary and secondary outcomes must be reported. Checklist for outcome measure data preparation can be found here, [Outcome Measure Data Preparation Checklist](#). Here are some templates for [Outcome Measure](#) and related [Statistical Analysis](#) of the data.
- [Adverse Events](#)
Table summary of anticipated and unanticipated serious, other (not including serious) adverse events and All-Cause mortality through the entire duration of the study. The required information for each serious or other adverse event section, includes the adverse event term, affected organ system, number of participants at risk, and number of participants affected, by study arm or comparison group. Here is the [Adverse Event Data Preparation Checklist](#).
- [Limitations and Caveats](#)
Information for significant limitation can be entered here that will help explain the study in more detail. For example, if a study was terminated early, you would describe the reason why in this section.
- [More information](#)
This section includes Disclosures of conflicts of interest and contact for questions about the clinical study results information.

4.0.3.1. Good cause extension request for delayed submission of results information:

The regulation at [42 CFR 11.44\(e\)\(1\)\(i\)](#) permits a responsible party to request an extension of the deadline for submitting clinical trial results information for good cause. The responsible party must submit the extension request via the ClinicalTrials.gov Protocol Registration and Results System (PRS) prior to the date (i.e., the day before) that results information would otherwise be due according to [42 CFR 11.44\(a\) through \(f\)](#).

The extension request must include

- a. Description of the reason(s) why clinical trial results information cannot be provided according to the deadline, with sufficient detail to allow for the evaluation of the request
- b. Estimate of the date on which the clinical trial results information will be submitted.

As of Jan 25th, 2022, responsible party cannot submit Good Cause Extension Request in the PRS for Delayed submission of Result Information on/ after the deadline, which is the due date for results information submission (1 year from the study's primary completion date).

The Director of the NIH will provide a response electronically to the responsible party indicating whether the requested extension demonstrates good cause and has been granted.

4.0.4 Record Maintenance and Expectations

Records registered on ClinicalTrials.gov must be maintained until either results are entered, or the primary and study completion dates have been entered for studies not requiring results reporting. This is true for any record submitted to the PRS for review, regardless of ATC determination or funding requirements. To maintain compliance with ClinicalTrials.gov expectations, records must be:

- Complete
- Accurate
- Up to date
- Free of errors

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The PRS administrator, or ClinicalTrials.gov Departmental Liaison, will notify investigators via email when problems exist in the record. However, investigators should be aware of any issues which currently exist in the record, or issues which may soon become problems, by regularly checking the record. In general, any changes to a study should be indicated in the ClinicalTrials.gov record within 30 days. Similarly, listed dates in the record must not be in the past for 'Anticipated' dates. Records must be updated at least once per year, even if nothing in the record has changed. In the event of no changes, the record verification date is updated to the current month and year, then submitted for review.

Review of the ClinicalTrials.gov record occurs with Continuing Review or modification submissions to the IRB. Investigators should plan to update their ClinicalTrials.gov record prior to these submissions, if necessary. In order to obtain IRB approval, the record must be up-to-date and free of error. However, if an IRB application will lapse before these updates can occur, a ClinicalTrials.gov Help appointment can be scheduled to address the updates outside of the IRB review, allowing for the investigator to avoid a lapse in IRB oversight.

As mentioned previously, the PRS administrator will also notify investigators via email when there are existing issues in a ClinicalTrials.gov record. This occurs outside of the IRB review and is another way to help investigators assure compliance with the registration and results reporting policies. Investigators receiving a communication for record updates from the ct-gov@uiowa.edu email have 2 weeks to either make the requested updates or respond to the email message with a plan for addressing the issue. If no response to the email is provided and the updates go unaddressed, the investigator's DEO will be notified and asked to assist the investigator in completing the requested tasks. Given the severe penalties to both the investigator and institution, and because records are a public document reflecting the University of Iowa, maintaining compliance is paramount.

Investigators who do not address required updates after help from the DEO is requested will be subject to a meeting with the PRS administrator, HSO Director, and Institutional Official to discuss research expectations at the University of Iowa.

5.0 Posting of the Informed Consent Document

The Human Subjects Office, via the PRS Administrator, tracks compliance under the revised Common Rule for uploading of consent documents to a public website for federally funded or supported clinical trials. The IRB tracks this compliance by asking the PI to respond 'Yes' or 'No' to this question on the HawkIRB form, VII.B.1.c. Before the IRB review staff are able to close a study, this question must have a 'Yes' response if the study is a clinical trial and utilizes federal funding. This is also addressed by the IRB at each Continuing Review if the study is closed to accrual and procedures. Publication of this document is typically done on ClinicalTrials.gov but can also be accomplished by posting to regulations.gov.

6.0 PI Departure/Transferring Records

Departing Responsible Parties and Record Owners must plan ahead before leaving the institution to assure paperwork is completed, records and data are transferred appropriately, and existing clinical and research endeavors are resolved. ClinicalTrials.gov PRS users must assure records and/or responsibilities are resolved prior to departure. To make this process easier follow the steps identified below to assure all records and data issues are resolved and can be appropriately transferred to a new institution.

6.0.1. PI Departure

Investigators planning to leave the institution should notify their departments early, as soon as possible. This allows other committees to complete their processes, and assure all pending issues are addressed. The easiest and most efficient way to complete this step is by completing the [PI Departure Form](#). Responsible Parties are required to either close their study and complete the ClinicalTrials.gov record, transfer an ongoing record to their new institution, or name a new PI as Responsible Party for the project to continue at UI. For Record Owners who enter data into a record, the PRS administrator

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should be contacted to name a new Record Owner for the study. If no replacement Record Owners are available, this will default to the PI and Responsible Party of the study.

6.0.2. PRS Records Transfer

To transfer a PRS record from one institution to another, you will need the following information:

- 1) The Official Title and NCT number of the record(s) to be transferred
- 2) The name of the institution where records will be transferred
- 3) Agreement from the new institution that a record transfer is acceptable
- 4) Registration in the PRS account at the new institution

With this information in place, you may request a transfer by emailing the PRS team at register@clinicaltrials.gov. Transfer requests should CC the University of Iowa PRS Administrator (ct-gov@uiowa.edu) and the PRS Administrator of the new institution.

The PI Departure Form will notify the PRS Administrator of the planned departure. Once notified, the PRS Administrator will email the investigator and assist in the record transfer process.

7.0 Help and Assistance

The best source of help can be found on ClinicalTrials.gov via the 'Help' links within each module, and the help menu of the PRS homepage. Additional [help](#) and [tutorials](#) can be found on the ClinicalTrials.gov public site. Additionally, the [Human Subjects Office website](#) provides a condensed version of this information on their ClinicalTrials.gov page.

7.0.1. ClinicalTrials.gov Working Group

The ClinicalTrials.gov Working Group is a group of departmental liaisons who are nominated by departments and trained by the PRS administrator to assist investigators in their respective departments in completing their PRS records and addressing reviewer comments.

Responsibilities of a Departmental Liaison include:

- Collaborate with the IRB Compliance Program and the Human Research Protections Program in the development and maintenance of policy and procedures that will improve compliance with regulations surrounding clinical trials.
- Serve on "ad hoc" working groups that evaluate specific issues and recommend potential improvements to the Network for adoption by the IRB Compliance Program and/or UI Human Research Protections Program.
- Raise potential issues within their respective division/area that are obstacles to complying with FDAAA 801 and requirements from other entities.
- Participate in educational activities about ClinicalTrials.gov; and
- Serve as a resource to other researchers for meeting regulatory as well as institutional requirements and developing best practices.

A complete listing of current ClinicalTrials.gov Working Group members can be viewed at our [page](#).

To request help from a member of the ClinicalTrials.gov Working Group, complete a [Help Request Form](#).

Departmental Requests to add a member to the Working Group can be sent to the PRS Administrator by emailing ct-gov@uiowa.edu.

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8.0 Additional Policies

The federal regulations (FDAAA801; 42 CFR 11) are not the only rules and requirements regarding registration and results reporting on ClinicalTrials.gov. In an effort to show support for the ClinicalTrials.gov initiative, other organizations have adopted policies relating to ClinicalTrials.gov. The two policies that will affect most investigators are those put forth by the NIH and the ICMJE.

8.0.1. NIH Policy

The NIH requires any clinical trial utilizing NIH funding to register and report results on ClinicalTrials.gov. However, NIH has defined 'clinical trial' slightly differently than the federal regulations. An NIH clinical trial is defined 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 biomedical or behavioral outcomes.'

This means that a study not meeting the registration requirements may in fact be required to register on ClinicalTrials.gov if the study utilizes NIH funding. The inclusion of behavioral interventions and outcomes in the definition of 'clinical trial' may be a new concept for many investigators.

As of January 25, 2018, all NIH funding applications/proposals must apply to one of three funding opportunities:

- 1) Clinical Trial Not Allowed
- 2) Clinical Trial Required
- 3) Clinical Trial Optional

An additional funding opportunity was announced November 29, 2018:

- 4) Basic Experimental Studies with Humans

While not all basic science meets the ACT definition, those that do are required to register and report results on ClinicalTrials.gov. Investigators should be familiar with this policy to be aware of any reporting requirements. NIH will ultimately determine if they consider a study they fund to be a clinical trial under their definition and will notify investigators of this decision in their award letter.

8.0.2. International Committee of Medical Journal Editors (ICMJE) Policy

ICMJE journals require all investigators wishing to publish in [their journals](#) to register their clinical trial on ClinicalTrials.gov prior to enrolling the first subject. This regulation differs from 42 CFR 11 and FDAAA 801 where investigators have 21 days after enrolling the first subject to register the trial. The ICMJE defines a clinical trial as any research project that prospectively assigns people or a group of people to an intervention, with or without concurrent comparison or control groups, to study the relationship between a health-related intervention and a health outcome.

Health-related interventions are those used to modify a biomedical or health-related outcome; examples include drugs, surgical procedures, devices, behavioral treatments, educational programs, dietary interventions, quality improvement interventions, and process-of-care changes. Health outcomes are any biomedical or health-related measures obtained in patients or participants, including pharmacokinetic measures and adverse events. The ICMJE does not define the timing of first participant enrollment, but best practice dictates registration by the time of first participant consent.

In addition to registration, the ICMJE requires all manuscripts submitted that report clinical trial results to contain a data sharing statement. As of July 1, 2018, all clinical trial results are required to have a data sharing statement. As of July 1, 2019, a data sharing plan is required in the trial's registration. ClinicalTrials.gov currently offers the option to indicate if data sharing occurs through the IPD (individual participant data) statement. If this statement is answered 'Yes,' the required elements of the ICMJE policy will be requested and can be used as a data sharing plan.

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8.0.3. Regulations and Policies Relating to ClinicalTrials.gov (Federal Regulations, NIH and ICMJE policy)

Element	Federal Regulations (42 CFR 11)	NIH Policy	ICMJE Policy
Scope/Applicability	<p>Applicable clinical trials of FDA-regulated drug, biological, and device products and pediatric post-market surveillance studies of devices required by the FDA under the FD&C Act.</p> <p>Does not apply to phase 1 trials or small feasibility studies.</p> <p>Applicable clinical trials are (1) clinical trials of drug and biological products that are controlled, clinical investigations, other than phase 1 investigations of a product subject to FDA regulation; and (2) prospective clinical studies of health outcomes comparing an intervention with a device product against a control in humans (other than small feasibility studies) or any pediatric post-market surveillance studies required by FDA under the FD&C Act. Applies to public and private sector sponsors and other entities who meet the definition of a responsible party.</p>	<p>All clinical trials funded wholly or partially by NIH.</p> <p>Includes phase 1 clinical trials and trials that do not involve any FDA regulated product such as trials involving only behavioral interventions.</p> <p>Applies to NIH-funded clinical trials where applications or proposals are received by NIH on or after the policy's effective date.</p> <p>Applies to NIH-conducted clinical trials initiated on or after the policy's effective date.</p>	<p>All clinical trials which wish to publish in an ICMJE journal, or its affiliates, must register prior to enrolling the first subject. Currently, only registration is mandated.</p>
Timeframe for registration on ClinicalTrials.gov	Not later than 21 days after enrollment of the first participant.	Not later than 21 days after enrollment of the first participant.	Prior to enrollment of first subject.
Registration data elements to be submitted to ClinicalTrials.gov	Elements defined in the final rule. Consists of descriptive information, recruitment information, location and contact information, and administrative data.	Elements defined in the final rule. Consists of descriptive information, recruitment information, location and contact information, and administrative data.	Elements defined in the final rule. Consists of descriptive information, recruitment information, location and contact information, and administrative data.
Timeframe for results information submissions to ClinicalTrials.gov	Not later than 12 months after primary completion date; possible delay of up to an additional 2 years for trials of unapproved products or of products for which initial FDA marketing approval or clearance is being sought, or approval or clearance of a new use is being sought.	Not later than 12 months after primary completion date; possible delay of up to an additional 2 years for trials of unapproved products or of products for which initial FDA marketing approval or clearance is being sought, or approval or clearance of a new use is being sought.	Not mandated in policy but must meet the requirements of FDAAA 801.
Results data elements to be submitted to ClinicalTrials.gov	Elements defined in the final rule. Includes participant flow, demographic and baseline characteristics, outcomes and statistical analyses, adverse events, the protocol, and statistical analysis plan, and administrative information.	Elements defined in the final rule. Includes participant flow, demographic and baseline characteristics, outcomes and statistical analyses, adverse events, the protocol, and statistical analysis plan, and administrative information.	Elements defined in the final rule. Includes participant flow, demographic and baseline characteristics, outcomes and statistical analyses, adverse events, the protocol, and statistical analysis plan, and administrative information.
Potential Consequences of Non-compliance	<p>Identifying clinical trial record as non-compliant in ClinicalTrials.gov.</p> <p>For Federally funded trials, grant funding can be withheld if required reporting cannot be verified.</p> <p>Civil monetary penalties of up to \$12,462 per day</p>	<p>May lead to suspension or termination of current grant or contract funding</p> <p>It can affect future funding decisions.</p> <p>Identifying clinical trial record as non-compliant in Clinical Trials.gov</p>	<p>Inability to publish in ICMJE or affiliated journal</p>

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8.0.4. Policies Specific to the University of Iowa

- **Unique protocol ID** – The unique protocol ID must be input as the IRB number of the approved study. This is so that a link exists between the HawkIRB application and the ClinicalTrials.gov records, which allows PRS administrators to track progress and assure information is accurate and up-to-date.
- **Responsible party designation** – The responsible party is the person or entity who initiates the protocol. If the protocol was initiated by an industry sponsor, they are responsible for creating and maintaining the study record. If the investigator initiated the protocol, then they are re responsible party who must create and maintain the record. This is represented in ClinicalTrials.gov under the ‘Sponsor/Collaborators’ module of the protocol section by selecting ‘Sponsor-Investigator’ as the responsible party and selecting the investigator’s name from the drop-down menu. Note, the ‘Principal Investigator’ designation is reserved for industry sponsor-initiated studies where a ‘Principal Investigator’ is designated by the sponsor as the responsible party. This designation is not appropriate in most situations at the University of Iowa and should be discussed with your PRS administrator if you feel this is an appropriate designation.

9.0 REFERENCES

ACT Checklist

https://prsinfo.clinicaltrials.gov/ACT_Checklist.pdf

ClinicalTrials.gov

<https://clinicaltrials.gov/>

Final Rule (42 CFR 11) –

<https://www.federalregister.gov/documents/2016/09/21/2016-22129/clinical-trials-registration-and-results-information-submission>

Food and Drug Administration Amendment Act Section 801 (FDAAA 801) –

<https://www.gpo.gov/fdsys/pkg/PLAW-110publ85/pdf/PLAW-110publ85.pdf>

ClinicalTrials.gov Checklist

<https://hso.research.uiowa.edu/sites/hso.research.uiowa.edu/files/ClinicalTrials.gov%20Checklist.pdf>

ICMJE policy

<http://www.icmje.org/recommendations/browse/publishing-and-editorial-issues/clinical-trial-registration.html>

International Committee of Medical Journal Editors (ICMJE) Policy

<http://www.icmje.org/recommendations/browse/publishing-and-editorial-issues/clinical-trial-registration.html>

Nation Institutes of Health (NIH) Policy

<https://www.federalregister.gov/documents/2016/09/21/2016-22379/nih-policy-on-the-dissemination-of-nih-funded-clinical-trial-information>

NIH Clinical Trial definition

<https://grants.nih.gov/policy/clinical-trials/definition.htm>

Policy for Protection of Human Research Subjects - 45 CFR 46 –

<https://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/index.html>

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Protocol Registration and Results System (PRS)

<https://register.clinicaltrials.gov>

PRS Helpful Hints for Results Reporting

<https://prsinfo.clinicaltrials.gov/ResultsExamples.pdf>

PRS User's Guide

<https://register.clinicaltrials.gov/prs/html/prs-users-guide.html>

Protocol Data Element Definitions

<https://prsinfo.clinicaltrials.gov/definitions.html>

Protocol Review Criteria

<https://prsinfo.clinicaltrials.gov/ProtocolDetailedReviewItems.pdf>

Public Health Service Act (PHA) –

<https://www.gpo.gov/fdsys/pkg/USCODE-2011-title42/html/USCODE-2011-title42-chap6A-subchapIII-partA-sec282.htm>

Results Data Elements Definitions

https://prsinfo.clinicaltrials.gov/results_definitions.html

Results Review Criteria

<https://prsinfo.clinicaltrials.gov/ResultsDetailedReviewItems.pdf>

Accreditation Standard: I.1.A; I.1.B; I.1.D; I.1.F; I.5.D; II.5.B; III.2.D	Date Reviewed:
Unit: Compliance	Version #: 2
File Location: L:\HSO\Monitoring\Clinical Trials.Gov\Policy\SOP	Owner: PRS Administrator
Approval: Michele Countryman	Approval: