



Grand Valley State University Institutional Review Board (IRB)	
<i>G-20: ClinicalTrials.gov Registration</i>	
Issued: August 18, 2020	Office of Research Compliance & Integrity

The Department of Health and Human Services (DHHS) and the Food and Drug Administration (FDA) each define the term “*clinical trial*” differently. If your trial meets either of these definitions, it may be necessary to register it on ClinicalTrials.gov (CT.gov). Follow the steps in the decision tree below to determine what is needed.

Definitions of *clinical trial*:

- DHHS Definition: **Clinical trial** means a clinical investigation, clinical study, or research study in which human subject(s) are prospectively assigned, according to a protocol, to one or more interventions (or no intervention, placebo, or other control) to evaluate the effect(s) of the intervention(s) on biomedical or health-related (including behavioral health-related) outcomes. [Combined 42 CFR 11.10 and 45 CFR 46.102(b)]
- FDA Definition: Utilize this [flowchart](#) to determine if the study is considered an “**applicable clinical trial.**” [Section 801 of the FDA Amendments Act (FDAAA)]

For assistance in determining if the research is a clinical trial, contact the Office of Research Compliance and Integrity (ORCI): 616-331-3197 or rci@gvsu.edu.

Decision Tree:

Question	No	Yes
1. Is this an applicable clinical trial (FDA definition), or will the study assess the safety or effectiveness of an FDA-regulated product (drug, device or biologic)?	Continue to next question.	Contact ORCI for assistance before proceeding: 616-331-3197 or rci@gvsu.edu .
2. Is this a clinical trial (DHHS definition) funded by the National Institutes of Health?	Continue to next question.	Utilize Checklist A.
3. Is this a clinical trial (DHHS definition) funded by a federal department or agency (other than the NIH) that has signed onto the Common Rule for the Protection of Human Subjects?	Continue to next question.	Utilize Checklist B.
4. Is this a clinical trial (DHHS definition) in which the research results will be submitted for publication in a journal that follows the International Committee of Medical Journal Editors (ICMJE) recommendations?	Continue to next question.	Utilize Checklist C.
5. Is the research required to be registered on CT.gov for any other reason (i.e. required by sponsor, discipline-specific expectation, etc.)?	The study does not need to be registered on CT.gov.	Utilize Checklist C and fulfill any additional sponsor or project requirements.

Checklist A: NIH Funding

Applicability: This checklist is to be used for clinical trials that have or will receive funding from the NIH and that do not involve the use of an FDA-regulated investigational product.

When working through grant submission process

1. Protocol development: Strongly recommend use of the NIH [Clinical e-Protocol Writing Tool](#) for several reasons:
 - a. The tool has templates for both Social/Behavioral clinical trials and Biomedical clinical trials.
 - b. The tool allows multiple collaborators to access and edit the protocol.
 - c. The protocol template mirrors the ClinicalTrials.gov (CT.gov) registration fields and results submission fields.
 - d. At the conclusion of the research, the comprehensive stand-alone research protocol needs to be uploaded to CT.gov. (Note that this cannot be the IRB application.) The protocol must be kept up-to-date with each amendment.

Some institutes at NIH only require a protocol synopsis, not a full protocol. Be aware that CT.gov requires a full protocol, regardless of what the funding agency requires.

2. When developing the research timeline, keep in mind that you need to account for initial IRB review time (1-2 months) and CT.gov posting review time (2-3 months).

Working through IRB submission process

1. All personnel are required to have current training and Conflict of Interest (COI) disclosures on file:
 - a. Responsible Conduct of Research training (every 3 yrs)
 - b. Human Subjects Research training (every 3 yrs)
 - c. Good Clinical Practice training (every 3 yrs)
 - d. Conflict of Interest training (every 4 yrs)
 - e. Conflict of Interest disclosure form in IRBManager (annually) – Note that the general disclosure in the IRB application is not sufficient to meet this requirement. The COI disclosure form must be completed by each individual every year.
2. Include the following required statements *-exactly as written-* in the consent form:
 - a. “A description of this clinical trial will be available on <http://www.ClinicalTrials.gov>, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.”
 - b. If the research is exempt, the above statements do not need to be included in the consent.

IRB approval obtained, research not yet started

1. Post the research on CT.gov. Per the regulations, registration must occur no later than **21 calendar days** after enrolling the first participant. However, if you intend to seek publication in a [journal](#) that follows the recommendation of the International Committee of Medical Journal Editors (ICMJE), CT.gov registration is required to be completed prior to the first enrollment.
2. CT.gov registration is handled by the Protocol Registration and Results System (PRS). PRS will review the submitted registration and return it for changes if it does not meet their format and requirements. Be aware that PRS posts their questions and required changes publicly in an effort to ensure high quality registrations are received the first time.
3. Helpful tips for entering registration information can be found here: [Protocol Registration Review Criteria](#). ORCI is available to assist in registering the clinical trial on CT.gov.

Study started and ongoing

1. The entire CT.gov listing must be reviewed not less than **once every 12 months**. Information from CT.gov is pulled into [eRA Commons](#) when completing the required Research Performance Progress Report, serving as a useful reminder to complete this annual requirement.
2. Amendments
 - a. If the protocol is amended in such a manner that changes are communicated to human subjects in the clinical trial, updates to any relevant clinical trial registration information data elements must be submitted not later than **30 calendar days** after the protocol amendment is approved by the IRB.
 - b. Overall Recruitment Status must be updated not later than **30 calendar days** after any change in overall recruitment status.
 - c. Individual Site Status must be updated not later than **30 calendar days** after a change in status.
 - d. IRB Status must be updated not later than **30 calendar days** after a change in status.
 - e. Study Start Date must be updated not later than **30 calendar days** after the first subject is enrolled.
 - f. Primary Completion Date must be updated not later than **30 calendar days** after the clinical trial reaches its actual primary completion date. Will also need to submit the actual number of participants enrolled.
 - g. Study Completion Date must be updated not later than **30 calendar days** after the clinical trial reaches its actual study completion date.
 - h. Responsible Party, Official Title of Responsible Party, and Responsible Party Contact Information must be updated not later than **30 calendar days** after a change. (Generally, the Responsible Party is the principal investigator.)
 - i. All other fields are updated at the time of the annual review, occurring not less than **once every 12 months**.
3. After recruitment is closed but no later than **60 days** after the last study visit by any subject: Post on CT.gov one IRB-approved informed consent form that was used to recruit participants. Post a blank one, not one with a signature. There may have been several IRB-approved versions of the consent; any one can be posted as long it was used by at least one participant.

Primary endpoint reached

1. **1 year** after the primary completion date: Submit results information to CT.gov. The results are not considered “submitted” until after PRS review is complete, and this review can take up to 3 months. To account for this review time, it is best to submit the results for PRS review no later than **9 months** after the primary completion date.
2. This is required even if data collection is ongoing for secondary endpoints and adverse event resolution.
3. You will need to include the full protocol and statistical analysis plan (if not included in protocol), including all amendments approved by the IRB.
4. Helpful tips for entering results information can be found here: [Results Review Criteria](#).

Secondary endpoints reached and resolution of adverse events

1. Secondary endpoints: Submit on CT.gov the remaining results information for secondary outcomes no later than **1 year** after the date on which the final subject is examined or receives an intervention for the purposes of final data collection. The results are not considered “submitted” until after PRS review is complete, and this review can take up to 3 months. To account for this review time, it is best to submit the results for PRS review no later than **9 months** after the date the final subject is examined or receives an intervention for the purposes of final data collection.
2. Adverse events: For additional adverse event information, submit on CT.gov **1 year** after the date of collection for additional adverse event information. The results are not considered “submitted” until after PRS review is complete, and this review can take up to 3 months. To account for this review time, it is best to submit the results for PRS review no later than **9 months** after the date of collection for additional adverse event information.
3. If the protocol or statistical analysis plan was revised after submission of the primary endpoint results but before submission of the secondary endpoint results, the revised protocol or statistical analysis plan must be submitted to PRS prior to submission of the secondary endpoint results.

Potential Consequences of Noncompliance (42 CFR 11.66)

1. Any person who violates these requirements is subject to civil monetary penalties.
2. Any person submitting false or misleading information is subject to civil or criminal judicial actions.
3. GVSU, as the institution holding the grant, can lose any remaining funding for the grant.
4. Any future grants to GVSU from the federal agency will not be released, thereby jeopardizing all federally-funded research at the institution.
5. The principal investigator may be investigated for research misconduct or noncompliance, consistent with applicable GVSU policies.

References and Resources

- [Behavioral and Social Sciences protocol requirement](#)
- [Biomedical protocol requirement](#)
- [NIH information on clinical trials](#)
- [PRS registration template](#)
- [NIH requirement for CT.gov](#)
- [Regulatory text for 42 CFR 11](#)
- [Regulatory text for 45 CFR 46 \(Revised Common Rule\)](#)
- [ICMJE requirement for CT.gov registration](#)

Checklist B: Funding from a Common Rule agency

Applicability: This checklist is to be used for clinical trials that do not involve the use of an FDA-regulated investigational product and that have or will receive funding from a [federal agency](#) that has signed onto the Revised Common Rule (except NIH).

Your funding agency does not require you to post your study on CT.gov; however, you may choose to do so if you wish. Note, however, that other sponsor and/or journal publication requirements still apply if you choose not to post on CT.gov, as indicated below. Read this checklist closely.

When working through grant submission process

When developing the research timeline, keep in mind that you need to account for initial IRB review time (1-2 months) and ClinicalTrials.gov (CT.gov) posting review time (2-3 months), if you choose to post on CT.gov.

Working through IRB submission process

1. All personnel are required to have current training on file:
 - a. Responsible Conduct of Research training (every 3 yrs)
 - b. Human Subjects Research training (every 3 yrs)
2. If funded by a Public Health Service (PHS) agency or office, the following additional requirements apply. Check with your Program Officer or the GVSU Office of Sponsored Programs to determine if your sponsor is part of PHS.
 - a. Conflict of Interest training (every 4 yrs)
 - b. Conflict of Interest disclosure form in IRBManager (annually) – Note that the general disclosure in the IRB application is not sufficient to meet this requirement. The COI disclosure form must be completed by each individual every year.

IRB approval obtained, research not yet started

1. Register the research on CT.gov if you intend to seek publication in a [journal](#) that follows the recommendation of the International Committee of Medical Journal Editors (ICMJE). CT.gov registration is required to be completed prior to the first enrollment.
2. If you will not publish in an ICMJE journal, you can choose to register on CT.gov. It is not required.
3. CT.gov registration is handled by the Protocol Registration and Results System (PRS). PRS will review the submitted registration and return it for changes if it does not meet their format and requirements. Be aware that PRS posts their questions and required changes publicly in an effort to ensure high quality registrations are received the first time.
4. Helpful tips for entering registration information can be found here: [Protocol Registration Review Criteria](#). ORCI is available to assist in registering the clinical trial on CT.gov.

Recruitment is closed

After recruitment is closed but no later than **60 days** after the last study visit by any subject:

1. If the research is registered on CT.gov: Post on CT.gov one IRB-approved informed consent form that was used to recruit participants. Post a blank one, not one with a signature. There may have been several IRB-approved versions of the consent; any one can be posted as long it was used by at least one participant.
2. If the research was not registered on CT.gov: Post on Regulations.gov one IRB-approved informed consent form that was used to recruit subjects. Follow the steps on this [OHRP website](#) to complete the posting. Ensure that you save your receipt and comment tracking number.

Research is complete

1. If the research was registered on CT.gov, log into CT.gov to change the research status to “complete.”
2. There is no requirement to post the protocol, statistical analysis plan or results on CT.gov.

Potential Consequences of Noncompliance

1. Failure to follow these required steps may lead to early termination of the grant by the sponsor, and future grants from the sponsor to the institution may not be supported, thereby jeopardizing federally-funded research at the institution.
2. The principal investigator may be investigated for research misconduct or noncompliance, consistent with applicable GVSU policies.

References and Resources

- [PRS registration template](#)
- [Regulatory text for 42 CFR 11](#)
- [Regulatory text for 45 CFR 46 \(Revised Common Rule\)](#)
- [ICMJE requirement for CT.gov registration](#)

Checklist C: Publication Only

Applicability: This checklist is to be used for non-FDA regulated research that has no federal funding and will seek publication in a [journal](#) that follows the International Committee of Medical Journal Editors (ICMJE) recommendations.

IRB approval obtained, research not yet started

1. Register the research on ClinicalTrials.gov (CT.gov). Registration is required to be completed prior to the first enrollment.
2. CT.gov registration is handled by the Protocol Registration and Results System (PRS). PRS will review the submitted registration and return it for changes if it does not meet their format and requirements. Be aware that PRS posts their questions and required changes publicly in an effort to ensure high quality registrations are received the first time.
3. Helpful tips for entering registration information can be found here: [Protocol Registration Review Criteria](#). ORCI is available to assist in registering the clinical trial on CT.gov.

Study started and ongoing

1. Keep the research updated in CT.gov as the research progresses, such as updating the research status to indicate that enrollment is open. You will receive automated emails as a reminder to complete the required annual reviews.

Research is complete

1. Log into CT.gov to change the research status to “complete.”
2. There is no requirement to post the protocol, consent form, statistical analysis plan or results on CT.gov.

References and Resources

- [PRS registration template](#)
- [ICMJE requirement for CT.gov registration](#)