

Clinical Trials Registration

1.0 Purpose

The purpose of this Policy is to outline the requirements for clinical trials registration and results reporting on ClinicalTrials.gov and expectations for Wright State University investigator adherence with these requirements. Additionally, this policy outlines the requirements for posting of clinical trial informed consent forms for federally funded clinical trials where the posting requirement will be fulfilled through ClinicalTrials.gov.

2.0 Scope

This policy applies to all clinical trials (as defined below) requiring registration and result reporting that is conducted by Wright State University faculty, staff and students and clinical trials for which the Wright State Institutional Review Board (IRB) acts as the IRB of record for an external entity (e.g., Premier Hospitals, Dayton VAMC, Wright State Physicians).

3.0 Definitions

- 3.1 **2018 Common Rule:** The U.S. Department of Health and Human Services and fifteen other Federal Departments and Agencies issued final revisions to the Federal Policy for the Protection of Human Subjects, the Common Rule. Effective July 19, 2018.
- 3.2 **Access List:** A list of account holders within the PRS that are granted access to a study. A user granted access to a record in this manner can perform all of the same actions on the record as if they were the record owner, with the exception of modifying the Record Access List.
- 3.3 **Aggregate Results:** Data collected from individual-level records that have been combined for statistical or analytical purposes and that are maintained in a form that does not permit the identification of individuals.
- 3.4 **Intervention** means both the physical procedures by which information or biospecimens are gathered (e.g., venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.
- 3.5 **Grantee:** Recipient institution of a grant or cooperative agreement from a federal agency.
- 3.6 **Final Rule:** Effective on January 18, 2017, the Final Rule for Clinical Trials Registration and Results Information Submission details the requirements for submitting registration and summary results information, including adverse event information, for specified clinical trials of drug products (including biological products) and device products and for pediatric postmarket surveillances of a device product to ClinicalTrials.gov (42 CFR Part 11).

- 3.7 **NCT Number:** The National Clinical Trial number is an identification that ClinicalTrials.gov assigns a study when it is registered. The NCT number is in the format “NCTXXXXXXXX”. Until an NCT number is assigned, the study is not registered. The NCT number must be included on claims for items and services provided in clinical trials that are qualified for coverage as specified in the Medicare National Coverage Determination Manual, Section 310.1.
- 3.8 **Primary (endpoint) Completion Date:** The date that the final subject was examined or received an intervention for the purposes of final collection of data for the primary outcome. This applies whether the clinical trial concluded according to the pre-specified protocol or was terminated
- 3.9 **Principal Investigator (PI):** The individual who is responsible and accountable for conducting the clinical trial.
- 3.10 **PRS:** The Protocol Registration and Results System is the online system that allows account holders within the institution to register, update and report results on ClinicalTrials.gov. The PRS can be accessed at <https://register.clinicaltrials.gov>.
- 3.11 **Record Owner:** Any account holder that creates a new record is automatically assigned as the Record Owner. The Record Owner will receive periodic emails from ClinicalTrials.gov whenever there are problems that require attention.
- 3.12 **Responsible Party:** The sponsor of the clinical study, as defined in 21 CFR 50.3; or the principal investigator of such clinical study if so designated by a sponsor, grantee, contractor, or awardee, so long as the principal investigator is responsible for conducting the study, has access to and control over the data from the clinical study, has the right to publish the results of the study, and has the ability to meet all of the requirements for the submission of clinical study information. For a pediatric post-market surveillance of a device product that is not a clinical trial, the responsible party is the entity who FDA orders to conduct the pediatric post-market surveillance of the device product.
- 3.12.1 The sponsor may designate a principal investigator as the responsible party if such principal investigator meets all of the following requirements: is responsible for conducting the study; has access to and control over the data from the study; has the right to publish the results of the study; and has the ability to meet all of the requirements for submitting and updating clinical study information.
- 3.13 **Study Completion Date:** The date the final participant was examined or received an intervention for purposes of final collection of data for the primary and secondary outcome measures and adverse events (for example, last participant’s last visit), whether the clinical study concluded according to the pre-specified protocol or was terminated. Once the clinical study has reached the study completion date, the responsible party must update the Study Completion Date to reflect the actual study completion date.

- 3.14 **Secondary ID:** Any identifier(s), other than the organization's Unique Protocol ID or the NCT number that is assigned to the clinical study. This includes any unique clinical study identifiers assigned by other publicly available clinical trial registries. If the clinical study is funded in whole or in part by a U.S. Federal Government agency, the complete grant or contract number must be submitted as a Secondary ID.
- 3.15 **Sponsor:** The entity (for example, corporation or agency) that initiates the study
- 3.16 **Unique Protocol ID:** Any unique identifier (ID) assigned to the protocol by the sponsor. At Wright State, the Unique Protocol ID is the IRB number.

4.0 Policy

- 4.1 It is the policy of the Wright State University that the following new or ongoing clinical trials shall be registered at <http://www.clinicaltrials.gov>:
- 4.1.1 Applicable clinical trials defined by Title VIII of the Food and Drug Administration Amendment Act of 2007 (FDAAA);
 - 4.1.2 Clinical trials funded, either in whole or in part, by the National Institutes of Health (NIH);
 - 4.1.3 Qualifying clinical trials which will render claims for items and services to the Center for Medicare and Medicaid Services (CMS)
 - 4.1.4 Clinical trials that meet the clinical trial definition of the International Committee of Medical Journal Editors (ICMJE) and, the results of which, the investigator plans to publish in a member journal.
- 4.2 **Accountability:**
- 4.2.1 It is the responsibility of the Principal Investigator to ensure registration and results reporting are completed and updated, and in the timeframes required, by FDAAA, NIH, CMS and/or ICMJE.
 - 4.2.2 It is the Principal Investigator's responsibility to upload the required documents per the Final Rule for Clinical Trials Registration and Results Information Submission and the 2018 Common Rule.

5.0 Procedures

5.1 Definition of Clinical Trial:

The definition of clinical trial differs across federal policies, regulations and other sources.

- 5.1.1 **Applicable Clinical Trial, or ACT (FDAAA):**
Includes interventional studies (with one or more arms) of FDA-regulated drugs, biological products or devices that meet one of the following conditions:

- the trial has one or more sites in the U.S.;
- the trial is conducted under an FDA investigational new drug application (IND) or investigational device exemption (IDE); or
- the trial involves a drug, biologic or device that is manufactured in the U.S. or its territories and is exported for research.

There are two types of FDAAA-defined applicable clinical trials which must be registered and results reported:

- **Applicable Clinical Drug Trial:** A controlled clinical investigation, other than a Phase I clinical investigation, of a drug or biological product subject to FDA regulation; and
- **Applicable Clinical Device Trial:** A controlled trial with health outcomes of devices subject to FDA regulation, other than small feasibility studies or pediatric post-market surveillance required by FDA.

Registration is required for applicable clinical trials (ACT) initiated after September 27, 2007 or ongoing as of December 26, 2007.

Trials that are excluded:

- (Non-serious/life-threatening) Phase 1 drug trials, including studies in which drugs are used as research tools to explore biological phenomena or disease processes
- Small clinical trials to determine the feasibility of a device or a clinical trial to test prototype devices where the primary outcome measure relates to feasibility and not to health outcomes
- Trials that do not include drugs, biologics, or devices (e.g., behavioral interventions)
- Non-interventional (observational) clinical research, such as cohort or case-control studies
- Trials that were ongoing* as of September 27, 2007, and reached the Completion Date before December 26, 2007

5.1.2 Clinical Trial (**NIH**):

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.

- NIH requires registration and results reporting for all NIH-supported clinical trials, regardless of study phase, type of intervention, or whether or not they are subject to FDAAA.

If you answer YES to ALL four of the following questions, your study is considered a clinical trial per the NIH definition:

1. Does the study involve human participants?
2. Are the participants prospectively assigned to an intervention?
3. Is the study designed to evaluate the effect of the intervention on the participants?
4. Is the effect being evaluated a health-related biomedical or behavioral outcome?

Your study is considered to meet the NIH definition of a clinical trial even if:

- Your study uses healthy participants, or does not include a comparison group (e.g., placebo or control)
- Your study is only designed to assess the pharmacokinetics, safety, and/or maximum tolerated dose of an investigational drug
- Your study utilizes a behavioral intervention
- Your study uses an intervention for the purposes of understanding fundamental aspects of a phenomenon.

Your study is NOT considered to meet the NIH definition of a clinical trial if:

- Your study is intended solely to refine measures.
- Your study involves secondary research with biological specimens or health information.

5.1.3 Qualifying Trial (**CMS**):

The activity must be a clinical trial that qualifies for coverage (as specified in CMS Section 310.1 of the Medicare National Coverage Determination Manual) and the purpose of the trial must be the evaluation of an item or service that falls within a Medicare benefit category (e.g., physicians' services, durable medical equipment, diagnostic test, etc.). The trial must have therapeutic intent and must enroll patients with diagnosed disease, not only healthy volunteers.

5.1.4 Clinical Trial (**ICMJE**):

A clinical trial is 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 defined as any biomedical or health-related measures obtained in patients or participants, including pharmacokinetic measures and adverse events.
- This definition includes Phase I studies.

5.1.5 Studies supported by a foundation who is a signatory to World Health Organization, International Clinical Trials Registry Platform (ICTRP):

- Many Non-governmental organizations (NGOs) and foundations such as the Bill and Melinda Gates Foundation, and the Wellcome Trust require registration and results reporting as part of contractual obligations for funding.

5.2 Responsible Party Determination

5.2.1 For Wright State-engagement of single-site studies, Wright State (sponsor) should be listed as responsible party.

- Dual Affiliation: Investigators may have dual affiliations at both Wright State University and local hospitals, clinics, or other academic institutions. In these cases, the investigator should determine which affiliation has primary engagement in the clinical trial. Typically, your primary affiliation is at the institution where you get your paycheck and/or the institution where you are primarily on-duty in any capacity (e.g., as an employee or student), unless Wright State is the prime awardee of the funding.
- Wright State Engagement Examples:
 - Wright State is receiving funding for the research (including any funding for salary support) through a grant, contract, or cooperative agreement.
 - Research is funded by Wright State internal (college or departmental) funds.
 - Research is being used to fulfill requirements associated with a Wright State role.
 - Students performing research to fulfill a programmatic requirement such as thesis or dissertation. This requirement would apply for graduate students or medical students who are enrolled in a dual M.D./PhD. Program.
 - Staff/Faculty performing research as part of their employment with and on behalf of Wright State.

5.2.2 For clinical trials occurring at Premier Health, Wright State Physicians, and Dayton VA Medical Center studies in which the Wright State IRB is acting as IRB of record, and Wright State University is determined to not be engaged, the respective relying facility will be the responsible party. These clinical trials should be registered under the respective facility account and not the Wright State University clinicaltrials.gov account. Investigators will need to comply with the respective facility policy regarding registration of clinical trials.

5.2.3 For multi-site trials:

- The holder of the IND, IDE, or HDE from the FDA will be designated as the responsible party
- The overall principal investigator for the study, and/or the investigator who meets all the requirements of responsible party as outlined in FDAAA 801.

5.3 Registration

Principal Investigators are responsible to register clinical trials at clinicaltrials.gov, review the content of the information uploaded to the registry to verify completeness and accuracy, and ensure all data-entry activities occur within required time frames, as follows:

5.3.1 FDAAA:

The Principal Investigator must register and input required clinical trial information through the Protocol Registration System (PRS) at the ClinicalTrials.gov website *no later* than 21 days after enrollment of the first participant (<https://www.clinicaltrials.gov/ct2/manage-recs/fdaaa>).

5.3.2 NIH:

The Principal Investigator must register and input required clinical trial information at the ClinicalTrials.gov website no later than 21 days after enrollment of the first participant (<https://www.nih.gov/news-events/summary-hhs-nih-initiatives-enhance-availability-clinical-trial-information>).

5.3.3 CMS:

The Principal Investigator must register and input required clinical trial information and obtain an NCT# at the ClinicalTrials.gov website before submitting claims for such services to CMS.

5.3.4 ICMJE:

The Principal Investigator must register with an ICMJE qualified publicly-accessible registry at or before the first patient is enrolled in the study as a condition for publication in a participating journal (<http://www.icmje.org/about-icmje/faqs/clinical-trials-registration>).

Studies registered on ClinicalTrials.gov must be registered through the Wright State University organization account at the clinicaltrial.gov website. The IRB will assign an IRB Protocol Number at the time the IRB application is accepted for review in RSP Gateway. The Principal Investigator should initiate study registration once the IRB Protocol Number is assigned. If the study involves multiples sites, the lead site and/or industry sponsor will be the responsible party.

5.4 Updating Records

Principal Investigators are responsible to keep clinical trial records continually accurate, up-to-date, and verify that data-entry occurs within the required time frames, as follows:

5.4.1 FDAAA, NIH, CMS and ICMJE require the following:

- Registration information must be updated no less than once every twelve months even if there are no changes;
- The following data elements must be updated within 30 days after a change occurs:
 - Study start date
 - Intervention name(s)
 - Availability of Expanded Access
 - Expanded Access status
 - Overall recruitment status
 - Explanation for change in status
 - Actual enrollment data
 - Individual site status
 - IRB status
 - Completion Date
 - Responsible Party
 - Official Title
 - Contact Information
 - Trial closure (regardless of the reason for closure— completion, low enrollment, etc.)

5.5 Results Reporting

Principal investigators are responsible to report results of clinical trials registered at a www.clinicaltrials.gov, review the record for accuracy and ensure data-entry occurs within required time frames, as follows:

5.5.1 **FDAAA & NIH:** Aggregate results and adverse event reporting on ClinicalTrials.gov must occur ***within 12 months of the Primary (endpoint) Completion Date***; Results for the *secondary outcome measure(s)* must be submitted **no later than 12 months** after the study completion date.

5.4.1 **CMS & ICMJE:** If the study qualifies as a clinical trial under FDAAA or NIH, results and event reporting must occur ***as indicated above***. If the study does not qualify as a clinical trial under FDAAA or NIH, ***results reporting is voluntary***.

Detailed instructions for submission of study results are found on the ClinicalTrials.gov website at <https://clinicaltrials.gov/ct2/manage-recs/how-report>.

5.6 Transfer of PI Responsibilities

During the course of a clinical trial, the PI may relocate to another institution or otherwise be unavailable to fulfill his/her role responsibilities as PI. Before leaving the University, the PI must work with their Department Head and/or Research Dean to ensure an orderly transition of his/her responsibilities to the new PI at the University or to initiate transfer of the registry account/record(s) and PI responsibilities to the new institution.

If a clinical trial remains at the University and there are continuing registry reporting obligations without a named PI, then the Department Head or Research Dean must personally assume or appoint a PI to serve and assume any remaining reporting obligations.

5.7 Other Posting Responsibilities

5.7.1 As mandated per the 2018 Common Rule:

- Posting (uploading) one IRB-approved informed consent form used to recruit study participants on a publicly available Federal website after recruitment closes, and no later than 60 days after the last study visit, if applicable.
- Any proprietary or personal information (such as names and phone numbers) must be redacted prior to posting the informed consent form.

5.7.2 As required per the Final Rule:

- Uploading the IRB-approved protocol and statistical analysis plan in a timely manner to ClinicalTrials.gov.
- Responding to registry reviewer requests for information or changes, as applicable, in a timely fashion.

5.8 Other Policy Requirements

- 5.8.1 Each PRS user must have their own account. Account sharing is not allowed.
- 5.8.2 The “Unique Protocol ID” must be the Wright State IRB number.
- 5.8.3 Any grant/funding number(s) must be listed as a “Secondary ID.”
- 5.8.4 The clinical trial PI must be assigned as “Record Owner.”
- 5.8.5 The “Responsible Party” must be designated as the “Sponsor.”

5.9 Penalties/Consequences:

- 5.9.1 On August 12, 2020 the Food and Drug Administration (FDA) released the final guidance on [Civil Money Penalties Relating to the ClinicalTrials.gov Data Bank](#).

Investigators should be aware of the following:

- Failure to submit clinical trial results information or the submission of false or misleading information may lead to civil monetary penalty and/or withholding of or loss of current and future grant funding
 - Failure to submit a required certification or knowingly submitting a false certification to the FDA may lead to civil monetary penalty
 - Failure to adhere to clinical trial registration and results submission compliance rules may lead to posting of Notice of non-compliance by FDA and NIH
- 5.9.2 If a violation is identified, a preliminary notice of noncompliance will be issued to the responsible party for the applicable record(s). Failure to comply with the requirements relating to applicable clinical trials may result in further FDA regulatory action, including the issuance of a Notice of Noncompliance, civil money penalties, injunction, and/or criminal prosecution.
 - 5.9.3 If a violation is not corrected within 30 days, an initial civil money penalty of not more than \$12,103 may be assessed. An additional \$12,103 may be assessed for each day until the violation is corrected.

6.0 Responsibilities and Authorities

6.1 Principal Investigators

The University requires compliance with clinical trials registration and results reporting. If a PI fails to comply with this policy, the Human Research Protection Office will notify the applicable department chair(s) and research dean(s). Failure to comply will result in notification to the IRB of record noting regulatory noncompliance in research registration and/or results reporting.

- Should any Investigator receive a “Preliminary Notice of Noncompliance (Pre-Notice) Letter” from Clinicaltrials.gov, they should immediately contact the Wright State Human Research Protection Office at irb-rsp@wright.edu.
 - HRPP staff will work with the investigator to review the trial(s) cited by the letter to resolve any potential violations fully and within 30 calendar days.
 - Any civil monetary penalties will be paid by the Investigator’s Department/Division.
- Should any investigator receive any notice related to ClinicalTrials.gov during an FDA inspection, they should immediately contact Wright State Human Research Protection Office at irb-rsp@wright.edu.

6.2 The Wright State HRPP

The Wright State HRPP is responsible for maintaining this policy and ensuring the clinical trial registration procedure is compliant and well supported.

7.0 Records

All records related to clinical trial registration will be stored and maintained in accordance with any Wright State policy, federal regulations and sponsor requirements associated with the clinical trial.

8.0 References

8.1 FDAAA 801:

- <https://clinicaltrials.gov/ct2/manage-recs/FDAAA>

8.2 Clinical Trials Registration and Results Information Submission (Final Rule):

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

8.3 Final Rule (42 CFR Part 11) Information:

- <https://prsinfo.clinicaltrials.gov/>

8.4 NIH Elaboration Document of Responsible and Applicable Clinical Trial:

- <https://prsinfo.clinicaltrials.gov/ElaborationsOnDefinitions.pdf>

8.5 NIH Policy & Compliance ClinicalTrials.gov and FDAAA: FAQs

- https://grants.nih.gov/ClinicalTrials_fdaaa/faq.htm

8.6 ClinicalTrials.gov website:

- www.clinicaltrials.gov

8.7 2018 Common Rule:

- <https://www.hhs.gov/ohrp/regulations-and-policy/regulations/finalized-revisions-common-rule/index.html>

8.8 2018 Common Rule – Clinical Trial Informed Consent Form Posting:

- <https://www.hhs.gov/ohrp/regulations-and-policy/informed-consent-posting/index.html>

8.9 ICMJE FAQ:

- <http://icmje.org/about-icmje/faqs/>

8.10 Center for Medicare and Medicaid Services (CMS):

- <https://www.cms.gov/Medicare/Coverage/ClinicalTrialPolicies/index.html?redirect=/ClinicalTrialPolicies>
- <https://www.cms.gov/Outreach-and-Education/Medicare-Learning-Network-MLN/MLNMattersArticles/Downloads/SE1344.pdf>
- https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/downloads/ncd103c1_part14.pdf

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