Title: ClinicalTrials.gov Registration and Results Reporting Guidance	
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I. PURPOSE

The purpose of this guidance document is to outline the process for registering, results reporting, and managing of Investigator-initiated interventional clinical trials through ClinicalTrials.gov.

II. ACCOUNTABILITY

It is the responsibility of the Principal Investigator to ensure ClinicalTrials.gov registration and results reporting are completed and trial information is updated on the ClinicalTrials.gov website as required.

III. DEFINITIONS

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.

Applicable Clinical Trial (ACT): This Food and Drug Administration Amendment Act of 2007 (FDAAA) definition of clinical trials includes interventional studies (with one or more arms) of FDA-regulated drugs, biological products, or devices.

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.

Clinical Trial (ICMJE): As defined by the International Committee of Medical Journal Editors (ICMJE), a clinical trial is a research project that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes.

ClinicalTrials.gov: A registry and results database of publicly and privately supported clinical studies of human participants conducted nationally and/or internationally that serves as the mechanism for fulfilling registration and results reporting requirements of FDAAA.

Food and Drug Administration Amendment Act of 2007 (FDAAA), Section 801: A federal statute, enacted September 27, 2007 that requires registration of an Applicable Clinical Trial (ACT) that is initiated after September 27, 2007 or ongoing as of December 26, 2007.

Grantee: Recipient institution of a grant or cooperative agreement from a federal agency.

International Committee of Medical Journal Editors (ICMJE): A group of general medical journal editors. They are the authors of *The Uniform Requirements for Manuscripts Submitted to Biomedical Journals*.

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.

Principal Investigator (PI): The individual who is responsible and accountable for conducting the clinical trial.

Qualifying Trial: A Center for Medicare and Medicaid Services (CMS) designation for clinical trials that qualify for coverage as specified in the "Medicare National Coverage Determination (NCD) Manual," Section 310.1. The purpose of the trial must be the evaluation of an item/service that falls within a Medicare benefit category (e.g., physicians' services, durable medical equipment, diagnostic test). The trial must have therapeutic intent and must enroll patients with diagnosed disease not only healthy volunteers.

Responsible Party (RP): University of Kentucky defines "Responsible Party" as the Principal Investigator who is responsible for conducting a clinical trial, has access to and control over the data from the clinical trial, has the right to publish the results of the trial, and has the ability to meet all of the requirements under this policy.

National Clinical Trial (NCT) Number (NCT Number/NCT #): A unique identifier that has been assigned to a study that has been successfully registered on ClinicalTrials.gov.

Protocol Registration System (PRS): The PRS is a web-based data entry system used to register a clinical study or submit results information for a registered study. You must have a PRS account to register study information on ClinicalTrials.gov.

IV. Commitment Statement

University of Kentucky complies with FDAAA, NIH, CMS, and ICMJE clinical trial registration and reporting requirements.

The Principal Investigator of an Investigator-initiated, interventional clinical trial that meets FDAAA, NIH, CMS, ClinicalTrials.gov registration and reporting requirements is responsible for posting the requisite information on University of Kentucky's organizational account on ClinicalTrials.gov.

The Principal Investigator of all interventional clinical studies that would like to be considered for publication within an ICMJE journal must register the clinical trials in a public trials registry.

Registration and results reporting must occur within the timeframe set by FDAAA, NIH, CMS and/or ICMJE, as applicable with whichever timeframe is earliest.

A. PROCEDURES

a. Registration

Registration and results reporting of clinical trials is REQUIRED if a clinical trial meets any of the following criteria:

1. FDA regulated clinical trials [other than phase 1 clinical investigations, of drugs or biological products subject to Food and Drug Administration (FDA) regulation];

2. National Institutes of Health funded Clinical Trials (fully or partially funded);

3. A clinical trial that the PI plans to publish in an International Committee of Medical Journal Editors (ICMJE) member journal;

   Note: The ICMJE clinical trial registration policy requires public, prospective registration in an acceptable public registry or in the World Health Organization (WHO) International Clinical Trials Portal. It is important to understand that ICMJE requires Principal Investigators to adhere to the registration guidelines of the chosen registry. However, by the conditions set forth by FDAAA 801, registration of a clinical trial on ClinicalTrials.gov requires the posting of summary results data.

4. Qualifying clinical trial for which reimbursement for items and services will be sought from the Center for Medicare and Medicaid Services.

   Note: The National Clinical Trial (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 (NCD) Manual," Section 310.1

b. Registration/Record Updates

i. For Applicable Clinical Trials, University of Kentucky Principal Investigators are ultimately responsible for:
- ensuring that clinical trials are registered in ClinicalTrials.gov in a timely manner;
- reviewing the content of the clinical trial information posted on ClinicalTrials.gov;
- reviewing the clinical trial record for any inconsistencies and/or errors;
- reviewing the clinical trial record as required to verify that updating is taking place as required.

ii. It is the responsibility of the Principal Investigator to register the trial in accordance with the following timelines:
- FDAAA requires that the RP (or designee) for an ACT must submit required clinical trial information through the PRS **no later than 21 days after enrollment of the first participant.**
  - https://www.clinicaltrials.gov/ct2/manage-recs/fdaaa
- The 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. These studies should be registered **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
- ICMJE requires trial registry **at or before first patient enrollment** as a condition for publication
  - http://www.icmje.org/about-icmje/faqs/clinical-trials-registration/

iii. Principal Investigator Responsibilities for Updating ClinicalTrial.gov Records
- Registration information must be updated no less than once every **6 months**.
- If recruitment status for the study changes (e.g., recruitment suspended), the registration must be updated within **30 days**.
- If the trial is complete (whether concluded or terminated prior to conclusion), registration must be updated within **30 days**.

c. Results Reporting

Aggregate results reporting, including reporting of adverse events, are required if the trial meets one of the following requirements:
- The trial meets the definition of an Applicable Clinical Trial specified in FDAAA. Reporting aggregate results and adverse events on ClinicalTrials.gov must occur within 12 months of the Primary (endpoint) Completion Date; or

- The trial is NIH-supported, in whole or in part. Results submission are required no later than one year after the trial's Primary Completion Date; or
- A study is registered on University of Kentucky's organizational account and is identified as a probable ACT/non-probable ACT based on its study information on ClinicalTrials.gov.

d. Transfer of Principal Investigator Responsibilities

During the course of a clinical trial, the Principal Investigator may relocate to another institution or otherwise be unavailable to fulfill Principal Investigator responsibilities. Before leaving the University, the Principal Investigator is responsible for working with the ClinicalTrials.gov Specialist to ensure an orderly transition of his/her responsibilities to the new Principal Investigator at University of Kentucky or to initiate transfer of the ClinicalTrials.gov account/record(s) and Principal Investigator responsibilities to the departing Principal Investigator's new institution.

If a clinical trial remains at University of Kentucky, and there are continuing ClinicalTrials.gov reporting obligations without a named PI, then the Dean or Department Chair is responsible for assuming the obligations or appointing a PI to serve to meet any remaining reporting obligations.

e. Compliance with this Plan

University of Kentucky requires compliance with ClinicalTrials.gov requirements for registration and results reporting.

Office of Corporate Compliance is responsible for auditing ClinicalTrials.gov requirements and for identifying noncompliance. The Office of Corporate Compliance notifies the PI and ClinicalTrials.gov Specialist in cases of noncompliance.

If the Principal Investigator does not comply with this plan, the Office of Corporate Compliance notifies the applicable Dean(s). The ClinicalTrials.gov Specialist is responsible for coordinating compliance with Deans, ORI, and OSPA.

V. REFERENCES

- FDAAA 801: https://clinicaltrials.gov/ct2/manage-recs/fdaaa
- 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
- NIH Elaboration Document of Responsible and Applicable Clinical Trial: https://prsinfo.clinicaltrials.gov/ElaborationsOnDefinitions.pdf
- NIH Policy & Compliance ClnicalTrials.gov and FDAAA: Frequently Asked Questions https://grants.nih.gov/ClinicalTrials_fdaaa/faq.htm
- ClinicalTrials.gov website: www.clinicaltrials.gov
- ICMJE FAQ: http://icmje.org/about-icmje/faqs/
- CMS Medicare Clinical Trial Policies https://www.cms.gov/Medicare/Coverage/ClinicalTrialPolicies/index.html?redirect=/ClinicalTrialPolicies
- Center for Medicare and Medicaid Services (CMS):
  - 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_part4.pdf

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