1.29 ClinicalTrials.gov Reporting

1.0. Purpose

The purpose of this policy is to describe the requirements for registration and compliance with ClinicalTrials.gov.

2.0. Policy

It is the policy of the Organization that:

- 2.1. FDA regulated trials that meet the definition of an "applicable clinical trial" (ACT) will be registered and updated on ClinicalTrials.gov in compliance with HHS regulations at 42 CFR 11 (Final Rule for Clinical Trials Registration and Results Information Submission).
  - 2.1.1. Investigators are required to adhere to the statutory provisions of 42 CFR 11 (rather than the abbreviated provisions described in this policy when there are discrepancies), as well as clarifications and definitions found at www.clinicaltrials.gov.
- 2.2. All NIH funded clinical trials will be registered and updated as required on ClinicalTrials.gov in compliance with the NIH Policy on the Dissemination of NIH-Funded Clinical Trial Information.
- 2.3. All Qualifying clinical trials which will render claims for items and services to the Center for Medicare and Medicaid Services (CMS) will be registered and updated on ClinicalTrials.gov as specified in the "Medicare National Coverage Determination (NCD) Manual," Section 310.1.
- 2.4. If an investigator voluntarily registers a study on ClinicalTrials.gov even though registration is not required, all ClinicalTrials.gov requirements and UNMC HRPP policies related to ClinicalTrials.gov reporting apply.

3.0. Definitions

- 3.1. Clinical Trial:
  - 3.1.1. Per 42 CFR 11.10(a) a clinical trial is a “clinical investigation (or clinical study) in which human subject(s) are prospectively assigned, according to a protocol, to one or more interventions (or no intervention) to evaluate the effect(s) of the intervention(s) on biomedical or health-related outcomes”
  - 3.1.2. Per NIH Policy NOT-OD-16-149 a clinical trial is 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.”
    - 3.1.2.1. For the purposes of this Policy, the regulatory definition at 42 CFR 11.10(a) and the definition in NIH policy are treated as synonymous. The NIH definition of "clinical trial" is, however, broader than the term "applicable clinical trial" as defined in 42 CFR 11 (below).
    - 3.1.2.2. The NIH definition of a clinical trial includes “Basic Experimental Studies involving Humans” (BESH) that meet both the definition of basic research and the NIH definition of a clinical trial. BESH are subject to NIH clinical trials policies such as registration and results reporting.
  - 3.1.3. Per ICJME 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.”
- 3.2. Applicable Clinical Trial (ACT):
  - 3.2.1. An applicable device clinical trial means a clinical trial or study that meets the conditions listed in 42 CFR 11.22(b).
  - 3.2.2. ACTs generally include interventional studies (with one or more arms) of FDA-regulated drugs, biological products, or devices that meet one of the following conditions:
    - 3.2.2.1. The trial has one or more sites in the United States.
    - 3.2.2.2. The trial is conducted under an FDA investigational new drug application or investigational device exemption.
    - 3.2.2.3. The trial involves a drug, biologic, or device that is manufactured in the United States or its territories and is exported for research.
  - 3.2.3. ACTs include the following:
    - 3.2.3.1. Trials of drugs and biologics: Controlled clinical investigations, other than phase 1 clinical investigations, of drugs or biological products subject to Food and Drug Administration (FDA) regulation.

        - 3.2.3.2. Trials of devices: 1) Controlled trials with health outcomes of devices subject to FDA regulation, other than small feasibility studies, and 2) pediatric post-market surveillance required by FDA.
- 3.3. Responsible Party:
    - 3.3.1. The sponsor of the trial will be considered the responsible party unless and until a principal investigator has been designated the responsible party in accordance with 42 CFR 11.4(c)(2).
    - 3.3.2. If an ACT or clinical trial is being conducted under an IND or IDE, then the holder of the IND or IDE is the responsible party regardless of how the clinical trial is being funded.
    - 3.3.3. For clinical trials not conducted under an IND or IDE:
        - 3.3.3.1. If the clinical trial is being conducted under a grant or sponsored research agreement, the funding recipient is generally considered to be Responsible Party.
        - 3.3.3.2. If the clinical trial is being conducted under a contract, the funder is generally considered to be the responsible party
        - 3.3.3.3. If there is no funding agreement supporting the clinical trial, the person or entity who initiated the clinical trial by preparing and/or planning the clinical trial, and has authority and control, is considered to be the responsible party.
    - 3.3.4. The sponsor of the clinical trial may designate the principal investigator to be the responsible party, if the PI satisfies the requirements of 42 CFR 11.4(c)(2).
    - 3.3.5. For NIH funded clinical trials, the awardee is usually the Responsible Party. If he/she is not the Responsible Party, then he/she is still obligated to coordinate with the responsible party to ensure that all regulatory requirements are met.
- 3.4. Record Owner: ClinicalTrials.gov Protocol Registration and Results System (PRS) account holder who creates a study record in PRS and is authorized by the Responsible Party to enter information into the PRS.

4.0. Investigator Responsibilities

The following describes the responsibilities of the PI if he/she is the Responsible Party. If he/she is not the Responsible Party, then the PI is responsible only for assuring the IRB Application correctly reflects that the research study is registered with clinicaltrials.gov and that the NCT number is accurate. Otherwise, this section does not apply.

- 4.1. The PI must ensure the following trials are registered in the ClinicalTrials.gov PRS system:
    - 4.1.1. FDA regulated trials that meet the definition of an "applicable clinical trial" (ACT) as above.
        - 4.1.1.1. The following types of studies are generally excluded from the registration and results submission requirements of 42 CFR 11. This is not a complete list.
            - 4.1.1.1.1. Phase 1 drug trials, including studies in which investigational drugs are used as research tools to explore biological phenomena or disease processes
            - 4.1.1.1.2. 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
            - 4.1.1.1.3. Trials that do not include drugs, biologics, or devices (such as behavioral interventions)
            - 4.1.1.1.4. Non-interventional (observational) clinical research (such as cohort or case-control studies)
        - 4.1.1.2. FDA regulated trials that do not meet the definition of ACT, or that do not otherwise require registration per 42 CFR 11 may still require registration if they are an NIH funded clinical trial, or are a qualifying clinical trial which will render claims for items and services to the CMS (per section 2.0 above).
    - 4.1.2. All NIH-funded clinical trials
        - 4.1.2.1. All NIH-funded awardees and investigators conducting clinical trials will register and report the results of their trial in Clinicaltrials.gov regardless of study phase, type of intervention, or whether they are subject to 42 CFR 11. *Note: For example, NIH-funded phase 1 clinical trials of an FDA-regulated product are covered by this policy as are clinical trials studying interventions not regulated by the FDA, such as behavioral interventions.*
        - 4.1.2.2. The investigator is responsible for submitting to the ORA a copy of the award letter or other documentation from the NIH which specifies whether the trial constitutes a clinical trial subject to NIH Policy NOT-OD-16-149.
    - 4.1.3. All Qualifying clinical trials which will render claims for items and services to the Center for Medicare and Medicaid Services (CMS) will be registered and updated on ClinicalTrials.gov as specified in the "Medicare National Coverage Determination (NCD) Manual," Section 310.1.
    - 4.1.4. Though not a requirement of the Organization, investigators should be aware that the International Committee of Medical Journal Editors (ICMJE) requires and recommends that all clinical trials be registered in a public registry at or before the time of first participant enrollment as a condition of consideration for publication. ICJME accepts registration in any registry that is a primary register of the WHO International Clinical Trials Registry Platform (ICTRP), including ClinicalTrials.gov. A listing of non-ICJME journals that follow ICJME's recommendations is available on the ICJME website.
    - 4.1.5. Though not a requirement by the Organization, investigators should be aware that

funders, may require registration and compliance with a publicly available registry.
- 4.2. The PI is responsible for assuring that the IRB Application correctly reflects that a research study is registered with clinicaltrials.gov and that the NCT number is accurate. If registration is done after initial approval, a change request will be required.
- 4.3. If a research study which does not require registration is voluntarily registered with clinicaltrials.gov, then the responsible party is obligated to satisfy all requirements noted in this policy.
- 4.4. If the clinical trial is not registered with ClinicalTrials.gov the PI must provide justification why the trial is not registered.
- 4.5. The PI must update the ClinicalTrials.gov record in accordance with Section 801 of FDAAA (https://clinicaltrials.gov/ct2/manage-recs/fdaaa) and 42 CFR 11.64. This may apply to some changes, study status, and annual update.
- 4.6. The PI is responsible for uploading required documents in accordance with 42 CFR 11.48(a)(5).
- 4.7. The PI is responsible for ensuring the submission of all appropriate study results as defined in 42 CFR 48 at the conclusion of the study, in accordance with in 42 CFR 11.42.
- 4.8. Should the PI leave the Organization, the PI is responsible for assuring that the record is transferred to a new Responsible Party, the record is resolved (completed, terminated, or withdrawn) with all applicable information entered, or the record is transferred to the PI's new Institution (applicable only to on-going studies).
- 4.9 If a study subject to this policy is completed (that is, when the investigator files a completion report), the IRB protocol must remain open and active until the ClinicalTrials.gov record is resolved.

5.0. ORA responsibilities

The following describes the responsibilities of the ORA where faculty, student or employee of the Organization is the Responsible Party for a record on ClinicalTrials.gov; otherwise, the UNMC HRPP Policies do not apply.

- 5.1. For studies where registration on ClinicalTrials.gov is required, ORA will not issue full approval of any protocol where the Responsible Party is part of the Organization until the trial is registered and NCT number is issued.
  - 5.1.1. Under certain limited circumstances, full approval may be granted before issuance of the NCT number, provided registration has been completed (for example, if a Letter of Award or grant funding is dependent on IRB approval). In those circumstances, a letter of IRB approval will be provided, but subject enrollment may not begin, and funds may not be spent, until the NCT number is provided as a Request for Change in protocol.
- 5.2. Approval of any subsequent IRB submissions will not be issued until the ClinicalTrials.gov record is in compliance. The IRB ORA Analyst serving as the PRS Administrator will communicate the problems with the Responsible Party and Record Owner, and ensure the problems are resolved appropriately.
- 5.3. The PRS Administrator will routinely review the Organization's ClinicalTrials.gov records for problems and will notify the Responsible Party and Record Owner, and ensure the problems are resolved appropriately.
- 5.4. The PRS Administrator will review the ClinicalTrials.gov record when a protocol amendment is submitted and will ensure that applicable changes are appropriately updated on the record.
- 5.5. Investigators who are non-compliant with ClinicalTrials.gov requirements or this HRPP Policy may be subject to disciplinary actions as per HRPP policy 8.4 (Review of Noncompliance Involving the PI and Study Personnel), and per the Office of the Vice-Chancellor for Research.

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Revised 1/6/2023 - Added requirement that CMS qualifying clinical trials must be registered and updated as required on ClinicalTrials.gov; specifically noted that BESH constitute clinical trials subject to this policy; added recommendation that clinical trials that meet the clinical trial definition of The International Committee of Medical Journal Editors (ICMJE) be registered and updated as required on ClinicalTrials.gov; clarified that if an investigator voluntarily registers a study on ClinicalTrials.gov even though registration is not required, all ClinicalTrials.gov requirements and UNMC HRPP policies related to ClinicalTrials.gov reporting apply; added that should the PI or the Record Owner leave the Organization, the PI is responsible for assuring that the Responsible Party and/or Record Owner are updated in the PRS database; revised ORA responsibilities and processes; added that investigator is responsible for submitting documentation from NIH specifying whether the trial constitutes a clinical trial; text reorganized and stylistic changes made for clarity. {Approved Chris Kratochvil (Institutional Official), Bruce Gordon (Assistant Vice Chancellor for Regulatory Affairs,

Executive Chair)}

Board notified: 1/16/2023

Revised 3/20/2023 - Provided regulatory reference for designation of “applicable clinical trials”; simplified “ORA Responsibilities” and deleted specific procedures; simplified “Investigator Responsibilities”; added that “If a study subject to this policy is completed ... the IRB protocol must remain open and active until the ClinicalTrials.gov record is resolved” (section 4.9); stylistic changes. {Approved Chris Kratochvil (Institutional Official), Bruce Gordon (Assistant Vice Chancellor for Regulatory Affairs, Executive Chair)}

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