DIVISION OF RESEARCH & INNOVATION Research Integrity & Compliance	**Institutional Review Board Standard Operating Procedures**

Title: ClinicalTrials.gov Registration

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Approval/Date:

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PURPOSE

The purpose of this Standard Operating Procedure (SOP) is to define Research Integrity and Compliance (RIC), Institutional Review Board (IRB) program, and Researcher procedures for the registration and results reporting of clinical trials to ClinicalTrials.gov.

SCOPE

This SOP delineates systematic process activities and functions for compliance with the US Department of Health and Human Service, Office for Human Research Protections (OHRP) and Common Rule requirements, and University of North Texas (UNT) requirements for the management, coordination, and operation of the Institutional Review Board program. It applies to all staff members who are engaged in the operations and support of the Institutional Review Board, and to all UNT Researchers performing human subjects research.

DEFINITIONS/ ABBREVIATIONS

1. Definitions

1.1 *Applicable Clinical Trials (ACTs):*Studies either initiated after September 27, 2007, or initiated on or before that date and were still ongoing as of December 26, 2007, and meeting the qualifications for registration as defined in section 402(j) of the Public Health Service Act and conforming amendments to the Federal Food, Drug, and Cosmetic FD&C Act (FD&C Act). As reflected in 42 CFR 11.10, ACTs generally include interventional studies (with one or more arms) of FDA-regulated drug, biological, or device products that meet one of the following conditions:

- The trial has one or more sites in the United States

- The trial is conducted under an FDA investigational new drug application or investigational device exemption
- The trial involves a drug, biological, or device product that is manufactured in the United States or its territories and is exported for research.

A complete definition can be located on the "Checklist and Elaboration for Evaluating Whether a Clinical Trial or Study is an Applicable Clinical Trial (ACT)."

1.2 *Clinical Trial*: 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. (International Committee of Medical Journal Editors (ICMJE) Definition of Clinical Trial)

1.3 *IRB Analyst:* Staff member of Research Integrity and Compliance that performs administrative activities, pre-reviews, reviews, and approvals for the Institutional Review Board program.

1.4 *Principal Investigator:* The primary individual responsible for the preparation and conduct of a research grant, sponsored project, or human subjects research study, in compliance with applicable laws, regulations, and institutional policy governing the conduct of research.

1.5 Protocol Registration and Results System (PRS): Website for entering and updating ClinicalTrials.gov records https://register.clinicaltrials.gov/

1.6 Record Owner: This individual can be the Principal Investigator or a designated research team member that is responsible for updating the ClinicalTrials.gov record and ensuring that it is updated in a timely manner. The owner must maintain communication so that the protocol record is released by the PI (Responsible Party) in the required time frame.

1.7 Researcher: Any individual performing various tasks related to the conduct of human subjects research activities, including but not limited to obtaining informed consent from subjects, collecting and analyzing data, interacting with subjects, and communicating with the IRB.

1.8 Responsible Party: The individual with complete access to trial data and rights to publish. The Responsible Party for Investigator Initiated studies is the Principal Investigator. The Responsible Party may designate individuals to help complete the ClinicalTrials.gov record, however, the final responsibility of review and approval lies with the Responsible Party. The Responsible Party has the sole authority to release a record.

2. Abbreviations

2.1 ACTs- Applicable Clinical Trials
2.2 IRB- Institutional Review Board
2.3 OHRP- Office for Human Research Protections
2.4 PI- Principal Investigator
2.5 PRS- Protocol Registration and Results System
2.6 RIC- Research Integrity and Compliance
2.7 SOP/SOPs - Standard Operating Procedure(s)

RESPONSIBILITIES

This SOP is applicable to all members of Research Integrity and Compliance and Institutional Review Board members who are involved in record keeping, reviewing, or approving research studies for the Institutional Review Board program. This SOP is also

applicable to all UNT researchers performing human subjects research under the oversight of the UNT Institutional Review Board.

PROCEDURE

1. The U.S. Food and Drug Administration (FDA) is the government agency that requires registration of clinical trials. Section 801 of the Food and Drug Administration Amendments Act of 2007 (FDAAA 801 or US Public Law 110-85) passed on September 27, 2007 requires mandatory registration and results reporting for certain clinical trials of drugs, biologics, and devices of all "Applicable Clinical Trials" initiated on or before September 27, 2007, and is ongoing as of December 27, 2007. This legislation coupled with the Final Rule for Clinical Trials Registration and Results Information Submission creates the regulatory requirements and procedures for ClinicalTrials.gov.
   1.1 According to the Food and Drug Administration Amendments Act of 2007:
      1.1.1 Penalties may include civil monetary penalties up to $10,000 fine for failing to submit or for submitting fraudulent information to ClinicalTrials.gov.
      1.1.2 After notification of noncompliance, the fine may go up to $10,000 per day until resolved.
      1.1.3 For federally funded grants, penalties may include the withholding or recovery of grant funds.
2. **Researcher Responsibilities**
   2.1 According to federal law, the 'Responsible Party' is responsible for reporting results to ClinicalTrials.gov. Research Integrity and Compliance may help make determinations if studies need to be registered.
   2.2 For trials being conducted under a funding agreement, grant (e.g. NIH awards) or department/internal funding, the funding recipient is considered the Responsible Party. Because the PI is in best position to understand the research protocol study results and adverse events, the institution will designate the Principal Investigator to assume the role of the Responsible Party. According to federal law, the Principal Investigator can serve as a Responsible Party if that individual:
      2.2.1 Is responsible for conducting the trial
      2.2.2 Has access to and control over the data from the clinical trial
      2.2.3 Has the right to publish the results of the trial
   2.3 In situations where UNT serves as the primary site for a clinical trial and the institution is determined to be the "Responsible Party," the responsibility will fall to the Principal Investigator.
   2.4 To obtain PRS access to register a study or study results, the "Responsible Party" must contact oric@unt.edu.
      2.4.1 The requestor must provide full name, institutional e-mail address, IRB number and title of the protocol. If the requestor is not the PI, an e-mail from the PI to the oric@unt.edu is required to create or change access. Please note that the PI of the study will need to have a ClinicalTrials.gov account in order to approve and release the record. You may request that at the same time if the PI does not have an account yet.
      2.4.2 Once an account is created you will be notified by the administrator and will receive an e-mail from the Protocol Registering System (PRS) to modify your password.
      2.4.3 Instructions to create, edit, approve, and release a study record will be provided to the PI and record owner. Additionally, instructions for creating, editing, approving, and releasing a study record are available on the main ClinicalTrials.gov website.

2.5 The Responsible Party is ultimately responsible for ensuring the studies are registered with ClinicalTrials.gov and updated appropriately at required intervals and released to the public database. The PI may be contacted by Research Integrity and Compliance if their protocol record is delinquent and needs to be updated. However, it is the sole responsibility of the Responsible Party to ensure the timelines are met. If the protocol record remains delinquent one month after initial reminder, without acceptable activity/progress, Research Integrity and Compliance will notify the PI and department chair.

2.6 Timelines for registration and study updates are strict. These include:

2.6.1 Registration- Registration should occur prior to the enrollment of the first subject but NO LATER than 21 days after the first subject is enrolled. A study is considered registered once the Responsible Party releases the record to PRS for review.

2.6.2 Active Enrollment- Updates or verifications must be made every 6 months. The record must be verified even if no changes need to be made.

2.6.3 Closed to Enrollment or Pending Results- Updates or verifications must be made annually. The record must be verified even if no changes need to be made.

2.6.4 Changes in Study Status- The record must be updated within 30 days of the status change.

2.6.5 Results Submission- Results must be submitted no later than 1 year after the primary completion date. Delayed submission of results is only permitted in certain circumstances. See 42 CFR 11.44 for details.

2.7 Please note that records cannot be deleted once they have been issued an NCT number, even after the study has been completed. There are limited circumstances when a record can be removed. Please contact oric@unt.edu for further details.

2.8 Penalties for noncompliance may include the following:

2.8.1 Under 42 CFR 11, civil and monetary penalties exist for noncompliance. Monetary penalties can be up to 10,000 US dollars a day.

2.8.2 Grant funding can be withheld until the required clinical trial information has been submitted.

2.8.3 Journals can refuse to publish data from studies that are noncompliant.

2.8.4 Noncompliance with UNT procedures and policies, 42 CFR 11, and other requirements could result in corrective actions that may include reporting of noncompliance to the IRB.

3. **Transferring a Record**

3.1 Research Integrity and Compliance will aid in all record transfers:

3.1.1 If the Responsible Party or PI is leaving UNT, they should inform oric@unt.edu, prior to leaving, to ensure that their ClinicalTrials.gov record is appropriately monitored or transferred.

3.1.2 The Responsible Party or PI can be reassigned to an alternative party within the University. The record may also be transferred to the new institution.

REFERENCES

1. US Department of Health and Human Service, Office for Human Research Protections (OHRP)
2. https://grants.nih.gov/policy/clinical-trials/reporting/index.htm
3. https://grants.nih.gov/policy/clinical-trials/reporting/understanding.htm
4. Checklist and Elaboration for Evaluating Whether a Clinical Trial or Study is an Applicable Clinical Trial (ACT)

5. International Committee of Medical Journal Editors (ICMJE) Definition of Clinical Trial

APPENDICES

1. UNT IRB SOP