UTHealth Human Subjects Protection Program
Policy and Procedures

Clinical Trial Registration and Results Reporting

POLICY

It is the policy of The University of Texas Health Science Center at Houston ("UTHealth") that clinical trials be registered and their results be reported at ClinicalTrials.gov in conformance with all relevant regulations and policies, including federal regulations and the National Institutes of Health (NIH) policy.

Clinical Trials That Must be Registered

Under this policy, clinical trials must be registered at https://clinicaltrials.gov/ if they meet any of the following criteria:

1. Applicable Clinical Trials: Applicable Clinical Trials, as defined by FDAAA section 801 and the Final Rule for Clinical Trials Registration and Results Information Submission (42 CFR Part 11), must be registered. Results must also be entered to ClinicalTrials.gov for all Applicable Clinical Trials.
2. NIH-funded Clinical Trials: All clinical trials funded in whole or in part by the NIH must be registered. Results must also be entered to ClinicalTrials.gov for all NIH-funded clinical trials.
3. Qualifying Clinical Trials: Registration and a resulting NCT # is required for qualifying clinical trials, which are clinical trials in which claims for items and services provided in the clinical trial may be submitted to the Center for Medicare and Medicaid Services.

Responsible Party

The entity or individual responsible for registration of a clinical trial and subsequent results submission is called the Responsible Party.

1. For UTHealth PI-initiated studies not conducted under an IND or IDE, the University is listed as the Sponsor, and as the Sponsor, the University designates the Responsible Party role to the UTHealth PI. The PI of the study as listed in iRIS is the Responsible Party. For UTHealth PI-initiated studies conducted under an IND or IDE, the University is not listed as the Sponsor and instead the UTHealth PI who holds the IND or IDE is listed as the Sponsor-Investigator, as well as the Responsible Party.
2. For industry-sponsored studies, the industry sponsor is usually the Responsible Party. Only one record should be created for a trial, and the UTHealth PI is advised to check with the industry sponsor to verify registration. There are a few cases where it is appropriate for the industry sponsor to delegate the Responsible Party role to the UTHealth PI—UTHealth PIs are advised to consult with UTHealth's Clinical Trials Resource Center (CTRC) (clinicaltrials@uth.tmc.edu) before deciding to accept this responsibility.
3. For multi-site studies, the lead site or cooperative group is the Responsible Party. The UTHealth PI is advised to check with the lead site to verify registration.

Timelines

It is the responsibility of the UTHealth Principal Investigator (PI), as Responsible Party, to ensure that the following are completed on time.

1. Registration: Applicable Clinical Trials and NIH-funded trials must be registered no later than 21 days after enrollment of the first participant; however, because the International Committee of Medical Journal Editors (ICMJE) requires that trials be registered at or before the time of first participant enrollment, it is best to register trials before enrollment of the first participant.
2. Updates: ClinicalTrials.gov records for Applicable Clinical Trials and NIH-funded trials must be updated at least once per year, and 15 or 30 calendar days after certain defined changes.

3. Results Entry: Results for Applicable Clinical Trials and NIH-funded clinical trials must be entered no later than 12 months after the "Primary Completion Date," which is defined as "the date that the final participant was examined or received an intervention for the purposes of final collection of data for the primary outcome, whether the clinical study concluded according to the pre-specified protocol or was terminated."
4. Protocol Upload: The most recent IRB-approved protocol must be uploaded to ClinicalTrials.gov at the time of results entry.

Responsibilities of the UTHealth PI in the Role of Responsible Party

It is the responsibility of the UTHealth PI as Responsible Party to perform the following ClinicalTrials.gov-related duties as required by the federal regulations and the NIH policy:

1. Determine if ClinicalTrials.gov registration is required.
2. Determine if results submission and protocol upload are required.
3. Be aware of and adhere to the due dates for registration, record updates, results entry, and protocol upload.
4. Initiate registration, record updates, results entry, and protocol upload, as applicable.
5. Ensure entry of all required registration, record update, and results information, as well as upload of protocol, as applicable.
6. Review all information entered to the ClinicalTrials.gov record to verify completeness and accuracy and subsequently "Approve" and "Release" the record.
7. Respond to ClinicalTrials.gov PRS staff reviewer requests by due dates.
8. Share correspondence related to ClinicalTrials.gov compliance (such as notice of an FDA audit or issuance of an FDA Pre-Notice or Notice of Noncompliance letter) with the UTHealth PRS Administrator at clinicaltrials@uth.tmc.edu.
9. If NIH or other federal funding is received after the time of initial submission to the IRB, promptly notify CTRC (clinicaltrials@uth.tmc.edu).
10. Notify the UTHealth PRS Administrator of any change in Responsible Party for clinical trials where the UTHealth PI is the Responsible Party.
11. If leaving UTHealth, notify the UTHealth PRS Administrator and ensure that all responsibilities under this policy have been met before departure.

PROCEDURES

Identifying Clinical Trials for Registration: For studies that are initially reviewed by UTHealth's full Institutional Review Board (IRB) at a convened meeting, the UTHealth PRS Administrator will make a determination of whether a clinical trial must be registered per FDAAA, the Final Rule, NIH policy, and/or the ICMJE recommendations. For UTHealth-PI initiated clinical trials (i.e., studies in which the UTHealth PI is the Responsible Party), if the UTHealth PRS Administrator determines that registration is required per FDAAA, the Final Rule, NIH, or ICMJE, then CTRC will notify the PI and other contacts listed in iRIS. The UTHealth PRS Administrator does not review studies undergoing expedited initial IRB review, and UTHealth PI's are encouraged to consult with CTRC (clinicaltrials@uth.tmc.edu) in determining whether their expedited studies must be registered per FDAAA, the Final Rule, NIH policy, and/or the ICMJE guidelines. The Policy does not mandate registration of studies that are only subject to the ICMJE guidelines for registration (and not to FDAAA, the Final Rule, or the NIH policy for registration and results reporting); however, because ICMJE journals may not publish reports of clinical trials if the trial was not registered before enrollment began, UTHealth PIs are strongly encouraged to prospectively register these trials in order to avoid issues with publication.

Registration Process: The UTHealth PI is responsible for initiating and completing registration at ClinicalTrials.gov by the legal and NIH due date; however, the UTHealth PRS Administrator is available upon request to assist. Study teams with little to no experience with ClinicalTrials.gov are strongly encouraged to work with a UTHealth PRS Administrator (clinicaltrials@uth.tmc.edu) to register together. UTHealth PI-Initiated studies are registered through UTHealth's organizational PRS account (Organization ID is UTexas_Houston). To request a personal account within UTHealth's organizational account, contact the UTHealth PRS Administrator at clinicaltrials@uth.tmc.edu.

Record Update Process: The ClinicalTrials.gov record must be updated at least once per year, and 15 or 30 days after the changes detailed on page 11 at https://prsinfo.clinicaltrials.gov/FinalRuleChanges-16Sept2016.pdf. The UTHealth PI is responsible for initiating and completing updates to the ClinicalTrials.gov record; however, the UTHealth PRS Administrator is available upon request to assist.

Results Entry Process: The UTHealth PI is responsible for initiating and completing results entry at ClinicalTrials.gov by the legal and NIH due date; however, the UTHealth PRS Administrator is available upon request to assist, and study teams are strongly encouraged to use this assistance. For Applicable Clinical Trials and NIH-funded clinical trials, all required results information is due to ClinicalTrials.gov no later than 1 year after the trial's Primary Completion Date, defined as the "date that the final subject was examined or received an intervention for the purposes of final collection of data for the primary outcome, whether the clinical trial concluded according to the pre-specified protocol or was terminated." For example, even if the trial was terminated before meeting the enrollment target and only one or two participants were enrolled, the study team may believe that analyzing the data from these few participants may not be significant; however, the regulations and NIH policy still require results entry if any data were collected. It is the responsibility of the UTHealth PI to be aware of the results due date and to enter results to ClinicalTrials.gov by that due date.

Protocol Upload Process: The UTHealth PI is responsible for ensuring that the protocol is uploaded at ClinicalTrials.gov by the legal and NIH due date; however, the UTHealth PRS Administrator is available upon request to assist. For Applicable Clinical Trials and NIH-funded clinical trials, the full IRB-approved protocol must be uploaded to the record at the time of results entry and will be publicly displayed. Before upload of the protocol to ClinicalTrials.gov, contact the UTHealth PRS Administrator, who will coordinate a review of the protocol by the Office of Technology Management (OTM) and Sponsored Projects Administrations (SPA) team for any personally identifiable, trade secret, or confidential commercial information, all of which will need to be redacted from the protocol. The UTHealth PRS Administrator will provide guidance on the legally required methods for redaction and preparation of the file for upload to ClinicalTrials.gov.

Noncompliance with Policy: If the UTHealth PI does not fulfill the Responsible Party responsibilities listed in this policy, then the matter will be escalated to the PI's Department Chair. If the issue is still not resolved, then it will be escalated to UTHealth's Executive Vice President and Chief Academic Officer or designee, who will determine appropriate enforcement actions if the record is not brought into compliance in a timely fashion. The UTHealth PRS Administrator may also share information about the noncompliance with the Committee for Protection of Human Subjects. Please also see the following section of this policy titled, "External Penalties for Noncompliance."

Departure of UTHealth PI who is Responsible Party: If a UTHealth PI who is a Responsible Party plans to leave the University, then the PI must ensure that they have met all of their responsibilities under this policy before their departure, as well as notify CTRC (clinicaltrials@uth.tmc.edu).

If the Primary Completion Date (defined as "the date that the final participant was examined or received an intervention for the purposes of final collection of data for the primary outcome, whether the clinical study concluded according to the pre-specified protocol or was terminated") is on or before the UTHealth PI's departure date and if the study will remain at UTHealth, then the ClinicalTrials.gov record will remain in the UTHealth PRS account. If results entry is required by the federal regulations or NIH policy, then it is the responsibility of the departing UTHealth PI to enter results information before departure from UTHealth. If results entry is not required by the federal regulations or NIH policy, then it is the responsibility of the departing UTHealth PI to update and close out the record before departure from UTHealth.

If at the time of the UTHealth PI's departure date the record will remain in the UTHealth PRS account as described above and there are any remaining reporting obligations, and/or if the study is ongoing and the study will remain at UTHealth, then it is the responsibility of the departing PI before leaving UTHealth to transfer the Responsible Party role to another UTHealth PI, who will take on all responsibilities for the record. It is the responsibility of the departing PI to ensure that the new PI has all the necessary information, including study documents and study data to fulfill the obligations as Responsible Party. If a UTHealth PI has departed without naming a new PI to the role of Responsible Party, then the departing PI's department chair is responsible for appointing another PI to assume the role of Responsible Party to fulfill all obligations related to ClinicalTrials.gov.

If the study will move with the PI to the new institution, then the ClinicalTrials.gov record must be transferred to the new institution's PRS account. Before leaving UTHealth, the PI must contact the UTHealth PRS administrator (at clinicaltrials@uth.tmc.edu) to initiate transfer of the record to the new institution.

Arrival of PI who is Responsible Party: If a PI joins UTHealth and brings an ongoing clinical study for which there is a ClinicalTrials.gov record and for which the PI is designated as the Responsible Party, then the PI must contact the PRS administrator at their previous institution, as well as UTHealth's PRS administrator (at clinicaltrials@uth.tmc.edu), to initiate transfer of the record to UTHealth. Before UTHealth will accept a record from another institution, the record must be updated and in compliance with federal regulations and NIH policy.

If a study reaches the Primary Completion Date before the PI's start date at UTHealth and if the study will remain at the PI's previous institution, then the CinicalTrials.gov record will remain in the previous institution's PRS account and will be subject to the previous institution's policy on ClinicalTrials.gov.

DEFINITIONS

1. **Federal Definition of "Applicable Clinical Trial":**
   1.1. "Applicable Clinical Trial," as defined by the Final Rule for Clinical Trials Registration and Results Information Submission (regulation 42 CFR Part 11): https://prsinfo.clinicaltrials.gov/ACT_Checklist.pdf. In summary, "Applicable Clinical Trials" are interventional trials of drugs and biologics (other than phase 1 drug studies), interventional trials of devices (other than device feasibility studies), and pediatric post-market surveillance studies.
2. **NIH Definition of "Clinical Trial":**
   2.1. "Clinical trial," as defined by NIH: https://grants.nih.gov/policy/clinical-trials/definition.htm
   2.2. Case Studies illustrating NIH's definition of "clinical trial": https://grants.nih.gov/policy/clinical-trials/case-studies.htm
   2.3. FAQs on NIH's definition of "clinical trial": https://grants.nih.gov/grants/policy/faq_clinical_trial_definition.htm
   2.4. NIH decision tree: https://grants.nih.gov/policy/clinical-trials/CT-decision-tree.pdf
3. **ICMJE Definition of "Clinical Trial":**
   3.1. "Clinical trial," as defined by ICMJE: http://icmje.org/recommendations/browse/publishing-and-editorial-issues/clinical-trial-registration.html
4. **Definition of "Primary Completion Date":** The Final Rule, FDAAA Section 801, and the NIH policy define "Primary Completion Date" as "the date that the final participant was examined or received an intervention for the purposes of final collection of data for the primary outcome, whether the clinical study concluded according to the pre-specified protocol or was terminated. In the case of clinical studies with more than one primary outcome measure with different completion dates, this term refers to the date on which data collection is completed for all of the primary outcomes."
5. **Definition of "Responsible Party":** The Final Rule, FDAAA Section 801, and the NIH policy define "Responsible Party" as "the sponsor of the clinical trial, as defined in 21 CFR 50.3; or the principal investigator of such clinical trial if so designated by a sponsor, grantee, contractor, or awardee, so long as the principal investigator is responsible for conducting the 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 part for the submission of clinical trial information."

RELEVANT REGULATIONS, POLICIES, AND GUIDANCE

1. **Federal Regulations**
   1.1. Final Rule for Clinical Trials Registration and Results Information Submission (regulation 42 CFR Part 11): https://www.federalregister.gov/documents/2016/09/21/2016-22129/clinical-trials-registration-and-results-information-submission
   1.2. FDAAA Section 801: https://www.gpo.gov/fdsys/pkg/PLAW-110publ85/pdf/PLAW-110publ85.pdf#page=82
   1.3. Paper describing changes to law enacted by Final Rule: https://www.nejm.org/doi/full/10.1056/nejmsr1611785
   1.4. Table comparing requirements of Final Rule with the requirements of FDAAA Section 801: https://prsinfo.clinicaltrials.gov/FinalRuleChanges-16Sept2016.pdf
   1.5. FAQs on the Final Rule: https://clinicaltrials.gov/ct2/manage-recs/faq#42CFRPart11
   1.6. Definitions for registration: https://prsinfo.clinicaltrials.gov/definitions.html
   1.7. Definitions for results entry: https://prsinfo.clinicaltrials.gov/results_definitions.html

2. **NIH Policy**
   2.1. Notice on NIH policy (NOT-OD-16-149): https://grants.nih.gov/grants/guide/notice-files/NOT-OD-16-149.html
   2.2. NIH policy: https://grants.nih.gov/policy/clinical-trials/reporting/understanding/nih-policy.htm and https://www.federalregister.gov/documents/2016/09/21/2016-22379/nih-policy-on-the-dissemination-of-nih-funded-clinical-trial-information
   2.3. Table comparing key elements of the Final Rule with the NIH policy: https://www.nih.gov/news-events/summary-table-hhs-nih-initiatives-enhance-availability-clinical-trial-information
3. **ICMJE Recommendations**
   3.1. ICMJE recommendations for registration: http://icmje.org/recommendations/browse/publishing-and-editorial-issues/clinical-trial-registration.html
   3.2. FAQs on ICMJE's registration recommendations: http://www.icmje.org/about-icmje/faqs/clinical-trials-registration/
   3.3. List of journals following ICMJE recommendations: http://www.icmje.org/journals-following-the-icmje-recommendations/
4. **HOOP 168** – Conduct of Research
5. **HOOP 92** - Research Data Ownership, Retention, and Access

EXTERNAL PENALTIES FOR NONCOMPLIANCE

1. **FDA:** Under the Final Rule and FDAAA Section 801, the FDA has the ability to issue fines of at least $10,000 a day.
   1.1. FDA guidance on penalties for ClinicalTrials.gov noncompliance: https://www.fda.gov/media/113361/download
   1.2. FDA may conduct inspections for ClinicalTrials.gov compliance: https://www.fda.gov/media/75927/download and https://www.fda.gov/downloads/ICECI/EnforcementActions/BioresearchMonitoring/ucm133770.pdf
2. **NIH:**
   2.1. NIH funding may be suspended or withheld, for both individual studies and institutions as a whole.
   2.2. Past performance at ClinicalTrials.gov may affect future funding decisions.
3. **ICMJE:** Journals following the ICMJE recommendations may refuse to publish studies that were not registered before the time of first participant enrollment: http://icmje.org/recommendations/browse/publishing-and-editorial-issues/clinical-trial-registration.html
4. **AllTrials FDAAA TrialsTracker:**
   4.1. AllTrials FDAAA TrialsTracker tracks and publicly posts studies out of compliance with results reporting regulations: https://fdaaa.trialstracker.net/

If you find errors in this document, please contact CTRC at clinicaltrials@uth.tmc.edu.

Effective:	01/01/2022
Revision History:	