1000 PR.1 Clinical Trial Registration and Reporting Results; Consent Form Posting on ClinicalTrials.gov Website

1. Purpose
This procedure outlines the process for identifying clinical trials conducted at Yale that require registration by the Yale investigator, registering the trials at ClinicalTrials.gov, and monitoring of the progress of the trials to comply with the continuing reporting requirement.

2. Scope
This procedure applies to clinical trials where Yale serves as the Responsible Party, i.e. entity responsible for the clinical trial and for submission of clinical trial information. For the industry authored and sponsored clinical trials, the Sponsor serves as the responsible party. Registration requirements of these clinical trials fall outside of the scope of this procedure.

3. Overview
In accordance with HRPP Policy 1000: Clinical Trial Registration and Reporting Requirements (HRPP Policy 1000), certain research studies that meet the NIH definition of a clinical trial or the FDA definition of applicable clinical trial require registration in a public database by a Responsible Party. The HRPP Policy 1000 also outlines the Centers for Medicare and Medicaid Services (CMS) clinical trial identifier requirement for all billing claims related to clinical trials outlined in the Medicare National Coverage Determination (NCD) Manual, Section 310.1–Pub. 100-03, as well as requirements established by the International Committee of Medical Journal Editors (ICMJE) related to trial registration.

HRPP Policy 1000 and the procedures outlined below apply to biomedical (e.g., School of Medicine, School of Public Health, School of Nursing, etc.) and non-biomedical studies (e.g., Faculty of Arts and Sciences.)

ClinicalTrials.gov is one of the searchable, public registries, and results database for clinical studies and is Yale’s registry of choice for all trials that meet the regulatory and institutional registration and reporting requirements.

Yale CTgov Team is located within the Yale Center for Analytical Sciences (YCAS). The team offers assistance to Yale investigators with ClinicalTrials.gov registration and reporting requirements. In collaboration with the Human Research Protection Program (HRPP), the CTgov team also ensures compliance with ClinicalTrials.gov requirements.

---

1 For description, see 42 CFR Part 11.10 and NIH Policy (NOT-OD-16-149).
4. Initial identification and Registration

4.1 Information collected in IRES IRB
The PI must provide a research protocol and additional protocol related documents to the IRB for review and approval. In addition, the IRES IRB application requires the PI to answer questions related to the proposed research. The following information is collected in the IRES IRB application, which is used to identify a clinical trial that may require registration:

- Answers to the questions: 'Does the study prospectively assign research subjects to one or more interventions? and a follow-up: 'Does the study have a health-related biomedical or behavioral outcome?'. Affirmative responses indicate that the research study most likely meets the NIH definition of a clinical trial.
- Funding source(s);
- Designation of the research as Interventional vs. Observational;
- Designation of the research as investigator-initiated study (vs. industry authored);
- Phase of the study using definitions from ClinicalTrials.gov;
- Use of drugs, biologics, and/or devices.

The completeness of the information in the IRES IRB submission is verified by the HRPP staff upon receipt of the submission. In addition, the HRPP staff will indicate any of the federal agencies with oversight authority, e.g. FDA, NIH.

4.2 HRPP Identification
Upon receipt, HRPP staff identify the following types of studies:

- PI-initiated studies meeting the NIH definition of a clinical trial (regardless of funding)
- Studies meeting the FDA definition of a clinical trial
- All NIH-funded research

4.3 Notification to Yale CTgov Team
The HRPP staff will use Manage Ancillary Review function in IRES IRB to notify Yale CTgov Team about the submission of a protocol meeting the criteria described above. The study will proceed to the IRB for review, per HRPP procedure. The Yale CTgov Team will review the submission and will submit the Ancillary Review within 3 business to indicate one of the following:

- Registration is required;
- Registration is recommended but not required;
- Registration is not required nor recommended.

The determination will be documented in IRES IRB. The HRPP Regulatory Analyst who requested Ancillary Review and the IRB Coordinator assigned to the submission will be notified when the determination from Yale CTgov Team is submitted.

4.4 HRPP/IRB Actions when registration is required
If the Yale CTgov Team’s determination is that registration is required, the HRPP Regulatory Analyst will inform the Principal Investigator (PI) and the PI Proxy via a comment posted in the study record that a registration is required prior to the final IRB approval. The PI will be referred to work with the Yale CTgov Team to complete the registration process. The IRB of record (internal Yale IRB or external IRB) will be notified that final approval is not to be granted until the National Clinical Trial (NCT) identifier (registration number) has been received and documented in IRES IRB. The PI will receive a reminder about their obligations related to the reporting requirements.

---

2 Medical journals may require registration of clinical trials in a public trial registry within a specified timeframe as a condition of consideration for publication. Currently, investigators are encouraged to register clinical trials to be able to publish in peer-reviewed journals. In the future, the University may require registration of all clinical trials regardless of funding. At that time, this SOP will be revised to indicate only two options: 'Registration is required' and 'Registration is not required.'
4.5 HRPP/IRB Actions when registration is NOT required but recommended
If the Yale CTgov Team’s determination is that registration is not regulatorily required but recommended, the HRPP Regulatory Analyst will inform the Principal Investigator (PI) and the PI Proxy via a comment posted in the study record that a registration is recommended. The PI will be referred to work with the Yale CTgov Team to complete the registration process. No action is taken if the registration is not required nor recommended.

4.6 Registration
The Yale CTgov Team offers assistance with the registration (e.g. creation of the password in Clinical Trials Protocol Registration System (PRS) and help answer the questions). Per PI’s request, the Yale CTgov Team can complete the registration in Clinical Trials Protocol Registration System (PRS) per PRS instructions: https://clinicaltrials.gov/ct2/manage-recs/how-register

5. Monitoring of Registered Studies
Registered clinical trials require updates to the record such as protocol amendments at least on annual basis (it is recommended that the Record Verification Date be updated every 6 months, even when there are no changes to the record). Changes in enrollment status and completion dates must be updated within 30 days of the change. The Principal Investigator is asked about the enrollment status in IRES IRB at the time of protocol modification and continuing review submitted to the IRB.

5.1 Studies under Yale IRB purview: Modifications
The PI must submit modifications to the research protocol for IRB review and approval. Upon receipt of the modifications to registered clinical trials where Yale serves as the Responsible Party, Yale HRPP will use Manage Ancillary Review function to notify Yale CTgov Team if the modification:
- Changes the inclusion/exclusion criteria;
- Changes study measures or the study design;
- Modifies study timelines e.g. interim analysis;
- Adds/removes study sites if Yale serves as the coordinating center.

The CTgov Team will reach out directly to the Principal Investigator to inform him/her about the requirement to update the study. The Yale CTgov Team will copy the HRPP Compliance and Quality group on the communication.

5.2 Studies under Yale IRB purview: Continuing Reviews
Yale HRPP will notify the Yale CTgov team when a request for continuing review has been submitted to the IRB. The study will proceed to the IRB for review, per HRPP procedure. Clinical trials that were approved without a requirement for continuing review will be assessed for the need for updates on the anniversary of the initial approval or the approval of the last continuing review. The CTgov Team will reach out directly to the Principal Investigator to inform him/her about the requirement to update the study at least annually. The Yale CTgov Team will copy the HRPP Compliance and Quality group on the communication.

5.3 Studies under external IRB purview
The Yale CTgov Team will reach out directly to the Principal Investigator every 6 months starting with the initial approval to verify that no new updates are required to the study. The Yale CTgov Team will copy the HRPP Regulatory, Compliance, and Quality group on the communication.

5.4 Clinical Trials where External Entity serves as the Responsible Party
On monthly basis, the YaleCTgov team runs a CMS report regarding clinical trial related claims. The report includes the name of the Hospital and/or practice submitting the claim. If there is no NCT # (National Clinical Trial registration number) associated with the claim, the YaleCTgov will reach out to the PI of the protocol at Yale and request the evidence of the registration from the
sponsors. The Yale CTgov Team will copy the HRPP Compliance and Quality group on the communication.

6. Posting of Clinical Trial Consent Form

For federally funded clinical trials approved after January 21, 2019 or approved prior to that date but converted to the revised rule after January 21, 2019, one IRB-approved version of the consent form must be posted on a public federal website. The current website of choice is clinicaltrials.gov. The consent form must be posted after the enrollment closes and no later than 60 days after the last study visit. An IRB approved consent form will be uploaded to the website at the time of the first update to the record (either after the first applicable amendment update, continuing review, or 6th month check-in). YCAS may redact the consent forms per allowable redactions.

7. Reporting Results

The HRPP staff will notify the Yale CTgov Team by using Manage Ancillary Review function in IRES IRB when a request to close a registered clinical trial has been submitted. The Yale CTgov Team will contact the PI to verify the status of the result reporting. Yale CTgov will submit the Ancillary Review in IRES IRB within 3 business days to confirm that the study can be closed. Should the research protocol require any changes, the HRPP will reject the submission and request modification to the protocol prior to study closure.

8. Escalation

If the Investigator is noncompliant with registration, reporting, and/or posting requirements, the following escalation steps will occur:

8.1 The Yale CTgov Team will send a reminder to the PI to address the noncompliance. The PI will have 10 business days after the date of the reminder to address the noncompliance. If the PI does not become compliant within the specified timeframe, the Yale CTgov Team will notify the HRPP within 5 business days regarding the PI’s noncompliance.

8.2 The HRPP Director or designee (HRPP Regulatory, Compliance, and Quality Team) will send a reminder to the PI and the PI’s department chair (with a cc to CT.gov Team to address the noncompliance. The PI will have 5 business days after the date of the reminder to address the noncompliance. If the PI does not become compliant within the specified timeframe, the HRPP Director or designee (HRPP Regulatory, Compliance, and Quality Team) will notify the Institutional Official within 5 business days regarding the PI’s noncompliance.

8.3 The Institutional Official will send a reminder to the PI and the PI’s department chair to address the noncompliance. The PI will have 5 business days to address the noncompliance. If the PI does not become compliant within the specified timeframe, the Institutional Official will consider one or more of the following actions until the noncompliance is rectified, including:
  • Administrative hold on the study until the noncompliance is rectified.
  • Administrative hold on all of the PI’s studies pending IRB review until noncompliance is rectified.
  • Restriction of submissions of initial studies to the IRB until the noncompliance is rectified.

9. Reports to the Institution

The HRPP (in collaboration with the Yale CT.gov Team) will issue a regular report to the HRPP Director, YCCI Deputy Director, and Institutional Official. The reports will include the following information:

- Total number of clinical trials approved in the reporting period
- Number of clinical trials where Yale is not the Responsible Party
- Number of clinical trials where Yale is the Responsible Party
- Number of NIH funded clinical trials registered by Yale as the Responsible Party in the reporting period
• Number of non-NIH funded clinical trials registered by Yale as the Responsible Party in the reporting period
• Number of clinical trials with Yale serving as the Responsible party that were closed in the reporting period
• Number of clinical trials requiring updates from Yale
• Number of clinical trials due for result reporting in the reporting period

10. Related Information
Policy: HRPP Policy 1000, Clinical Trial Registration and Reporting Requirements
Work Instructions: 1000 WI.1, Clinical Trial Registration and Monitoring

11. Revision History

<table>
<thead>
<tr>
<th>Version Date</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>March 11, 2019</td>
<td>Initial effective date.</td>
</tr>
</tbody>
</table>