ClinicalTrials.gov Registration and Results (CTRR) Taskforce

Best Practice and General Procedure

ClinicalTrials.gov Record Maintenance
Where the Institution is the Sponsor/Responsible Party

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Best Practices for PRS Admins to Maintain ClinicalTrials.gov Records

- **Access Reporting Tools or Notifications** for relevant Clinical Trials Management System (CTMS), Institutional Review Board (IRB) application, or other source of truth for Institutional trials to receive alerts about study status changes, final enrollment numbers, and protocol amendments that should be reflected in the public record within 30 days of the change.

- **Develop Email Communication Best Practices** that provide continuing education for the study team (ie, always define Primary and Study Completion date when referenced) and explicitly indicate what action is requested by what date.

- **Document Protocol Version Date:** Utilize the Secondary ID field to keep track of the Protocol Version that is reflected in the public record.

- **Create Email Scripts:** Save relevant email scripts (for record verification, protocol amendments, study status, completion dates, results required, etc) as drafts in your email client. Text can be easily cut and pasted into an email thread to preserve history of communication.

- **Create an Escalation Plan** to encourage study teams to communicate in a timely manner.

- **Consider a 6-month Record Verification Process:** Per FDAAA Law, Annual Verification is required if the record has not otherwise been updated. A 6-month verification process can help study teams in maintaining compliant records, particularly with respect to Primary Completion Date determination and Results Module due dates.

- **Open the Results Module for Completed NIH-Funded Trials:** NIH-funded clinical trials that are non-ACTs will fall off the 'Active Records' list when they've reached study completion. To keep track of their subsequent results submission, open the results module to add the trial to the 'problem' list.

- **Share Results Due Calendar Reminders with Study Teams.** When Actual Primary Completion has been reached, mark the service line calendar with monthly reminders until the Results Reporting due date. Share with the study team for a passive reminder about their upcoming results due date. Use this calendar reminder to save all relevant results module communication updates (save to all occurrences).

Purpose

ClinicalTrials.gov records are dynamic and require routine maintenance to remain compliant. The [Institution] ClinicalTrials.gov Service assists Study Teams to maintain accurate records.

ClinicalTrials.gov Records require the following maintenance:

- Update of Anticipated Study Start Date to Actual Start Date (date of first participant consent) within 30 days
- Update of Study Status Changes within 30 days
- Update of Anticipated Enrollment to Actual Enrollment at Closed to Accrual
- Update of ClinicalTrials.gov records to reflect applicable institutional study changes including protocol amendments, change of Principal Investigator, participating site

- additions or withdrawal, and funding/collaborator changes as required within 30 days of change
- Upload of a consent form that was used to consent participants any time after the trial is closed to recruitment, but no later than 60 days after the last study visit by any subject (for federally funded studies, as applicable)
- Annual Verification if there have been no other Study Changes, or more frequently per Institutional policy
- Update of Anticipated Primary and Study Completion Dates to Actual Completion Dates
- Submission of Results within 1 year of Primary Completion Date
- Submission of remaining results with 1 year of Study Completion Date, if different than Primary Completion Date

Data curated and rigorously maintained in a CTMS can be a source of truth for study status changes, accrual, protocol amendments, and study completion dates per ClinicalTrials.gov. IRB applications can be sourced for IRB-approved protocol amendments.

Procedure

This document provides a process for ClinicalTrials.gov Records Maintenance. Access to a CTMS, IRB applications, and their reporting tools are critical to ClinicalTrials.gov records maintenance. The Planning Report in the ClinicalTrials.gov Protocol Registration and Results System (PRS) Administrative console is critical for proactive maintenance of records.

1. Status Changes

The [PRS Administrator / Record Owner or Study Team designee on the record access list] updates the study status in the ClinicalTrials.gov record, using one of the following processes:

a. **Proactive:** [PRS Administrator] runs a report out of [CTMS] at a predetermined frequency agreed on by the Institution (e.g. weekly or bi-monthly) to identify status changes. [PRS Administrator] updates the Study Status in the ClinicalTrials.gov record, assuming [CTMS] is the source of truth.

- Set up the report using a start date and end date that covers the reporting frequency, (e.g. for a one or two week period from Sunday to Sunday)
- Download and open the report - consider saving it for historical documentation to [Service Folder]. Add the date the report was run in the following format _YYYYMMDD to the end of the file name.
- Log into the PRS and update the status for ClinicalTrials.gov records the [Institution] is responsible for

  (1) 'Open' the Protocol Section of the ClinicalTrials.gov Registration Record

  (2) 'Edit' the Study Status section to change the Overall Status

  (3) If status is changed to 'Closed to Accrual' in [CTMS], then the 'Anticipated' Enrollment number should be changed to an 'Actual' enrollment number

  - 'Edit' the Study Design section
  - Update the Enrollment with the final number
  - Change 'Anticipated' to 'Actual', click Save

  (4) Release the record for PRS review

b. **Proactive:** [PRS Administrator] runs a report out of [CTMS] at a predetermined frequency agreed on by the Institution (e.g. weekly or bi-monthly) to identify status changes. [PRS Administrator] contacts the Record Owner and requests updates to the record within the required timelines (within 30 days of study status change). The Study Team updates the study status on the ClinicalTrials.gov record, [PRS Administrator] releases it for PRS review

c. **Proactive:** Enable automated email notifications at a predetermined frequency directly from the [CTMS or IRB application] to assist with study status updates.

d. **Reactive:** [PRS Administrator] learns of a study status change through the course of study communications regarding protocol amendments or annual verification, follow (1) - (4) above.

2. **Changes to Trial Records**

The [PRS Administrator / Record Owner or Study Team designee on the record access list] makes changes to the ClinicalTrials.gov record to reflect applicable institutional study changes including protocol amendments, change of Principal Investigator, participating site additions or withdrawal, and funding/collaborator changes as required.

a. Proactive: [PRS Administrator] runs a report out of the [IRB application] at a predetermined frequency agreed on by the Institution (e.g. weekly or bi-monthly) to identify IRB approvals [Initial Approvals, Change Reviews, and Continuing Reviews]

- Log into [reporting tool] and select relevant parameters
- Input a start date and end date that covers a predetermined frequency agreed on by the Institution (e.g. weekly or bi-monthly) to identify changes
- Download the Report and Save it to [relevant folder]
- For each study with a ClinicalTrials.gov record for which the [Institution] is responsible

(1) Initial IRB Approvals or Submissions, as relevant

- Reach out to the study team to offer ClinicalTrials.gov registration assistance

(2) Approved Change Reviews / Protocol Amendments

- Log into [IRB application] and locate the record
- Identify approved changes

(i) The [PRS Administrator] reviews the current version of the protocol with 'Tracked Changes' to assist in amending the ClinicalTrials.gov record.

1. Unless otherwise agreed upon, the [PRS Administrator] seeks approval from the Study Team prior to making changes to the record. If approved, the [PRS Administrator] updates the record and the Protocol Version Date in the Secondary ID field and approves and releases the record to keep the record current.
    a. [PRS Administrator] emails the Study Team, indicating changes made per amendment, OR
    b. [PRS Administrator] waits for PRS notification that the Study Team has updated the record and releases it for PRS review.

(3) Approved Continuing Reviews

- Log into [IRB application] and locate the record
- View the continuing review. Use this opportunity to reach out to the study team if the study status listed on the Continuing Review differs from the ClinicalTrials.gov record.

b. **Reactive**: [PRS Administrator] finds out about protocol amendments during the Annual Verification Process and ensures that the ClinicalTrials.gov record accurately reflects the most recently approved protocol.

3. Proactive Planning Report Actions

The [PRS Administrator] has administrative access to the Planning Report, found under the ‘Records’ menu in the ClinicalTrials.gov PRS system. This interface is used to identify ClinicalTrials.gov records that require updates, including Updating Study Start Dates, Annual Verification of Records, Updating Primary and Study Completion Dates, and Results Reporting Due Dates. Planning Report Actions can take place on a monthly basis.

a. **Navigate to the Planning Report**

- Click on ‘Action Expected’
- Click on the ‘Show/Hide Columns’ button
- Select the following columns
    - Protocol ID
    - ClinicalTrials.gov ID
    - Brief Title
    - FDAAA
    - Update Expected
    - Results Expected
    - All Results Expected
    - NIH Grants
    - Study Type
    - Phase
    - Intervention Type
    - Study Start Date
    - Primary Completion Date
    - Study Completion Date
    - Verification Date

- Download and Open the spreadsheet. Consider saving it for historical documentation purposes to [relevant folder]

- Format the report as applicable, ie add a ‘Notes’ column, set a filter on the top row

b. **Update Study Start Dates –** Typically, a study is registered to ClinicalTrials.gov prior to ‘Open to Accrual’ and participant enrollment. At this time, the study has an *Anticipated* Study Start Date. The *Actual* Study Start Date is the day that the first participant consented to take part in the study.

- Sort the Study Start Date from newest to oldest

(1) Trials with [CTMS]: Scroll down or filter to a date that is about one month prior to the current date – and review [CTMS] records for those studies to see if they have started consenting participants.

- Advance the Anticipated start date by 1 month if the date has passed and they have not yet enrolled anyone, or
- Set Study Start Date to actual and input the date of first participant consented, or if

(2) Trial is not in [CTMS] or [CTMS] is not the source of truth: Reach out to the Study Team to confirm Actual Study Start Date or if the study start date should be advanced

c. **Annual Verification of Records** – If nothing else changes in a ClinicalTrials.gov record, the record requires at least Annual Verification to ensure that it remains accurate. [Institution] can increase the required verification frequency to ensure more regular record review and update. Using the previously downloaded Planning Report

- Sort the Verification Date from Oldest to Newest
- Contact Study Teams for which Annual Verification is due in the next 1-2 months.

(1) Log into [CTMS] or [IRB application], ensure there were no protocol amendments or status changes since last verified

- Communicate with the Study Team:

(i) Request updates to or confirmation of the Anticipated Primary and Study Completion Dates

(ii) Request they update the Verification Date (or offer to do this for them)

(iii) Include link to the public record so they are aware of its contents

- Update the Verification Date, as requested

d. **Updating Primary and Study Completion Dates –** Actual Primary and Study Completion Dates are moving targets with definitions that are often confusing to the Study Team. Study Completion Dates per ClinicalTrials.gov often coincide with the last person off-study. Part of proactive records maintenance, the Anticipated Primary and Study Completion dates can be tracked in the Planning Report and either advanced or made Actual when the Anticipated Date has been reached. Using the previously downloaded Planning Report:

- Filter the 'Primary Completion Date Type' by 'Anticipated'
- Sort the 'Primary Completion Date' from Oldest to Newest
- For any Primary Completion Date that has passed or is Anticipated this month

(1) Log into [CTMS], if applicable

- If the Study Status is Open to Accrual: Reach out to the Study Team to confirm they are still enrolling and if so, suggest advancing the Anticipated Primary Completion Date (and Study Completion Date by the same timeframe)

- If the Study Status is 'Closed to Accrual':

(i) If the timeframes of the Primary and Secondary Outcome Measures are different, it is possible that the Primary Completion date has been reached even if all participants are still On Study. If possible, confirm the date of last enrollment via [CTMS] and calculate the estimated primary completion date using the longest primary outcome time frame (if more than one primary outcome) to see if potential record edits are needed. Contact the Study Team to confirm as needed.

(ii) If IRB approval was issued on or after January 21st 2019, follow-up with the Study Team and request they attach a consent form used to consent participants to the study as required by the Common Rule in the Documents section of the ClinicalTrials.gov record.(45 CFR 46.116(h)(1)). Consent forms can be posted any time after the trial is closed to recruitment, but no later than 60 days after the last study visit by any subject.

i. Confirm with Study Team which consent form was used to enrolled participants
ii. Save the consent form as a PDF/A to the [relevant study folder]
iii. From the PRS Record Summary Page, 'Open' the Document Section
iv. Click 'New Document'
v. Select 'Informed Consent Form' from the Document Type
vi. The Document Date is the date the IRB approved the consent form
vii. Upload the ICF

- If all Participants are Off Study, reach out to the Study Team to confirm the Actual Primary and Study Completion Dates

(i) If the Actual Primary Completion Date is verified AND the study is an ACT or requires results per NIH Policy, initiate Results Reporting communication with the Study Team.

1. **Important:** IF the clinical trial requires results per NIH Policy and is NOT an ACT – it will fall off of the 'Actions Expected' list on the Planning Report as soon as the Actual Study Completion Date is entered. To keep it on the Planning Report, **consider opening the results module to put it on the 'Problem' list or tracking separately per another preferred Institutional method.**

2. If ALL data has been collected (Actual Primary AND Study Completion Dates)

a. Check to see if the study is federally funded, if YES, then

b. Check to see when the initial IRB approval was, if on or after January 21, 2019, ensure a consent form used to consent participants to the study is uploaded to the documents section of the ClinicalTrials.gov record if it hasn't been already, within 60 days of the last study visit. See section (d) (1) (ii) above for more details.

(2) If there is not a [CTMS] or [CTMS] is not the source of truth, reach out to the Study Team to ask that they update their Primary / Study Completion Dates

- See section (d) (1) (ii) above for more details if Actual completion dates are met.

- Un-filter the 'Primary Completion Date Type' column
- Filter the 'Study Completion Type' column by 'Anticipated'
- Sort the 'Study Completion Date' from 'Oldest to Newest'
- For any Study Completion Date that has passed or is Anticipated this month

(1) Confirm that the Primary and Study Completion Dates should be different (look at the outcome measure 'Time Frame' for each as a guide).

(2) Log into [CTMS] (as applicable) and note if all participants are off study, reach out to the Study Team to update the Study Completion Date to reflect the final collection of data for the primary and secondary outcome measures and adverse events (for example, last participant's last visit).

1. If ALL data has been collected (Actual Study Completion Date)

a. Check to see if the study is federally funded, if YES, then

b. Check to see when the initial IRB approval was, if on or after January 21, 2019, ensure a consent form that was used to consent participants to the study is uploaded to the documents section of the ClinicalTrials.gov record if it hasn't been already, within 60 days of the last study visit. See section (d) (1) (ii) above for more details.

e. **Results Reporting Due Dates (per FDAAA**) – Results are due within one year of the Primary and Study Completion Dates for pACTs or ACTs. Using the previously downloaded Planning Report:

- Clear All Filters
- Filter ‘Primary Completion Date Type’ to ‘Actual’
- Sort ‘Results Expected’ Column from Oldest to Newest
- Filter ‘FDAAA’ Column to ‘pACT’ and ‘ACT’ (uncheck ‘Blanks’)

(1) The studies with ‘late results’ (results due prior to current date) will top the list.

- Check in to see if any communication with the Study Team requires escalation

(2) For ‘results expected’ due dates that are eminent (1-6 months from the current date), ensure that communication with the Study Team has started

(3) Mark the [service line] Calendar with monthly reminders until the due date for each study.

- Note the PI name, NCT number, and due date in the Title
- Write the Study Title, primary completion date, and relevant notes about who is working on the results or details about their progress in the body, save to all occurrences.
- Share this Calendar reminder with the study team to passively alert them to their results due date.

f. **Results Reporting Due Dates (per NIH Policy) -** Results are due within one year of the Primary and Study Completion Dates for all clinical trials funded by NIH. Using the previously downloaded Planning Report:

- Clear All Filters
- Filter ‘Primary Completion Date Type’ to ‘Actual’
- Filter ‘FDAAA’ column to show only ‘blanks’ – [All trials per FDAAA are already on the ‘results expected’ list]

- Filter out ‘Blanks’ from ‘NIH Grants’ column – [This column is sourced from the collaborators section, populated when an NIH grant is input into the Secondary ID field]

  (1) NIH policy (Results Due) may apply to any studies that remain on the spreadsheet

  - Check the email communications for evidence of results requirement determined at registration, or
  - Send Study Team follow up email to confirm results reporting requirement

    Tip: Unless the Result Module is open, NIH-funded clinical trials will not be on the Planning Report if Actual Study Completion has been met. QC recently completed studies with NIH-funding and open the results module to ensure it stays on the tracking list. [PRS Administrator] can easily delete the results module if it is not required and has not yet been submitted.

  (2) Results are due within 1 year from the Actual Primary Completion Date

  (3) Mark the [service line] Calendar with monthly reminders until the due date for each study.

  - Note the PI name, NCT number, and due date in the Title
  - Write the Study Title, primary completion date, and relevant notes about who is working on the results or details about their progress in the body, save to all occurrences.
  - Share this Calendar reminder with the study team to passively alert them to their results due date.

4. **Escalation Best Practices**

For instances when the Study Team or POC does not respond to emails regarding results reporting deadlines, it can be quite beneficial to include a Department Chair, Vice President of Research, etc. in the correspondence. Escalation to leadership should be done at least 14-30 days before the results are due.

Glossary

ACT: Applicable Clinical Trial

CT.gov: ClinicalTrials.gov (https://register.clinicaltrials.gov/)

CTMS: Clinical Trial Management System

FDA: Food and Drug Administration, federal agency of the US Department of Health and Human Services.

FDAAA: Food and Drug Administration Amendments Act

ICF: Informed Consent Form

IRB: Institutional Review Board

NCT: National Clinical Trial, the NCT number is assigned by ClinicalTrials.gov upon acceptance of the registration record

NIH: National Institute of Health

PI: Principal Investigator

POC: Point of Contact

PRS: Protocol Registration and Results System

PRS Administrator: Person who releases [institutional] ClinicalTrials.gov records for PRS Review

Study Team: This is the research group that includes the PI, study coordinators, and program managers per the IRB application / [CTMS]

SOP: Standard Operating Procedure

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