August 6, 2019

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Clinical Research Newsletter

A Newsletter for Clinical Research Professionals

Announcements

- Introduction to RecruitMe sessions will be offered on August 14, 2019 and September 13, 2019. To attend a session, please RSVP here.

  To post your trial or for additional inquiries, please contact recruitme@columbia.edu.

- The Final Rule has been in effect since January 18, 2017 for clinical trials registration and results submission on *ClinicalTrials.gov*. For assistance, please contact CU Administrators.

- An optional Good Clinical Practice (GCP) training module is now available in Rascal *TC3450 – Good Clinical Practice (GCP)*.

- The Human Research Protection Office (HRPO) Liaison Service now takes place at the Presbyterian Hospital, 622 West 168 Street, 10th floor: Ask for the IRB Liaison Service at the Reception Desk.

  Walk-in Hours:
  Mondays, 3 to 4pm
  Wednesdays, 10 to 11am
  Thursdays, 10 to 11am

Clinical Trials Office, Columbia University

ClinicalTrials.gov — Submitting Results Information

What is the ClinicalTrials.gov results database?

The National Library of Medicine (NLM) maintains ClinicalTrials.gov, an online database of federally and privately supported clinical studies and their results, which includes any initiated, ongoing, and completed or terminated research. The data is self-reported by study sponsors or investigators to demonstrate protocol adherence and complement medical literature. It is a free service of the U.S. National Institutes of Health (NIH) to make study findings available to the public and different audiences.

ClinicalTrials.gov is not only a searchable registry of clinical trials with information about a trial's purpose and design, but also a repository of the reported summary results for these clinical trials.

Why must results data be reported?

Submission of results information is required to be completed by the responsible party, or sponsor of "applicable clinical trials" (see checklist for evaluating an ACT) by federal law. The Final Rule (42 CFR Part 11) clarifies and expands the regulatory requirements and procedures for submitting results information for certain trials to ClinicalTrials.gov in accordance with U.S. Public Law 110-85, Title VII (also known as FDAAA 801).

Sponsors of clinical trials funded by NIH are also required by a recent NIH policy (NIH Policy on the Dissemination of NIH-Funded Clinical Trial Information) to register and report results on ClinicalTrials.gov for clinical trials initiated **AND** awarded by the NIH on or after January 18, 2017.

In addition to satisfying legal and funding requirements, many medical journal editors require registration of clinical trials in a public trials registry prior to enrollment of first participant as a condition of consideration for publication (ICMJE Recommendations for the Conduct, Reporting, Editing and Publication of Scholarly Work in Medical Journals).

In recent years, multiple advocacy and watchdog groups that monitor and track compliance on ClinicalTrials.gov have generated reports, published papers and posted unfavorable messages on public platforms such as Twitter. These reports often target and criticize the individual investigators and institutions for not sharing their clinical trial results.

Are there potential consequences for failing to submit results?

The Final Rule outlines the potential criminal and civil monetary penalties (up to $11,569 per day) of noncompliance against the responsible party, and the withholding of remaining or future funds (e.g., NIH, HHS) from a grantee for failure to submit results information.

Which trials must have results submitted to ClinicalTrials.gov?

The responsible party is expected to report results for all clinical trials subject to FDAAA/Final Rule on ClinicalTrials.gov. Clinical trials that do not necessarily meet FDAAA's definition of an ACT (e.g., clinical trials examining a behavioral intervention or phase 1 drug product) but are funded by NIH would be subject to NIH Policy and follow the same results submission requirement as the Final Rule.

Reporting Requirement	**FDAAA** (Effective in 2007) **Final Rule** (January 18, 2017)	**NIH Policy*** (January 18, 2017)	**ICMJE** (Effective in 2005)
Scope	Registration and Results Reporting	Registration and Results Reporting	Registration only (Results Reporting encouraged)
Phase	Not Phase 1	All	All
Intervention Type	Drug, biologic and device products regulated by FDA	All, including behavioral intervention	All
Funding Source	Any	NIH	Any

* Initiated and awarded by the NIH on or after January 18, 2017.

When does results information need to be submitted to ClinicalTrials.gov?

The deadline for results entry is determined by the completion (final) date of data collection. In general, results information must be submitted no later than 1 year after the completion date for trials subject to FDAAA/Final Rule or NIH Policy.

There are two types of completion dates: Primary Completion Date and Study Completion Date.

	Primary Completion Date	**Study Completion Date**
	Definition: Final data collection date for the primary outcome measure [anticipated or actual].	*Definition: Final data collection date for the primary and secondary outcome measures and adverse events [anticipated or actual].*
Scope	**Primary Outcome Measure**	**Secondary Outcome Measure Adverse Event Information**
	Definition: Data measure(s) of greatest importance specified in the protocol.	*Definition: Data measure(s) of lesser importance but pre-specified in the protocol.*
Outcome Measure Example	Maximum Tolerated Dose	Overall Survival Rate
Completion Date	June 2020	June 2025
Results Expected Date	June 2021 ↓ ONE YEAR AFTER	June 2026 ↓ COMPLETION DATE

REMINDER

Responsible party must update the Primary Completion Date and Study Completion Date on ClinicalTrials.gov to reflect any change to the completion dates (including actual dates) once they have been reached within 30 calendar days of the change.

What does results information consist of?

The summary of results data is entered into the **Results Section** of a record through the Protocol Registration and Results System (PRS), the same platform where the responsible party enters the study information at the time of trial registration. The following data elements are required for results reporting if collected:

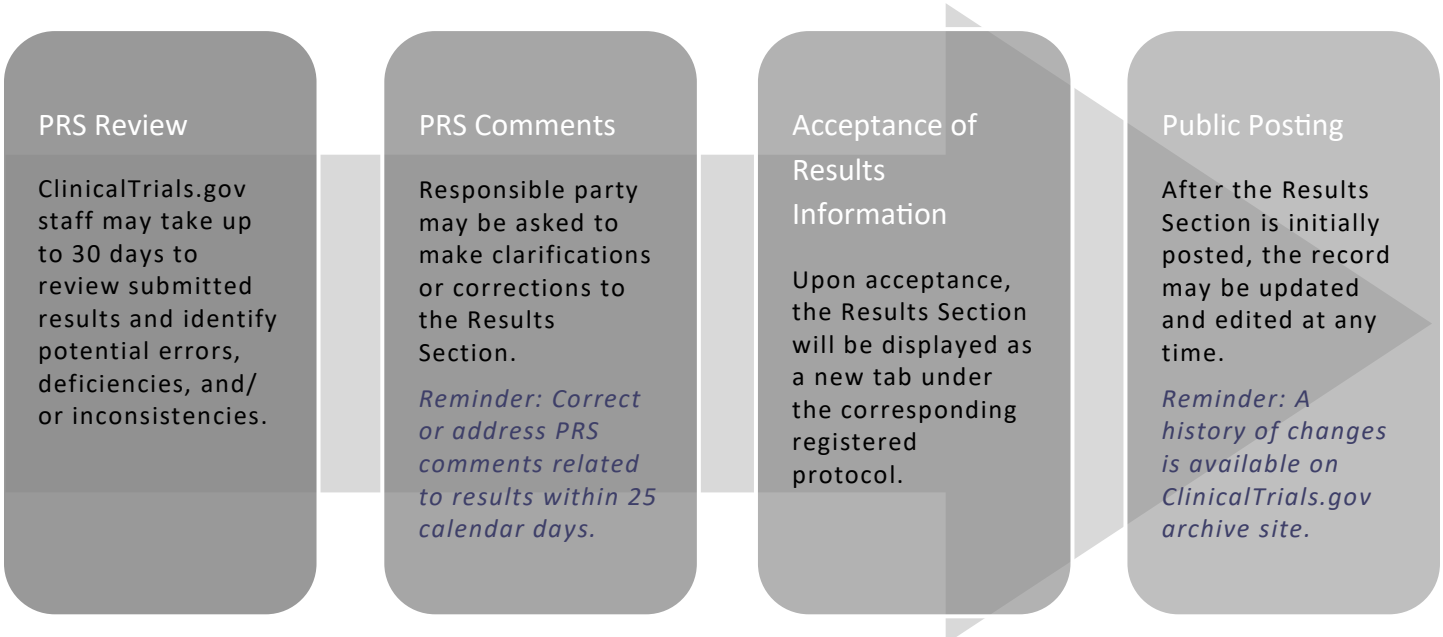
4 SCIENTIFIC MODULES[1]	DEFINITIONS
Participant Flow	Information on the progress of subjects through each stage of a study in a tabular format, including the actual number of subjects who started and completed the study (identical in purpose to a CONSORT flow diagram).
Baseline Characteristics	A table of demographic and baseline values (e.g., age, gender, race/ethnicity, study-specific measures) presented by study arm ("arm") AND for the entire study population.
Outcome Measures	Data for each primary and secondary outcome measure by arm, and statistical analyses if desired.
Adverse Events	Three tables summarizing adverse events: • Deaths due to any cause, with the number and frequency of such events by arm. • Serious adverse events (SAEs), grouped by organ system, with the number and frequency of such events by arm. • Non-serious AEs that exceed a specified (usually 5%) frequency in any arm.

[1] See *page 5* Example Studies for Results Data Entry link for actual PRS screenshots of the modules.

The Final Rule requires a copy of full study protocol and statistical analysis plan (SAP) to be uploaded in the **Document Section** of a record at the time of results information submission. These study documents must be the latest versions used for data analysis, and must be in PDF Archive (PDF/A) format.

What happens after data has been entered and released (submitted) in PRS?

The record will go through the following review process (see below). The responsible party should check back in PRS until the results information has been accepted and posted publicly on ClinicalTrials.gov.



Frequently Asked Questions

1. Am I required to submit results information for a study that was terminated early and did not reach target sample size (only 3 out of 35 subjects were enrolled)?

Yes. If the study is subject to FDAAA/Final Rule or NIH policy (see HHS/NIH summary table), the responsible party must submit any available raw data collected for the 3 subjects, even if the collected data will not be analyzed. At minimum, information should be available to complete the **Participant Flow** and **Baseline Characteristics** modules.

If data is not collected or analyzed for any of the outcome measures (**Outcome Measures** module), the responsible party may enter "0" in the "Overall Number of Participants Analyzed" field and the reason why data is not collected or analyzed in the "Analysis Population Description" field, and leave the data table blank. The same applies for the **Adverse Events** module, where the reason can be entered in the "Arm/Group Description" field.

2. Can I upload (attach) my manuscript or article directly on ClinicalTrials.gov in lieu of completing the Results Section of a record?

No. Completing the Results Section ensures that all required data elements are available for ClinicalTrials.gov staff to perform data quality review. The results information entered through PRS also allows ClinicalTrials.gov staff to generate comments and request additional information in a systematic way.

3. Do I have to upload a protocol and statistical analysis plan (SAP) for my ClinicalTrials.gov record?

Only certain studies need to have study documents uploaded. Full study protocol and SAP are only required with results information submission for studies with a Primary Completion Date on or after January 18, 2017 (see Final Rule).

4. PRS will not accept the study documents I uploaded. Why did this happen?

The uploaded documents must be 1) in English; 2) in PDF/A format; and 3) include a cover page with the official study title, the NCT number, and the version date of the document. Keep in mind that uploaded documents will be posted and available publicly. The responsible party should ensure that the documents do not include any personally identifiable information (PII) of the subjects, trade secrets and/or confidential commercial information.

5. What if I am not ready to submit data by the results expected date?

The responsible party may delay submission of results information in limited circumstances by submitting a delayed results request. There are 2 types of requests: Certification and Extension Requests.

CERTIFICATION REQUEST: Responsible party can postpone the disclosure of study data or proprietary information on the public registry if the trial is studying an unapproved product that is still under development by the manufacturer; or if the manufacturer has sought or will seek FDA approval for a new use of a product studied in the trial within 1 year.

EXTENSION REQUEST: Responsible party can submit a written request that demonstrates "good cause" (reasons why clinical trial results information cannot be provided according to the deadline), and a new estimated date on which the clinical trial results information will be submitted (generally up to 2 years). The NIH Director will review and grant or decline the request. **Note:** Pending publication is not considered a "good cause" for delayed submission.

You should submit a request **prior to** the actual results expected date. Doing so will ensure your record remains compliant as you are preparing for data entry. Requests can be submitted using the "Delayed Results" link in the **Results Section** of the record.

DO'S OF RESULTS SUBMISSION

1. Do plan ahead to meet specified timeframes.
2. Do enlist extra help from qualified personnel, such as a statistician, to assist.
3. Do retain your data per study protocol and study arms.
4. Do check on the status of your results submission until it is posted publicly.
5. Do update the Protocol Section before starting the Results Section.
6. If available, cite your relevant publication(s) in the Protocol Section of the record.

Resources

- Training materials and online presentations, such as the Final Rule Webinar Series hosted by the National Library of Medicine (NLM), are available on the ClinicalTrials.gov website.
- ClinicalTrials.gov Results Review Criteria: Describes review criteria for each scientific module in the results section of the study record submitted to the results database (June 2018).
- Example Studies for Results Data Entry: Screenshots of fictional records to illustrate key concepts for results entry in PRS.
- Summary Table of HHS/NIH Initiatives and ICMJE Guidelines to Enhance Availability of Clinical Trial Information.

For more information on submitting study documents or results deadline extension requests, please contact the Clinical Trials Office at ClinicalTrialsGov@cumc.columbia.edu.

Clinical Trials Office (CTO)

Our mission is to facilitate quality clinical trial research by providing the CU research community with comprehensive administrative services that help move trials quickly from initial proposal through contract execution. We also provide regulatory support for FDA-regulated research.

We're on the Web!

Visit us at:

https://research.columbia.edu/content/clinical-trials-office

CRC Help:

CRChelp@columbia.edu

IND/IDE Help:

INDhelp@columbia.edu

PRS Help:

ClinicalTrialsGov@cumc.columbia.edu

RecruitMe:

recruitme@columbia.edu

A Word on Informed Consent Form Upload

Studies subject to the revised Common Rule (effective since January 21, 2019) have the option of posting consent documents on ClinicalTrials.gov or Regulations.gov. If you choose to utilize Regulations.gov, ensure that your desired key words (such as CUMC IRB Number) are present in the documents. For more information on Regulations.gov, please see NIH's Guidance on Posting Informed Consent Forms for NIH-Funded Clinical Trials.

Research Summer Camp: The Need to Become Leaner and More Innovative