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Background

Section 801 of the Food and Drug Administration Amendments Act (FDAAA) of 2007, also known as U.S. Public Law 110-85, added requirements for registering trials, updating trial information and reporting trial results in ClinicalTrials.gov. The ClinicalTrials.gov "basic results" database was launched in September 2008. The final rule for Clinical Trials Registration and Results Information Submission (42 CFR 11), which clarifies and expands the requirements in FDAAA, was released in September 2016. Both registration and results reporting are accomplished through the ClinicalTrials.gov Protocol Registration System (PRS).

The NIH Policy on the Dissemination of NIH Funded Clinical Trial Information (NOT-OD-16-149) expands the scope of trials for which aggregate results and summary adverse event information must be reported by including all clinical trials funded in whole or in part by the NIH. Although specific trials covered by the NIH policy may or may not also be considered as applicable under the statute (FDAAA) and regulation (42 CFR 11), the NIH policy's *reporting requirements* are those of the statute and regulation.

Noncompliance with these requirements could result in civil monetary penalties and withholding or recovery of funds from federal grants.

Responsible Personnel

Principal Investigator

Responsible Party

Medical Director, Clinical Research Support

Director, Clinical Research Support

Abbreviations and Acronyms

ACT: Applicable Clinical Trial (42 CFR 11.10)

CMS: Center for Medicare and Medicaid Services

CRS: Clinical Research Support

FDA: Food and Drug Administration

FDAAA: Food and Drug Administration Amendments Act

FHCRC: Fred Hutchinson Cancer Research Center

ICMJE: International Committee of Medical Journal Editors

IRB: Institutional Review Board

NCI: National Cancer Institute

NCI-CTRP: NCI's Clinical Trials Reporting Program

NCT ID: National Clinical Trials ID, *ClinicalTrials.gov*

NIH: National Institutes of Health, HHS

PCD: Primary Completion Date (42 CFR 11.10)

PI: Principal Investigator

PRMS: Protocol Review and Monitoring System

PRS: Protocol Registration and Results System, *ClinicalTrials.gov*

RP: Responsible Party (42 CFR 11.10)

SC: Seattle Children's

SCD: Study Completion Date (42 CFR 11.10)

SRC: Scientific Review Committee

SCCA: Seattle Cancer Care Alliance

UW: University of Washington

Definitions

Applicable Clinical Trial: A term used in the FDAAA statute, which includes the following types of trials:

- **Trials of drugs and biologics.** Controlled clinical investigations, other than phase 1 clinical investigations, of drugs or biological products subject to Food and Drug Administration (FDA) regulation

- **Trials of devices.** 1) Controlled trials with health outcomes of devices subject to FDA regulation, other than small feasibility studies, and 2) pediatric postmarket surveillance required by FDA

Note:

- A clinical investigation of a drug can be an Applicable Drug Clinical Trial under FDAAA even if it does not require an IND, and a clinical investigation of a device can be an Applicable Device Clinical Trial whether or not an IDE is required.

- The scope of FDAAA and 42 CFR 11 is limited to "Applicable Clinical Trials," a term which has a narrower definition than "Clinical Trial." The scope of the NIH Policy (NOT-OD-16-149) encompasses the broader definition of “Clinical Trial.”

For the complete statutory (FDAAA) definition and more information on the meaning of "applicable clinical trial," see 42 CFR 11.10 or Elaboration of Definitions of Responsible Party and Applicable Clinical Trial. (Source: ClinicalTrials.gov)

Cancer Consortium: An NCI-designated Comprehensive Cancer Center comprised of: Fred Hutchinson Cancer Research Center (FHCRC), University of Washington (UW), Seattle Children’s (SC), and Seattle Cancer Care Alliance (SCCA).

Clinical Trial: A research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes. This definition encompasses phase 1 trials of FDA-regulated drug and biological products, small feasibility studies of FDA-regulated device products, and studies of any intervention not regulated by the FDA, e.g., behavioral interventions. This definition of "clinical trial" is broader than the term "applicable clinical trial" as defined in the regulation. (Source: NIH)

ClinicalTrials.gov: A public database developed by the U.S. National Institutes of Health (NIH), provided through its National Library of Medicine (NLM), that meets FDAAA and ICMJE requirements.

Interventional Study Type: Participants are assigned prospectively to an intervention or interventions according to a protocol to evaluate the effect of the intervention(s) on biomedical or other health related outcomes. (Source: ClinicalTrials.gov)

Primary Completion Date: 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. In the case of clinical trials 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. (Source: PRS)

Responsible Party: The sponsor of the clinical trial or the principal investigator (PI) of such clinical trial if so designated by a sponsor, grantee, contractor, or awardee, so long as the PI 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 42 CFR 11 and FDAAA for the submission of clinical trial information.(Source: ClinicalTrials.gov)

Study Completion Date: The date the final participant was examined or received an intervention for purposes of final collection of data for the primary and secondary outcome measures and adverse events (for example, last participant’s last visit), whether the clinical study concluded according to the pre-specified protocol or was terminated. (Source: PRS)

Policy

Cancer Consortium Investigators are responsible for ensuring registration of any clinical trial in which their role is Principal Investigator, regardless of whether the Consortium PI meets the definition of Responsible Party. If the Consortium PI meets the definition of Responsible Party, they are responsible for ensuring the accuracy of all ongoing trial information in the ClinicalTrials.gov system, including the recruitment status, summary of adverse event information, and trial results, according to the FDA Amendments Act (FDAAA) and 42 CFR Part 11.

Procedures

Registration

Although the PI is responsible for ensuring registration, Clinical Research Support (CRS) staff manages the initial ClinicalTrials.gov registration of investigator-initiated, Consortium clinical trials on behalf of the Responsible Party (the Principal Investigator) and the Sponsor (FHCRC or UW).

- The Consortium PI is responsible for registering the trial directly in the ClinicalTrials.gov Protocol Registration System (PRS), within the timeframes specified in 42 CFR 11, if the PI meets the definition of Responsible Party for a non-cancer-related clinical trial that is applicable under the FDAAA statute or covered by the NIH policy. . Registration with ClinicalTrials.gov of clinical trials that are neither applicable under FDAAA nor covered by the NIH policy may still be required by policies such as those of CMS or ICMJE (both of which require registration prior to enrolling participants). PRS is accessible at https://register.clinicaltrials.gov.

- Clinical trials for which the Consortium PI does not meet the definition of Responsible Party are generally registered with ClinicalTrials.gov by the external lead organization, such as industry-sponsored trials, NCI National Clinical Trials Network trials, and trials coordinated by other Cancer Centers.

Registrations managed by Clinical Research Support

CRS staff submits the protocol, consent and a specific set of trial data to NCI-CTRP to fulfill the NCI's requirements. In return, NCI-CTRP provides a trial summary report, which is used by CRS staff to create the initial ClinicalTrials.gov record. ClinicalTrials.gov staff review the trial record, which may involve more than one review cycle if comments are issued to which responses are required. The trial is considered to be completely registered when ClinicalTrials.gov assigns an NCT ID, after the trial record has been reviewed and accepted.

In consideration of the following rules and policies, CRS staff initially registers trials with NCI-CTRP immediately following SRC approval to allow enough time for production of the trial summary report, data processing and reviews.

- The NCT ID is required by CMS for all billing claims.
- ICMJE requires registration before the first participant is enrolled as a condition of consideration for publication.
- Registration is required no later than 21 days after the first participant is enrolled to comply with the NIH funding policy and the FDA Amendments Act.

CRS staff continues to manage amendments, updates and status changes in ClinicalTrials.gov until it is time to transfer management of the trial record to the Principal Investigator (the Responsible Party) for results reporting.

Registrations managed by the Principal Investigator

Cancer Consortium Principal Investigators who meet the definition of Responsible Party for non-cancer-related clinical trials need a ClinicalTrials.gov account in order to register their trials. The Consortium's ClinicalTrials.gov Administrator creates individual user accounts under the institutional account (either UWashington [FH/UWCC group] or FHCRC) and provides basic system instructions to investigators and study teams.

Updates to Trial Information in ClinicalTrials.gov:

The FDAAA and 42 CFR Part 11 specify update requirements. In general, if the PI meets the the definition of Responsible Party, the PI must review and verify all trial information in the ClinicalTrials.gov system not less than once every 12 months. The final rule also specifies certain data elements that must be updated within 30 calendar days of a change. Notice of changes in recruitment status must be provided as soon as possible, but no later than 30 days after such changes. For trial records managed by CRS, it is the responsibility of the PI to inform CRS's ClinicalTrials.gov administrator within 10 business days of any change in overall recruitment status or the occurrence of the actual Primary Completion Date.

Additionally, the Responsible Party must respond to comments issued by a ClinicalTrials.gov reviewer within 15 days, to correct or address all apparent errors, deficiencies, and/or inconsistencies.

Results and Adverse Events

A Cancer Consortium Principal Investigator who meets the definition of Responsible Party for an Applicable Clinical Trial under FDAAA and/or a Clinical Trial funded by NIH must submit clinical results and summary adverse event information directly in the ClinicalTrials.gov Protocol Registration System (PRS) at https://register.clinicaltrials.gov, according to FDAAA and 42 CFR Part 11.

The standard deadline for reporting results data is no later than 1 year after the Primary Completion Date (as defined in 42 CFR Part 11.10). Delayed submission of results information is allowed in some circumstances, such as if the sponsor is seeking FDA approval for an investigational product (detailed in 42 CFR Part 11.44). The regulation also specifies deadlines for reporting outcomes of secondary endpoints and/or additional adverse event information.

Additionally, the Responsible Party must correct or address all apparent errors, deficiencies, and/or inconsistencies within 25 days of notification or discovery.

Clinical Research Support does not report results or adverse events for any trials. The Consortium's ClinicalTrials.gov Administrator creates individual user accounts when management of a trial is transferred to the PI for results reporting.

Results Deadlines

- The primary completion date and study completion date must be identified and reported no later than thirty days after each occurs.
- Clinical trial results, a summary of adverse events and a copy of the updated protocol and statistical analysis plan (if not included in the protocol) must be submitted to ClinicalTrials.gov no later than 1 year after the primary completion date.
- If data collection is still continuing for any of the secondary endpoints at the time of the initial results information submission, one or more additional results submission deadlines will apply, with the final submission deadline occurring no later than 1 year after the study completion date.
- Submission of results may be delayed according to guidelines specified by the regulation if the product under investigation does not yet have FDA approval (either initial approval or approval for a new use that is not included in the current package labeling).

Departing Investigator Responsibilities

- If a faculty member who serves as Responsible Party for a clinical trial leaves the Consortium before all required data have been reported to ClinicalTrials.gov, it must be determined whether the Responsible Party (RP) will continue to hold the role of RP or have the role of RP transferred to another individual in the Consortium. When appropriate, the Consortium can accept the role of RP.

Applicable Regulations & Guidelines

21 CFR 50 – Protection of Human Subjects

FDA Amendments Act of 2007, Section 801 (FDAAA or Public Law 110-85)

42 CFR 11 – Clinical Trial Registration and Results Information Submission

NOT-OD-16-149 – NIH Policy on Dissemination of NIH-Funded Clinical Trial Information

NOT-CA-15-011 – NCI Clinical Trial Access Policy

International Committee of Medical Journal Editors (ICMJE) clinical trial registration policy

CR 8401 – Center for Medicare and Medicaid Services (CMS)

Attachments / Related References

Related References:

- ClinicalTrials.gov Protocol Registration System (PRS): https://register.clinicaltrials.gov
- FDAAA section 801 Requirements: http://clinicaltrials.gov/ct2/manage-recs/fdaaa
  - Data definitions: https://prsinfo.clinicaltrials.gov/definitions.html
- Checklist for Evaluating Whether a Clinical Trial or Study is an Applicable Clinical Trial (ACT): https://prsinfo.clinicaltrials.gov/ACT_Checklist.pdf
- NCI Clinical Trial Access Policy: https://grants.nih.gov/grants/guide/notice-files/NOT-CA-15-011.html
- NIH Policy on the Dissemination of NIH Funded Clinical Trial Information: https://grants.nih.gov/grants/guide/notice-files/NOT-OD-16-149.html
- ICMJE: http://www.icmje.org/recommendations/browse/publishing-and-editorial-issues/clinical-trial-registration.html
- CMS: https://www.cms.gov/Outreach-and-Education/Medicare-Learning-Network-MLN/MLNMattersArticles/Downloads/SE1344.pdf

Version Review History	
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