



ClinicalTrials.gov Noncompliance Procedure

I. Purpose

The purpose of this document is to describe the Weill Cornell Medicine (WCM) ClinicalTrials.gov Program's Standard Operating Procedure (SOP) for escalating Principal Investigator noncompliance with institutional ClinicalTrials.gov requirements for record updates and summary results or with other applicable ClinicalTrials.gov regulations, policies, and/or terms of the grant, including:

- Title VII of the Food and Drug Administration Amendments Act Section 801 (FDAAA 801)
- Department of Health and Human Services (DHHS) Final Rule for Clinical Trials Registration and Results Information Submission (45 CFR 11)
- National Institutes of Health (NIH) Policy on the Dissemination of NIH-funded Clinical Trial Information
- International Committee of Medical Journal Editors (ICMJE) Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals ("The Uniform Requirements")
- Centers for Medicare and Medicaid Services (CMS)
- Requirements from funders such as the Patient-Centered Outcomes Research Institute (PCORI), the Bill & Melinda Gates Foundation, and VA Office of Research and Development (VAORD)

II. Revisions from Previous Version

None.

III. Definitions

Clinical Trial Definitions will be applied when determining which escalation procedure is applicable.

- **Applicable Clinical Trial, or ACT (FDAAA 801):** A clinical trial as defined by Title VII of the Food and Drug Administration Amendments Act (FDAAA 801), the Final Rule, and as guided by the ACT Checklist (https://prsinfo.clinicaltrials.gov/ACT_Checklist.pdf). Generally includes interventional studies (with one or more arms) of FDA-regulated drugs, biological products or devices that meet one of the following conditions:
 - (a) The trial has one or more sites in the U.S or a U.S. territory.; **or**
 - (b) The trial is conducted under an FDA investigational new drug application (IND) or investigational device exemption (IDE); **or**
 - (c) The trial involves a drug, biologic or device that is manufactured in the U.S. or its territories and is exported for study in another country.

ClinicalTrials.gov registration is required for applicable clinical trials (ACT) initiated after September 27, 2007 or ongoing as of December 26, 2007.

- **Clinical Trial (NIH):** 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.

NIH requires registration and public posting of summary results on ClinicalTrials.gov for all wholly or partially NIH-supported clinical trials, regardless of study phase, type of intervention, or whether or not they are subject to FDAAA 801. All WCM awardees of NIH funded clinical trials are subject to the NIH Policy and this ClinicalTrials.gov policy.

- **Clinical Trial (ICMJE):** A research project that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes—includes drugs, biologics, devices, surgical procedures, and behavioral treatments (see The Uniform Requirements for Manuscripts Submitted to Biomedical Journals). This definition includes Phase I studies.
- **Qualifying Trial (CMS):** A clinical trial that qualifies for coverage (as specified in CMS Section 310.1 of the Medicare National Coverage Determination Manual) and the purpose of the trial must be the evaluation of an item or service that falls within a Medicare benefit category (e.g., physicians' services, durable medical equipment, diagnostic test, etc.). The trial must have therapeutic intent and must enroll patients with diagnosed disease, not only healthy volunteers.

Completed: When the ClinicalTrials.gov record has passed the internal Quality Control (QC) process such that the WCM ClinicalTrials.gov Administrator can submit the record to ClinicalTrials.gov for public posting.

Enrollment: The estimated total number of participants to be enrolled (target number) or the actual total number of participants that are enrolled in the clinical study.

Human Subjects Protection Review Board Status: An indication in the ClinicalTrials.gov record as to whether a clinical study has been reviewed and approved by at least one human subjects protection review board or such review is not required per applicable law (for example, 21 CFR Part 56, 45 CFR Part 46, or other applicable regulation).

Individual Site Status: The recruitment status of each participating facility in a clinical study.

NCT (National Clinical Trial Number): An eight-digit number that is assigned to identify the ClinicalTrials.gov record and is issued when the registration is publicly posted on ClinicalTrials.gov.

Overall Recruitment Status: The recruitment status for the clinical study as a whole, based upon the status of the individual sites. If at least one facility in a multi-site clinical study has an Individual Site Status of "Recruiting," then the Overall Recruitment Status for the study must be "Recruiting."

Primary Completion Date: The date that the final subject was examined or received an intervention for the purposes of final collection of data for all of the primary outcome measure.

PRS (Protocol Registration and Results System): (<http://register.clinicaltrials.gov>) The system used to complete data entry for the purposes of public posting of study information on ClinicalTrials.gov. Each sponsoring entity has an assigned PRS organizational account.

Record Verification Date: The date on which the Principal Investigator last verified the clinical study information in the entire ClinicalTrials.gov record for the clinical study, even if no additional or updated information is being submitted.

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, the last participant's last visit), whether the clinical study concluded according to the pre-specified protocol or was terminated.

IV. Policy

1. Principal Investigators are responsible for maintaining the completeness and accuracy of ClinicalTrials.gov registrations and summary results records in a timely manner and in accordance with the WCM ClinicalTrials.gov Policy and with applicable ClinicalTrials.gov regulations, policies, and/or terms of the grant.

2 Record Updates

2.1 The Principal Investigator/designee must update a given ClinicalTrials.gov record:

- 2.1.1 No less than once every 12 months to review the complete ClinicalTrials.gov record for accuracy and to update the Record Verification Date, even if no other updated information is submitted at the time; and

2.1.2 Proactively and within the timelines specified in the table below for the following data elements:

Data Element	Deadline for Updating (i.e., not later than the specified date)
Study Start Date	30 calendar days after the first subject is enrolled (if the first human subject was not enrolled at the time of registration).
Intervention Name(s)	30 calendar days after a nonproprietary name is established.
Overall Recruitment Status	30 calendar days after a change in overall recruitment status.
Individual Site Status	30 calendar days of a change in status of any individual site.
Human Subjects Protection Review Board Status	30 calendar days after a change in status.
Primary Completion Date	30 calendar days after the clinical trial reaches its actual primary completion date.
Enrollment	At the time the primary completion date is changed to "actual," the actual number of participants enrolled must be submitted.
Study Completion Date	30 calendar days after the clinical trial reaches its actual study completion date.
Device Product Not Approved or Cleared by U.S. FDA	15 calendar days after a change in approval or clearance status has occurred.

3 Summary Results

3.1 At WCM, Principal Investigators are responsible for submitting completed summary results, when required by applicable regulations, policies, and/or terms of the grant, to ClinicalTrials.gov within 9 months of the Primary Completion Date for primary outcome measures and within 9 months of the Study Completion Date for secondary outcome measures (unless the data for one or more secondary outcome measures were collected at the same time as for primary outcome measures (or earlier), in which case those secondary outcome measure data are due at the same time as the primary outcome measure data).

3.2 To facilitate the WCM ClinicalTrials.gov Administrator's timely notification to a Principal Investigator/designee of the results deadline and so Human Research Compliance can provide timely assistance to the Principal Investigator, it is imperative that the Principal Investigator complete proactive updates of the Primary Completion Date and Study Completion Date in accordance with the deadlines stipulated in this policy.

4 PRS Review Comments Requiring Record Edits

4.1 At WCM, Principal Investigators are responsible for responding to ClinicalTrials.gov PRS Review Comments by completing ClinicalTrials.gov record edits within the timelines specified in the table below:

Comment Type	Registration	Results
Major Comment(s) <i>(Response Required)</i>	Within 7 calendar days of notification from the WCM ClinicalTrials.gov Administrator	Within 14 calendar days of notification from the WCM ClinicalTrials.gov Administrator
Advisory Comment(s) <i>(Response Optional)</i>	Same as above.	Same as above.

V. Procedure

1. Record Updates for ACTs, NIH-Funded Clinical Trials, or Studies Funded by Other Entities That Require Summary Results (e.g., PCORI)

1.1. The WCM ClinicalTrials.gov Administrator shall, on an annual basis, send a two-week deadline notice and one courtesy reminder to the Principal Investigator/designee to update the ClinicalTrials.gov record.

1.2. If the update is not completed by the deadline specified in the two-week notice, the WCM ClinicalTrials.gov Administrator shall notify the following individuals that the Principal Investigator/designee has 7 calendar days to complete the update before further escalation:

- Principal Investigator/designee
- Department Chief Administrative Officer
- Executive Director, Human Research Protection & Compliance
- Assistant Dean, Clinical Research Compliance/Institutional Official

1.3. If the update is not completed within 7 calendar days, then the Assistant Dean, Clinical Research Compliance/Institutional Official may suspend the institution's approval to conduct the research study. When this enforcement action is taken, the following individuals shall be notified:

- Principal Investigator/designee
- Department Chief Administrative Officer
- Department Chair
- Division Chief
- Executive Director, Human Research Protection & Compliance
- Assistant Director, Regulatory Compliance, Human Research Compliance

2. Record Updates for non-ACTs and Clinical Trials Not NIH- or PCORI-funded

2.1. The WCM ClinicalTrials.gov Administrator shall, on an annual basis, send a two-week deadline notice and one courtesy reminder to the Principal Investigator/designee to update the ClinicalTrials.gov record.

2.2. If the update is not completed by the deadline specified in the two-week notice, then the WCM ClinicalTrials.gov Administrator shall notify the Principal Investigator/designee that the noncompliant ClinicalTrials.gov record has been added to a list of noncompliant records organized by department and distributed on a quarterly basis to the following individuals:

- Department Chief Administrative Officer
- Executive Director, Human Research Protection & Compliance
- Assistant Director, Regulatory Compliance, Human Research Compliance
- Executive Director, Joint Clinical Trials Office (if non-cancer study listed)
- Director, Cancer Clinical Trials Office (if cancer study listed)
- Associate Director for Clinical Research at the Sandra and Edward Meyer Cancer Center (if cancer study listed)

2.3 The noncompliant ClinicalTrials.gov record shall remain on the list until the Principal Investigator/designee has completed the update.

3. Summary Results for ACTs, NIH-Funded Clinical Trials, or Studies Funded by Other Entities That Require Summary Results (e.g., PCORI)

3.1. Upon the Principal Investigator/designee updating the ClinicalTrials.gov record's Primary Completion Date and/or Study Completion Date from "anticipated" to "actual," the WCM ClinicalTrials.gov Administrator shall immediately send a results deadline notice followed later by two courtesy reminders to the Principal Investigator/designee as the results deadline approaches.

3.2. If the summary results are not completed by the deadline specified in the results deadline notice, then the WCM ClinicalTrials.gov Administrator shall notify the following individuals that the Principal Investigator is required to meet with the WCM ClinicalTrials.gov Administrator and Assistant Director, Regulatory Compliance, Human Research Compliance promptly to provide a plan for how the Principal Investigator is going to complete the results record within the next 30 calendar days:

- Principal Investigator/designee
- Department Chief Administrative Officer
- Assistant Dean, Clinical Research Compliance/Institutional Official
- Executive Director, Human Research Protection & Compliance
- Assistant Director, Regulatory Compliance, Human Research Compliance

3.3. If the summary results are not completed within 30 calendar days, then the Assistant Dean, Clinical Research Compliance/Institutional Official shall notify the following individuals that (a) the Institutional Review Board (IRB) will not conduct a review of any new initial IRB submissions for the Principal Investigator until such time as the results record is completed and (b) the Principal Investigator's department shall be held responsible for paying any civil monetary penalties levied against the institution (\$10,000 per noncompliant record per day and adjusted for inflation going forward) as a consequence of the noncompliance:

- Principal Investigator/designee
- Department Chief Administrative Officer
- Department Chair
- Division Chief
- Senior Associate Dean, Clinical Research
- Executive Director, Human Research Protection & Compliance
- Assistant Director, Regulatory Compliance, Human Research Compliance
- Executive Director, Joint Clinical Trials Office (if non-cancer study)
- Director, Cancer Clinical Trials Office (if cancer study)
- Associate Director for Clinical Research at the Sandra and Edward Meyer Cancer Center (if cancer study)

3.4 If the summary results are not completed within 30 days of the notification from the Assistant Dean, Clinical Research Compliance/Institutional Official, the Senior Associate Dean, Clinical Research may remove some or all of the Principal Investigator's research privileges until such time as the results record is completed and, in doing so, shall notify the following individuals:

- Principal Investigator/designee
- Department Chief Administrative Officer
- Department Chair
- Division Chief
- Assistant Dean, Clinical Research Compliance/Institutional Official
- Executive Director, Human Research Protection & Compliance
- Assistant Director, Regulatory Compliance, Human Research Compliance
- Executive Director, Joint Clinical Trials Office (if non-cancer study)
- Director, Cancer Clinical Trials Office (if cancer study)
- Associate Director for Clinical Research at the Sandra and Edward Meyer Cancer Center (if cancer study)

4. Summary Results for non-ACTs and Clinical Trials Not NIH- or PCORI-funded

- 4.1. Because summary results are not required for studies that have only registered on ClinicalTrials.gov due to ICMJE requirements, there is no results escalation procedure in place for non-ACTs and clinical trials not NIH- or PCORI-funded.

5. PRS Review Comments for Registrations (All Trial Types)

- 5.1. Because a consequence of nonresponse to PRS Review Comments for registrations is that ClinicalTrials.gov does not assign an NCT # and thus the trial cannot initiate at WCM, there is no escalation procedure in place for a failure to respond to PRS Review Comments for registrations.

6. PRS Review Comments for Results (All Applicable Trial Types)

- 6.1. The WCM ClinicalTrials.gov Administrator shall, upon notification from ClinicalTrials.gov, send a two-week deadline notice to the Principal Investigator/designee with one courtesy reminder as the deadline approaches.

- 6.2. If the record edits are not completed by the deadline specified in the two-week deadline notice, the WCM ClinicalTrials.gov Administrator shall notify the following individuals that the Principal Investigator/designee has 7 calendar days to complete the record edits before further escalation:

- Principal Investigator/designee
- Department Chief Administrative Officer
- Executive Director, Human Research Protection & Compliance
- Assistant Dean, Clinical Research Compliance/Institutional Official

- 6.3. If the record edits are not completed within 7 calendar days, then the Assistant Dean, Clinical Research Compliance/Institutional Official shall notify the following individuals that (a) the Institutional Review Board (IRB) will not conduct a review of any new initial IRB submissions for the Principal Investigator until such time as the record edits are completed and (b) the Principal Investigator's department shall be held responsible for paying any civil monetary penalties levied against the institution (\$10,000 per noncompliant record per day and adjusted for inflation going forward) as a consequence of the noncompliance:

- Principal Investigator/designee
- Department Chief Administrative Officer
- Department Chair
- Division Chief
- Senior Associate Dean, Clinical Research
- Executive Director, Human Research Protection & Compliance
- Assistant Director, Regulatory Compliance, Human Research Compliance
- Executive Director, Joint Clinical Trials Office (if non-cancer study)
- Director, Cancer Clinical Trials Office (if cancer study)
- Associate Director for Clinical Research at the Sandra and Edward Meyer Cancer Center (if cancer study)

- 5.4 If the record edits are not completed within 7 days of the notification from the Assistant Dean, Clinical Research Compliance/Institutional Official, the Senior Associate Dean, Clinical Research may remove some or all of the Principal Investigator's research privileges until such time as the results record is completed and, in doing so, shall notify the following individuals:

- Principal Investigator/designee
- Department Chief Administrative Officer
- Department Chair
- Division Chief
- Assistant Dean, Clinical Research Compliance/Institutional Official
- Executive Director, Human Research Protection & Compliance

- Assistant Director, Regulatory Compliance, Human Research Compliance
- Executive Director, Joint Clinical Trials Office (if non-cancer study)
- Director, Cancer Clinical Trials Office (if cancer study)
- Associate Director for Clinical Research at the Sandra and Edward Meyer Cancer Center (if cancer study)

VI. References

WCM ClinicalTrials.gov Policy,

https://research.weill.cornell.edu/sites/default/files/policy_forms/wcm_ct.gov_policy_final_v1.0_3.07.18.pdf

FDAAA 801, <https://www.govinfo.gov/content/pkg/PLAW-110publ85/pdf/PLAW-110publ85.pdf#page=82>

Clinical Trials Registration and Results Information Submission (Final Rule; 42CFR11),

<https://www.federalregister.gov/documents/2016/09/21/2016-22129/clinical-trials-registration-and-results-information-submission>

ACT Checklist, https://prsinfo.clinicaltrials.gov/ACT_Checklist.pdf

NIH Policy on the Dissemination of NIH-Funded Clinical Trial Information, <https://grants.nih.gov/policy/clinical-trials/reporting/understanding/nih-policy.htm>

International Committee of Medical Journal Editors (ICMJE) Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals (“The Uniform Requirements”), <http://www.icmje.org/icmje-recommendations.pdf>

CMS Medicare Clinical Trial Policies,

<https://www.cms.gov/Medicare/Coverage/ClinicalTrialPolicies/index.html?redirect=/ClinicalTrialPolicies>