Guidance on CTgov Registration & Results Reporting Requirements

The purpose of this guidance is to help you determine when an **Investigator-Initiated Trial (IIT**) requires registration and results reporting. This guidance integrates institutional (UNC), National Institutes of Health (NIH), U.S. Food and Drug Administration (FDA) rules for Applicable Clinical Trials (ACTs), Centers for Medicare & Medicaid Services (CMS), and publication requirements (International Committee of Medical Journal Editors (ICMJE)) decision points, timelines, and common pitfalls.

Regulatory Drivers

There are four main rule bodies that influence trial registration and reporting requirements. In addition, contractual obligations, especially for PCORI funding, may also impose these requirements and should be evaluated on a case-by-case basis. Each rule body should be assessed independently as more than one may apply:

Rule Body	Register When	Report When	Notes
ICMJE	Before 1st enrollment (signing of informed consent)	N/A	Required for publication eligibility
NIH	Within 21 days of 1st enrollment	Within 12 months of primary outcome data collection	Includes pilot, feasibility, and BESH trials. See NOT-OD-16-149 for NIH policy on the Dissemination of Clinical Trial Information. Visit Clinical Trial Requirements for Grants and Contracts, NIH Clinical Trial Definition, National Cancer Institute, Decision Tool, NIH Case Study Examples, and FAQs.
ACT (FDA)	Within 21 days of 1st enrollment	Within 12 months of primary outcome data collection	Studying approved/unapproved FDA-regulated intervention. See checklist for evaluating ACTs and FAQs.
CMS	Before 1st participant enrollment	N/A	Effective 01/01/2014, the NCT number is required on claims for services in qualifying clinical trials. Enter the NCT in OnCore to ensure it appears on claims and prevent payment delays.
Additional Drivers			
Contract	As agreed	As agreed	Failure to comply is a breach
PCORI*	As agreed	As agreed	*Mandated funding terms include registration & reporting typically including observational trials

Decision Points

Use the questions below to help determine if your trial requires registration and results reporting. A 'Yes' response to any of the following questions indicates that registration and reporting requirements may apply and should be further evaluated. Not all questions must be answered 'Yes' for this determination to apply. See the decision tree provided below.

1. For all Investigator-Initiated Trials (IITs), is the study interventional?
   - According to CTgov, a trial qualifies as an interventional clinical trial when participants are prospectively assigned to an intervention(s) based on a protocol, with the goal of evaluating the effect of the intervention(s) on biomedical or other health related outcomes.

   - In clinical research, the distinction between interventional and observational studies hinges on how participants are assigned to receive treatments, interventions, or exposures.

     ❖ A study is considered **interventional** when participants are prospectively assigned to one or more interventions according to a protocol, with the intent to evaluate the effects of those interventions. Assignment may occur through randomization, stratification, or investigator decision, if it is planned and protocol-driven.

     ❖ A study is considered **non-interventional (observational**) when the assignment to treatment or exposure is not directed by the protocol or researcher. Instead, participants receive interventions or engage in behaviors as part of routine practice or natural circumstances, and researchers observe outcomes without influencing the assignment process.

     These definitions align with the FDA's August 2023 guidance, which emphasizes that non-interventional studies do not involve protocol-specified assignment and that interventional studies actively assign interventions to evaluate their effects.

     Use Inclusion Criteria to Clarify Study Type
     Inclusion criteria help clarify whether a study is interventional or observational. Keep this in mind when writing the study protocol.

     - In **interventional** trials, inclusion criteria are defined by the protocol and used to determine eligibility for receiving the intervention. These criteria may be medical, behavioral, psychological, social or other factors. The key factor is that assignment to the intervention is prospective and protocol-driven, not based on routine care or participant choice.

     - In **observational** studies, inclusion criteria reflect that the intervention or exposure occurred independently of the research protocol. The study does not direct or alter how participants receive the intervention or engage in the behavior.

     Understanding and clearly documenting this distinction is essential for:
     - Accurate trial registration (e.g., CTgov)
     - Appropriate IRB review pathways
     - Correct informed consent procedures
     - Meeting FDA and regulatory compliance standards

See also: Is This an Interventional Clinical Trial or Observational Study? How- and Why- It Is Important to Write Protocols That Make This Distinction Clear | WCG.

2. Does the trial evaluate the effect of the intervention(s) on health related biomedical, behavioral, or other health-related outcomes? (Wording of "Clinical Trial" definitions varies by rule body)

3. Are there plans to publish the study findings? (ICMJE, see also What is the ICMJE definition of a clinical trial?)

4. For an NIH-funded trial, does it:
   - Involve human subjects?
   - Use one or more interventions?
   - Prospectively assign human subjects to an intervention?
   - Evaluate a health-related biomedical, behavioral outcome?

   See also NIH Case Study Examples.

5. Is the study evaluating an approved or unapproved FDA-regulated intervention outside routine care?

6. Will research-related cost be billed to CMS?

7. Is there a contractual requirement for registration/results reporting?

8. Is the study PCORI-funded?

If your investigator-initiated trial (IIT) requires registration, follow the timelines below. For studies intended for publication, the ICMJE registration requirement must be met—this requirement has the strictest timeline.

Before creating a record in CTgov, the study must be submitted to the UNC Institutional Review Board (IRB), even if not yet approved. **Important:** Studies with "approval in principle" or 118-type approvals under 45 CFR 46.118 do not satisfy the IRB submission requirement

Timeline Tracker

Requirement	Deadline	Notes
ICMJE Registration	Before enrollment (i.e., 1st consent signed)	Required for publication
NIH Registration	Within 21 days of first enrollment	Required for NIH-funded clinical trials
ACT Registration	Within 21 days of first enrollment	Required for trials studying an FDA-regulated product
Results Reporting	Within 12 months of last primary outcome data collection	Required for NIH and ACT and contractual terms in some cases
CMS registration	Before enrollment (i.e., 1st consent signed)	Required before billing to CMS to ensure payment.

UNC maintains two CTgov or Protocol Registration and Results System (PRS) accounts: one for oncology-related trials and another for all other trial types. Contact Melahat Canter at Lineberger Comprehensive Cancer Center (LCCC) for oncology trials or Monica Coudurier for non-oncology trials.

After creation in the UNC-held CTgov account, records must be released to CTgov for them to begin QC review. NCT number assignment follows successful QC review and marks official registration. CTgov will send an email to the Record Owner with the NCT number upon completion of the QC review.

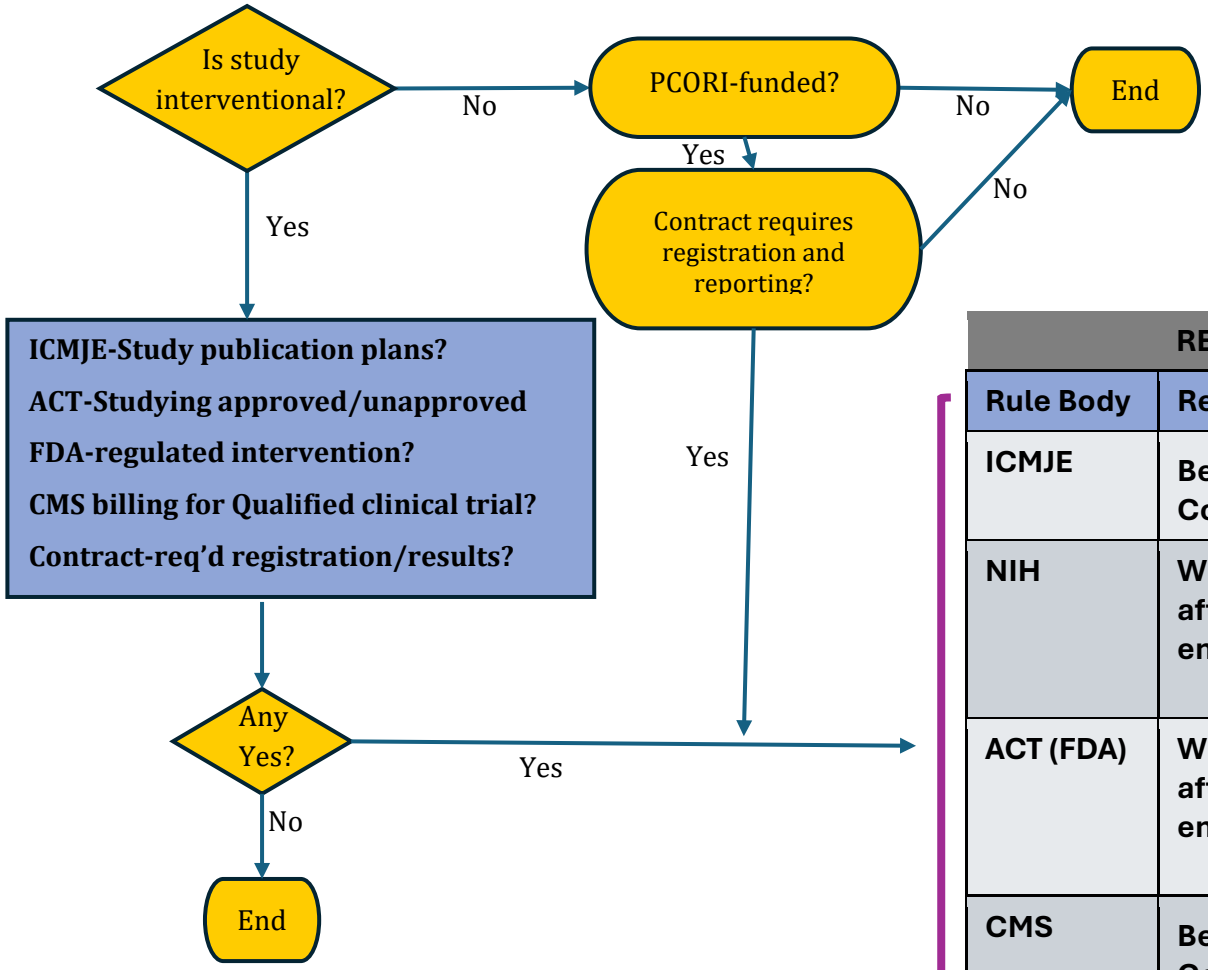
Common Pitfalls

❌ Assuming small trials (e.g., pilot, feasibility) don't require registration
❌ Registering *after* enrollment starts (violates ICMJE)
❌ Believing only drug/device trials need registration
❌ Assuming that only unapproved/uncleared drug/device/biologic trials need registration
❌ Waiting until after publication to report results

Roles & Responsibilities

Role	Responsibility
Principal Investigator (PI)	**Ensures Registration and Results Reporting** All tasks related to registration, results reporting, and study record updates on CTgov are delegated by the University to the Principal Investigator (PI). While certain activities—such as initial registration and ongoing record maintenance—may be delegated to qualified study team members, both CTgov and UNC expect that results reporting is performed by an individual with a thorough understanding of the study's design, conduct, and outcomes, and who is proficient in statistical analysis. The PI remains ultimately accountable for the accuracy and completeness of the CTgov record, including timely updates and results submissions, regardless of any delegation. This ensures compliance with federal regulations, institutional policies, and supports transparency in clinical research.
Compliance Team	Provides guidance

Quick Reference for Interventional & PCORI-Funded Trials



REGULATORY DRIVERS

Rule Body	Register When?	Report When?
ICMJE	Before 1st Inf Consent signed	Not Applicable
NIH	Within 21 days after enrollment	Final by 12 months of primary outcome data collection
ACT (FDA)	Within 21 days after enrollment	Final by 12 months of primary outcome data collection
CMS	Before 1st Inf Consent signed	Not Applicable
Contract-Req'd	As agreed	As agreed

Reporting results in CTgov requires a formal protocol even if SRC and IRB do not require this.