

Clinical Trials

Background

Clinical trials have historically been viewed as research projects investigating a drug, device, or biologic regulated by the Food and Drug Administration (FDA). The concept of a clinical trial, however, expanded in 2014 when the National Institutes of Health (NIH) adopted a definition encompassing a wide range of trial types: mechanistic, exploratory/developmental, pilot/feasibility, behavioral, and more. The Office for Human Research Protections will be implementing the same definition as the NIH.

What is a clinical trial?

Three separate definitions determine what federal agency rules apply for the conduct of a clinical trial. These definitions are not mutually exclusive:

National Institutes of Health

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.

Human Subject Common Rule

Clinical trial means 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 the interventions on biomedical or behavioral health-related outcomes.

Food and Drug Administration

FDA has defined "*clinical investigation*" to be synonymous with "*research*". "*Clinical investigation*" means any experiment that involves a test article and one or more human subjects, and that either must meet the requirements for prior submission to the FDA...or the results of which are intended to be later submitted to, or held for inspection by, the FDA as part of an application for a research or marketing permit.

A simple test to determine if the activity is a clinical trial is to answer the following questions:

1. Does the study involve human participants?
2. Are the participants prospectively assigned to an intervention?
3. Is the study designed to evaluate the effect of the intervention on the participants?
4. Is the effect being evaluated a health-related biomedical or behavioral outcome?

*If the answer is 'yes' to all questions then the study is a clinical trial.

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What is a health-related outcome?

Any outcome looking at “health” is considered health-related. “Health” is considered physical, mental, emotional, and behavioral. The NIH goes on to state that all NIH funded activity investigating biomedical or behavioral health outcomes is a clinical trial given the purpose of the NIH. It is important to note that only one outcome need to investigate biomedical or behavioral health to be considered a clinical trial.

If the study is not designed to assess whether a prospectively assigned intervention modifies a behavioral outcome, the study is not a clinical trial.

What is an intervention for purposes of determining if a research study is a clinical trial?

Intervention includes both physical procedures by which data or biospecimens are gathered and manipulations of the subject’s environment that are performed for the purpose of modifying one or more health-related biomedical or behavioral processes and/or endpoints.

Examples include: drugs/small molecules/compounds; biologics; devices; procedures (e.g., surgical techniques); delivery systems (e.g., telemedicine, face-to-face interviews); strategies to change health-related behavior (e.g., diet, cognitive therapy, exercise, development of new habits); treatment strategies; prevention strategies; and, diagnostic strategies (e.g. venipuncture).

Studies that involve secondary research with biological specimens or health information are not clinical trials. Educational studies, such as those with outcomes focusing on memorization, or retention and recall of information to assess teaching methods, are not clinical trials.

What are the requirements to conduct a clinical trial?

The requirements listed below are not mutually exclusive. All rules may apply if the clinical trial meets the regulatory definitions above or are funded or supported by a federal agency.

All projects deemed a clinical trial must include:

- Paragraph in the informed consent describing that the study is posted on [Clinicaltrials.gov](https://clinicaltrials.gov).
- Submit a clinicaltrials.gov registration number as part of the IRB submission.

Food and Drug Administration

If the project involves a drug or device (e.g., test article) the FDA rules apply. This means that the investigational item may require an investigational new drug or device application (IND or IDE) from the FDA before the research may proceed.

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National Institutes of Health

If the project is NIH funded or supported investigators must:

- Use a single IRB for non-exempt, multi-site clinical trials for application due dates on/after January 25, 2019. It is important to note that for NIH clinical trials, the requirement to use a single IRB occurs sooner than for all other federally funded or supported clinical trials. This date is January 19, 2020.
- Complete Good Clinical Practice (GCP) training expectations for NIH staff, grantees, and contractors that went into effect January 2017 (see: <https://grants.nih.gov/grants/guide/notice-files/NOT-OD-16-148.html>).
- Register and report clinical trial information on CT.gov (contact David Faguy for information on obtaining an account)
- Have updated peer review criteria that will be included in FOAs for clinical trial applications and solicitations for due dates on/after January 25, 2018. (refer to Sponsored Projects for questions)
- New Human Subject Information form requirements for clinical trials that will be included in updated application forms (FORMS-E) for due dates on/after January 25, 2018, and contract solicitations published as of January 25, 2018. This form requests human subject and clinical trials information at the study level.

Extending the Common Rule to All Clinical Trials

The NIH rule does not apply to non-federally funded clinical trials. However, the FDA rules may still apply.

Resources

NIH clinical requirements for grants and contracts: <https://grants.nih.gov/policy/clinical-trials.htm>