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Frequently Asked Questions: NIH Clinical Trial Definition

QUESTIONS ABOUT THE CLINICAL TRIAL DEFINITION

- **What is the difference between clinical research and a clinical trial?**

  Clinical trials are clinical research studies.

  Clinical research includes all research involving human participants. It does not include secondary studies using existing biological specimens or data collected without identifiers or data that are publicly available. (https://humansubjects.nih.gov/glossary)

  Clinical trials are clinical research studies involving human participants assigned to an intervention in which the study is designed to evaluate the effect(s) of the intervention on the participant and the effect being evaluated is a health-related biomedical or behavioral outcome.

- **How can researchers determine whether a proposed study is a clinical trial?**

  The following questions should be used to determine whether a study meets the NIH clinical trial definition:

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

  If the answers are all "yes," the study is a clinical trial.
  If any answers are "no," the study is not a clinical trial

- **Does the primary outcome of a study need to be a health-related outcome in order for a study to be considered a clinical trial?**

  If any outcome is health-related and the answers to the four questions are all yes, then the study is meets the clinical trial definition. You should note, though, that all NIH-funded research investigating biomedical or behavioral outcomes is considered to be health-related. Hence, if the outcome is biomedical or behavioral, the study may be a clinical trial (if the answers to the other three questions are "yes"). Many clinical trials are "mechanistic" or "exploratory" falling outside the realm of efficacy or effectiveness trials.

- **What is the difference between the clinical trial definition in the revised Common Rule and the NIH clinical trial definition?**

  NIH considers the two definitions to have the same meaning.

Revised Common Rule §__.102(b): "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."
https://www.gpo.gov/fdsys/pkg/FR-2017-01-19/pdf/2017-01058.pdf

NIH clinical trial definition: "A research study in which one or more human subjects are prospectively assigned to one or more interventions4 (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes." (Oct 23, 2014)
https://grants.nih.gov/grants/guide/notice-files/NOT-OD-15-015.html

- **Does risk to human participants factor into whether a study is considered to be a clinical trial?**

  Risk is not part of the NIH clinical trial definition. NIH considers the study to be a clinical trial as long as all elements of the NIH clinical trial definition are met.

- **What is the sub-definition of "intervention"?**

  An intervention is defined as a manipulation of the subject or subject's environment 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.

- **Are measurements the same as interventions?**

  No; measurements are used to evaluate outcomes.

- **Does the NIH clinical trial definition apply to foreign awards?**

  Yes; the NIH clinical trial definition applies to all NIH-funded studies.

- **How will NIH educate researchers?**

  NIH is providing updated information, tools, and resources to the research community as guidance around the NIH clinical trial definition. See resources at:
  https://grants.nih.gov/policy/clinical-trials.htm

  Additionally, NIH staff are prepared to help educate researchers on whether their studies meet the NIH clinical definition.

SPECIFIC CASES

- **If a proposed clinical study includes a plan for addressing incidental findings, is the study considered to be a clinical trial?**

  No; having a plan for addressing incidental findings does not determine whether a study is considered to be a clinical trial. To determine whether your study meets the NIH clinical trial definition, please refer to the four questions above that outline the criteria.

- **Are studies that propose to evaluate a clinical intervention or to develop a diagnostic tool considered to be clinical trials?**

  It depends; studies that involve prospective assignment of human participants to an intervention, which may be a clinical intervention or development of a diagnostic tool, and that are designed to evaluate an effect of the intervention on the participant, where the effect is a biomedical or behavioral health outcome, are clinical trials. (See Case Study #7b). Studies designed only to validate the sensitivity or specificity of a tool are not clinical trials (See Case Study #7a).

- **Are studies that elicit the opinions or preferences from human participants considered to be clinical trials?**

  No; studies eliciting opinions or preferences are not considered to be health-related outcomes.

- **Are observational studies, which do not include an intervention, considered to be clinical trials?**

  No; in order to meet the NIH clinical trial definition there must be an intervention.

- **Are studies that involve only healthy participants considered to be clinical trials?**
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  Yes; studies involving healthy participants are considered clinical trials if all elements of the NIH clinical trial definition are met.

- **Are studies that are not designed to impact diagnoses or treatment of patients considered to be clinical trials?**

  It depends; studies that meet all elements of the NIH clinical trial definition are considered to be clinical trials. (See Case Studies #8a-c)

- **Are studies designed to investigate whether a technique can be used to measure a response in research participants considered to be clinical trials?**

  No; in order to meet the NIH clinical trial definition there must be an intervention.

- **Are studies designed to compare two approved diagnostic or therapeutic devices considered to be clinical trials?**

  No; a study must be designed to evaluate the effect of the intervention on the human participant to meet the NIH clinical trial definition.

- **Must a health-related outcome be permanent or lasting in order for a study to be a clinical trial?**

  No; a transient health-related outcome is sufficient for a study to be considered a clinical trial, as long as all other elements of the NIH clinical trial definition are met.

- **Are studies that coordinate with health-care providers where the outcome is measured in their patients considered to be clinical trials?**

  Yes; in these studies, both the health-care providers and patients are human participants, and the health care providers become part of the intervention. The study is considered to be a clinical trial as long as all other elements of the NIH clinical trial definition are met. (See Cast Study #20)

- **Are studies with just a few research participants considered to be clinical trials?**

  Yes; the NIH clinical trial definition specifies that there must be one or more human participants involved in the study. The study is considered to be a clinical trial if all elements of the NIH clinical trial definition are met.

- **Are studies ancillary to clinical trials considered to be clinical trials as well?**

  Yes; studies ancillary to clinical trials are themselves are considered to be clinical trials if all elements of the NIH clinical trial definition are met.

- **Are studies that use correlational designs considered to be clinical trials?**

  No; studies using correlational designs to prospectively associate biomedical parameters with other health-related measures, but do not involve an intervention, do not meet the NIH clinical trial definition.

- **Are studies designed to understand a disease mechanism considered to be clinical trials?**

  Yes; studies that are designed to evaluate the effect of an intervention on a research participant, and meet all other elements of the clinical trial definition, meet the NIH clinical trial definition.

- **Are studies that compare two different methods of diagnosing a disease in patients to determine the reliability of a new method, but have no intention of using the results to inform the clinical care of the patients considered to be clinical trials?**

  No; studies that involve a comparison of methods and that do not evaluate the effect of the interventions on the participant do not meet the NIH clinical trial definition.

- **Are studies that evaluate the effect of an intervention on research participants, but do not have a comparison group (e.g., placebo, control) considered to be clinical trials?**

  Studies need not include a comparison group to meet the NIH clinical trial definition. As long as all of the elements of the NIH clinical trial definition are met, the study would be considered to be a clinical trial.