NIH Definition of a Clinical Trial

Definition: 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.

For more information see NIH webpage and FAQ: https://grants.nih.gov/policy/clinical-trials/definition.htm
NIH Decision Tree

Case Studies:
https://grants.nih.gov/policy/clinical-trials.case-studies.htm
Prospectively Assigned refers to a pre-defined process (e.g., randomization) specified in an approved protocol that stipulates the assignment of research subjects (individually or in clusters) to one or more arms (e.g., intervention, placebo, or other control) of a clinical trial.

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.
NIH Definition of Clinical Trial

A "health-related biomedical or behavioral outcome" is defined as the pre-specified goal(s) or condition(s) that reflect the effect of one or more interventions on human subjects’ biomedical or behavioral status or quality of life.

Examples include: positive or negative changes to physiological or biological parameters (e.g., improvement of lung capacity, gene expression); positive or negative changes to psychological or neurodevelopmental parameters (e.g., mood management intervention for smokers; reading comprehension and/or information retention); positive or negative changes to disease processes; positive or negative changes to health-related behaviors; and, positive or negative changes to quality of life.
Clinical Trial FOA’s

Effective on or after January 25, 2018, NIH will require that all applications involving one or more clinical trials be submitted through a Funding Opportunity Announcement (FOA) specifically designed for clinical trials.

The FOA/RFP must explicitly state it will accept clinical trials.
Clinical Trial - NRSA’s

Special requirements for NIH NRSA series applications

Training – T – Awards:
Institutional Training awards do not support clinical trials (with the exception of some D43 and K12 awards).

- All Training (T) FOAs will be designated as “Clinical Trial Not Allowed” in Section II. Award Information, but will indicate that appointed trainees are permitted to obtain research experience in a clinical trial led by a mentor or co-mentor.

- Some D43 and K12 FOAs will be designated as “Clinical Trial Optional” in Section II. Award Information
Clinical Trial - NRSA’s

Special requirements for NIH NRSA series applications

Fellowships (F) awards
The NIH encourages fellows to receive training in clinical research, however, NIH supported fellows are not permitted to conduct a clinical trial independently.

- All Fellowship (F) FOAs will be designated as ‘No Independent Clinical Trials’ in Section II. Award Information, but will indicate that applicants are permitted to propose research experience in a clinical trial led by a sponsor or co-sponsor
- Fellowship applicants proposing to gain mentored training in a clinical trial will be instructed to provide details of their contribution to the study in the Research Strategy rather than in the clinical trial specific fields on the PHS Human Subjects and Clinical Trials Information form.
- NIH expects the mentor or individual receiving support for the clinical trial to assume overall responsibility of the trial.
Clinical Trials – Career Awards (K)

Career Development awards may support either independent clinical trials or a mentored research training experience, depending on the FOA.

- FOAs that indicate ‘Clinical Trial Required” in the title and in Section II. Award Information will support independent clinical trials conducted by the applicant

- FOAs that indicate “No Independent Clinical Trials” in the title and in Section II. Award Information permit the applicant to propose research experience in a clinical trial led by a sponsor or co-sponsor
  - Career Development applicants proposing to gain mentored training in a clinical trial will be instructed to provide details of their contribution to the study in the Research Strategy rather than in the clinical trial specific fields on the PHS Human Subjects and Clinical Trials Information form.
  - NIH expects the mentor or individual receiving support for the larger trial to have the overall responsibility of the trial.
Clinical Trial Policy Changes

**Good Clinical Practice Training**
Effective January 1, 2017 NIH expects all NIH-funded clinical investigators and clinical trial staff who are involved in the design, conduct, oversight, or management of clinical trials to be trained in Good Clinical Practice (GCP).

Policy on Good Clinical Practice Training for NIH Awardees Involved in NIH-funded Clinical Trials (NOT-OD-16-148)

**Clinical Trials Protocol Template**
If your application includes phase 2 or 3 clinical trials that require Investigational New Drug application (IND) or Investigational Device Exemption (IDE) applications, a NIH-FDA template with instructional and sample text can help you write your protocols. Use of this template is optional. Exemption (IDE) applications, a NIH-FDA template with instructional and sample text can help you in writing your protocols.

NIH and FDA Release Protocol Template for Phase 2 and 3 IND/IDE Clinical Trials (NOT-OD-17-064)

**Clinicaltrials.gov Registration and Reporting**
A new regulation and NIH policy expanded Clinicaltrials.gov registration and reporting to ALL NIH-funded clinical trials. All NIH-funded clinical trials are expected to register and submit results information to Clinicaltrials.gov for competing applications and contract proposals submitted on or after 01/18/2017.

NIH Policy on the Dissemination of NIH-Funded Clinical Trial Information (NOT-OD-16-149)
Clinical Trial Policy Changes

**Clinical Trial-Specific Funding Opportunities**
Effective January 25, 2018, all grant applications with plans to conduct clinical trials must be submitted in response to an FOA which specifically states that clinical trials are allowed. All current parent announcements will no longer allow clinical trials. There will be some new parent announcements that will allow clinical trials, and the specifics will depend upon the discipline. Some of the institutes will be joining certain parent announcements specifically for clinical trials, but that’s something to be determined by each individual IC.

Policy on Funding Opportunity Announcements (FOA) for Clinical Trials (NOT-OD-16-147)
NIH Plans for Clinical Trial Specific Parent R01 and Parent R21 Funding Opportunity Announcements (NOT-OD-18-010)

**Clinical Trial-Specific Review Criteria**
New review criteria will be used to evaluate applications proposing clinical trials or clinical trial research experience. New questions related to the following areas will be used to review clinical trials: significance, investigator(s), innovation, approach, environment, and study timeline.

The NIH Announces New Review Criteria for Research Project Applications Involving Clinical Trials (NOT-OD-17-118)
Clinical Trial Policy Changes

**New Human Subjects and Clinical Trial Information Form**
A new Human Subjects and Clinical Trial Information form will be included in the new FORMS-E Application Packages and will be required for all applications with due dates on or after January 25, 2018. This new form consolidates all Human Subjects and Clinical Trial related information into one place and expands the information required for studies that meet the NIH definition of a clinical trial.

New NIH "FORMS-E" Grant Application Instructions Available for Due Dates On or After January 25, 2018 (NOT-OD-17-119)

**Single IRB Policy for Multi-Site Research**
For applications with due dates on or after January 25, 2018, and contract solicitations published on or after January 25, 2018, NIH expects that all sites participating in multi-site studies, which involve non-exempt human subjects research funded by the NIH, will use a single Institutional Review Board (sIRB) to conduct the ethical review required for the protection of human subjects.

NOT-OD-16-109 Scenarios to Illustrate the Use of Direct and Indirect Costs for Single IRB Review under the NIH Policy on the Use of a Single IRB for Multi-site Research
NOT-OD-18-003 Guidance on Exceptions to the NIH Single IRB Policy