The Changing Landscape

Tulane HRPO Information Session
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Overview

• Revised NIH Definition of Clinical Trials
• Registration and Submission to ClinicalTrials.gov
• Implications of the Revised Common Rule
Revised NIH Definition of Clinical Trials
NIH Clinical Trials

• Replaces the current clinical trial definition in relevant extramural and intramural NIH policies, guidance, and instructional materials.

• Issued on October 23, 2014 and took effect January 25, 2015 (not really new).

• With broader definition, many more studies are classified as clinical trials
NIH Clinical Trials

Revised 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.
NIH Clinical Trials

• **Prospectively Assigned**: 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**: 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.
NIH Clinical Trials

- Health-related Biomedical or Behavioral Outcome: 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.
Decision Tree for NIH Clinical Trial Definition

Does the study involve human participants research?

YES

Are participants prospectively assigned to an intervention?

NO

YES

Is the study designed to evaluate the effect of the intervention on the participants?

NO

YES

Is the effect being evaluated a health-related biomedical or behavioral outcome?

NO

YES

This study is a clinical trial.

The study is NOT a clinical trial.
Case Studies

Case Study #1:
The study involves the recruitment of research participants who are randomized to receive one of two approved drugs. It is designed to compare the effects of the drugs on the blood level of a protein.
Case Studies

Case Study #2:
The study involves the recruitment of research participants with disease X to receive an investigational drug. It is designed to assess safety and determine the maximum tolerated dose of the drug.
Case Studies

Case Study #3a:
The study involves the recruitment of research participants with disease X to test an investigational in vitro diagnostic device (IVD). It is designed to evaluate the ability of the device to measure the level of an antibody in blood.
Case Study #3b:
The study involves the recruitment of research participants with disease X to be evaluated with an investigational in vitro diagnostic device (IVD). The study is designed to evaluate how knowledge of certain antibody levels impacts clinical management of disease.
Case Studies

Case Study #3b:
The study involves the recruitment of research participants with disease X to be evaluated with an investigational in vitro diagnostic device (IVD). The study is designed to evaluate how knowledge of certain antibody levels impacts clinical management of disease.
Case Studies

Case Study #4:
The study involves the recruitment of healthy volunteers who will be randomized to different durations of sleep deprivation (including no sleep deprivation as a control) and who will have stress hormone levels measured. It is designed to determine whether the levels of stress hormones in blood rise in response to different durations of sleep deprivation.
Case Studies

Case Study #5:
The study involves the recruitment of individuals to receive a new behavioral intervention for sedentary behavior. It is designed to measure the effect of the intervention on hypothesized differential mediators of behavior change.
**Case Studies**

**Case Study #6:**

The study involves the recruitment of healthy adolescent volunteers followed over time to assess brain development and factors that influence brain development. Participants are administered a battery of standard measures at each visit including blood draws, surveys, various cognitive performance measures (e.g., working memory tasks), and brain scans (e.g., fMRI) to assess the association of these measures over time.
Case Study #7:
The study involves the recruitment of healthy volunteers who are randomly assigned (either between-subject or within-subject in a counterbalanced design) to one of two experimental conditions to enhance or interfere with cognitive performance. The effects of these conditions on cognitive performance (e.g., working memory) and brain function during the cognitive performance task are measured (e.g., fMRI).
NIH Clinical Trials

Implications:

• Training in Good Clinical Practice (GCP)
  • All NIH-funded clinical investigators and clinical trial staff who are involved in the design, conduct, oversight, or management of clinical trials are required to be trained in Good Clinical Practice (GCP) [Effective January 1, 2017]

• Clinical trial-specific Funding Opportunity Announcements (FOAs)
  • All grant applications & contract proposals involving one or more clinical trials must be submitted through an FOA or Request for Proposal (RFP) specifically designated for clinical trials [Effective for due dates on/after January 25, 2018]

• New Human Subjects & Clinical Trials Information Form
  • Consolidates human subjects, inclusion enrollment, and clinical trial information into one form [Effective for due dates on/after January 25, 2018]

• Expanded registration and results reporting in ClinicalTrials.gov
Submitting and Reporting to ClinicalTrials.gov
ClinicalTrials.gov

NIH Policy on Dissemination of NIH-Funded Clinical Trial Information

• All clinical trial applications requesting support for a trial that will be initiated on/after January 18, 2017 must register and report the results in ClinicalTrials.gov
ClinicalTrials.gov

In order to comply with the NIH Policy on Clinical Trial Dissemination, awardees must:

- Submit a plan in the application that outlines compliance with the expectations of the policy
- Register the clinical trial no later than 21 days after enrolling the first participant
- Submit summary results no later than one year after primary completion date
ClinicalTrials.gov

• Determine which regulations and/or policies apply
  • Is your study an “Applicable Clinical Trial” (ACT) - is it an FDA-regulated clinical trial?
    • If so, both NIH and FDA requirements must be met.
    • If not, only NIH requirements must be met.
  • Certify compliance in NIH grant applications and progress reports.
ClinicalTrials.gov

- Determine who is responsible for clinical trial registration and results reporting.
  - If it is an ACT (FDA-regulated) then it is the sponsor or PI if designated by the sponsor
  - If it is not (only NIH funded) then it is the grant recipient or investigator
ClinicalTrials.gov

• Ensure the responsible entity registers the clinical trial no later than 21 days after enrolling the first subject.
• Ensure the responsible entity updates information in the clinical trial record at least once every 12 months.
• Ensure the responsible entity reports summary results not later than a year after clinical trial completion date.
ClinicalTrials.gov

• Go to https://clinicaltrials.gov/ct2/manage-recs to see instructions on how to:
  • Apply for an account
  • Register a study
  • Edit study record
  • Submit results
Revisions to the Common Rule
Revisions to the Common Rule

Federal Policy for the Protection of Human Subjects; Final Rule

Federal Register / Vol. 82, No. 12 / Thursday, January 19, 2017

• Generally, the new regulations will go into effect in one year, i.e., January 2018.

• January 2020 is the effective date for the requirements related to cooperative research (i.e., the single IRB requirements).

• New administration has put all new regulations on hold for further study. Unclear how it affects this rule.
Major Changes

- IRBs covered as well as institutions
- Biospecimens included in definition
- Additional exemptions
- Limited review of some exemptions
- Broad consent for data/specimens research
- Changes to presentation of information in consent
- Single IRB review required for cooperative research
Implications

• Some research that needed expedited review now would be exempt (behavioral interventions, identifiable sensitive surveys, etc.).

• Future use of data only requires “broad consent” – only need general description of types of research that might be done (along with usual consent information).

• IRBs will have to evaluate how information is presented to subjects (key information presented first and organization must facilitate comprehension).

• Single IRB review required for multi-site cooperative research.