NIH – Funded Clinical Trials

Impact of NIH Policies in Research Administration

- Good Clinical Practice
- Single IRB
- Registration & Reporting
- Clinical Trial Review Criteria
- New Application Forms
- Clinical Trial FOAs
Purpose of Reforms & Policy Changes

In 2016, NIH announced initiatives targeted to enhance and improve:

**Efficiency**
Enhance the efficiency of how research studies involving human participants are conducted

**Transparency**
Promote a culture of transparency in research in order to advance public health

**Accountability**
Ensure that NIH can appropriately identify and report on their clinical trials portfolio to ensure proper stewardship

**Timely Reporting**
Decrease the time it takes investigators to publicly report study results
Reforms & Initiatives

To enhance the stewardship of research involving human subjects, NIH is implementing the following:

**All Research Involving Human Participants**

- New forms to collect human subjects information
- Use of a single Institutional Review Board (IRB) for multi-site studies

**Research that Meets the NIH Definition of a Clinical Trial**

- Training in Good Clinical Practice (GCP)
- Clinical trial-specific Funding Opportunity Announcements (FOAs)
- New review criteria
- Expanded registration and results reporting in ClinicalTrials.gov
How Does NIH Define a Clinical Trial?

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.

Learn more at https://grants.nih.gov/policy/clinical-trials/definition.htm
Unpacking the Definition (Part I)

**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.

*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
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.

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
• positive or negative changes to quality of life
NIH Definition of a Clinical Trial is Broad

• Definition was **clarified** and **broadened** in October 2014

• Encompasses a wide range of types of trials, including:
  – Mechanistic
  – Exploratory
  – Pilot/Feasibility
  – Behavioral

• With broader definition, many more studies are classified as clinical trials
Questions to Ask PIs

Does the study...

- Involve one or more **human subjects**?
- **Prospectively assign** human subject(s) to intervention(s)?
- Evaluate the **effect of intervention(s)** on the human subject(s)?
- Have a **health-related biomedical or behavioral outcome**?

If “yes” to ALL of these questions, the study is considered a clinical trial
Why is it important to know if it is a clinical trial?

Knowing if the research meets the NIH definition of a clinical trial impacts:

- Selection of a funding opportunity announcement (FOA)
- How the Research Strategy and human subjects sections of the application is written
- What policies and regulations need to be complied with

Learn more at: https://grants.nih.gov/policy/clinical-trials/definition.htm
Data Safety Monitoring Plan (DSMP)

✓ All clinical trials require monitoring
✓ Monitoring should be commensurate with risks
✓ Monitoring should be commensurate with size and complexity
Clinical Trial Reforms & Initiatives

- Good Clinical Practice
- Single IRB
- Registration & Reporting
- Clinical Trial Review Criteria
- Clinical Trial FOAs
- New Application Forms
Good Clinical Practice Training Requirement

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)

Good Clinical Practice training establishes:

- Standards for clinical trial implementation, data collection, monitoring, and reporting
- Responsibilities of investigators, sponsors, monitors, and institutional review boards

- Training should be refreshed every 3 years to stay up to date with regulations, standards, and guidelines – At UD via www.CITIProgram.org

Learn more at https://grants.nih.gov/policy/clinical-trials/good-clinical-training.htm
Funding Opportunity Announcements (FOAs) for Clinical Trials

Effective for due dates on/after January 25, 2018 – 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.

Clinical Trial-specific FOAs allow NIH to:

- identify proposed clinical trials
- ensure that key pieces of clinical trial-specific information are submitted with each application
- uniformly apply clinical trial-specific review criteria

**Important:** Adding a clinical trial to a non-clinical trial application is no longer permitted via the prior approval process. Grantees must submit competitive renewal.
How to Determine if an FOA Accepts Clinical Trials?

FOA Title (new FOAs)

- Participating Organization(s)
  - National Institutes of Health (NIH)
- Components of Participating Organizations
  - National Cancer Institute (NCI)

Funding Opportunity Title
- Early Phase Clinical Trials in Imaging and Image-Guided Interventions (R01 Clinical Trial Required)

FOA Section II. Award Information

Application Types Allowed
- New
- Resubmission
- Revision

The OER Glossary and the SF424 (R&R) Application Guide provide definitions of all application types.

Clinical Trial?
- Required: Only accepting applications that propose clinical trial(s)

Tip: Check your FOA at least 30 days before the due date for any updates
Clinical Trial Designations for FOAs

Effective for due dates on/after January 25, 2018 – all FOAs will be designated as one of the following in Section II of the FOA:

- Clinical Trial Required
- Clinical Trial Not Allowed
- Clinical Trial Optional
- No Independent Clinical Trials: *only for Career Development (K) & Fellowship (F)

Tip: Contact your Program Official or the Scientific/Research contact listed in Section VII of the FOA to ensure you are submitting to the correct announcement
Special Considerations for Training, Fellowship, and Career Development FOAs

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

**Fellowship (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

**Career Development (K) awards:** Career Development awards may support either independent clinical trials or a mentored research training experience, depending on the FOA

Learn more at [https://grants.nih.gov/policy/clinical-trials/specific-funding-opportunities.htm](https://grants.nih.gov/policy/clinical-trials/specific-funding-opportunities.htm)
Review Criteria for Clinical Trials

FOAs that accept clinical trials will include new review criteria

Scored Review Criteria

✓ Significance
✓ Investigator
✓ Innovation
✓ Approach
✓ Environment

Additional Review Criteria

✓ Study Timeline & Milestones

Tip: Read the FOA carefully and be sure the application addresses the review criteria appropriately
New Human Subjects & Clinical Trials Information Form

A primary component of NIH’s clinical trial reform is the creation of a new application form that:

- **Consolidates** human subjects, inclusion enrollment, and clinical trial information into one form
- Collects information at the **study-level**
- Uses **discrete form fields** to capture clinical trial information and provide the level of detail needed for peer review
- Presents key information to reviewers and staff in a **consistent format**
- **Aligns** with ClinicalTrials.gov (where possible) for future data exchange with ClinicalTrials.gov

January 25, 2018 – First due dates for new FORMS-E Application Packages
How Does the Human Subjects & Clinical Trials Information Form Impact Applicants?

New form collects information previously included in the Research Strategy

Applicants will now be instructed to:

- Use the PHS Human Subjects and Clinical Trials Information form to capture detailed study information

- Use the Research Strategy section to discuss the overall strategy, methodology, and analyses of proposed research, but *do not duplicate* information collected in the PHS Human Subjects and Clinical Trials Information form

**Tip:** Applicants should familiarize themselves with the new Human Subjects and Clinical Trial Information form to ensure information is captured appropriately in the application
Changes to the Appendix Policy

Effective for due dates on/after January 25, 2018 – Since the new Human Subjects and Clinical Trials Information form collects key elements from the protocol, the optional protocol submission will be removed from the Appendix Policy.

**Parent FOAs**

- Will **NOT** allow inclusion of the protocol in the application
- ✓ If the protocol is included, the application will be sent back

**IC issued FOAs**

- ✓ Protocols and other materials allowed only when specified as required in the FOA

Resources for the Human Subjects & Clinical Trials Information Form

✓ Explore the new Annotated Form Set for FORMS-E
✓ Take a video tour of the new Human Subjects and Clinical Trial Information form

A Walk-through of the PHS Human Subjects and Clinical Trials Information Form

NIH National Institutes of Health Office of Extramural Research

July 2017
Single Institutional Review Board (sIRB) Policy for Multi-site Research

Effective for due dates on/after January 25, 2018 – NIH expects that all 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.

sIRB policy aims to:

- Streamline IRB review process to enhance research efficiency
- Reduce unnecessary administrative burdens and inefficiencies

What Does the sIRB Policy Apply To?

- Domestic sites of NIH-funded multi-site studies where each site will conduct the same protocol involving non-exempt human subjects research

- Includes research supported through:
  - Grants
  - Cooperative agreements
  - Contracts
  - NIH Intramural Research Program

- sIRB policy does not apply to career development, research training, or fellowship awards
sIRB Plan for Applicants/Offerors

Application/proposal must include a plan that:

- Describes the use of an sIRB that will be selected to serve as the IRB of record for all study sites
- Confirms that participating sites will adhere to the sIRB Policy and describes how communications between sites and sIRB will be handled

The UD IRB Office needs to be notified by the PI of any sIRB plans being proposed at the time of proposal.

**Tip:** sIRB Plan attachment will be included in the new Human Subjects & Clinical Trials Information form
NIH Policy on Dissemination of NIH-Funded Clinical Trial Information

Effective for applications due on/after January 18, 2017 – 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

NIH dissemination policy:

- Extends previous HHS laws and regulations to apply to all NIH-funded clinical trials, including the defined subset of “applicable clinical trials”

- Increases the availability of information to the public about clinical trials

Learn more at https://grants.nih.gov/policy/clinical-trials/reporting/index.htm
Registering & Reporting Requirements for 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

Learn more at https://grants.nih.gov/policy/clinical-trials/reporting/index.htm
NIH Resources

Website on Clinical Trial Requirements for Grants and Contracts:
https://grants.nih.gov/policy/clinical-trials.htm

Training Resources: https://grants.nih.gov/policy/clinical-trials/training-resources.htm

- Slides
- Human Subjects/Clinical Trials Questionnaire
- Videos
- Training opportunities

Help spread the word!
UD Resources

Human Subjects in Research:
http://www1.udel.edu/research/preparing/humansub.html

Clinical Trials:
http://www1.udel.edu/research/clinicaltrials/

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F.A.Q.

• Does this project involved human subjects?
• Application says it involves human subjects...is it a clinical trial?
• What is required by the UD IRB for review and approval of Human Subjects research?
• Do all research with human subjects and multiple sites require Data Use Agreements (DUAs)?
• What is a reliance agreement? What do I need under the sIRB requirement?