UCLA CTSI
Clinical and Translational Science Institute

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Practical Approaches to NIH's New Human Subjects and Clinical Trials Updates

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Prepared by: Robin Faria and LeeAnna Bowman-Carpio
CTSI Grants Submission Unit (GSU)

Overview of Major Changes

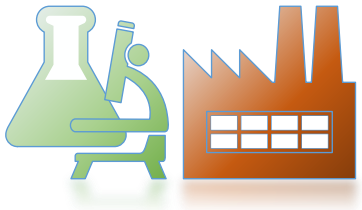
1. New Clinical Trial Definition
2. Reissued NIH FOAs
3. NIH Application Updates for Human Subject and Clinical Trial Studies
4. Integration with ClinicalTrials.gov

New Clinical Trial Definition

1. Does the study involve human subjects?
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 that will be evaluated a health-related biomedical or behavioral outcome?

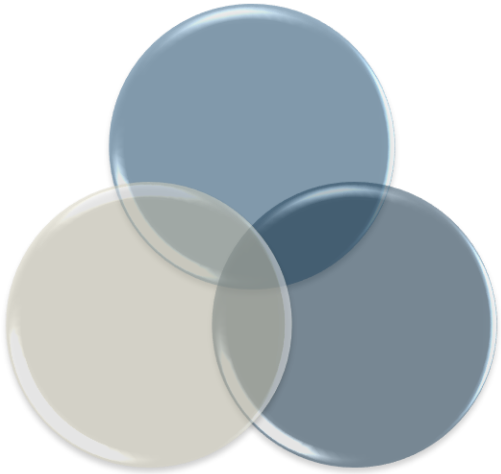
Yes to All? Your Study is a Clinical Trial, even if it does not involve a drug or device.

Review case studies at: https://grants.nih.gov/policy/clinical-trials/case-studies.htm



Implications

1. Broader definition of clinical trials
2. Investigators who have not previously had research classified as CT will have to familiarize themselves with ClinicalTrials.gov requirements
3. Change has led to overlap between ClinicalTrials.gov requirements and NIH application forms



NIH FOA Changes

NIH grants (including parent grants) have been reissued or revised

NIH Research Project Grant (Parent R01 Clinical Trial Required) PA-18-485

NIH Research Project Grant (Parent R01 Clinical Trial Not Allowed) PA-18-484

New Application Form

PHS Human Subjects and Clinical Trials Information Form

1. Changes to Existing Components
2. Addition of New Components
3. Integration with ClinicalTrials.gov

Revised Components

1. Protection of Human Subjects
2. Inclusion of Women, Minorities, and Children
   - *The two documents are now combined into one*
3. Eligibility Criteria
4. Statistical Design and Power
5. FDA-Regulated Interventions

New Components

1. Individual Study Titles
2. Conditions or Focus of the Study
3. Recruitment and Retention Plan
4. Study Timeline
5. Single IRB Plan
6. Overall Structure of the Study Team
7. Brief Summary
8. Narrative Study Description
9. Interventions
10. Outcome Measures
11. Dissemination Plan

PHS Human Subjects and Clinical Trials Information Form

Check Form for Errors Save

Study Record: PHS Human Subjects and Clinical Trials Information

OMB Number: 0925-0001
Expiration Date: 03/31/2020

* Always required field

Section 1 - Basic Information

1.1. * Study Title (each study title must be unique)

1.2. * Is this Study Exempt from Federal Regulations? ☐ Yes ☐ No

1.3. Exemption Number ☐1 ☐2 ☐3 ☐4 ☐5 ☐6 ☐7 ☐8

1.4. * Clinical Trial Questionnaire

If the answers to all four questions below are yes, this study meets the definition of a Clinical Trial.

1.4.a. Does the study involve human participants? ☐ Yes ☐ No

1.4.b. Are the participants prospectively assigned to an intervention? ☐ Yes ☐ No

1.4.c. Is the study designed to evaluate the effect of the intervention on the participants? ☐ Yes ☐ No

1.4.d. Is the effect that will be evaluated a health-related biomedical or behavioral outcome? ☐ Yes ☐ No

1.5. Provide the ClinicalTrials.gov Identifier (e.g., NCT87654321) for this trial, if applicable

Section 2 – Study Population Characteristics

Section 2 - Study Population Characteristics

2.1. Conditions or Focus of Study

X

Add New Condition

2.2. Eligibility Criteria

2.3. Age Limits **Minimum Age** **Maximum Age**

2.4. Inclusion of Women, Minorities, and Children Add Attachment Delete Attachment View Attachment

2.5. Recruitment and Retention Plan Add Attachment Delete Attachment View Attachment

2.6. Recruitment Status

2.7. Study Timeline Add Attachment Delete Attachment View Attachment

2.8. Enrollment of First Subject

Inclusion Enrollment Report(s)

Add Inclusion Enrollment Report

Section 3 – Protection and Monitoring Plans

Section 3 - Protection and Monitoring Plans

3.1. Protection of Human Subjects | Add Attachment | Delete Attachment | View Attachment

3.2. Is this a multi-site study that will use the same protocol to conduct non-exempt human subjects research at more than one domestic site?

☐ Yes ☐ No ☐ N/A

If yes, describe the single IRB plan | Add Attachment | Delete Attachment | View Attachment

3.3. Data and Safety Monitoring Plan | Add Attachment | Delete Attachment | View Attachment

3.4. Will a Data and Safety Monitoring Board be appointed for this study?

☐ Yes ☐ No

3.5. Overall Structure of the Study Team | Add Attachment | Delete Attachment | View Attachment

Section 4 – Protocol Synopsis

Section 4 - Protocol Synopsis

4.1. Brief Summary

4.2. Study Design

4.2.a. Narrative Study Description

4.2.b. Primary Purpose

4.2.c. Interventions

X	Intervention Type	
	Name	
	Description	

Add New Intervention

4.2.d. Study Phase

Is this an NIH-defined Phase III clinical trial? ☐ Yes ☐ No

Section 4 – Protocol Synopsis

4.2.e. Intervention Model

4.2.f. Masking ☐ Yes ☐ No

☐ Participant ☐ Care Provider ☐ Investigator ☐ Outcomes Assessor

4.2.g. Allocation

4.3. Outcome Measures

X	**Name**	
	Type	
	Time Frame	
	Brief Description	

Add New Outcome

4.4. Statistical Design and Power Add Attachment | Delete Attachment | View Attachment

4.5. Subject Participation Duration

4.6. Will the study use an FDA-regulated intervention? ☐ Yes ☐ No

4.6.a. If yes, describe the availability of Investigational Product (IP) and Investigational New Drug (IND)/Investigational Device Exemption (IDE) status

Add Attachment | Delete Attachment | View Attachment

4.7. Dissemination Plan Add Attachment | Delete Attachment | View Attachment

2.7 Study Timeline (NEW)

NIH: Provide a description or diagram describing the study timeline.
The timeline should be general (e.g. “one year after notice of award”), and should not include specific dates.

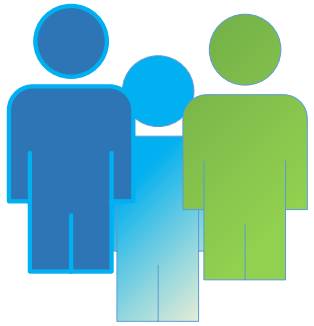
Review Criteria - NEW:
Describe timeline in detail taking into account:

- Start-Up activities
- Anticipated rate of enrollment
- Planned follow-up assessment
- Timeline must be feasible and well justified
- If applicable, project incorporates efficiencies and existing resources (CTSAs, networks, EMRs, databases, and patient registries) to increase efficiency of patient enrollment
- Address potential challenges and correspondent solutions (i.e. strategies re: enrollment shortfalls)

3.1 Protection of Human Subjects (Revised)

Items Removed

- Justification for proposed use of human subjects
- Description of age range and health status of subject population
- Sample plan, and rationale for involvement of vulnerable populations
- Recruitment and Informed Consent
- FDA IND/IDE test articles



3.1 Protection of Human Subjects (Revised)

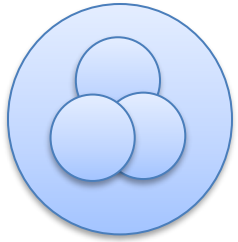
Items Added

- Study design
- Need to provide details on previously collected biospecimens considerations Need to specify potential risks for each intervention separately
- Emphasis on caveats for adults unable to consent
- Incidental findings
- Vulnerable Populations
- Clarification that compensation is not a benefit

3.2 Single IRB Plan (sIRB) (NEW)

1. Describe how you will comply with the NIH Policy on the use of sIRB for multi-site research.
2. Provide the name of the IRB that will serve as the sIRB of Record (Reviewing IRB Institution).
3. Indicate that all identified participating sites have agreed to rely on the proposed sIRB and that any sites added afterward will rely on the sIRB.
4. Briefly describe how communications between sites will, prior to initiating the study, sign an authorization/reliance agreement that will clarify the roles and responsibilities of the sIRB and participating sites.
5. Indicate which institution or entity will maintain records of the authorization/reliance agreements and of the communication plan.
6. Note: Do NOT include the authorization/reliance agreements or communication plan(s).

Contact UCLA IRB Reliance for guidance before completing:
irbreliance@research.ucla.edu



4.1 Brief Summary

NIH:

4.1 Brief Summary

Limited to 5,000 characters

Enter a brief description of objectives of the protocol, including the primary and secondary endpoints

Include brief summary of the study hypothesis

Summarize for the lay public

ClinicalTrials.gov:

5. Study Description

Brief Summary

Definition: A short description of the clinical study, including a brief statement of the clinical study's hypothesis, written in language intended for the lay public.

Limit: 5,000 characters.

4.2.a Narrative Study Description

NIH:

4.2.a Narrative Study Description

Limited to 32,000 characters

Enter a narrative description of the protocol, including more technical information

Do NOT include the entire protocol

Do NOT duplicate information elsewhere (i.e. Eligibility Criteria, Outcomes)

Describe your plans for assignment of participants

Describe your plans for delivery of interventions

Show that your methods for sample size and data analysis are appropriate given those plans

For trials that randomize groups or deliver interventions to groups, special methods are required

See https://researchmethodsresources.nih.gov/ for additional guidance

ClinicalTrials.gov:

Detailed Description

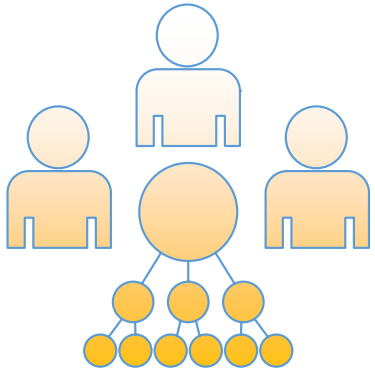
Definition: Extended description of the protocol, including more technical information (as compared to the Brief Summary), if desired. Do not include the entire protocol; do not duplicate information recorded in other data elements, such as Eligibility Criteria or outcome measures.

Limit: 32,000 characters.

4.4 Statistical Design and Power (Revised)

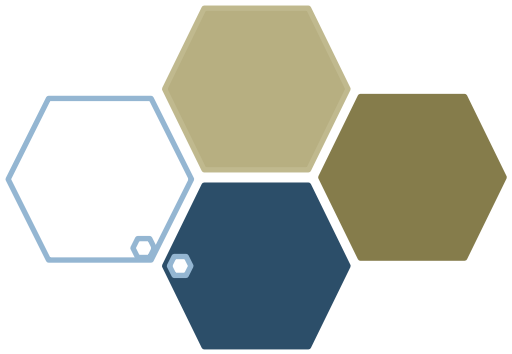
Recommendations:

- Information and new forms cannot be duplicative
- Where overlap potential exists, consider using Research Strategy for higher-level analysis and leave details in Statistical Design and Power
- Think about citing other components (i.e. “See statistical design and power for more information”)
- Spend more space in RS on Rigor and Transparency



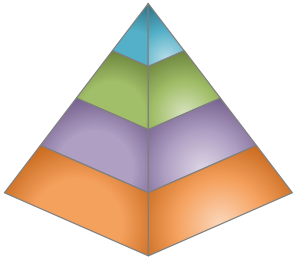
Challenges

- Numerous new uploads and text fields will require increased coordination between PIs, admins, and fund managers
- Awareness of text field requirements vs. document upload requirements
- New components and detailed statistical requirements will necessitate an earlier start for planning applications
- PIs will need to familiarize themselves with the new Clinical Trial definition



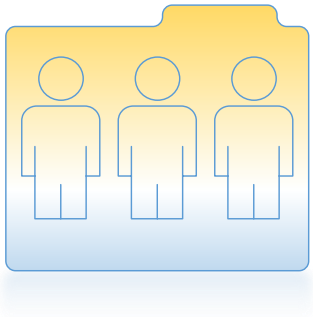
Burden Statement

- NIH allows for costs to be budgeted associated with burden of collecting and reporting ClinicalTrials.gov information
- Estimated as:
  - 8 hours for response to initial registration
  - 2 hours each for 8 updates during course of the trial
  - 40 hours per response for initial results submission
  - 10 hours for 2 substantive updates to the results info



In Development

- Interactive Collection Form
- Website (now live!)
- Working Group
  - The CTSI is coordinating a working group to identify resources and experts to provide guidance on the new application requirements
- Collecting Examples
  - We are currently soliciting examples of successful protocols, timelines, and other components.



Key Takeaways

- Plan early for new requirements
- Review revisions to existing components
- Be aware of relocation of components
- Avoid potential redundancy
- Think proactively about ClinicalTrials.gov registration

START EARLY AND BE ENGAGED

Additional Resources

- NIH SF 424 FORMS E: https://grants.nih.gov/grants/how-to-apply-application-guide/forms-e/general-forms-e.pdf
- ClinicalTrials.gov definitions: https://prsinfo.clinicaltrials.gov/definitions.html
- Does your study meet the definition of a CT? https://grants.nih.gov/ct-decision/index.htm
- NIH Infopath Questionnaire - Determine What Type of Human Subjects Protections are Needed: https://humansubjects.nih.gov/questionnaire
- NIH Case Studies: https://grants.nih.gov/policy/clinical-trials/case-studies.htm

Questions?

For Additional Questions

Tel: 310-267-4258
Email: gsu@mednet.ucla.edu
Website: https://ctsi.ucla.edu/pages/Hsapps