Clinical and Translational Science Institute

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

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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
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 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
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
Study Record: PHS Human Subjects and Clinical Trials Information

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

1.4. * 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

### 2.1. Conditions or Focus of Study

```
X
```

[Add New Condition]

### 2.2. Eligibility Criteria

```
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### 2.3. Age Limits

<table>
<thead>
<tr>
<th>Minimum Age</th>
<th>Maximum Age</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### 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

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### 2.7. Study Timeline

Add Attachment | Delete Attachment | View Attachment

### 2.8. Enrollment of First Subject

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Inclusion Enrollment Report(s)

[Add Inclusion Enrollment Report]
### Section 3 - Protection and Monitoring Plans

3.1. Protection of Human Subjects

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

3.3. Data and Safety Monitoring Plan

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

- [ ] Yes
- [ ] No

3.5. Overall Structure of the Study Team
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

<table>
<thead>
<tr>
<th>Intervention Type</th>
<th>Name</th>
<th>Description</th>
</tr>
</thead>
</table>

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

4.2.g. Allocation

4.3. Outcome Measures

<table>
<thead>
<tr>
<th>Name</th>
<th>Type</th>
<th>Time Frame</th>
<th>Brief Description</th>
</tr>
</thead>
</table>

Add New Outcome

4.4. Statistical Design and Power

4.5. Subject Participation Duration

4.6. Will the study use an FDA-regulated intervention?

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

4.7. Dissemination Plan
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)
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
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
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.**
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/](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.
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
• 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
• 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
• 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