The Changing Policy Landscape for Clinical Trials

CCTS Monthly Forum

Denise McKenzie
CCTS Forum: Agenda

- Does Your Study Meet the NIH Clinical Trial Definition?
  - Clinical Trial or Clinical Research
- NIH Dissemination Plan
  - Required For All NIH-Funded Clinical Trials
- NIH: Forms-E
  - Required to Use On or After January 25, 2018
- ICMJE Data Sharing Plan
  - Data Sharing Statements July 1, 2018
- FDAAA Tracker
  - Enforcing Penalties
ClinicalTrials.gov 2017

• January 18, 2017: Regulators issued clarifications of the requirements
• April 18, 2017: Penalty phase was applied
• June 29, 2017: Upload Protocol & Statistical Analysis
• Consent Form to include the NCT # and:
  • If the protocol meets the definition of a clinical trial, it must be registered on Clinical Trials.gov and you must include the following language:
    • A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.
Decision Tree for NIH Clinical Trial Definition

Decision Tree for NIH Clinical Trial Definition

Does the study involve human participants research?

- YES
- NO

Are participants prospectively assigned to an intervention?

- YES
- NO

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

- YES
- NO

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

- YES
- NO

This study is a clinical trial.

The study is NOT a clinical trial.
NIH Non-Clinical Trials

- Studies that involve secondary research with biological specimens or health information, or studies that are intended solely to refine measures are not considered clinical trials.
- Review extensive list of “Case Studies”
- NIH advises to consult with your program officer should your research
Registering & Reporting?

When Does a Study Have to be Registered on ClinicalTrials.gov?
(Evaluate all requirements)

1. Requirement 1: NHLBI Dissemination Policy
   - Does the study receive NHLBI funding?
     - Yes: Proceed to Requirement 2
     - No: Proceed to Requirement 3

2. Requirement 2: FDA/NIH and Regulatory Subpart C
   - Is the study an interventional clinical trial?
     - Yes: Proceed to Requirement 3
     - No: Proceed to Requirement 1

3. Requirement 3: ICMEI Publication Requirements
   - Is the study an interventional clinical trial?
     - Yes: Proceed to Requirement 4
     - No: Proceed to Requirement 1

4. ICMEI policy applies Registration (but not results) is required
   - Not required by the publishers

The 3 main requirements are shown here; other requirements may apply.

Applicable Clinical Trial
Registration and results reporting is required
FDAAA 801 Registering & Reporting?

- Is the study an interventional clinical trial?
- Is it an FDA-regulated clinical investigation of a drug, biologic, or device?
- Is it conducted under an IND/IDE?
- Is it other than a phase 1 or device feasibility?
ICMJE Registering & Reporting?

- Prospectively assigns individuals to an intervention, with or without concurrent comparison or control groups, to study the relationship between a health-related intervention and a health outcome.

- Includes drugs, surgical procedures, devices, behavioral treatments, educational programs, dietary interventions, quality improvement interventions, and process-of-care changes.

- Requires registration of clinical trials in a public trials registry at or before the time of first patient enrollment as a condition of consideration for publication.
NIH Dissemination Plan

• Applicants seeking NIH funding will be required to submit a plan for the dissemination of NIH-funded clinical trial information that will address how the expectations of the policy will be met.

• Upon receipt of an award, an awardee will be obligated to adhere to their plan through the terms and conditions of the award.

• The required plan can be a brief statement explaining whether the applicant intends to register and submit results information to ClinicalTrials.gov as outlined in the policy.
Dissemination Plan Request sent to an Investigator (Northwestern)

• As you may be aware, all clinical trial applications submitted on or after January 18, 2017 are to include a dissemination plan for clinical trials to be submitted for documentation in the official grant file. Please see guide notice NOT-OD-16-149. Our records indicate that we have not received this required documentation for the above-referenced grant. The plan can be brief, but at a minimum it must contain sufficient information to assure that:

• (1) the applicant will ensure that clinical trials under the award are registered and results information is submitted to ClinicalTrials.gov as outlined in the policy and according to the specific timelines stated in the policy;

• (2) informed consent documents for the clinical trial(s) will include a specific statement relating to posting of clinical trial information at ClinicalTrials.gov; and

• (3) the recipient institution has an internal policy in place to ensure that clinical trials registration and results reporting occur in compliance with policy requirements.

• Please submit a dissemination plan for the above mentioned grant via the AOR by (Date).
UAB Policy For ClinicalTrials.gov Registration

Effective January 18, 2017, NIH issued its Policy on Dissemination of NIH-Funded Clinical Trial Information.

As part of grant applications or proposals, Principal Investigators seeking NIH funding will be required to submit a plan for the dissemination of NIH-funded clinical trial information that will address how the expectations of this policy will be met. NIH-funded investigators conducting clinical trials funded in whole or in part by the NIH will be required to comply with all terms and conditions of award, including following their plan for the dissemination of NIH-funded clinical trial information. See sample below.
Sample NIH Plan for Dissemination

As Principal Investigator for this study, I will comply with the NIH Policy on the Dissemination of NIH-Funded Clinical Trial Information in NIH Guide Notice NOT-OD-16-149. All clinical trials for this project will be registered in ClinicalTrials.gov no later than [date]. As PI, I will be responsible for registering the trial and will ensure that information in the clinical trial record is updated at least once every 12 months and I will ensure that results are reported no later than one year after the clinical trial primary completion date.

The consent form for this clinical trial will contain language specifying that the study is registered at clinicaltrials.gov. The required wording on all consent forms by the University of Alabama at Birmingham (UAB) Institutional Review Board for Human Use is:

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

The UAB Center for Clinical and Translational Science (CCTS) works with investigators to ensure that they meet the requirements of ClinicalTrials.gov in a timely fashion, and that all clinical trials comply with requirements for registration and reporting as specified in NOT-OD-16149. The CCTS maintains a web site (https://www.uab.edu/ccts/news/clinicaltrials-gov-whats-new) specifically for the purpose of updating investigators regarding changes to ClinicalTrials.gov. The CCTS also offers one-on-one training to assist investigators in initiating and maintaining their ClinicalTrials.gov entry.
NIH New Requirements

FORMS-E

Good stuff to know when developing support in system-to-system solutions for FORMS-E application forms.

August 2017
NIH New Requirements

Two major changes impact applications submitted for due dates on or after January 25, 2018.

- Applicants are required to use FORMS-E.  
  New NIH "FORMS-E" Grant Application Forms and Instructions Coming for Due Dates On or After January 25, 2018 - NIH Guide Notice NOT-OD-17-062, Release Date: April 27, 2017

- Applications that include one or more clinical trials must be submitted in response to funding opportunity announcements (FOA) that allow for clinical trials.  

Application form packages are designated alphabetically to indicate the most recent version  
(e.g., FORMS-D, FORMS-E)
New Forms Aligned With The New Definition

Goals of this Effort?

• Distinguish between clinical trials and clinical research studies
• Enhance the precision of the information NIH collects, tracks and reports
• Improve dissemination, transparency and accountability
• Encourage advances in the design, conduct and oversight of clinical trials
• Align with ClinicalTrials.gov (where possible) and position us for future data exchange with ClinicalTrials.gov
NIH FORMS-E

Focus of changes:

- Majority of changes related to human subjects and clinical trials data collection
  - Consolidation of data fields collected on multiple forms into new PHS Human Subjects and Clinical Trials Information form
Research & Related Other Project Information
PHS Human Subjects and Clinical Trials Information

Please complete the human subjects section of the Research & Related Other Project Information form prior to completing this form.

The following items are taken from the Research & Related Other Project Information form and displayed here for your reference. Any changes to these items must be made on the Research & Related Other Project Information form, and may impact the data fields you are required to complete on this form.

When HS-its is on R&R Other Project Information form, applicants answer a single question and associated attachment and are done with this form.

When HS-its on R&R Other Project Information form, applicants can enter study information.

Information populated from R&R Other Project Information form for reference.
PHS Human Subjects and Clinical Trials Information

Section 1: Basic Information

Full study records are comprised of 5 sections.

Although feature may not be available for initial rollout, we hope to be able to pull data from ClinicalTrials.gov into ASSIST to reduce data entry.
PHS Human Subjects and Clinical Trials Information
Section 2: Study Population Characteristics
# Section 2: Inclusion Enrollment Report

## Inclusion Enrollment Report Data Collection

### Inclusion Enrollment Report

1. "Using an Existing Dataset or Resource":
   - Yes
   - No

2. Enrollment Location Type:
   - Domestic
   - Foreign

3. Enrollment Country(ies):
   - United States of America

4. Enrollment Location(s):
   - Enter up to 500 characters

5. Comments:
   - Enter up to 500 characters

### Cumulative (Actual) Report

**Used when Existing Data Source or Resource = Yes**

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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
PHS Human Subjects and Clinical Trials Information
Section 5: Other Clinical Trial-Related Attachments

Section 5 - Other Clinical Trial-related Attachments

5.1. Other Clinical Trial-related Attachments

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## Forms Updated in FORMS-E

### Agency-specific forms
- PHS 398 Career Dev. Award Supp.
- PHS 398 Cover Page Supplement Form
  - PHS 398 Modular Budget
  - PHS 398 Research Plan
  - PHS 398 Research Training Program Plan
  - PHS 398 Training Budget & Subaward
  - PHS Additional Indirect Costs
  - PHS Assignment Request Form
  - PHS Fellowship Supp. Form
  - PHS Inclusion Enrollment Report
    - No longer used
    - Rolled into new PHS Human Subjects and Clinical Trials Information form

### Federal-wide forms
- SF424 (R&R)
- Project/Performance Site Location(s)
- R&R Other Project Info
- R&R Sy/key Person Profile (Expanded)
- R&R Budget & Subaward
  - 5 YR, 10 YR, MP
- SF424C – Construction Budget
- SBIR/STTR Information

### Resources
- Annotated Form Sets
- High-level Summary of Form Changes in FORMS-F Application Packages
- Preview of FORMS-F Grant Application Form Changes
High-level Summary of Form Changes: FORMS-E

Agencies periodically update application forms in order to remain current with the most recent form sets available through Grants.gov and approved by the Office of Management and Budget and to align data collection with current policies.

NH and some other agencies served by NIH use the "Competitive ID" field of Grants.gov application packages for quick and easy identification of the form versions used in an application package.

NH will require the use of application packages with a Competition ID of "FORMS-E" for due dates on or after January 25, 2018. Applications prepared using "FORMS-D" application packages for due dates after January 24, 2018 will not be reviewed.

Changes to Agency-specific NHLBI Forms Included in "FORMS-E" Application Packages:

The majority of form changes introduced in FORMS-E packages relate to the consolidation of human subjects and clinical trial information form. The new form also expands clinical trial data collection to ensure the appropriate level of information for review and to improve oversight.

NHX 596 Career Development Award Supplemental Form:
- Updated OMB Expiration Date to 08/31/2020
  - Removed Human Subjects Section, including the following attachments:
    - Protection of Human Subjects
    - Data Safety Monitoring Plan
    - Inclusion of Women and Minorities
    - Inclusion of Children
  - Renumbered form fields
  - Made minor text edits

NHX 598 Cover Page Supplement:
- Updated OMB Expiration Date to 08/31/2020
  - Removed Human Subjects Section, including:
    - "Clinical Trial" question
    - "Agency Defined Phase III Clinical Trial" question
  - Renumbered form fields
  - Made minor text edits

NHX 599 Modular Budget:
- Updated OMB Expiration Date to 08/31/2020

NHX 599 Research Plan:
- Updated OMB Expiration Date to 08/31/2020
  - Removed Human Subjects Section, including the following attachments:
    - Protection of Human Subjects
    - Data Safety Monitoring Plan

Updated: 06/20/2017
Common Rule Changes

COMMON RULE

• We are preparing our systems for the expected implementation of the Common Rule this January.

• Although HHS has not yet confirmed the targeted January 2018 implementation date, we hope to include the new exemption codes in FORMS-E to avoid multiple form updates
  • Will use validations to prevent use of new codes if implementation date is delayed

• Only change to our application forms is the addition of two human subjects exemption codes (7 and 8)
  • R&R Other Project Information
    • Waiting on OMB approval
  • PHS Human Subjects & Clinical Trials Information

Learn more about the Common Rule
New ICMJE Policy

- Data Sharing Statement: publication requirement
- For trials that start enrolling participants on or after January 1, 2019, ICMJE will require data sharing statements in the ClinicalTrials.gov registration as a condition of publication
- (These statements will be required in manuscripts submitted to ICMJE journals starting in July 2018)
- In ClinicalTrials.gov, the data sharing statement is entered in the IPD Sharing Statement module
FDAAA Trials Tracker

FDAAA 2007 is a law that requires certain clinical trials to report results. After a long wait, it effectively comes into force from Feb 2018. The FDA are not publicly tracking compliance. So we are, here.

Who’s sharing their clinical trial results?

Filter trials by status:
- On
- Overdue
- Off
- Ongoing
- Reported
- Late

Showing 1 to 10 of 216 entries

Absorption and Safety With Sustained Use of Salbutamol Evaluation (ASSURE) Study in Patients With Cystic Fibrosis Receiving Enteral Feeding (pdcT)

Alveolar Therapeutics Inc.
NCT02795651
2017-03-30
31
Questions & Discussion
Stay Connected

- [www.uab.edu/ccts](http://www.uab.edu/ccts)
- [205-934-7442](tel:205-934-7442)
- [ccts@uab.edu](mailto:ccts@uab.edu)
- [PCAMS – 1924 7th Ave South](http://ccts.uab.edu)
- [@cctsnetwork](https://twitter.com/cctsnetwork)
- Search: cctsnetwork
Resources

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