NIH Clinical Trial Requirements

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NIH Policies

- Clinical Trials Registration
  - January 18, 2017
- Good Clinical Practice (GCP) Training
  - January 1, 2017
- Certificates of Confidentiality
  - October 1, 2017

NIH Policy

On January 18, 2017, an expanded policy of the National Institutes of Health (NIH) went into effect that requires:

- clinical trials funded in whole or in part by the NIH are registered at ClinicalTrials.gov, AND
- that results information of these trials is submitted to ClinicalTrials.gov

Purpose of Registration

- Transparency in tax-funded research
- Available trials and results
- Ethical obligation to report results when volunteers contribute their time as study participants in prospective experiments
- Maximize information and improve
  - Better design
  - Reduce duplication
  - Allows scientists to build upon solid results

NIH Definition of 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**

Breakdown of Definition

- **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.

Breakdown of definition (cont'd)

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 or 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

Breakdown of definition (cont'd)

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

Clarification of Definition

- If procedures and tasks are being performed to measure and describe, but not to modify then the study is **NOT** a clinical trial
- Refer to case study # 18 a-f at: https://grants.nih.gov/policy/clinical-trials/case-studies.htm

Questions to Ask

Per the NIH, there are 4 questions researchers must ask in order to determine if the study is a clinical trial as defined by NIH:

1. Does the study involve human participants?
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?

If the answer is “yes” to all four questions, then the NIH considers this study to be a clinical trial

Case Studies and FAQ's

- Case studies and FAQs are living documents and will evolve as we work under this new definition and policy together
- If unsure whether your human subjects study meets the NIH definition of a clinical trial, ask the NIH program official (scientific contact) listed in the funding opportunity announcement or on NIH's website who is responsible for your area of research

Grant Application Form Changes

- Effective for due dates on/after January 25, 2018, all grant applications involving one or more clinical trials must be submitted through an FOA specifically designated for clinical trials (FORMS-E)
- Consolidation of human subjects and inclusion enrollment report information from previous collected multiple forms into a new PHS Human Subjects and Clinical Trials Information Form (FORMS-E)

Clinical Trial Information on FORMS-E

FORMS-E Application:

- Consolidates human subjects, inclusion enrollment, and clinical trial information into one form
- Collects information at 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

BU CRC Information

- PRS Administrator: IRB Director
  - Create new accounts
- 62 records in ClinicalTrials.gov
- Statistical consultation
  - Obtain while designing study as most errors are related to poor study design and lack of valid outcome measures
  - BU CTSI consulting services at: http://www.bu.edu/ctsi/support-for-research/
  - Biostatistical consultations every Tuesday from 11:00 AM to 12 noon in Evans 747 or by appointment

BMC/BUMC Information

- PRS Administrator BMC/BUMC:Karla Damus damusk@bu.edu
  - Create new accounts
  - Assist with registration, outcome measures, updating, and responding to ClinicalTrials.gov comments
  - Assist with results reporting
- 209 records in BMC; 159 records in BUMC CTgov databases
- CRRO consultation
  - For pre and post IRB assistance, ICF, DSMP, etc http://www.bumc.bu.edu/crro/services-request-form/
- Statistical consultation
  - Biostatistical consultations every Tuesday from 11:00 AM to 12 noon in Evans 747 or by appointment http://www.bu.edu/ctsi/support-for-research/

Clinical Trials Registration: Food and Drug Administration Amendments Act (FDAAA)

- **FDAAA**: Food and Drug Administration Amendments Act (Section 801): Requires registration and results reporting for applicable clinical trials either initiated after September 27, 2007, or initiated on or before that date and were still ongoing as of December 26, 2007.
- **Applicable Clinical Trial:** Applicable Clinical Trials include the following:
  - Trials of drugs and biologics: Controlled clinical investigations, other than phase 1 clinical investigations, of drugs or biological products subject to Food and Drug Administration (FDA) regulation
  - Trials of devices: 1) Controlled trials with health outcomes of devices subject to FDA regulation, other than small feasibility studies, and 2) pediatric postmarket surveillance required by FDA

Clinical Trials Registration: International Committee of Medical Journal Editors (ICMJE)

- The ICMJE member journals implemented the expanded definition of clinically directive trials for all trials that began enrollment on or after July 1, 2008
- The ICMJE clinical trial registration policy requires prospective registration of all interventional clinical studies, but does not require results reporting for registered trials.

Clinical Trials Registration: International Committee of Medical Journal Editors (ICMJE)

The ICMJE's expanded definition is: any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes. Health-related interventions include any intervention used to modify a biomedical or health-related outcome (for example, drugs, surgical procedures, devices, behavioral treatments, dietary interventions, and process-of-care changes). Health outcomes include any biomedical or health-related measures obtained in patients or participants, including pharmacokinetic measures and adverse events. Purely observational studies (those in which the assignment of the medical intervention is not at the discretion of the investigator) will not require registration.

Reporting Requirements

Comparison of Clinical Trial Reporting Requirements			
Reporting Requirement	**ICMJE**	**FDAAA & Regulations**	**NIH Policy**
What	Registration	Registration and Results Reporting	Registration and Results Reporting
Scope	Clinical Trials (any)	Applicable Clinical Trials	NIH-funded Clinical Trials
Phase	All	All except for Phase 1 or device feasibility	All
Intervention Type	All	Drug, Biological, and Device products regulated by the FDA	All (including behavioral interventions)
Enforcement	Refusal to publish	Criminal proceedings and civil penalties (up to $10,000/day)	Withdrawal/loss of funding

BU CRC/BUMC Outreach

- Ct.gov National Taskforce
  - Organizations/institutions nationwide
  - NIH/Ct.gov staff participate in monthly call
  - Deliverables/resources created by the Taskforce are reviewed by NIH/Ct.gov staff
- Ct.gov Harvard Catalyst Regulatory Sub-committee
- Federal Demonstration Partnership (FDP)
- Council on Governmental Relations (COGR)

Clinical Trials Registration Resources

- NIH Policy on the Dissemination of NIH-Funded Clinical Trial Information: https://s3.amazonaws.com/public-inspection.federalregister.gov/2016-22379.pdf
- Checklist: https://prsinfo.clinicaltrials.gov/ACT_Checklist.pdf
- FAQ's for NIH Definition of a Clinical Trial: https://grants.nih.gov/grants/policy/faq_clinical_trial_definition.htm
- NIH Case Studies: https://grants.nih.gov/policy/clinical-trials/case-studies.htm

Good Clinical Practice (GCP) Training

- On January 1, 2017, a new policy of the National Institutes of Health (NIH) went into effect that requires all NIH-funded investigators and staff who are involved in the conduct, oversight, or management of clinical trials to be trained in Good Clinical Practice (GCP).
- The policy applies to all active grants and contracts, no matter what point they are in the life cycle of the trial.

NIH GCP Resources

- Policy on Good Clinical Practice Training for NIH Awardees Involved in NIH-funded Clinical Trials: https://grants.nih.gov/grants/guide/notice-files/NOT-OD-16-148.html
- Frequently Asked Questions: https://grants.nih.gov/grants/policy/faq_nih_good_clinical_practice.htm#5154

Certificates of Confidentiality

- On October 1, 2017 the NIH updated its policy for issuing Certificates of Confidentiality
- Applies to all research that was commenced or ongoing on or after December 13, 2016
- Policy applies to all biomedical, behavioral, clinical, or other research funded wholly or in part by the NIH, whether supported through grants, cooperative agreements, contracts, other transaction awards, or conducted by the NIH Intramural Research Program, that collects or uses **identifiable, sensitive** information

Certificates of Confidentiality

- Certificates of Confidentiality are issued by the National Institutes of Health (NIH)
- A Certificate of Confidentiality (Certificate) protects the privacy of research participants enrolled in biomedical, behavioral, clinical or other research:
  - With limited exceptions, researchers may not disclose names or any information, documents or biospecimens containing identifiable, sensitive information.
  - The Certificate prohibits disclosure in response to legal demands, such as a subpoena

Certificates of Confidentiality

- Under the new policy, the investigator will not need to apply for a Certificate. All eligible research studies that are funded by NIH are automatically issued a certificate under the NIH Policy on Certificates of Confidentiality
- To determine if a study (which is conducted or supported by NIH) qualifies for a Certificate of Confidentiality, the investigator must answer the following question:
  - Is the activity biomedical, behavioral, clinical, or other research?

Certificates of Confidentiality

If the answer is "YES", investigator must consider the questions below:

- Does the research involve Human Subjects as defined by 45 CFR 46?
- Are you collecting or using biospecimens that are identifiable to an individual as part of the research?
- If collecting or using biospecimens as part of the research, is there a small risk that some combination of the biospecimen, a request for the biospecimen, and other available data sources could be used to deduce the identity of an individual?
- Does the research involve the generation of individual level, human genomic data?

Certificates of Confidentiality

- If the answer to **ANY ONE** of the four questions above is "YES", then this NIH policy will apply and will be considered to have a Certificate of Confidentiality by the NIH
- Clarification from NIH:
  - **ALL** NIH funded research that meets the Common Rule definition of human subjects research is now covered by a CoC, even if the topic of the research is not particularly "sensitive"
  - Under the prior COC authority, the notion of sensitive had a role in determining if a CoC was warranted. This has now changed and the criteria for sensitive have been removed from the NIH website.

Certificates of Confidentiality

- If a study is covered under the policy, the consent form must include language about the protections and exceptions allowed with the Certificate
- The NIH has updated the required consent form language
- The language is at the following website: https://humansubjects.nih.gov/coc/suggested-consent-language

CoC Resources

- Updated policy is located at: https://grants.nih.gov/grants/guide/notice-files/NOT-OD-17-109.html
- NIH FAQ's website at: https://humansubjects.nih.gov/coc/faqs

Contact Information

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