Human Subjects
Office of Research
UNIVERSITY OF GEORGIA

NIH Policy Application

Maricia Dilan, IRB Professional

mdilan@uga.edu

Policy Environment Scan - NIH

- NIH Clinical Trial registration requirements
  - Consent Form posting
- NIH Data Sharing and Management
- NIH Certificate of Confidentiality (CoC)

ClinicalTrials.gov

A website and online database of clinical research studies and their results operated by the National Library of Medicine of the National Institutes of Health (NIH)

- Initially developed to help potential subjects with life-threatening illnesses find trials in which they might want to participate
- Enhance design of clinical trials and prevent duplication of unsuccessful or unsafe trials
- Increase the efficiency of drug and device development processes

Since that time, registry has come to serve many other purposes for a variety of users

Trial Registration and Results Submission Purposes

Trial Registry Purposes and Benefits for Various Groups

Registry Purpose	Group That Benefits
Fulfill ethical obligations to participants and the research community	Patients, the general public, the research community
Provide information to potential participants and referring clinicians	Patients, clinicians
Reduce publication bias	Users of the medical literature
Help editors and others understand the context of study results	Journal editors, users of the medical literature
Promote more efficient allocation of research funds	Granting agencies, the research community
Help institutional review boards (IRBs) determine the appropriateness of a research study	IRBs, ethicists

Source: Zarin DA, Keselman A. Registering a clinical trial in ClinicalTrials.gov. *Chest*. 2007;131(3):909-12. [Full Text]

Results Database Purposes and Benefits for Various Groups

Results Database Purpose	Group That Benefits
Provide a public record of basic study results in a standardized format	Researchers, journal editors, IRBs, ethicists
Promote the fulfillment of ethical obligations to participants and the overall contribution of research results to medical knowledge	Patients, the general public, the research community
Reduce publication and outcome reporting biases	Users of the medical literature
Facilitate systematic reviews and other analyses of the research literature	Researchers, policymakers

Source: Tse T, Williams RJ, Zarin DA. Reporting "basic results" in ClinicalTrials.gov. *Chest*. 2009;136(1):295-303. [Full Text]

ClinicalTrials.gov Registration

Studies must be registered if they:

- Involve drugs, devices, or biologics that are regulated by the FDA
- Are federally funded (or privately funded) and meet the definition of clinical trial
- There is plan to publish the results in a medical journal and study meets the clinical trial definition of the International Committee of Medical Journal Editors (ICMJE)

ClinicalTrials.gov Registration (cont.)

- Can be registered at anytime [ClinicalTrials.gov or Regulations.gov (Docket ID: HHS-OPHS-2018-0021)]

  NOTES:

  i) FDA – within 21 days of enrollment of the first participant

  ii) ICMJE – prior to enrollment of the first participant

- Consent Form Posting – After the clinical trial is closed to recruitment, and no later than 60 days after the last study visit by any subject

- Done by the responsible party (sponsor or PI)

NIH – is it a clinical trial?

Definition of 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

Definition of BESH:

Basic Experimental Studies involving Humans (BESH) are studies that fall within the NIH definition of a clinical trial and also meet the definition of basic research

NOTE: *All BESH meet the NIH definition of a clinical trial, but not all clinical trials are BESH.*

Clinical Trial Decision Tree

Use the following four questions to determine the difference between a clinical study and a clinical trial:

- Does the study involve human participants?
- Are the participants prospectively assigned to an intervention?
- Is the study designed to evaluate the effect of the intervention on the participants?
- Is the effect being evaluated a health-related biomedical or behavioral outcome?

Note: If the answers to the 4 questions are yes, your study meets the NIH definition of a clinical trial, even if…

- You are studying healthy participants
- Your study does not have a comparison group (e.g., placebo or control)
- Your study is only designed to assess the pharmacokinetics, safety, and/or maximum tolerated dose of an investigational drug
- Your study is utilizing a behavioral intervention
- Only one aim or sub-aim of your study meets the clinical trial definition

Is there an intervention?

- **It is useful for BESH investigators to think of an experimental intervention as an independent variable, which the investigator changes or controls. The intervention (i.e., independent variable) will have a direct effect on a participant which can be measured (i.e., directly effects a dependent variable which is tested and measured in an experiment)**

- In contrast to BESH, researchers conducting observational studies do not control an independent variable. They observe and measure variables of interest (in some cases, over time) and look for relationships between them. The variables are measured, but not manipulated

NIH Data Sharing and Management

NIH Data Sharing Policy (2003 requirements apply because proposal was received by NIH prior to January 2023)

Data sharing options:

- **Depositing data in a data archive**
- **Depositing data in a data enclave**
- **Distributing data under the auspices of the investigator** who is responsible for storing, managing, and sharing of the data. The investigator also vets and makes decisions on access requests. Some investigators doing this may choose to form collaborations with other investigators

What does the IRB look for?

- The rights and privacy of human research participants who participate in NIH-sponsored research must be protected at all times. It is the responsibility of the investigators, their institution and reviewing Institutional Review Board (IRB) to protect the rights of research participants and the confidentiality of the data.

- In general, it is inappropriate for the Principal Investigator (PI) to:

    1. Place limits on the research questions or methods other investigators might pursue with the data
    2. Require authorship as a condition for sharing the data

- Investigators who are planning to share data should discuss with research participants as part of the informed consent process:

    1. The potential risks posed by data sharing, and
    2. The steps taken to address those risks

The DRAFT DUA

Below are several ways for investigators to protect the privacy of human participants when sharing data:

- Remove identifiers from the data prior to sharing
- In addition to removing direct identifiers such as name, address, telephone numbers, and Social Security Numbers, researchers should consider removing indirect identifiers and other information that could reveal participants' identities. Identification from indirect identifiers is a higher risk for participants from small geographic areas, rare populations, or in linked datasets
- Adopt strategies to minimize risks of unauthorized disclosure of personal identifiers
- Although not required, PI may withhold part of the data to reduce the risk of subject identification. Alternatively, they may statistically alter the data in ways that will not compromise secondary analyses but will protect each subjects' identities
- When entering into a Data Use Agreement (DUA), include conditions for protecting confidentiality and privacy (e.g., CoC consideration)

Certificate of Confidentiality (CoC)

- A formal confidentiality protection authorized by the Public Health Service Act (PHSA) [Sec 301(d)(42 U.S.C. 241(d)] to protect the privacy of human research participants enrolled in biomedical, behavioral, clinical and other forms of sensitive research by withholding identifying characteristics from those not connected to the research

CoC Protections:

- All copies of identifiable, sensitive information collected by a CoC recipient
- Immune from the legal processes and is not admissible as evidence (unless participant consents to this disclosure)
- Last in perpetuity

NOTE: *Regulations focus on the identifiability of the information and not on the sensitivity of the information*

NIH-Funded vs Privately-Funded/Unfunded Studies

NIH-Funded Study:

- NIH-funded study is automatically deemed to be issued a CoC. Hence, CoC does not need to be requested
- NIH does not issue a physical certificate for NIH-funded research projects. The following provides protection:
  - NIH CoC Policy
  - Notice of Award
  - NIH Grants Policy Statement for grant awards
  - NIH DGS Contract Handbook- Special Contracts Requirements for R&D Contracts
- CoCs automatically cover research activities and do not need to be extended or amended while the research remains funded by NIH. It continues for the duration of a no-cost extension

Privately-Funded Study/Unfunded Study

- Request to NIH should be made, but NIH issuance of Certificates is discretionary
- CoC issuance limits to single project, not to multiple projects
- Once CoC expired, a new request should be submitted. NIH System does not process extensions

Other HHS-Agencies and Other Federal Departments and Agencies also issue CoC

- Centers for Disease Control and Prevention (CDC)
- Food and Drug Administration (FDA)
- Health Resources and Services Administration (HRSA)
- Indian Health Service (IHS)
- Substance Abuse and Mental Health Services Administration (SAMHSA)

- Investigators whose research is funded by CDC, HRSA, IHS, or SAMHSA should contact the Certificate Coordinators at their funding agency to determine how to obtain a CoC.

- Investigators whose research is funded by an HHS agency, other than NIH, CDC, FDA, HRSA, IHS, or SAMHSA, or a non-HHS Federal Department or Agency may request a Certificate of Confidentiality for specific research projects that collect or use identifiable, sensitive information through the online NIH CoC system.

Policy Environment Scan - 45 CFR 46

Consent

- Key Info Section
- Intention re: Future Use of Data and Data Sharing
- A statement regarding whether clinically relevant research results, including individual research results, will be disclosed to subjects, and if so, under what conditions
- CoC required language
- ClinicalTrials.gov required language
- For research involving biospecimens, whether the research will (if known) or might include whole genome sequencing

NIH Required Statements – Consent Form

- **Certificate of Confidentiality (CoC)**

"To help us protect your privacy, we [choose one: will obtain or have obtained] a Certificate of Confidentiality from the National Institutes of Health. With this Certificate, the researchers can refuse to disclose information that may identify you, even by a court subpoena, in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings. The researchers will use the Certificate to resist any demands for information that would identify you, except as explained below.

The Certificate cannot be used to resist a demand for information from personnel of the United States Government that is used for auditing or evaluation of federally funded projects or for information that must be disclosed in order to meet the requirements of the FDA.

A Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers may not use the Certificate to withhold that information. However, if we learn about abuse of a child or elderly person or that you intend to harm yourself or someone else, or about certain communicable diseases, we will report that to the proper authorities."

- **ClinicalTrials.gov**

"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. ClinicalTrials.gov is a website that provides information about federally and privately supported clinical trials. You can search this website at any time."

Policy Environment Scan - 45 CFR 46

Subpart D

- Parent means a child's biological or adoptive parent
- Guardian means an individual who is authorized under applicable State or local law to consent on behalf of a child to general medical care
- Research Involving children checklist Section B
- Waiver of Consent checklist Section A

Policy Environment Scan – UGA HRPP

- Deception
- Compensation
- Recruitment (Community Engagement)

IRB 1 - Memory Review

- Does the study staff need to include someone with the appropriate training and experience to assess harm related to responding to sensitive questions or to provide immediate support/care?
- Is the protocol sufficient to respond to incidents during/after testing? Are there sufficient safety assessments and communication plans?
- Does there seem to have been sufficient community engagement in the design of the study and materials?
- Is the plan related to return of results (incidental findings and individual study results) appropriate?

Helpful Links

- 45 CFR 116 - General Requirements for Informed Consent
- Clinical Trials Registration and Results Information Submission
- Why Should I Register and Submit Results?
- Informed Consent Posting Instructions (2022)
- Submit Studies to ClinicalTrials.gov PRS
- Clinical Study Frequently Asked Questions
- Grants & Funding (NIH Central Source for Grants and Funding Information
- Certificate of Confidentiality

Thank you!