An Overview of NIH Policies on Human Subjects

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Objectives

- Identify NIH policies pertaining to research involving human subjects
- Determine when research involving human subjects is a clinical trial
- Review considerations when applying for an NIH award for research that involves human subjects
- Identify NIH resources for investigators conducting research involving human subjects
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Human Subjects Research Policies

- Inclusion across the lifespan
- Inclusion of Women and Minorities
- Human Subjects Education
- Certificates of Confidentiality
- Disseminating Clinical Trial Information
- FOA Policies
- BESH
- GCP Training
- Human Fetal Tissue
- Clinical Trials Policies
- Data and Safety Monitoring

Human Subjects Research
When do NIH Human Subjects Policies Apply?

- Research activities that involve Human Subjects (HS)
  - Human subjects defined in the Common Rule
  - Some HS policies apply to clinical research (e.g., Inclusion)
  - Some HS policies apply only to clinical trials (e.g., Data and Safety Monitoring)
- NIH policies complementary or in addition to the Common Rule
Decision Tool: Am I Doing Human Subjects Research?

The Office of Extramural Research (OER) has developed a quick decision tool that should assist you with determining if your research involves human subjects, may be considered exempt from Federal regulations, or is not considered human subjects research. This tool should not be used as the sole determination of exemption.

**Note:** Please keep in mind that this tool uses the pre-2018 requirements, so stay tuned for the upcoming changes with the final revisions to the Federal Policy for the Protection of Human Subjects (the Common Rule). For more information, please visit OHRP’s page.  

### QUESTION ONE

Please check which best describes your research:

- [ ] For the purpose of this study, at some point there will be an intervention or interaction with subjects for the collection of specimens or biological material or data (including health or clinical data, surveys, focus groups or observation of behavior).
- [ ] This study will involve only the use of secondary analysis of biological material/tissue/specimens or data not collected specifically for this study.
- [ ] This study will involve materials/specimens or data from deceased individuals only.
Required Education In the Protection of Human Research Participants

• **All key personnel** must have education on the protection of human research participants:
  • Individuals responsible for design and conduct of the research
  • Also applies to key personnel at performance sites
• One-time training
Certificates of Confidentiality (CoC) (1 of 2)

• Applicable NIH research ongoing or awarded as of December 13, 2016 is deemed to be issued a Certificate

• **Must not disclose identifiable, sensitive information**:  
  • In any Federal, State, or local civil, criminal, administrative, legislative, or other proceeding  
  • To any other person not connected with the research

• Disclosure permitted **only** when:  
  • Required by Federal, State, or local laws (e.g., reporting child or elder abuse, mandatory disease reporting)  
  • With participants’ consent  
  • For other scientific research
Certificates of Confidentiality (CoC) (2 of 2)

• CoC protects “covered information”
  • Names or any information, documents, or biospecimens
  • If there is a small risk that covered information can be combined with other data to determine individual’s identity

• CoC applies to all copies of the data
  • Secondary researchers must uphold CoC protections
  • Covered information protected in perpetuity
Human Fetal Tissue (HFT)

- NIH implemented the HHS Policy, effective June 5, 2019
- Applicants must provide:
  - a justification of the use of HFT,
  - details regarding procurement and costs,
  - information about how the applicant/contract offeror will use HFT
- NIH will not accept modular budgets for applications for research involving HFT
- Applications that do not address all required information will be administratively withdrawn and not reviewed
Inclusion (1 of 2)

• Inclusion of women and minorities in all NIH funded or supported clinical research mandated by law

• Additional requirements for Phase III clinical trials
  • Can study be expected to identify potential differences by sex/gender, race, and/or ethnicity
Inclusion (2 of 2)

- Must include individuals across the lifespan when conducting clinical research, unless there is a scientific or ethical reason to exclude
- Policies Goal: ensure individuals are included in clinical research in a manner appropriate to the scientific question under study
Single IRB Requirement

Revised Common Rule Cooperative Research Provision at 45 CFR 46.114(b)

• All cooperative research projects are expected to abide by the cooperative research provision, when applicable

NIH sIRB Policy

• Nonexempt human subjects research studies with more than one domestic site are expected to use a single IRB
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How Does NIH Define 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**.
Clinical Trial Questionnaire

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 of the participants?

Is the effect that will be evaluated a health-related biomedical or behavioral outcome?

Answers determine:

- ✓ Appropriate FOA type
- ✓ Application form requirements
- ✓ Review criteria for evaluation
- ✓ Requirement for registration and results reporting
- ✓ Requirement for GCP training

**If YES to all questions, study is a clinical trial**
Clinical Trial Decision Tool

Decision Tool: Does Your Human Subjects Research Study Meet the NIH Definition of a Clinical Trial?

To learn more about the considerations for each question, use the decision tool below:

Note for ancillary studies: When answering the following questions, take into account only the work being proposed in the ancillary study, not the work being done in the parent project.

QUESTION ONE

Does the study involve human participants?

Unsure how to respond? Our case studies and FAQs may help you decide.

- Yes
- No

Does Your Human Subjects Research Study Meet the NIH Definition of a Clinical Trial?
Funding Opportunity Announcement (FOA) for Clinical Trials

• Applications involving clinical trials must be submitted to clinical-trial specific FOAs

• Applications submitted to incorrect FOA will be administratively withdrawn

• Purpose:
  • Improve NIH’s ability to identify proposed clinical trials
  • Ensure key pieces of trial-specific information are submitted with each application
  • Uniformly apply trial-specific review criteria
Dissemination of NIH-Funded Clinical Trial Information

Policy Requires Registration and Reporting:

- **SUBMIT** - a plan in the application outlining compliance with the policy
- **REGISTER** - no later than 21 days after enrolling the first participant
- **REPORT** - summary results no later than one year after primary completion date
Basic Experimental Studies with Humans (BESH) FOAs (1 of 2)

• BESH studies meet definition for both:
  • Basic Research
  • NIH clinical trial

• NEW BESH Website

Guide Notices
NOT-OD-18-212 & NOT-OD-21-088
Published
July 20, 2018 & March 23, 2021
Basic Experimental Studies with Humans (BESH) FOAs (2 of 2)

- Interim flexibilities for registration and results reporting through September 24, 2023.
- Registration and results reporting is still expected for BESH FOAs, but with flexibility to use alternative publicly available platforms (other than Clinicaltrials.gov)
- NOTE: This flexibility ONLY applies to BESH studies funded through BESH FOAs
Good Clinical Practice Training (GCP)

• All NIH-funded clinical investigators and clinical trial staff involved in the design, conduct, oversight, or management of clinical trials should be trained in GCP

• GCP training can be achieved through:
  • class or course
  • academic training program
  • certification from a recognized clinical research professional organization

• Training should be refreshed every 3 years
Data and Safety Monitoring

- Clinical trials must submit a Data and Safety monitoring plan
  - Address overall data and safety monitoring framework
  - Describe procedures for adverse event reporting
  - Identify the monitor (e.g., PI, independent safety monitor, DSMB, etc.)
- Data and Safety Monitoring Board (DSMB) generally required for NIH-defined phase III trials

Guide Notices
NOT-98-084 & NOT-OD-00-038
Published
June 10, 1998 & June 5, 2000
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# Using the Human Subjects and Clinical Trial Form

<table>
<thead>
<tr>
<th>Form Section</th>
<th>If answered “No” to any questions in Clinical Trial Questionnaire</th>
<th>If answered “Yes” to all questions in Clinical Trial Questionnaire</th>
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</thead>
<tbody>
<tr>
<td>Section 1 Basic Information</td>
<td>Required</td>
<td>Required</td>
</tr>
<tr>
<td>Section 2 Study Population Characteristics</td>
<td>Required; some fields optional if exemption 4</td>
<td>Required</td>
</tr>
<tr>
<td>Section 3 Protection and Monitoring Plans</td>
<td>Some fields required; some fields optional</td>
<td>Required</td>
</tr>
<tr>
<td>Section 4 Protocol Synopsis</td>
<td>Not permitted</td>
<td>Required</td>
</tr>
<tr>
<td>Section 5 Other Clinical Trial-related Attachments</td>
<td>Not permitted</td>
<td>Required only if specified in FOA</td>
</tr>
</tbody>
</table>

Human Subjects and Clinical Trials Information Form
Plan Protection of Human Subjects
(1 of 3)

1. Risks
   - Study population, assignment and procedures
   - Sources of materials – access to identifiers
   - Potential Risks for ALL research interventions: physical, psychological, social, legal

2. Adequacy of Protection Against Risks
   - The consenting process
   - Procedures to minimize identified risks, including protecting participant privacy
   - Additional protections for vulnerable subjects
Plan Protection of Human Subjects (2 of 3)

3. Potential Benefits of Research to Human Subjects and Others
   • Discuss risks in relation to anticipated benefits
   • In some cases, there is no direct benefit to subjects
   • Do not include financial compensation

4. Importance of Knowledge to be Gained
   • Discuss in relation to risks
Plan Protection of Human Subjects (3 of 3)

• Don’t assume reviewers will understand what you mean
  • Explain how, what, when, where, why and who
• Common human subject issues identified in peer review:
  • Physical or psychological risks not adequately addressed
  • Inadequate protections for vulnerable populations
  • Source of specimen and/or data
  • Incidental findings not addressed
  • Missing or inadequate Data & Safety Monitoring Plans
Multi-site Study Considerations

• In general, funding recipient is considered engaged in human subjects (HS) research when nonexempt research involves HS

• **All** engaged sites must have:
  • FWA (can be covered under recipient’s FWA)
    • [Extending a FWA to Cover Collaborating Investigators](#)
  • IRB Approval
    • U.S. sites to rely on one IRB under 45 CFR 46.114
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Useful Resources: Human Subjects Protections and Inclusion

- NIH Human Subjects Research Home Page
- NIH Clinical Trial Requirements for Grants and Contracts
- NIH Basic Experimental Studies Involving Humans (BESH)
- Office for Human Research Protections (OHRP) Home Page
Questions