An Overview of NIH Policies on Human Subjects

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National Institutes of Health Office of Extramural Research

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

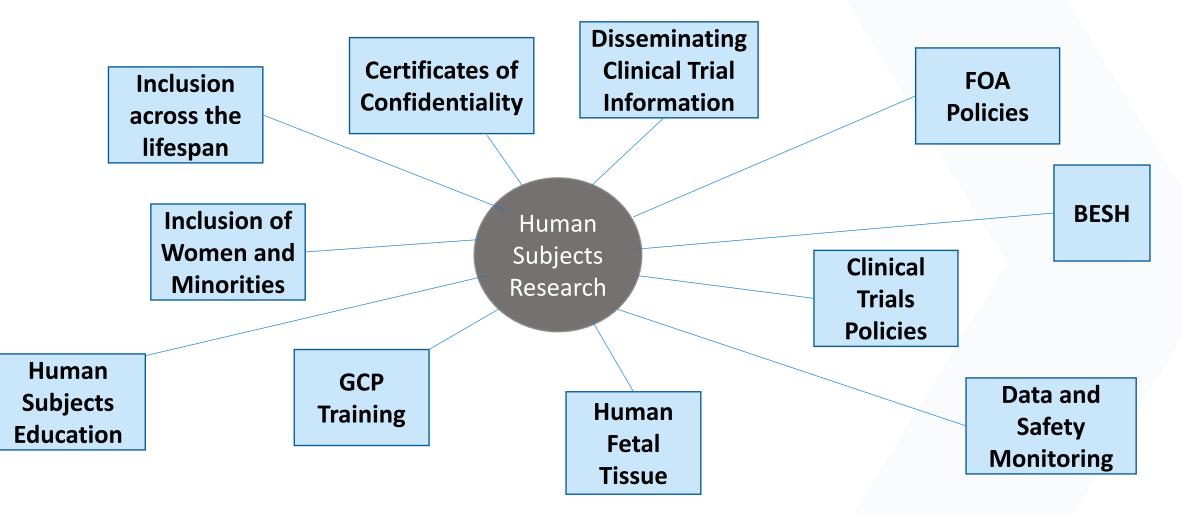


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Human Subjects Research Policies



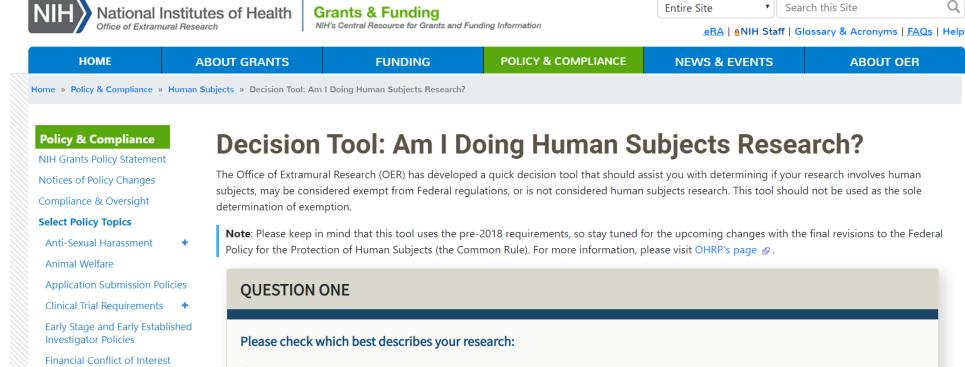


When do NIH Human Subjects Policies Apply?

- 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



- 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).
- O 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.



Human Subjects Research

Research

Definition of Human Subjects

Due and Deet Assessed Due and

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

Guide Notices <u>NOT-OD-00-039</u> & <u>NOT-OD-11-061</u> *Published* June 5, 2000 & September 5, 2001



Certificates of Confidentiality (CoC)

- 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) cont'd

- CoC protects "covered information"
 - Names or any information, documents, or biospecimens
 - If there is a small risk that covered information can be combined wither 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

Guide Notice <u>NOT-OD-17-109</u> *Published* September 7, 2017



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,

Guide Notices <u>NOT-OD-19-128</u> & <u>NOT-OD-19-137</u> *Published* July 26, 2019 & August 23, 2019

- 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

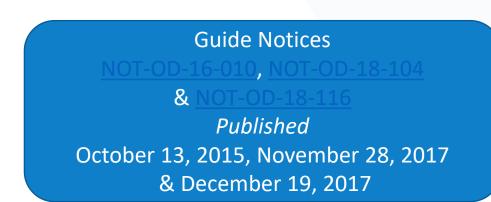
- Inclusion of women and minorities in all NIH funded or supported clinical research mandated by law
- Additional requirements for Phase III clinical trials
 - Can study be expected to identify potential differences by sex/gender, race, and/or ethnicity





Inclusion cont'd

- 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





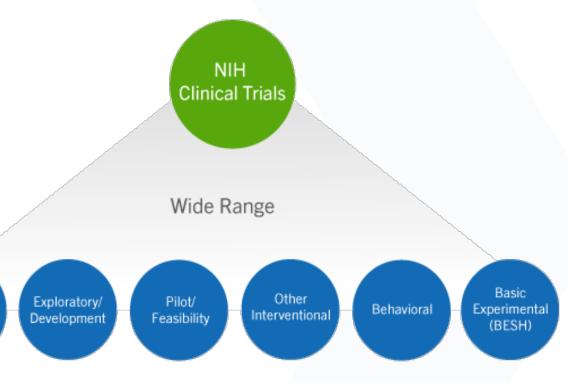
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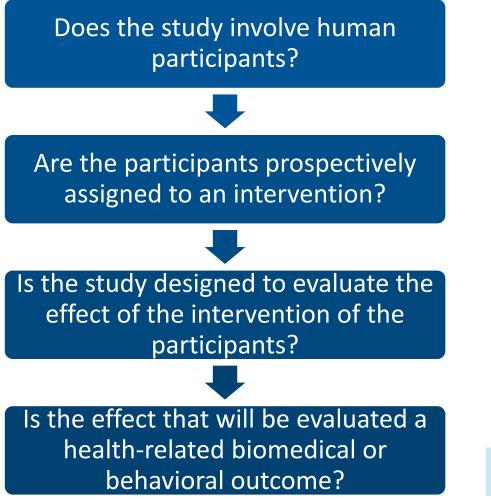
How Does NIH Define a Clinical Trial?

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 Mechanistic interventions on health-related biomedical or behavioral outcomes





Clinical Trial Questionnaire



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 <u>all</u> 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

O No

Next



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:

Guide Notice: <u>NOT-OD-16-147</u> Published September 16, 2016

- 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



Basic Experimental Studies with Humans (BESH) FOAs

- BESH studies meet definition for **BOTH**:
 - Basic Research
 - NIH clinical trial

Guide Notices <u>NOT-OD-18-212</u> & <u>NOT-OD-19-126</u> *Published* July 20, 2018 & July 24, 2019

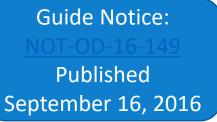
- *NIH extended interim policy flexibilities for registration and results reporting through September 24, 2021
- Registration and results reporting is still expected for BESH FOAs, but with *flexibility to use alternative publicly available platforms (other than Clinicaltrials.gov)
- *NOTE: The flexibilities only apply to BESH studies funded through BESH FOAs



Dissemination of NIH-Funded Clinical Trial Information

Policy Requires Registration and Reporting:

- **SUBMIT** a plan in the application outlining compliance with the policy
- REGISTER the clinical trial no later than 21 days after enrolling the first participant
- REPORT Submit summary results no later than one year after primary completion date



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



Guide Notice: <u>NOT-OD-16-148</u> Published September 16, 2016



Data and Safety Monitoring

- Clinical trials must submit a Data and Safety monitoring plan
 - Address overall data and safety monitoring framework

Guide Notices <u>NOT-98-084</u> & <u>NOT-OD-00-038</u> *Published* June 10, 1998 & June 5, 2000

- 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



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Using the Human Subjects and Clinical Trial Form

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



Plan Protection of Human Subjects

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 cont'd

- 3. Potential Benefits of Research to Human Subjects and Others
 - Discuss risks in relation to anticipated benef**^
 - 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 cont'd

- 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)
 - <u>http://www.hhs.gov/ohrp/policy/guidanceonalternativetofwa.html</u>
 - IRB Approval
 - U.S. sites to rely on one IRB under <u>45 CFR 46.114</u>
 - Reliance agreement

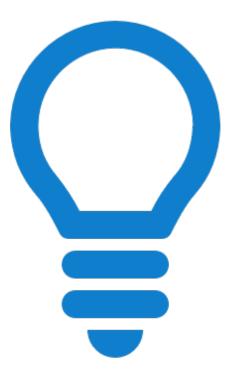
http://www.hhs.gov/ohrp/assurances/forms/irbauthagree.html

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Useful Resources: Human Subjects Protections and Inclusion



 NIH OER Human Subjects website <u>https://humansubjects.nih.gov</u>

• OHRP website

https://www.hhs.gov/ohrp/



Questions



