Office of Sponsored Programs (OSP) Roundtable

New NIH Human Subjects Requirements

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Agenda

- Updated definition of Clinical Trial
- Single Institutional Review Board (sIRB) requirements
- Certificate of Confidentiality (CoC)
- Forms E - PHS Human Subjects and Clinical Trials Information Form

OSP Roundtable – New NIH Human Subjects Requirements

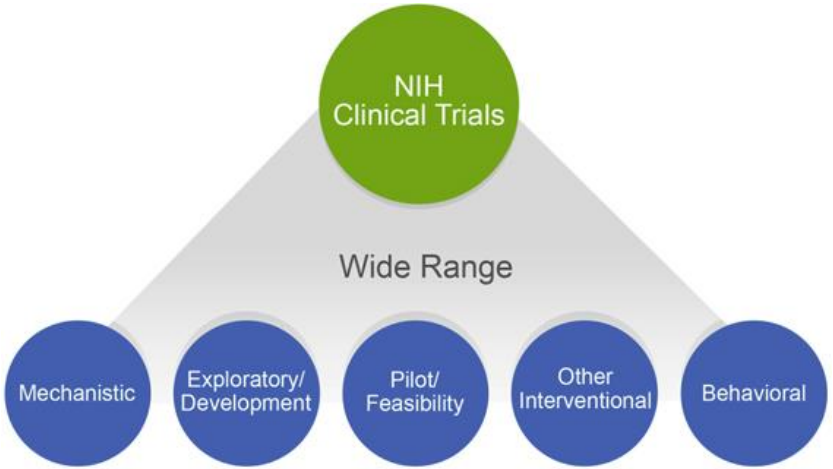
Updated Definition of Clinical Trial

What has changed?

- NIH's definition of clinical trial has been updated to communicate a much broader applicability:

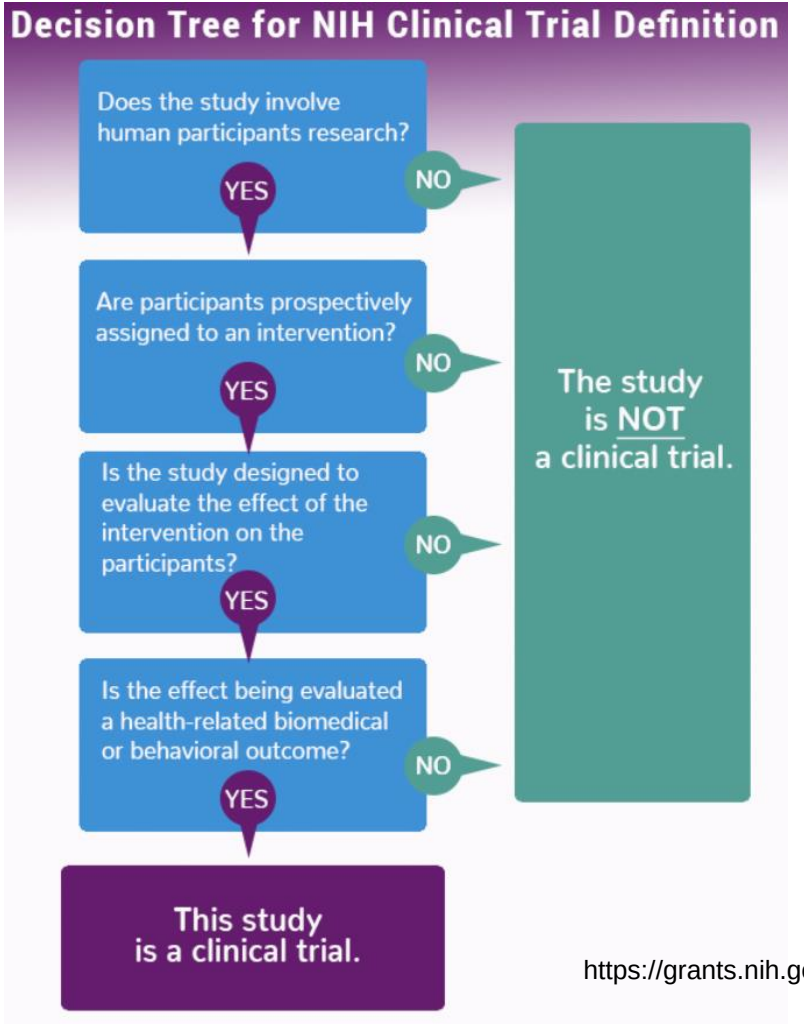
"A research study in which one or more **human subjects** are **prospectively assigned** to one or more **interventions** (which may include placebo or other control) to evaluate the effects of those interventions on **health-related biomedical or behavioral outcomes**."

NIH Policy Notice NOT-OD-15-015 (October 23, 2014)
https://grants.nih.gov/grants/guide/notice-files/NOT-OD-15-015.html



Breaking down the definition

- **Prospectively assigned:** a pre-defined process (e.g., randomization) by which research participants are assigned to one or more arms (e.g., intervention, placebo, or other control) of a study
- **Intervention:** a manipulation of the research participant or their environment (e.g., use of a wearable device such as a Fitbit; diet or exercise; surgical technique)
- **Health-related Biomedical or Behavioral Outcome:** a pre-specified goal or condition that reflects the effect of the intervention(s) on participants' biomedical or behavioral status or quality of life (e.g., improvement of lung capacity; changes to psychological wellbeing)



https://grants.nih.gov/policy/clinical-trials/CT-decision-tree.pdf

Example 1

A study involves the recruitment of school children to evaluate two different tools for monitoring food intake. Food consumption behavior will be measured by asking children to activate a pocket camera during meals and to use a diary to record consumed food. Changes to eating behavior will be assessed.

- **Does the study involve human participants?** Yes, children are human participants.
- **Are the participants prospectively assigned to an intervention?** Yes, the participants are prospectively assigned to two food monitoring methods.
- **Is the study designed to evaluate the effect of the intervention on the participants?** Yes, the study is designed to determine whether using the monitoring methods changes eating behavior.
- **Is the effect being evaluated a health-related biomedical or behavioral outcome?** Yes, eating behavior is a health-related outcome.

This study is a clinical trial.

Example 2

A study involves the recruitment of children at two schools to monitor eating behavior. Children's food choices will be monitored using a remote food photography method. Food consumption and the accuracy of food monitoring methods will be assessed.

- **Does the study involve human participants?** Yes, the children participating in this study are human participants.
- **Are the participants prospectively assigned to an intervention?** No, not in this context. The study involves observing and measuring eating behavior, but not modifying it. This is an observational study.

This study is not a clinical trial.

What are the implications of this change?

- With this broader definition, many more studies are classified as clinical trials and are therefore subject to additional human subjects compliance requirements, including;
  - All researchers on the protocol for the NIH-funded clinical trial study must complete training in Good Clinical Practice (GCP).
  - The study must be registered within 21 days of enrollment of first participant on ClinicalTrials.gov and must provide summary results and updates about the study as required.
  - For clinical trials funded by any federal agency, all consent forms must be posted online (website TBD) after the study is closed to recruitment and within 60 days of the end of data collection.

What are the implications of this change?

- Researchers and administrators will need to determine whether the project meets the definition of a clinical trial ***prior to submitting a proposal to NIH for funding consideration***.**Effective for due dates on or after January 25, 2018, NIH will require all applications involving one or more clinical trials be submitted through a Funding Opportunity Announcement (FOA) specifically designated for clinical trials.**

Due Dates on or after January 25, 2018	All clinical trial applications **MUST** be submitted to an FOA that allows clinical trials

- NIH is revising and reissuing all Parent Funding Opportunity Announcements (FOAs) to specify whether or not a proposal involving a clinical trial study will be accepted. See NIH Policy Notice NOT-OD-18-106 https://grants.nih.gov/grants/guide/notice-files/NOT-OD-18-106.html.

Next Steps: Cornell Researchers

- **All** researchers;
  - Prior to starting your NIH proposal, determine whether your project is a clinical trial. Ask the Cornell IRB Staff at irbhp@cornell.edu for help if you are not sure!
  - Work with your pre-award administrator and OSP Grant & Contract Officer to apply to the correct NIH Funding Opportunity Announcement (FOA).
  - Add a few days to your proposal planning and preparation timeline.
- Clinical Trial researchers;
  - Have all study team members take Good Clinical Practices (GCP) training http://www.oria.cornell.edu/training/citi/login/index.cfm
  - Familiarize yourself with Clinicaltrials.gov and set up an account https://grants.nih.gov/policy/clinical-trials/reporting/steps.htm

Next Steps: Research Administrators

- Become familiar with;
  - The updated definition and determination criteria for clinical trials
  - Clinicaltrials.gov and the reporting requirements
  - Updated NIH Funding Opportunity Announcements (NOT-OD-18-106)
  - Forms E, especially the new PHS Human Subjects and Clinical Trials Information Form
- Work with all NIH researchers to;
  - Determine whether their project is a clinical trial. Ask the Cornell IRB Staff at irbhp@cornell.edu for help if you are not sure!
  - Ensure all proposals, both those that are and are not clinical trials, are submitted to the correct NIH Funding Opportunity Announcement (FOA)
- Add a few days to your proposal planning and preparation timeline.

NIH Resources

- Guidance

NIH's Definition of a Clinical Trial Website
https://grants.nih.gov/policy/clinical-trials/definition.htm

NIH's Clinical Trials FAQs
https://grants.nih.gov/grants/policy/faq_clinical_trial_definition.htm

NIH's Clinical Trial Case Studies Website
https://grants.nih.gov/policy/clinical-trials/case-studies.htm

NIH's Good Clinical Practice (GCP) Training Website
https://grants.nih.gov/policy/clinical-trials/good-clinical-training.htm

- Policy

NIH Policy Notice NOT-OD-15-015: Notice of Revised NIH Definition of "Clinical Trial"
https://grants.nih.gov/grants/guide/notice-files/NOT-OD-15-015.html

NIH Policy Notice NOT-OD-17-118: NIH Announces New Review Criteria for Research Project Applications Involving Clinical Trials
https://grants.nih.gov/grants/guide/notice-files/NOT-OD-17-118.html

NIH Policy Notice NOT-OD-18-106: Policy on Funding Opportunity Announcements (FOA) for Clinical Trials Takes Effect 1/25/2018
https://grants.nih.gov/grants/guide/notice-files/NOT-OD-18-106.html

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Single Institutional Review Board (sIRB) Requirements

What is a single Institutional Review Board (sIRB)?

- One IRB that is responsible for conducting an ethical review of, and coordinating, all human participant research performed at all the locations in a multi-site study.
- Role of the sIRB:
  - Conducts ethical review for studies at all sites, including recruitment, applications, consent forms, incident reports, data and privacy, in keeping with Common Rule requirements.
  - May also serve as Privacy Board (HIPAA Privacy Rule - use/disclosure of PHI for research).
  - Handles all changes to the study and ensure that they are uniformly implemented, ensure all concerns are addressed, maintain documentation, correspond with the NIH and regulators.
- Role of participating sites:
  - Rely on sIRB to carry out review functions and report to sIRB (unanticipated problems, study progress, information regarding local context issues), meet all IRB requirements for study at their site (local review, documentation, training, oversight, incident reporting, etc.)

What has changed?

- NIH has a new policy, intended to streamline the IRB review process, harmonize IRB requirements for an NIH-funded study, and reduce administrative burden.

All multi-site projects with non-exempt human participant research (clinical and non-clinical) where the same research protocol is conducted at more than one domestic site will be required to use a single Institutional Review Board (sIRB).

- Applies to all competing grant applications (new, renewal, revision, resubmissions) due on or after **January 25, 2018**, and all contract solicitations published starting January 25, 2018.
- Does not apply to international sites, or to Career Development (K), Research Training (T), or Fellowship (F) mechanisms.

What are the implications of this change?

- If the NIH proposal involves conducting the same research at multiple locations, the proposal ***must*** include an **sIRB Plan**
  - Plan must indicate the sIRB, confirm that participating sites will adhere to the sIRB Policy, describe communications between sites and sIRB
  - sIRB costs might be permitted as direct charges (Talk to you GCO!)
  - If awarded, all participating sites must execute an Authorization Agreement & the sIRB Plan will be incorporated into the Notice of Award (NOA) as a term and condition

The administrative responsibility of the Single IRB is very significant.
Do not assume Cornell can act as sIRB.
Contact Cornell IRB (irbhp@cornell.edu) well in advance of proposal submission.

NIH Resources

- Guidance

NIH's Single IRB policy for Multi-site Research Website
https://grants.nih.gov/policy/clinical-trials/single-irb-policy-multi-site-research.htm

- Policy

NIH Policy Notice NOT-OD-16-094: Final NIH Policy on the Use of a Single Institutional Review Board for Multi-Site Research
https://grants.nih.gov/grants/guide/notice-files/NOT-OD-16-094.html

NIH Policy Notice NOT-OD-18-003: Guidance on Exceptions to the NIH Single IRB Policy
https://grants.nih.gov/grants/guide/notice-files/NOT-OD-18-003.html

NIH Policy Notice NOT-OD-18-004: Guidance on Implementation of the NIH Policy on the Use of a Single Institutional Review Board for Multi-Site Research
https://grants.nih.gov/grants/guide/notice-files/NOT-OD-18-004.html

OSP Roundtable – New NIH Human Subjects Requirements

Certificates of Confidentiality

What is a Certificate of Confidentiality?

- A Certificate of Confidentiality (CoC) **protects the privacy of research participants** by prohibiting disclosure of participants' identifiable, sensitive information in response to legal demands, such as a subpoena.

What has changed?

- Effective **October 1, 2017**, for NIH-funded research active on December 13, 2016;
  - All research that collects or uses identifiable, sensitive information is deemed to be issued a CoC
  - No documentation will be given — determination of whether a CoC applies is left to the institution and researchers
  - Previously, obtaining CoC protections required an application to NIH-- not all requests were granted

- For **non-NIH studies**, PIs may request a CoC (the new, automatic issuance only applies to NIH studies) if they believe it is necessary to protect participants

What are the implications of this change?

- If a CoC applies to an NIH-funded study:
  - The IRB office will inform the PI during the approval process
  - The researcher may not disclose protected information to any person not connected with the research, including for legal proceedings
  - The consent should inform participants about the CoC
  - Collaborators & other recipients of identifiable information or biospecimens are subject to the same restrictions, and the PI is responsible for communicating this to collaborators

NIH Resources

- Guidance

NIH's Certificates of Confidentiality Website
https://humansubjects.nih.gov/coc/index

- Policy

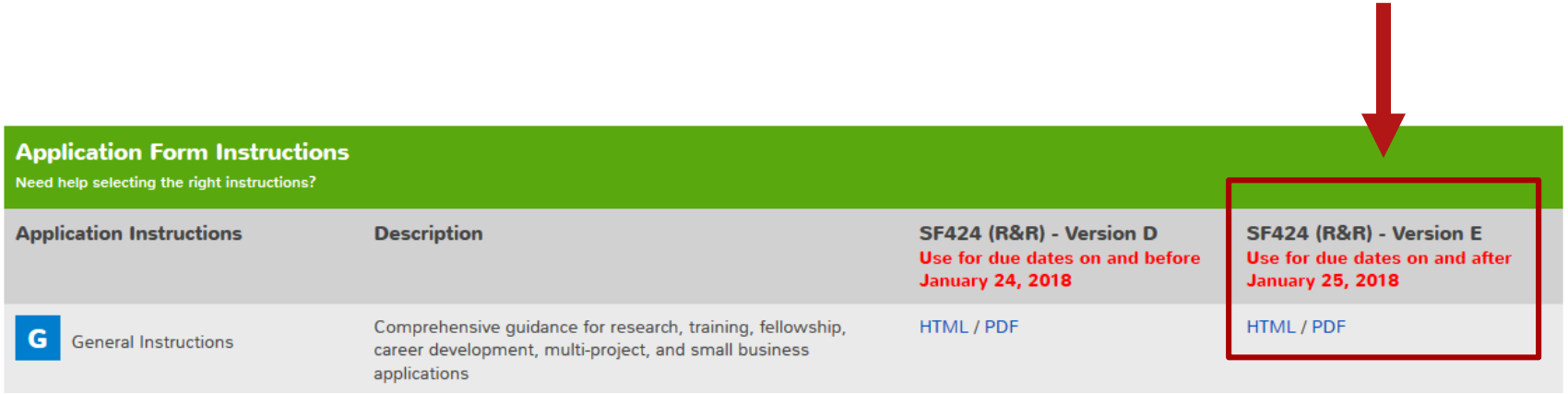
NIH Policy Notice NOT-OD-17-109: Notice of Changes to NIH Policy for Issuing Certificates of Confidentiality
https://grants.nih.gov/grants/guide/notice-files/NOT-OD-17-109.html

OSP Roundtable – New NIH Human Subjects Requirements

Forms E - PHS Human Subjects and Clinical Trials Information

SF 424 (R&R) Forms Version E

- Effective for due dates on or after **January 25, 2018**, the Forms E Application package, including the new Human subjects and Clinical Trials Information form, is required for all applications submitted to NIH.



Application Form Instructions

Need help selecting the right instructions?

Application Instructions	Description	SF424 (R&R) - Version D Use for due dates on and before January 24, 2018	SF424 (R&R) - Version E Use for due dates on and after January 25, 2018
G General Instructions	Comprehensive guidance for research, training, fellowship, career development, multi-project, and small business applications	HTML / PDF	HTML / PDF

https://grants.nih.gov/grants/how-to-apply-application-guide.html

PHS Human Subjects and Clinical Trials Information Form

- New form making it's debut in Forms E!
- Purpose:
  - Consolidates human subjects, inclusion enrollment, and clinical trial information previously collected across multiple agency forms
  - Incorporates structured data fields
  - Collects information at the study-level
- PHS 398 Research Plan has also been updated to remove the human subjects attachments Protection of Human Subjects, Data Safety Monitoring Plan, Inclusion of Women and Minorities, and Inclusion of Children.

PHS Human Subjects and Clinical Trials Information

View Burden Statement

OMB Number: 0925-0001
Expiration Date: 03/31/2020

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 fields must be made on the Research & Related Other Project Information form and may impact the data items you are required to complete on this form.

Are Human Subjects Involved? ☐ Yes ☐ No

Is the Project Exempt from Federal regulations? ☐ Yes ☐ No

Exemption number: ☐1 ☐2 ☐3 ☐4 ☐5 ☐6 ☐7 ☐8

If No to Human Subjects

Does the proposed research involve human specimens and/or data? ☐ Yes ☐ No

If Yes, provide an explanation of why the application does not involve human subjects research.

Add Attachment | Delete Attachment | View Attachment

Skip the rest of the PHS Human Subjects and Clinical Trials Information Form.

If Yes to Human Subjects

Add a record for each proposed Human Subject Study by selecting 'Add New Study' or 'Add New Delayed Onset Study' as appropriate. Delayed onset studies are those for which there is no well-defined plan for human subject involvement at the time of submission, per agency policies on Delayed Onset Studies. For delayed onset studies, you will provide the study name and a justification for omission of human subjects study information.

Other Requested Information

Add Attachment | Delete Attachment | View Attachment

Click here to extract the Human Subject Study Record Attachment

Study Record(s)

Attach human subject study records using unique filenames.

x 1) Please attach Human Subject Study 1 — Add Attachment | Delete Attachment | View Attachment

Add New Study

Delayed Onset Study(ies)

	Study Title	Anticipated Clinical Trial?	Justification
x		☐	Add Attachment | Delete Attachment | View Attachment

Add New Delayed Onset Study

Check Form for Errors | Save

Study Record: PHS Human Subjects and Clinical Trials Information

OMB Number: 0925-0001
Expiration Date: 03/31/2020

* Always required field

Section 1 - Basic Information

1.1. * Study Title (each study title must be unique)

1.2. * Is this Study Exempt from Federal Regulations? ☐ Yes ☐ No

1.3. Exemption Number ☐1 ☐2 ☐3 ☐4 ☐5 ☐6 ☐7 ☐8

1.4. * Clinical Trial Questionnaire

If the answers to all four questions below are yes, this study meets the definition of a Clinical Trial.

- 1.4.a. Does the study involve human participants? ☐ Yes ☐ No
- 1.4.b. Are the participants prospectively assigned to an intervention? ☐ Yes ☐ No
- 1.4.c. Is the study designed to evaluate the effect of the intervention on the participants? ☐ Yes ☐ No
- 1.4.d. Is the effect that will be evaluated a health-related biomedical or behavioral outcome? ☐ Yes ☐ No

1.5. Provide the ClinicalTrials.gov identifier (e.g., NCT87654321) for this trial, if applicable

Section 2 - Study Population Characteristics

2.1. Conditions or Focus of Study

x

Add New Condition

2.2. Eligibility Criteria

2.3. Age Limits — Minimum Age | Maximum Age

2.4. Inclusion of Women, Minorities, and Children — Add Attachment | Delete Attachment | View Attachment

2.5. Recruitment and Retention Plan — Add Attachment | Delete Attachment | View Attachment

2.6. Recruitment Status

2.7. Study Timeline — Add Attachment | Delete Attachment | View Attachment

2.8. Enrollment of First Subject

Inclusion Enrollment Report(s)

Add Inclusion Enrollment Report

Inclusion Enrollment Report

Remove Inclu

1. * Using an Existing Dataset or Resource ☐ Yes ☐ No

2. * Enrollment Location Type ☐ Domestic ☐ Foreign

3. Enrollment Country(ies)

Add New Country

4. Enrollment Location(s)

5. Comments

Planned

Racial Categories	Ethnic Categories				Total
	Not Hispanic or Latino		Hispanic or Latino		
	Female	Male	Female	Male	
American Indian/ Alaska Native	0	0	0	0	0
Asian	0	0	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0	0	0
Black or African American	0	0	0	0	0
White	0	0	0	0	0
More than One Race	0	0	0	0	0
Total	0	0	0	0	0

Cumulative (Actual)

Racial Categories	Ethnic Categories									Total
	Not Hispanic or Latino			Hispanic or Latino			Unknown/Not Reported Ethnicity			
	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	
American Indian/ Alaska Native	0	0	0	0	0	0	0	0	0	0
Asian	0	0	0	0	0	0	0	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0	0	0	0	0	0	0	0
Black or African American	0	0	0	0	0	0	0	0	0	0
White	0	0	0	0	0	0	0	0	0	0
More than One Race	0	0	0	0	0	0	0	0	0	0
Unknown or Not Reported	0	0	0	0	0	0	0	0	0	0
Total	0	0	0	0	0	0	0	0	0	0

< Previous Report | Report 1 of 1 | Next Report >

|<< First Report | Delete Report | Last Report >>|

Section 3 - Protection and Monitoring Plans

3.1. Protection of Human Subjects — Add Attachment | Delete Attachment | View Attachment

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 — Add Attachment | Delete Attachment | View Attachment

3.3. Data and Safety Monitoring Plan — Add Attachment | Delete Attachment | View Attachment

3.4. Will a Data and Safety Monitoring Board be appointed for this study?

☐ Yes ☐ No

3.5. Overall Structure of the Study Team — Add Attachment | Delete Attachment | View Attachment

Section 4 - Protocol Synopsis

4.1. Brief Summary

4.2. Study Design

4.2.a. Narrative Study Description

4.2.b. Primary Purpose

4.2.c. Interventions

X	Intervention Type	
	Name	
	Description	

Add New Intervention

4.2.d. Study Phase

Is this an NIH-defined Phase III clinical trial? ☐ Yes ☐ No

4.2.e. Intervention Model

4.2.f. Masking ☐ Yes ☐ No

☐ Participant ☐ Care Provider ☐ Investigator ☐ Outcomes Assessor

4.2.g. Allocation

4.3. Outcome Measures

X	Name	
	Type	
	Time Frame	
	Brief Description	

Add New Outcome

4.4. Statistical Design and Power — Add Attachment | Delete Attachment | View Attachment

4.5. Subject Participation Duration

4.6. Will the study use an FDA-regulated intervention? ☐ Yes ☐ No

4.6.a. If yes, describe the availability of Investigational Product (IP) and Investigational New Drug (IND)/Investigational Device Exemption (IDE) status — Add Attachment | Delete Attachment | View Attachment

4.7. Dissemination Plan — Add Attachment | Delete Attachment | View Attachment

Section 5 - Other Clinical Trial-related Attachments

5.1. Other Clinical Trial-related Attachments — Add Attachments | Delete Attachments | View Attachments

NIH Resources

- Guidance

PHS Human Subjects and Clinical Trials Information Form Walk-through
https://www.youtube.com/watch?v=nz9NWFhYOG8

New Human Subjects and Clinical Trial Information Form Website
https://grants.nih.gov/policy/clinical-trials/new-human-subject-clinical-trial-info-form.htm

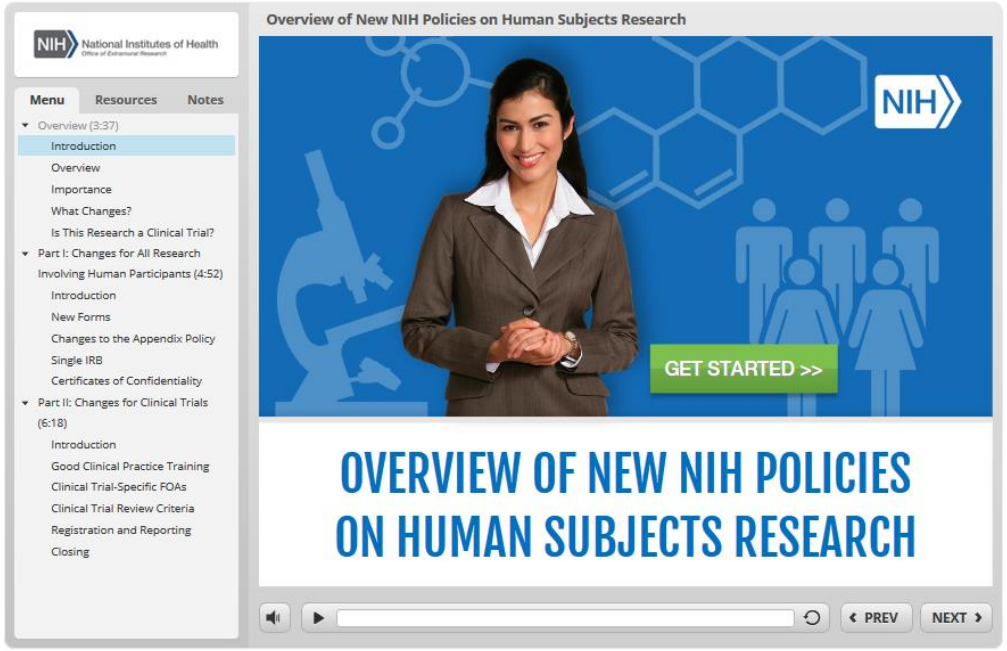
Annotated Forms Version E For NIH Grant Applications due on/after January 25, 2018
https://grants.nih.gov/grants/ElectronicReceipt/files/Annotated_Forms_General_FORMS-E.pdf

- Policy

SF 424 (R&R) Forms Version E – Significant Changes
https://grants.nih.gov/grants/how-to-apply-application-guide/forms-e/general/g.120-significant-changes.htm

SF 424 (R&R) Forms Version E – PHS Human Subjects and Clinical Trials Information Guidelines
https://grants.nih.gov/grants/how-to-apply-application-guide/forms-e/general/g.500-phs-human-subjects-and-clinical-trials-information.htm

Overview of New NIH Policies on Human Subjects Research



https://grants.nih.gov/policy/clinical-trials/tutorial/story_html5.html?lms=1

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Questions?

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